Influence of the Elevation of the Left Ventricular Diastolic Pressure on the Values of the First Temporal Derivative of the Ventricular Pressure (dP/dt)

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Purpose *– To assess the effects of the elevation of the left ventricular end-diastolic pressure (LVEDP) on the value of the 1st temporal derivative of the ventricular pressure (dP/dt).*

Methods *– Nineteen anesthetized dogs were studied. The dogs were mechanically ventilated and underwent thoracotomy with parasympathetic nervous system block. The LVEDP was controlled with the use of a perfusion circuit connected to the left atrium and adjusted to the height of a reservoir. The elevation of the LVEDP was achieved by a sudden increase in the height of a reservoir filled with blood. Continuous recordings of the electrocardiogram, the aortic and ventricular pressures and the dP/dt were performed.*

Results *– Elevation of the LVEDP did not result in any variation of the heart rate (167±16.0bpm, before the procedure; 167±15.5bpm, after the procedure). All the other variables assessed, including systolic blood pressure (128±18.3mmHg and 150±21.5mmHg), diastolic blood pressure (98±16.9mmHg and 115±19.8mmHg), LVEDP (5.5±2.49 and 9.3±3.60mmHg), and dP/dt (4,855 ± 1,082 mmHg/s and 5,149±1,242mmHg/s) showed significant increases following the expansion of the ventricular cavity. Although the elevation of the dP/dt was statistically significant, 6 dogs curiously showed a decrease in the values of dP/dt.*

Conclusion *– Sudden elevation of the LVEDP resulted in increased values of dP/dt; however, in some dogs, this response was not uniform.*

Key words: Frank-Starling mechanism, dP/dt, ventricular function

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The rate of change in pressure with time (dP/dt), usually known as the 1st temporal derivative of ventricular pressure, is one of the parameters employed for the assessment of the left ventricular function.

In the 60's and 70's, the maximal values of dP/dt (dP/dtmax) were largely employed to assess the inotropic capacity of the heart [1-4]. From the studies conducted at that time, it was suggested that dP/dt did not reliably reflect the inotropic state. The concept that finally prevailed was that dP/dtmax had limited practical applications as an indicator of the inotropic capacity [5]. The major limitation [6,7] was the lack of specificity of this parameter, since other factors, in addition to myocardial inotropic capacity, interfered with the maximal value of dP/dt. The factors capable of interfering with the values of the dP/dtmax include: the afterload [7,8], the preload [9,10] and the presence of myocardial hypertrophy [2,11].

The correct interpretation of the relationship between the degree of myocardial stretching (preload) and dP/dt is particularly complex. According to the most traditional version of the concepts related to ventricular function, the inotropic capacity of the heart and the variation of the performance of the heart as a result of change in the muscular length during rest (Frank-Starling mechanism) were considered independent myocardial characteristics. Yet, the influence of the Frank-Starling mechanism on dP/dtmax would not be related to changes in the inotropic capacity of the heart. For this reason, variations in the ventricular volume occurring during the evaluation of dP/dt max would preclude an exact definition of the inotropic state.

Advances in the knowledge of the physiological basis of myocardial contraction make this traditional view questionable, currently allowing alternative explanations. More recent information [12-17] about the subcellular adjustments involved in the relationship between the ventricular stretching during rest and the mechanical performance of the ventricles indicate that myocardial stretching interferes with the degree of activation of the contractile phenomenon, i.e., with myocardial contractility. The identification of

a functional interaction between the Frank-Starling mechanism and myocardial contractility requires adequate concepts related to the validity of dP/dtmax when evaluating the inotropic capacity of the heart in the presence of changes in the preload.

A number of authors have described a direct relationship between the increase of the ventricular volume and the values of dP/dt [1,18-20]. Others [3,21,22], however, report lack of association between both parameters. It should be underscored that these studies were conducted according to protocols that established a period of time for the stabilization of the preparation after elevation of the preload, thus allowing circulatory accommodation. Consequently, the direct relationship between the ventricular volume and dP/dt was influenced by the circulatory adjustment.

In a study conducted in our laboratory, using preparations of isolated canine hearts, we noted that the sudden ventricular dilation was invariably followed by an increase in the values of dP/dt [15]. In this experiment, the behavior of dP/dt was only indicative of the response of the heart to the expansion of the ventricular cavity. No similar protocol was conducted in canine hearts in situ.

Thus, the objective of this study was to assess the behavior of the values of dP/dtmax after a sudden increase in the diastolic pressure of the left ventricle (LV) and to discuss these findings in light of the current concept relating myocardial stretching and myocardial contractility.

Methods

Nineteen dogs, weighing 19.6±4.4kg (x±sd), were studied. The dogs were anesthetized with meperidine (2.0mg/kg) intramuscularly combined with an intravenous mixture of chloralose (60mg/kg) and urethane (600mg/kg). After being anesthetized, the dogs were placed in the horizontal supine position, intubated and mechanically ventilated. Catheterization of the femoral vein was performed for drug administration and fluid replacement. Subsequently, a median thoracotomy with pericardiotomy was performed. A catheter (length: 4cm; internal diameter: 1.4mm) was inserted into the left ventricular cavity through puncture of the apex, and the extremity of another catheter, which was inserted through the femoral artery, was placed in the ascending aorta. The distal tips of these catheters were connected to Statham P23-ID transducers, which were coupled to amplifiers (1205 model, with VR-12 polygraph**,** Electronics for Medicine). In order to control the ventricular filling pressure, a perfusion circuit connected to the left auricle and to the external jugular veins was designed. The circuit (fig. 1) contained tubes, a reservoir with a level limiting system, a stick to sustain the reservoir, allowing its movement in the vertical direction, and a perfusion pump.

The pressures of the LV and the aorta, the dP/dt and a bipolar lead of the electrocardiogram were continuously monitored. After the surgical procedures and administration of atropine (0.5mg/kg IV), the preparation was allowed to rest for 30min to reach stabilization. The reservoir

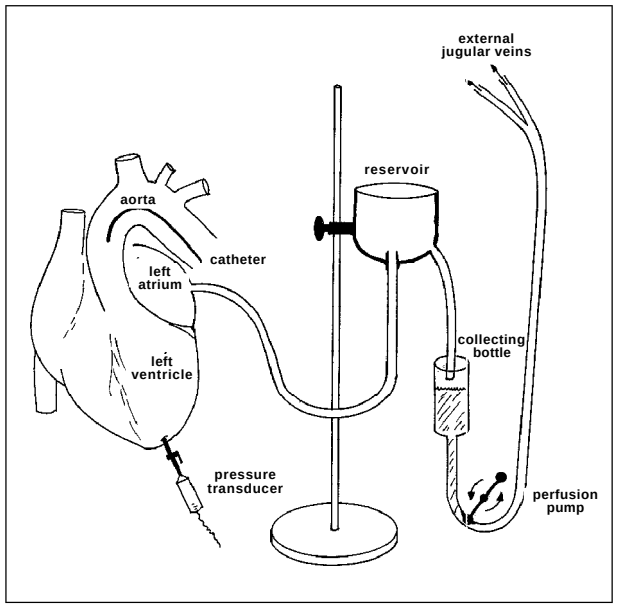

Fig. 1 – Schematic representation of the perfusion circuit used in the experiment.

was filled with blood and its height was adjusted so that the blood level in its interior corresponded to the left atrial pressure. During 10s of sustained expiratory apnea, the reservoir was suddenly elevated to promote a rapid increase in atrial pressure. These maneuvers enabled the recording of the ventricular and aortic pressures, as well as of dP/dt, in a control scenario and during the elevation of the ventricular filling pressure.

In order to assess the significance of the variations in the values of dP/dtmax, the Student t test for paired values was employed; when the differences whose probabilities depended on chance were <5% ($p<0.05$), they were considered statistically significant. To characterize the magnitude of the increase of the left ventricular end-diastolic pressure (LVEDP), of the systolic blood pressure (SBP) and of the diastolic blood pressure (DBP), 95% confidence intervals were constructed.

Results

The mean values and the standard deviations of the variables assessed in the control scenario and during the elevation of the LV dfiastolic pressure are exhibited in Table I. The heart rate did not show significant variation (167 ± 16.0bpm and 167±15.5bpm). In all dogs, increased values of SBP, DBP and LVEDP were observed. The SBP increased from 128±18.3mmHg to 150±21.5mmHg, and the 95% confidence interval for the variation was 17.7-26.5mmHg. The DBP increased from 98±16.9mmHg to 115±19.8mmHg, and the 95% confidence interval for the variation was 12.9-22.2mmHg. The LVEDP increased from 5.5±2.49mmHg to 9.3±3.60mmHg, with a 95% confidence interval of 2.94-4.64mmHg for the variation. In regard to dP/dtmax, there was an increase from 4,855±1,082mmHg/s to 5,149±1,242mmHg/s and it was statistically significant (p=0.0169). The analysis

Table I - Hemodynamic data in the control scenario and during elevation of the left ventricular diastolic pressure

	Control	Elevation
HR (bpm)	167±16.0	167±15.5^{ns}
SBP (mmHg)	128±18.3	150±21.5*
DBP (mmHg)	98±16.9	115±19.8*
LVEDP (mmHg)	5.5±2.49	9.3±3.60*
dP/dt_{max} (mmHg/s)	4,855±1,082	5,149±1,242#

HR- heart rate; SBP- systolic blood pressure; DBP- diastolic blood pressure; LVEDP – left ventricular end-diastolic pressure; dP/dt_{max}- maximal value of the 1st temporal derivative of the ventricular pressure; #- p<0,05; ns- p>0,05; *- the elevation occurred in all dogs.

of the individual data of this variable (fig. 2) enabled us to verify that, unexpectedly, and on a significant number of occasions (6 dogs), the values of the dP/dtmax decreased following the elevation of the ventricular filling pressure.

Discussion

The increased values of dP/dt noted in this study are in accordance with previously reported data, when we induced similar ventricular stretching in isolated canine hearts perfused with the blood of another dog [15]. The decreased values of dP/dt observed in the present study were completely unexpected, considering the previous experiment. In the preparation of isolated heart, the ventricular expansion was followed by an increase in the values of dP/dt in all the experiments [15].

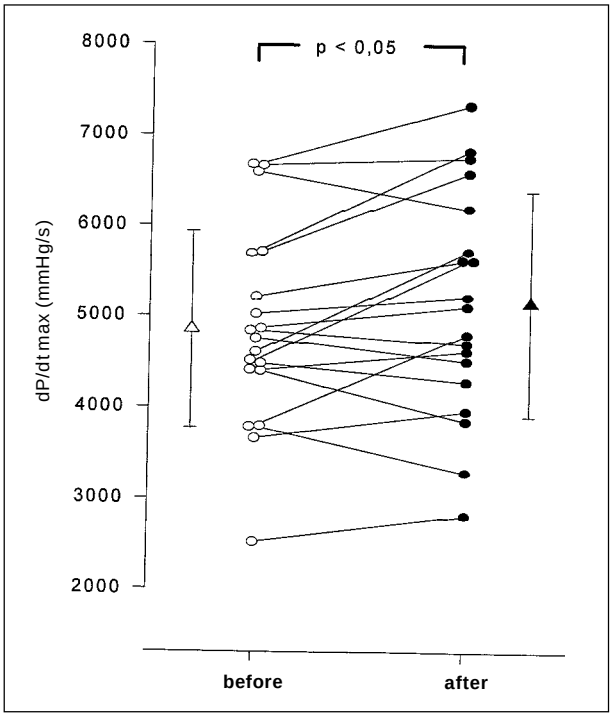

Fig. 2 – Individual values of the 1st temporal derivative of the ventricular pressure (dP/dt) before and after the elevation of the left ventricular end-diastolic pressure.

In this study, the fact that the values of dP/dtmax might have been influenced by the increase of blood pressure (BP), changes in the viscoelasticity of the myocardium and the Frank-Starling mechanism must be taken into account.

The increase of the aortic pressure could affect the values of dP/dt, inducing variations in the afterload [8,23], in the perfusion pressure and in the coronary flow [24-27]. A series of publications [3,7,8,23] report that the maximal values of dP/dt are directly proportional to the levels of BP; others [9,28,29], however, suggest that the aortic pressure has no influence on the dP/dt. The great variability of the models and the investigational protocols employed in these studies may be considered the determining factor of the controversial results. The authors who assessed the relationship between these 2 variables considered that, during oscillations of BP, the values of dP/dt may be modified as a result of variations in the afterload or in the coronary perfusion. Studies conducted in our laboratory [29-31], whose methods were similar to those used in the present study, showed that, in the experimental conditions that we used, the sudden increase in the aortic pressure did not affect the values of dP/dtmax.

Another phenomenon that must be considered as a factor that might affect the ventricular function when BP is abruptly increased is the Anrep effect. The current concept about the Anrep effect is that, after a sudden increase in BP, a transient decrease of the inotropic capacity of the heart is observed, due to subendocardial ischemia. As a result of an autoregulatory vasodilation [15,32,33], the perfusion of the heart is promptly restored, allowing the recovery of the inotropic capacity of the myocardium. As we performed the assessments of dP/dtmax a few seconds after the heart load (preload and afterload) underwent variation, there is a possibility that the Anrep effect might be responsible for the decrease in the values of dP/dtmax observed in some dogs in our study; that is, the evaluation of the dP/dt may have occurred during a period when a transient myocardial ischemia was taking place. In addition, some authors [34-36] noted a worsening of the myocardial perfusion as a result of the elevation of the diastolic pressure in the left ventricular cavity. This was also a consequence of the collapse of the subendocardial coronary vessels. The abnormal myocardial perfusion is likely to be the mechanism accounting for the decrease in the values of dP/dt noted in some experiments.

Considering the characteristics of our protocol, another aspect to be considered is the viscoelasticity of the myocardium [12,37-39]. The viscoelastic component of the cardiac muscle confers resistance against the acute alterations in the muscular length [37,38,40]. This resistance depends on the rate of stretching and on the initial muscle length [40-42]. Thus, LeWinter et al [37] noted that, to obtain the same value of LVEDP, the greatest dilation of the LV was seen when the maneuver of increasing the diastolic pressure was done slowly. In our study, it is not possible to determine precisely the influence of viscoelasticity in our results. However, if we consider that these factors would likely have influenced our

results, this would be towards limiting the magnitude of ventricular dilation, probably decreasing the effects of the Frank-Starling mechanism.

The main effect of the volume infusion maneuver performed in our study was the improvement of the ventricular performance as a result of the Frank-Starling mechanism. Improvement of the ventricular performance is currently considered a result of the contributing physical factors and of factors that alter the intensity with which the contraction is activated [12-15,17,43,44]. The physical factors are related to the spatial disposition of the myofilaments, that is, myocardial stretching provides an increased spatial interaction between the myofilaments, increasing the number of active links between myosin and actin, and eventually improving the ventricular performance. The factors that activate contraction are related to myocardial contractility. It has been demonstrated that myocardial stretching increases the transarcolemmal inflow of calcium [44-46], intensifies the release of calcium by the sarcoplasmic reticulum [13,47,48] and increases the affinity of troponin C for calcium [49-52]. It is believed that the main factor that contributes to the improvement of the ventricular performance as a result of stretching is the improved myocardial contractility [13,49,53]. Thus, our findings of increased values of dP/dtmax as a result of the elevation of the left ventricular diastolic pressure are likely to be a spontaneous result of the intensification of the process by which contraction is activated. If this statement is correct, the current focus on the relationship between preload and dP/dt, which considers the modifications due to stretching inadequate signs of deviations of the contractile state, will no longer prevail. Rather, the oscillations of dP/dt occurring in these circumstances may indicate the degree to which the contraction is activated secondary to the mobilization of factors that intervene in the kinetics of calcium.

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