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Exergy model of human heart

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Abstract:

In the past few years, exergy analysis has been applied to human body in order to understand its exergy behavior aiming at, ultimately, collaborating with medical area, by means of diagnosis and treatment of pathologies. Exergy behavior of human body as a whole has already been determined by few authors for standard and healthy subjects. A first attempt to study the effects of obesity on life expectancy by the light of exergy concepts has also been performed. However, this work came to the conclusion that higher body fat *per se* does not lead to higher mortality among obese people; the focus must be turned to obesity-related diseases, which are mostly related to impaired cardiovascular functions. Thus, the next step towards the comprehension of the effects of pathologies on exergy behavior of human body is to understand human heart by the exergy point of view. In the present work, an exergy model of human heart is developed. The heart is divided into two control volumes: left heart, which pumps arterial blood from the lungs to the organs, and right heart, which pumps venous blood from the organs to the lungs. In both left and right hearts, exergy metabolism, exergy transfer associated to heat of metabolism, difference of exergy of blood flows and performed work are taken into account. Exergy metabolism is determined from values of oxygen consumed and carbon dioxide produced by heart tissues available from thermal model of human body, which also provides the temperature of the heart, utilized to determine Carnot factor and, then, exergy transfer associated to heat metabolism, and partial pressures of oxygen and carbon dioxide in arterial and blood flows. Work performed by the heart is determined by means of pressure-volume diagrams. Then, it is possible to determine destroyed exergy and exergy efficiency of the heart at rest and also for walking and running. Moreover, these values can be confronted to those obtained for the whole body, estimating the percentage of destroyed exergy of the body that is attributed to the heart. The model can be applied to healthy subjects and also to individuals with hypertension or any other pathology that affects some input of the model.

Keywords:
Exergy analysis, human heart, destroyed exergy, exergy efficiency.

1. Introduction

Exergy analysis is a well-established tool to evaluate the quality of energy conversion processes and it has already been applied to a wide variety of industrial systems. According to Szargut [1], a promising area for application of exergy analysis is the evaluation of living organisms to determine their exergy behavior aiming for a better understanding of living and aging processes from thermodynamic point of view, what is expected to help predicting long-term behavior of living organisms under different conditions.

Batato [2] was the first to apply exergy analysis to human body and he concluded that the metabolism on exergy basis is the most relevant variable in exergy balance. With emphasis in thermal comfort, Prek [3,4], Prek and Butala [5], Simone et al. [6] and Mady et al. [7] used the exergy analysis as a tool to obtain relations between destroyed exergy in human body and thermal comfort and thermal sensation indexes. Mady et al. [8] performed exergy analysis during physical activity and observed that the exergy efficiency increases with exercise intensity and also with age.

Albuquerque-Neto et al. [9] and Henriques et al. [10] proposed exergy models of respiratory system. The former assumed metabolism as a heat source, air composed only of oxygen and carbon dioxide and the reference state was assumed at the tissues. The latter considered metabolism as a chemical reaction, air composed of nitrogen, oxygen and carbon dioxide and the reference state as the environment. The results obtained by Henriques et al. [10] indicated that the efficiency of respiratory system is reduced at high altitudes and under physical activity, while the exergy efficiency of human body increases for both parameters.

Exergy analysis was also applied in studies of aging process. Hershey [11] and Silva & Annamalai [12] claim that there is a maximum cumulative value of entropy generated along lifespan. Thus, they proposed entropy generation as a more suitable quantity to evaluate life progression. This idea was extrapolated to the use destroyed exergy by Mady et al. [13]. Taking anthropometric data of a standard Brazilian male from birth to 80 years, cumulative destroyed exergy for basal conditions is 3091MJ/kg. Since exergy metabolism is responsible for most part of the exergy destroyed in the body [14], physiological conditions characterized by metabolic alterations tend to incur in lifespan modifications as well. With that in mind, Henriques et al. [15] performed the first attempt to evaluate how metabolic alterations in obese affect life expectancy. They altered body composition of the model in order to get to metabolic rate and mass close to real values for control, moderately obese and obese people and then applied exergy analysis. The results were conflicting with statistic data about mortality among obese population [16], which led to the conclusion that the shorter life expectancy observed in this group is due to the development of obesity-related diseases, not to the sole presence of a thicker fat tissue and higher metabolic rate. Therefore, in order to better evaluate the impact of obesity in exergy behavior and life span, it is necessary to study how the obesity-related diseases impact physiological, not only morphological, aspects of human body.

According to the American Heart Association, obesity is a major modifiable risk factor of cardiovascular disease and the accumulation of cholesterol leads to stiffening and narrowing of arteries and, ultimately, to hypertension, stroke, myocardial infarction and sudden death, among others [17]. Moreover, cardiovascular diseases are the major cause of death among obese [18]. For that reason, the next step towards the understanding of exergy behavior of human body under pathological conditions is developing an exergy model of human heart. In the present work, a model of human heart with its exergy flows and transfers will be proposed. Then, the exergy analysis will performed for basal, walking and running conditions and the results will be confronted with those obtained previously for human body and respiratory system [10]. Moreover, a first attempt of determining destroyed exergy in the heart of a lean person with hypertension will be performed based on experimental data available in the literature [19].

2. Methods

2.1. Exergy model

Human heart can be divided into two parts: right and left. Right heart receives venous blood from the organs through the venae cavae and pumps it to the lungs by the pulmonary artery. After gas exchange in the respiratory system, arterial blood flows through pulmonary veins to left heart and then, after being pumped, goes to the other organs by the aorta. Figure 1a depicts human heart and its blood flows. The period of cardiac cycle where the heart is filled with blood is called diastole, while the contraction period is called systole. A pressure-volume diagram of left ventricle during cardiac cycle is shown in Figure 2. The yellow area indicates the work performed over the heart. The steps of the active pumping process are filling, isovolumetric contraction, ejection and isovolumetric relaxation. In medical literature, more emphasis is usually given to the ventricle because the atrium works just as a pre-pump to aid the filling process of the ventricle.

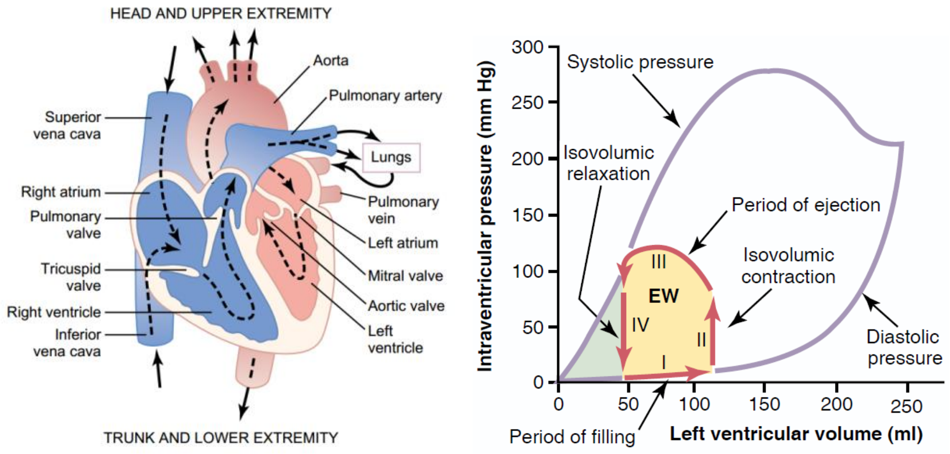

Fig. 1: Representation of human heart (a) and pressure-volume diagram of left ventricle (b) [20].

In Figure 1a it can be seen that both left and right parts are composed of an atrium and a ventricle that are separated by a valve, which operates passively. For that reason, in the model of Figure 2, atrium and ventricle are assumed as constituting only one chamber. It was also assumed that each heart has only one inlet and one outlet with cross sectional area equivalent to the sum of those of the real arteries and veins.

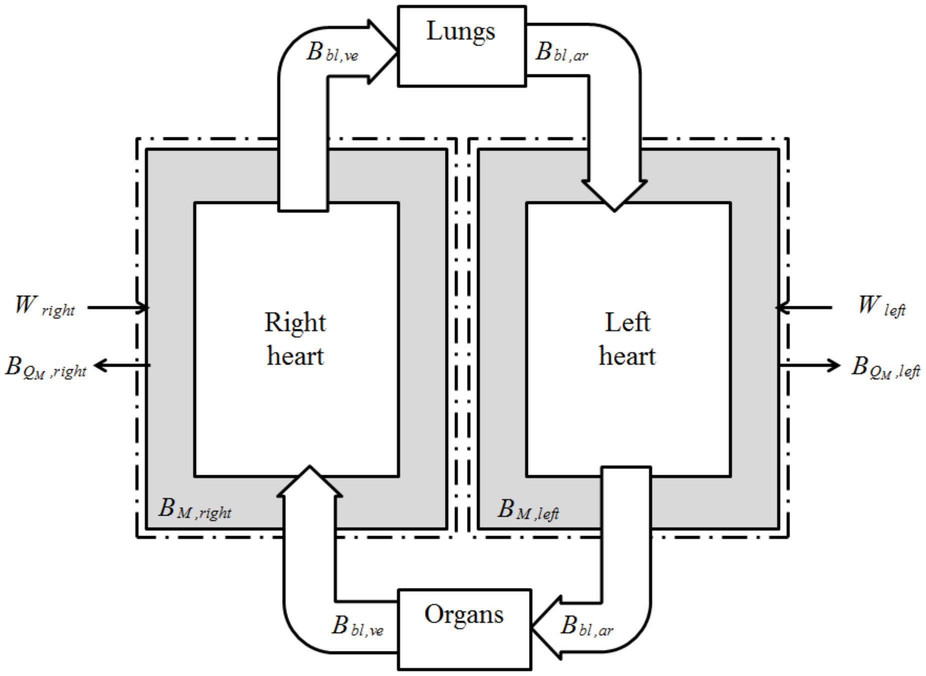

Fig. 2: Model of human heart.

Although the heart operates cyclically, the calculus was performed assuming continuous and steady operation in order to determine the terms of energy and exergy balances. To perform the exergy analysis, the following parcels are taken into account, as shown in Figure 2: exergy metabolism of cardiac muscle ($B_{M,heart}$), exergy transfer rate associated to the heat released by heart metabolism ($B_{QM,heart}$), exergy flow rates of venous ($B_{bl,ve}$) and arterial blood ($B_{bl,ar}$) and power performed by cardiac muscle (W_{heart}). The control volume is placed outside heart cavity in order to take into account exergy parcels associated to heart metabolism. As can be seen in the pressure-volume diagram of Figure1b, the work is performed over human heart. Destroyed exergy of left and right heart are shown in (1) and (2), respectively. Total destroyed exergy in human heart is the sum of left and right parcels.

$$B_{d,left} = B_{M,left} - B_{Q_M,left} + B_{bl,ar}\big|_{in} - B_{bl,ar}\big|_{out} + W_{left} = B_{M,left} - B_{Q_M,left} - \Delta B_{bl,ar} + W_{left}, \quad (1)$$

$$B_{d,right} = B_{M,left} - B_{Q_M,right} + B_{bl,ve}\big|_{in} - B_{bl,ve}\big|_{out} + W_{right} = B_{M,left} - B_{Q_M,right} - \Delta B_{bl,ve} + W_{right}, \quad (2)$$

Heart metabolism, on exergy and energy basis, are calculated by means of the expressions presented by Mady and Oliveira-Junior [14] using the values of oxygen consumed and carbon dioxide produced by heart tissue instead of the values for the whole body, as shown in (3) and (4), respectively. The ratios of exergy and energy metabolism of each part of the heart to total heart metabolism was assumed as equal to the ratios of power. All activity parameters are greater for the left side of the heart because it has to pump oxygenated blood to every organ and the right side only has to pump the blood till the lungs. Equation (5) illustrates the determination of $B_{QM,heart}$.

$$B_{M,heart} = 9501 m_{O_2,heart} + 3963 m_{CO_2,heart}, \quad (3)$$

$$M_{heart} = 11371 m_{O_2,heart} + 2366 m_{CO_2,heart}, \quad (4)$$

$$B_{Q_M,heart} = Q_{M,heart}\left(1 - \frac{T_0}{T_{heart}}\right) = \left(M_{heart} + W_{heart}\right)\left(1 - \frac{T_0}{T_{heart}}\right), \quad (5)$$

Exergy rate of blood flow (B_{bl}) is composed of kinetic ($B_{bl,kin}$) and physical ($B_{bl,ph}$) parcels. $B_{bl,kin}$, as shown in (6) is a function of blood flow velocity, which is obtained from values of mass flow rate, cross sectional areas of arteries and veins and density of blood.

$$B_{kin} = m_{bl}\frac{{V_{bl}}^2}{2}, \quad (6)$$

Physical exergy of blood flow is determined in (7), (8) and (9) as a combination of physical exergy of liquid and gaseous parts.

$$B_{bl,ph} = B_{bl,liq} + B_{bl,g} = B_{bl,liq} + B_{bl,O_2} + B_{bl,CO_2}, \quad (7)$$

$$B_{bl,liq} = m_{bl}\left[c_{bl}\left(T_{bl} - T_0 - T_0 \ln\frac{T_{bl}}{T_0}\right)\right], \quad (8)$$

$$B_{bl,g} = m_g\left[c_{p,g}\left(T_{bl} - T_0 - T_0 \ln\frac{T_{bl}}{T_0}\right) + R_g T_0 \ln\frac{P_{g,bl}}{P_{g,0}}\right], \quad (9)$$

Looking back at (1) and (2), it is possible to observe that destroyed exergy rate depends on the difference between exergy of blood flow in the inlet and the outlet of the control volume. Different cross sectional areas of arteries and veins lead to different inlet and outlet velocities, which alters kinetic exergy parcel. About the physical exergy, the difference between inlet and outlet is due to heart metabolism that consumes oxygen and produces carbon dioxide, altering the concentration and, consequently, partial pressures of these gases in the outlet.

In order to determine pumping power of the heart, filling and ejection processes shown in Figure 2 are assumed to occur at constant pressure. Equations (10) and (11) were proposed by Alexander [21] as a way to determine pumping power of left and right hearts, respectively. He recommends the use of mean systolic brachial artery pressure (P_{sb}) and mean pulmonary wedge pressure (P_{pw}) as filling and ejection pressures, respectively, for the left heart and mean systolic pulmonary artery pressure (P_{sp}) and right ventricular end-diastolic pressure (P_{rd}) as representative of filling and ejection pressures for the right heart. Cardiac output (CO), which represents the blood flow rate, is used to obtain pumping power. Thus, the heart is assumed as an isentropic pump.

$$W_{left} = CO\left(P_{sb} - P_{pw}\right), \qquad (10)$$

$$W_{right} = CO\left(P_{sp} - P_{rd}\right), \qquad (11)$$

Human heart is treated as a pump; however, differently from the industrial devices, the performed power is an output, which is obtained by means of exergy metabolism. Analogously to the efficiency determined in [20] on energy basis, exergy efficiency of the heart is:

$$\eta_{ex,heart} = \frac{W_{heart}}{B_{M,heart}}, \qquad (12)$$

2.2. Input data

Data related to the energy balance of human body, such as mass flow rates, temperatures and partial pressures, are necessary to perform the exergy analysis of human heart for rest, walking and running conditions. This type of information is obtained by means of the results of the simulations done by Henriques et al. [10] for the same conditions. Values of pressure needed to determine work performed by the heart are available at Horwich et al. [22], but only at rest. Myiai et al. [23] conducted a series of experiments to determine the effect of exercise on blood pressure. They came to the conclusion that only systolic pressures are significantly affected. Using the results of their experiments and mathematical tools, an equation that describes systolic pressure as a function of workload (W_{body}) is obtained, as displayed in (13). The increment of blood pressure corresponding to the workload increase is applied to the reference values of [22] in order to obtain systolic brachial artery and systolic pulmonary artery pressures for walking and running.

$$P_s = 3\times10^{-5}W_{body}^3 - 0.0037W_{body}^2 + 0.3716W_{body} + 126.6 \qquad (13)$$

Frohlich et al. [19] performed an experiment where cardiovascular parameters, including systolic and diastolic blood pressure, were measured in lean and obese people with and without hypertension. The results of energy balance used as reference [10] are just for lean people, so, this preliminary analysis of the impact of hypertension in human heart will be performed only for this group. The experiment [19] provides only systolic and diastolic pressures. It was assumed that the increase observed for mean systolic pressure, which is 34.9%, is also applicable to systolic brachial artery and systolic pulmonary artery pressures, as well as the increase of 29.3% of diastolic pressure may be applied to pulmonary edge and right ventricular end-diastolic pressures. Hypertension leads to increased oxygen consumption and, consequently, greater heart metabolism in order to perform more power to overcome arteries resistance. The augmentation of 35.4% in heart metabolism was assumed based on experimental data provided by Strauer [24].

3. Results and Discussion

From the proposed model and data available in the literature, exergy analysis was applied to human heart and the main results are displayed in Figures 3 to 7. In Figure 3, it is possible to observe how left and right hearts contribute to total exergy destruction in the organ for both normotensive and hypertensive for different levels of physical activity, which are indicated in the graphs as the workload imposed to the body due to the exercise. It can be seen that destroyed exergy increases with exercise intensity and also in the presence of hypertension as a consequence of the augmentation of pumping power and exergy metabolism that occur as a response for the higher systolic and diastolic pressures. Regarding physical activity, the increase is also attributed to higher cardiac output. Between normotensive and hypertensive, increases of total destroyed exergy of 24.0%, 18.0% and 16.7% are accounted at rest, walking and running, respectively.

As expected, destroyed exergy is greater in the left part of the heart than in the right one due to higher power and exergy from nutrients required to pump arterial blood to all organs. Figure 4 depicts how the contribution of the left part to total exergy destruction varies as a function of workload for normotensive and hypertensive. From Fig. 4 it is possible to infer that $B_{d,left}$ always corresponds to more than 80% of $B_{d,heart}$, but this ratio has different behaviors for normotensive and hypertensive . In case of hypertension, the ratio is greater and also increases with exercise intensity, while it is almost constant, varying less than 1% for normotensive. This is another evidence of the pronounced effect of hypertension on left part of the heart that, ultimately, leads to hypertrophy of left ventricle, which is one of the morphological outcomes of hypertension. Observing the individual exergy parcels, it becomes clear that the difference between exergy flows of bloodstream in the outlet and the inlet of the control volume (ΔB_{bl}) is the responsible for this behavior.

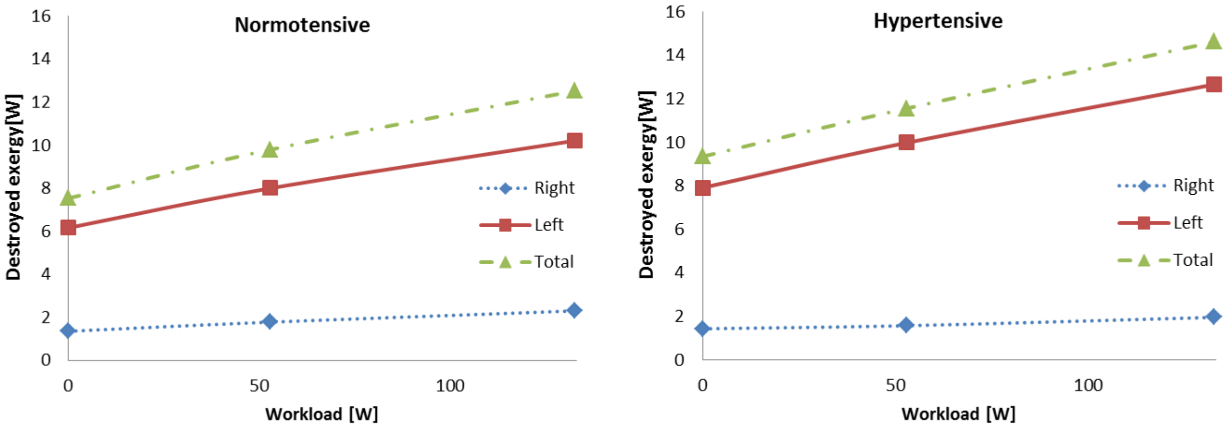

Fig. 3: Destroyed exergy as a function of exercise intensity for normotensive (a) and hypertensive (b).

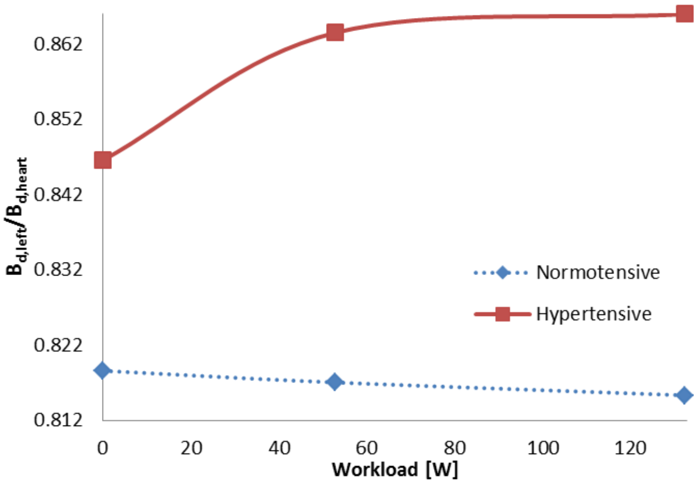

Fig. 4: Ratio of destroyed exergy in left heart ($B_{d,left}$) to total destroyed exergy in the heart ($B_{d,heart}$) as a function of workload for normotensive and hypertensive.

Figure 5 displays the values of ΔB_{bl} in left and right parts of the heart for normotensive and hypertensive. A marked increase in ΔB_{bl} with exercise intensity is observed in case of hypertension for both left and right hearts. This more pronounced increase is due to the higher values of blood pressure, which are directly related to the partial pressures of oxygen and carbon dioxide in bloodstream. According to (9), the relation between partial pressures of the gas in bloodstream and in the reference environment is taken into account in the calculus of the exergy of the gas inside the natural logarithm. When the independent variable is smaller than one, this kind of function is negative and presents a rapid increase. For values above one, it is positive and its evolution is slow. Carbon dioxide partial pressure in bloodstream is greater than that of reference environment. Thus, its exergy is positive and do not suffer great influence from a certain value of pressure on. On the other hand, in the cases evaluated, partial pressure of oxygen in the blood is smaller than that of reference environment, which makes its exergy negative. However, the greater the blood pressure, the closer the oxygen gets to the reference environment. Therefore, its exergy becomes closer to zero rapidly and the total exergy of bloodstream increases.

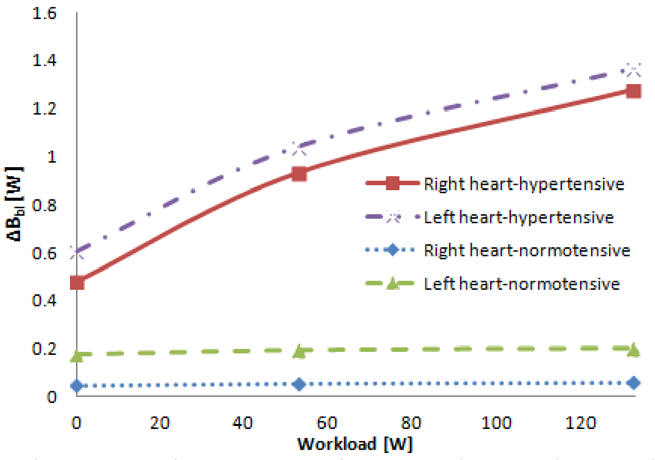

Fig. 5: Difference between exergy flow of bloodstream in the outlet and in the inlet (ΔB_{bl}) of left and right heart for normotensive and hypertensive.

Based in data of $B_{d,body}$ available in the literature [10], the contribution of the heart to total exergy destroyed in the body is plotted in Figure 6. It can be observed that under physical activity, a smaller part of $B_{d,body}$ is attributed to the heart in comparison to rest condition. This indicates that the effect of exercise is more pronounced in other organs of the body. However, a trend of increase is observed from walking to running, what may indicate that light activities affects more other organs than the heart, while more vigorous activities have greater effect on the exergy destroyed in the heart than in the other organs.

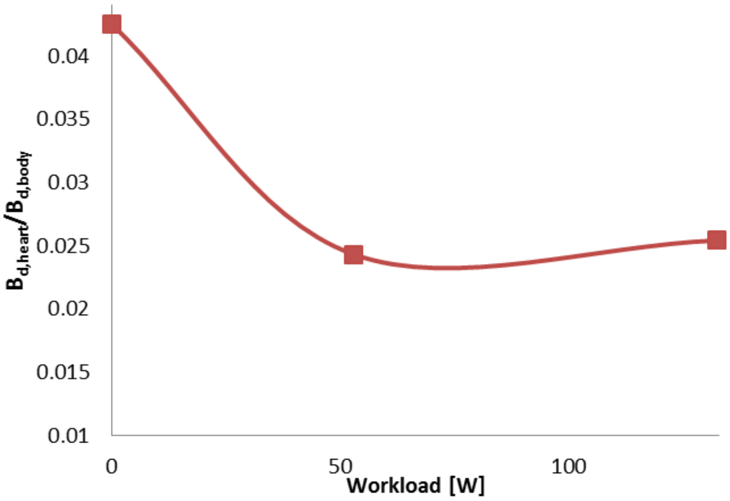

Fig. 6: Contribution of destroyed exergy in the heart ($B_{d,heart}$) to exergy destroyed in the whole body ($B_{d,body}$).

The analysis of exergy efficiency was also performed based on [10] and the results are presented in Figure 7. Since the increase of systolic and diastolic pressures, necessary to the calculus of pumping power, are, respectively, 34.9% and 29.3%, and the increment of metabolism is 35.4% for hypertension, there is no significant difference between exergy efficiency of heart between the groups, which is coherent with information from medical literature [25]. But it can be noticed that exergy efficiency of the heart increases with exercise level in a rate greater than that observed for the whole body, reinforcing the hypothesis raised in last paragraph about the effect of vigorous exercise. As emphasized in [10], the lungs work, basically, as a mass exchanger. For that reason, their exergy efficiency is very high, presenting negative variations for physical exercise only at the third decimal place.

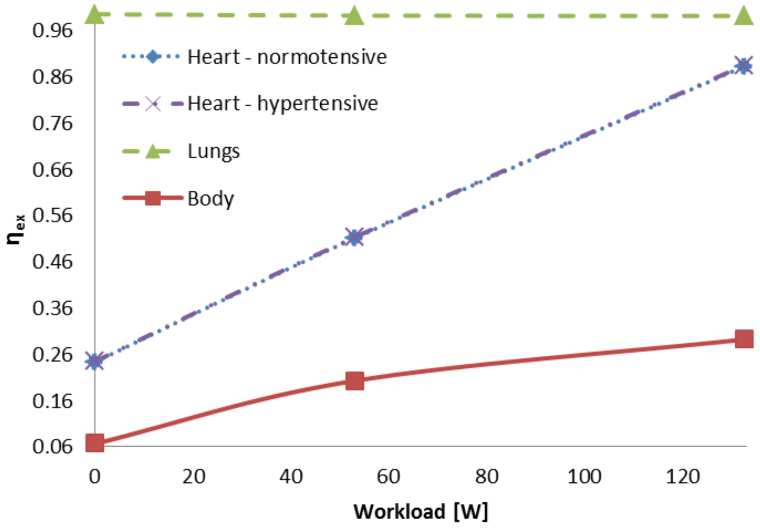

Fig. 7: Exergy efficiency (η_{ex}) of human body, heart with and without hypertension and lungs as a function of workload.

4. Conclusions

An exergy model of human heart was proposed and applied for three different levels of physical activity and also for lean subjects with and without hypertension. Results of destroyed exergy showed that both exercise and hypertension increase the exergy destruction in human heart due to the augmentation of blood pressure and consequent increment of pumping power and exergy metabolism. In all the evaluated scenarios, the exergy destroyed in the left part of the heart was greater than that of the right part. For hypertensive group, the contribution of the left part to the total exergy destroyed was greater than in the normotensive and increased with exercise level. This augmentation is mathematically explained by the natural logarithm of the ratio of partial and reference pressures present in the calculus of the exergy flow of bloodstream, what boosts the impact of higher blood pressure on the value of exergy flow.

By means of data available in the literature, exergy behavior of human heart was compared to that of the whole body. It was observed that the parcel of destroyed exergy of human body attributed to the heart decreases for walking but tends to increase at greater workloads, indicating the role played by the heart in more vigorous activities. About the variation of exergy efficiency as a function of workload, there was no difference between normotensive and hypertensive heart by reason of the proportional increase of power and exergy metabolism. Exergy efficiency of heart increases at a greater rate than that of human body. This fact, added to the participation of destroyed exergy of the heart in the total value, reinforces the importance of this organ during high intensity exercises.

On account of the numerous diseases related to the heart and the circulatory system, the present work represents a small but important step towards the understanding of the impacts of pathologies on exergy behavior of human body. In the near future, it is expected that this research field can deliver some effective results to help diagnosis and treatment of diseases.

Acknowledgements

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Nomenclature

B	exergy rate and flow rate, W
c	specific heat capacity, J/kg.K
CO	cardiac output, m^3/s
m	mass flow rate, kg/s
M	metabolism, W
P	pressure, Pa
Q	heat transfer rate, W
R	gas constant, J/kg.K
T	temperature, K
V	velocity, m/s
W	performed power, W

Greek symbols

η	exergy efficiency

Subscripts and superscripts

0	reference
ar	arterial
bl	blood
CO2	carbon dioxide
d	destroyed
ex	exergy
g	gas
in	inlet
kin	kinetic
liq	liquid
M	metabolic
O2	oxygen
out	outlet
ph	physical
pw	pulmonary wedge
QM	heat released by metabolism
rd	right ventricular end-diastolic

s	systolic
sb	systolic brachial artery
sp	systolic pulmonary artery
ve	venous

References

[1] Szargut J., Exergy Analysis. Research in Progress Thermodynamics 2005; 7(3): 31-33.

[2] Batato M., Borel L., Deriaz O., Jequier, E., Analyse exergétique théorique et expérimentale du corps humain. Entropie 1990;26(153-154):120-130.

[3] Prek M., Thermodynamic analysis of human heat and mass transfer and their impact on thermal comfort. International Journal of Heat and Mass Transfer 2005; 48(3-4):731-739.

[4] Prek M., Thermodynamical analysis of human thermal comfort. Energy 2006; 31(5):732-743.

[5] Prek M., Butala, V., Principles of exergy analysis of human heat and mass exchange with the indoor environment. International Journal of Heat and Mass Transfer 2010; 48(25-26):731-739.

[6] Simone A., Kolarik J., Iwamatsu T., Asada H., Dovjak M., Schellen L., Shukuya M., Olesen B.W., A relation between calculated human body exergy consumption rate and subjectively assessed thermal sensation. Energy and Buildings 2011; 43(1):1-9.Prigogine I., Wiame J., Biologie et Thermodynamique des phenomenes irreversibles. Experimentia 1946; 2(11):451-453.

[7] Mady C. E. K., Ferreira M. S., Yanagihara J. I., Oliveira Junior S., Human body exergy analysis and the assessment of thermal comfort conditions. International Journal of Heat and Mass Transfer 2014; 77:577-584.

[8] Mady C. E. K., Albuquerque Neto C., Fernandes T. L., Hernandez A. J., Saldiva P. H. N., Yanagihara J. I., Oliveira-Junior S., Exergy performance of human body under physical activities. Energy 2014; 62:370-378.

[9] Albuquerque-Neto C., Pellegrini L.F., Ferreira M.S., Oliveira Jr S., Yanagihara J.I., Exergy analysis of human respiration under physical activity. International Journal of Thermodynamics 2010;13 (3):105-109.

[10] Henriques I.B., Mady C.E.K., Albuquerque-Neto C., Yanagihara J.I., Oliveira-Junior, S., The effect of altitude and intensity of physical activity on the exergy efficiency of respiratory system. International Journal of Thermodynamics 2014; 17:265-273.

[11] Hershey D. Entropy theory of aging systems. London: Imperial College Press, 2010.

[12] Silva C., Annamalai K., Entropy generation and human aging: lifespan entropy and effect of diet composition and caloric restriction diets. Journal of Thermodynamics 2009; 2009:1-10.

[13] Mady C. E. K.; Henriques, I. B.; Oliveira-Junior S., Exergy analysis of human body and lifespan: a first approach. In: COBEM, 2013, Ribeirão Preto. Proceedings of the 22th International Congress of Mechanical Engineering, 2013.

[14] Mady C. E. K., Oliveira-Junior, S., Human body exergy metabolism. International Journal of Thermodynamics 2013; 16(2):73-80.

[15] Henriques I.B., Mady C.E.K., Oliveira-Junior, S., Obesity and exergy behavior of human body: a first approach. In: ECOS 2014, Turku. Proceedings of the 27th International Conference on Efficiency, Cost, Optimization, Simulation and Environmental Impact of Energy Systems, 2014.

[16] Prospective Studies Collaboration, Body-mass index and cause-specific mortality in 900000 adults: collaborative analyses of 57 prospective studies. Lancet 2009; 373:1083-96

[17] Poirier P., Eckel R.H., Cardiovascular consequences of obesity. Drug Discovery Today: Therapeutic Strategies- Cardiovascular diseases 2008; 5(1):45-51.

[18] Alexander J.K., Obesity and the heart. Current Problems in Cardiology 1980; 5(1); 1-41.

[19] Frohlich E.D., Messerli F.H., Reisin E., Dunn F.G., The problem of obesity and hypertension. Hypertension 1983; 5(5):71-79.

[20] Guyton A. C., Hall J. E., Textbook of medical physiology. 11th ed., 2006, Elsevier.

[21] Alexander J. K., Obesity and Cardiac Performance. The American Journal of Cardiology 1964; 14:860-865.

[22] Horwich T.B., Fonarow G.C., Hamilton M.A., MacLellan W.R., Woo M.A., Tillisch J.H., The relationship between obesity and mortality in patients with heart failure. Journal of the American College of Cardiology 2001; 38(3):789-795.

[23] Miyai N., Arita M., Miyashita K., Morioka I., Shiraishi T., Nishio I., Blood pressure response to heart rate during exercise test and risk of future hypertension. Hypertension 2002; 39:761-766.

[24] Strauer B.E., Myocardial oxygen consumption in chronic heart disease: role of wall stress, hypertrophy and coronary reserve. The American journal of cardiology 1979; 44(4):730-740.

[25] Kameyama T., Asanoi H., Ishizaka S., Yamanishi K. Fujita M., Sasayama S., Energy conversion efficiency in human left ventricule. Circulation 1992; 85:988-996.