Assessment of the work efficiency with exergy method in ageing muscles and healthy and enlarged hearts

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Abstract: Thermodynamic aspects of skeletal and cardiac muscle work performance are assessed with the data obtained from the literature. Since the second law muscle work efficiency decreases with declining metabolic energy conversion efficiency in the mitochondria, followed by structural failure of the muscles during ageing, the thermodynamic aspects of the muscle work ageing process were simulated by incorporating the decreasing second law muscle work efficiency with the exercise data obtained with the healthy young adults. Within limits of the data analysed here, glucose utilisation ability of the cardiac muscle appears to be the most critical factor determining its work performance. The left and the right ventricles of the enlarged heart had the ability of utilising approximately 3.5 and 2.7 times less glucose, respectively, than their healthy counterparts. The work performance and the entropy generation by the enlarged and the healthy hearts maintained the same ratios.
Keywords: ageing mitochondria; exergy destruction; heart; muscle work performance; second law efficiency.

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1 Introduction

The second law of thermodynamics accounts for the dissipation of energy via entropy production in any process, including the living organisms (Schrödinger, 1944). Organisms manage a combined entropy process in every constituent of their systems, a change in any subsystem affects others and the entire system (Schrödinger, 1944;
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Luo, 2009; Molnar et al., 2011; Boregowda et al., 2012; Garland, 2013). Entropy generation in organisms was extensively studied (Prigogine and Wiame, 1946; Zottin and Zottin, 1967; Balmer, 1982; Aoki, 1994; Rahman, 2007; Silva andAnnalama, 2008; Silva and Annalama, 2009; Neto et al., 2010); while some of the recent studies have been focusing explicitly on exercise (Rahman, 2007; Silva andAnnalama, 2008; Silva and Annalama, 2009; Neto et al., 2010; Henriques et al., 2014) some of them were also referred to as valuable tools in physiology (Muñoz-Diosdado and Galvez-Coyt, 2010; Uehara and Koibuchi, 2011; Davogusto and Taegtmeyer, 2015).

1.1 Muscle work

In muscles, chemical exergy is converted into work via biochemical reactions. The number of moles of ATP produced as a result of the catabolism depends on the type of the nutrient and the metabolic pathway. For example, 30 to 38 moles of ATP are produced during oxidation of one mole of glucose (Genc et al., 2013) as expressed with the following apparent reaction:

\[
30 \text{ADP} + 30 \text{P} \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O}
\]

Similarly, ATP utilisation for work production may be summarised as:

\[
\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i
\]

When exergy harvested from this reaction is employed for performing muscle work, the conversion ratio of the nutrients into ATP is determined by the metabolic efficiency, and the conversion of ATP into muscle work is determined by the muscle work efficiency. In Figure 1, exergy efficiency of the metabolism, \(\eta_m\), and exergy efficiency of the mechanical work, \(\eta_m\), are described with the equations:

\[
\eta_m = \frac{\text{ATP exergy}}{\text{nutrients exergy}}
\]

\[
\eta_m = \frac{\text{muscle work}}{\text{ATP exergy}}
\]

The product of the metabolic and mechanical work efficiencies can be expressed in the 2nd law efficiency:

\[
\eta_2 = \eta_m \cdot \eta_m
\]

The efficiency of muscle contraction measures how much external work is obtained from the input of chemical energy (Jubrias et al., 2008). The first law efficiency, also called the mechanical or thermodynamic efficiency, is defined as:

\[
\eta_1 = \frac{W}{\Delta H}
\]

where \(W\) is the work actually produced and \(\Delta H\) is the apparent enthalpy change of the reaction described in equation (1). Energy supply by other substrates, e.g., fats are not
assessed here to limit the scope of the study. The second law efficiency is defined as the ratio of the actually produced work to the maximum available work:

$$\eta = \frac{W}{W_{\text{max}}} = \frac{W}{\Delta G},$$

(7)

where $\Delta G$, $\Delta S$ are the apparent Gibbs free energy and apparent entropy, respectively of the reaction described in equation (1). After substituting $\Delta G = \Delta H - T\Delta S$ in equation (7), $\Delta S$ may be expressed as

$$\Delta S = \Delta H - \frac{W}{\eta}. \quad (8)$$

The muscle work efficiency, $\eta_p$, in equation (8) is actually the parameter which determines the entropy generation by the muscle during work performance (Gibbs and Chapman, 1974; Heglund and Cavagna, 1987; Barclay, 1996; Barclay and Weber, 2004; Smith et al., 2005; Barclay, 2008; Barclay, 2012; Sorgüven and Özilgen, 2015). Studies on the muscle work efficiency are important for the diversity of disciplines and applications; for example, rehabilitation, sports biomechanics, ergonomics, etc. (Mariunas et al., 2008). The capability of sustaining a given level of muscular activity depends on the balance between the exergy requirements of the activity and the metabolic capacity of the exercising muscle to provide exergy (Holloszy and Coyle, 1984; Westerblad et al., 1991; Barclay, 1994). If the energetic requirements surpass the capacity to provide exergy, the level of activity cannot be maintained and muscles fatigue is experienced (Barclay, 1994).

Figure 1  Schematic description of the metabolic and the mechanical muscle efficiencies on the conversion of the exergy of the nutrients to muscle work

From a thermodynamic perspective, the heart can be regarded as a machine that converts part of the utilised exergy into work when it pumps blood. In the course of the contraction of the cardiac muscle, most of the consumed chemical exergy is transformed into heat and a much lesser portion into work. The ratio of the work and the chemical exergy expenditure is $\eta_p$. This is also called the efficiency of the cardiac contraction, or basically heart efficiency (Muñoz-Diosdado and Galvez-Coyt, 2010). The metabolic efficiency is an essential factor of the efficiency of ATP supply to requirement matching. In the case that the heart efficiency of ATP utilisation, e.g., mechanical efficiency
as described in Figure 1 and equation (4) reduces, more ATP would be required per unit work, and thus the myocardial oxygen consumption rate would increase. If the cardiac ATP generation efficiency diminishes, myocardial oxygen consumption rate rises; cardiac output may still decrease owing to the insufficient quantities of ATP supply (Yaniv et al., 2013).

### 1.2 Ageing

Ageing causes mass and quality loss in the muscles (Loeb et al., 2005; Peterson et al., 2012) and increases in the entropy of the body (Schrödinger, 1944; Balmer, 1982; Hayflick, 2007; Salminen and Kaarniranta, 2010). The loss of skeletal muscle proteins reduces the number of mitochondria (Lenaz, 1998, Lenaz et al., 2000). Muscle mitochondrial dysfunction leads to metabolic disturbances (Conley et al., 2000; Menshikova et al., 2006). With the decline in mitochondrial activity, the rate of the ATP generation slows down (Stucki, 1980; Cairns et al., 1998), the lower rate of ATP generation causes fatigability (Santanasto et al., 2015). Increased energy need for pumping ion in active transportation may also cause a decrease in the muscle efficiency (Shigenaga et al., 1994). As a result, the muscle cells of the aged people become different than those of the young people (Toussaint et al., 1995). The elderly people may usually perform low levels of exercise efficiently and have a slow routine in daily living activities (Martin et al., 1992; Rooyackers et al., 1996; Woo et al., 2006). Schematic description of the changes occurring in the muscles during ageing is summarised in Figure 2.

Kiriazis and Gibbs (2000), while investigating the effect of ageing on the work output and efficiency of rat papillary muscle reported that the mechanical work performance efficiency, \( \eta_m \), was not influenced by ageing, it was actually the metabolic exergy efficiency, \( \eta_{me} \), what decreased by ageing (Kiriazis and Gibbs, 2000). Figueiredo et al. (2008), argue that the age-related increase in the levels of oxidative stress and damage on the mitochondrial biomolecules becomes progressively more apparent with ageing (Figueiredo et al., 2008). When the cellular capacity for the repair is not sufficient, this increased damage leads to accumulation of the dysfunctional proteins, impaired membrane integrity and increased levels of the mutant mitochondrial DNA. These damaged cellular compounds proliferate irreversibly through mitochondrial and cellular divisions and cause reduction of the intact mitochondria and the maximal mitochondrial function, and the maximal energetic capacity of skeletal muscle fibres. This progressive loss of mitochondrial redundancy may not limit its capacity to supply the cellular energetic demands at basal metabolic conditions, but may limit the functionality of myofibrils during situations with higher energetic requirements. Ageing damage occurring to the metabolic pathways may not be confined to metabolism, but eventually propagate to the mechanical work performing sites of the muscles (Figueiredo et al., 2008). The age-related muscle changes start in the fourth decade of the life of the people and cause weakness and disabilities (Nair, 2005). Decreases in the synthesis rates of several muscle proteins, specifically of myosin heavy chain and mitochondrial proteins, occur with age. Reduction in mitochondrial biogenesis and ATP production leads to decreases in mitochondrial DNA and messenger RNA. Reduced ATP production could be the basis of reduced muscle protein turnover (Nair, 2005). In the studies with rats, decrease in \( \eta_D \) was caused by the declining efficiency \( \eta_{me} \) of the metabolic
pathways only, probably because of the short life span of the rats (Kiriazis and Gibbs, 2000), where probably the rats did not have opportunity of spreading the damage to the mechanical work performing sites of the muscle. The development of a heart failure is related to reduced energy metabolism, transient increase in Ca\(^{2+}\), reduction in the ATP production capacity and subsequent reduction in the total ATP concentration and oxygen utilisation in both basal and high-demand situations. The decline of these functions occurs only at high demand in healthy ageing. In chronic heart failure; levels of the reactive oxygen species (ROS) increases, myocardial antioxidant reserve decreases, the PCr/ATP (phosphocreatine/adenosine triphosphate) ratio reduces, and NADH/NAD\(^{+}\) ratio rises over the entire age range of the heart work.

**Figure 2** Schematic description of the changes occurring during ageing in skeletal muscle (see online version for colours)
1.3 Exercising

In short-term, exercise blood glucose plays a vital role in the substrate supply to the exercising skeletal muscle. During the forearm and leg exercises, glucose uptake by the working muscles rises 20 to 35-fold above that of the basal level (Jorfeldt and Wahren, 1970; Wahren et al., 1971). At exercise intensities, below 75% of the maximal oxygen uptake (Saltin and Karlsson, 1971), blood glucose accounts for almost the total carbohydrate consumption (Ahlborg et al., 1974; Ahlborg and Felig, 1982). Glycogen stored in the muscle tissues and the liver serves as a vital energy reserve, especially after the depletion of the glucose.

Muscle tenderness, stiffness, and ache are often related with weakness. Breathing pump muscles can also limit the physical performance in the healthy subjects and athletes (Ribeiro et al., 2012). Exercise enhances muscle protein synthesis and mitochondrial biogenesis (Kiriazis and Gibbs, 2000; Nair, 2005). Systematic exercise can increase the life span (Guiney and Machado, 2013). Sedentary men, undergoing long-term maintained aerobic oxidative training have higher PCR/ATP ratio in comparison with the untrained controls (Perseghin et al., 2009). There is a correlation between the positive influence of exercise and changes in the ATP supply-to-demand mechanisms in ageing people (Colcombe et al., 2004).

Presence of approximately 4 millimolar of ATP in a muscle fibre is sufficient to maintain a full contraction for 1–2 s. The most preferred energy source to reconstitute ATP is phosphocreatine. This high-energetic phosphate bond containing substance has a slightly higher amount of free energy than that of an ATP bond. The total amount of phosphocreatine in the muscle fibre is limited. The combination of ATP and phosphocreatine may provide energy to cause maximal muscle contraction for 5–8 seconds (Guyton and Hall, 2011). The second most preferred energy source is glycolysis. This rapid enzymatic breakdown of the glycogen to pyruvic acid and lactic acid liberates energy to convert ADP to ATP; and then ATP can be used directly for additional muscle contraction and also to re-form the phosphocreatine storage. The ATP, phosphocreatine and glycolysis mechanisms are important energy pathways under anaerobic conditions to energise the muscle contraction for 1–2 min, depending on the anaerobic capacity of a person. The third and the least preferred energy source is oxidative metabolism. More than 95% of all energy used by the muscles for long-term contraction is derived from the oxidative metabolism of carbohydrates, fats and proteins. By far, the greatest proportion of energy comes from fats for periods of 2–4 h. Generally, as much as one-half of the energy can come from stored carbohydrates (Guyton and Hall, 2011).

1.4 Cardiac cycle

Cardiac cycle describes the phases of contraction and relaxation of the heart that drive blood flow throughout the body to deliver nutrients to the cells to maintain the metabolic activity and remove the waste. It refers to a complete heartbeat from its generation and extends until the beginning of the next beat, so includes the diastole (part of the cycle when the heart refills with blood), the systole (contraction, the phase when the blood is pumped out), and the intervening pause. The frequency of the cardiac cycle is determined by the heart rate. Each beat of the heart includes five major stages. The first two stages, involve the movement of blood from the atria into the ventricles. The next three stages
include the movement of blood from the ventricles into the pulmonary artery (in the case of the right ventricle) and the aorta (in the case of the left ventricle).

Cardiac output is the quantity of blood pumped into the aorta by the heart in a minute. The left ventricle pumps blood throughout the body (systemic circulation) while a right ventricle sends blood to the lungs for oxygenation and elimination of carbon dioxide (pulmonary circulation). For young healthy men, under resting conditions, cardiac output averages about 5.5 L/min (Guyton and Hall, 2011). However, the heart has the potential to maximise its cardiac output above normal. This is called the cardiac reserve and is about 300% to 400% in the healthy sedentary individuals and may increase a little more in athletically trained people. During exercise, circulation of the cardiac output to specific tissues is adjusted according to the metabolic activity of the tissue and most of the cardiac output is devoted to the working skeletal muscles (Harms, 2000). Blood circulation is directed to tissues depending on their metabolic activity. For example, inactive skeletal muscles of the body receive a very low amount of blood, e.g., 4 mL/ (min 100 g of muscle), while it can increase up to 20 times in exercise when muscle metabolic activity increases. Therefore, a heart allows operation at different pressures in the left and right ventricles with the help of heart valves. Cardiac reserve declines with ageing. A thermodynamic model has recently been offered by Henriques et al. (2016), to analyse heart work in a simple way (Henriques et al., 2016).

Cardiac cycle causes an increase in the randomness, e.g., entropy, of the cardiac tissue, which eventually may lead to cardiac damage (Dini et al., 2012). Annamalai and Silva (2012) analysed the entropy stress on the organs over the life span and ranked them in the order of entropy generation, where heart appeared to be the highest entropy generating and the most entropy-stressed organ. Weakening in the peripheral skeletal muscle function may be a factor in the pathophysiology of heart failure (Clark et al., 1996). Reduced expression of mitochondrial transcription factors and mitochondrial proteins are involved in the mechanisms leading to mishandling of energy in the heart failure (Ventura-Clapier et al., 2004; Barclay, 2008). Reducing the high-energy phosphate production in the enlarged heart, reduces coronary circulation, which then can restrict the nutrient and oxygen transfer to the cardiac muscle cells at high workloads (Sack et al., 1996; Razeghi et al., 2001). Energy need of the cardiac muscles can be satisfied under aerobic situations only (Beloukas et al., 2013). The heart is capable of providing its energy from the oxidation of the fatty acids, glucose, lactate and other substrates available for oxidation (Taegtmeyer, 2000). In heart failure, enzymes involved in fatty acid oxidation may be down-regulated and cause the shift of the myocardial energy substrates from fatty acids to glucose (Sack et al., 1996; Razeghi et al., 2001).

Enlarged heart (cardiomegaly) may be caused by dilatation of the heart muscles or increase in the volume of an organ or tissue (hypertrophy) due to the enlargement of its component cells when placed under a high workload for a prolonged period of time. Some cardiac hypertrophy is reversible, such as that seen in athletes and pregnant women. Pathologic hypertrophy is the result of diseases that place increased demand on the heart, such as chronic hypertension, myocardial infarction, and damage to the valves. Left ventricular hypertrophy is the most common type of hypertrophic heart disease (Mayo Clinic, 2017). It is generally believed that the main myocardial energy resource changes from fatty acid β-oxidation to glycolysis for the duration of hypertrophy. The change from fatty acid to carbohydrate metabolism in hypertrophy appears as a measure to sustain the efficiency of the heart by providing glucose to the metabolism (Taegtmeyer, 2000). In hypertrophy, proliferation in glycolysis and glycolytic enzymes is seen, but
more lactate accumulates. Metabolic adjustment becomes unsatisfactory with decreasing
capacity to oxidise glucose leading to reduced efficiency (Leong et al., 2003). The
enlarged heart is not capable of sustaining its energetic reserve. Changes in myocardial
high-energy phosphates were recognised in the animal models and the hearts of the
people with left ventricle hypertrophy or heart failure.

Heart failure creates problems in energy generation, transfer and utilisation.
Reduction in the creatine kinase activity, PCr/ATP ratio and fluxes and changes in the
isoenzyme patterns are among the characteristics of cardiac failure (Ingwall, 1993;
Nascimben et al., 1996; Neubauer et al., 1997; De Sousa et al., 1999; Dzeja et al., 2000;
Ye et al., 2001; Spindler et al., 2003; Weiss et al., 2005). Moreover, the efficiency of the
ATPases depends on sufficient energy supply and the effective extraction of the end
products of ATP hydrolysis (Ventura-Clapier et al., 2004). Besides reduced energy
generation, there is also some indication for the waste of energy at the cellular level in
cardiac dysfunction. The enlarged heart has decreased mechanical efficiency that
increases the energy cost of the work production in the heart (Schipke, 1994; Ashrafian,
2002; Saavedra et al., 2002; Ashrafian et al., 2003). Accompanied by other cellular
deficiencies, the decline in metabolic fluxes of the enzymatic systems involved in energy
transfer may cause energy restriction and therefore may be a key reason triggering
cardiac failure (Ventura-Clapier et al., 2004).

1.5 Muscle metabolism in heart failure

Patients suffering from heart failure complain continuously of muscular weakness and
exercise intolerance because heart failure influences the rest of the body as well. Changes
in the energy metabolism influence both the cardiac and skeletal muscles via acquired
metabolic myopathy, e.g., a muscle fibre disease (Katz, 2002). The enlargement of the
cardiac pump stimulates neuro-hormonal processes influencing the whole-body strength
which affects the cardiac and skeletal muscle function and structure. Decreased maximal
exercise capacity of the heart failure patients associates inadequately with central
dynamics of blood flow. This has led to the conclusion that the factors outside the heart
may also be involved in the muscle faintness and enlarged fatigability of the patients.
Consideration has thus been concentrated on factors such as changes in vascular function
and intrinsic skeletal muscle irregularities that may appear in this disease (Drexler and
Coats, 1996; Poole-Wilson and Ferrari, 1996). There are relatively few studies on skeletal
muscle function in heart failure. Damaged calcium homeostasis, decreased force and
slower contractile kinetics were observed to be not related to the intrinsic contractile
proteins (De Sousa et al., 2000; Lunde et al., 2001). Therefore, changes in the contractile
protein profile may not be the main factor for exercise intolerance in heart failure.
Alternatively, great metabolic deficiencies have been explained in skeletal muscles from
heart failure patients and animals. Skeletal muscles in heart failure show a reduced
mitochondrial volume that associates with the aerobic capacities of the patients,
proposing the main payment of changed oxidative metabolism to exercise intolerance in
heart failure (Drexler et al., 1992). It is generally recognised that heart failure influences
mitochondrial capacity and regulation, and phosphotransfer systems in both cardiac and
skeletal muscles (Coats, 1996; Hardie and Pan, 2002). These metabolic failures may
result from reduced transcription of mitochondrial proteins or from increased
mitochondrial degradation. Heart failure stimulates histological, metabolic and functional
adjustments in the inspiratory muscles, e.g., muscles which induce inhalation, as well.
This inspiratory muscle faintness, which takes place in 30% to 50% of the heart failure patients, is related to the decrease in the functional capacity, the decline in the quality of life and with a poor prognosis in these individuals (Ribeiro et al., 2012).

Failure in energy metabolism is progressively thought as an essential determining factor in the development of the disorder, in spite of the variety of source and of clinical indication of heart failure (Lopaschuk et al., 2002; Ashrafian et al., 2003; Watkins, 2003). Heart failure is a multi-organ disorder, disturbing diverse cell types and generating multiple neuro-hormonal activations. Inside muscle cells, this pathology influences most intracellular organelles and pathways. In myocytes, calcium and energy homeostasis are intrinsically linked so that influencing one will automatically be reflected on the other. The reduced efficiency of mechanical transduction and insufficient calcium uptake and release result in a mismatch between energy generation and utilisation, and may affect calcium homeostasis and contractility, e.g., the ability for self-contraction. It is therefore not surprising that improving calcium homeostasis results in improved cardiac energetics (Del Monte et al., 2001) and that in turn improving myocardial energetics regulates calcium cycling (Hasenfuss et al., 2002; Liao et al., 2002). Steady failure in several steps in myocardial energetic signaling, along with compromised compensatory mechanisms, triggers the failure of the whole cardiac energetic system, finally contributing to myocardial dysfunction (Ventura-Clapier et al., 2004).

In physiology, where thermodynamics is not typically used, instead of the second law efficiency, as defined in equation (7), cardiac output (CO) is used to evaluate the performance of the heart:

\[ CO = HR \times SV, \]  

(9)

where, HR is the heartbeat rate and SV is the stroke volume. In the present study, CO of the healthy heart was calculated from the Wiggers diagram as 5.15 L/min when HR and SV were 75 beats/min and 73.6 mL/min, respectively. A detailed description of the Wigger’s diagram is provided by Klabunde (2012). The mean arterial pressure (MAP) is the weighted average arterial pressure calculated as over one cardiac cycle and used together with CO to evaluate the efficiency of the pumping pressure of the heart:

\[ MAP = \frac{1}{3} \left( P_{sys} + 2P_{dias} \right), \]  

(10)

where, \( P_{sys} \) and \( P_{dias} \) are the systole and diastole pressures, respectively. One of the purposes of this study is employing the fundamental principles of thermodynamics, while analysing the biological phenomena, and demonstrating that these phenomena may be assessed by using equation (7) instead of equation (9).

2 Methodology

Mass, energy, exergy and entropy balances are performed around the muscles to calculate the glucose consumption, energy utilisation, exergy destruction and entropy generation. A human heart is modelled as the left and the right ventricle muscle subsystems in the present study.
2.1 Muscle work performance by the left and right heart in one beat

The heartbeat data was adapted from Guyton and Hall (2011). Heartbeat rate was 75 beats/min and the duration of each cycle was 0.8 s. The coronary artery and the left main coronary artery resting blood flows were 0.25 L/min. An energy balance around the muscle system (Figure 3) requires:

\[ Q - W + \sum_{i} (mh)_{in} - \sum_{i} (mh)_{out} = \Delta E = 0, \]

where \( i = 1, 2, 3 \) and 4 refer to glucose, oxygen, carbon dioxide and water, respectively. Heartbeat works of the left and right ventricles were calculated from the Wiggers diagrams, standard diagrams used in physiology for a cardiac cycle. During contraction under the steady-state conditions \( \Delta E = 0 \). Heat released during work performance from the muscles was calculated from equation (11) with the data presented in Table 1. In equation (11), the exergy analysis was demonstrated for a process in J, not in W, therefore the analysis carried out in this study were actually integrated exergy analyses. Exergy destroyed in the blood stream was calculated as:

\[ \text{Ex}_{\text{destroyed}} = Q \left(1 - \frac{T_0}{T}\right) - W + (\text{mex})_{in} - (\text{mex})_{out}, \]

where \( T \) is the temperature at the boundary of the muscle and \( T_0 \) is the reference temperature. The specific exergy of the species is calculated from their chemical composition and thermophysical state:

\[ ex = ex_a + h - T_0 s - \sum x_i \mu_i^0, \]

where \( \mu_i^0 \) is the chemical potential of the pure species and \( \text{Ex}_{\text{destroyed}} \) may be regarded as the exergy destruction in the blood stream, and equals to the multiplication of entropy accumulation in the blood stream and the body temperature as provided in equation (14). All the analyses were based on the assumption that the muscles were at the body temperature of 37°C and heat was released to the environment at 25°C, during the muscular activity. Here \( T = T_{in} \) is the temperature at the boundary of the muscle system, and \( T_0 = T_{out} \) is the reference temperature. Exergy of formation of each chemical is listed in Table 1, both when \( T_0 = T_{out} = 25^\circ C \), and \( T = T_{in} = 37^\circ C \). Muscle work performance is achieved with the consumption of ATP; heat generation is an inevitable part of the process and equals to 2/3 of the enthalpy change of the glucose to metabolic end-product conversion reactions. After assuming that heat transfer from blood to the muscle occurs at 37°C and from the muscle to air at 25°C, \( S_{\text{gen}} \) (J/K) for the muscle was calculated as:

\[ S_{\text{gen}} = \frac{\text{Ex}_{\text{destroyed}}}{T_0}. \]

Work performance data are adapted from the literature (Table 2).
Table 1 Chemical composition, mass, heat capacity, enthalpy of formation, absolute entropy and chemical exergy of the constituents entering and leaving through the system boundaries

<table>
<thead>
<tr>
<th>Chemical species</th>
<th>Mass input to System I (g)</th>
<th>Mass output from System I (g)</th>
<th>$\Delta h_f^0$ (kJ/g)</th>
<th>$C_p$ (kJ/g K)</th>
<th>$\Delta h_{310K}^{**}$ (kJ/g)</th>
<th>$s^0$ (kJ/g K)</th>
<th>$ex^0$ (kJ/g)</th>
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<tbody>
<tr>
<td>System – Muscle cycle</td>
<td></td>
<td></td>
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<tr>
<td>Glucose</td>
<td>$2.1 \times 10^{-4}$*</td>
<td>$-7.05$</td>
<td>$1.25 \times 10^{-3}$</td>
<td>$-7.04$</td>
<td>$1.16 \times 10^{-3}$</td>
<td>$11.47$</td>
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<tr>
<td>Oxygen</td>
<td>$2.2 \times 10^{-4}$*</td>
<td>$-3.8 \times 10^{-1}$</td>
<td>$9.20 \times 10^{-4}$</td>
<td>$-3.7 \times 10^{-1}$</td>
<td>$6.41 \times 10^{-3}$</td>
<td>$2.7 \times 10^{-1}$</td>
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<tr>
<td>Carbon dioxide</td>
<td>$3 \times 10^{-4}$*</td>
<td>$-15.93$</td>
<td>$8.40 \times 10^{-4}$</td>
<td>$-15.92$</td>
<td>$4.89 \times 10^{-3}$</td>
<td>$-3.11$</td>
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<tr>
<td>Water</td>
<td>$1.2 \times 10^{-4}$*</td>
<td>$-15.97$</td>
<td>$4.18 \times 10^{-3}$</td>
<td>$-15.92$</td>
<td>$5.05 \times 10^{-4}$</td>
<td>$-9.24$</td>
<td></td>
</tr>
</tbody>
</table>

*The stoichiometry of the reaction $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$, the molar concentrations are converted into mass concentrations.

**Calculated by $\Delta H_{310K}^f = \Delta H_f^0 + CpdT$.

Figure 3 The schematic description of the energy, e.g., ATP, supply during muscle contraction process
Table 2 Numerical values of the glucose consumption rate, exergy destroyed and the entropy generation in the muscles with the second law work performance efficiencies $\eta_{II} = 0.17$, $\eta_{II} = 0.3$ and $\eta_{II} = 0.42$

<table>
<thead>
<tr>
<th>Work (J)</th>
<th>$\eta_{II}$</th>
<th>Glucose consumed (mmol/min)</th>
<th>Exergy destroyed (J)</th>
<th>Entropy generation (J/K)</th>
<th>References</th>
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<td>122</td>
<td>$\eta_{II} = 0.17$</td>
<td>11.13</td>
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<td>2.134</td>
<td>Arm</td>
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<td></td>
<td>$\eta_{II} = 0.30$</td>
<td>6.308</td>
<td>305.5</td>
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<td>(Volianitis and Secher, 2002)</td>
</tr>
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<td></td>
<td>$\eta_{II} = 0.42$</td>
<td>4.505</td>
<td>182</td>
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<td>$\eta_{II} = 0.42$</td>
<td>14.29</td>
<td>577.3</td>
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Table 2 Numerical values of the glucose consumption rate, exergy destroyed and the entropy generation in the muscles with the second law work performance efficiencies $\eta_{II} = 0.17$, $\eta_{II} = 0.3$ and $\eta_{II} = 0.42$ (continued)

<table>
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<tr>
<th>Work (J)</th>
<th>$\eta_{II}$</th>
<th>Glucose consumed (mmol/min)</th>
<th>Exergy destroyed (J)</th>
<th>Entropy generation (J/K)</th>
<th>References</th>
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<td>1.706</td>
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<td>1.824</td>
<td>104.2</td>
<td>0.349</td>
<td>Leg cardiac output exp1 (Strange, 1999)</td>
</tr>
<tr>
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<td>$\eta_{II} = 0.30$</td>
<td>1.034</td>
<td>50.08</td>
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<td>$\eta_{II} = 0.42$</td>
<td>0.738</td>
<td>29.83</td>
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<td>40</td>
<td>$\eta_{II} = 0.17$</td>
<td>3.649</td>
<td>208.5</td>
<td>0.699</td>
<td>Leg cardiac output exp2 (Strange, 1999)</td>
</tr>
<tr>
<td></td>
<td>$\eta_{II} = 0.30$</td>
<td>2.068</td>
<td>100.1</td>
<td>0.336</td>
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</tr>
<tr>
<td></td>
<td>$\eta_{II} = 0.42$</td>
<td>1.477</td>
<td>59.67</td>
<td>0.200</td>
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<tr>
<td>20</td>
<td>$\eta_{II} = 0.17$</td>
<td>1.824</td>
<td>104.2</td>
<td>0.349</td>
<td>Leg exp1 (Strange, 1999)</td>
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<td>$\eta_{II} = 0.30$</td>
<td>1.034</td>
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<td>40</td>
<td>$\eta_{II} = 0.17$</td>
<td>3.649</td>
<td>208.5</td>
<td>0.699</td>
<td>Leg exp2 (Strange, 1999)</td>
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<tr>
<td></td>
<td>$\eta_{II} = 0.30$</td>
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<tr>
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<td>$\eta_{II} = 0.42$</td>
<td>1.477</td>
<td>59.67</td>
<td>0.200</td>
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</tr>
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</table>

3 Results and discussion

3.1 Thermodynamic analysis of the skeletal muscle system

Mass of glucose consumed in the muscle was calculated after substituting 3.868 kJ/kmol for the Gibbs free energy of the apparent glycolysis reactions and 180.16 kg/kmol for the molar mass of glucose in equation (15) (Çatak et al., 2015):
Assessment of the work efficiency with exergy method in ageing muscles

\[ m_{\text{glucose}} = \frac{W}{180.16 \cdot \frac{\eta_{\text{II}}}{3.86 \cdot \frac{W}{m_{\text{glucose}}}}} \]  

(15)

In the previous studies, the first law efficiencies based on the research carried out on animals, such as frog and mouse were between 0.14 and 0.35 and the second law efficiencies are between 0.17 and 0.42 (Smith et al., 2005). Numerical values of the work performed, glucose consumed, exergy destroyed and entropy generated are calculated for the second law efficiencies of 0.17, 0.3 and 0.42 (Table 2). While doing the same amount of muscular work, decreases were observed in glucose consumption, exergy destruction and entropy generation with the increasing 2nd law efficiency (Figure 4), implying that as the efficiency increases, a larger fraction of the chemical exergy of glucose is converted into work. In Figure 4(a), glucose consumption at \( W = 0 \) describes its use either for the basal metabolism or the depletion of the cellular reserve. The slope of this line is the inverse second law efficiency, e.g., \( \text{slope} = 1/\eta_{\text{II}} \). The plots given in Figure 4 are linear, since the data were obtained with healthy young subjects only. If we attempt to utilise the data obtained with the elderly or unhealthy people we would not be able to obtain linear relations. Figure 4(b) and (c) show that the exergy destruction and entropy generation in the muscles increase as a response to the attempts to higher work production in the ageing muscle systems. In the present study, entropy generation is calculated from exergy destruction. Although these two physical quantities give the same information in the forthcoming studies we will refer to entropy generation as a measure of the inefficiency while comparing the healthy and the malfunctioning organs, therefore we wanted to be consisted with our other publications and both exergy destruction and entropy generation are reported here.

Cross-sectional studies show that the elder adults utilise more energy than their younger counterparts to do the same activity due to their lower muscle work performance efficiency (Martin et al., 1992; Conley et al., 2000; Malatesta et al., 2003; Mian et al., 2006; Ortega and Farley, 2007). Figure 4(b) and (c) show that this observation may be caused by higher exergy destruction and entropy generation at lower second law muscular work performance efficiencies (Mogensen et al., 2006). The results given in Figure 4(b) and (c) may imply that the young individuals who improve their muscular work efficiency by exercise may experience lower exergy destruction and lower entropy generation.

The decline of either the metabolic exergy efficiency, \( \eta_{\text{m1}} \), or the mechanical work performance efficiency, \( \eta_{\text{m2}} \), by ageing causes a drop in the second law muscle work performance efficiency. The ageing process of two different people following path 1 and 2 are assessed in Figure 5. In the examples given in Figure 5, thermodynamic analysis starts at the age of 20, when the 2nd law efficiency is 0.42 and at the age of 80 the 2nd law efficiency becomes 0.17; Figure 5(c) visualises the allocation of the exergy driven from one mole of glucose for each path of ageing described here. At the age of 60, a person who is following to path 2 does more work compared to a person who is ageing by following path 1. His muscles cause smaller amounts of exergy destruction and generate less entropy, in comparison with the person who is following path 2.
Figure 4  Glucose consumption: (a) exergy destruction; (b) and entropy generation; (c) rates during muscle work performance with the 2nd law efficiencies of $\eta_{II} = 0.17$, $\eta_{II} = 0.3$ and $\eta_{II} = 0.42$ (see online version for colours)
Figure 5  Muscle work production and exergy destruction in exercise during utilisation of one mole of glucose when: (a) the second law muscle work efficiency is constant either as 0.42 or 0.17; (b) decline of the second law efficiency follows a steady path through the entire life span and (c) decline of the second law efficiency occurs gradually until the age of 70 and then becomes faster (see online version for colours)
3.2 Thermodynamic analysis of the cardiac heart muscle system

The heart is an open system with moving boundaries, pressure and the volume of the left and right ventricles changes throughout the heartbeat. Left ventricle pressure remains at 10 mmHg for the first part (i.e., 0–0.4 s) of the cardiac cycle (Figure 6(a)) while the blood flows into the left ventricle doubles its size (Figure 6(b)). When heart muscles contract, left ventricle pressure rises drastically to above 120 mmHg to drive the blood from the left ventricle chamber into the aorta, by opening the aortic valve (Figure 6(a)). Meanwhile, the left ventricle volume exhibits a sharp decrease, because nearly half of the blood in the left ventricle is sent to the body through the aorta (Figure 6(b)).

Figure 6 (a) Variation of the pressure in the left and right ventricles of the healthy heart and (b) variation of the volume in the left and right ventricles of the healthy heart (see online version for colours)

Pressure and volume changes in the left and right ventricles of the enlarged heart are plotted in Figure 7(a) and (b), respectively. An enlarged heart is chosen to represent the
case referring to an unhealthy heart mostly because it is a common heart failure and may also refer to a structural deformation, not a muscle decease. The pressure in the left ventricle of an enlarged heart was approximately half of the pressure in the left ventricle of the healthy heart; implying that the enlarged heart cannot build as high pressure in the left ventricle as the healthy heart. The lower pressure in the left ventricle disturb the operation of the aortic valve and change the magnitudes of CO and MAP. However, the right ventricle pressure was 15% less in the enlarged heart. Effect of decrease in the pressure of the left and the right ventricles was accompanied with an increase in the left and right ventricle volumes, for example, the left and right ventricle volumes increased nearly by 50% and 15% compared to those of the healthy heart, respectively.

**Figure 7** (a) Variation of the pressure in the left and right ventricles of the enlarged heart and (b) variation of the volume in the left and right ventricles of the enlarged heart

For the present case, $P_{sys}$ and $P_{dias}$ and MAP were 121.5, 76.88 and 91.75 mmHg, respectively for the healthy heart. The magnitude of the MAP indicates how well the
aortic valve functions when the pressure reaches to 80 mmHg. Once pressure and volume variation in the left and right ventricles are obtained, pressure can be plotted against volume to examine the relation between pressure and volume for a single cardiac cycle as illustrated in Figure 8(a). Variation of pressure along with volume implies boundary work; therefore, the enclosed areas in Figure 8(a) were the work done by the left and right ventricle walls of the heart. The work done by the left and right ventricles were calculated as 0.9607 J and 0.1969 J, respectively. These results indicate that the heart does approximately five times more work to drive blood from left ventricle to the body, compared to that of the work done by the right ventricle, which sends CO₂ rich blood to the pulmonary circulation. In general, Wigger diagrams are significantly similar for the healthy people of the same gender, body characteristics and age, but they are significantly different for the people with unhealthy hearts. Therefore, the results of the analyses based on the pressure vs. time and volume vs. time profiles described in Figure 7 and the pressure vs. volume profile of Figure 8(b) would be case specific and different for every unhealthy heart.

Figure 8  Wigger diagrams for the: (a) healthy and (b) enlarged hearts
Change of pressure along with volume in the enlarged heart illustrated quite different curves than those of the healthy heart as shown in Figure 8. Boundary works for left and right ventricles were calculated by taking the numerical integral of the enclosed areas of Figure 8 as $0.2812 \text{ J}$ and $0.0723 \text{ J}$, respectively. Furthermore, nearly 50% decrease in CO indicates that the internal organs and tissues would not receive sufficient amount of blood in the body of the person of the enlarged heart; 30% drop in MAP of the same person may imply an operational problem in the aortic valve, since it is activated only when a certain pressure is applied on the upstream side.

Table 3 shows the variation of the glucose consumption rate, exergy destruction rate and the entropy generation rate with the second law efficiency in a single beat in the cardiac muscles of a healthy person at heartbeat rate of 75 beats/min (one beat = 0.8 s, left ventricular beat work $= 9.607 \times 10^{-4} \text{ kJ}$). Tables 4 and 5 show the glucose consumption and the exergy destruction and the entropy generation in the same heart. Similar analysis is presented for the enlarged heart in Tables 6 and 7, where the left ventricular beat work was $2.812 \times 10^{-4} \text{ kJ/beat}$ and that of the right ventricle heart muscles was $7.23 \times 10^{-5} \text{ kJ/beat}$. Tables 3–7 and Figure 9 show that as the efficiency increases, a larger fraction of the chemical exergy of glucose is converted into work. Therefore, the amount of the glucose required to achieve the same work decreases as the efficiency increases. When the heart rate increases from 60 beats/min to 140 beats/min, cycle time decreases from 1 s to 0.43 s, as a result glucose consumption and absorption from the blood increase (Figure 9) and the heart can do more work in a minute.

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<tr>
<th>$\eta$</th>
<th>$m_{\text{glucose}}$ (mol/beat)</th>
<th>$m_{\text{glucose}}$ (mmol/min)</th>
<th>Glucose concentration in the blood (mmol/L)</th>
<th>Ex$_{\text{destroyed, muscle}}$ (kJ/beat)</th>
<th>S$_{\text{gen, muscle}}$ (kJ/K)/beat</th>
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<td>0.22</td>
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<td>$1.77 \times 10^{-1}$</td>
<td>$1.55 \times 10^{-3}$</td>
<td>$5.21 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.42</td>
<td>$5.91 \times 10^{-7}$</td>
<td>$4.43 \times 10^{-2}$</td>
<td>$1.29 \times 10^{-1}$</td>
<td>$1.43 \times 10^{-3}$</td>
<td>$4.81 \times 10^{-6}$</td>
</tr>
</tbody>
</table>

It was observed in Figure 8 that the left and the right ventricles of the healthy heart do approximately 3.5 and 2.7 times more work, respectively, than their counterparts in the enlarged heart. Such a major change in the work performance may be observed because of several reasons. The limiting cases may include:
• Coronary arteries may deliver less nutrients, while the heart rate, muscle work efficiency, exergy destruction and entropy generation rates remain the same.

• Coronary arteries may deliver the same amounts of nutrients, while the heart rate remains the same, but muscle work efficiency decreases causing an increase in exergy destruction and entropy generation rates. The decrease of the muscle work efficiency may be caused by the decline of either the metabolic efficiency or the mechanical efficiency of the cardiac muscles or both as depicted in Figure 1.

These limiting cases may arise at the onset of the health problem, and propagate later to alter the muscle structure, for example, a problem starting by metabolic inefficiency will inevitably extend to cause mechanical efficiency and then cause changes in the heart rate, muscular work efficiency, exergy destruction and entropy generation rates.

Table 4  Variation of the glucose consumption rate in the person heart muscles with the different second law efficiencies at a heart rate of 60 and 140 beats per min in the left ventricle (healthy rest subject left ventricular one beat work = $9.607 \times 10^{-4}$ kJ)

<table>
<thead>
<tr>
<th>$\eta_{II}$</th>
<th>Heart rate (beat/min)</th>
<th>Cycle time-time (sec)</th>
<th>Glucose consumed (mmol/min)</th>
<th>Glucose absorbed from the blood flow (mmol/litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.17</td>
<td>60</td>
<td>1</td>
<td>$8.76 \times 10^{-2}$</td>
<td>0.3506</td>
</tr>
<tr>
<td>0.17</td>
<td>140</td>
<td>0.43</td>
<td>$2.04 \times 10^{-1}$</td>
<td>0.8181</td>
</tr>
<tr>
<td>0.42</td>
<td>60</td>
<td>1</td>
<td>$3.55 \times 10^{-2}$</td>
<td>0.1419</td>
</tr>
<tr>
<td>0.42</td>
<td>140</td>
<td>0.43</td>
<td>$8.27 \times 10^{-2}$</td>
<td>0.3311</td>
</tr>
</tbody>
</table>

Table 5  Variation of the glucose consumption, exergy destruction and the entropy generation rates with the second law efficiency in the right ventricle muscles of the person with the healthy heart at heart rate of 75 beats/min (one beat 0.8 s and healthy rest subject right ventricular one beat work = $1.969 \times 10^{-4}$ kJ).

<table>
<thead>
<tr>
<th>$\eta_{II}$</th>
<th>$m_{glucose}$ (mol/beat)</th>
<th>$m_{glucose}$ (mmol/min)</th>
<th>Glucose concentration in the blood (mmol/L)</th>
<th>$E_{X_{destroyed, muscle}}$ (kJ/beat)</th>
<th>$S_{gen, muscle}$ (kJ/K)/beat</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.17</td>
<td>$2.99 \times 10^{-7}$</td>
<td>$2.24 \times 10^{-2}$</td>
<td>$8.98 \times 10^{-2}$</td>
<td>$1.02 \times 10^{-3}$</td>
<td>$3.44 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.22</td>
<td>$2.31 \times 10^{-7}$</td>
<td>$1.73 \times 10^{-2}$</td>
<td>$6.94 \times 10^{-2}$</td>
<td>$7.46 \times 10^{-4}$</td>
<td>$2.50 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.26</td>
<td>$1.96 \times 10^{-7}$</td>
<td>$1.46 \times 10^{-2}$</td>
<td>$5.87 \times 10^{-2}$</td>
<td>$6.00 \times 10^{-4}$</td>
<td>$2.01 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.3</td>
<td>$1.69 \times 10^{-7}$</td>
<td>$1.27 \times 10^{-2}$</td>
<td>$5.09 \times 10^{-2}$</td>
<td>$4.93 \times 10^{-4}$</td>
<td>$1.65 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.34</td>
<td>$1.49 \times 10^{-7}$</td>
<td>$1.12 \times 10^{-2}$</td>
<td>$4.49 \times 10^{-2}$</td>
<td>$4.10 \times 10^{-4}$</td>
<td>$1.38 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.4</td>
<td>$1.27 \times 10^{-7}$</td>
<td>$9.54 \times 10^{-3}$</td>
<td>$3.81 \times 10^{-2}$</td>
<td>$3.18 \times 10^{-4}$</td>
<td>$1.07 \times 10^{-6}$</td>
</tr>
<tr>
<td>0.42</td>
<td>$1.21 \times 10^{-7}$</td>
<td>$9.09 \times 10^{-3}$</td>
<td>$3.63 \times 10^{-2}$</td>
<td>$2.93 \times 10^{-4}$</td>
<td>$9.85 \times 10^{-7}$</td>
</tr>
</tbody>
</table>

The behaviour of the left and the right ventricles are described in Figure 9 for both the healthy and the enlarged hearts. The enlarged heart could use considerably less glucose, perform less work and generate lower entropy at the same heartbeat, in comparison with
Assessment of the work efficiency with exergy method in ageing muscles

the healthy heart at the same efficiency. Equation (8) implies that entropy generation increases with substrate utilisation; therefore, right ventricles of the people with healthy heart generated more than 2.5 times of the entropy than those of the people who have enlarged heart. Meanwhile, the left ventricles of the people with healthy hearts generated 3.4 times more entropy than those with an enlarged heart. Glucose consumption rate increases with the heartbeat rate (Figure 9(a)). When the second law efficiency was 0.40, glucose consumption increased linearly with the heartbeat rate; on the other hand, at lower efficiency, glucose consumption increased more rapidly with the heart rate than that described by the linear relation. Figure 9(b) is plotted for the case of a constant heartbeat rate of 75 beats/min; therefore, the maximum glucose consumption is lower in Figure 9(b) than that of Figure 9(a).

Table 6  Variation of the glucose consumption, exergy destruction and the entropy generation rates with the second law efficiency in the left ventricle muscles of the person with the enlarged heart at heart rate of 75 beats/min (one beat 0.8 s and enlarged rest subject left ventricular one beat work = 2.812 × 10⁻⁴ kJ)

<table>
<thead>
<tr>
<th>ηII</th>
<th>m_glucose (mol/beat)</th>
<th>m_glucose (mmol/min)</th>
<th>Glucose concentration in the blood (mmol/L)</th>
<th>Ex_destroyed, muscle (kJ/beat)</th>
<th>S_gen, muscle (kJ/K)/beat</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.17</td>
<td>4.27 × 10⁻⁷</td>
<td>3.20 × 10⁻²</td>
<td>1.28 × 10⁻¹</td>
<td>1.46 × 10⁻³</td>
<td>4.92 × 10⁻⁶</td>
</tr>
<tr>
<td>0.22</td>
<td>3.30 × 10⁻⁷</td>
<td>2.47 × 10⁻²</td>
<td>9.91 × 10⁻²</td>
<td>1.06 × 10⁻³</td>
<td>3.57 × 10⁻⁶</td>
</tr>
<tr>
<td>0.26</td>
<td>2.79 × 10⁻⁷</td>
<td>2.09 × 10⁻²</td>
<td>8.38 × 10⁻²</td>
<td>8.57 × 10⁻⁴</td>
<td>2.87 × 10⁻⁶</td>
</tr>
<tr>
<td>0.3</td>
<td>2.42 × 10⁻⁷</td>
<td>1.81 × 10⁻²</td>
<td>7.26 × 10⁻²</td>
<td>7.04 × 10⁻⁴</td>
<td>2.36 × 10⁻⁶</td>
</tr>
<tr>
<td>0.34</td>
<td>2.13 × 10⁻⁷</td>
<td>1.60 × 10⁻²</td>
<td>6.41 × 10⁻²</td>
<td>5.86 × 10⁻⁴</td>
<td>1.96 × 10⁻⁶</td>
</tr>
<tr>
<td>0.4</td>
<td>1.81 × 10⁻⁷</td>
<td>1.36 × 10⁻²</td>
<td>5.45 × 10⁻²</td>
<td>4.55 × 10⁻⁴</td>
<td>1.52 × 10⁻⁶</td>
</tr>
<tr>
<td>0.42</td>
<td>1.73 × 10⁻⁷</td>
<td>1.29 × 10⁻²</td>
<td>5.19 × 10⁻²</td>
<td>4.19 × 10⁻⁴</td>
<td>1.40 × 10⁻⁶</td>
</tr>
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</table>

Table 7  Variation of the glucose consumption, exergy destruction and the entropy generation rates with the second law efficiency in the right ventricle muscles of the person with the enlarged heart at heart rate of 75 beats/min (cycle time = 0.8 s, left ventricular resting beat work/cycle = 7.23 × 10⁻⁵ kJ)

<table>
<thead>
<tr>
<th>ηII</th>
<th>m_glucose (mol/beat)</th>
<th>m_glucose (mmol/min)</th>
<th>Glucose concentration in the blood (mmol/L)</th>
<th>Ex_destroyed, muscle (kJ/beat)</th>
<th>S_gen, muscle (kJ/K)/beat</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.17</td>
<td>1.09 × 10⁻⁷</td>
<td>8.24 × 10⁻³</td>
<td>3.29 × 10⁻²</td>
<td>3.76 × 10⁻⁴</td>
<td>1.26 × 10⁻⁶</td>
</tr>
<tr>
<td>0.22</td>
<td>8.49 × 10⁻⁸</td>
<td>6.37 × 10⁻³</td>
<td>2.54 × 10⁻²</td>
<td>2.74 × 10⁻⁴</td>
<td>9.20 × 10⁻⁷</td>
</tr>
<tr>
<td>0.26</td>
<td>7.18 × 10⁻⁸</td>
<td>5.39 × 10⁻³</td>
<td>2.15 × 10⁻²</td>
<td>2.20 × 10⁻⁴</td>
<td>7.39 × 10⁻⁷</td>
</tr>
<tr>
<td>0.3</td>
<td>6.23 × 10⁻⁸</td>
<td>4.67 × 10⁻³</td>
<td>1.86 × 10⁻²</td>
<td>1.81 × 10⁻⁴</td>
<td>6.07 × 10⁻⁷</td>
</tr>
<tr>
<td>0.34</td>
<td>5.49 × 10⁻⁸</td>
<td>4.12 × 10⁻³</td>
<td>1.64 × 10⁻²</td>
<td>1.51 × 10⁻⁴</td>
<td>5.06 × 10⁻⁷</td>
</tr>
<tr>
<td>0.4</td>
<td>4.67 × 10⁻⁸</td>
<td>3.50 × 10⁻³</td>
<td>1.40 × 10⁻²</td>
<td>1.17 × 10⁻⁴</td>
<td>3.92 × 10⁻⁷</td>
</tr>
<tr>
<td>0.42</td>
<td>4.45 × 10⁻⁸</td>
<td>3.33 × 10⁻³</td>
<td>1.33 × 10⁻²</td>
<td>1.07 × 10⁻⁴</td>
<td>3.62 × 10⁻⁷</td>
</tr>
</tbody>
</table>
3.3 Energy metabolism in heart failure

It was assumed in Figure 10 that blood arrives at the right and left sides of both healthy and enlarged hearts with the same glucose and oxygen concentrations. The left and right sides of the healthy heart utilise all the available glucose and oxygen; whereas the enlarged heart does not have the ability to do so. Therefore, a fraction of the glucose and oxygen exits the heart without being utilised. Heart muscle is an extremely oxidative tissue and generates more than 90% of its energy at the mitochondria. Mitochondria are located along the muscle filaments and occupy nearly 30% of the cardiac muscle space. There is a continuous space available for diffusion of oxygen between the mitochondria. Heart uses more than 90% of its oxidative capacity during the period of the maximal
exercise, in such a case there is no excess capacity for providing more energy in case of an attempt for over utilisation (Mootha et al., 1997). There is a strong association between oxygen utilisation, cardiac work performance, and global cellular ATP and phosphocreatine concentrations. Ca²⁺ plays an essential role in starting and regulating the strength of cardiac contraction. There appears to be a relation between the Ca²⁺ handling in the tissue and heart failure (Esposito et al., 1999; Kubalova et al., 2005; Bers, 2006), but postulation of the control of the excitation and contraction of the heart muscles by Ca²⁺ ions only, and ignoring other factors mentioned in this study is not adequate (Shimizu et al., 2002). The reduced oxidative capacity of the enlarged cardiac muscles will restrict cardiac work as the minimum for high workloads as described in Figure 8, because of the severe association between oxygen consumption and work. On the other hand, even in basal situations the cellular levels of ATP and PCr in addition to the PCr/ATP ratio, all of which are regulated by oxidative phosphorylation, are changed in heart failure (Ventura-Clapier et al., 2004). Chronic heart failure is linked with morphological irregularities of mitochondria for example enlarged number, decreased size and compromised structural integrity (Schaper et al., 1991). In animal models of heart failure and in the tissues from the heart failure patients, mitochondria have been reported to be structurally atypical and reduced in number, or more abundant but smaller in size. In addition, the function of these mitochondria appears to be impaired and expression of the mechanism of the electron transport chain is decreased (Ormerod et al., 2008).

Figure 10 Exergy charts for the operation of: (a) healthy left; (b) enlarged left; (c) healthy-right and (d) enlarged right hearts (see online version for colours).

Thermodynamic aspects skeletal muscles and cardiac muscles are assessed in this study with the limited data obtained from the literature. The second law muscle work efficiency decreases as a result of the reduction of the metabolic energy conversion in the
mitochondria and the following structural failure during ageing as described in Figure 1. Data pertinent to the healthy young people are employed to simulate the ageing process in terms of the declining second law muscle work efficiency. Within limits of the data analysed here, glucose utilisation ability of the cardiac muscles appears to be the most critical factor determining their work performance. The left and the right ventricles of the healthy heart has the ability of utilising approximately 3.5 and 2.7 times more glucose, respectively, than their enlarged-heart counterparts. The ratios of the work performance and entropy generation of the healthy and the enlarged are the same as those of glucose utilisation by the healthy and the enlarged hearts. Recently Değerli and Özilgen (in press) argued that the glucose utilisation ability of the mixed cultures of Saccharomyces cerevisiae and Lactobacillus plantarum during leavening of dough are determined by the ratio of the microbial species and the temperature of the culture. The factors, which limit the glucose utilisation rates in the cardiac muscle cells need to be studied further to make a meaningful contribution to the failure of the heart.

4 Conclusion

The argument which is presented here, implies that thermodynamic analyses, when combined with medical practices may make a significant contribution to developing the measures to prevent the skeletal muscle and heart failure. More vigorous work and interdisciplinary data are needed to develop reliable procedures for the prevention of heart failure.

References


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Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_p$</td>
<td>Specific heat capacity</td>
<td>kJ/kg K</td>
</tr>
<tr>
<td>$ex$</td>
<td>Specific exergy</td>
<td>kJ/kg</td>
</tr>
<tr>
<td>$Ex$</td>
<td>Total exergy</td>
<td>kJ</td>
</tr>
<tr>
<td>$h$</td>
<td>Specific enthalpy</td>
<td>kJ/kg</td>
</tr>
<tr>
<td>$H$</td>
<td>Total enthalpy</td>
<td>kJ</td>
</tr>
<tr>
<td>$m$</td>
<td>Mass</td>
<td>kg</td>
</tr>
<tr>
<td>$MW$</td>
<td>Molecular weight</td>
<td>kg/kmol</td>
</tr>
<tr>
<td>$Q$</td>
<td>Heat</td>
<td>kJ</td>
</tr>
<tr>
<td>$s$</td>
<td>Specific entropy</td>
<td>kJ/kg K</td>
</tr>
<tr>
<td>$S$</td>
<td>Total entropy</td>
<td>kJ/K</td>
</tr>
<tr>
<td>$T$</td>
<td>Temperature</td>
<td>K</td>
</tr>
<tr>
<td>$W$</td>
<td>Work</td>
<td>kJ</td>
</tr>
</tbody>
</table>
### Assessment of the work efficiency with exergy method in ageing muscles

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔE</td>
<td>Energy change</td>
<td>kJ</td>
</tr>
<tr>
<td>η_II</td>
<td>The second law efficiency</td>
<td>Fraction or percentage</td>
</tr>
<tr>
<td>η_m1</td>
<td>Exergy efficiency of the metabolism</td>
<td></td>
</tr>
<tr>
<td>η_m2</td>
<td>Exergy efficiency of the mechanical work</td>
<td></td>
</tr>
<tr>
<td>µ</td>
<td>Chemical potential</td>
<td>kJ/kmol</td>
</tr>
</tbody>
</table>

### Subscripts

- 0: Restricted dead state
- ch: Chemical
- exp: Experiment
- gen: Generation
- i: Any species
- in: Inlet
- out: Outlet