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Echocardiographic assessment of cardiac function in the rabbit : a preliminary study

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Summary — A technique for obtaining M-mode echocardiograms in sedated adult rabbits of both sexes, New Zealand and California breeds, is described. Despite the fact that with rabbits there are certain technical difficulties in obtaining the M-mode echocardiograms, our preliminary results indicate that the following measurements could be the most useful and accurate : 1) left ventricular systolic time intervals; 2) right ventricular systolic time intervals; 3) right ventricular end-diastolic dimension; 4) left atrial internal dimension; 5) left ventricular end-diastolic and end-systolic dimensions; 6) systolic slope of the interventricular septum; 7) mid-diastolic partial closure of the mitral valve (EF slope); and 8) systolic slope of the posterior aortic wall.

echocardiography — cardiac function — rabbit

Résumé — *Evaluation de la fonction cardiaque par échocardiographie chez le lapin : une étude préliminaire. La technique décrite permet d'obtenir des échocardiogrammes en mode-TM chez les lapins adultes tranquilisés de race New Zealand et California. Bien qu'il y ait, chez le lapin, certaines difficultés techniques pour l'obtention de ces enregistrements, nos résultats préliminaires indiquent que les mesures suivantes pourraient être très utiles et précises : 1) intervalles de temps systoliques du ventricule gauche; 2) intervalles de temps systoliques du ventricule droit; 3) dimension fin de diastole du ventricule droit; 4) dimension interne de l'atrium gauche; 5) dimensions fin de diastole et fin de systole du ventricule gauche; 6) pente systolique du septum interventriculaire; 7) pente de fermeture meso-diastolique de la valvule mitrale (pente EF); 8) pente systolique de la paroi aortique postérieure.*

échocardiographie — fonction cardiaque — lapin

Introduction

The rabbit has been widely used in cardiovascular research in both chronic

and acute experiments (Ruckebusch, 1977; Ewald and Greg, 1983; Fox, 1984; Gross, 1985).

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There are numerous reports on measurements and parameters obtained using non-invasive techniques such as electrocardiography (Hamlin and Smith, 1960; Ruckebusch, 1977; Fox, 1984; Lolov and Lolov, 1985), vectorcardiography (Lolov and Lolov, 1983; Lolov and Lolov, 1984), radiology (Gibbs and Hinton, 1981), blood pressure (Ruckebusch, 1977; Fox, 1984; Gross, 1985a) and systolic time intervals measured on the carotidogram (Long *et al.*, 1982; Long *et al.*, 1983), that have been performed to evaluate the cardiac function of the rabbit in both normal and diverse pathological states.

Despite the fact that M-mode echocardiography has been, for some time, a common non-invasive technique which is highly accurate in evaluating cardiac function clinically and experimentally (Shah and Gramiak, 1974; Hamrath and Schlüter, 1983; Gross, 1985b), it has not yet been used successfully in the rabbit.

The aim of our report is to describe a method for obtaining M-mode echocardiograms in sedated rabbits, which could be extremely useful in evaluating cardiac function under different conditions in these animals.

Materials and Methods

Twenty New Zealand and California strain, male and female rabbits between 2 and 4 kg from the Centro Experimental Agrícola-Ganadero of la Diputación de Cadiz, were used to develop the technique.

The echocardiograms were obtained using a 5 MHz non-focused transducer connected to a Smith-Kline Echoline 20A System with a Cambridge Honeywell recorder.

The 20 rabbits were sedated with intramuscular ketamine (35 mg/kg) and placed supine on a surgical table. Electrocardiographic leads were attached to each extremity

with subcutaneous needles. After this procedure the ventral area of the chest was shaved.

After identification of the apical impulse, the transducer was placed on the same intercostal space, perpendicular to the chest wall. Tilting the transducer, the mitral valve echos were localized (Fig. 1). From this "starting point" of reference, standard views as described by Feigenbaum (1976) at the apex, left atrioventricular valve (mitral), anterior mitral leaflet, aortic root, right atrioventricular valve (tricuspid) and pulmonic valve were recorded (Fig. 2).

At the beginning of the study, a needle following the same path of the ultrasonic beam was inserted into the heart of 3 rabbits, to record the wave pressure of the ventricles in order to assure that these were the expected chambers.

Results

The 4 standard views of the heart have been recorded by M-mode echocardiographic study and have enabled us to obtain the measurements (Fig. 2) described below.

Position 1

This is an echocardiographic cut of the left ventricle at the level of the posterior papillary muscle or its environments. A portion of the right ventricular chamber is crossed by the ultrasonic beam. Figure 3 demonstrates how to obtain the left ventricular interval diameters used in the evaluation of cardiac function.

Position 2

This view is defined by the presence of the distinct M-like shape of the anterior mitral leaflet and the w-like shape of the

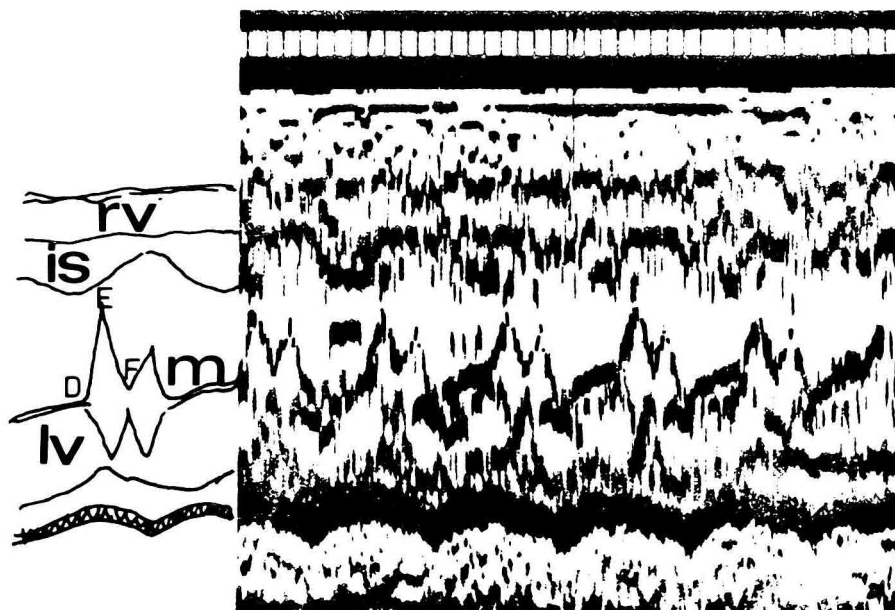


Fig. 1. Echocardiographic view of the mitral valve. This echocardiographic cut corresponds to position 2 in the text. Mitral valve (m) is the first structure to be identified as a 'starting point'. On the left of the figure the most important structures of the view are drawn in schematic form : right ventricle (rv), interventricular septum (is) and left ventricular chamber (lv). Inside the left ventricle the M-like image of the anterior mitral leaflet and the W-like image of the posterior leaflet are apparent. Points D (beginning of the valve opening), E (the fully open position) and F (the semiclosed position of the valve) are clearly identified.

posterior one, inside the left ventricular chamber. Points E, F and D are easily identified in Figure 1 as well as the limits of the right ventricle, interventricular septum and posterior wall of the left ventricle. Interval ventricular diameters can also be measured in this position.

Position 3

The structures cut by the ultrasonic beam in this position are : right ventricle, interventricular septum (near the aortic root), anterior mitral leaflet, and left atrium (near mitral ring). In Figure 4 a pass from left ventricle to aortic root is shown in an attempt to explain the echocardiographic

interrelations between interventricular septum, anterior mitral leaflet and aortic root.

Position 4

In this situation the right ventricle outflow tract, aortic valve and left atrium are crossed by the ultrasonic beam. The opening and closing of the aortic valve cusps can be easily identified on the echograms making it possible to measure left ventricular systolic time intervals (Fig. 5).

Tricuspid valve

This valve could be reached moving the ultrasonic beam from its departure

position (mitral valve) to the right side of the thorax. In this view, the anterior tricuspid leaflet, right atrium, interatrial septum and left atrium were recorded (Fig. 6).

Pulmonary valve

Starting from position 4, it was possible to register the pulmonary echogram moving the echo-beam slightly to the left. In most cases, only the posterior cusp of the pulmonary valve could be recorded as is the case in humans (Fig. 7).

Discussion

The advantages of the rabbit as a cardiovascular research subject have been recognized by numerous authors (Ruckebusch, 1977; Ewald and Greg, 1983; Fox, 1984; Gross, 1985a). The main advantages are : low cost, high rate of reproduction and easy management. In addition, the rabbit has certain characteristics which make it a useful cardiovascular research subject, such as, the possibility of using standard recording

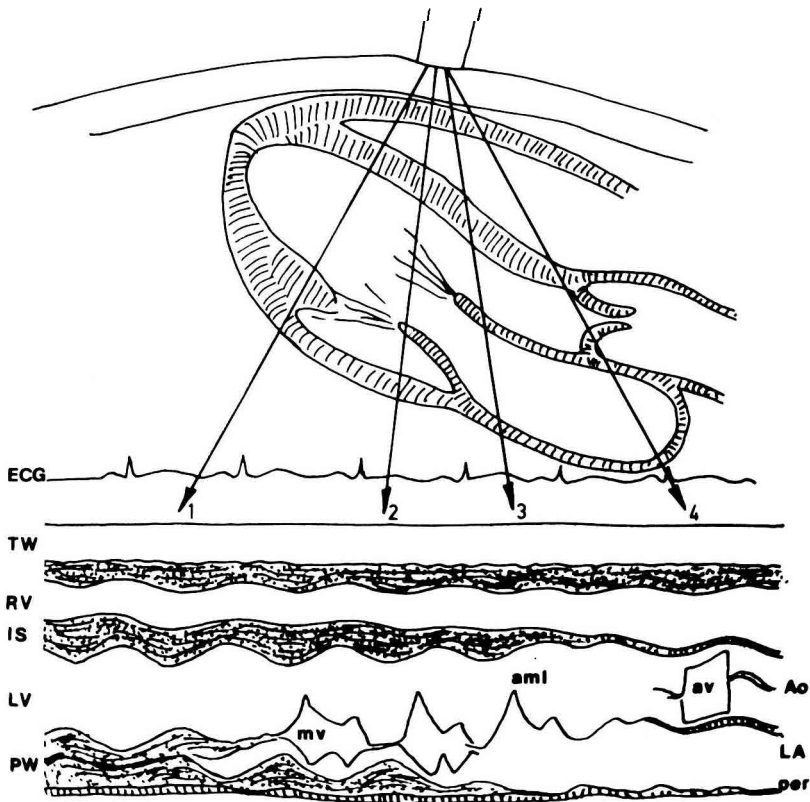


Fig. 2. The 4 basic echocardiographic cuts. This scheme modified from Feigenbaum (1976), shows the 4 basic positions described in the text. The upper part of the figure is a drawing of a long axis cut of the rabbit heart showing those structures that participate in each cut. The lower part of the figure is a schematic echogram containing the 4 basic views. Abbreviations : ECG : electrocardiogram; TW : thoracic wall; RV : right ventricle; LV : left ventricle; IS : interventricular septum; PW : posterior wall; mv : mitral valve; aml : anterior mitral leaflet; av : aortic valve; Ao : aorta; LA : left atrium; per : pericardium.

equipment (Ruckebusch, 1977; Lolov and Lolov, 1983, 1984, 1985); easy approach to arterial and venous system (Long *et al.*, 1982, 1983; Wingerd, 1985); relatively large heart size in relation to thoracic volume (Gibbs and Hinton, 1981) and human-like myocardial responses after administration of certain cardiotoxic drugs (Jaenke, 1974, 1976; Long *et al.*, 1982, 1983).

Two forms of assessing cardiac involvement in the rabbit under different pathological states have traditionally been used. First, acute or chronic studies with euthanasia of the animals and subsequent postmortem histopathological and morphological studies, despite their accuracy, are very costly, require a large series of animals and are highly time

consuming. Second, chronic studies using non-invasive techniques are inexpensive and need few animals but have the main disadvantages of low accuracy and low sensitivity in the early detection of the impaired cardiac function.

M-mode echocardiography has been used in humans and dogs as an excellent method for the evaluation of cardiac function (Shah and Gramiak, 1974; Feigenbaum, 1981; Hamrath and Schlüter, 1983; Gross, 1985b) but to date it has not been adapted to the rabbit model (Long *et al.*, 1982, 1983; Fox, 1984; Gross, 1985a and b). In our opinion, this could be due to technical problems resulting from the special situation of the thorax and heart in rabbits, and from the difficulty in finding some

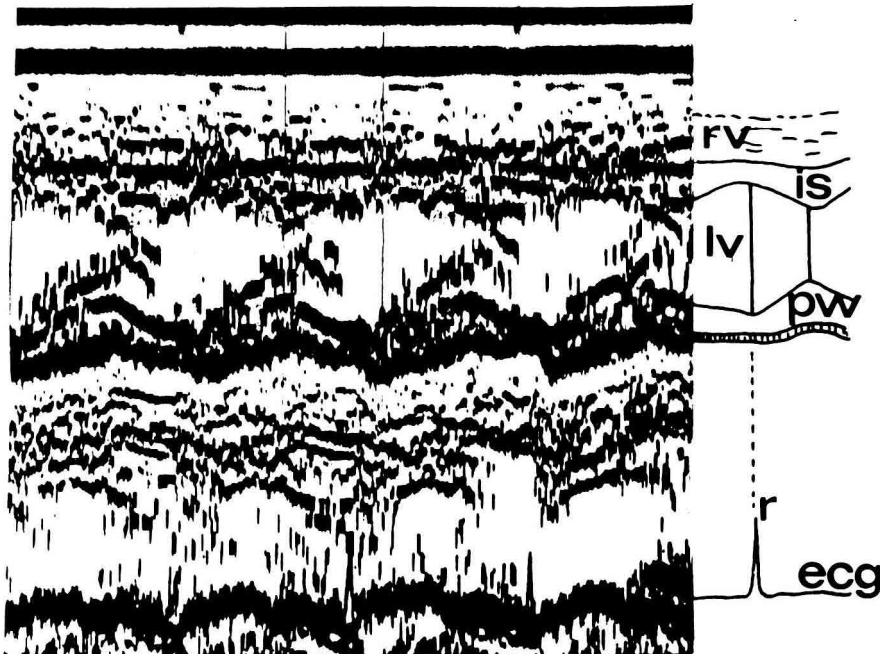


Fig. 3. Echocardiographic view of both ventricles (position 1). The left ventricular chamber (lv) clearly shows the characteristic systolic/diastolic motion between the interventricular septum (is) and posterior wall (pw). End-systolic and end-diastolic dimensions can be easily obtained: end-diastolic, coincident with the r peak of the ECG; and end-systolic between the nearest points of the septum and posterior wall in systole.

sedative drugs which do not have deleterious cardiovascular effects (Fox, 1984; Gross, 1985a).

Ketamine (35 mg/kg) provides a good sedative state for 40 min in the rabbit, with a minimum of respiratory and blood pressure depression (Sanford and Colby, 1980; Blake *et al.*, 1982). Using adequate neonate transducers and with little experience, the anatomical difficulty of the rabbit can be overcome.

The standard echo-views described by Feigenbaum (1976) were obtained in all 20 white rabbits, although some structures were more difficult to obtain than others. For instance, it was very difficult to record the aortic cusps throughout systole, probably due to their thin consistency; however, their point of opening and closing could be easily identified, thus enabling the measurement of left ventricular systolic time intervals. In

our study, the pulmonary valve was the most time consuming structure to record.

Useful information was obtained from the echocardiographic images described herein for evaluating cardiac function in rabbits, applying the measurements described by most authors (Shah and Gramiak, 1974; Feigenbaum, 1976; Rogers *et al.*, 1979; Shah, 1979; Feigenbaum, 1981).

Admittedly, some difficulties were encountered in obtaining certain concrete structures in the rabbit using M-mode echocardiography as stated before. However, this is not sufficient reason to consider this technique as less valuable. As we have demonstrated, it is possible to obtain a great deal of information about cardiac function using the measurements (Fig. 8) described below.

Systolic time intervals of the left ventricle and the pre-ejection period

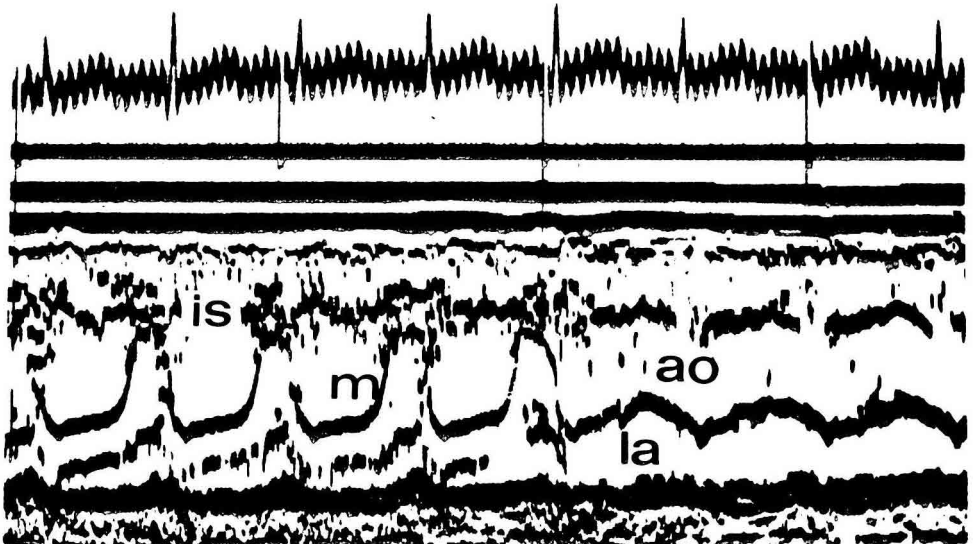


Fig. 4. Echocardiographic view of anterior mitral leaflet (position 3). The right and left ventricular cavities separated by interventricular septum (is) can be clearly identified. The mitral valve (m) can be seen moving inside the left ventricle. To the right of the figure the interrelations between these structures and the aortic root (ao) and left atrium (la) are shown.

(PEP) and ejection period (EP) are dependent upon the contractile state of the left ventricle as well as upon the other variables, such as pre- and afterload (Wayne, 1973; Lewis, 1985). These parameters measured them in position 4 (Fig. 6).

Systolic time intervals of the right ventricle can be measured in the pulmonary valve position.

Right ventricular end-diastolic dimension and left atrial interval dimension give additional information about cardiac function. They may be enlarged only under significant contractile depression (Demaria *et al.*, 1984). The

former parameter was obtained from positions 1 and 2, and the latter from position 4.

Left ventricular end-diastolic dimension and left ventricular end-systolic dimension are the previously explained diameters of the left ventricle. Useful cardiac function data obtained from these parameters have been previously reported in man and some experimental models (Shah and Gramiak, 1974; Feigenbaum, 1976; Rogers *et al.*, 1979; Feigenbaum, 1981; Hamrath and Schlüter, 1983; Demaria *et al.*, 1984; Fulkerson, 1985; Gross, 1985b). But the most direct, yet simple information that can be obtained from the echo, is

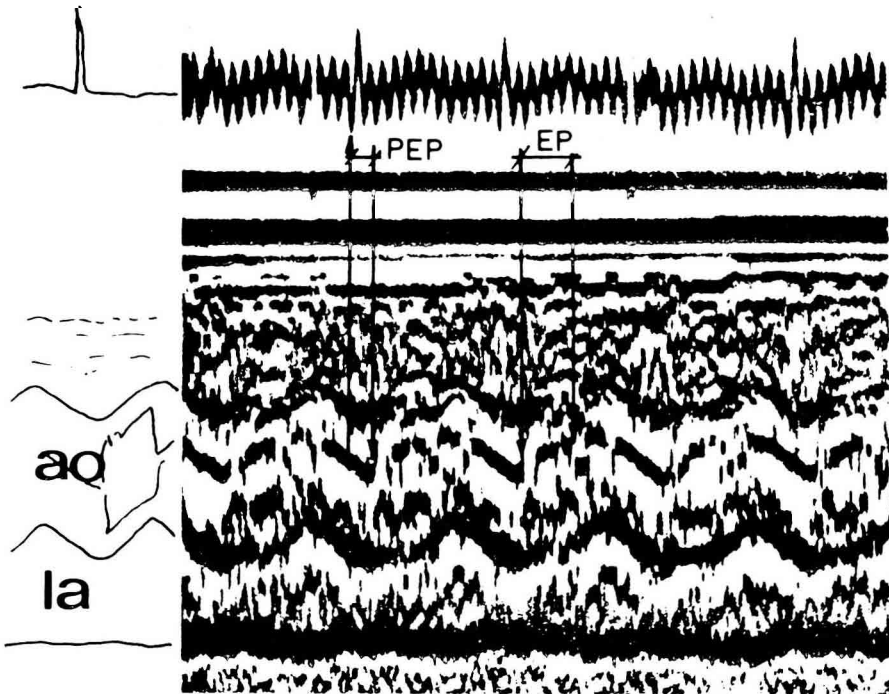


Fig. 5. Echocardiographic cut of aortic root and left atrium (position 4). In this echogram, the structures represented are : right ventricle, aortic root (ao) showing its valvular cusps, and left atrium (la). Both valvular cusps come together in one line of echos in the middle of the aorta during diastolic filling in the opposite direction during systolic ejection. The systolic time intervals of the left ventricle can be measured without difficulty on the figure. Pre-ejection period (PEP) is measured from the onset of the QRS complex to the opening point of the cusps. Ejection period (EP) represents the time during which the valve is open.



Fig. 6. Echocardiographic view of the tricuspid valve. The M-like image of the tricuspid valve (tv) is clearly identified. Beneath it, the echos from the interatrial septum (ias) separate both atrial cavities (la and ra).

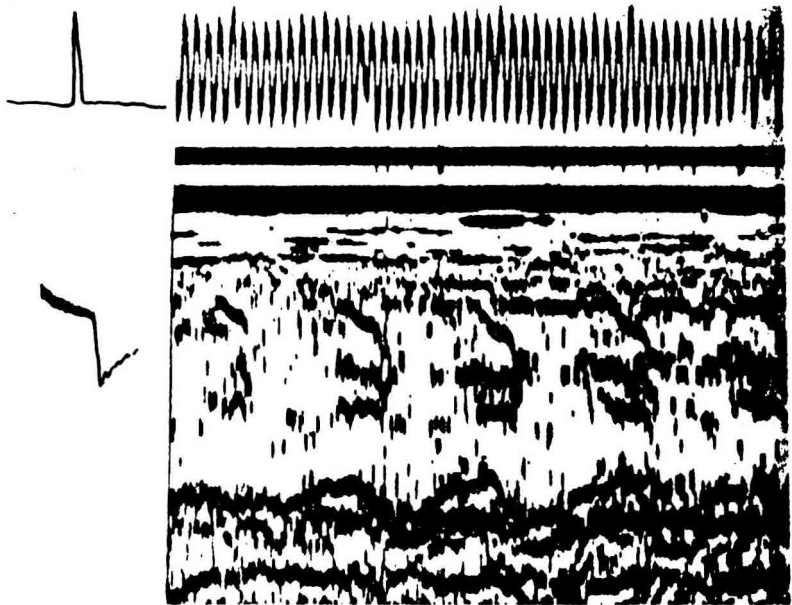


Fig. 7. Echocardiographic view of the pulmonary valve. It is only possible to obtain the echos from the posterior cusp. This condition leads to the characteristic shape shown in the figure. In most cases, however, these echograms allow measurement of the pre-ejection period of the right ventricle.

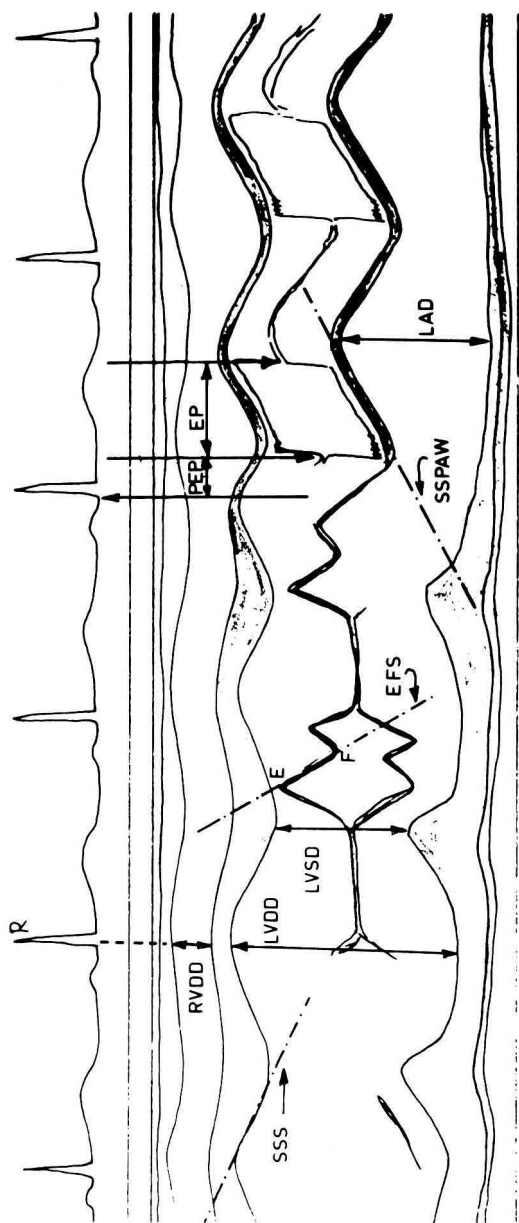


Fig. 8. This diagram summarizes all the measurements that can be made in the echocardiographic evaluation of the cardiac function. Abbreviations : **SSS** : systolic slope of the septum; **LVDD** : left ventricular end-diastolic dimension; **LVSD** : left ventricular end-systolic dimension; **RVDD** : right ventricular end-diastolic dimension; **LAD** : left atrial interval dimension; **EF slope** : early diastolic posterior motion of mitral valve; **SSPAW** : systolic slope of the posterior aortic wall; **PEP** : pre-ejection period; **EP** : ejection period.

fractional shortening (= LVDD-LVSD/LVDD). These can be measured in positions 1 and 2.

Systolic slope of the septum indicates the mean velocity of the systolic posterior movement of the interventricular septum on the left ventricular side (inferior side in the echograms in positions 1 and 2). In the absence of segmentary changes in left ventricular contractility, it can be extrapolated to the total contractility.

Early diastolic posterior motion of mitral valve, or EF slope, represents the rate of left ventricular filling or left atrial emptying and it is therefore used as an important indicator of flow across the mitral valve and mitral valve function. It can be measured in positions 2 and 3.

Systolic slope of the posterior aortic wall indicates the mean velocity of the systolic anterior movement of the aortic root, and represents the rate of left ventricular emptying. This was determined in position 4.

We are currently working on a large series of normal white rabbits in order to establish the normal echocardiographic values and to improve the technique for assessing the cardiac function more accurately.

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