# QUANTITATION OF MEASUREMENTS IN AN ISOLATAD HEART PREPARATION

Ergun F. Sabar, M.D. (*)

*Ventricular function curves, tension curves and compliance curves can be drawn as straight lines and represented by regression equations by limiting the related measurements to a range between end-diastolic pressures of* 0-10 *mmHg. This has been done in an isolated heart preparation and the resulting curves were analysed stastically. It has been shown that the slope of these curves reflects the exact physiological significance of its related curve. Therefore, it is concluded that the number representing the slope of a curve can be used as a quantitative measurement to asses changes in myocardial contractility during an experiment or to compare it with other meassurements of the same parameter.*

It is well established that the ventricular function curve (VFC), relating the external stroke work of the heart to the end-diastolic pressure(EDP) or the end-diastolic volume (EDV), is one of the most reliable physiological measurements of myocardial contractility. Although they have been used in many experiments upon the heart on a comparative basis, e.g. to detect any difference in myocardial activity before and after the injection of a certain drug (1,2), no attempt has been made to give them an absolute value, which could in turn be compared with other meassurements of myocardial performance.

The purpose of this paper is to present a statistical analysis of fifty-nine ventricular function curves obtained during experiments on isolated hearts in twenty-nine dogs in an attempt to find a quantitative value for each, which would reflect its exact physiological significance.

---

(*) Chairman, Dept, of Surgery, Ataturk University Medical Faculty Erzurum, Turkey.

## Material and Methods

The preparation used in these experiments. consists of an isolated dog's heart perfused by an extracorporeal circulation. The venous return is from a basket placed in the right atrium and the arterial return is to the aortic arch and the coronary arteries through the left sub-clavian artery. When the descending aorta is cross-clamped and the superior and the inferior vena cavae are tied, the perfusion circuit is reduced to coronary sinus return and coronary perfusion (Fig. 1).

The oxygenation is accomplished by a small disc oxygenator, which is primed from the dog, while the dog's blood volume is expended with about 800 cc. of Rheomacrodex before the bypass is started. The coronary perfusion pressure is monitored through a catheter placed in the aortic arch and the temperature of the perfusate is kept constant.

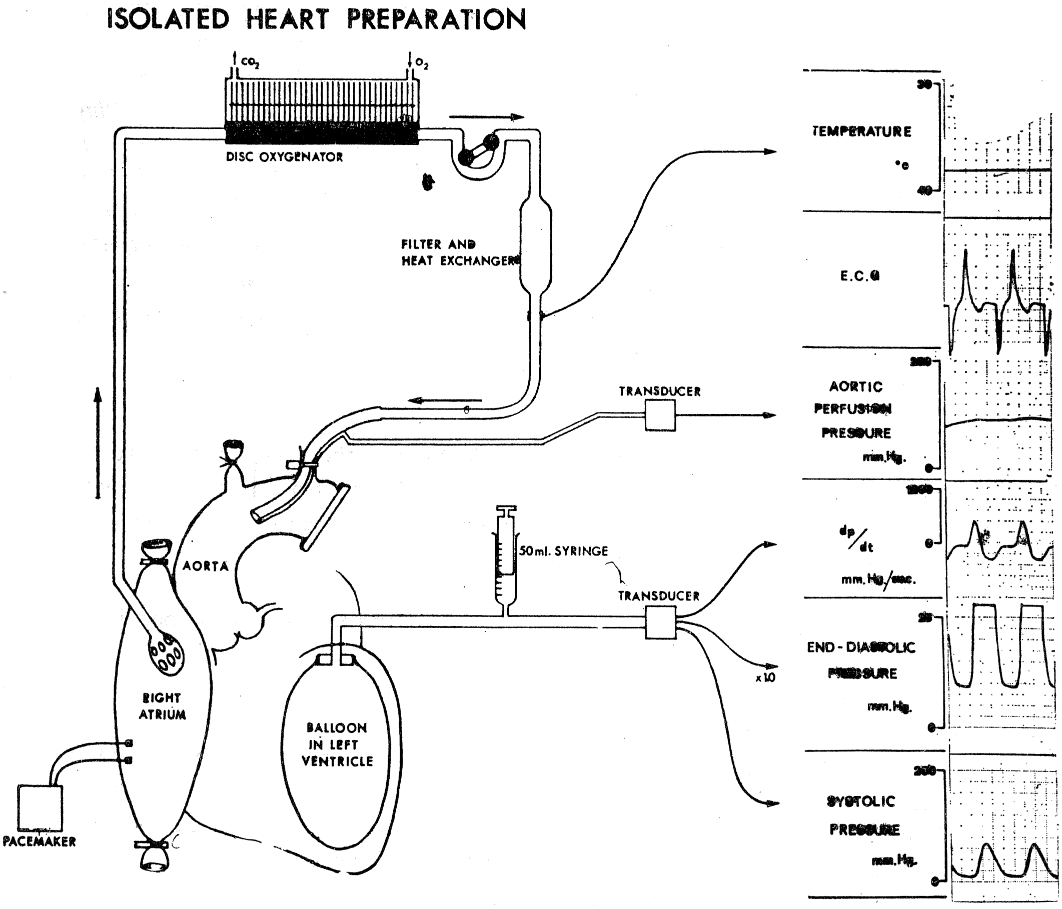
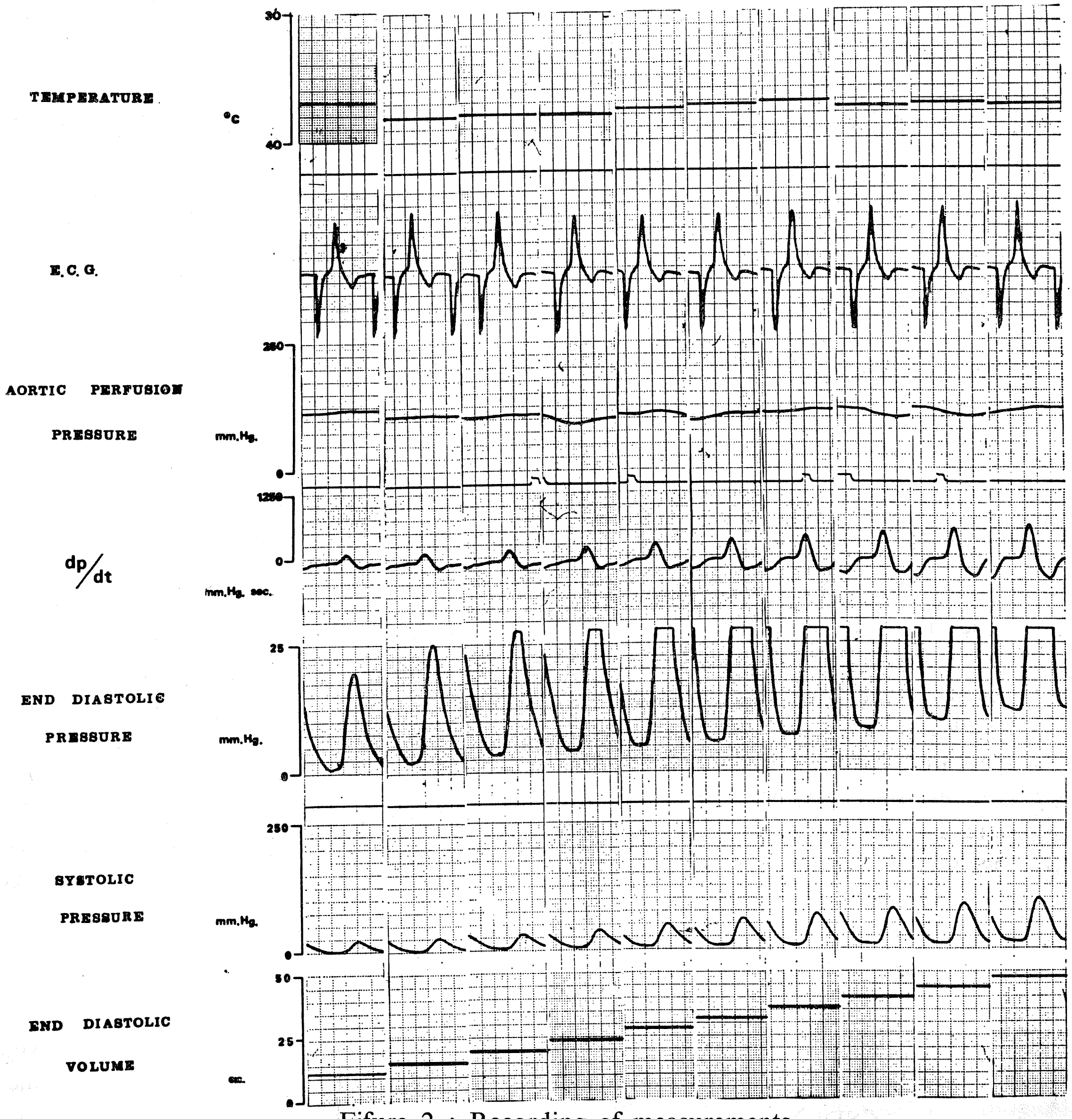


Figure 1 : The experimental preparation

By putting small amounts of fluid in an oversized balloon placed in the left ventricle through the mitral valve, the end-diastolic pressure can be varied. The systolic pressure produced by the contraction corresponding to that end-diastolic pressure and volume can then be measured.

The heart is paced at a constant rate after crushing the atrioventricular node. The temperature of the perfusate, the electrocardiogram, the coronary perfusion pressure, the left ventricular systolic pressure and the left ventricular end-diastolic pressure are recorded on a direct writing oscillograph with a paper



Fifure 2 : Recording of measurements on a direct writing oscillograph speed of 5 cm./sec. The end-diastolic volume corresponding to the different stages of the recording is measured by the amount of fluid introduced into the balloon and recorded also (Fig. 2).

The maximum tension at the endocardial surface of the left ventricular myocardium at its equatorial section, assuming that it has the shape of a sphere (3), is calculated by the formula:

$T=P \pi r^2$ where,

$P=$ left ventricular systolic pressure, and,

$r=$ radius of a sphere containing the same amount of fluid.

The developed pressure is defined as the systolic pressure less the end-diastolic pressure.

The values for maximum tension, developed pressure and the end-diastolic volume are plotted against their corresponding end- diastolic pressures, and three sets of curves are obtained, reflecting the response of the myocardium to various degrees of diastolic preload. These are called respectively, tension curves, ventricular function curves and compliance curves. They are drawn from a regression equation, using the formula (4):

$$Y=r\left(\frac{SD_y}{SD_X}\right)(X-M_X)+M_y \text{ , or,}$$

$$X=r\left(\frac{SD_X}{SD_y}\right)(Y - M_y) + M_X$$

where, $SD_X$=standart deviation of x,

$SD_y$=Standart deviation of Y

$M_X$=mean of x,

$M_y$=mean of y,

r=correlation coefficient Pearson r, which is calculated from the formula:

$$r=\frac{n(\sum XY)-(\sum X)(\sum Y)}{\sqrt{[n(\sum X^2)-(\sum X)^2][n(\sum Y^2)-(\sum Y)^2]}}$$

where, n = number of observations,

$(\sum XY)$=sum of XY,

$(\sum X)^2$=sum of X squared,

$(\sum X^2)$=sum of squared X.

All correlations between slopes of different curves are calculated from the formula for Pearson r correlation coefficient.

## Results and Discussion

A function curve, whether it is plotted as tension, developed pressure or external work against end-diastolic pressure, is S shaped. The initial portion of the curve where the end-diastolic pressure is below zero is relatively flat, reflecting small elevations in output for comparatively large increases in end-diastolic pressure. This is due to an increase in end-diastolic residual volume. The flattening of the curve re-occurs once the end-diastolic pressure exceeds 12 mmHg. This is due to the incapacity of the myocardium to cope with the very high inflow volumes. The physiologically important part of the curve, which is between the end-diastolic pressure of 0-12 mmHg. is a relatively steep straight line. Therefore, all curves obtained during these experiments are expressed as straight lines and are drawn only between end-diastolic pressures of 0 and 10 mmHg.

Ventricular function curves are expressed as the regression of developed pressure on the end-diastolic pressure and the slope given for each curve reflects this relationship-the bigger the number, the steeper the slope.

When an increase in contractility occurs the ventricular function curve becomes steeper and moves higher and to the left of the previous one, reflecting a higher developed pressure generated from the same or lower end-diastolic pressure. The reverse happens when a decrease in contractility occurs. Therefore, the family of ventricular function curves obtained from the same heart under different conditions or from different hearts performing at different states of contractility displays a fan-like arrangement. The slopes of these curves therefore should not only reflect their steepness but also their levels, because their steepness will increase as the slopes move higher and to the left. It is therefore impossible for curves corresponding to different levels of developed pressures to have the same slopes.

To check this assumption we have plotted the slopes of different ventricular function curves against their respective developed pressures from an end-diastolic pressure of 10 mmHg. because this is the level where the curves diverge maximally, while still being straight lines (Fig. 3). The correlation is highly sinificant (Pearson r=0.849, p= 0.004) and we can conclude that the number obtained as the slope of the ventricular function curve reflects confidently not only the steepness but also the level, namely the complete physiological significance of that curve -the higher the number, the higher and steeper the curve and the better the performance of the myocardium.

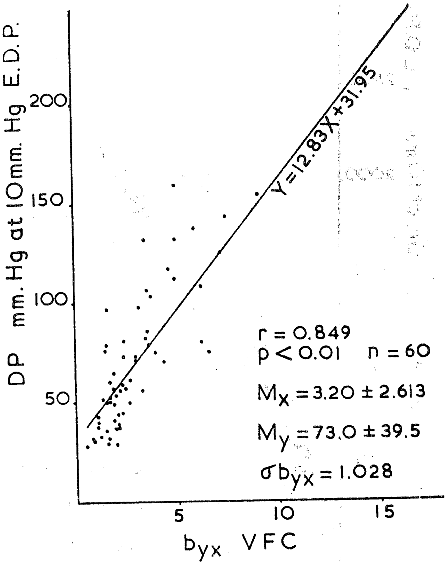


Figure 3 : Correlation between the slopes of the ventricular function curves and their developed pressures

Tension curves are plotted as maximum tension in grams against end-diastolic pressure and expressed as the regression of tension upon pressure. In Fig. 4 the slopes of these curves are plotted against the maximum tensions at an end-diastolic pressure of 10 mmHg. It shows a highly significant correlation (Pearson r=0.781, p=0.004) and proves that they also display a fan-like arrangement and that the slope represents their total physiological significance.

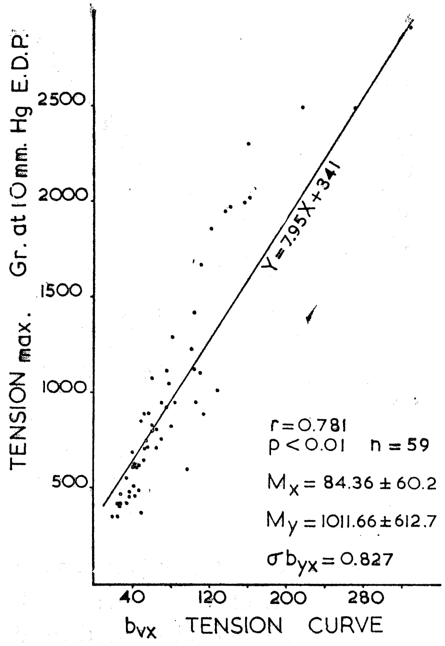


Figure 4 : Correlation between the slopes of tension curves and their developed tensions

The measurement of tension is a step further towards the isolated muscle strip preparation and takes into account both the developed pressure, irrespective of the end-diastolic pressure, and the volume and the radius of the ventricle. The tension curves in this preparation show its relation to initial fibre length. Fig. 5 shows the correlation between the slopes of ventricular function curves and the slopes of tension curves which is highly significant (Pearson $r=0.887$, $p=0.002$) and proves that both are measurements of the same parameter although using different components.

Compliance curves are presented as the regression of end-diastolic pressure upon end -diastolic volume and their slope represents only the steepness of the curves, their level depending upon the size of the heart.

The ventricular function curve drifts higher and to the left of the previous one if an increase in myocardial contractility occurs. This shows that an increased amount of work is done for the same end-diastolic pressure. We have shown that also for a given end-diastolic volume, which can be kept constant in this preparation, the end-diastolic pressure is lowered by this increase in contractility. Therefore,

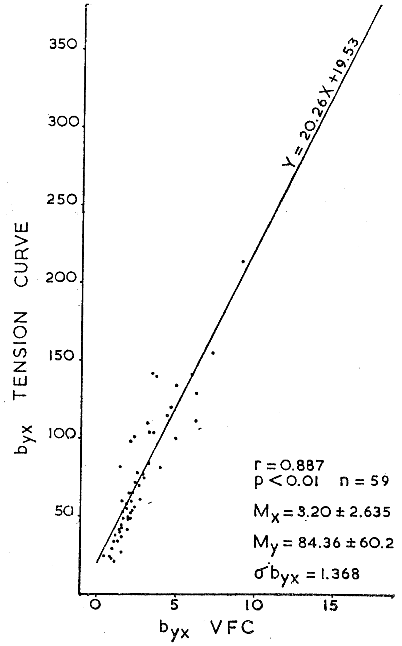


Figure 5 : Correlation between the slopes of the ventricular function curves and the slopes of tension curves

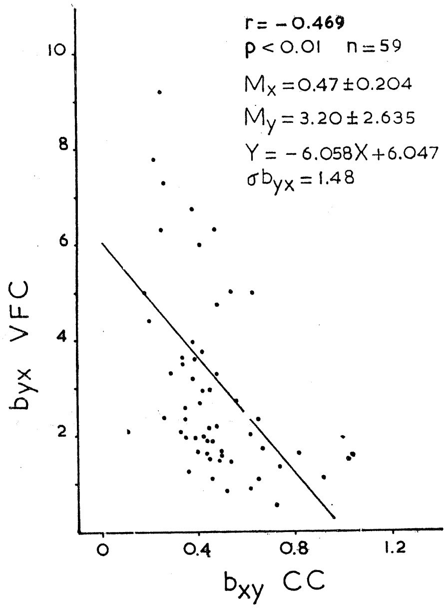


Figure 6 : Correlation between the slopes of ventricular function curves and the slopes of of compiance curves

an increase in diastolic compliance of the ventricle must have occured, which in turn means that the heart has had to relax more completely in order to perform at a higher level. The calculated correlation between the slopes of compliance curves and the slopes of ventricular function curves on 59 measurements were found to be highly significant (Pearson r=0.469, p= 0.008) (Fig. 6), indicating that the higher the myocardial contractility, the more compliant the ventricle is, or in other words, the myocardium requires good relaxation to be able to perform with a good level of contractility.

## Conclusions

By limiting the measurements of developed pressure, tension and end-diastolic volume to a range between end-diastolic pressures of 0-10 mmHg, it is possible to draw ventricular function curves, tension curves and compliance curves as straight lines and express them by regression equations. The slope of the regression equation is shown to be representitive of the physiological significance of its curve. This provides a quantitative value for each curve, instead of merely stating that one is better or worse compared to another one. This is valuable for quantitating changes in myocardial function during the course of an experiment and in comparing physiological evaluations with other measurements of myocardial activity.

## ÖZET

İzole edilmiş bir kalp preparatından elde edilmiş olan 59 vantrikül fonksiyon eğrisi, 0-10 mmHg. diastol sonu basınçları arası ölçülerek, regresyon denklemleri ile ifade edilmiştir. Bu şekilde elde edilen eğrinin meyilini gösteren rakkamın, o eğrinin fizyolojik vasıflarını da doğru olarak aksettirdiği ispat edilmiştir. Bu şekilde, vantrikül fonksiyon eğrilerinin kıymetini rakamlarla ifade edebilmek mümkün olmuş ve vantriküllerin kontraktilitesini başka ölçülerle mukayese imkânı sağlayan kantitatif bir ölçü elde edilebilmiştir.

## References

1- Braunwald, E., Bloodwell, R. D., Goldberg, L.I. and Morrow, A. G.: Studies on Digitalis IV. Observations in man on the effects of Digitalis preparations on the contractility of the non-failing heart and on total vascular resistance.
J. Clin. Invest. **40:** 52, 1961

2- Cotten, M. deV. and Stopp, P,E.: Action of digitalis on the non-failing heart of the dog.
Amer. J. Physiol. **192**: 114, 1958

3- Covell, J.W., Ross, J.Jr., Taylor, R., Sonnenblick, E.H. and Braunwald, E: Effects of increasing frequency of contraction on the force-velocity relation of left ventricle.
Cardiovasc. Res. **1**: 2, 1967

4- Guilford, J.P.:

Fundamental statistics in psychology and education.
Mc Graw - Hill Book Company, Inc. 1956