SYSTOLIC TIME INTERVALS - MEASUREMENT IN THE DOG THROUGH THE USE OF APEXCARDIOGRAPHY

by

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INTRODUCTION

Systolic time interval measurement is a diagnostic tool that has been utilized in human medicine to assess cardiac function. It has not been used in the dog because of technical problems in recording the time interval externally. This study was conducted in order to obtain normal values for systolic time intervals in the dog through utilization of an apexcardiogram and to record dogs with chronic valvular disease and mitral insufficiency in order to quantitate their abnormalities.

PAPER I

SYSTOLIC TIME INTERVALS - MEASUREMENT IN NORMAL DOGS THROUGH THE USE OF APEXCARDIOGRAPHY

INTRODUCTION

Use of systolic time intervals (STI) has gained in popularity in human medicine in the last decade as a means of assessing left ventricular function, primarily due to the ease of recording, minimal expense, minimal time involvement, and no anesthetic requirement. The outstanding factor in this method of assessment is the diagnostic knowledge obtained. Data obtained is reliable and valuable in initial evaluation and in follow-up therapy. The main value for the clinician is detection of altered states of contractility in congestive heart failure and assessment of myocardial response to positive inotropic agents (e.g., digitalis.

Systolic time intervals have not been utilized in veterinary cardiology because the method used in the human is not applicable to the dog. Therefore, an alternative method to define the intervals needed to be devised for this species.

The apexcardiogram is a recording of the excursions of the apex beat against the chest wall. The initial contraction of the left ventricle is from base to apex, forcing the ventricular walls to bulge laterally against the thoracic cage. When the left ventricular systolic pressure reaches aortic diastolic pressure the aortic valve opens and the entire left ventricle collapses upon itself, taking it away from the chest wall. Due to this phenomenon the initiation of contraction and the point where the aortic valve opens can be detected on the apexcardiogram. Utilizing an electrocardiogram, phonocardiogram, and apexcardiogram the systolic time intervals can be measured and utilized.

The following study fulfilled two goals: 1) it examined the relationship of the apexcardiogram to intra-cardiac events in order to validate the technique utilized, and 2) it determined normal values in both sexes over a wide range of heart rates against which abnormal subjects could be compared.

LITERATURE REVIEW

In 1921 Wiggers[12] published his findings describing the phases of the cardiac cycle in the dog. Systole was divided into three consecutive periods - the periods of isometric contraction, maximal ejection, and reduced ejection. The start of isometric contration began with a rise in intraventricular pressure or the onset of the first vibration of the first heart sound. Its conclusion and the beginning of the ejection phases was the opening of the aortic valve as signaled by a rise in aortic pressure. The cessation of ejection was indicated by the beginning of the incisural notch. One additional phase was delineated between the end of systole and the beginning of diastole. It was designated the proto-diastolic phase which included the time between the start of the incisura and the second heart sound. This phase has fallen out of use today in clinical measurements and is included as a portion of the ejection period.[8,11]

Weissler[10] published his data on systolic time intervals in the human in 1968. All times were recorded externally through the use of an electrocardiogram, a phonocardiogram, and a carotid pulse wave tracing. He measured the following time intervals: 1) the total electromechanical systole (QS_2) was measured from the start of the QRS complex to the first high frequency vibration of the aortic component of the second heart sound; 2) the left ventricular ejection time (LVET) was measured from the beginning of the upstroke of the carotid pulse wave tracing to the incisura; and 3) S_1S_2 was measured as the interval between the first and second heart sounds. The following intervals were calculated from these measurements: 1) the pre-ejection period (PEP) was derived by subtracting the LVET from QS_2; 2) the time from beginning depolarization to the first heart sound (Q-1) was derived by subtracting S_1S_2 from QS_2, representing electro-mechanical delay; and 3) the isovolumetric contraction time (ICT) was derived by subtraction LVET from S_1S_2.

Weissler established normal values for man and recorded abnormalities in Phase III and IV congestive heart failure patients. A summary of significant findings includes: 1) the LVET shortened significantly with increasing heart rate while the pre-ejection period shortened slightly; 2) QS_2 and LVET were significantly longer in females than in males; 3) the PEP and ICT were of the same magnitude in both sexes; 4) the ICT remained constant with heart rate; 5) in left ventricular failure the PEP was prolonged and the LVET was shortened; and 6) the shortened LVET and prolonged PEP correlated well with cardiac and stroke indices in patients with left ventricular disease undergoing cardiac catheterization.

Another index, the ratio of PEP to LVET, has since been added to the above measurements. In man this ratio is a constant number at heart rates below 110 beats per minute and increases in left ventricular failure.[3]

Various time intervals have been compared to internal indices since Weissler's original work. Martin, et. al.[6] found that the LVET was the same when measured internally and externally while the PEP and ICT were not equal but exhibited good linear relationship. Others[3,8,13] have concluded that PEP and PEP/LVET correlated well with the ejection fraction (ejection volume/left ventricular end diastolic volume).

Ahmed, et. al.[1] outlined the criteria to determine the ability of an index to measure left ventricular contractility. They concluded that it should: 1) detect the contractile deficit in clinically manifest failure; 2) yield normal values in cardiac diseases which do not affect left ventricular contractility; 3) exhibit appropriate changes with positive and negative inotropic influences; 4) reflect the state of left ventricular inotropy uninfluenced by pump-function alterations due solely to preload, afterload, and other factors; 5) be sensitive to contractile deficits which may exist in the absence of clinically overt failure; and 6) exhibit close correlations with selected, validated, independent measures of contractility. Their study satisfactorily demonstrated PEP and PEP/LVET to fulfill all the criteria. They concluded the PEP is responsible for most of the change in PEP/LVET with altered contractility but PEP/LVET was advantageous because it was not affected by heart rate. They also concluded that PEP and PEP/LVET correlate better with measures of contractility (dp/dt) than with measures of performance (cardiac index, stroke volume) because performance measurements are more affected by preload, afterload, and heart rate than contractility. Weissler[10] stated that LVET correlated more closely with stroke volume and cardiac index since it is a measurement of the time the aortic valve is open.

The aforementioned method for measuring systolic time intervals cannot be applied to the dog. The carotid artery is buried deep within cervical tissue and inaccessible to pulse wave recording. The femoral pulse wave lacks an incisura and cannot be utilized.[4]

Another method to be considered utilizes apexcardiography.[2] The apexcardiogram is recorded by applying a transducer over the left apex beat and recording the excursions of the left chest wall. Willems, et. al.[15] have shown a close correlation between the beginning of the upstroke of the apexcardiogram and the onset of mechanical systole in the dog. A good correlation was also shown between the peak dp/dt and the "E" point on the apexcardiogram (Figure 1). Peak dp/dt occurs intimately with the onset of ejection.

Through the simultaneous recordings of an apexcardiogram, electrocardiogram and phonocardiogram the following measurements could be evaluated: 1) The pre-ejection period (PEP), as measured from the onset of the QRS complex to the "E" point on the apexcardiogram; 2) the systolic upstroke time (SUT), which corresponds to the isovolumetric contraction time, by measuring from the onset of the upstroke of the apexcardiogram to the "E" point; 3) total electromechanical systole (QS_2) measured from the onset of the QRS complex to the initial vibrations of the second heart sound. The left ventricular ejection time could then be calculated by subtracting the PEP from QS_2 (Figure 2).

Still another means of assessing contractility via the use of the apexcardiogram has been evaluated in man. The premise for this measurement is that dp/dt is affected to some degree by preload and afterload. Time from the onset of the rise of the dp/dt curve to its peak (t-dp/dt) is unaffected by preload or afterload. Time measurements from the start of the upstroke of the first derivative of the apexcardiogram to its peak (t-peak Δ ACG) correlate well to t-dp/dt (Figure 3). The method also demonstrates excellent correlation to changes induced by beta-adrenergic stimulation and blockade.[7] Thus, an external time measurement can be utilized that is unaffected by preload or afterload.

Studies of systolic time intervals in the dog are limited. Talley, et. al.[9] compared the use of PEP in the dog to t-dp/dt and to the maximal dp/dt divided by intantaneous left ventricular pressure and reported good correlation to these refined measurements of contractility. They also noted that PEP did not alter with heart rate when the rate was enhanced by electrical pacing. The conclusion was that shortening of the PEP with naturally occurring increased heart rate is due to adrenergic influences that affect both rate and myocardial contractility. Hamlin, et. al.[5] have found PEP actually lengthens when the R-R interval shortens in pronounced sinus arrhythmia.

MATERIALS AND METHODS

The initial phase of the study compared internally recorded points in the systolic cycle to corresponding events recorded by apexcardiography in the dog and compared results to previously published research data.[9] This phase was included in order to establish that the technique utilized was valid. Five pairs of normal mesocephalic dogs were studied. Each pair consisted of a male and female of equal weight. The weight pairs consisted of 9, 13.5, 17, 21.5, and 26 kilograms. Each dog was anesthetized using thiamylal sodium intravenously without prior atropinization and maintained under anesthesia with halothane. A surgical exposure of the left carotid artery was performed. An 8-French double lumen catheter was guided down the arterial channel to a point where the distal lumen of the catheter was lying within the left ventricular cavity. The second lumen, which was 12 cm. proximal to the distal lumen, rested in the root of the aorta. An electrocardiograph lead was selected in which the Q wave was visible. The apexcardiogram was recorded from the left apex beat. Simultaneous recordings of the aortic pressure curve, left ventricular pressure curve, apexcardiogram and electrocardiogram were taken on an Electronics for Medicine DR-8 multichannel recorder at 200 mm./sec. Comparisons between the initiations of the upstroke of the left ventricular pressure wave and the apexcardiogram were noted. Comparisons between the "E" point of the apexcardiogram and the initial aortic pressure rise were also recorded (Figure 1).

The second phase of the study established normal systolic time interval values in dogs of various weights, breeds, heart rates, and in both sexes. Twenty male and twenty female dogs were recorded on an Electronics for Medicine DR-8 multichannel recorder at 100 mm./sec. Each dog was given 1 mg. per kg. of Diazepam[a] intravenously prior to recording in order to control shaking and allow electrode placement. All recordings were taken in left lateral recumbency. An electrocardiogram, left apexcardiogram, and first derivative curve of the apexcardiogram were recorded simultaneously. Immediately following, an electrocardiogram and a high frequency phonocardiogram were recorded simultaneously. The following measurements were derived: 1) The QS_2; 2) the PEP; 3) the SUT; 4) the t-peak Δ ACG; 5) the LVET; and 6) the PEP/LVET (Figure 4). Three complexes were measured for each dog. The results were averaged and plotted on a graph against heart rate. All measurements were calculated to the nearest 5 msec. Regression equations and standard deviations were computed. Statistical analysis was performed for each measurement.

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[a]Valium, Roche Laboratories, Nutley, New Jersey.

RESULTS

A. Comparative Values

Upstroke Initiation

During the simultaneous apexcardiogram, left ventricular pressure curve recordings, 7 of 10 dogs exhibited no measurable difference between the beginning of the systolic wave of the left apexcardiogram and the rise of the left ventricular pressure curve. In the remaining three dogs the mean time difference was less than 10 msec. with the apexcardiogram following the left ventricular pressure curve in each case (Table 1, Column A).

Peak Upstroke

In 4 of 10 dogs the "E" point of the apexcardiogram coincided with the onset of aortic pressure rise. Of the remaining 6 dogs, 5 followed the pressure rise by mean time differences less than 8 msec. One dog's "E" point preceded the aortic pressure rise by a mean time difference of 3 msec. (Table 1, Column B).

B. Normal Values

All data was divided into two equal groups based on sex. The male regression equations revealed each interval that was measured to be significantly related to heart rate. The interval with the greatest relation was LVET with a regression equation of 221.864-0.671 HR (Figure 5) followed by PEP (96.605-0.209 HR) (Figure 6), SUT (70.170-0.156 HR) (Figure 7), t-peak Δ ACG (43.477-0.079 HR) (Figure 8), and PSP/LVET (0.392 + 0.001 HR) (Figure 9).

Females did not show a similar correlation. Only LVET had a regression equation that was significant in relation to heart rate (172.810-0.310 HR) (Figure 10). PEP (76.087 - 0.073 HR) (Figure 11), SUT (56.938 - 0.062 HR) (Figure 12), t-peak Δ ACG (36.489 - 0.031 HR) (Figure 13), and PEP/LVET (0.423 + 0.001 HR) (Figure 14) were not significant in relation to heart rate.

DISCUSSION

Results of comparing the internal and external cardiac events recorded with our technique compared favorably with the measurements recorded by Willems, et. al.[13] Therefore, it was concluded that the apexcardiographic technique as utilized was a valid means of determining the point of initial contraction and the point of aortic valve opening.

Results of measuring systolic time intervals on normal subjects revealed a marked difference between male and female populations. Each time interval of the male population exhibited a more prolonged measurement at slow heart rates in comparison to the female population. The male population's time intervals then exhibited a more marked influence with heart rate than the female population's time intervals, exhibiting a rapid decline as heart rate increased. The female's time intervals showed little variance with heart rate except in the case of LVET. The relationship between PEP and LVET in each population was similar at varying heart rates resulting in the PEP/LVET ratio being very similar in males and females. PEP/LVET also varied mildly with heart rate. Therefore, its measurement may be a convient method to determine dysfunction and to follow response to therapy.

However, measurement of individual time intervals will oftentimes give more benefit in situations where contractility is more affected than ejection and vice versa. Mitral insufficiency results in a shortened LVET, oftentimes with no prolongation of the PEP. If utilized as an indicator for determining the severity of the regurgitance the obtained LVET must be compared with normal regression analysis for the particular sex involved. Alternately cardiomyopathy will result in prolonged measurements of contractility (PEP, SUT, t-peak ACG). Mitral insufficiency oftentimes accompanies congestive cardiomyopathy because of annular dilatation resulting in a concomitant decrease in LVET. Both values need to be analyzed in this situation.

Systolic time interval measurement holds promise as a diagnostic tool in three areas of clinical cardiology. They are: 1) as a means of detecting heart failure states; 2) as a means of assessing if the patient requires digitalis glycoside therapy; and 3) as a means of assessing the patient's response to therapy.

A common clinical entity encountered in canine medicine is the miniature or toy breed dog that is presented with a cough and a cardiac murmur. The differential diagnosis usually includes mitral insufficiency with congestive heart failure, chronic pulmonary disease and tracheal malformations. The differentiation is oftentimes difficult, especially since a combination of disease processes may be present. Systolic time interval measurement may provide a rapid and inexpensive means of determining if heart failure is present.

Congestive heart failure may not always include a significant loss of myocardial contractility. Congestive failure due to the hypertrophic form of cardiomyopathy or infundibular hypertrophic subaortic stenosis are good examples. Contractility in these cases may be normal or augmented. Positive inotropic agents (e.g., digitalis) are contraindicated and this fact could be better realized through systolic time interval measurement. Therapy with negative inotropic agents (e.g., propanalol) could then be instituted and assessed.

Many patients in whom digitalis glycosides are utilized are still digitalized to a point of toxicity. This is especially true in a patient that does not respond well to digitalis therapy clinically. Until now there has been no practical way of assessing how the myocardium is responding to medication. Systolic time interval measurement provides the means of evaluating the patient who responds to a minimal amount of digitalis by returning to normal and the patient who does not respond to therapy. Thus, the clinician is alerted that alternate medications need to be utilized. This type of evaluation should reduce the number of toxicity states encountered.

Systolic time interval measurement may also enable the clinician to avoid the potential problem of chronic overdigitilization. The primary beneficial effect of digitalis is to stimulate a failing myocardium to increase its power output. This requires increased work and increased oxygen utilization by the myocardium. At optimal levels of digitalis its negative chronotropic effect and its ability to reduce ventricular size offset the increase in oxygen need. However, in theory, if the myocardium were to be overstimulated with digitalis the oxygen requirement could reach a level that could not be offset. The end result would be a chronically hypoxic myocardium, an enhanced failure state, and the premature demise of the patient. Through systolic time interval measurement the minimal amount of glycoside needed to correct a contractility deficit should be able to be achieved. It is estimated in human medicine that in many patients only one-fourth of a digitilizing dose is needed to correct deficient myocardial contractility. If this statement holds true in veterinary medicine we may be doing many of our patients a disservice.

In addition to assessing a patient's response to digitalis therapy, systolic time interval measurement may also be utilized to assess response to other positive inotropic agents, to negative inotropic agents, and possibly to vasodilator therapy in the future.

SUMMARY

Systolic time interval measurement involves determining the pre-ejection period, systolic upstroke time, time to the peak of the first derivative curve of the apexcardiogram, and the left ventricular ejection time. A method for measurement in the dog utilizing apexcardiography was evaluated. The technique involved was compared to previous research and found to correlate well.

Normal values were established for an equal number of males and females. Results revealed a marked difference between the two populations. The male population's intervals varied markedly with heart rate while only the left ventricular ejection time varied in the female population. Regression analysis and statistical analysis was performed for each time interval.

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TABLE 1

Comparison values obtained through simultaneous left ventricular pressure, aortic pressure and apexcardiographic recordings.

Case #	Sex	Wt.	A Upstroke Initiation	B Peak Upstroke
847	Fe	9 kg	+3	+3
1145	M	9 kg	0	0
891	Fe	13.5 kg	0	0
813	M	13.5 kg	+0	-3
231	Fe	18 kg	+8	+8
782	M	18 kg	0	+4
883	Fe	22.5 kg	0	+5
858	M	22.5 kg	0	+3
816	Fe	27 kg	+10	0
863	M	27 kg	0	0
		Range	+3-+10	-3-+8

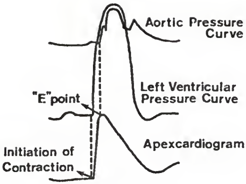


FIGURE 1

The comparisons made between events measured through cardiac catheterication and apexcardiography.

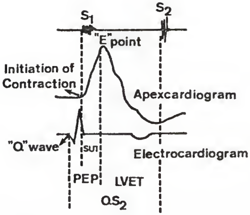


FIGURE 2

Systolic time interval measurements made by utilizing an apexcardiogram.

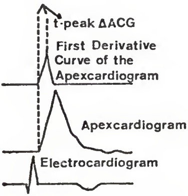


FIGURE 3

The measurement method for t-peak Δ ACG.

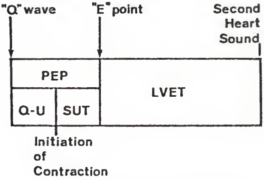


FIGURE 4

Graphic representation of systolic time interval measurements made by utilizing an apexcardiogram.

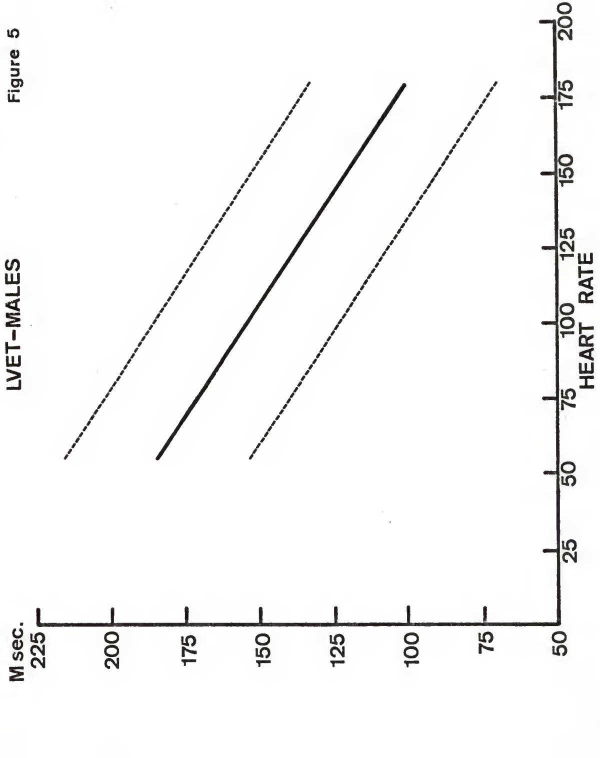

LVET-MALES
M sec.
225
200
175
150
125
100
75
50
25
50
75
100
125
150
175
200
HEART RATE

Figure 5

Figure 6

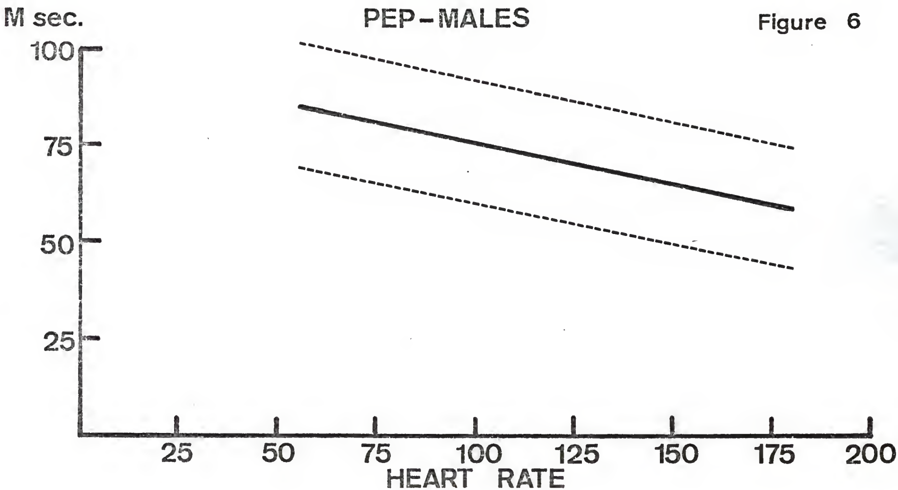

PEP-MALES
M sec.
100
75
50
25
25
50
75
100
125
150
175
200
HEART RATE

Figure 7

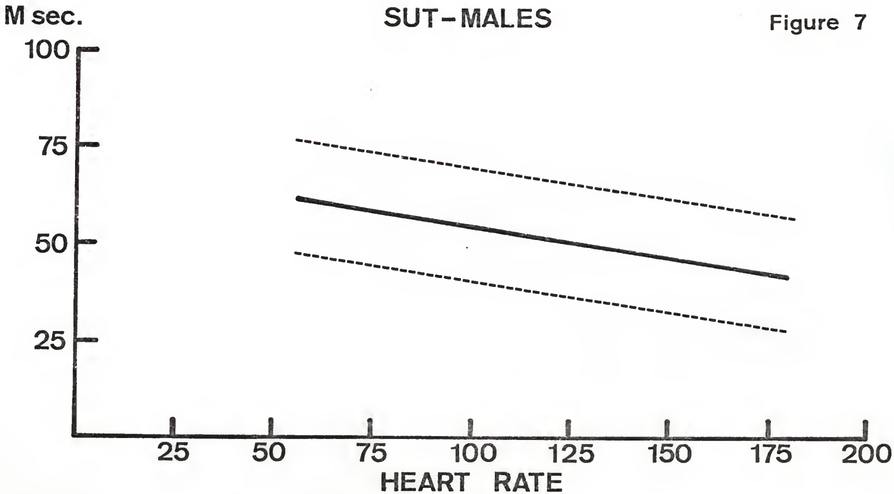

SUT-MALES
M sec.
100
75
50
25
25
50
75
100
125
150
175
200
HEART RATE

Figure 8

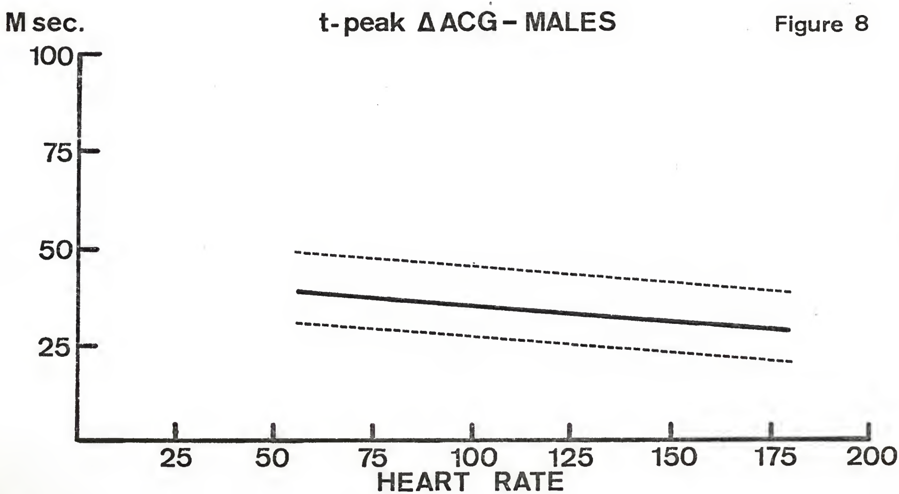

M sec.
t-peak ΔACG – MALES
100
75
50
25
25
50
75
100
125
150
175
200
HEART RATE

Figure 9

PEP/LVET - MALES

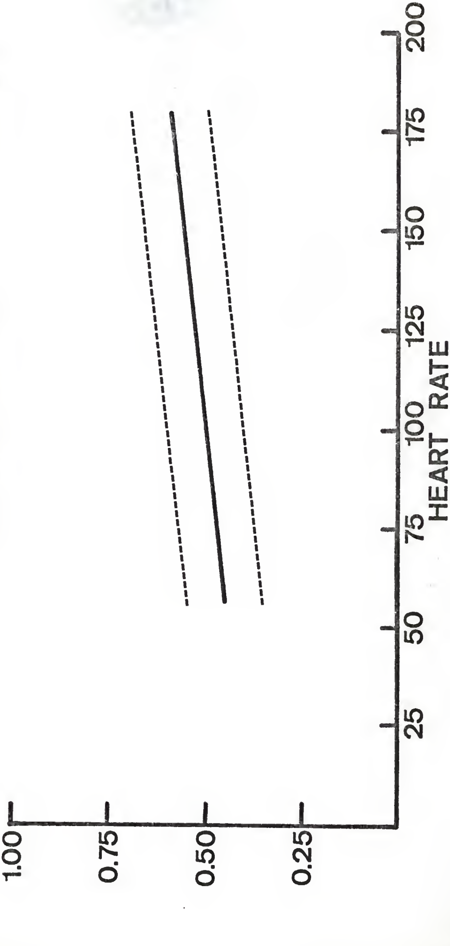


Figure 10

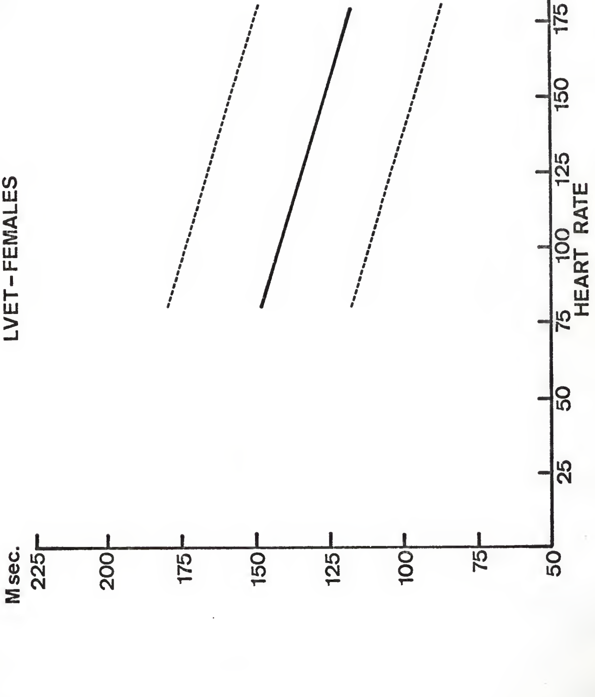

LVET - FEMALES
M sec.
225
200
175
150
125
100
75
50
25
50
75
100
125
150
175
200
HEART RATE

Figure 11

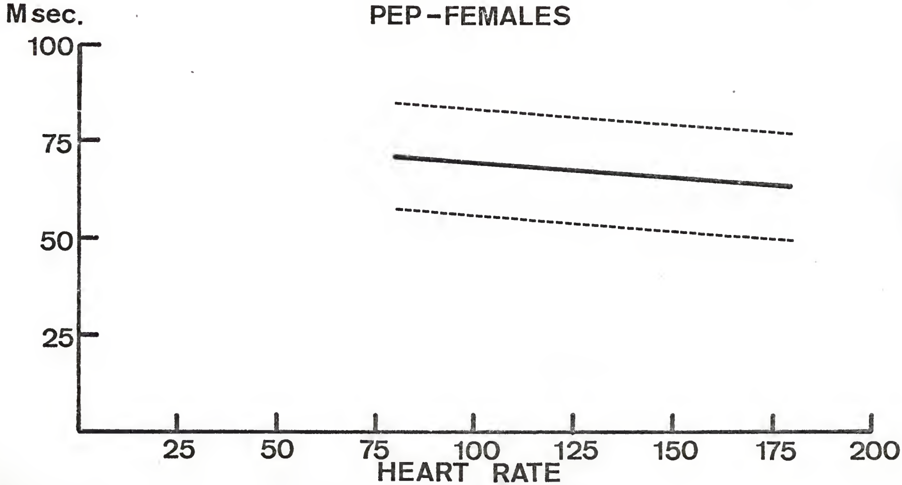
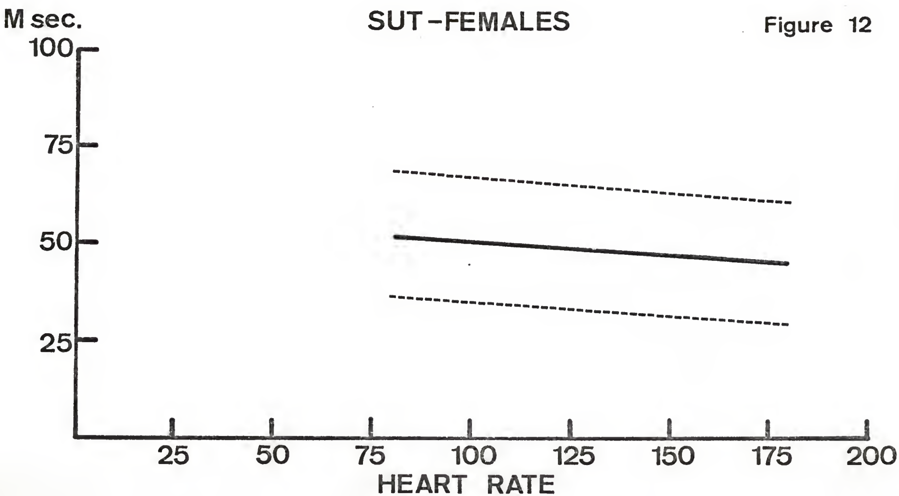
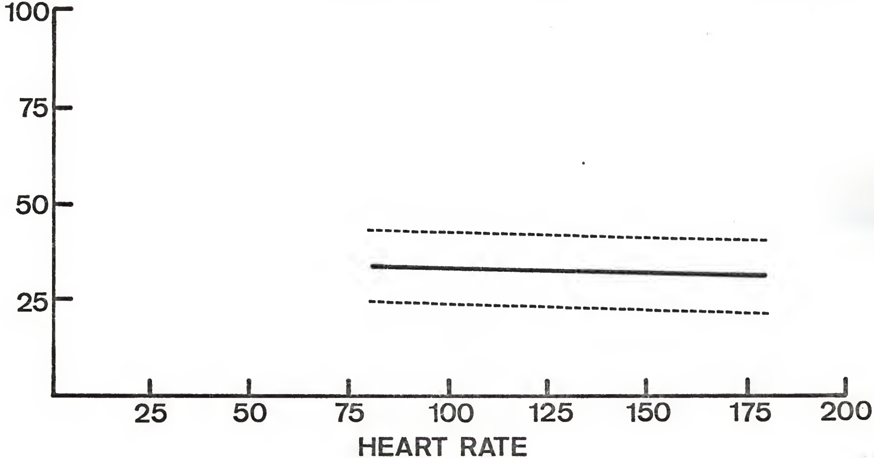

PEP-FEMALES
M sec.
100
75
50
25
25
50
75
100
125
150
175
200
HEART RATE

Figure 12


SUT-FEMALES
M sec.
100
75
50
25
25
50
75
100
125
150
175
200
HEART RATE

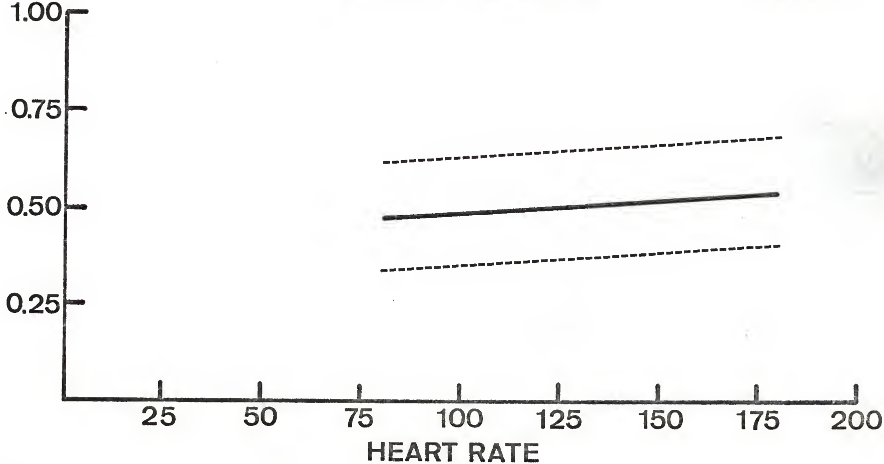
t-peak ΔACG-FEMALES

Figure 13



PEP/LVET FEMALES

Figure 14



PAPER II

SYSTOLIC TIME INTERVALS MEASURED WITH APEXCARDIOGRAPHY IN DOGS WITH MITRAL INSUFFICIENCY

INTRODUCTION

Systolic time interval (STI) measurement, utilizing an apexcardiogram (ACG) has been standardized for the dog.[6] The time intervals for which normal intervals have been established include the pre-ejection period (PEP), systolic upstroke time (SUT), left ventricular ejection time (LVET), time to peak of the first derivative curve of the ACG (t-peak Δ ACG) and a ratio of PEP/LVET. It has been established that all systolic time interval measurements decrease as heart rate increases in the male dog while only the LVET shortens significantly in the female. Regression equations plus standard deviations have been formulated in respect to heart rate for each measurement (Table 1).

It has been established that systolic time intervals show significant change in heart failure in man and that the time intervals tend to normalize on digitalis therapy. It is the purpose of this paper to 1) detail the abnormalities found in STI in dogs with mitral insufficiency in various phases of congestive heart failure and to 2) evaluate their response to digitalis glycosides when indicated.

LITERATURE REVIEW

Weissler[8] has discussed the effects that congestive heart failure have on systolic time intervals in man. He found the PEP to lengthen, the LVET to shorten, and total electro-mechanical systole (QS_2) to remain essentially constant. The lengthened PEP was due to both an increase in the time from QRS initiation to the first heart sound (Q-1) and an increase in the isovolumetric contraction time. The patients studied were afflicted with arteriosclerotic heart disease, hypertensive cardiovascular disease or primary myocardial failure.

Kitchiner, et. al.[5] measured STI in human patients with mitral incompetence. All patients were digitilized at the time of recording. The PEP in each case was normal. The LVET was shortened and related directly to forward stroke index. The greater the degree of regurgitance, the more advanced the heart failure and the shorter the LVET. This was reflected in an increased PEP/LVET ratio.

It is realized that mitral insufficiency is a unique cardiovascular lesion. The afterload against which the ventricle must eject is low because of the low impedance pathway via the regurgitant leak. Due to this fact left ventricular wall tension is not increased above normal limits. Left ventricular pressure is attained via fiber shortening rather than wall tension. Fiber shortening requires little oxygen consumption compared to building wall tension so myocardial failure takes a longer period of time to develop.[2] For this reason a patient can oftentimes live for several years with a mitral valve lesion before decompensating. There is evidence that when congestive heart failure does ensue it is due to the degree of regurgitance[1] and to a depressed inotropic state.[7] However, the depressed inotropic state is masked in most measurements of contractility, including PEP, due to the favorable unloading conditions which occur during early systole.[3] Therefore, refined measurements of contractility, such as Vmax need to be utilized to quantitate the myocardial weakness.

The effects of digitalis on systolic time intervals in patients with congestive heart failure have been studied in man.[9] The patients evaluated had arteriosclerotic, hypertensive, or primary myocardial disease. It was demonstrated that reductions in QS_2 and PEP were the most consistent findings. LVET also shortened but was less consistent. The changes in PEP and LVET correlated significantly with other indices of cardiac function.

The effects of digitalis glycosides on patients with congestive heart failure due to mitral insufficiency can be expected to be similar except for the LVET. In mitral insufficiency, enhancing contractility will reduce the mitral annular dilatation therefore decreasing the mitral regurgitant flow.[1] It may also decrease the left ventricular end systolic volume, resulting in more complete emptying of the chamber. For these reasons the LVET could be expected to increase after digitalis administration.

MATERIALS AND METHODS

A total of thirteen patients were selected for evaluation. Patient selection was based on the presence of a Grade III/VI or greater murmur characteristic of mitral insufficiency and a history of no previous inotropic therapy. Routine analysis of the patient by history, physical examination, radiography, and electrocardiography was performed and the patient placed in a phase of chronic mitral valvular fibrosis as described by Ettinger and Suter.[4]

For purposes of data collection each case was given 1 mg/kg of diazepram[a] intravenously. This produced sufficient sedation to abolish muscular shaking and allow electrode placement. Systolic time interval recordings were taken on an Electronics for medicine DR-8 multichannel recorder at 100 mm./second. The patient was placed in left lateral recumbency. A simultaneous electrocardiogram, apexcardiogram, and first derivative curve of the apexcardiogram were recorded. Immediately thereafter a simultaneous electrocardiogram and phonocardiogram were recorded. Either a high frequency or medium frequency channel on the phonocardiogram was utilized to define the second heart sound, depending on the character of the murmur.

The phases of systole measured are as follows: 1) total electromechanical systole (QS_2) was measured from the Q wave of the electrocardiogram to the first vibration of the second heart sound; 2) The pre-ejection period was measured from the Q wave to the "E" point on the apexcardiogram; 3) the systolic upstroke time (SUT) was measured

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[a]Valium, Roche Laboratories, Nutley, New Jersey.

from the start of the upstroke of the apexcardiogram to the "E" point; and 4) the time to the peak of the first derivative curve of the apexcardiogram (t-peak Δ ACG) was measured from the beginning of the upstroke of the first derivative curve to its peak. Phases of systole that were calculated from the above time intervals were: 1) the left ventricular ejection time, calculated by subtracting PEP from QS_2; and 2) the ratio PEP/LVET (Figures 1, 2, 3).

All measurements were calculated to the nearest 5 msec. Three complexes were measured from each patient and averaged for data analysis.

RESULTS

All measurements were compared to a normal regression equation $\pm$ two standard deviations for each sex and each particular measurement. The time interval was then recorded as within normal limits or abnormal. Results are tabulated in Table 2. An asterisk marks each value that was considered abnormal.

All contractility measurements (PEP, SUT, t-peak Δ ACG) were within normal limits for dogs in Phase I mitral insufficiency. Only one value was considered more abbreviated than normal for LVET in Phase I.

The one case placed in Phase II mitral insufficiency was on furosemide and theophylline therapy at the time of recording. Contractility measurements were normal but LVET and subsequently PEP/LVET were prolonged.

All patients in Phase III possessed normal contractility measurements before therapy. Dogs #112 and #116 progressed to an abnormal PEP following procainamide therapy and returned to normal following digoxin administration. The SUT and t-peak Δ ACG showed variable response with procainamide therapy but each was within normal limits following digoxin. Except for dog #116 each subject possessed a LVET shorter than normal. In dogs given procainamide these values became more abbreviated. Digoxin therapy resulted in moderate prolongation of LVET. The ratio PEP/LVET followed the change in LVET in each case.

DISCUSSION

Systolic time interval measurement is a clinical diagnostic tool useful in determining the presence of heart failure due to contractile deficits or altered ejection. It also is extremely useful in determining response to therapy.

Systolic time intervals have been utilized in human mitral insufficiency patients to determine the severity of the regurgitant leak and determine the severity of phase of congestive heart failure.[5]

Mitral insufficiency is a cardiac defect whereby a percentage of the left ventricular stroke volume is ejected into the left atrium. Ejection fraction (total stroke volume/left ventricular end diastolic volume) may be normal or increased but the forward stroke volume becomes progressively diminished as the mitral valve orifice widens. When a mitral regurgitant orifice is present a percentage of the stroke volume is ejected into the left atrium before the aortic valve opens. The percentage of regurgitance is in linear correlation to the size of the mitral valve lesions. Therefore, ejection of blood takes place prior to the aortic valve opening, during the pre-ejection phase. When the aortic valve does open, blood flows in both directions. Due to these actions the period of ejection or LVET is shortened. The shortening of the LVET is linearly related to the size of the mitral orifice and to the severity of the congestive heart failure.

In the present study, patients in Phase I of mitral regurgitation showed LVET measurements generally within normal limits. One dog did show an abbreviated LVET but the value obtained was borderline. The patient studied in Phase II exhibited a shortened LVET. Patients in

Phase III consistently exhibited abbreviated LVET's. The ejection times shortened further on negative inotropic therapy and lengthened on positive inotropic medication.

Evaluations of contractility measurements (PEP, SUT, t-peak Δ ACG) did not reveal variance from normal in any phase of mitral insufficiency. However, this does not mean that contractility is not affected in mitral insufficiency patients in congestive heart failure. Due to altered loading conditions present in mitral insufficiency and to favorable unloading during the pre-ejection and ejection phases of systole, the depressed inotropic state is masked in many routine criterions for contractility.[3] However, the depressed inotropic state is in linear relationship to the amount of regurgitant flow.[7] Therefore, the phase of congestive heart failure and the amount of inotropic depression should be able to be evaluated through LVET measurement. Unfortunately, response to positive inotropic therapy cannot be unequivocally assessed by a return of abnormal values to normal. PEP measurements, however, do shorten within the normal range and inability to further abbreviate the measurements may signal adequate levels of digitalis.

Negative inotropic therapy resulted in prolongation of the PEP in the two cases studied. Systolic time interval measurement in both patients was extremely valuable in evaluating the myocardial response to procainamide and the subsequent return to normal values following administration of digoxin.

Evaluation of the ratio of PEP/LVET revealed this method of study to correspond to the LVET in each case. Thus, it may be a useful criterion to measure since the normal values are almost identical in the male and female, making it more convenient to evaluate.

SUMMARY

Systolic time interval measurement was undertaken in dogs with mitral insufficiency in Phases I, II, and III of congestive heart failure. Results demonstrated that all values are normal in Phase I with the PEP staying normal and the LVET becoming significantly abbreviated in Phases II and III. Response to positive inotropic therapy in Phases II and III was characterized by a moderate prolongation of the LVET and the PEP shortening. Negative inotropic therapy resulted in prolonged contractility measurements and the LVET becoming shorter.

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TABLE 1

Regression equations obtained for systolic time intervals measured in the dog through the use of an apexcardiogram.

	Male	Females
PEP	96.605 - 0.209 HR	76.087 - 0.073 HR
SUT	70.170 - 0.156 HR	56.938 - 0.063 HR
t-peak ACG	43.477 - 0.079 HR	36.489 - 0.031 HR
LVET	221.864 - 0.671 HR	172.810 - 0.310 HR
PEP/LVET	0.392 - 0.001 HR	0.423 - 0.001 HR

TABLE 2

SYSTOLIC TIME INTERVALS IN DOGS WITH MITRAL INSUFFICIENCY

Sex	No.	Phase	Medication	HR	PEP	LVET	SUT	t-peak	PEP/LVET
M	108	I	None	130	70	120	47	28	.583
M	109	I	None	145	72	133	47	32	.581
M	110	I	None	140	75	110*	52	33	.682*
Fe	111	I	None	155	60	110	43	33	.545
Fe	115	I	None	160	65	125	42	32	.520
Fe	120	I	None	165	60	135	42	28	.444
Fe	102	I	None	140	58	142	42	28	.412
M	118	II	Furosemide; Theophylline	180	65	103*	48	37	.629*
Fe	113a	III	None	200	75	65*	57	33	1.154*
	113b	III	0.24 mg. total Digoxin	200	58	82*	43	18	.716*
	113c	III	0.32 mg. total Digoxin	190	65	75*	53	22	.872*
	113d	III	0.025 mg. b.i.d. Digoxin	180	60	70*	40	23	.857*
Fe	117a	III	12.5 mg. s.i.d. Furosemide	185	78	42*	63	25	1.890*
	117b	III	.12 mg. 48 hours Digomain	200	58	62*	40	20	.949*
M	112a	III PCV's	None	100	82	108*	53	37	.754*
	112b	III	250 mg. t.i.d. Procainamide 40 mg. b.i.d. Furasemide	130	92*	100*	65	45*	.900*
	112c	III		110	70	130	50	37	.540
Fe	116a PAT PVC's	III	None	140	78	137	58	28	.574
	116b	III	125 mg. t.i.d. Procainamide	110	90*	90*	67*	37	1.000*
	116c	III	125 mg. t.i.d. Procainamide .20 mg. 24 hours Digomain	130	70	150	57	28	.467
Fe	121	III	None	200	57	75*	35	22	.733*

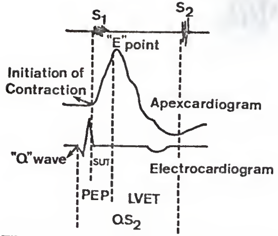

FIGURE 1

Systolic time interval measurements made by utilizing an apexcardiogram.

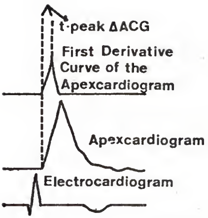

FIGURE 2

The measurement method for t-peak Δ ACG.

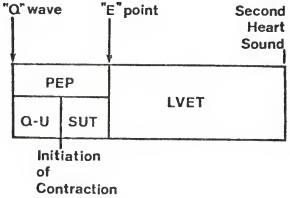

FIGURE 3

Graphic representation of systolic time interval measurements made by utilizing an apexcardiogram.

A P P E N D U M

No.	Case #	Sex	Wt.	Upstroke Initiation	Peak Upstroke
1	847	Fe	9 kg	0	+4
2	847	Fe	9 kg	+10	+6
3	847	Fe	9 kg	0	0 +3
1	1145	M	9 kg	0	0
2	1145	M	9 kg	0	0
3	1145	M	9 kg	0	0
1	891	Fe	13.5 kg	0	0
2	891	Fe	13.5 kg	0	0
3	891	Fe	13.5 kg	0	0
1	813	M	13.5 kg	0	−4
2	813	M	13.5 kg	0	−5
3	813	M	13.5 kg	0	−3
1	231	Fe	18 kg	+8	+9
2	231	Fe	18 kg	+8	+6
3	231	Fe	18 kg	+7	+10 +8
1	782	M	18 kg	0	+4
2	782	M	18 kg	0	+4
3	782	M	18 kg	0	+4 +4
1	883	Fe	22.5 kg	0	+7
2	883	Fe	22.5 kg	0	+5
3	883	Fe	22.5 kg	0	+4 +5
1	858	M	22.5 kg	0	+5
2	858	M	22.5 kg	+5	+4
3	858	M	22.5 kg	−4	0 +3
1	816	Fe	27 kg	+12	+9
2	816	Fe	27 kg	+10	−6
3	816	Fe	27 kg	+9	−4 0
1	863	M	27 kg	0	0
2	863	M	27 kg	0	0
3	863	M	27 kg	0	0 0
				Avg. +1	+3

Sex	No.	HR	PEP	LVET	SUT	t-peak da/dt	PEP/ LVET
M	1	55	85	205	52	35	.415
M	2	65	70	165	57	42	.424
Fe	17	80	75	155	58	35	.484
Fe	18	80	75	148	58	35	.517
M	41b	85	89	172	62	45	.516
M	10	90	87	173	62	38	.501
M	13	90	85	155	62	40	.548
M	24	90	83	167	65	37	.500
Fe	26	90	68	132	55	35	.52
Fe	27	90	65	112	43	32	.582
Fe	29	90	78	138	62	35	.57
Fe	40	90	60	140	40	33	.429
M	43	90	73	162	53	32	.455
M	48	100	77	127	53	35	.598
M	23	105	78	142	58	33	.553
Fe	30	105	68	132	57	37	.494
M	46	110	78	162	62	42	.485
Fe	14	110	73	158	48	30	.469
Fe	19	110	67	153	48	35	.435
M	31	110	83	158	62	38	.532
M	35	110	63	127	48	25	.501
Fe	37	110	70	150	47	37	.467
Fe	45	110	62	137	45	30	.446
Fe	12	120	80	140	62	38	.571
Fe	20	120	80	140	65	45	.571
Fe	9	120	60	120	45	30	.500
M	38	120	58	132	38	32	.444
M	32	125	70	130	55	30	.538
Fe	15	130	65	125	45	28	.520
Fe	21	130	65	120	43	23	.542
Fe	22	130	60	140	40	35	.429
M	36	130	60	150	38	30	.467
M	49	130	60	130	40	27	.462
Fe	33	140	65	155	50	30	.419
M	34	150	65	135	48	32	.481
M	47	150	72	127	48	35	.579
Fe	28	170	73	107	53	33	.69
M	44	175	60	95	40	33	.632
M	11	180	63	107	48	30	.594
Fe	16	180	55	115	42	30	.478

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SYSTOLIC TIME INTERVALS - MEASUREMENT
IN THE DOG THROUGH THE USE OF APEXCARDIOGRAPHY

by

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Systolic time interval (STI) measurement consists of dividing systole into a pre-ejection phase (PEP), systolic upstroke time (SUT), time to peak of the first derivative curve of the apexcardiogram (t-peak ACG) and left ventricular ejection time (LVET). It is utilized as a diagnostic tool in order to assess cardiac function.

Systolic time interval measurement in the dog has previously been recorded only through invasive or surgical techniques. Measurement in man is carried out externally via recording an electrocardiogram, carotid pulse wave form, and phonocardiogram simultaneously. This method cannot be utilized in the dog as the carotid artery is buried deep in cervical tissue and is inaccessible to transducer pickup. An external means of recording systolic time intervals has been evaluated in man. Relationships between apexcardiography and events in the cardiac cycle, notably initiation of contraction and aortic valve opening, have been studied in the dog. A procedure using apexcardiography to delineate systolic time intervals warranted evaluation in the dog.

This study was divided into three phases. Phase I consisted of recording simultaneous left ventricular and aortic pressure curves plus an apexcardiogram in ten normal dogs. Corresponding points were compared in order to judge the ability of the apexcardiographic method utilized to measure the onset of left ventricular contraction and the initiation of ejection. Phase II measures systolic time intervals in forty, unanesthetized, normal dogs. The normal subjects consisted of a wide range of breeds, weights, and heart rates equally divided between males and females. Phase III measured time intervals in dogs in three separate stages of congestive heart failure.

Results of Phase I demonstrated that the technique utilized compared favorably with previously described techniques. Phase II revealed that systolic time intervals vary with heart rate and that there is a marked variance between male and female populations. Normal values, including regression equation and standard deviations were established. Phase III revealed that the left ventricular ejection time shortens with progressively worsening congestive heart failure associated with mitral insufficiency. The pre-ejection period failed to delineate the loss of contractility that is known to accompany mitral insufficiency. Therapeutic administration of digoxin shortened the PEP further and lengthened the ejection time significantly.