Comparative Mechanical Study of Isolated Papillary Muscle from Wistar-Kyoto and Wistar Rats

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SUMMARY

Isolated papillary muscles have often been used in myocardial mechanical function studies. The objective of the present study was to compare the mechanical function of papillary muscle isolated from left ventricle between Wistar (W) and Wistar-Kyoto (WKY) rats of different ages (1, 3, 6 and 12 months), in order to examine whether there is a difference in intrinsic mechanical properties of muscle between the two rat strains. Muscles were perfused with Krebs-Henseleit solution at 28°C and studied isometrically and isotonically at a stimulation rate of 0.2 Hz. The W and WKY showed statistically significant differences during both isometric and isotonic contractions. During isometric contraction, (1) the peak developed tension (DT) and + dT/dt were lower in WKY rats in the 1 mo groups, (2) the resting tension (RT) was greater in WKY at 3, 6 and 12 mo, (3) time to peak tension (TPT) was greater in WKY at 3 and 12 mo, (4) time for tension to fall from peak to 50% of peak tension (RT 1/2) was greater in WKY at 3 mo and (5) – dT/dt was lower in WKY at 1 and 3 mo. During isotonic contraction, (1) the peak shortening (PS) and – dL/dt were lower in WKY at 12 mo, (2) the time to peak shortening (TPS) was greater in WKY at 3 and 12 mo; (3) + dL/dt was lower in WKY at 3, 6, and 12 mo and (4) the relative variation of length (Lmax-PS)/Lmax was greater in WKY at 6 and 12 mo. These data showed a difference in mechanical behaviour of the papillary muscle between Wistar and Wistar-Kyoto rats of different age. (Jpn Heart J **35**: 333–343, 1994)

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SINCE Frank's description of responses of the isolated frog heart to diastolic tension variations,[1] many studies have attempted to characterize the behav-

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ior of the heart as a pump under different conditions.[2-6] However, the complex geometry of the cardiac chamber impedes the study of myocardial contraction. Since Abbott & Mommaerts[7] demonstrated that cat papillary muscles display some of the mechanical properties of isolated heart muscle, these preparations have been used as a research tool in cardiology.[8-15]

One of the remarkable characteristics of this method is that the muscle needs to be embedded for its nutrition. Thus, it is necessary to utilize small diameter muscle in order to allow optimal nutrition and oxygenation of the muscle fibers.[16,17] These experimental conditions can be reached when rat papillary muscles are employed. Wistar and Sprague-Dawley rats are most frequently used. The Wistar-Kyoto strain has not been utilized as a control, because they are precursors of spontaneously hypertensive rats,[18,19] and, therefore, many have altered cardiac performance.

The purpose of this experiment was to determine whether Wistar-Kyoto rat papillary muscle can be utilized as a control preparation. The intrinsic contractile performance of papillary muscles removed from the left ventricle of Wistar-Kyoto and Wistar rats was compared in this investigation.

Materials and Methods

Male Wistar and Wistar-Kyoto rats at age 1, 3, 6 and 12 months were studied. After decapitation, the heart was removed rapidly and placed in oxygenated Krebs-Henseleit solution[20] at 28°C. Trabecular carneae and papillary muscle were dissected carefully from the left ventricle, mounted between two spring clips, and placed vertically in a chamber containing Krebs-Henseleit solution with 5.50 mM glucose.

The composition of the Krebs-Henseleit solution was as follows: 118.5 mM NaCl, 4.69 mM KCl, 2.52 mM $CaCl_2$, 1.16 mM $MgSO_4$, 1.18 mM KH_2PO_4, 5.50 mM glucose, and 25.88 mM $NaHCO_3$. The PO_2 of the perfusate was maintained between 550 and 600 mmHg by passing 95% O_2 and 5% CO_2 through sintered glass disks located at the bottom of the muscle chamber. The temperature was maintained at 28°C. The lower spring clip was attached to a Kyowa model 120T–20B force transducer by a thin steel wire (1/15,000 inch), which passed through a mercury seal at the bottom of the chamber. The upper spring clip was connected by a thin steel wire to a rigid lever arm above which a micrometer stop was mounted for the adjustment of muscle length. The lever arm was made from magnesium with a ball-bearing fulcrum and a lever arm ratio of 4:1. A displacement transducer (Hewlett-Packard, 7 DCDT—050) was mounted above the short end of the lever arm. Preparations were stimulated 12 times/min with 5 ms square wave pulses through parallel platinum electrodes, at

voltages which were approximately 10% greater than the minimum required to produce a maximal mechanical response.

After a 60-min period during which the preparations were permitted to shorten while carrying light loads, muscles were loaded to contract isometrically and stretched to the apices of their length-tension curves.

After a 5-min period during which preparations performed afterloaded isotonic contractions, muscles were again placed under isometric conditions, and the apex of the length-tension curve (L_{max}) was determined carefully. A 15-min period of stable isometric contraction was imposed prior to the experimental period. One isometric contraction was then recorded for later analysis. In addition, isotonic contraction parameters were obtained, using the lightest preload able to maintain the L_{max}.

The following parameters were measured from isometric contractions: peak developed tension (DT; g/mm^2), resting tension (RT; g/mm^2), time to peak tension (TPT, ms), maximum rate of tension development (+dT/dt; g/mm^2/s), time for tension to fall from peak to 50% of peak tension ($RT^1/_2$; ms) and maximum rate of tension decline (– dT/dt; g/mm^2/s). For isotonic contractions, the following parameters were assessed: peak shortening (PS; mm), time to peak shortening (TPS; ms), maximum velocity of isotonic shortening (+dL/dt; ML/s), maximum velocity of isotonic relengthening (– dL/dt; ML/s), and relative variations of length (L_{max} –PS)/L_{max}. At the end of each experiment the muscle length at L_{max} was measured and the muscle between the two clips was blotted dry and weighed. Cross-sectional areas were calculated from the muscle weight and length by assuming cylindrical uniformity and a specific gravity of 1.00. All force data were normalized for the muscle cross-sectional area and all length data were normalized by the muscle length (L_{max}).

Body weight (BW), heart weight (HW), left ventricular weight (LVW), right ventricular weight (RVW), atrial weight (AW), HW/BW, LVW/BW, RVW/BW and AW/BW ratios were measured for all groups of animals. Parameters used to characterize individual papillary muscles were muscle length (ML), muscle weight (MW) and muscle cross-sectional area (XS). Values are presented as means ± SD. The comparison between groups was made by analysis of variance and *post hoc* Tukey tests. The level of significance was considered at 5% or 1%.

Results

General characteristics of the rats at 1, 3, 6 and 12 months (mo) are shown in Table I. Body weight was greater in Wistar-Kyoto (WKY) rats than Wistar (W) rats in the 3 mo and 6 mo groups only ($p < 0.01$). The same effect was observed for heart and left ventricle weights. Right ventricle and atria weights were signifi-

Table I. General Characteristics of the Wistar and Wistar-Kyoto Rats

	Rats	Age (months)			
		1	3	6	12
Body weight	W	113±8	289±10	438±18	463±38
(g)	WKY	110±9	335±15	504±46	482±19
	p	NS	<0.01	<0.01	NS
Heart weight	W	0,43±0,03	0,75±0,05	1,17±0,09	1,31±0,10
(g)	WKY	0,45±0,04	1,01±0,10	1,33±0,10	1,30±0,07
	p	NS	<0,01	<0.01	NS
LV weight	W	0,30±0,03	0,54±0,04	0,84±0,07	0,92±0,07
(g)	WKY	0,32±0,03	0,74±0,07	0,97±0,08	0,95±0,06
	p	NS	<0,01	<0.01	NS
RV weight	W	0,09±0,01	0,16±0,01	0,23±0,02	0,27±0,03
(g)	WKY	0,09±0,01	0,20±0,03	0,25±0,02	0,24±0,02
	p	NS	<0.01	<0.01	<0,01
A weight	W	0,04±0,01	0,06±0,01	0,09±0,01	0,12±0,03
(g)	WKY	0,04±0,01	0,08±0,01	0,10±0,02	0,11±0,01
	p	NS	<0.01	<0.05	<0.05
$\frac{HW}{BW} \times 10^3$	W	3,83±0,33	2,62±0,21	2,66±0,17	2,84±0,26
	WKY	4,10±0,22	3,02±0,20	2,64±0,13	2,70±0,17
	p	<0.01	<0.01	NS	NS
$\frac{LV}{BW} \times 10^3$	W	2,67±0,20	1,87±0,16	1,92±0,15	1,99±0,16
	WKY	2,90±0,17	2,20±0,15	1,93±0,11	1,97±0,13
	p	<0.01	<0.01	NS	NS
$\frac{RV}{BW} \times 10^3$	W	0,78±0,15	0,55±0,05	0,53±0,04	0,59±0,07
	WKY	0,79±0,08	0,58±0,07	0,51±0,03	0,51±0,04
	p	NS	NS	NS	<0.05
$\frac{A}{BW} \times 10^3$	W	0,39±0,08	0,19±0,03	0,21±0,03	0,26±0,06
	WKY	0,42±0,08	0,24±0,03	0,21±0,03	0,22±0,02
	p	NS	<0.05	NS	NS

Values are means ± SD; $n = 12$; W = Wistar; WKY = Wistar-Kyoto; LV = left ventricle; RV = right ventricle; A = atria; HW = heart weight; BW = body weight; $p < 0.05$ or $p < 0.01$ as compared with Wistar rats; NS = not significant ($p > 0.05$).

cantly greater in WKY than W rats in the 3 mo and 6 mo groups, but in the 12 mo groups they were greater in the W than WKY. Heart and left ventricle weight-to-body weight ratios were greater ($p < 0.01$) in WKY than W rats in the 1 mo and 3 mo groups. The right ventricle weight-to-body weight ratio was lower ($p < 0.05$) in WKY than W rats only at 12 mo. The atria weight-to-body weight ratio was greater ($p < 0.05$) in the WKY than W rats in the 3 mo group.

As shown in Table II, papillary muscle weights were higher in WKY than the W rats in the 1 mo and 3 mo groups. The muscle lengths from WKY were greater than those from W ($p < 0.01$) in the 3 mo and 6 mo groups. The cross-sectional areas of papillary muscles from WKY were greater than those from W ($p < 0.01$) in the 1 mo group only.

Table III summarizes data from isometric contractions obtained from papillary muscle preparations at Lmax. The DT and +dT/dt were significantly lower in the WKY compared with W rats only in the 1 mo group. The RT was greater

Table II. General Characteristics of Left Ventricular Papillary Muscles

	Rats	Age (months)			
		1	3	6	12
MW	W	1,78±0,37	4,25±1,13	5,28±1,36	6,58±1,25
(mg)	WKY	3,08±1,39	5,45±0,83	6,14±1,22	5,91±1,16
	p	<0.01	<0.05	NS	NS
ML	W	4,01±0,50	5,24±0,69	5,90±0,62	6,67±0,76
(mm)	WKY	4,27±0,66	6,37±0,60	6,72±0,57	6,71±0,84
	p	NS	<0.01	<0.01	NS
XS	W	0,44±0,10	0,80±0,17	0,89±0,17	0,98±0,13
(mm^2)	WKY	0,71±0,26	0,86±0,13	0,91±0,14	0,88±0,15
	p	<0.01	NS	NS	NS

Values are means ± SD; $n = 12$; W = Wistar; WKY = Wistar-Kyoto; MW = muscle weight; ML = muscle length at Lmax (length of muscle at maximum developed isometric force); XS = muscle cross-sectional area; $p < 0.05$ or $p < 0.01$ as compared with Wistar rats; NS = not significant ($p > 0.05$).

Table III. Isometric Contraction Data

	Rats	Age (months)			
		1	3	6	12
DT	W	9,52±1,81	8,78±1,26	7,72±1,34	7,46±1,08
(g/mm^2)	WKY	7,85±2,53	8,30±1,33	8,70 ±1,51	8,20±1,73
	p	<0.05	NS	NS	NS
RT	W	0,55±0,15	0,52±0,14	0,47±0,23	0,37±0,11
(g/mm^2)	WKY	0,61±0,21	0,70±0,20	0,95±0,29	0,63±0,27
	p	NS	<0.05	<0.01	<0.01
TPT	W	148±14	174±18	182±16	192±16
(ms)	WKY	155±12	187±15	194±10	206±17
	p	NS	<0.05	NS	<0.05
+dT/dt	W	104±18	91±17	77±16	66±12
($g/mm^2/s$)	WKY	81±24	79±16	82±15	72±15
	p	<0.01	NS	NS	NS
$RT_{1/2}$	W	206±37	204±19	231±24	230±33
(ms)	WKY	211±32	246±25	248±23	232±42
	p	NS	<0.01	NS	NS
−dT/dt	W	28±5	31±7	22±3	24±5
($g/mm^2/s$)	WKY	24±7	23±4	23±3	23±5
	p	<0.05	<0.01	NS	NS

Values are means ± SD; $n = 12$; W = Wistar; WKY = Wistar-Kyoto; DT = peak developed tension; RT = resting tension; TPT = time to peak tension; +dT/dt = maximum rate of tension development; − dT/dt=maximum rate of tension decline; $RT_{1/2}$ = time for tension to fall from peak to 50% of peak tension; $p < 0.05$ or $p < 0.01$ as compared with Wistar rats; NS: not significant ($p > 0.05$).

in WKY than W rats at 3, 6 and 12 mo; there was no significant difference at 1 mo (Figure 1). The TPT was greater in WKY compared with the W group at both 3 and 12 mo ($p < 0.05$, Figure 2). The $RT^1/_2$ was greater ($p < 0.01$) in the WKY than the W group at 3 mo. Finally, the −dT/dt was lower in the WKY compared to W rats at 1 ($p < 0.05$) and 3 ($p < 0.01$) mo.

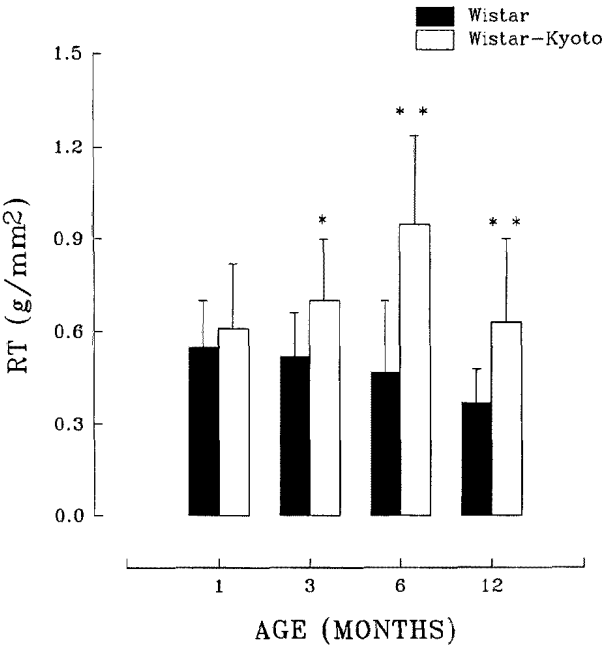

Figure 1. Resting tension (RT) is shown for muscles from Wistar and Wistar-Kyoto rats. $*p < 0.05$, $**p < 0.01$.

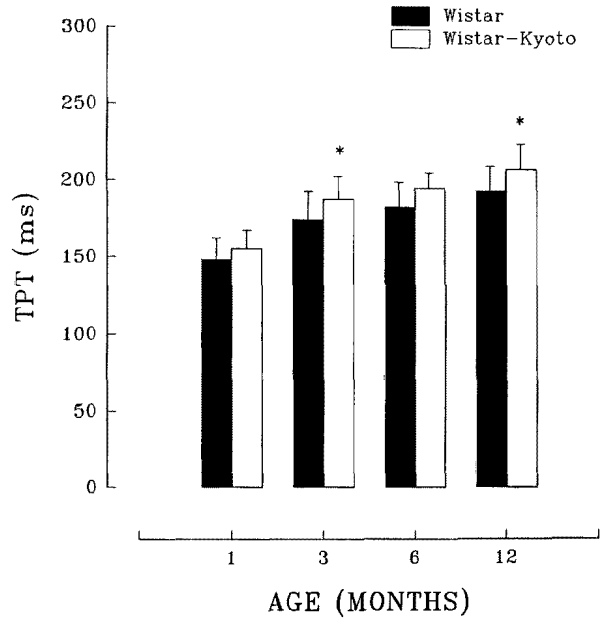

Figure 2. Time to peak tension (TPT) is shown for muscles from Wistar and Wistar-Kyoto rats. $*p < 0.05$.

Table IV. Isotonic Contraction Data

	Rats	Age (months)			
		1	3	6	12
PS	W	1,10±0,11	1,46±0,24	1,46±0,24	1,69±0,33
(mm)	WKY	1,16±0,19	1,59±0,30	1,49±0,21	1,46±0,24
	p	NS	NS	NS	<0.05
TPS	W	169±16	184±14	197±13	196±17
(ms)	WKY	173±8	203±12	207±11	209±15
	p	NS	<0.01	NS	<0.05
$\frac{L_{max} - PS}{L_{max}}$	W	0,74±0,02	0,73±0,03	0,75±0,03	0,75±0,03
	WKY	0,73±0,02	0,75±0,03	0,78±0,02	0,78±0,03
	p	NS	NS	<0.01	<0.01
+dL/dt	W	2,62±0,23	2,87±0,47	2,76±0,60	2,86±0,60
(ML/s)	WKY	2,48±0,27	2,45±0,55	2,17±0,35	2,15±0,47
	p	NS	<0.05	<0.01	<0.01
−dL/dt	W	3,50±0,63	4,35±0,80	3,62±0,73	4,14±0,95
(ML/s)	WKY	3,52±0,57	4,45±0,58	3,62±0,60	3,53±0,68
	p	NS	NS	NS	<0.05

Values are means ± SD; $n = 12$; W = Wistar; WKY = Wistar-Kyoto; PS = peak shortening; TPS = time to peak shortening; $(L_{max} - PS)/L_{max}$ = relative variation of length; + dL/dt = maximum velocity of isotonic shortening; − dL/dt = maximum velocity of isotonic relengthening; ML = muscle length; $p < 0.05$ or $p < 0.01$ as compared with Wistar rats; NS = not significant ($p > 0.05$).

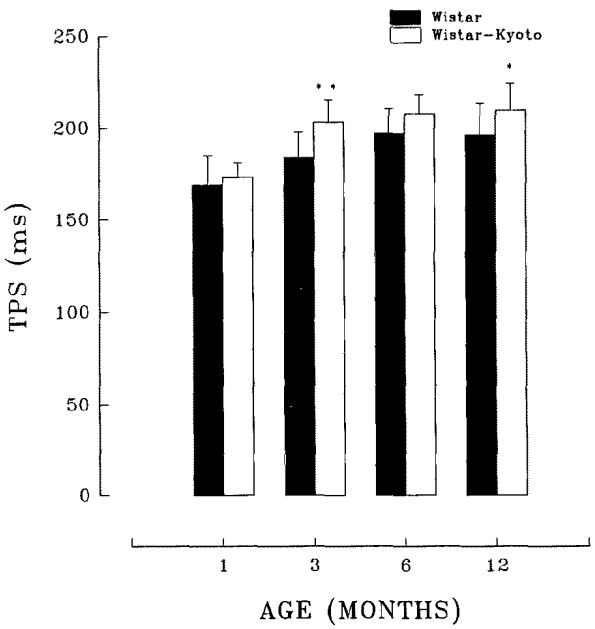

Figure 3. Time to peak shortening (TPS) is shown for muscles from Wistar and Wistar-Kyoto rats. *$p < 0.05$, **$p < 0.01$.

Data from isotonic contractions are shown in Table IV. Both the peak shortening and − dL/dt were lower ($p < 0.05$) in the WKY compared to W rats

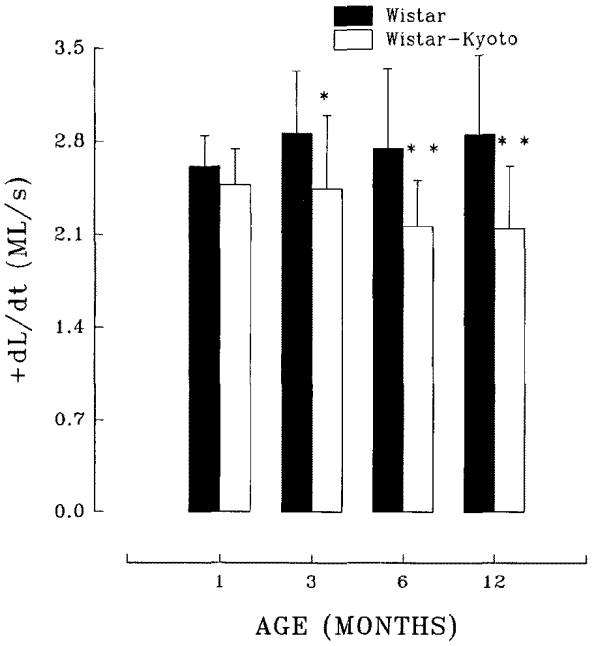

Figure 4. Maximum velocity of isotonic shortening (+dL/dt) is shown for muscles from Wistar and Wistar-Kyoto rats. *$p < 0.05$, **$p < 0.01$.

only in the 12 month old group. The TPS was greater in WKY than W rats at 3 ($p < 0.01$) and 12 ($p < 0.05$) mo (Figure 3). $(L_{max} - PS)/L_{max}$ was greater ($p < 0.01$) in WKY compared to W rats in both 6 and 12 months old groups. Finally, the +dL/dt values were significantly lower in WKY than W rats at 3, 6 and 12 months (Figure 4).

Discussion

The papillary muscles of the rat left ventricle are used widely for the evaluation of myocardial function. A review of studies shows that basal values of normal muscles obtained from isometric or isotonic contractions can be very discrepant.[21-24] This variability in data may reflect methodological differences between experiments.

When the cardiac mechanical function is studied using isolated papillary muscles, two main factors can affect the results: (1) inadequate oxygenation and (2) damage to the ends of the papillary muscle preparations.[16,17,25] Because isolated papillary muscle oxygenation is achieved through diffusion, the use of a cardiac fiber with a large cross-sectional area may produce a hypoxic core in the muscle. Most authors use muscles with cross-sectional areas whose upper limits are between 1.0 and 1.5 mm^2.[14,22,24,26-28] Another factor that changes the papillary

muscle mechanical function is damage to ends of the cardiac fibers, secondary to the attachment to the experimental apparatus.[25] The present experiment attempted to minimize the effect of these factors by (a) using muscles with cross-sectional areas less than 1.2 mm^2 (Table II) and (b) producing consistent damage to the ends of muscle across preparations and that the damaged ends were similar for all. Thus, we believe that these factors did not differentially affect the experimental groups.

The present study showed differences between the cardiac muscle mechanical properties of Wistar and Wistar-Kyoto rats. These differences were verified in isometric and/or isotonic parameters which varied according to the age of the animals. For example, 1 month old rats showed different mechanical behaviour in the values of the parameters of isometric contraction (DT, +dT/dt and − dT/dt). For 12 mo old animals, the difference in myocardial function was expressed through data from the isometric (RT and TPT) and isotonic contractions [PS, TPS, + dL/dt, − dL/dt and $(L_{max} - PS) / L_{max}$]. Further, the RT was significantly greater in WKY rats rather than in W rats in the 3, 6 and 12 mo old groups (Figure 1). Other parameters, such as TPT and TPS were greater in WKY rats (3 and 12 mo) than in W rats of the same age (Figures 2 and 3).

To our knowledge, there are no previous comparison studies of the biochemical, morphological or electrophysiological aspects of heart or papillary muscles of Wistar and Wistar-Kyoto rats. This fact makes it difficult to find explanations for the mechanical behaviour differences noted between the papillary muscles of the two rat strains.

The reason for the difference among the values of the peak developed tension by one-month-old Wistar and Wistar Kyoto rats might lie in their morphological features. One-month-old Wistar-Kyoto rats showed muscles with cross-sectional areas significantly greater than in Wistar rats (Table II). Bing and Frezza[29] reported an inverse relation between normalized developed tension and the cross-sectional area of isometrically contracting papillary muscles at Lmax. Therefore, it is probable that the difference between the cross-sectional areas of the papillary muscles is responsible for the DT values observed in both groups. However, the reasons for the DT behavior in both groups may lie in the metabolical processes which control the excitation-activation-contraction coupling of the cardiac cell.

The data of Table IV and Figure 4 show that +dL/dt was significantly smaller in WKY rats than in W rats (3, 6 and 12 mo). Former studies had shown a correlation between the velocity of muscle shortening and the relative amounts of myosin isozymes in isolated papillary muscles of rabbits and rats.[30,31] Therefore, it is suggested that the myocardium of WKY rats has less myosin ATPase activity than W rat myocardium.

It can be concluded from the present study that there are mechanical behavior differences between the muscles of W and WKY rats. These differences are manifested in parameters obtained from isometric and isotonic contractions in various age groups. There is no information in the literature which can lead to the determination of the mechanisms responsible for specific differences in mechanical behavior between both Wistar and Wistar-Kyoto rats.

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References

1. Frank O: Zur dynamic des herzmuskels. Ztschr f Biol 32: 370, 1895. Translated by Chapman CB and Wasserman E. On the dynamics of cardiac muscle. Am Heart J **58**: 282 and 467, 1959
2. Sarnoff SJ, Berglund E: Ventricular function I. Starling's law of the heart studied by means of simultaneous right and left ventricular function in the dog. Circulation **9**: 706, 1954
3. Sonnenblick EH, Downing SE: Afterload as a primary determinant of ventricular performance. Am J Physiol **204**: 604, 1963
4. Ross J Jr: The assessment of myocardial performance in man by hemodynamic and cineangiographic technics. Am J Cardiol **23**: 511, 1969
5. Hunter WC: End-systolic pressure as a balance between opposing effects of ejection. Circ Res **64**: 265, 1989
6. Elzinga G, Westerhof W: How to quantify pump functions of the heart. Circ Res **44**: 303, 1979
7. Abbott BC, Mommaerts WFHM: A study of inotropic mechanisms in the papillary muscle preparation. J Gen Physiol **42**: 533, 1959
8. Sonnenblick EH: Implications of muscle mechanisms in the heart. Fed Proc **21**: 975, 1962
9. Sonnenblick EH: Force-velocity relation in mammalian heart muscle. Am J Physiol **202**: 931, 1962
10. Hoffman BF, Bassett AL, Bartelstone HJ: Some mechanical properties of isolated mammalian cardiac muscle. Circ Res **23**: 291, 1968
11. Sonnenblick EH: Effects of altered loading in contractile events in isolated rat papillary muscle. Circ Res **24**: 521, 1969
12. Parmley WW, Chuck L: Length-dependent changes in myocardial contractile state. Am J Physiol **224**: 1195, 1973
13. Gillebert TC, Sys SU, Brutsaert DL: Influence of loading patterns on peak length-tension relation and on relaxation in cardiac muscle. J Am Coll Cardiol **13**: 483, 1989
14. Conrad CH, Brooks WW, Robinson KG, Bing OHL: Impaired myocardial function in spontaneously hypertensive rats with heart failure. Am J Physiol **260**: H136, 1991
15. Cicogna AC, Padovani CR, Nardi SC, Okoshi MP: Efeito do envelhecimento sobre o comportamento mecânico dos músculos papilares de ratos Wistar. Arq Bras Cardiol **60**: 215, 1993
16. Snow TR, Bressler PB: Oxygen sufficiency in working rabbit papillary muscle at 25°C. J Mol Cell Cardiol **9**: 595, 1977
17. Paradise NF, Schmitter JL, Surmitis JM: Criteria for adequate oxygenation of isometric kitten papillary muscle. Am J Physiol **241**: H348, 1981
18. Okamoto K, Aoki K: Development of a strain of spontaneously hypertensive rats. Jpn Circ J **27**: 282,

1963

19. Yamori Y: Development of the spontaneously hypertensive rat (SHR) and of various spontaneous rat models, and their implications. *in* Experimental and Genetic Models of Hypertension, ed by Jong W, Elsevier, Amsterdam, p 224, 1984 (Handbook of Hypertension, 4)
20. Krebs HA, Henseleit K: Untersuchungen uber die Harnstoffbildung im Tierkörper. Hoppe Seylers Z Physiol Chem **210**: 33, 1932
21. Henderson AH, Brutsaert DL, Parmley WW, Sonnenblick EH: Myocardial mechanics in papillary muscles of the rat and cat. Am J Physiol **217**: 1273, 1969
22. Capasso JM, Malhotra A, Remily RM, Scheuer J, Sonnenblick EH: Effects of age on mechanical and electrical performance of rat myocardium. Am J Physiol **245**: H72, 1983
23. Cicogna AC, Bing OHL: Influência da anestesia e/ou degolamento sobre o comportamento mecânico de músculos papilares isolados de ventrículo esquerdo de ratos. Arq Bras Cardiol **53**: 197, 1989
24. Bing OHL, Brooks WW, Conrad CH, Sen S, Perreault CL, Morgan JP: Intracellular calcium transients in myocardium from spontaneously hypertensive rats during the transition to heart failure. Circ Res **68**: 1390, 1991
25. Donald TC, Reeves DNS, Reeves RC, Walker AA, Hefner LL: Effect of damaged ends in papillary muscle preparations. Am J Physiol **238**: H14, 1980
26. Bing OHL, Brooks WW, Wiegner AW: Myocardial mechanics in two models of pressure overload hypertrophy. Perspect Cardiovasc Res **8**: 167, 1983
27. Poggesi C, Reggiani C, Bottinelli R, Ricciardi L, Minelli R: Relaxation in atrial and ventricular myocardium; activation decay and different load sensitivity. Basic Res Cardiol **78**: 256, 1983
28. Cicogna AC, Padovani CR, Brooks WW, Schine L, Robinson KG, Conrad CH, Gaasch WH, Bing OHL: Protective effects of diltiazem on the mechanical performance of the hypoxic myocardium. Brazilian J Med Biol Res **26**: 859, 1993
29. Bing OHL, Frezza WA: PO_2 modulated performance of cardiac muscle. Am J Physiol **231**: 1620, 1976
30. Pagani ED, Julian FJ: Rabbit papillary muscle myosin isozymes and the velocity of muscle shortening. Circ Res **54**: 586, 1984
31. Brooks WW, Bing OHL, Blaustein AS, Allen PD: Comparison of contractile state and myosin isozymes of rat right and left ventricular myocardium. J Mol Cell Cardiol **19**: 433, 1987