REGIONAL WALL THICKENING DYNAMICS AS AN INDEX OF REGIONAL MYOCARDIAL FUNCTION

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ABSTRACT -- Biplane roentgen angiograms of isolated, metabolically supported working canine left ventricles were analysed for rates of wall thickening during the systolic phase of cardiac cycle. Left atrial filling pressure, aortic outflow resistance, heart rate, and coronary flow were independently controlled. Values for peak rate of wall thickening, normalized for instantaneous wall thickeness, were closely similar for anterior and lateral free walls of all ventricles under similar hemodynamic conditions. Rate of wall thickening varied linearly with steady state heart rate and coronary artery flow. Little change in rate of thickening was achieved over a considerable range of filling pressures but there was a consistant but small decrease in rate of thickening with elevated aortic outflow resistance. The data support the conclusion that rate of ventricular wall thickening is a good index of inotropic state and/or perfusion of regional myocardium.

INTRODUCTION

Detection of the localized effect of coronary artery stenosis or occlusion is a major reason for development of a regional index of myocardial function. Intrinsic cardiac compensatory mechanisms may compensate for localized myocardial functional impairment so that global cardiac function (e.g., stroke volume) may remain essentially within normal limits until fairly extensive regional myocardial impairment is present. Consequently, a method which permits evaluation of regional myocardial function should provide an earlier index of the effect of small areas of myocardial ischemia than is achieved by indices of global cardiac function (Goldstein and DeJong, 1974). Several techniques have been proposed (Herman et al., 1967; Harris et al., 1974) but these quantitate motion patterns of regional endocardium relative to either the "opposite" endocardium or some other point of reference such as the line drawn through the aortic valve and apex. Unlike these techniques, in which the quantitative value of regional function could be markedly affected by the normal or abnormal behavior of the other regions of the heart, the use of regional wall dynamics (Dumensil et al., 1974) is little affected by the "idiosyncrasies" of the particular reference point chosen. Moreover, one would expect that regional wall thickening relates more directly to the regional myocardium than regional motion of the endocardium which may be affected by factors other than the regional wall contractile function.

A number of clinical (Chesebro et al., 1976; Roy et al., 1975) and experimental studies (DeJong and Goldstein, 1974; Sasayama et al., 1976) suggest that rates of wall thickening during the systolic phase of the cardiac cycle correlate well with presence of regional myocardial ischemia. On the basis

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of these and other similar studies we propose to quantitatively test the hypothesis that the rate of thickening of myocardial wall during the systolic phase of the cardiac cycle is an index of regional myocardial contractile function.

It is to be expected that the magnitude and rate of muscle cell shortening (and hence wall thickening) will be affected by variations in preload (venous filling), afterload (peripheral arterial resistance), and heart rate in addition to coronary perfusion. In intact animals these variables are interdependent and difficult to control so that the relative effects of these variables on rate of wall thickening is difficult to evaluate. For this reason we used an isolated, metabolically supported working left ventricle preparation which allowed a high degree of control of these variables (Ritman et al., 1975).

METHOD

Animal Preparation

Five dogs (13-16 kg) were anesthetized with pentobarbital 15 mg/kg and a thoracotomy performed. The left common coronary artery was cannulated and perfused with arterial blood from a larger, heparinized donor dog. The pulmonary artery, veins, vena cava, and the main branches of the thoracic aorta were ligated and divided. The aorta itself was then also cannulated and divided. The free right ventricular and right atrial walls were resected. The coronary sinus blood was collected in a funnel positioned beneath the heart and returned to the femoral vein of the donor dog. The His bundle was divided and the atrium and ventricle paced independently at a computer-controlled interval and rate with bipolar electrodes sewn into the exposed right ventricular and atrial endocardium. The isolated left ventricle and atrium were suspended from the aortic cannula and connected to a circuit via which aortic blood was returned to the left atrium. The donor dog supplied blood to the coronary circulation via a rotary pump to control coronary flow. The "systemic circuit" of the isolated left ventricle included a cannulating electromagnetic flowmeter, a windkessel, a Starling resistor to provide systemic resistance, and a reservoir to control the left atrial filling pressure. The circuit could be "broken" just downstream to the Starling resistor so that the output of the isolated ventricle could be measured volumetrically. This circuit was filled with isotonic Ringer's dextran with 12% Renovist (i.e., 45 mg Iodine/ml). Left ventricular, left atrial, and aortic pressures were measured by fluid-filled 6-F catheters and Statham P23Db strain gauges.

Imaging Technique

The biplane x-ray-video systems were adapted to ensure maintenance of constant signal levels and operated in pulse mode. Each 60/second x-ray pulse was from 1 to 2 milliseconds in duration. The video images were recorded on videotape for subsequent analysis. Up to 16 channels of analog information (Sturm et al., 1974) such as the pressures, electrocardiographic information, and identification codes were recorded by video pulse height modulation.

Experimental Procedure

The preparations functioned at physiological levels (aortic pressure greater than 80 mm Hg) for at least three hours. Once a uniform concentration of contrast medium in the "systemic circuit" was achieved, the isolated ventricle was subjected to various interventions. During each intervention, a

roentgen angiographic sequence was recorded on videotape. The angiographic record was subsequently transferred from videotape to video disc for detailed stop-action analysis. After each controlled hemodynamic variable (such as left atrial filling pressure) was changed, several minutes were allowed for stabilization of function and then direct volumetric measurement of the isolated ventricular output was obtained while maintaining a constant aortic resistance and filling pressure. During some sequences, coronary flow was decreased stepwise from approximately 120% to 30% of control (1 ml/gm/min). Myocardial oxygen consumption was calculated from the difference of oxygen content between arterial and coronary sinus blood multiplied by coronary flow. There were four sequential protocols performed in each preparation. First, the heart rate was selected, the preparation allowed to equilibrate for several minutes, and an angiographic sequence recorded for approximately 20 seconds. This was performed at selected heart rates between 60 and 180 b/minute. Second, the preload was changed by altering the level of fluid in the left atrial reservoir. Filling pressure was changed and following equilibration, an angiographic sequence of approximately 20 seconds was recorded. This was performed at selected filling pressure up to 21 mm Hg. Heart rate was maintained at 120 b/minute. Third, the afterload was changed by altering the Starling resistor pressure from 60 to 100 mm Hg in a stepwise manner and recordings taken much like the filling pressure procedure. Finally, at fixed filling and afterload pressures, the coronary flow was altered stepwise by control of the pump setting.

Data Reduction

The biplane video images were analyzed by a computer-based operator-interactive border recognition and measurement system (Ritman et al., 1973). The 10-bit digital values corresponding to the horizontal and vertical position of several hundred border recognition points around each epicardial and endocardial silhouette were measured and transferred to digital tape for subsequent analysis. The pressure data recorded on the same videotape were also measured electronically and recorded on the same digital magnetic tape. Ventricular chamber volume and wall thickness at selected intervals between apex and base, and the time rate of change of these values were derived from these data and displayed as illustrated in Figure 1. Ventricular chamber volume was calculated using Simpson's rule. The computer-based method used to compute regional wall thickness (taken to be the shortest distance between the endo- and epicardial surfaces in the selected segment of the wall) and time rate of thickening is described elsewhere (Dumensil et al., 1974). The hearts used in these studies were of very similar size, hence any differences of rates of thickening due to scale were minimized. However, in each ventricle, the rate of wall thickening was seen to be dependent on wall thickness. As can be appreciated in Figure 2 rate of thickening increased with increased wall thickness from apex to base of the ventricle. In order to minimize the possible role of wall thickness we used the following "normalization" approach.

The basic assumption used in this normalization is that the myocardium is essentially incompressible so that any change in myocardial length results in an inverse thickness change. For sake of simplicity of the model, we assume all myocardial fibers to be circumferential. This assumption is not essential but is probably reasonable in the myocardium midway between apex and base and is supported by data presented in the work os Sasayama et al. (1976), who measure wall thickness and circumference directly with ultrasound crystals sutured to myocardium. Figure 3 illustrates the variables in this model of the relationship between wall thickness and myocardial muscle wall length.

$T_w \cdot L \cdot H = M$ (see Figure 3 for meaning of symbols) (1)

If the myocardium is essentially incompressible, time rate of change of muscle mass is zero.

$$d(T_w.L.H)/dt = d(M)/dt = 0 \quad (2)$$

$$L.H.d(T_w)/dt + T_w.H.d(L)/dt + T_w.L.d(H)/dt = 0 \quad (3)$$

"Thickening" of the transverse slice (in apex to base directional) is considered negligible, i. e.,

$$d(H)/dt = 0 \quad (4)$$

Rearrangement of remaining non-zero terms results in the following relationships:

$$(dL/dt)/L = -(dT_w/dt)/T_w \quad \text{or} \quad d(\ln L)/dt = -d(\ln T_w)/dt \quad (5)$$

This model suggests that normalized "velocity" of myocardial shortening in the circumferential direction is proportional to the negative normalized rate of wall thickening. This model is very similar to that proposed by Gould et al. (1976).

RESULTS

Global Ventricular Function

The functional performance levels of all ventricles used in this analysis were comparable to that expected for denervated ventricles of similar size in the intact dog. Average ventricular output ranged from 0.6 l/min at aortic diastolic pressure greater than 100 mm Hg or low coronary flow (less than 50 ml/100 gm/min) to a maximum of 1.65 $\pm$ 0.3 l/min at aortic diastolic pressure less than 50 mm Hg and control coronary flow (approximately 100 ml/100 gm/min). That these functional characteristics were produced by ventricles which were not in failure is suggested by the fact that stroke volume increased with atrial filling pressure elevated up to 21 mm Hg.

Regional Myocardial Wall Dynamics

Wall thickness was measured 60 times per second at selected levels between the base and apex of the videoroentgenograms. The wall thickness values were obtained in up to 10 sequential cardiac cycles.

The dynamic pattern of wall thickening at one region of the free wall through several cardiac cycles is illustrated in Figure 1. Systolic thickening of the wall in the selected region commences at the beginning of the isovolumetric contraction period and the rate of wall thickening is at a maximum at the time of maximum ejection rate. The magnitude of the maximal rate of wall thinning during the midpoint of the rapid filling phase of diastole is about as rapid as the maximum rate of thickening during the midpoint of the ejection phase. Minimum wall thickness is achieved during end-diastole. Peak rate of wall thickening averaged around 2.0 wall thicknesses per second (range 1.1 to 2.5) under control conditions.

The effects of total coronary flow on wall dynamics is illustrated in

Figure 4 and effect of steady state heart rate, aortic diastolic pressure and left atrial filling pressure on wall dynamics is illustrated in Figure 5.

The data in Figure 4 show that rate of wall thickening during systolic phase decreases linearly with total coronary flow. If 1 ml/gm/min is taken to be normal coronary flow, then these data also indicate that supranormal flow in this preparation can increase rate of wall thickening to values greater than control values. The data in Figures 4 and 5 indicate that the normalized rate of wall thickening in different parts of the ventricle corresponded closely over the full range of induced change in rate of wall thickening.

DISCUSSION

The magnitude of the rates of wall thickening observed in these isolated ventricles, supported by a donor dog anesthetized with pentobarbital, possibly have little direct applicability to intact unanesthetized man and experimental animals. However, several features of these data may be of importance for the interpretation of wall dynamics in the intact, in situ heart.

First, the rate of dynamic blood volume changes as a contributor to rates of wall thickening can be estimated from the data of Gaasch and Bernard (1977). In the unlikely event that the entire 15% wall blood content is squeezed out completely during the approximately 0.3 seconds of systole and no pure thickening of the muscle occurs, then an estimated normalized wall thickening rate of 0.45 wall thickenings per second would result. Consequently, physiologically significant changes in rates of thickening that suggest myocardial function changes should be greater than 0.5 thicknesses per second if there is to be no doubt about the change.

Second, wall dynamics are highly dependent on factors that are known to affect velocity of shortening such as coronary flow (Goldstein and DeJong, 1974), heart rate and afterload (aortic diastolic pressure). These observations support the hypothesis that normalized rate of systolic wall thickening is an index of circumferential shortening. As illustrated in the middle panel of Figure 5, an increased afterload can be expected to result in a decreased rate of wall thickening. The data presented in the left panel of Figure 5 show lack of change in rate of wall thickening with increase in muscle length (wall thinning due to increased filling pressure). Apparently the increased tension generating capacity resulting from the increased preload is cancelled out by the increased afterload resulting from the distension of the ventricle and the associated increase in radius of curvature of the wall.

The fact that regional wall thickening reflects myocardial function is not new. A new point, however, is that changes in the anterior and lateral free walls of the left ventricle are similar under various hemodynamic conditions.

In conclusion, the results of this study suggest that wall thickening dynamics change with afterload (aortic diastolic pressure), oxygen delivery (coronary flow), and stimulus frequency (heart rate) much like the shortening behavior of isolated papillary muscle preparations (Sonnenblick, 1962; Sutton et al., 1980). The data presented here suggest that comparison of wall dynamics (wall thickening values) in one region of the heart wall with another region — when heart rate, filling pressure and aortic pressure are identical — is the context within which wall dynamics should be used.

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REFERENCES

CHESEBRO, J.H., RITMAN, E.L., FRYE, R.L., SMITH, H.C., CONNOLLY, D.C., RUTHERFORD, B.D., DAVIS, G.D., DANIELSON, G.K., PLUTH, J.R., BARNHORST, D. A., and WALLACE, R.B. (1976), "Videometric analysis of regional left ventricular function before and after aortocoronary artery bypass surgery", J. Clin. Invest. 58:1339-1347.

DEJONG, J.W., and GOLDSTEIN, S. (1974), "Changes in coronary venous inosine concentration and myocardial wall thickening during regional ischemia in the pig", Circ. Res. 35:111-116.

DUMENSIL, J.G., RITMAN, E.L., FRYE, R.L., GAU, G.T., RUTHERFORD, B.D., and DAVIS, G.D. (1974), "Quantitative determination of regional left ventricular wall dynamics by roentgen videometry", Circulation 50:700-708.

GAASCH, W., and BERNARD, S. (1977), "The effect of acute changes in coronary blood flow on left ventricular end-diastolic wall thickness", Circulation 56:593-598.

GOLDSTEIN, S., and DEJONG, J.W. (1974), "Changes in left ventricular wall dimensions during regional myocardial ischemia", Am. J. Cardiol. 34:56-62.

GOULD, K.L., KENNEDY, J.W., FRIMER, M., POLLACK, G.H., and DODGE, H.T. (1976), "Analysis of wall dynamics and directional components of left ventricular contraction in man", Am. J. Cardiol. 38:322-331.

HARRIS, L.D., CLAYTON, P.D., MARSHALL, H.W., and WARNER, H.R. (1974), "A technique for the detection of asynergistic motion in the left ventricle", Comput. Biomed. Res. 7:380-394.

HERMAN, M.V., HEINLE, R.A., KLEIN, M.D., and GORLIN, R. (1967), "Localized disorders in myocardial contraction: asynergy and its role in congestive heart failure", N. Engl. J. Med. 277:222-232.

RITMAN, E.L., STURM, R.E., and WOOD, E.H. (1973), "Biplane roentgen videometric system for dynamic (60/second) studies of the shape and size of circulatory structures, particularly the left ventricle", Am. J. Cardiol. 32(2): 180-187.

RITMAN, E.L., TSUIKI, K., DONALD, D., and WOOD, E.H. (1975), "Regional myocardial shape and dimensions of the working isolated canine left ventricle. IN: Harrison, D.C., Sandler, H., and Miller, H.A.: Cardiovascular Imaging and Image Processing, Theory and Practice. 72:129-137.

ROY, P., FRYE, R.L., TAJIK, A.J., CHESEBRO, J.H., RITMAN, E.L. and GAU, G.T. (1975), "Regional left ventricular function by echocardiography and roentgen videometry", Circulation II 52:234.

SASAYAMA, S., FRANKLIN, D., ROSS, J. JR., KEMPER, W.S., and MCKOWN, D. (1976), "Dynamic changes in left ventricular wall thickness and their use in analysing cardiac function in the concious dog", Am. J. Cardiol. 38: 870-879.

SONNENBLICK, E.H. (1962), "Force-velocity relations in mammalian heart muscle", Am. J. Physiol. 202:931-939.

STURM, R.E., RITMAN, E.L., HANSEN, R.J., and WOOD, E.H. (1974), "Recording of multi-channel analog data and video images on the same video tape or disc", J. Appl. Physiol. 36:761-764.

SUTTON, M.G.ST. JOHN, RITMAN, E.L., and PARADISE, N.F. (1980), "Biphasic changes in maximum relaxation rate during progressive hypoxia in isometric kitten papillary muscle and isovolumic rabbit ventricle", Circ.Res. 47(4):516.

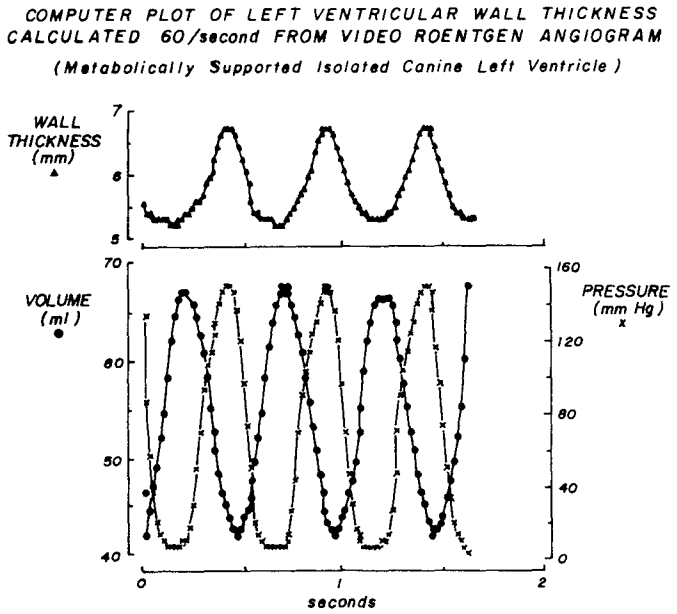


Figure 1. Computer-generated plot of simultaneous recordings of left ventricular pressure, computed left ventricular volume and wall thickness obtained at a point on the free wall midway between apex and base during three successive cardiac cycles (Reproduced with permission from Ritman et al., (1975)).

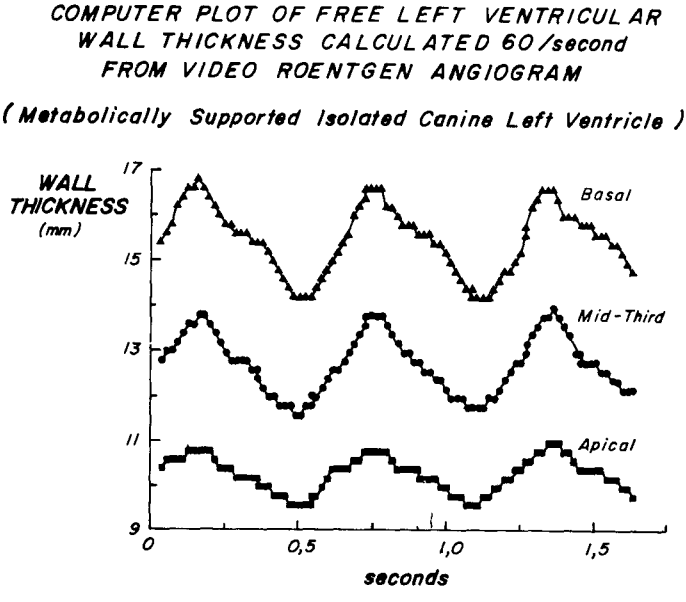
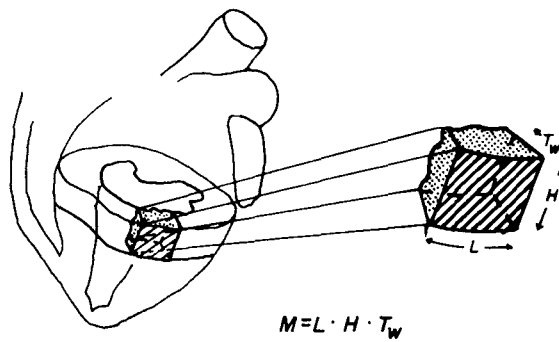


Figure 2. Dynamic sequence of left ventricular wall thickness values measured simultaneously in one ventricle at 60/sec intervals during three successive cardiac cycles. The upper trace was obtained from near the base, the middle trace from midway between base and apex, and the lower trace from near the apex.

RELATIONSHIP OF REGIONAL MYOCARDIAL
WALL THICKNESS DYNAMICS
TO MYOCARDIAL LENGTH DYNAMICS



$$M = L \cdot H \cdot T_w$$

$$\frac{dM}{dt} = 0; \quad \frac{dH}{dt} = 0$$

$$\therefore -\frac{dL}{L} = \frac{dT_w}{T_w}$$

Figure 3. Schematic representation of relationship between change in myocardial cell length (in circumferential direction) and wall thickness. Basic assumption is that muscle wall is incompressible. The fractional change in wall thickness is used as a normalization for minimizing the effect of heart size on the value and rate of wall thickening during systole.

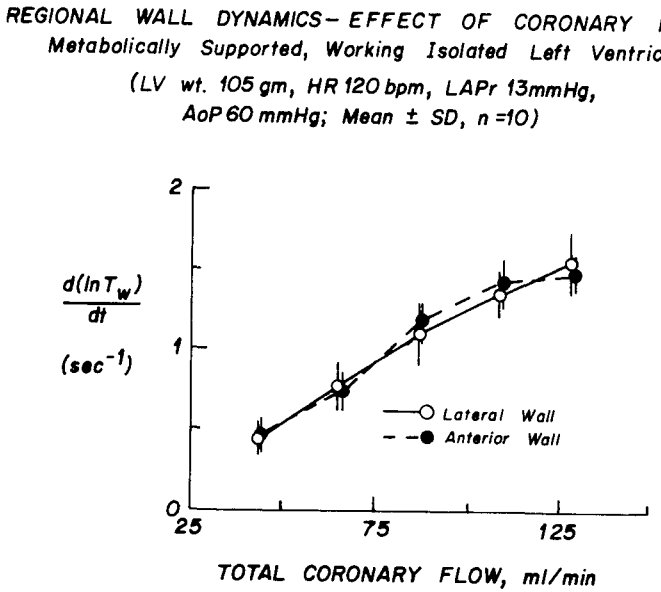


Figure 4. Effect of total coronary flow on normalized rate of wall thickening of isolated left ventricle. Control coronary flow is approximately 1 ml/gm myocardium/min. The dashed line represents data from the anterior free wall and it corresponds closely to the data obtained in the lateral free wall. In both walls an average and one standard deviation obtained from 10 sequential cardiac cycles is displayed. The data are from a 105 gm ventricle paced at 120 b/min, left atrial pressure of 13 mm Hg and aortic Starling resistor pressure of 60 mm Hg.

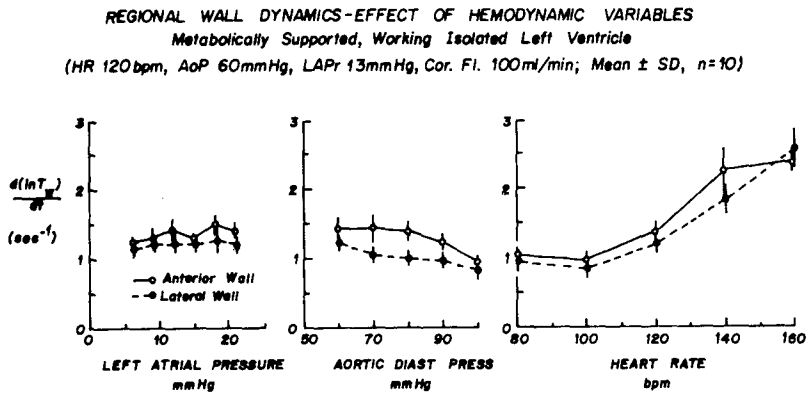


Figure 5. Effect of three hemodynamic variables on normalized rate of thickening of one 105 gm isolated left ventricle. The dashed line joins data points obtained in the lateral free wall and the solid line joins values obtained in anterior free wall. In both walls an average and one standard deviation obtained from 10 sequential cardiac cycles is displayed. The sequences were obtained at coronary flow of 1 ml/gm/min, left atrial pressure of 13 mm Hg, aortic Starling resistor pressure of 60 mm Hg, and heart rate of 120 b/min except for the variable parameter.

DINÂMICA DO AUMENTO REGIONAL DE ESPESSURA DE PAREDE COMO UM INDICADOR DE FUNÇÃO REGIONAL DO MIOCÁRDIO

RESUMO--Angiogramas roentgen biplanares de ventrículos esquerdos - caninos, isolados e mantidos funcionando metabolicamente, foram analisados em termos da taxa de aumento de espessura da parede durante a fase sistólica do ciclo cardíaco. A pressão de enchimento de átrio esquerdo, a resistência à saída de fluxo na aorta, a frequência cardíaca e o fluxo coronariano foram controlados independentemente. Valores para o pico da taxa de aumento de espessura da parede, normalizado para valores instantâneos de espessuras de paredes, foram similares para paredes livres nas partes anterior e lateral de todos os ventrículos sob condições hemodinâmicas similares. A taxa de aumento de espessura de parede variou linearmente com a frequência - cardíaca de estado permanente e fluxo arterial de coronária. Pouca mudança ocorreu na taxa de aumento da expessura da parede para uma faixa considerável de pressões de enchimento mas houve uma consistente, porém pequena, diminuição nesta taxa para valores elevados da resistência ao fluxo de saída da aorta. Os resultados levam a concluir que a taxa de aumento da espessura da parede ventricular é um bom indicador do estado inotrópico e/ou perfusão regional do miocárdio.