ASSESSMENT OF LEFT VENTRICULAR FUNCTION IN PATIENTS ON RENAL DIALYSIS AND AFTER TRANSPLANTATION ECHO DOPPLER CARDIOGRAM STUDY

THESIS

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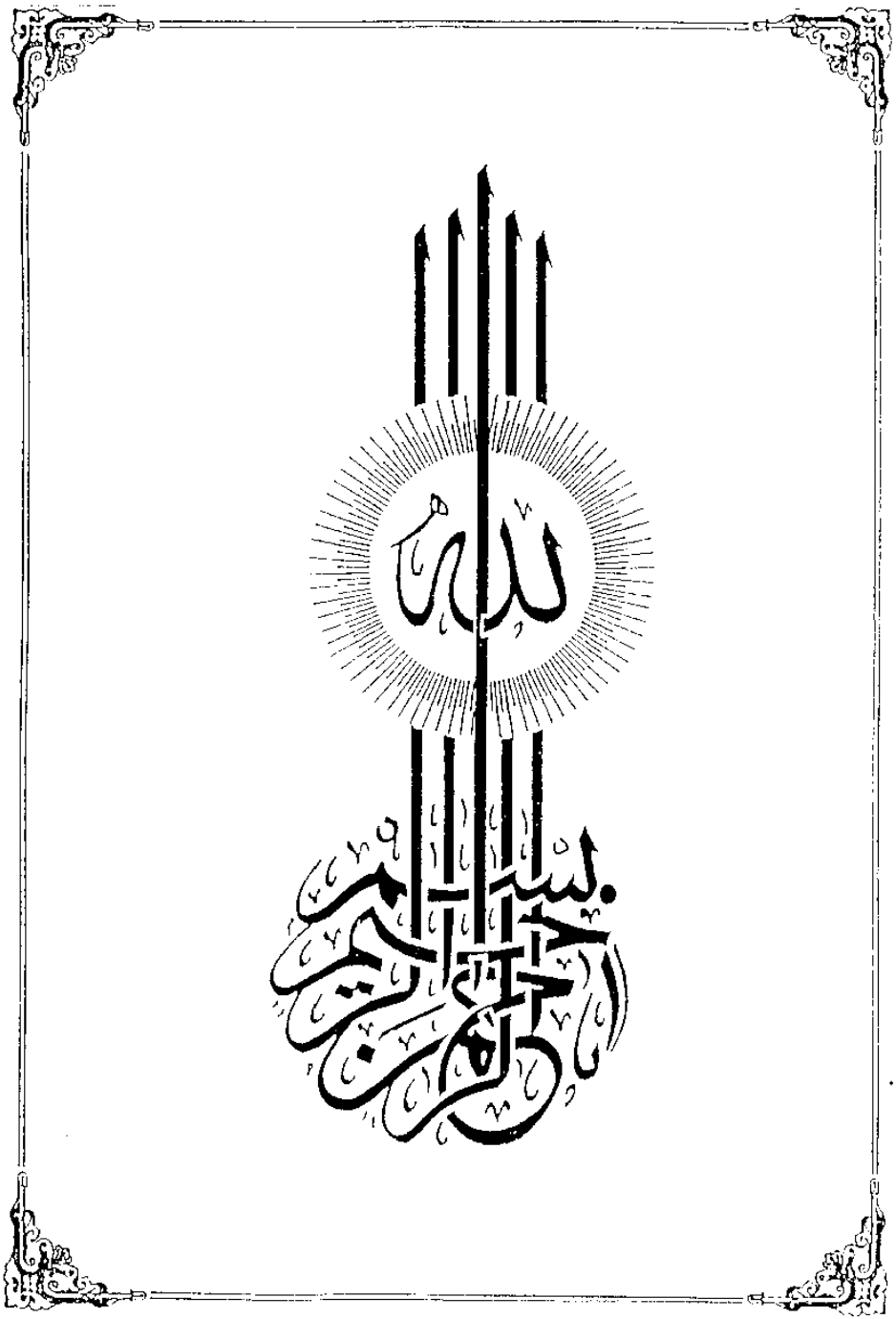

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INTRODUCTION

The subject of cardiac affection by chronic renal failure as well as by different modes of renal replacement therapy, is an important one. Cardiac death is a principal cause of death in such patients (Ritz, 1978). Numbers of renal failure patients are enormously increasing in our country, there is also a growing success rate of kidney transplantation in Egypt. This work was introduced with the impetus to help throw more light on effects of different modes of renal replacement therapy-commonly in use in our country- on the heart. Inspite of the fact that heart affection in uremia was known as early as the beginning of last century (Van-Stone, 1983), yet, many facts are still desputable and remain unclear. Even the broad lines of cardiac affection in uremia are still a matter of controversy; for example, uremic cardiomyopathy is still a desputable topic and its existance is questionable; the role of diastolic malfunction in uremic heart dysfunction and its implict on symptomatology; the effect of different risk factors, which are enormous, on the heart in uremia, ... etc.

This work is divided into four main sections; a review of the literature, methodology, results and a final discussion in which we correlate our results with those in the literature, and drive conclusions.

The review section consists of four chapters. The first and second deal with basis of diastolic and systolic functions and malfunctions. Of course, both subjects are too wide to be included in one, two, or more chapters, as they are the material of some textbooks. However, these two chapters were introduced with the purpose of making clear some of the methodologic

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aspects in this thesis as well as to serve the subsequent discussion of the results. The third chapter deals with cardiac affection under different modes of dialysis. The fourth chapter introduces the few reports available in the literature about the subject of effects of kidney transplantation on cardiac performance.

Aim of the Work:

(1) Assessment of left ventricular function in patients on renal dialysis programs.

(2) Studying the effects of renal transplantation on the myocardial function.

(3) Throwing more light on the entity of "uremic cardiomyopathy".

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REVIEW OF LITERATURE

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SECTION ONE

CHAPTER ONE

DIASTOLIC FUNCTION OF LEFT VENTRICLE

Cardiologists were aware of diastolic function since more than half a century. In 1923, Henderson stated "..., in the heart, diastolic relaxation is a vital factor, and not merely a mechanical stretching like that of a rubber bag. Being vital, it is variable". (Henderson 1923). This still holds true.

Diastolic malfunction may result in a wide array of symptoms starting from dyspnea at effort up to congestive heart failure and pulmonary oedema (Himelman, 1988).

Left ventricular diastolic dysfunction is now recognized as a significant cause of cardiac symptoms even in patients with apparently normal systolic ventricular functions (Rousseou, 1981) (Aroesty, 1985). It has been tantalizing to speculate that an abnormal index of diastolic function can be used to identify patients who will subsequently develop systolic abnormalities or left ventricular dysfunction. It is not clear whether all patients will eventually develop symptoms of either diastolic or systolic dysfunction. Thus, the predictive value of abnormal indexes of diastolic function is not known (Lew, 1989).

Diastole can be divided into an early period of active energy consuming relaxation, followed by a passive phase (Grossman, 1976) (Pasipoularides, 1986). Overlap occurs between these two phases and it depends on the uniformity and completeness of the relaxation process (Rankin 1980).

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So, diastolic malfunction can be classified broadly into two groups: **(1)** those related to left ventricular relaxation and early filling, and **(2)** altered passive pressure-volume characteristics and reduced compliance. The former was mostly derived from data obtained in man with cardiac catheterization, radionucleotide and echocardiographic techniques. In contrast, abnormalities of left ventricular compliance were mostly documented in experimental studies. (Foud 1987) (Pasipoularides, 1986).

Following the isovolumic relaxation period, filling occurs in three phases. Immediately after mitral valve opening, there is a period of rapid filling lasting up to 200 m sec, when approximately 70% of stroke volume enters the ventricle. In mid-diastole, or diastasis, volume changes little, and finally the remaining 30% enters during left atrial systole. These three phases are only apparent at rest. As heart rate increases, diastasis becomes shorter and rapid filling merges with atrial systole (Gibson 1983).

As the aortic valve closes, pressure falls rapidly in the left ventricle, and continues to do so after the mitral valve opens. The greater part of the rapid filling occurs as ventricular pressure is falling rather than rising. During diastasis, left ventricular pressure and volume both remain virtually constant. During atrial systole pressure may increase by up to 5 mmHg. So, it is apparent that ventricular filling cannot be considered as balloon inflation, since at the time of peak filling ventricular pressure falls rather than rises. However, it seems likely that the ventricle is deformed at end-systole, with energy stored in its wall as elastic forces, and with the onset of relaxation it shows a striking tendency to return to its end-diastolic shape (Gibson 1983).

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FACTORS INFLUENCING EARLY LEFT VENTRICULAR FILLING: Table I

In contrast to alterations in passive compliance, changes in early diastole are more dependent on dynamic factors (Table I). The delay in early left ventricular filling may develop early in the evolution of disease when ejection fraction, cardiac output, peak left ventricular ejection rates are still normal (foud, 1980) (Inouye, 1985) (Appleton, 1986).

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Table (1): Factors influencing early left ventricular (LV) filling (fouad, 1987)

(1) Structural (anatomic) factors:

- **(a)** Left ventricular hypertrophy.
- **(b)** Right ventricular hypertrophy.
- **(c)** Fibrosis, or infiltrations e.g. amyloidosis.

(2) LV dynamics

- **(a)** Systolic performance (inotropic state)
- **(b)** Loading conditions (preload and afterload)
- **(c)** Heart rate.

(3) Sympathetic drive to the heart.

(4) Coronary blood flow and myocardial perfusion.

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*** Left ventricular hypertrophy:**

In 1984, Fouad et al performed a cross-sectional study for 23 untreated hypertensive patients and revealed a negative correlation between left ventricular mass and the maximum rate of early left ventricular filling. However, the role of hypertrophy, per se, was questioned. Comparison of hypertrophy due to hypertension, with "physiologic" hypertrophy, did not support a direct relationship between left ventricular mass and left ventricular peak filling rate (Colan 1985). Hypertrophy that occurs in response to the stimulus of chronic exercise, in atheletes for example, (that is, physiologic hypertrophy) does not appear to result in similar abnormalities in early diastolic function. Colan et al showed that athletes have significant increase in left ventricular mass. Despite this absolute increase in left ventricular mass, the peak rate of left ventricular dimension increase and wall thining are significantly increased. Athletes may show eccentric or concentric hypertrophy but various studies using echocardiography or catheterisation showed no deterioration in diastolic function (Carew, 1978) (Bersohn, 1977). These findings denote that hypertrophy per se is not the contributing factor but the mechanism that underlies it. However, it should be noted that athletes are usually assessed in the "unloaded" state (that is, hemodynamic stress that leads to hypertrophy was not active at the time of evaluation), whereas, in general, subjects with aortic stenosis or hypertension are assessed with the hemodynamic load present.

However, impaired speed of relaxation, due to marked pathologic left ventricular hypertrophy, occurs regardless of whether it is due to pressure overload or volume overload (Eichhorn, 1982).

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Effect of Afterload on diastolic function:

Blood pressure level and left ventricular afterload have an important role on early left ventricular filling. Most investigators reported that increased afterload prolonges left ventricular relaxation (Gaasch, 1980) (Karliner, 1977) (Choong, 1988). While increasing left ventricular end-systolic stress did slow left ventricular filling, actual systolic blood pressure levels did not prove to be the major determinant of left ventricular relaxation or early filling either in man (fouad, 1984) or in dogs (Bahler, 1985). Another complicating factor is the duration of increase in afterload, Gaash et al., 1985, clearly demonstrated a marked difference in alteration in diastolic indexes between acute and steady-state changes in afterload. Dogs with chronic arterio-venous fistula demonstrate a progressive increase in left ventricular end-diastolic volume, without a further increase in left ventricular end-diastolic pressure beyond that observed during the early acute phase of volume overloading. A right ward displacement (along the volume axis) of the entire diastolic pressure dimension relationship occurs, and the slope of this curve is steeper, indicating increased chamber stiffness (McCullagh, 1972). Fig. (1).

Effect of preload:

Raff and Glantz, 1981, reported that changes in relaxation could occur due to changes in perload. They found that volume loading slows relaxation and increases the time constant (T) of left ventricular isovolumetric pressure decline. However Karliner et al., 1977, reported that primary changes in afterload produced changes in T, but volume infusion did not produce such changes. Gaasch et al., 1980, found that modest changes in left ventricular preload did not influence T, but when volume loading was sufficient to produce an

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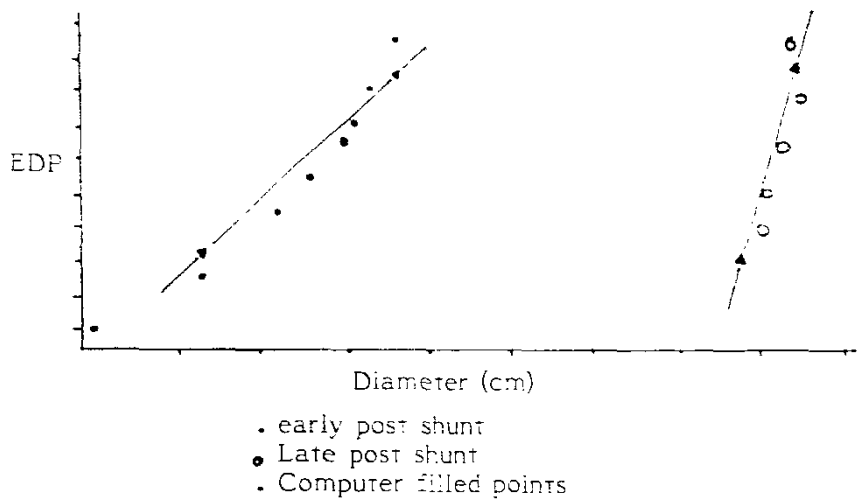

Fig. (1): Relation between left ventricular end-diastolic pressure (EDP) and left ventricular diameter at end-diastole (cm) in one dog studied early and late during the course of chronic volume overloading by means of an arteriovenous fistula. Each curve relating end-diastolic pressure to end-diastolic diameter was obtained by acute transfusion and bleeding. The shift to the right and increase in the slope of the pressure-diameter relation between the early post-shunt study (closed circles) and the study many weeks after the occurrence of chronic cardiac dilatation (open dots) are apparent;the slope change reflects a reduction in diastolic compliance. (Quoted from McCullagh et al., 1972).

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increase in aortic pressure, T increased. Further investigation on intact dog heart using single-beat intact heart intervention, and isolated cardiac muscle, showed that the maximum rate of isometric tension decline is independent on preload, and primary changes in preload do not affect isovolumetric relaxation rate (Gaasch, 1986). Using dogs on right heart bypass, and changing preload independently by pumping blood into femoral arteries, Chong et al. (1988) claimed that the peak velocity of early left ventricular filling varies directly with left ventricular filling. Stoddard et al. (1989) studied the influence of preload on indexes of diastolic function; left ventricular end-diastolic pressures were decreased with nitroglycerin and increased with contrast medium injections. They found that a decrease in preload decreased the peak filing velocity and time-velocity integral during early diastole in Doppler transmitral measurements (E-wave) but not during atrial systole (A-wave) resulting in lower E/A ratio mimicking a pattern of diastolic function impairment. An increase in preload increased both Doppler E & A wave peak velocities, but it did not change the E wave to A-wave ratio or the percentage of atrial contribution to filling. Left ventricular chamber stiffness constants did not change with either an increase or decrease in preload. The investigators concluded that a decrease in perload alters the Doppler filling pattern to mimic diastolic dysfunction, whereas an increase in preload may alter the Doppler filling pattern to mask diastolic dysfunction. In fact, an increase in preload increased both E & A wave peak velocities because peak filling rate or peak early filling velocity is linearly related to the left atrial pressure and the peak early diastolic transmitral gradient. (Choong, 1987) (Courtois, 1988). A direct relation between the left atrial pressure and peak atrial filling velocity (A wave) has also been described (Choong, 1988) (Courtois, 1988). However, altering preload with nitroglycerin and contrast did not alter the chamber stiffness (Stoddard, 1989).

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