Correlation Between Exercise Tolerance and Left Ventricular Diastolic and Systolic Functions Assessed by Echo-doppler Before and AfterAdministration of Captopril in Patients with Dilated Cardiomyopathy

Thesis

Submitted in the partial fullfilment
for master degree in cardiology

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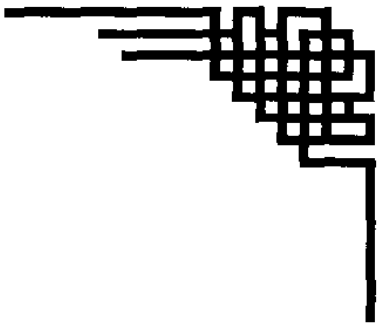
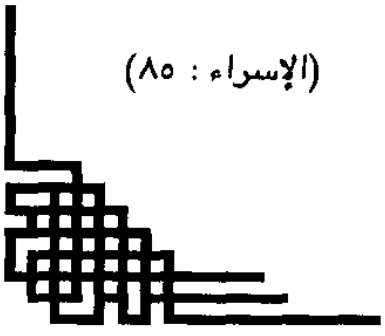
1994

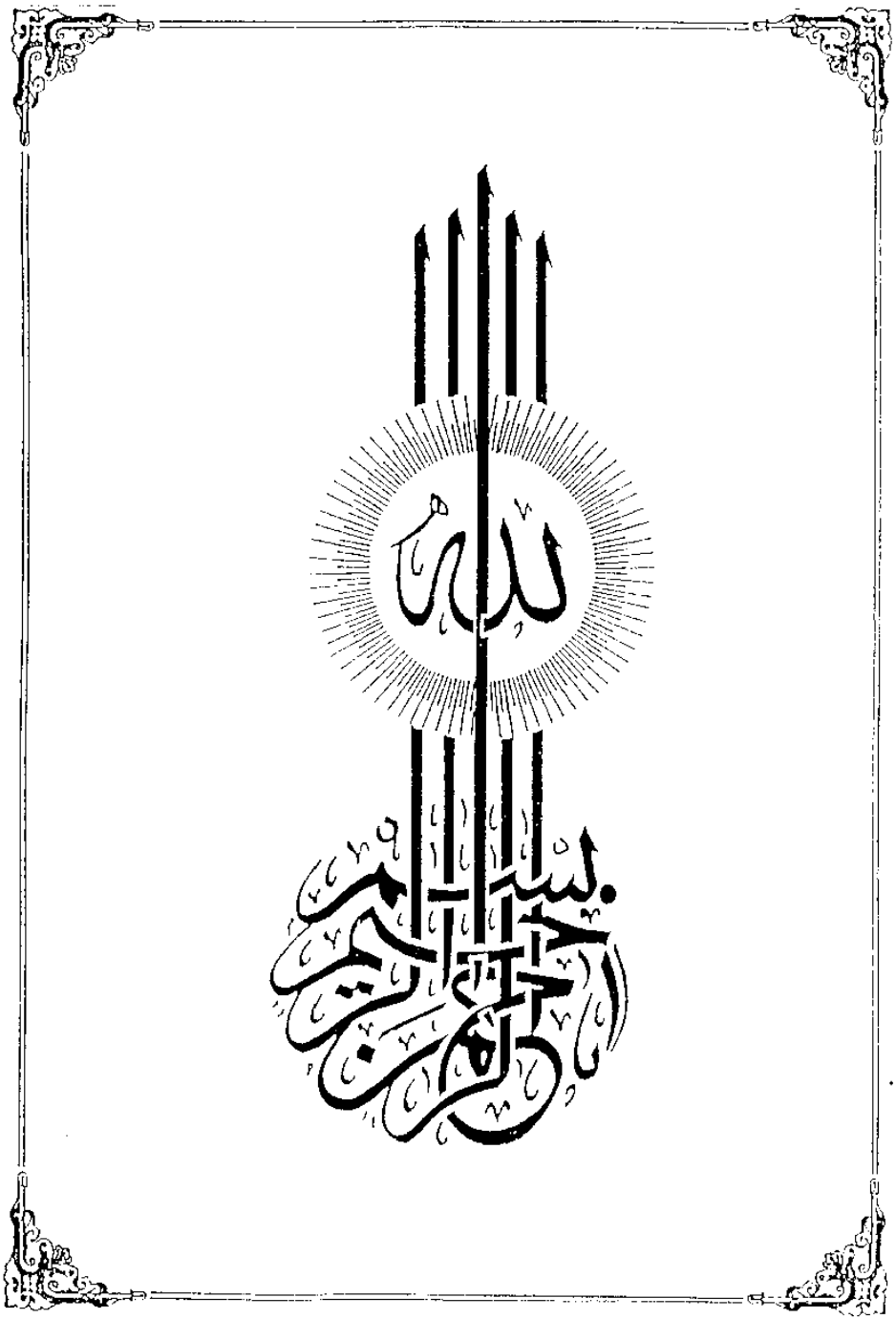


بسم الله الرحمن الرحيم

«وما أوتيتم من العلم إلا قليلاً»

(الإسراء : ٨٥)





Acknowledgement

First and Foremost, thanks to GOD, the most beneficial and merciful.

I would like to express may profound gratitude and my immense appreciation to ***Prof. Dr. Adel El-Atribi*** *, professor of cardiology, faculty of medicine, Ain Shams university, who offered his precious time, kind instructions and reassuring advice for supervising this study.*

I am also deeply indebted to ***Dr. Mervat Abou El-Maati****, lecturer of cardiology, faculty of medicine, Ain Shams university, she has spared no effort to provide me with the knowledge, experience, guidance and encouragement necessary for fulfilling my work.*

I am truely grateful to ***Dr. Hani Abd El-Razek*** *consultant of cardiology, National Embaba Heart Institute, for his enormous unlimited help, great care and assistance to start this study and to follow it up till completion.*

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INTRODUCTION AND AIM OF THE WORK

Introduction :

Idiopathic dilated cardiomyopathy is an enigmatic and in many ways, frustrating disease. It is diagnosed with increasing frequency and in some parts of the world may account for up to 30% of all cardiac deaths. (1)

Current concepts of cardiomyopathy are changing and this disease entity is a focus of investigation on many fronts, yet we still know relatively little about the condition and several questions are completely unanswered. Is it one disease or many? Is it the same disease in parts of the world? What's the etiology or are there multiple etiologies? recent studies have shed light upon the natural history, with newer methods of diagnosis possibly leading to detection at an earlier stage. Crucial factors that distingwish between patients who survive and those who die still need to be established. Finally in the face of what is generally to be poor prognosis as documented by most natural history studies, it must be realized that definitive therapy is unavailable.

Aim of the work :

The aim of this work is to study the effects of oral captopril given for 1 - 2 weeks to patients with dilated cardiomyopathy on exercise tolerance and left ventricular function.

REVIEW OF LITERATURE

His clinical and pathological description, founded on a series of cases which he obsereved, fit well into what is described today as idiopathic cardiomyopathy.

He considered the clinical disorder and the pathological changes in the myocardium to be the result of a preceedig acute myocarditis, he also believed that the pathological changes were chronic and non inflamatory which eventually led to "myocardial failure".

Shortly, after krehl's observations and reports, other reports by Feidler (3) in 1899 and by Josserand and Gallavardin (4) in 1901 resulted in the introduction of other new terms to descibe forms of idiopathic myocardial disease.

Fielder's consepts were based upon clinical and pathological studies of 5 young adults, with a similar illness, fatal in 4 of them. The illness was charactarized by rapidly developing progressive biventricular heart failure without high fever or symptoms of sepsis. At autopsy, the heart. Was the chief site of disease where the predominant changes were localized to the interfibrillary (interstitial) tissue of the heart muscle with only minimal parenchymal changes.

He considered these changes to be one of the "interstitial myocarditis" not due to diphtheria, scarlet fever, nor sepsis but to some microrganisms or its toxins which directly localized its action to the heart mscle this perhaps was the first suggestion that an invasive organism or its toxins might be cardiotrophic with ability to localize to myocardium.

Dr. Wallace bridgen, in his work 1956, (5) gave a masterly

account of "unknown myocardial disease".

In this work he clarified the great confusion which existed at that time about the obscure aspect of heart disease. He reported 50 cases of isolated heart. muscle disease (cardiomyopathy) seen at london national heart hospital between (1949 and 1956) and on basis of clinical history, physical examination, laboratory investigation and necropsy he placed 42 of these cases into broad ateological groups (5).

The term cardiomyopathy, meaning heart muscle disease, has now passed into medical termenology and has accumulated a vaste literature, not all of which is as definitive as was Bridgen's study (6) (7) (8). Professor John Goddwin returned to the subject of cardiomyopathies in his St. Gyres lecture for 1969 (9) based on a decade of clinical study at the royal post graduate medical school at Hammersmith.

The matter was still obscure but it was now possible to group primary cardiomyothies as congestive, hypertrophic or restrictive.

Many subsequent studies followed, some presented new terms and classifications (10) (11), others discussed natural history, diagnostic criteria, haemodynamic assessment of the dilated failing heart. (12) and the role of differnt therapeutic regimens (13) (14) (15) (16).

Advancements in general scientific concepts especially in immunochemistry, immunology and genetic and molecular biology (17) (18) (19) (20) have greatly contributed to our better understading of this condion. But despite this prolonged work our

insight into this problem remains limited with many questions regarding aetiological factors; and efficacy of different lines of therapy, ect... awaiting further hard and talentive research work.

Definition :

Cardiomyopathies comprise a heterogenous group of heart muscle disease of unknown cause or causes (21) pathophysiologically, they are categorized into three relatively distinct enteties : dilated cardiomyopathy, hypertrophic cardiomyopathy which may be obstructive or non obstructive and restrictive cardiomyopathy. (22) while impaired ventricular. Filling is a primary feature of hypertrophic and restrictive cardiomyopathies, dilated cardiomyopathy has been characterized as a form of cardiomyopathy. In which there is impaired function of the heart as a pump with dilatation of the ventricles and reduced systolic function.(228) The condition generally recognized by dilatation of both left and right ventricles with varying degrees of hypertrophy. Recently patients, with severe global reduction in systolic function with minimal dilatation have been described. (23).

In the past, dilated cardiomyopathy received many disgnations icluding idiopathic cardiac hypertrophy, idiopathic cardiomegally, primary myocardial disease, diffuse myocardial disease, myocardiopathy and familial myocardial disease. The world health organization / international society of cardiology task force on cardiomyopathies specifically relates that it is "heart muscle disease or diseases of unknown cause or causes." the prior

definition of primary and secondary cardiomyopathies is now redundant (21). The later referred to conditions in which the cardiac abnormality existed in association with another systemic disease for example, amyloidosis or haemochromatosis.

It is evident, therefore, that idiopathic dilated cardiomyopathy is a diagnosis of exclusion.

It should be emphasized that severe systolic dysfunction due to coronary, hypertensive or valvular diseases not be termed.

However, cardiomyopathy i.e. idiopathic dysfunction may coexist with these common disorders, and clinical differentiation of cause and effect may be difficult. For instance, a generalized global dysfunction with one vessel coronary artery disease, mild systemic hypertention, or mitral stenosis are all examples of coexistence of two unrelated disorders. In some instances a judgment of possible cause and effect versus concurrence of unrelated conditions may provide considerable difficulty. (24).

Incidence :

Congestive heart failule affects more than 2 million americans and is increasing in prevelance (25). The most common cause of congestive heart failure in North America and Europe is coronary art. Diseases (7). Deaths due to cardiomyopathy are only 2% (in white) and 5% (in blacks) as frequent as those considered to be due to ischaemic heart disease in the United States. (26).

In 1982 the age - adjusted prevelence rate for persons aged.

35 - 74 years were as follows : white males 11 per 100.000, white females 4.4 per 100.000

Black males 27 per 100.000 and a black females 11 per 100.000. In this age bracket, the male to female ratio was 2.5:1 in white and 2.4:1 in blacks. The black to white ratio was 2.4:1 in males and 2.6:1 in females. The rate for all ages rose from 4 to 14.5 5 per 100.000 (an increased of 263%), and all age groups were affected. (26). In a two year study in Denmark in 1980 - 1981, 41 cases of confirmed dilated cardomyopathy were identified, giving an estimated incidence of at least 0.7 cases per 100.00 residents. (29).

This latter incidence rate is much lower than the Swedish experience which was an instance of 7.5 cases per 100.000 inhabitants per year betwen. 1970 and 1979 with a male to female ratio of 3:1 and a mean age 47y. The prevelance of dilated cardiomyopathy in England has been estimated to be 8.3 cases per 100.000 population (30). A mayo clinic population based study in Olmsted county, Minnesota, found an incidence, rate of 5.4 per 100.000 population (31).

In summary, the incidence of dilated cardiomyopathy in Western hemisphere is approximately 7 - 10 per 100.000 persons per year, but there are a lack of epidemiological data particularly with regard to Africa and Asia. Newer methods of diagnosis and earlier recognitions of the disease will likely alter the incidence rate.

Pathology :

- Gross picture : the typical features of dilated cardiomyopathy are dilatation of all four cardiac chambers (32 - 35). Heart weights at autopsy are usually 400 - 750 gm (normal weight is 300 gm) but may be in excess of 1000 gm.

Hypertrophy is present despite of normal wall thickness due to the degree of dilatation. Thrombi are found in over 50% of non anticoagulated patients and are usually multiple and located in the left ventricular apex (34). There are no specific pathological features in the epicardium and in the endocardium but non specific thickening and fibrosis are present. It should be emphasized that fibrosis' is usually patchy but more prominent in the subendocardium. Hudson noted frequent fibrotic involvement of the endocardium in the area of origin of left fasicle, which correlates with the high frequency of left bundle branch block. (36). There is also often dilatation and thickening of the mitral and tricuspid value rings in association with chronic atrioventricular valve regurgitation, but cause or effect arc unestablished. The coronary artries are usually normal or have mild, heamodynamically insignificant atherosclerosis (37).

Recently in a small group of patient, clinical and haemodynamic findings that are similar to those seen in dilated cardiomyopathy have been reported, though this group had only minimal cardiac dilatation.

Althaugh in the majority of patients enlargmet of the left ventricle is greater than that of the right (32), selective right ventricular dilatation has been noted by several investigators (38-41).

In general the size of the left ventricular cavity and the heart

weight are proportional to the severity and duration of the symptoms of D.C.* (42).

- Histological findings: histological findings on light microscopy are non specific with similar patterns being found in patients with valvular, coronary and congenital heart disease. In dilated cardiomyopathy, the histological appearance is variable and reflects neither the clinical nor the haemodynaminc severity of the disease the findings actually may be normal in the face of severe congestive heart failure, but as a rule the histological examination is abnormal but nonspecific (32, 33) the most frequent findings are variability in myofibril size, hyperchromatic enlarged nuclei, myofibrillar degeneration and necrosis, increase interstitial collagenous tissue and fibrosis and cellular hypertrophy these findings are seen more commonly in the left ventricle than in the right.

In comparison with the epicardium, the endocardium and subendocardium have the greatest degree of fibrosis (33).

Histochemically, myocardial level of creatine kinase, glycogen, succinic dehydrogenase and mitochondrial enzymes have been found to be decreased by varring degrees (224, 225, 226). Lactate dehydrogenase (LDH) specifically the LDH5 isoenzyme has been shown to be elevated in myocardial biopsy specimens and correlates with heamodynamic decompensation (227). This is propably a non specific secondary finding. Measurement of contractile protein synsthesis by quantitating cardiac specific messenger ribonucleic acid (RNA) from biopsy

* D.C. = Dilated cardiomyopathy.