Taurine attenuates cardiac remodeling after myocardial infarction ☆

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After myocardial infarction, cardiac remodeling is associated with progressive ventricular dysfunction and cardiovascular death [1]. Therefore, the objective of this study was to investigate the effect of taurine on cardiac remodeling induced by myocardial infarction in rats.

All experiments were approved by the Animal Ethics Committee of our institution. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

Male Wistar rats weighing 200–250 g were allocated into the following three groups: Group C (n = 10): the rats were submitted to surgery, but they did not undergo coronary occlusion; Group MI (n = 31): the rats were submitted to coronary occlusion; Group MI-T (n = 30): the rats were submitted to coronary occlusion and treated with taurine (3% in drinking water). The dose of taurine and route of administration have been shown to modulate cardiac remodeling [2]. The methods were performed as previously described [2–7].

Considering our results, the cardiac taurine levels were higher in the MI-T in comparison with the other groups (C = 0.100 ± 0.04 μmol/g, MI = 0.175 ± 0.07 μmol/g, MI-T = 0.419 ± 0.187 μmol/g; p = 0.022). The infarct size was not different among the infarcted groups (MI = 31.3 ± 11.5%, MI-T = 31.7 ± 10.4%). Taurine attenuated the increase in the left atrium, the left ventricular (LV) mass, the LV posterior wall thickness (PWT), and the interventricular septum thickness induced by infarction. With regard to the functional variables, taurine did not improve systolic dysfunction induced by coronary occlusion. On the other hand, taurine attenuated the diastolic dysfunction caused by infarction (Table 1).

In relation to metalloproteinase (MMP)-2 and -9, the taurine group showed intermediated values between the C and MI groups. The same phenomenon was observed for the Nrf-2 values. In addition, taurine treatment decreased the GSH-Px and caspase-3 levels, in comparison with the MI group. On the other hand, taurine treatment increased the lactate dehydrogenase, β-hydroxyacylcoenzyme A dehydrogenase, and citrate synthase levels in comparison with controls, as shown in Table 1.

In conclusion, taurine attenuated morphological and functional variables after three months following coronary occlusion. Importantly, this effect was related to decreased apoptosis, oxidative stress, and MMP-2 and MMP-9 activation and was associated with improved cardiac energy metabolism.

Table 1
Echocardiographic, biochemical and molecular data.

Variables	C (n = 6)	MI (n = 6)	MI-T (n = 6)
Caspase 3 ($U/cm^2 \times 10^3$)	0.026 ± 0.03	0.47 ± 0.35*	0.11 ± 0.12#
MMP-2	542 (356–723)	1250 (1180–1270)*	622 (343–964)
MMP-9	991 (836–1065)	3150 (2010–3735)*	1190 (1055–1505)
LDH (nmol/mg protein)	618 ± 128	943 ± 167	1283 ± 236*
OHADH (nmol/mg protein)	82 (80–91)	182 (129–232)	341 (250–419)*
CS (nmol/mg protein)	384 (336–408)	508 (422–563)	669 (542–768)*
GSH-Px (nmol/mg protein)	624 ± 165	821 ± 203*	494 ± 74#
Nrf-2	0.63 ± 0.21	0.25 ± 0.16*	0.42 ± 0.14
LA (mm)[a]	5.3 ± 0.7	6.8 ± 1.0*	6.1 ± 0.8*#
PWT (mm)[a]	1.4 (1.31–1.46)	1.59 (1.53–1.7)*	1.5 (1.4–1.6)*#
IVRT/R-$R^{0.5}$ (ms)[a]	78.5 ± 21.6	100 ± 21.3*	91.1 ± 19.7

C: control animals; MI: infarcted animals; MI-T: infarcted animals supplemented with taurine; MMP: metalloproteinase; LDH: lactate dehydrogenase; OHADH: β-Hydroxyacylcoenzyme A dehydrogenase; CS: citrate synthase; GSH-Px: glutathione peroxidase; Nrf-2: nuclear-factor-E2-related factor; LA: left atrium; PWT: left ventricular posterior wall thickness; IVRT/R-$R^{0.5}$: isovolumetric relaxation time normalized for heart rate. Data are expressed as the mean ± SD or medians (including the lower quartile and upper quartile).
[a] (C, n = 10; MI, n = 21; MI-T, n = 22).
* p < 0.05 versus C.
\# p < 0.05 versus MI.

References

[1] Zornoff LA, Paiva SA, Duarte DR, Spadaro J. Ventricular remodeling after myocardial infarction: concepts and clinical implications. Arq Bras Cardiol 2009;92:157–64.
[2] Denipote F, Ardisson LP, Azevedo PS, et al. Influence of taurine on cardiac remodeling induced by tobacco smoke exposure. Cell Physiol Biochem 2011;27:291–8.
[3] Minicucci MF, Azevedo PS, Martinez PF, et al. Critical infarct size to induce ventricular remodeling, cardiac dysfunction and heart failure in rats. Int J Cardiol 2011;151:242–3.
[4] Paiva SA, Novo R, Matsubara BB, et al. β-Carotene attenuates the paradoxical effect of tobacco smoke on the mortality of rats after experimental myocardial infarction. J Nutr 2005;135:2109–3113.
[5] Ardisson LP, Minicucci MF, Azevedo PS, et al. Influence of AIN-93 diet on mortality and cardiac remodeling after myocardial infarction in rats. Int J Cardiol 2012;156:265–9.

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[6] Azevedo PS, Minicucci MF, Chiuso-Minicucci F, et al. Ventricular remodeling induced by tissue vitamin A deficiency in rats. Cell Physiol Biochem 2010;26:395–402.

[7] Rafacho BP, Santos P, Assalin HB, et al. Role of vitamin D in the cardiac remodeling induced by tobacco smoke exposure. Int J Cardiol 2012;155:472–3.

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Golden Ratio is beating in our heart

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Definition of systole and diastole such as systolic time intervals, electromechanical systole, and left ventricular ejection time have been studied for decades in terms of left ventricular systolic and diastolic function by using methods such as electrocardiograms, phonocardiogram and plethysmographic carotid pulse, M mode and Doppler echocardiography. Physiological systole lasts from the onset of isovolumic contraction to the peak of the ejection phase, so that physiological diastole commences as the LV pressure starts to fall [1]. In contrast, cardiologic systole is demarcated by the interval between the first and the second heart sounds, lasting from the first heart sound to the closure of the aortic valve. The remainder of the cardiac cycle automatically becomes cardiologic diastole [1]. Similarly the occurrence of second heart sound by means of closure of semilunar valves and opening of atrioventricular valves coincides with the end of T wave on electrocardiography. In electrocardiography diastole starts with the end of T wave. There is a slight electromechanical delay from the onset of QRS complex to the onset of first heart sound [2]. As a general perception the beginning of left ventricular systole coincides with the R wave on electrocardiography. It was not our aim to redefine or assess systolic and diastolic phases or their interaction with disease situations.

The ratio Φ:1 has been known since antiquity as the Golden Ratio or the Golden Mean or Number, for its apparent esthetic pleasure. The Golden Ratio is the ratio between two lines of unequal length, where the ratio of the lengths of the shorter to the longer is the same as the ratio between the lengths of the longer and the sum of the lengths, $a/b = b/(a + b)$. The Golden Ratio is also linked, through golden geometric shapes like triangles, rectangles, and pentagrams, to the equiangular spiral. Golden geometric shapes have the property that the ratio between the lengths of their sides is the Golden Ratio. The Golden Ratio has been used extensively in ancient and modern architecture, painting, and music, and is manifest in many forms in nature [3–7].

We aimed to assess the ratio of cardiac phases namely diastole and systole and whether that ratio is close to Golden Ratio.

One hundred and sixty two healthy subjects were included in the study, all subjects had electrocardiogram after 15 min of resting in the supine position. Subjects younger than 20 years and older than 40 years were not included. Subjects were recruited from the hospital staff or healthy relatives of the out-patients. Subjects with any known systemic disease infection, malignancy, valvular heart disease, and subjects who had been receiving any drugs were excluded from the study. Additionally subjects with heart rate <60 beats/min and >80 beats/min or right bundle branch block, left bundle branch block, atrial fibrillation and QRS duration >10 ms were not included in the study. None of the subjects had been receiving any medication. Systolic phase defined as the time between the tip of R wave and the end of the T wave on electrocardiography. Diastolic phase was calculated by subtracting the systolic phase from the R–R interval. Diastolic phase duration/systolic phase duration and R–R/diastolic phase duration were calculated for each patient. Electrocardiograms were recorded with 25 mm/s rate after 15 min of rest at supine position.

Mean age of the patients was 32 ± 7 years. Time intervals are given in Table 1. To rule out the effects of heart rate on diastolic duration we restricted the heart rate in between 60 and 80/min. In these heart rate intervals there were significant negative correlations of diastole/systole ratio with heart rate as expected ($r = -0.66$, $p < 0.001$, Fig. 1). However there was no correlation of diastole/systole ratio with age ($r = -0.09$, $p = 0.25$). Diastolic time interval to systolic time interval ratio was 1.611 and the R–R/diastole ratio was1.618.

The Fibonacci series, discovered in 1202 by the Italian Leonardo di Pisa, or Fibonacci, is a sequence of numbers for which, beginning with 0 and 1, the successive term is the sum of every two previous consecutive terms. The Fibonacci series begins 0, 1, 1, 2, 3, 5, 8, 13, 21, 34… Fibonacci series has been proven useful in the modeling of biological and financial systems as well as in electronics and music [3]. The ratio between a term and the term preceding it in the series approaches Φ:1 or approximately 1.618:1.

It has been recently proposed that the distribution of coronary arteries reveals a morphological spread that follows Fibonacci series of

Table 1
Time intervals in cardiac cycles.

Variables	Mean
Diastolic time (msn)	536 ± 66
Systolic time (msn)	333 ± 22
R–R intervals (msn)	866 ± 73
Diastole/systole	1.611
Heart rate (pulse/min)	69 ± 5
R–R intervals/diastole ratio	1.618
Age (years)	32 ± 7

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