RADIONUCLIDE ANGIOGRAPHIC EVALUATION OF THE EFFECT OF INTRAVENOUS OXYFEDRINE ON LEFT VENTRICULAR FUNCTION IN PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE

THESIS

Submitted In Partial Fulfilment For
The Master Degree of Cardiology

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A C K N O W L E D G E M E N T

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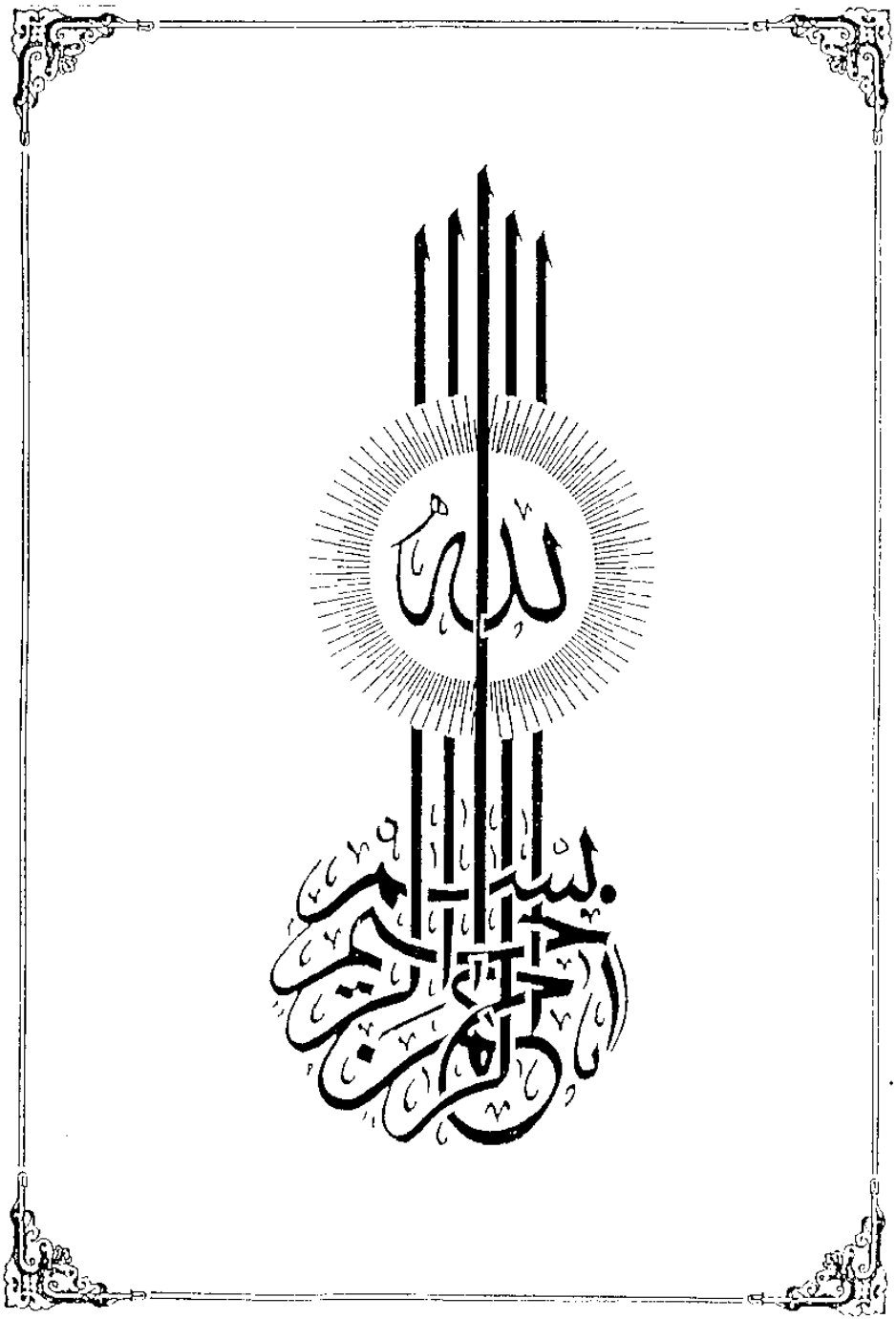

C O N T E N T S

INTRODUCTION

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Before designing any line of treatment in patients with coronary artery disease, it is of paramount importance to assess left ventricular performance . This is because of the known fact that there are some potent anti-anginal drugs such as propranolol which is known to have a myocardial depressant effect and it could not be used safely in patients with left ventricular dysfunction .

Up till this moment, search for an ideal anti-anginal drug which could improve coronary perfusion, decrease oxygen consumption and improve myocardial contractility is still going on .

Oxyfedrine is a new anti-anginal drug which is claimed to have such an ideal action (Dirschingen et al., 1982 and Whittington and Raftery, 1982) .

The aim of the present work is to evaluate the effect of intravenous oxyfedrine on myocardial contractility .

REVIEW OF LITERATURE

Physiology Of Cardiac Contraction

A) Mechanics of Cardiac Contraction :

Cardiac contraction can be readily studied in-vitro by mounting a mammalian cardiac muscle . The preferred myocardial segment is the papillary muscle because of the parallel arrangement of its fibers . The ends of the muscle are fixed, and the muscle is allowed to contract isometrically. The three most important mechanical characteristics of the cardiac muscle are :

1) Length-active tension relationship .
2) Force-velocity relationship .
3) Force-velocity-length relationship .

1) Length-active tension relationship :

The development of active tension during isometric contraction by the myocardium can be altered by changing initial muscle length, and the relation between these two variables constitutes the length-active tension curve (Fig. 1). When the muscle is stimulated to contract isometrically , the length of the muscle at which the resultant force developed is maximal is termed L_{max} (Mommaerts , 1964) .

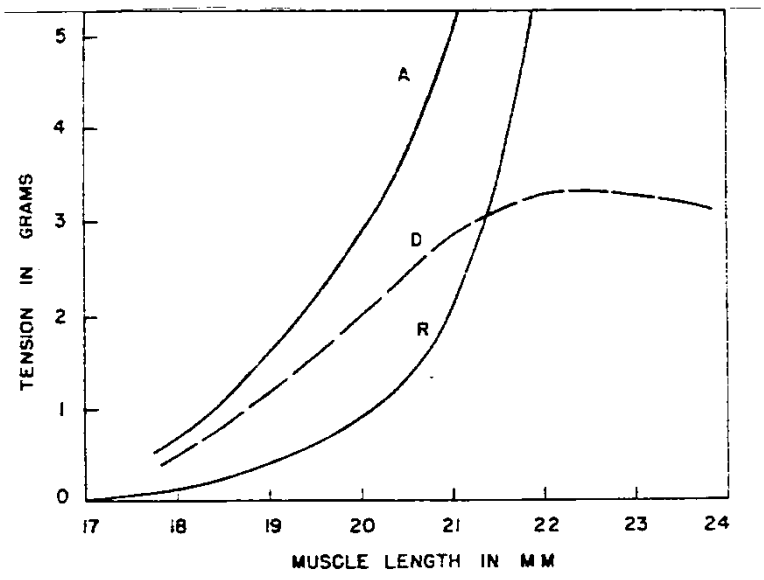

Fig.(1): Representative force-length or tension-length diagram for cardiac muscle . R : resting tension; A : Total active tension ; D: Developed Tension (The tension added by contraction or A - R) . Note significant resting tension at shortest length (After Mommaerts, 1964) .

The strength of individual isometric cardiac contraction is modified by two major influences : (1) a change in initial muscle length or preload and (2) a change in contractility (Sonnenblick, 1962) .

2) Force-velocity relationship :

It is the study of shortening characteristics of the muscle when the length of the muscle is changed while its tension is maintained at constant level i.e. under isotonic contraction . The extent and maximum velocity of shortening for each contraction depends on the total load (Pre-load + afterload), and the inverse relation between force developed and velocity of contraction constitutes the force-velocity curve (Fig. 2) .

As the load is increasing , the velocity of shortening decreasing. Conversely , when the load is smallest , the velocity of shortening is greatest . The maximum velocity of unloaded shortening is called V_{max} (Abbott and Mommaerts, 1959) .

When the contractility is augmented, the entire curve is shifted upwards and to the right with an increase in both force and velocity (Fig. 3) (Sonnenblick, 1967) .

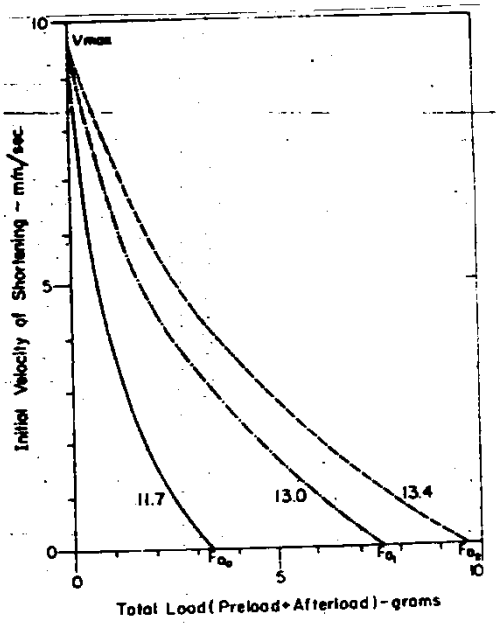

Fig. (2): Relation between peak velocity and initial length of the muscle (After Abbott and Mommaerts,1959).

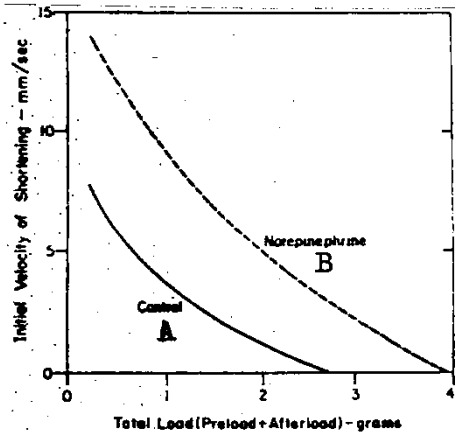

Fig. (3): Effect of norepinephrine. A= Before ; B= After . (After Sonnenblick, 1967) .

3) Force-velocity-length relationship :

With the development of Hill model of the contractile element (Fig. 4), a wide variety of circumstances can be studied during both isometric and isotonic contractions .

During isotonic contraction, the muscle (CE) moves in a predictable manner across the surface, describing the relation between force, length and velocity (Figure 5) . With activation (onset of contraction), the contractile element (CE) rises into a hypothetical force velocity curve (right projection of the curve A) . As the force is increasing, the velocity of contractile element is decreasing until the afterload is reached, after which shortening proceeds across the surface . As shown in Fig. (5 B) , the velocity of shortening between the two points B and C depends on the level of the force-velocity-length plane (Brutsaert and Sonnenblick, 1973) .

B) Contractility and Inotropism :

If one is accustomed to think in the term of contractility, it should be defined strictly as the capability for becoming short in response to a stimulus . Inotropism : is the positive or negative modification of the basic contractile force .

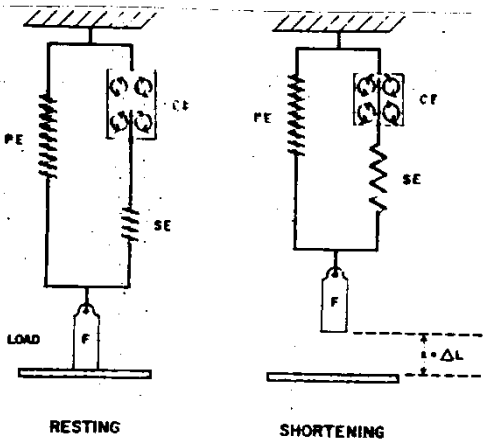

Fig. (4): A hypothetical muscle model of Hill .
When the contraction is isometric, the CE shortens and generates force by stretching the SE , but overall change in length is prevented . When the overall muscle is shortening at a constant load, the contraction is isotonic . The change in length with contraction is $X = \Delta L$.

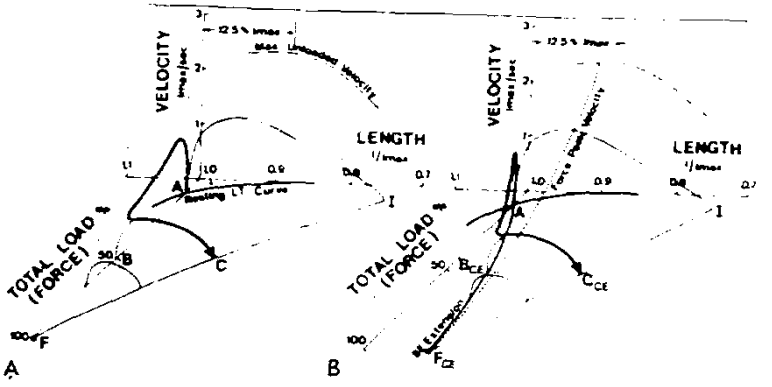

Fig. (5): Force - velocity - length relationship .
(After Brutsaert and Sonnenblick, 1973).

Inotropic intervention appears to operate by changing the intensity of the active state and its duration . However, the inability to measure the inotropic effect directly instead, we must rely on determination of the outcome parameters from the change in contractility . In other words , a fundamental modification of the basic contractile state with inotropism is unlikely i.e. contractility per se does not change, but its manifestations can be modified (Fracis, 1979) .

Positive and negative inotropic agents :

Myocardial contractility is increased by activation of the myocardium, which is mediated in one form or another by an enhanced availability of Ca^{2+} ions inside the cell . Increased calcium ions delivery by catecholamines including norepinephrine, epinephrine and isoproterenol , through their action on adenyl cyclase system . Digitalis glycosides also enhance contractility but act by inhibiting the Na^{+}-K^{+}-stimulated ATPase in the cell surface membrane , which appear to leave larger amounts of Ca^{2+} within the muscle fiber . Contractility is also increased, to some degree, by cartico-steroids, aldactone, angiotensin, serotonin and glucagon . Myocardial contractility is decreased by hypoxia and by many drugs, including barbiturates, quinidine, propranolol , procainamide and lidocaine (Hurst, 1982) .