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THE UNIVERSITY OF ALBERTA

The Natural History of Left Ventricular Abnormal Wall Motion Following Anterior Myocardial Infarction Using Two Dimensional Echocardiography

by

Bruce A. Sussex M.B.B.S.

A Thesis Submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the Degree of Master of Science

In

Experimental Medicine

Department of Medicine

Edmonton, Alberta

Fall, 1984

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ABSTRACT

Over the last 15 years, a large effort has been made to demonstrate reduction in the extent of ischaemic injury and subsequent myocardial necrosis with specific therapies during myocardial infarction in man. Such research has been hampered by a lack of suitable methods for quantifying infarct size in man. Decreased wall motion has been shown to be a sensitive indicator of myocardial ischaemia and infarction. This study was done to evaluate the natural history of left ventricular abnormal wall motion (AWM) after acute anterior myocardial infarction by two dimensional echocardiography (2D echo). Sixteen patients with acute anterior myocardial infarction underwent up to 10 serial 2D echo studies up to 6 months after infarction. Serial short-axis and long axis images were recorded and the extent of total abnormal wall motion (AWM) was computed for each section. Total AWM was defined as hypokinesis plus akinesis plus dyskinesis. Over the 6 months of the study there were no significant differences in extents of AWM in the group as a whole but there was a significant decrease in extent of total AWM and extent of akinesis plus dyskinesis of approximately 20% ($p < 0.05$) in those 5 patients with small infarctions (as determined by a peak creatine kinase (CK) less than 1150 I.U.). This decrease occurred over the full 6 months of the study. No change was seen in extent of dyskinesis alone. Among 10 patients with medium to large infarctions all developed diastolic shape distortion suggestive of aneurysm, but LV dilation negated any absolute changes in extent of abnormal wall motion. No clinical events predicted the changes in

abnormal wall motion over time within the group. The extent of total AWM showed a good correlation with peak serum CK ($r = 0.70$, $p < 0.01$ and extent of dyskinesis correlated with summated Q waves (on standard anterior chest leads of electrocardiogram done at 48 hrs). ($r = 0.65$, $p < 0.01$). Intraobserver reproducibility was satisfactory with a variation of measurement of AWM of 10%. Thus, two dimensional echocardiography is a reproducible method of estimating the extent of left ventricular asynergy. No significant changes in extent of AWM occurred in the 6 months post-infarction.

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Bruce Sussex

Cardiology Division

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November 30, 1983

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF FIGURES

INTRODUCTION

Ever since the studies of Tennant and Wiggers[1], it has been known that acute coronary occlusion resulted in rapid and dramatic changes in wall motion of the ischaemic region. They also showed that restoration of flow after brief occlusion resulted in complete return of normal wall motion. This was the first experiment to suggest reversibility of ischaemic injury. This concept has received major interest[2] since the introduction of coronary care units resulted in a major reduction in deaths from primary arrhythmias (2a). The size of ischaemic injury is now the major determinant of morbidity and mortality in acute myocardial infarction.[3] To test the hypothesis that the amount of ischaemic necrosis can be reduced during myocardial infarction, a reliable method to quantify myocardial infarct size is needed. Many studies have utilized wall motion abnormalities as an indicator of myocardial ischaemia. However, it was only with the advent of two dimensional echocardiography that repeated serial tomographic imaging of the heart in motion became practical in man (3a). This study was thus performed (1) to assess the feasibility and reproducibility of repeated two dimensional echocardiographic imaging after acute myocardial infarction; (2) to determine the natural history of abnormal wall motion in acute myocardial infarction in man as assessed by two dimensional echocardiography.

LITERATURE REVIEW

QUALITATIVE ASSESSMENT OF WALL MOTION

DEFINITIONS

A discussion of myocardial wall motion requires a definition of terms. Thus, the movement of the ventricular muscle mass relative to the ventricular cavity can be defined as ventricular wall motion. It can be divided into 4 components - isovolumic contraction and isovolumic relaxation - both with fixed volume but conformational change, and ejection phase and filling phase where wall movement is associated with change in volume.

Abnormal wall motion will be defined as decreased amplitude or abnormal direction of wall movement during systole associated with decreased systolic thickening. It is essential to introduce the parameter of wall thickening to exclude non-ischaemic causes of abnormal wall motion.

There is heterogeneity of contraction and thickening within the normal left ventricle (4,5,6) and this has to be considered when evaluating wall motion. Although abnormal patterns of wall motion within systole (biphasic, delayed) and during isovolumic relaxation are characteristic in ischaemia,[7] they can be recognized only by frame by frame analysis because the duration of these abnormal patterns is too short.

Wall motion is the product of the interaction of developed force through muscle fibre shortening against a resistance (electrochemical/mechanical coupling) and muscle fibre orientation.

MYOCARDIAL CONTRACTION

The mechanisms of actin and myosin interaction to initiate contraction and fibre shortening are well described.[8,9] Initiation of the normal processes of contraction and relaxation requires adenosine triphosphate (ATP). There is a translation of chemical energy (ATP) into mechanical energy in the movement of actin-myosin cross linkages that occurs during shortening. A "plasticizing" effect is provided by ATP, which allows dissociation. In its absence, actin and myosin can interact directly to form rigor complexes, which are neither amenable to regulation by Ca^{2+} concentrations nor fully reversible.

Calcium regulates the interaction of actin and myosin through the tropomyosin troponin complex. With low Ca^{2+} concentration, this complex inhibits binding of actin and myosin - ATP and it activates binding at high concentrations.

Excitation-contraction coupling is rapidly inactivated by ischaemia through the onset of hypoxia, acidemia and reduced levels of ATP. The latter results in the formation of the rigor complexes seen early after acute myocardial infarction.[10]

The sarcomeres in the mid wall of the myocardium operate at close to optimal resting length for tension development at normal endodiastolic pressures. The sarcomeres of the epicardium and endocardium are shorter. With dilation, a progressive "recruitment" occurs so that the epicardial and endocardial sarcomeres elongate. The sarcomeres resist stretching beyond 2.2 microns and further dilation can only occur with distraction - resulting in myocardial damage and subsequent

fibrosis. "Recruitment" results in increased force of contraction and improvement in cardiac function (Frank Starling mechanism).[11] Because of geometrical considerations there is relatively less shortening of the epicardial than the endocardial sarcomeres. The sequence of recruitment and the above geometric considerations have significant effect on wall motion patterns because of the variations in fibre architecture of the left ventricle and because ischaemic damage preferentially involves the subendocardium.

STRUCTURAL CONSIDERATIONS

The left ventricle has a complex geometry with inlet and outlet compartments aligned at 30° to each other. In diastole the anterior border of the heart (as seen on the RAO angiogram) is invariably concave to the cavity but the inferior border is frequently flat or convex in relation to the cavity. This relationship holds true in systole in normal hearts.[12]

To understand normal contraction patterns requires some knowledge of the fibre architecture of the heart. This has recently been reviewed.[13] The basis of our understanding of fibre orientation was stated by Krehl in describing the Triebwerk - a series of helical fibre paths passing from base to apex and from epicardium to endocardium and then continuing from apex to base and from endocardium to epicardium. The fibre pathways are not joined to each other and only a limited number of fibres are attached to the fibrous skeleton. These concepts were confirmed by Torrent-Guasp[14] using a dissection protocol that rigorously preserved the principal fibre path. Within this framework there are a number of regional variations. Histological

analysis of through-wall blocks have shown that the helix angle gradually changes from +90° (endocardium) to 0° (mid wall) to -90° (at epicardium) relative to the surface of the epicardium in mid chamber.[15] This structural relationship persists in systole.[16] By using cross-sectional slices of human hearts examined in rigor mortis, Greenbaum, et al.[17] have shown regional variations exist in fibre orientation.

At the base, the fibres are essentially circumferential in the mid-wall, sandwiched between longtitudinal fibres in the endocardium and obliquely running spiral fibres in the sub-epicardium.

At the mid-ventricle level, longtitudinal fibres are seen in the trabeculae and sub-endocardium, while circumferential fibres are present mid-wall especially in the septum. Spiral oblique fibres are subepicardial with longtitudinal fibres seen on the anterior and obtuse marginal surfaces.

Towards the apex the spiral oblique fibres are seen in both the sub-endocardial and sub-epicardial "layers" - there is no middle layer - and the two interdigitate. The wall is thinner and forms a vortex at the apex.

The orientation of fibres in the septum is almost exclusively circumferential towards the left ventricle except near the apex where spiral oblique fibres are seen.

There are extensive cross-over fibres both anteriorly and posteriorly between the right and left ventricle. The septum is morphologically part of the left ventricle by virtue of the circumferential fibres which are not seen in the right ventricle.

As a result of these regional differences in morphology there are variations in regional function.[4,5,6] The relative roles of the sub-endocardium and sub-epicardium in myocardial thickening and wall motion are important in the understanding of the effects of ischaemia on contraction.

Sub-endocardial thickening accounts for over 80% of total systolic thickening and therefore of overall pump function.[18] This is at least partly related to mechanical and geometric constraints on the epicardium and the incompressibility of the myocardium.[18] Thus, Sabbah et al demonstrated a reduction of internal dimension of the left ventricle (short axis) of 22% versus 6% for the external dimension.[18]

Part of the sub-endocardial thickening is produced by longitudinal shortening which occurs mostly due to movement of the base of the heart.[4] This shortening may be overestimated if there is apical cavity obliteration.[19]

In the normal ventricle, systolic ejection is achieved mainly through lateral apposition of walls.[20] Thus, fractional shortening of the short axis of the heart correlates well with ejection fraction in normal and diffusely abnormal ventricles.[19] However, fractional shortening (and thus wall motion) varies in extent from base to mid chamber (and by extrapolation, presumably to the apex).[4] In the study of Shapiro et al., fractional shortening at the base was 32$\pm$ 6% (mean $\pm$ S.D.) and for papillary level 37$\pm$ 5%. Epicardial motion at the base was much greater than at mid-chamber. This partly compensated for the reduced systolic thickening at the base. Septal thickening which contributes substantially to septal motion was significantly less than

that of the posterior wall at the crosssectional levels.

At mid-chamber levels, the posterior endocardium continues to move inwards after the aortic valve is closed. This delayed contraction occurs in the absence of conduction delay and suggests temporal dispersion of contraction. This delayed thickening is not due to diastolic myocardial engorgement because it does not occur at all cross-sectional levels. This non-uniformity is likely due to variations in fibre architecture rather than in local myocardial cell properties.

The relative changes in cavity dimensions and wall motion have been demonstrated by angiography.[19,21,22] In normal ventricles, long axis shortening is approximately 18%.[21,22] It is reduced in abnormal ventricles e.g. 13%,[19] 7%[22] especially in aortic stenosis where the long axis may lengthen in systole. However, changes in the short axis more closely reflect overall cardiac function provided the abnormality is diffuse.[19] Measurements of normal fractional shortening by cineangiogram 27%[19,22] are slightly less than those by ultrasound 36%.[23]

Technical problems associated with definition of endocardial edge may cause apparent regional differences. Using angiography to measure wall thickness, Mitchell[24] found that systolic thickness involved true thickening of the muscle and infolding of the trabeculae carnae. As trabeculation is not uniformly distributed over the left ventricular surface this gives rise to apparent variations in thickness an extent of wall motion. This is less of a problem with ultrasound measurement.

Rotational forces contribute to apparent non-uniformity of wall motion. Torsion about the long axis has been measured[15] by change in the fibre angle of myocardial muscle between diastole and systole. This change is 7° at the base and 19° near the apex. Using endocardial markers Rushmer et al.[25] showed a torsion relative to long axis of approximately 10° at mid-chamber. Errors of measurement of wall motion may then be made by rotation of a surface out of the plane of section.[26] This torsion produces potential energy that allows for active and rapid relaxation through derotation.

PHYSIOLOGICAL FACTORS

Dilatation of the left ventricle occurs in response to increases in preload or afterload or a decrease in contractility. The left ventricle dilates asymmetrically increasing mainly in the short axis dimension to assume a more spherical shape.[19] As this occurs, a disproportionate amount of the decrease in wall motion amplitude occurs in the short axis relative to the long axis. Thus, the relative amplitudes of regional contraction are partly dependent on the size of the cavity.

In the absence of change in cavity size or shape, changes in preload, afterload and contractility will not alter the relative amplitudes of regional wall motion. However, increased afterload will tend to decrease amplitude of wall motion whereas increased preload will tend to increase it.[9] In the absence of sympathetic discharge,

changes in heart rate do not significantly change cardiac output, but do change the end-diastolic size of the left ventricle and the amplitude of contraction.

Conduction disturbances cause temporal asynergy (asynchrony). This is associated with some shape change. Further, in left bundle branch block there may be an additive effect due to the asynchronous contraction of the two ventricles.

An increase in right ventricular filling volume or pressure causes a flattening and a left shift of the intraventricular septum - this causes a decrease in the septal/free wall dimension and an increase in anterior/posterior dimension of the left ventricle.[27] This shape change decreases the compliance of left ventricle and filling volume resulting in a fall in stroke volume. These changes are accentuated with acute cardiac dilation, but are seen to a mild degree with inspiration in the normal sized heart. A decrease in the amplitude of wall motion of the septum (but not of wall thickening) occurs relative to the posterior wall[28] and septal motion may become paradoxical.

ABNORMAL WALL MOTION WITHOUT ISCHAEMIA

Localized abnormalities of wall motion not related to the above factors are mostly due to ischaemic heart disease. However, there are a number of other causes of regional asynergy. These include abnormalities at the base of the heart in mitral valve prolapse and rheumatic mitral valve disease and in the septum in hypertrophic obstructive cardiomyopathy. Focal disease in the heart may occur with granulomatous

and infiltrative processes causing regional asynergy which may be associated with abnormal thickening. Thus, these conditions must be excluded before assessment of ischaemia by regional wall motion abnormalities is possible.

THE USE OF ABNORMAL WALL MOTION TO DETECT ISCHAEMIA

Changes in contractile function are the earliest externally detectable signs of ischaemia. Within 5 seconds of occlusion of a coronary artery there are characteristic changes of systolic thinning and paradoxical motion in the centre of the ischaemic zone.[29] These changes occur before any evidence of a current of injury on ECG and also before the onset of chest pain.[30]

A number of studies have been performed to determine the relationship between contractile function (demand) and myocardial blood flow (supply). Keeping myocardial work constant, Wyatt et al.[31] induced ischaemia by graded reductions in flow. Contractile function rapidly decreases when coronary perfusion pressure falls below 50 to 65 mm of Hg and coronary blood flow below 0.25 to 0.55 ml/min/g. The relationship is sigmoidal. The subendocardium is more sensitive to a decrease in blood flow than the subepicardium. Below a flow of 0.5 ml/min/g there is a steep decline in subendocardial length shortening. At a flow of 0 to 0.3 ml/min/g endocardial systolic shortening is lost.[32] Changes in endocardial segment length have been shown to closely parallel those of thickness measured by sonomicrometers[33] and echocardiography.[34]

The relationship between subendocardial length shortening and flow is important because of the greater contribution of the subendocardium to the amplitude of motion and thickening of the ventricular wall.[18] Further, reduction of blood flow to the subendocardium results in decreased systolic shortening of the subepicardium despite normal subepicardial blood flows.[32]

The amplitude and mean velocity of systolic wall motion is progressively decreased with graduated reductions in coronary blood flow.[35] Some systolic wall motion was maintained in these experiments despite complete coronary artery occlusion but blood flow did not fall below 25% of normal, presumably due to collaterals.

Many experiments have shown subepicardial sparing in acute myocardial infarction.[36,37,38] However, it is functionally tethered to the subendocardium. This makes amplitude of wall motion (and thickening) a relatively insensitive indicator of transmural extent of infarction as infarction involving greater than 20% of wall thickness is associated with systolic thinning and no significant change in the amount of thinning occurs as transmural extent of infarction increases.[39]

TETHERING

Weiss et al.[40] showed a positive correlation between circumferential extent of wall motion evaluated subjectively and the circumferential extent of infarction pathologically. However, the circumferential extent of myocardial infarction assessed by abnormal wall motion overestimated the extent of myocardial necrosis. This was due almost entirely to wall motion abnormalities in the region adjacent to scar. As these zones were within the occluded bed of the infarct,

they could have been severely ischaemic at the time of echo examination.[40] However, there is considerable controversy regarding this phenomenon. Kerber et al.[35] showed a decrease in function by M mode echocardiography in regions with normal perfusion but adjacent to ischaemic segments suggesting tethering of the normal myocardium to abnormal myocardium or the late results of transient ischaemia as suggested by Heyndrickx et al.[41] Wyatt et al.[42] not only found depressed function adjacent to infarcted tissue but also at a distance - the degree of depressed function being related to distance from the infarcted zone. These latter results were based on epicardial recordings which contribute only to a minor degree to overall cardiac function. Wyatt et al. suggested a "parallel fibre" hypothesis to explain their findings. Their experiments involved length gauge placement in a region where the myocardial fibres are in series. However, these results need to be cautiously applied to the endocardium and other sections of epicardium where fibre architecture is not so uniform. Heikkila et al.[43] and Banka et al.[44] failed to show any change in function of the posterior wall in response to left anterior descending artery occlusion.

In contradistinction to the above studies, others[29,45,46] have shown that areas remote from the infarct show increased function likely due to decreased afterload secondary to paradoxical bulging of the ischaemic segment (decreased afterload), slight end-diastolic dilation (Starling effect) and reflex sympathetic discharge.

In zones adjacent to infarction the issue is more complex. The intermediate function of the "border" zone may be related to severe

ischaemia, microscopic islands or peninsulas of infarction or sub-endocardial extent of infarction beyond areas of transmural infarction. Reversibility of asynergy can usually be induced in these zones by post-extrasystolic potentiation[47,48] or by nitroglycerin.[29,49,50,51] This contractile reserve within the ischaemic zone[52] may be the result of improved function of the residual normal myocardium or reversible ischaemia. The former is suggested by studies,[7] which show continuation of ischaemic patterns of contraction despite increased amplitude.

Several studies have suggested no significant lateral border zone exists,[38,53,54] although Jugdutt et al.[37] showed a lateral border zone width of 7 mm (mean). However, natural epicardial sparing does frequently occur.[38,53] In the former study, the transmural extent of infarction was slightly less at the borders than at the centre, which could in part explain the difference in response of the two zones to post-extrasystolic potentiation and nitroglycerin.

However, the overestimation of circumferential extent of infarction, the existence of an intermediate zone of function and its improvement with post-extrasystolic potentiation or nitroglycerin can all be at least partly explained by "tethering" - the transmission of wall motion of one region to an adjacent region. From a mechanical point of view, some degree of tethering is to be expected. However, the degree to which it contributes to the extent of abnormal wall motion, especially hypokinesis, but also akinesis, is unknown as are its effect on the severity of wall motion of the ischaemic zone.

ABNORMAL WALL MOTION AND THICKENING

As has been discussed already, epicardial dimensional shortening fraction is small and thus the major contribution to wall motion is thickening. Approximately 45% of this thickening is due to circumferential shortening, 40% radial shortening and 15% longtitudinal shortening.[20] Thus, thickening[39] and rate of thickening[43,55] are very sensitive in detecting changes in ischaemia. However, there are technical problems in measurement of thickness and rate of thickening in man.[24] Detection of the end-systolic endocardial edge may be difficult on LV angiograms and the epicardial border is often difficult to detect on two dimensional echocardiography. M-mode echocardiography is more suitable for examining changes over the cardiac cycle but is limited by small area and number of sampling sites.[56]

ABNORMAL WALL MOTION IN ISCHAEMIA AND INFARCTION

It has been shown that transient complete ischaemia (myocardial blood flow less than 0.1 ml/min/g) is indistinguishable from acute infarction when assessed by wall motion amplitude or thickening[47] despite the fact that these changes are completely reversible. Reversibility is related to the duration of the flow disturbance.[36] Occlusion for more than 20 minutes results in irreversible changes in the centre of the ischaemic zone both pathologically, and in terms of wall motion. Further, because of the relationship between myocardial blood flow and thickening,[32] abnormal wall motion may be present in the absence of infarction. The difference between these two functional states of the myocardium can be demonstrated by post-extrasystolic

potentiation[48] or nitroglycerin.[40] These interventions improve function in the chronically ischaemic zone, but not in the area of infarction. The improvement of function is reproduced by subsequent successful coronary bypass grafting to the vessel supplying the ischaemic zone.[58] The severity of the wall motion abnormality is partially predictive of reversibility.[50,58] Thus, paradoxical motion is rarely reversible, akinesis may be reversible and hypokinesis is frequently reversible. Whether or not this improvement is due to increased contraction of normal subepicardial zones or relief of the ischaemia, these findings show that wall motion cannot easily separate chronic ischaemia from infarction. Thus asynergy will tend to overestimate the extent of infarction.[40] Despite this, its assessment is valuable because it is the extent of abnormal motion and not actual extent of infarction, which determines function.[59] The size of this ischaemic and non-infarcted zone is variable.[59]

PATHOPHYSIOLOGICAL FACTORS AFFECTING WALL MOTION

The pathophysiological changes that occur with evolving myocardial infarction have a direct effect on the state of the myocardium and thus on the dynamics of its movement.

In dogs with induced acute coronary artery occlusions there is a time dependent change in function in the central ischaemic and marginal zones.[44,60,61] In the central ischaemic zone characteristic changes of systolic thinning with aneurysmal bulging occur due to loss of ejection tension.[44] The amplitude of this bulging is maximal between 15 minutes to 1 hour and decreases slowly over next 6 hours to

near zero. The reason for this change is a decrease in compliance. As cellular adenosine triphosphate (ATP) levels fall below 12 μ moles/g dry weight[10] in the ischaemic zone, free association of myosin and actin to form "rigor complexes" occurs without bound ATP. These "rigor complexes" stimulate rapid ATP hydrolysis and also result in decreased compliance of the central zone. This decreased compliance improves left ventricular function by reducing the negative effect of the aneurysmal bulging on overall stroke output.[60] This process is complete in all zones with ATP levels below 4 μ moles/g dry weight.

Segment lengths in the ischaemic zone also undergo stress relaxation within minutes of occlusion. The diastolic segment length increases by approximately 5% in the absence of any change in normal diastolic segment length.[62]

Much less work has been done on the behavior of the marginal zones that border the central ischaemic zone. These zones exhibit intermediate abnormalities of reduced systolic thickening and reduced systolic motion[33] associated with reduced ejection tension[63] and endocardial segment length shortening.[29] The size of this zone is controversial - from very small to equivalent to the size of the infarct. It is partly dependent on infarct size and geometry.[64] This controversy is partly related to limitations of methodology[54] and partly the result of varying interpretation of existing data. This zone is presumably a mixture of normal and necrotic tissue or a zone of ischaemia without infarction.[33]

The model of acute coronary occlusion in dogs has been very useful in understanding the pathophysiology of acute myocardial

infarction. However, human infarction is rarely due to sudden complete occlusion of a previously normal vessel. Occlusion may be transient, secondary to spasm, or incomplete - both resulting in a much higher percentage of contraction band necrosis than in acute complete occlusions.[36,65] Further, the infarction may occur over several days - especially if preceded by a history of pre-infarction angina.[66] This "stuttering" course of myocardial infarction[59,66,67] may be related either to a prolongation of the duration to complete necrosis in a single infarction or due to very early extensions of completed infarction - the extensions are almost always in the territory of the recently occluded artery.[66,68,69] These changes may be the result of local blood flow, metabolic, hormonal, haemorrheologic, haemodynamic or wall stress changes during the dynamic evolution of acute myocardial infarction. The influence of collaterals will be discussed later.

Reflow after temporary occlusion results in early development of oedema, cellular infiltrate and haemorhage associated with a broader band of contraction band necrosis,[36] although these changes are seen by 4 days in no reflow infarction - these changes profoundly affect the early changes in compliance of the ischaemic zone.[36]

COMPLIANCE

Compliance of the abnormal segment plays a major role in its behavior in the absence of contraction. Following myocardial infarction, a highly predictable series of histopathological changes occurs[70,71] although there is considerable variability in their extent and time course.

Initially, the central ischaemic zone becomes essentially avascular resulting in decreased tissue turgor. This, associated with loss of contractile function, leads to an increase in compliance[62] usually with systolic aneurysmal bulging. Early development of rigor complexes then tends to decrease compliance.[10] Subsequently, the mass and stiffness[72] of the infarct is increased by oedema, cellular infiltrate and variable amounts of haemorrhage.[36] Early in this phase, myocardial necrosis may also significantly affect compliance. In the healing phase the compliance decreases further as a result of increasing fibrosis with scar formation.[61,73]

A number of drugs have been shown to affect the healing process including methylprednisolone,[74] indomethacin[75] and ibuprofen[76] - the latter two drugs being commonly used for treatment of pericarditis associated with acute myocardial infarction. The end result of this interference with cellular repair is infarct expansion with significant diastolic segment length increase associated with major diastolic shape distortion and marked diastolic thinning of the affected myocardium. This process occurs in man in the absence of medications.[68,77]

This shape distortion is associated with significant decrease in pump function and thus with overall dilation of the ventricle.[78] As has been already stated,[19] this dilation is asymmetric, occurring more in the short axis than in the long axis altering the regional heterogeneity of wall motion amplitude. Further, increase in LV size increases wall stress and this results in a compensatory hypertrophy in the non-ischaemic zone[61] - an asymmetric hypertrophy which alters LV mechanics.

Conduction disturbance will result in asynchronous contraction which may have a more marked effect on overall LV performance in acute myocardial infarction depending on the compliance of the ischaemic segment. These can either be of bundle branch pattern or intraventricular conduction delay.

PRESENCE OF LV THROMBUS

It has been shown that in the absence of LV mural thrombus there is a sparing of an endocardial layer of up to 12 cells thick.[36,38,71] These cells develop into a dense layer of endocardial fibroelastosis.[79] This layer is non-compliant and tends to prevent aneurysmal bulging of the ischaemic myocardium. In the presence of mural thrombus, this layer of endocardium is lost.[79] The thrombus itself tends to decrease compliance, but with healing there is a greater likelihood of aneurysm formation. With time, the thrombus may be incorporated into the wall as collagenous scar [79] making endocardial definition difficult, and intefering with measurement of amplitude of motion and thickening of the affected segment.

LOCATION OF ABNORMAL WALL MOTION

Inferior myocardial infarctions have a better prognosis than anterior myocardial infarctions.[80] For equivalent sized infarctions, the frequency of aneurysm[81] and thrombus formation[82] is greater for anterior versus inferior infarcts. This suggests that the location of infarction may be an important variable in the subsequent process of healing.

Part of these differences are related to the extent of right ventricular involvement in the infarction process. Enzymatically estimated infarct size in inferior infarction includes both left and right ventricular necrosis. Thus, the extent of left ventricular infarction is greater in anterior than inferior infarcts. This results in greater depression of left ventricular function[83,84] and more widespread depression of regional function.[83] This latter study also suggested a degree of improvement in regional and global function not seen in Reduto's study.[84] Part of the difference may be related to the time interval from onset of symptoms to initial study (not specifically given in either study). However, it is possible that there are regional differences in the left ventricle in response to ischaemic injury due to mechanical or haemodynamic factors, collateral blood flow variability or fibre geometry.

In human infarction, the normality of coronary arteries not involved in the infarction cannot be assumed as it is for animal experiments. Severe stenosis of another coronary artery can induce motion abnormalities at a distance from the zone supplied by the occluded artery.[85,86] Weiss et al.[40] showed that in all but one of the segments judged to be akinetic but found to be normal pathologically, the abnormality was within the zone of an artery with at least a 75% stenosis.

Natural epicardial sparing occurs in human infarction[38] and is variable in extent. This is likely related to the degree to which collaterals can return myocardial blood flow towards normal balanced

against factors which increase myocardial oxygen demand. The development of collaterals in man takes time. Their presence at the time of acute infarction will be related to the duration of significant coronary artery stenosis.[87] Thus, the presence or absence of other coronary artery disease and of collaterals may have a significant effect on the ultimate infarct size, the presence of remote ischaemia and the extent and severity of wall motion abnormalities.

QUANTITATIVE ASSESSMENT OF ABNORMAL WALL MOTION

Gold Standard

The contrast left ventricular angiogram was the first in vivo method used to evaluate left ventricular wall motion in man. Quantitative information from angiography has been extensively validated against pathologically demonstrated infarction (65, 88) and coronary angiography (65, 89). As such, it has become the "gold standard" against which other newer imaging modalities have been judged. However other imaging modalities such as two dimensional echocardiography and radionuclide angiography do not reproduce the images of cineangiography and are not strictly comparable. Further, the value of comparison of extent of wall motion abnormalities with the extent of pathologically proven myocardial infarction is limited by the many dynamic factors which may influence regional wall motion (69). Thus, no true "gold standard" exists. Methods must be judged by their reproducibility and consistency with other experimental observations (90).

SUBJECTIVE VERSUS OBJECTIVE ASSESSMENT

Initial attempts to analyze cineangiograms relied on subjective assessment of wall motion - both in terms of extent and severity of abnormality. A grading system for severity of abnormal wall motion was established by Gorlin et. al (91) and extent was defined by the number of arbitrarily assigned segments (92) that were abnormal (93, 94). The great advantage of such an approach is simplicity. However, the reproducibility of the results is highly dependent on observer experience. An experienced observer may be fairly consistent but there may be significant inter-observer variation (94). A modification of this system is to use the end-diastolic outline to mark the extent of abnormal wall motion and express it as a percentage of the circumference (95). This percentage shows a close correlation with the size of infarction measured by accumulated release of CK-MB (88, 97) and to the impairment of global function (95, 98). These subjective methods have been used to evaluate abnormal wall motion demonstrated at echocardiography. Thus, Kisslo et al. examined the heart according to anatomic segments and related their findings to LV angiography (90). They found agreement in assessment of wall motion in 87% of all segments visualized by both methods. Echocardiography was less reliable in visualizing all segments (68%). Inadequate target identification was responsible for 23 of the 55 discrepancies bewteen the two methods (90). Heger et al. (99) showed that in a group of patients with acute myocardial infarction satisfactory visualization of the left ventricle was possible in 84%. Using a segmental approach the 2D echo reliably detected and determined the location of MI. They further showed agreement between 2D echo and autopsy findings in 94% of segments assessed

(99). Visser et al. (100) used a more extensive segmental approach to determine an estimate of infarct size and found a close correlation ($r = 0.87$) between CK-MB infarct size and the 2D Echo estimate of infarct size. Another modification of the segmental approach is the wall motion index (101-104). This index allows assessment of both extent and severity of abnormal wall motion and correlates closely with clinical subsets (101, 102), prognosis (102, 104) and infarct size as assessed by technetium pyrophosphate scanning (103) and thallium perfusion defects (103). Two other methods for quantitating extent of subjectively evaluated wall motion have used a similar approach to Field et al. (95) and expressed extent as a percentage of the endocardial diastolic circumference (40) or as a perimeter extent for serial studies (77). This method shows good correlation with pathological extent ($r = 0.90$) but 2D Echo consistently overestimates infarct size (40). Finally, subjectively evaluated wall motion abnormalities have been used to determine the extent of left ventricular surface area that is abnormal (105, 106) and this has also been shown to correlate closely with pathological (105) and CK (106) estimations of infarct size.

Objective Assessment

Although subjective assessment of abnormal wall motion has provided useful information, objective quantitation is more reproducible (107) especially in the evaluation of hypokinesis (94). For LV angiography a number of systems of superimposition of images in end-diastole and end-systole have been used (94, 107, 107a). Each method

makes assumptions that are not entirely true (108). Using a simple modification of the system of Herman et al. (109), Gelberg et al. showed that the area shrinkage method was superior to chord or perimeter shortening (110). Similar methods have been applied to cross-sectional images obtained by 2D Echocardiography. The endocardial outline is circular in normal studies and thus a geometric centre can be derived from which measurements of hemi-axial shortening, perimeter shrinkage and area shrinkage can be obtained (111). The area shrinkage method was again found to be the most reproducible (111). Further, of the 3 methods it has the most sensitivity, specificity and predictive accuracy in the detection of regional abnormal wall motion (112). However, major problems exist in the detection of hypokinesis because of the natural heterogeneity of wall motion as defined by these methods (5, 6). Thus, qualitative methods in 2D Echocardiography proved satisfactory for detecting sub-endocardial infarction (113, 114) where the most severe abnormality was hypokinesis in 50% of the patients (114) and in distinguishing between subendocardial infarction and normal studies in 85% of patients with chest pain and no prior infarction. Further, the technique can be used to show changes over time with specific treatment (105, 106) and in the early natural evolution of myocardial infarction (40, 100, 103, 104, 115).

Reproducibility

There are a number of limitations to the quantification of abnormal wall motion by two dimensional echocardiography (108). These can be divided into factors relating specifically to the technique of

echocardiography, those related to methods of quantification and those related to the variability of wall motion. The latter 2 have already been discussed.

The physical properties of ultrasound limit the resolution of the image in echocardiography. The reflection of ultrasound is dependent on the acoustic impedance of the medium. This is expressed as the half-power distance of the medium which is partly dependent on the frequency of ultrasound. Blood in motion has a high half-power distance and reflects virtually none of the ultrasonic beam whereas bone reflects nearly all the beam (116). The myocardium has variable reflectance depending on the amount of contained fibrous connective tissue (117, 118). It has been shown that these properties of attenuation and reflectance show predictable time related changes in areas of myocardial infarction (119, 120). The endocardial edge is frequently difficult to define (121) because it is a relative weak reflector of echoes and depends on absence of cavitary echoes for identification.

In the presence of stasis, secondary to cardiac dilation or myocardial infarction, blood may cause weak cavity echoes which may obscure the endocardial outline (82). Thrombus formation may have the same result (82). Because the endocardial edge is a weak reflector gain settings may be increased causing "blooming" - obscuring the underlying edge (108).

The resolution of any sector image can be divided into 3 components - axial, lateral and azimuthal. Axial resolution is constant at all levels of depth of field and is approximately 2.5 mm (122). Lateral and azimuthal resolution varies with depth of field from 2-3 mm in near field (123) to as much as 17 mm in far field (122).

These values depend on the instrumentation used and the energy of the beam (123). This resolution is also affected by the orientation of the edge to the beam. There is better resolution where the beam is at right angles to the edge than when it is nearly parallel. Further, reverberation may make edge detection more difficult and less reproducible and shadow effect due to intervening ribs can obscure detail.

These difficulties are magnified when defining epicardium where there is not a sharp image intensity interface (124) and where the signal/noise ratio is greatly reduced by ultrasound scatter in the adjacent lung tissue.

In specific patients further difficulty may be encountered because of chest configuration, obesity or emphysema.

For these reasons, the accuracy and reproducibility of 2D echocardiographic measurement of dimensions is less than M mode measurements (125, 126). However, part of this problem is related to loss of integrative data with stop frame analysis of 2D images, and lack of standards as to what constitutes the endocardial or epicardial edge (126). Parallax in measurement is also significantly greater on a curved monitor screen than with M mode format.

Finally, uncertainty as to the sector plane in space relative to long axis of the heart is only partly alleviated by recognition of internal landmarks such as mitral valve attachments. This uncertainty increases in ischaemic heart disease where normal anatomy may be distorted and particularly in all examinations of the apical region where no such landmarks exist (108). Further, due to translational and

rotational movements of the heart in space during systole, the image plane seen in diastole and systole may not be the same (26).

Despite these difficulties two dimensional echocardiography has been widely used to study acute myocardial infarction because it is non-invasive, portable and easily repeatable. It is capable of giving tomographic sections that view essentially all of the endocardium. It can give both structural and functional information. All of these attributes suggest a role in the serial evaluation of infarct limiting therapies. The purpose of this study was to establish a baseline for such evaluations.

STATEMENT OF THE PROBLEM

Principle Problems

(a) To assess the feasibility and reproducibility of repeated two dimensional echocardiographic imaging after acute myocardial infarction in man.

(b) To determine the natural history of abnormal wall motion in acute anterior myocardial infarction in man as assessed by two dimensional echocardiography.

Subsidiary Problems

(a) To determine, if possible, some of the clinical determinants of changes in abnormal wall motion over time in acute myocardial infarction.

(b) To establish a baseline of expected behavior of abnormal wall motion for the planning of future experiments designed to test the hypothesis that reduction of infarct size is possible with appropriate interventions.

METHODS AND PROCEDURE

Patients selected for study were those admitted to the University of Alberta Hospital with:

(1) A typical clinical history suggestive of acute myocardial infarction (MI)

(2) Typical ECG changes of acute MI.

Patients were excluded from the study if:

(1) There was a known history of previous myocardial infarction.

(2) Admission was delayed beyond 72 hours after the onset of symptoms

(3) Echocardiographic examination could not be performed within 96 hours of onset of symptoms for technical or logistical reasons.

(4) The initial two-dimensional echocardiographic study was considered unsatisfactory because of inadequate target identification.

(5) Subsequent ECG and cardiac enzyme evaluations failed to confirm acute infarction.

Patients were not excluded because of the presence of bundle branch block provided the other criteria for myocardial infarction were satisfied.

ECG's were performed (with the patient supine) on admission and repeated daily for the next 72 hours. The ST segments were evaluated according to the method of Hillis et al. (127) at 0.08 sec. after the J point for the 6 anterior (V) chest leads. The height of R (plus R) waves and the depth of Q waves was quantitated for the same leads and the results for all leads summated.

In the early part of the study echocardiographic examination was not performed for the first 48 hours after onset of symptoms because it was performed outside the coronary care unit. Thus, the group selected were those who survived to 48 hours and were stable enough to be transferred for examination. In the latter half of the study, patients were examined in the coronary care unit as soon as possible after admission. No attempt was made to control the treatment received by patients and all patients received normal care including opiates for pain, supplemental oxygen and prophylactic xylocaine for 24 hours and other medications as indicated.

There were 96 patients admitted to the University of Alberta Hospital with a diagnosis of acute MI during the 7 month period of enrollment. Of these, 51 patients presented with a first myocardial infarction. For technical reasons, only 41 patients actually had an initial echocardiographic examination. Of these, 33 patients were subsequently followed up, of whom the 16 patients with anterior MI represent the study population.

Echocardiograms were obtained using a phased array ultrasonograph (Toshiba Sonolayergraph or Varian 3400). A standard examination technique was used for each patient as previously described (128). The views obtained were:

(1) parasternal long axis

(2) apical four chamber view

(3) apical two chamber view

(4) serial parallel parasternal short axis views at mitral, chordal, papillary, low papillary and apical levels. (See Fig. 1)

All recordings were made in held end-expiration. The interrogating plane was considered optimal when the left ventricular outline was most nearly circular. Great care was taken to maintain constant transducer angulation for each short axis view, to keep the transducer perpendicular to the long axis of the heart and to move the transducer towards the apex in the line of that long axis. This usually required the patient to lie with a tilt to the left of between 30 and 60 degrees. Subsequent examinations were performed with approximately the same angle of tilt. An attempt was made to equally space the short axis views from base to apex. Images were recorded on videotape for subsequent analysis.

Echocardiographic examinations were performed within 96 hours of onset of symptoms with repeat examinations if possible on alternate days for the first week, pre-discharge, one month, two months, three months and at six months. At the time of each examination heart rate, blood pressure and medications were recorded. Clinical events noted included presence of hypotension, left ventricular failure, (including initial and maximal Killip class (129)), recurrent chest pain (including extension, expansion and pericarditis) and recurrent arrhythmias. Post-discharge events recorded included recurrent chest pain, myocardial infarction, onset of left ventricular failure, coronary bypass surgery and New York Heart Association functional class (130).

Blood samples for cardiac enzyme determinations were drawn routinely on admission, 8 hourly for the first 48 hours and once more at 72 hours. Calculation of CK Infarct size was made according to the method of Roberts et al. (131).

Method of Data Analysis

All echocardiograms were analyzed by one observer as part of a a larger study involving all 33 patients with first acute MI followed up. The observer was blinded to the identity of the patient and the timing of the examination relative to the onset of chest pain. Analysis was performed by a method similar to Gibson et al. (104). After each view had been identified (see Fig. 3), endocardial and where possible epicardial outlines were traced on plastic overlays from stop frames images of end-diastole and end-systole of the same cardiac cycle. The frame count number was noted for subsequent reproducibility studies. End- diastole was defined by placing a cursor on the peak of the R wave on the ECG. End-systole was determined at the beginning of each study by setting a cursor on the ECG tracing to coincide with aortic valve closure. The interval between the two cursors was assumed to be constant throughout the study. Still frame edge detection was augmented by too and fro playback for each view. Intracardiac landmarks were marked and where possible both right and left ventricular outlines were drawn. The end-diastolic tracing was superimposed on the end-systolic image and subsequent too and fro playback of the images in each view allowed the detection of abnormal wall motion. This was classified into 4 groups as defined by Gibson et al. (104).

(1) Normal

(2) Hypokinesis - a reduction of endocardial wall motion relative to a normal zone within the same section associated with a greater than 50% reduction in systolic thickening relative to normal zones as judged visually and with the aid of the end-systolic tracing.

(3) Akinesis - absence of endocardial motion associated with absence of wall thickening.

(4) Dyskinesis - Paradoxical motion - systolic outward motion of the endocardial edge associated with systolic thinning.

All degrees of wall motion abnormality were partially assessed by displaying the systolic image with the diastolic outline superimposed. The extent and severity of abnormal wall motion was marked on the end-diastolic outline and corrected on further playback analysis.

This process was repeated for all available sections for each examination.

During analysis of each section note was taken as to the presence or absence of ventricular thrombi and their location was marked on the tracings.

Image quality was empirically graded for each section according to endocardial edge definition:

(a) Good - all endocardium clearly visualized.

(b) Adequate - some small areas of endocardial drop-out but outline easily interpolated.

(c) Poor - significant regional endocardial drop-out making outline difficult to interpolate.

Despite initial screening before entry, a significant number of sections could not be analyzed because of insufficient endocardial detail in one or more quadrants. For this purpose a minimum of 50% of endocardial targets in each quadrant needed to be identified for successful analysis as suggested by Kisslo et al. (90). Results were tabulated for each view. The diastolic endocardial tracings were digitized electronically on a Hewlett Packard HP9835A digitizer to obtain:

(1) the length of the arc of abnormal wall motion - both the total extent and the extent of each degree of severity of abnormal wall motion.(See Fig. 2)

(2) the circumference for each section.

The reproducibility of these measurements by digitizer was checked by repeat digitization of 30 sections. Maximum error was 0.05 cm and averaged 0.02 cm.

Reproducibility of the detection of abnormal wall motion was determined by one observer by:

(a) repeat blinded analysis of the same examination in 20 patients

(b) blinded analysis of repeat examination done in 19 patients with past history of myocardial infarction and stable clinical status with no change in medications.

These results were analyzed in terms of circumferential extent (expressed as percentage of total circumference) of paradoxical motion and akinesis, total extent of abnormal wall motion and extent of paradoxical motion alone in all cross-sections.

Statistical Analysis

Not every patient had an examination at each time zone and not all examinations were complete. The long axis views were those most frequently obtained. Thus, it was possible to examine changes over time for a larger number of time zones in selected patients who had complete examinations. The time zones chosen were:

(a) 0 to 72 hours, 3 to 5 days, 8 to 10 days, 1 month, 3 months and 6 months

(b) 3 to 5 days, 6 to 7 days, 8 to 10 days, 1 month, 2 months, 3 months and 6 months

(c) 3 to 5 days, 6 to 7 days, 8 to 10 days, 1 month, 3 months and 6 months

When looking at all sections, the data was grouped into 4 time zones: 0 to 5 days, 8 to 14 days, 1 to 2 months and 3 to 6 months. Where a patient had more than one examination performed during a time frame, the mean value was used. The one patient who died within 24 hours of admission was excluded from analysis.

The data from the 2 long axis views (parasternal long axis and apical four chamber) was combined to obtain a mean - the long axis composite - the two views were considered to be 2 planes of the heart at 90° to each other. The mean values for each patient were grouped in the same way as for individual sections.

The mean values for each time zone for each section and each degree of severity of abnormal wall motion were compared using a two way ANOVA. Where the null hypothesis was rejected, the significance of differences was tested by multiple paired T tests. A p value less than 0.05 was regarded as significant.

The population was arbitrarily divided into two groups according to the peak value of serum creatine phosphokinase (CK).

Small infarction - less than 1150 I.U./ml.

Large infarction - greater than 1150 I.U./ml.

Because of small numbers, this analysis could only be performed for a few selected views.

The patient population was also divided according to:

(1) Summation of Q waves in the anterior chest leads of ECG at 48 hours

(a) less than 2 mV

(b) 2.0 to 4.5 mV

(c) greater than 4.5 mV

(2) extent of paradoxical motion on initial echocardiogram as assessed by the mean of the long axis views

(a) less than 8%

(b) 8 to 15%

(c) greater than 15%

(3) total extent of abnormal wall motion on echocardiogram as assessed by the mean of the long axis views at 3-5 days

(a) total A.W.M. greater than 35%

(b) total A.W.M. less than 35%

(4) extent of akinesis and paradox on echocardiogram as assessed by the mean of the long axis views at 3-5 days

(a) greater than 30%

(b) less than 30%

(5) according to clinical events in hospital

(a) increase in Killip class during admission

(b) unchanged Killip class during hospitalization

(6) according to recurrence of chest pain during follow-up

(a) angina or recurrent MI during follow-up

(b) no recurrent chest pain

Changes over time were tested for each group using the same statistical procedures as for the whole population.

Variability of assessments of extent of abnormal wall motion was calculated as the mean of differences between measurements for each view. Thus

$$\text{Mean Error \% Circumference} = \frac{\sum_{i=1}^{n} (x-y)}{n} \times 100\%$$

where x = first observation as % circumference
y = second observation as % circumference
n = numbers of pairs of observations
(x-y) is always considered as a positive number

The variability of measurement relative to the actual measurement was calculated for each section as

$$\text{Relative Error \%} = \frac{\text{Mean Error \% Circumference}}{\text{Mean value of A.W.M.}} \times 100\%$$

These calculations were repeated for each section and each degree of severity of abnormal wall motion. This was done for repeat analysis of the same examination (Reproducibility 1) and repeat examination and analysis of a stable patient with past history of myocardial infarction (Reproducibility 2).

The mean error % circumference for all examinations in all views was summated for each degree of severity for Reproducibility 1 and Reproducibility 2.

In the same way, the relative error % for all examinations in all views was summated for each degree of severity for each study.

Differences between Reproducibility 1 and Reproducibility 2 were then tested for significance by a student t test.

The proportion of variability due to repeat analysis relative to variability due to repeat examination was calculated for each degree of severity for mean error % and for relative error %. Differences were tested by a Chi squared test.

Linear regression analysis was used to correlate the echocardiographically determined extent of abnormal wall motion ng axis section at 0 to 5 days with peak CK, the sum of Q wave ıe anterior chest leads at 48 hours and ejection fraction (EF) determined echocardiographically. The extent of abnormal wall motion at 3-6 months was also correlated with the echocardiographically determined ejection fracton at that time.

Left ventricular ejection fraction was calculated by planimetry of the endocardial outlines of the two long axis sections in end-systole and end-diastole using a Simpson's rule for areas program. The long axis lengths were digitized and ejection fraction calculated using the Dodge-Sandler formula for two views (132).

All values were expressed as mean $\pm$ S.E.M.

RESULTS

There were 16 patients who were considered suitable for study. The in-hospital clinical data is shown in Table 1. The ages ranged from 29 to 76 years, with a mean of 56.1 $\pm$ 3.3 years. There were 13 males and 3 females. Admission Killip class score was (mean) 1.6 $\pm$ 0.1. There was a slight increase in overall Killip class score to mean 2.2 $\pm$ 0.2 during hospitalization. In 9 patients Killip class remained unchanged and in 7, it increased. Three patients had hypertension for more than 6 hours and two patients had significant hypotension unrelated to bradycardia or heart block. One of these patients progressed to cardiogenic shock and death within 13 hours of admission and was not included in subsequent analysis. Pericarditis occurred in 7 patients and infarct extension, verified by new enzyme elevations and ECG changes associated with chest pain, was confirmed in 3 patients. One patient developed an acute V.S.D. two days after admission and was treated surgically prior to discharge from hospital.

The ECG data is shown in Table 2. The first ECG was performed at 0.5 to 64 hours - mean 14.8 $\pm$ 5.2 hours - after the onset of chest pain although 10 of 16 patients had the first ECG within 8 hours. The location of the ischaemic changes was antero-septal (16), antero-lateral (12) and inferior (2). Two of the antero-septal MI's were sub-endocardial. The ST segments were not summated because of widely varying times of presentation. The summation of the R waves in the anterior leads at 48 hours was a mean 1.3 $\pm$ 0.3 mV but correlated poorly with other indices of infarct size (peak CK, extent of left ventricular

abnormal wall motion). The summation of Q waves in the anterior chest leads at 48 hours ranged from 0 to 6.8 mV with mean 3.7 ± 0.5 mV.

The enzyme data are shown in Table 3. The range in peak CK values was 231 to 4405 I.U., with a mean 1908 ± 296 I.U./ml. The range of CK Infarct sizes was 5.6 to 162.7 g/Eq, with a mean of 47.8 ± 10.2 g/Eq.

The follow-up data over the six months of the study and beyond is shown in Table 4. Recurrent angina occurred in 9 patients and progressed to myocardial infarction in 3 - although only in 1 within the 6 months of the echocardiographic study. The patient with a V.S.D. complicating MI had open heart surgery at one month post-infarction to repair the defect. The duration of clinical follow-up was 6 to 23 months, with a mean 12.4 ± 1.6 months. No patient died of primary cardiac causes during follow-up. However, two patients died of a C.V.A. and in both cases embolic stroke was suggested. At their last echocardiographic examination both had persistent LV apical thrombus (see Table 5).

The qualitative echocardiographic data is shown in Table 5. The delay in imaging the patients following onset of chest pain ranged from 5 to 94 hours with a mean of 53.1 ± 6.5 hours. All patients had apical, antero-septal and antero-lateral abnormalities. Echocardiography tended to suggest more extensive infarction than did ECG but otherwise agreement was good between the two methods. All except one patient had apical paradox and four patients also had some antero-septal paradox. Left ventricular thrombus was present in 12 of 16 patients on initial echocardiogram and was still present in 11 of

the 12 at 6 months although the morphology of the thrombus had changed from protruberant to mural. Biplane ejection fraction, calculated from the two long axis views (Longitudinal and Apical 4 Chamber) was 33.0 $\pm$ 1.8% on first echo examination and 35.0 $\pm$ 2.0% at the 6 month echo examination. The difference was not statistically significant.

Table 6 (a, b, c, d) describes the ability to obtain adequate quality serial echocardiograms in this study. For logistical reasons patients did not all have examinations at the prescribed times (see Table 6(b)). However, all patients were studied at the 4 time intervals given in Table 6(c). Although an echo examination was attempted in these 16 patients a total of 126 times not all views were successfully recorded. Table 6(d) gives a breakdown of success of recording individual sections these studies. At the start of the study Apical 2 Chamber and Low Papillary cross-sectional views were not routinely recorded and will be excluded from further consideration. Incorrect orientation of the view recorded increased in a step-wise manner from 0% at mitral valve cross-section to 7.9% at the apical cross-section. Similarly, inadequate definition sufficient to prevent analysis was more common at apical cross-section (9.5%) than mitral cross-section (0%). Thus if all cross-sections were attempted during the examination it can be assumed that inadequate visualization for the purposes of recording was also more frequent as the transducer was moved from base (0.8%) to apex (17.5%). These differences are most likely due to an inability to obtain a satisfactory apical window, interposing lung tissue and fewer internal landmarks for section recognition during both recording and playback analysis. This difficulty in lower left ventricular cross-sections resulted in a

smaller percentage of successful examinations and analysis of apical (65.1%) versus mitral (99.2%) cross-sections. Thus only 38.9% of all examinations were complete although 91.3% had 3 cross-sections.

The longitudinal and apical 4 chamber views were consistently imaged and analyzed but there was a significant number of examinations in which the apical 2 chamber view was inadequate for analysis. This was either the result of marked foreshortening or inadequate target visualization of the anterior wall.

The empirically assessed image quality of analyzed views is shown in Table 7. The image quality of the apical 4 chamber, mitral and chordal cross-sections was significantly better than for all other views. Image quality was poor more frequently in the longitudinal view and in the mid-papillary cross-section. In the longitudinal view there was usually poor posterior and apical wall definition. In mid-papillary cross-section there was usually poor lateral wall definition and occasionally poor posterior wall definition. Thus, in neither case did the area of poor definition have a major effect on the interpretation of abnormal wall motion in these anterior myocardial infarctions.

Figure 4 represents an actual tracing of stop frame video images in systole and diastole of mid-papillary cross-sections in one patient at initial examination and at 3 months. The relative positions of the papillary muscles and the posterior RV-interventricular septum intersection suggest that the 3 month study cross-section is slightly closer to the apex than in the initial study. But, as is shown below, the differences between the two studies in extent of AWM is unlikely to

to be explained on this basis. The extent of total AWM was 34.0% and 47.3%. The extent of akinesis plus paradox was 27. and 42.4%. The extent of paradox only was 10.9% and 18.8%. The increase in extent of AWM was associated with slight diastolic anterior wall thinning and marked diastolic shape distortion. In neither case is the view entirely circular suggesting a slightly oblique section but the changes are not significantly affected by this. Left ventricular thrombus had developed in this area of shape distortion (aneurysm).

Figures 5 (a, b, c) represent the results of serial evaluations of abnormal wall motion in one patient over the 6 months of the study plotted on a logarithmic scale for clarity. Each point represents one echocardiographic examination. This patient developed recurrent myocardial infarction after the 3 month study. Figure 5(a) shows the values for total AWM during the study. There was a non-significa t fall in extent of total AWM in the Longtitudinal and Apical 4 Chamber views over time until 3 months. The mean value of total AWM for 2-3 months and 6 months were 31.9% and 39.6%, $p < 0.05$ for Longitudinal view and 32.0% and 40.6% $p < 0.05$ for Apical 4 Chamber view. The increase was the result of a significant increase in AWM in the lateral wall on chordal 5.6% to 25.0%, $p < 0.01$ and Mid-Papillary 31.5% to 46%, $p < 0.05$ cross-sectional views. There were no significant changes in Low Papillary and apical cross-sections. Figures 5(b) and (c) show the serial values of akinesis plus paradox and paradox alone respectively. For akinesis plus paradox there were no significant differences over time for any views except Chordal and Mid-Papillary cross-sections which increased from 0% to 20.1%, $p < 0.01$ and 25.6% to

38.3%, $p < 0.05$ respectively for pre and post recurrent infarction studies. For paradox alone (Figure 5(c)) there were no significant changes over time except in Mid-Papillary cross-section which increased from 8.7% to 17.1%, $p < 0.05$ with the recurrent MI. As can be seen there is considerable scatter of the points reflecting the inherent variability of measurement.

The results of the follow-up study for each section are displayed in Figures 6, 7 and 8. In each case, for each section there are no significant differences between time zones by ANOVA testing. Because there were no significant differences shown, several time zones were combined so that all 15 patients were examined at each of the 4 time zones chosen. Once again for the whole group there were no significant changes over time by ANOVA testing (see Fig. 9).

To test the hypothesis that different sizes of infarction might behave differently over time, the patient population was divided arbitrarily into groups with small to large infarctions by three different methods.

Firstly, a level of peak serum CK of 1150 I.U./nl was used to divide the patients into two groups. The results are shown in Fig. 10 (a to e) for each view with an adequate number of patients. There was no significant differences in AWM over time in either group in the Chordal (Fig. 10 (d)) and Mid-Papillary (Fig. 10 (e)) cross-sections. However, for both the Longitudinal and long axis composite views there was a significant fall in extent of total AWM and akinesis plus paradox over time in the group with small infarcts. for the longitudinal view total AWM fell by 27.8% from the initial time zone to the 3-6 month studies, $p < 0.01$ and for the same time zones extent of akinesis plus

paradox fell 26.8%, $p < 0.01$. There was no change in extent of paradox alone. For the Apical 4 Chamber view (Fig. 10(b)) there was a non-significant decrease in total AWM of 15.4% but a 35.0% decrease in extent of akinesis plus paradox, $p < 0.01$. Once again there was no change in the extent of paradox alone. For the long axis composite there was a 21.9% decrease in extent of total AWM, $p < 0.05$ and a 26.8% decrease in extent of akinesis plus paradox, $p < 0.01$. There was no significant change for paradox alone. The changes were maximal at the last study period but appropriate graduated changes were seen at intermediate time zones. It has already been shown that there was no significant change in the overall group between 3 and 6 months. When these time zones were examined for small infarcts then a slight nonsignificant decrease in extent of both total AWM (7.0%) and akinesis plus paradox (10.7%) was seen in the long axis composite. This suggests that the decrease in extent of AWM continues for up to 6 months. The greater decrease in akinesis plus paradox coupled with no change in extent of paradox alone suggests that a significant amount of akinetic wall becomes hypokinetic over time and only a small amount of akinetic wall becomes normal. That this is so is further suggested by the fact that the initial extent of akinesis plus paradox is not significantly larger (28.8% versus 23.8%) than the extent of total AWM of the end of the study. The absolute extent of hypokinesis alone was not significantly larger (6.3% versus 5.6%) at 3-6 months versus the initial stud[illegible]

[illegible](a, b, c) displays the results when the patients are divided into [illegible]oups according to one ECG criterion for infarct size,

ΣQ at 48 hours. The numbers arbitrarily chosen were 0 > 2.0 mV, 2.0 > 4.5 mV and > 4.5 mV and divided the patients into 3 equal groups. Group 3 with ΣQ of 0 to 2.0 mV corresponded exactly to the patients with peak CK less than 1150 I.U. Those with the large infarctions (group 1) ($\Sigma Q_{48\ hrs} > 4.5$ mV) showed no significant changes with time for any degree of severity of wall motion abnormality and for any view tested (Longtitudinal, Apical 4 Chamber and the combined long axis composite). For the group with medium sized infarctions (group 2) ($\Sigma Q_{48\ hrs.}$ 2.0 > 4.5 mV) there were significant increases in extent of total AWM and of akinesis plus paradox for the Apical 4 Chamber view of 20.4%, $p < 0.05$ and 26.9%, $p < 0.05$ respectively. For the parasternal long axis view (Longtitudinal) the increases were not significant. However, for the combined long axis composite the increases were 16.7%, $p < 0.05$ and 19.9%, $p < 0.05$. There were no changes in any view in extent of paradox alone. The increases in extent were mainly related to changes in shape of the affected segments although lateral wall extension was seen in one patient. This diastolic shape distortion was seen in 10 patients at 6 months. All 5 patients with medium sized MI's had an apical aneurysm which was localized in 4 and diffuse in 1. Those 5 patients with large infarctions also had an aneurysm but in 4 of the 5 patients it was diffuse and in only 1 was it localized. Because of the method used to calculate circumferential extent, diffuse shape distortion will tend to underestimate increases in extent of AWM whereas segmental shape distortion will result in significant increases in % AWM.

Figure 12 displays the results for the long axis composite when the patients were divided according to the extent of paradox in the long axis composite on the first echocardiographic examination. The group with small infarcts (less than 8% paradoxical motion) was the same as the group with small infarcts by peak CK and $\Sigma Q_{48\ hrs}$. The other two groups overlapped with those divided by $\Sigma Q_{48\ hrs}$ but the results were similar. There was an increase of 13.0%, $p < 0.05$ and 16.4% $p < 0.05$ for total AWM and akinesis plus paradox respectively in the group with medium sized infarcts. For total AWM this change was gradual over the 6 months of the study but for akinesis plus paradox most of the change occurred in the first two weeks. For those with large infarction (paradoxical motion of greater than 15% on first study) there were no significant changes over time.

Table 8(a) and (b) display the results when the patients were divided according to the extent of abnormal wall motion on the 3-5 day examination - for akinesis plus paradox (a) and total AWM (b). There were no signficant within group differences over time for any degree of severity of AWM. This suggests that neither the initial extent of total AWM nor of akinesis plus paradox predicts those infarcts which will get smaller or larger as assessed by AWM. This result is at least in part related to the variability of measurement.

Table 9(a) and (b) display the results when the patients were divided according to clinical events - (a) increase in Killip class during admission versus unchanged and (b) angina or recurrent MI during follow-up versus no recurrent chest pain. From Table 9(a) it can be seen that an increase in Killip class during initial admission was not

associated with any significant increase in extent of AWM either on the pre-discharge studies (8-14 days) or subsequently. From Table 9(b) it can be seen that the occurrence of post-infarction angina (9 of 15 patients) did not effect the extent of abnormal wall motion over time and did not differentiate those patients with large or small infarctions (Between group differences not significant). Recurrent MI occurred in only 3 of 15 patients and in only 1 within the 6 month follow-up period. In this one patient recurrence of MI was associated with an increase in total AWM of 23.3% $p < 0.01$) and in akinesis plus paradox of 8.9%, N.S. in long axis composite versus the 2 and 3 month studies done prior to recurrent MI. In cross-sectional views the majority of the increase was seen in the chordal cross-section where total AWM increased from 5.6% to 25% and akinesis plus paradox from 0 to 20.1% (both $p < 0.01$). Extent of paradox alone was not significantly different.

There were no significant changes in extent of AWM for low papillary and apical cross-sections and no study at the mid papillary level was available for comparison at either 2 or 3 months. However, earlier studies had a mean of 8.7% whereas studies after the recurrent MI had a mean of 17.1%. Thus, the study was capable of detecting and localizing extensions to an existing MI in this one patient.

Correlation Studies

To assess the reliability of these studies, comparison was made with other indices of size of myocardial infarction. Thus, Figure 13 displays the relationship between peak CK and extent of AWM - of total

AWM, akinesis plus paradox and of paradox alone (from left to right). the slope of the three curves is similar at 128, 126 and 111 respectively. However, the intercept shift from -2450 (for total AWM) to 578 (for paradox alone) confirms that small infarcts rarely have significant akinesis and/or paradox whereas large infarctions usually do. The relationship is similar for total AWM and akinesis plus paradox (r = 0.70 and 0.66 respectively) but there is greater variability of extent of paradox in relation to peak CK (r = 0.54). This suggests that looking at extent of paradox alone is an unsatisfactory method of assessing infarct size but that total AWM and akinesis plus paradox are equally suitable. The relationship between the two variables was significant at $p < 0.01$ for total AWM and akinesis plus paradox and at $p < 0.05$ for paradox alone. Thus, although there is significant scatter reflecting the lack of precision of both variables the results suggest that AWM can be used as an indicator of infarct size.

Another measure of infarct size ($\Sigma Q_{48\ hrs.}$) was compared to the extent of AWM on the long axis composite and the relationship is shown in Figure 14. From left to right the independent variable is total AWM, akinesis plus paradox and paradox alone. As can be seen, the only significant relationship is between the extent of paradox alone and $\Sigma Q_{48\ hrs.}$, $p < 0.01$. The intercept is close to zero suggesting that paradoxical motion does not occur in the absence of significant Q waves in these anterior infarctions. The lack of a relationship between $\Sigma Q_{48\ hrs.}$ for both total AWM and akinesis plus paradox suggests that $\Sigma Q_{48\ hrs.}$ is a less satisfactory way of determining infarct size than AWM especially when the relationship between peak CK and AWM (Figure 13) is considered.

The relationship between extent of abnormal wall motion and global function is shown in Figures 15 and 16. As has already been shown in Figures 6-9 there are no significant differences in AWM over time nor is there a significant change in global function (LVEF 34±1.6 at 0-5 days and 35.0±2.0% at 3-6 months. The relationship between LVEF and extent of AWM - total AWM (left) and akinesis plus paradox (right) - is very similar for 0-5 day studies (Figure 15) and 3-6 month studies (Figures 16). The intercepts for total AWM are 60.8% and 60.3% for the 0.5 days and 3-6 month studies respectively. The intercepts for akinesis plus paradox is 57.2% and 56.4% respectively in the same studies. This suggests that the extent of hypokinesis has a slight but measurable effect on overall left ventricular function in this group of patients. Further, it suggests that analysis of hypokinesis on the echocardiogram is worthwhile despite methodological difficulties.

These correlations offer indirect evidence that AWM, as measured in these studies, reflects the extent of myocardial infarction.

Reproducibility

The extent to which the method of assessment of abnormal wall motion is reproducible has an important bearing on demonstration of significant differences between groups. Thus, reproducibility studies were undertaken. The results are summarized in Table 10. The absolute difference between two readings rather than the average difference from the mean was used because this approach estimates the random variation when comparing two time intervals. Two methods of looking at

variability were used - the actual difference between 2 readings (as a percentage of circumference) and the difference relative to the mean percent extent of abnormal wall motion. It is assumed in this study that the maximum variability should occur when a new study is performed and analyzed at a time separate from the original study. The minimum variability should occur when the same study is reanalyzed.

Tables 10(a) and (b) outline the results for variability of each view for each degree of severity. Mitral cross-section is not included in this study because in all but 2 patients studied this section was normal. The variability of 2 measurements of the same echo examination (Reproducibility 1) ranged from 1.80 to 4.69% of LV circumference. As the LV circumference decreases from base to apex in cross-sectional views the absolute error (in centimetres) remained fairly constant for all views. The range for total AWM was from 0.64 to 0.85 cm, for akinesis and paradox from 0.38 to 0.70 cm and for paradox alone from 0.47 to 0.74 cm.

The variability of measurement of extent of abnormal wall motion of two echocardiographic examinations performed and analyzed by the same observer (Reproducibility 2) ranged from 2.84 to 8.44% of LV circumference. The absolute error (in centimetres) ranged from 0.67 to 1.78 cm (total A.W.M), 0.70 to 1.57 cm (akinesis and paradox) and 0.47 to 1.05 cm (paradox only).

Total A.W.M. variability for Reproducibility 1 was significantly less than for Reproducibility 2 in 4 of 7 views. Comparable figures for akinesis and paradox were 5 of 7 views whereas in only 1 of 7 views was variability significantly different when assessing paradox

alone. However, in only 1 of 21 views was variability less for Reproducibility 2 than for Reproducibility 1.

The relative error was much larger (as a percentage) than the absolute error. The extent of AWM was the major determinant of the size of this error as would be expected with a relatively constant absolute error. Thus, relative error was largest in the chordal cross-section (where mean extent of AWM was smallest) and smallest in apical cross-section (where mean extent of AWM was largest.

Tables 10(c) and (d) reflect the magnitude of variability based on severity of AWM that was assessed. In all cases variability in Reproducibility 1 was significantly less than for Reproducibility 2. Further in Table 10(c) it can be seen that variability was greatest for total AWM. For Reproducibility 1 total AWM variability 3.28±0.10% was significantly greater than both other categories which were not significantly different from each other. For Reproducibility 2, paradox alone variability was significantly smaller than the other two. The differences between variability of total AWM (5.14±0.46%) and akinesis and paradox (4.61±0.41) failed to reach statistical significance. The reason for the differences in ability to assess the extent of AWM of varying severity between the two studies is not apparent.

Table 10(d) shows the results for relative error for variability at each degree of severity of AWM. Here, variability in Reproducibility 1 is significantly less than for Reproducibility 2. However, because of the dominating effect of the mean value of AWM on the relative error, for both studies paradox alone has the largest error. Thus, in this longtitudinal study, significant differences between

groups at different time intervals are most easily demonstrated for total AWM and least easily for paradox alone. Akinesis and paradox AWM is intermediate between them.

The proportion of the variability due to reanalysis of the same study relative to assumed maximal variability is shown in Table 10(e). The results show that significantly greater than 50% of the maximal error is related to simple reanalysis. This was true for absolute error (% circumference) but only true for relative error in assessment of paradox alone. The variability was similar for assessment of akinesis and paradox by both methods. Thus, the major source of variability in all studies with one observer is reanalysis of the same echocardiographic examination.

In all reproducibility studies, variability has been assessed as the absolute difference between 2 values. This is appropriate for comparison of single values. However, in comparing group data the mean error and relative error should be divided by 2 to give the average variation from the mean value. If this is done, the variability for all report studies will be half those shown in Tables 10(a), (b), (c) and (d).

DISCUSSION

The introduction of coronary care units has resulted in a major reduction in mortality secondary to arrhythmias in the first few days after acute myocardial infarction (2a). Residual mortality is now mainly related to the extent of myocardial necrosis (3, 59, 69). Thus, the objective in treatment of acute myocardial infarction has shifted from prevention of complications to active intervention to try and reduce the extent of myocardial necrosis (2). That this is theoretically possible has been shown in animal studies (29, 30, 133-140). However, verification of these results in man required a reliable method for non-invasive assessment of extent of myocardial infarction. Many studies have demonstrated that myocardial infarction results in left ventricular asynergy (1, 29, 39, 81, 84, 91, 93). Recent studies have shown that two dimensional echocardiography can reliably detect left ventricular asynergy (90, 141) and give a quantitative estimate of infarct size that is comparable to other methods (39, 40, 100, 103, 105, 142) although 2D Echocardiography consistently overestimates myocardial infarct size (40, 142). This study confirms the findings of others that echocardiography usually demonstrates larger abnormalities than would be predicted from the ECG (100, 104, 113, 143). It confirms the findings of others (100, 103, 144, 145) who have shown that in the period immediately after acute myocardial infarction no change in extent or severity of abnormal wall motion occurs although shape distortion occurs frequently (77, 146), but extends them to 6 months. However, in patients with a small myocardial infarction there is a gradual reduction of left ventricular abnormal wall motion over the 6 months.

This study does not address the issue of changes in the first 3 days after infarction. Thus, it is unlikely that the decrease seen subsequently in extent of abnormal wall motion in small infarctions is related to reversible acute ischaemia. Rather it is more likely due to increased density of the infarct zone (147) with increased fibrous tissue (71) and scar shrinkage (147). Recovery in marginal (hypokinetic) zones may be related to decreased ischaemia or secondary to hypertrophy (61) in response to decreased left ventricular function and abnormal wall stress. It is unlikely to be related to changes in compliance of the abnormal zone (and thus in tethering) because there was no change in the extent of paradoxical motion over time even in the small infarctions (although the amplitude of paradox was not assessed). From the work of Lieberman et al. (39) it is suggested that the major determinant of paradoxical motion at 48 hours post-infarction is the transmural extent of infarction. If this was greater than 20% then paradoxical motion was seen. In their study only a small number of segments were in the transition zone - thus the majority of paradoxical segments can be expected to have greater than 60% transmural extent. It is unlikely that significant functional change could occur in this setting where viable epicardium is insufficient to maintain regional shape (148). Any effect of scar shrinkage may be offset by the effects of infarct expansion which, when present, seems to be progressive (77).

In patients with large infarctions there was no change over time in the extent of abnormal wall motion as a % of left ventricular circumference. This was despite the fact that all 5 patients developed aneurysms. These aneurysms were diffuse and associated with marked

progresive left ventricular dilation as previously shown by Erlebacher et al. (78). In this setting no change in extent as a percentage of circumference can be demonstrated (78) even though changes in perimeter extent did occur in both this study and that of Erlebacher et al. (78) because parallel changes in circumference minimize percentage differences.

In the patients with medium sized infarcts there was an increase of 16.7% and 19.9% in extent of total AWM and akinesis plus paradox respectively. This was associated with clinically detected infarct extension in only one patient (versus 2 with large infarctions) - in this patient echocardiography also detected lateral extension of the infarction. Thus, the increase in extent in these medium sized infarcts appears mostly related to development of a shape distortion. Four of the five developed a discrete aneurysm without major left ventricular dilation. However, that this was of functional significance can be seen by the constant relationship between LVEF and the extent of AWM from 3-5 days to 3-6 months (Table 15, 16).

That an aneurysm developed in all 10 patients with mid to large infarctions is compatible with the canine model studies of Eaton et al. (148) where there was expansion of 81% of all transmural infarctions and in none with subendocardial infarctions.

In large part, the results of this study are dictated by the methodology used to assess the extent of AWM. The method used is that of Weiss et al. (40), which is a modification of that of Field et al. (96) for LV angiograms. The major limitations of the method of Eaton et al. (77) for anterior and posterior segment lengths is that it can

only be applied to cross-sections with constant internal lankmarks that are easily identifiable. It cannot be easily applied to long axis views nor to apical cross-sections. The method undoubtedly has greater sensitivity for detecting regional change - especially in the presence of shape distortion, but it was not used because of difficulty in obtaining the exact location of internal landmarks and its lack of general applicability to all sections. Further, no attempt was made to use quantitative measures which use a geometric centre (108) because such programs were not available. In the setting of shape distortion in diastole (aneurysm) or systole (paradoxical motion) the determination of the central point in the long axis of the ventricle for each section is complex and was beyond the scope of this study. However, such methodologies have the potential advantage of more effectively detecting changes related to shape distortion and true extension or shrinkage of the zone of abnormal wall motion.

This study demonstrated a progression of extent and severity of abnormal wall motion from the base to apex in these patients with anterior infarctions. This reflected a fairly constant infarct shape. The differences in extent of AWM between serial cross-sections was 15-20%. Thus, the small errors in reproducing the interrogating plane could produce variations in extent of 5-10%. In the serial studies this is particularly important because shape distortion makes determination of the plane of section and correct angulation more difficult and oblique sectioning more likely. Despite these potential problems, the major component of variability for the one observer/operator in this study was related to reanalysis of the same echocardiogram. The size

of this variability ranged from 0.38 to 0.85 cm. This is very similar to the 6 mm for inter-reader variation found by Eaton et al. (77) although higher than their intra-reader variation of 3 mm. This translates into a relative variability (in terms of standard deviation) of 5.2% to 9.6% for the one study and 8.8% to 14.6% for two studies. The relative error tends to be greatest where the extent of AWM is smallest, eg. Chordal cross-section. This is a potential problem in therapeutic studies because infarct salvage if possible would be expected to occur in proximal (basal) segments. Thus, this technique has the ability to demonstrate changes in extent of total AWM of greater than 20% but the magnitude of change would need to be much larger for small infarctions.

This study has delineated changes that occur in a small population of patients with anterior myocardial infarction. There is a need to confirm these findings in a larger series of patients with inferior as well as anterior infarctions because of their known differences in behavior (68). However, such studies need only concentrate on a small number of time intervals such as initial study, pre-discharge, 1 to 2 months and 3 to 6 months. Such studies and companion animal studies are needed to determine those factors which determine infarct healing and changes in abnormal wall motion over time after infarction.

CONCLUSIONS

(1) Two dimensional echocardiography is a reproducible method for estimating the extent of left ventricular asynergy in man.

(2) Using the perimeter extent of abnormal w. l motion relative to circumference as the method it appears that small infarctions heal with shrinkage and decrease in extent of left ventricular abnormal wall motion.

(3) No changes are seen in medium to large infarctions with this method because changes in morphology (aneurysm formation) are off-set by overall left ventricular dilation.

(4) The stability of extent of abnormal wall motion suggests that relatively few examinations over time are required to show the effects of treatment - both acutely and chronically

Table 1

Clinical Data

	Age	Sex	Killip Class Admit	Killip Class Max	Hypertension > 110mm (diast.)	Hypotension < 90 (syst.)	Pericarditis	Infarct Extension	Other
1	53	M	2	2	+	-	+	-	-
2	53	M	2	3	-	+	+	-	-
3	39	M	1	1	-	-	-	-	-
4	43	M	2	2	-	-	+	-	-
5	59	M	1	2	-	-	-	-	-
6	46	M	2	2	-	-	+	+	-
7	58	M	1	2	+	-	-	-	-
8	29	M	2	2	-	-	+	-	-
9	76	M	2	2	-	-	-	+	-
10	52	F	1	1	+	-	-	-	-
11	74	M	2	2	-	-	-	-	-
12	65	F	1	3	-	-	-	-	V.S.D.
13	49	M	1	3	-	-	+	+	-
14	59	M	1	2	-	-	+	-	-
15	74	F	2	2	-	-	-	-	-
16	69	M	2	4	-	+	-	-	-
	56.1 ±3.3		1.6 ±0.1	2.2 ±0.2					

N.B. Hypotension, Hypertension — Sustained for > 6 hours after admission

Table 2

ECG Data

	Time To 1st ECG (hrs)	Location of MI	Σ R (48 hrs) mV	ΣQ (48 hrs) mV
1	6.5	AS, AL	0.1	4.8
2	1.5	AS, AL	0.6	4.4
3	33.0	AS, AL	1.6	4.0
4	0.5	AS, AL	3.0	2.9
5	1.75	AS, AL	0.5	4.3
6	5.0	AS, AL	0.3	6.8
7	4.0	AS	0.4	3.7
8	13.5	AS, AL, InF	2.4	5.1
9	64.0	AS, AL	0.7	3.0
10	45.0	AS, AL	1.7	1.3
11	2.0	AS (Se)	4.0	0.39
12	3.0	AS, AL	0.2	3.7
13	51.0	AS, AL, InF	0.5	6.7
14	3.0	AS (Se)	1.9	0.0
15	2.5	AS	1.6	0.2
16	1.0	AS, AL	-	-
	14.8 $\pm$ 5.2		1.3 $\pm$ 0.3	3.7 $\pm$ 0.5

AS = Anteroseptal
AL = Antero-lateral
InF = Inferior
Se = Subendocardial

$\Sigma R_{48\ hrs}$ = Sum of R Waves, V_1 ..... 6 at 48 hrs

$\Sigma Q_{48\ hrs}$ = Sum of Q Waves, V_1 ..... 6 at 48 hrs

$Time_0$ hrs = onset of chest pain

Table 3

Enzyme Data

	Peak CK	Peak AST	Peak LDH	CK g/Eq
1	2736	321	950	45.9
2	2072	392	1188	38.3
3	1810	-	480	27.9
4	1629	188	585	35.9
5	2739	327	922	62.9
6	2919	178	1166	162.7
7	1192	203	530	24.3
8	4405	462	1289	71.5
9	1140	-	-	26.8
10	521	107	378	22.9
11	231	49	246	5.6
12	1970	480	983	40.7
13	3330	267	1187	99.3
14	841	177	539	14.5
15	1082	146	727	38.4
16	-	-	-	-
	1908 ± 296	254 ± 37	798 ± 92	47.8 + 10.2

CK = Creatine Phosphokinase

AST = Aspartate Transaminase

LDH = Lactic Dehydrogenase

CK g/Eq = Ck Infarct size calculated according to the method of Sobel et al.

Table 4

Follow-up Data

	Angina	Recurrent MI (Months)	Bypass Surgery (Months)	LVF	Duration Follow-up (Months)	Last NYHA	Cause of Death
1	Yes	Yes (4)	No	Yes	14	3	-
2	Occ	No	No	Yes	21	3	-
3	No	No	No	No	19	1	CVA
4	No	No	No	No	6	2	-
5	Yes	No	No	Yes	20	2	-
6	Occ	No	No	Yes	10	2	-
7	Yes	Yes (23)	No	No	23	2	-
8	No	No	No	No	13	2	-
9	No	No	No	No	7	1	-
10	Occ	No	No	No	7	2	-
11	Yes	Yes (8)	No	Yes	6	2	-
12	No	No	Yes (1)	Yes	13	2	-
13	Yes	No	No	Yes	12	3	CVA
14	Yes	No	No	No	13	1	-
15	No	No	No	Yes	14	2	-
16	IN	HOSPITAL	DEATH		13 (hrs)	4	Cardiogenic Shock
					12.4 $\pm$1.6	2.1 $\pm$0.2	

LVF = Left Ventricular Failure

NYHA = New York Heart Association Functional Class

Table 5

Echocardiographic Data

	From 1st Echo					From 6 mo. Echo	
	Time To First Echo (hours)	Location: Total AWM + Akinesis + Paradox	Location: Paradox Only	LV Thrombus	LVEF (Biplane) (%)	LV Thrombus	LVEF Biplane (%)
1	52	Ap, AS, AL Ap-Po	Ap, AS	+	28.6	+	23.7
2	76	Ap, AS, AL Ap-Po	Ap	+	36.8	+	28.2
3	94	Ap, AS, AL	Ap	+	41.5	+	35.8
4	56	Ap,AS,Al Ap,AS,AL Ap-Po	Ap, AS	+	35.0	+	35.5
5	50	Ap, AS, AL Ap-Po	Ap	+	34.0	+	30.4
6	68	Ap,AS, AL Ap-Po	Ap, AS	+	27.5	+	37.6
7	64	Ap, AS, AL Ap-Po	Ap, AS	+	32.6	+	28.7
8	30	Ap, AS, AL Ap-Po	Ap, AS	+	29.2	+	38.6
9	88	Ap, AS, AL Ap-Po	Nil	-	42.2	-	38.2
10	78	Ap, AS, AL Ap-Po	Ap	+	35.9	-	50.2
11	12	Ap, AL Ap-Po	Ap	-	35.2	-	48.3
12	58	Ap, AS, AL Ap-Po	Ap	+	31.1	+	31.2
13	57	Ap, AS, AL Ap-Po	Ap	+	20.9	+	24.4
14	30	Ap, AS, AL Ap-Po	Ap	+	44.7	+	44.1
15	31	Ap,AS,Al Ap,AS,Al Ap-Po	Ap	-	34.4	-	30.7
16	5	Ap,AS,Al, Ap,AS,AL B.S Ap-Po Ap-Po	Ap	-	19.0	-	-
Mean ± SEM	53.1 6.5				33.0 ±1.8		35.0 ±2.0

Ap = Apical, AS = Antero-Septal, B.S. = Basal-Septal, AL = Antero-lateral
Ap-Po = Apico-Posterior, LVEF = Left ventricular ejection fraction.

Table 6

Completeness of Echocardiographic Data

(a)	Number of patients studied	n = 16
	Total number of studies recorded	128
	Studies lost due to technical reasons	2
	Total number of studies analyzed	126

(b) Number of studies at specific time intervals

0 - 72 hours	13
72 hours - 5 days	15
6 - 7 days	10
8 - 10 days	13
2 weeks	13
1 month	14
6 weeks	7
2 months	13
3 months	14
6 months	14

(c) Number of patients studied at specific time intervals

0 - 5 days	n = 15
8 - 14 days	n = 15
1 - 2 months	n = 15
3 - 6 months	n = 15

Table 6 (continued)

(d) Number of individual sections obtained (possible 126)

View	Number Analyzed (%)	Not Recorded	Incorrect	Not Able To Analyze
Longtitudinal	124 (98.4)	0	2 (1.6)	0
Ap.4 Chamber	124 (98.4)	1 (0.8)	1 (0.8)	0
Ap.2 Chamber	68 (54.0)	41 (32.5)	8 (6.3)	9 (7.1)
Mitral XS	125 (99.2)	1 (0.8)	0	0
Chordal XS	120 (95.2)	4 (3.2)	1 (0.8)	1 (0.8)
Mid-Papillary XS	106 (84.1)	5 (4.0)	7 (5.6)	8 (6.3)
Low Papillary XS	76 (60.3)	39 (31.0)	6.3)	3 (2.4)
Apical XS	82 (65.1)	22 (17.5)	10 (7.9)	12 (9.5)

(e) Number of serial sections obtained (possible 126)

Views	Number analyzed (%)
Long axis composite	123 (97.6)
3 Cross-sections	115 (91.3)
4 Cross-sections	96 (76.2)
5 Cross-sections	49 (38.9)

Table 7

Image Quality

View	Good	Adequate	Poor
Longtitudinal n = 124	40%	29%	31%
Ap.4 Chamber n= 124	58%	27%	15%
Ap.2 Chamber n = 68	44%	37%	19%
Mitral XS n = 125	60%	25%	15%
Chordal XS n = 120	51%	25%	24%
Mid-Papillary XS n = 106	36%	35%	29%
Low Papillary XS n = 76	36%	30%	24%
Apical n = 82	44%	35%	21%

Percentage = % of images successfully analyzed

Table 8

Population divided into 2 groups according to extent of abnormal wall motion on echocardiogram at 3 - 5 days.

(a) Group 1 - total AWM greater than 35% n = 8
Group 2 - total AWM less than 35% n = 7

Long Axis Composite

		0-5 d	8-14 d	1-2 mo.	3-6 mo.
Total % AWM	Group 1 n = 8	36.49 ±0.64	36.94 ±1.51	35.28 ±1.44	34.2 ±[illegible]06
	Group 2 n = 7	29.04 ±1.39	29.62 ±1.43	30.61 ±1.98	29.70 ±2.83
Akinesis % + Paradox	Group 1 n = 8	31.[illegible]9 ±1.30	32.19 ±1.93	[illegible]70 ±[illegible].21	29.93 ±1.97
	Group 2 n = 7	24.63 ±1.31	24.94 ±2.49	25.57 ±3.14	23.88 ±3.24
Paradox % Only	Group 1 n = 8	14.84 ±1.66	14.36 ±1.90	14.86 ±1.40	13.85 ±1.63
	Group 2 n = 7	8.62 ±1.79	7.36 ±2.32	8.56 ±2.80	9.11 ±2.44

No within group differences are significant.

Table 8 (continued)

(b) Group 3 - Extent akinesis + paradox greater than 30%
Group 4 - Extent akinesis + paradox less than 30%

Long Axis Composite

		0-5 d	8-14 d	1-2 mo.	3-6 mo.
Total % AWM	Group 3 n = 6	36.76 ±0.87	37.31 ±1.66	35.81 ±1.57	35.88 ±1.04
	Group 4 n = 9	30.52 ±1.44	31.01 ±1.61	27 ±1.72	29.58 ±2.57
Akinesis % + Paradox	Group 3 n = 6	33.23 ±0.96	67 ±1.59	30.80 ±1.13	31.98 ±1.54
	Group 4 n = 9	24.91 ±0.93	25.57 ±2.22	25.75 ±2.45	23.86 ±2.59
Paradox % Only	Group 3 n = 6	16.68 ±0.98	15.09 ±2.07	15.48 ±1.64	15.10 ±1.28
	Group 4 n = 9	8.77 ±1.58	8.43 ±2.12	9.54 ±2.29	8.75 ±2.09

No within group differences are significant.

Table 9

Population divided into 2 groups according to clinical events.

(a) Group 5 - Increase in Killip class from admission
Group 6 - Killip class unchanged during hospitalization

Long Axis Composi

		0-5 d	8-14 d	1-2 mo.	3-6 mo.
Total % AWM	Group 5 n = 6	35.05 ±1.50	36.39 ±2.55	35.07 ±2.20	35.76 ±2.18
	Group 6 n = 9	31.66 ±1.68	31.62 ±1.37	31.79 ±1.57	29.59 ±2.23
Akinesis % + Paradox	Group 5 n = 6	30.15 ±2.54	32.21 ±2.35	30.16 ±2.81	30.51 ±2.64
	Group 6 n = 9	26.96 ±1.22	26.54 ±2.31	23.07 ±3.03	24.84 ±2.55
Paradox % Only	Group 5 n = 6	14.71 ±1.76	15.33 ±2.17	14.21 ±2.45	14.15 ±1.61
	Group 6 n = 9	10.09 ±1.91	8.27 ±2.01	10.39 ±2.22	9.61 ±2.09

No within group differences are significant.

Table 9 (continued)

(b) Group 7 - Angina during follow-up ± recurrent MI
Group 8 - No recurrent chest pain

Long Axis Composite

		0-5 d	8-14 d	1-2 mo.	3-6 mo.
Total % AWM	Group 7 n = 9	33.45 ±1.72	33.62 ±1.89	33.62 ±1.98	32.89 ±2.56
	Group 8 n = 6	32.36 ±1.77	33.39 ±2.27	32.32 ±1.58	30.91 ±2.32
Akinesis % + Paradox	Group 7 n = 9	28.30 ±1.82	29.31 ±2.46	28.40 ±2.47	27.62 ±3.07
	Group 8 n = 6	28.15 ±1.83	28.05 ±2.73	26.83 ±1.93	26.33 ±1.88
Paradox % Only	Group 7 n = 9	12.97 ±1.58	12.28 ±2.46	11.68 ±2.61	12.10 ±2.23
	Group 8 n = 6	10.39 ±2.76	9.31 ±2.18	12.28 ±1.78	10.41 ±1.83

No within or between group differences are significant.

Table 10

Reproducibility Studies

(a) Reproducibility studies of estimation of extent of AWM

Study	Longtitudinal			Apical 4 Chamber			Apical 2 Chamber		
Reproducibility 1	Mean Error % CIRC.	Mean Value A.W.M.	Relative Error %	Mean Error % CIRC.	Mean Value A.W.M.	Relative Error %	Mean Error % CIRC.	Mean Value A.W.M.	Relative Error %
Total AWM	2.33 ± 0.35	31.34	7.4	2.81 ± 0.54	30.60	9.2	2.96 ± 0.45	32.46	9.1
Akinesis + Paradox	2.40 ± 0.32	27.92	8.6	2.17 ± 0.30	26.58	8.2	2.06 ± 0.43	27.75	7.4
Paradox Only	2.70 ± 0.41	12.99	20.8	2.22 ± 0.42	11.10	20.0	2.02 ± 0.47	9.72	20.8
Reproducibility 2									
Total AWM	4.34 ± 0.84*	30.4	14.3	3.65 ± 0.60	31.47	11.6	3.06 ± 0.68	30.72	10.0
Akinesis + Paradox	3.75 ± 0.64*	28	13.7	3.73 ± 0.57*		13.2	4.64 ± 1.05*	26.24	17.7
Paradox Only	3.84 ± 0.97	13.47	28.5	2.84 ± 0.77		22.2	3.68 ± 0.86	10.66	34.5

Variability = Mean Error % CIRC. = $\frac{(x-y) \times 100}{n}$ where x = first observation % circumference, y = second observation % circumference, n = nos. of pairs of observations.

Relative error % = $\frac{\text{Mean Error \% CIRC}}{\text{Mean Value A.W.M.}} \times 100\%$

Reproducibility 1 = Repeat analysis of same echo by same observer, n = 20.
Reproducibility 2 = Repeat echo examination by same observer/technician in the same patients, n = 19.
Total AWM = Circumferential extent of abnormal wall motion (%).
Comparing Reproducibility 1 vs. Reproducibility 2 for each section, * $p < 0.05$, ** $p < 0.01$.

Table 10 (continued)

(b) Reproducibility studies. - Cross Sections

Study	Chordal			Mid-Papillary			Low Papillary			Apical		
Reprod. 1	M.E. %	M.V. A.W.M.	R.E. %	M.E. %	M.V. A.W.M.	R.E. %	M.E. %	M.V. A.W.M.	R.E. %	M.E. %	M.V. A.W.M.	R.E. %
Total AWM	3.34 ± 0.61	18.1	18.5	3.77 ± 0.64	35.5	10.6	3.65 ± 0.75	42.2	8.7	4.69 ± 0.96	60.9	7.7
Akinesis + Paradox	1.80 ± 0.51	9.8	18.3	1.79 ± 0.33	29.0	6.2	3.32 ± 0.81	34.2	9.7	3.37 ± 0.45	50.7	6.6
Paradox Only	-	-	-	2.51 ± 0.48	10.5	24.0	2.23 ± 0.60	14.8	15.0	3.04 ± 0.52	20.2	15.0
Reprod. 2												
Total AWM	6.30 ± 1.67*	17.6	35.9	6.09 ± 1.03*	34.2	17.8	8.44 ± 1.20*	43.6	19.4	3.67 ± 1.57	57.8	6.4
Akinesis + Paradox	3.30 ± 1.00	5.4	58.4	5.57 ± 1.31**	27.7	20.1	7.46 ± 2.58*	33.7	22.1	5.45 ± 1.30	48.6	11.2
Paradox Only	-	-	-	4.71 ± 1.08*	8.4	56.1	2.23 ± 0.94	15.4	14.4	3.95 ± 1.22	20.2	19.6

M.E. % = Mean Error % Circumference
M.V. AWM = Mean Value abnormal wall motion
R.E. % = Relative Error %
Comparing Reprod. 1 vs. Reprod. 2 for each section, * $p < 0.05$, ** $p < 0.01$

Table 10 (continued)

(c) Mean Error % for all views

	Reproducibility 1	Reproducibility 2	Significance
Total	3.28 ± 0.10	5.14 ± 0.46	$p < 0.005$
Akinesis + Paradox	2.34 ± 0.17	4.61 ± 0.41	$p < 0.001$
Paradox Only	2.47 ± 0.19	3.55 ± 0.40	$p < 0.01$
Mean	2.7 ± 0.15	4.47 ± 0.42	$p < 0.005$

N.B. for Reproducibility 1: Total significantly different from others, $P < 0.01$.

For Reproducibility 2: Total significantly different from Paradox only $p < 0.01$; Akinesis + Paradox significantly different from paradox only $p < 0.05$.

(d) Relative Error % for all views

	Reproducibility 1	Reproducibility 2	Significance
Total	10.4 ± 0.36	17.6 ± 0.98	$p < 0.001$
Akinesis + Paradox	9.5 ± 0.39	23.6 ± 1.69	$p < 0.001$
Paradox Only	19.1 ± 0.47	29.2 ± 1.43	$p < 0.001$
Mean	12.6 ± 0.41	23.3 ± 1.37	$p < 0.001$

N.B. for Reproducibility 1: Total and akinesis + paradox significantly different than paradox only $p < 0.001$.

For Reproducibility 2: Total significantly different from akinesis + paradox ($p < 0.005$) and paradox only ($p < 0.001$).

Akinesis + Paradox significantly different from paradox only $p < 0.01$.

Table 10 (continued)

(e) Proportions of Variability due to Reproducibility 1 and Reproducibility 2

	For Mean Error %			For Relative Error %		
	$\frac{R_1 \times 100\%}{R_2}$	$\frac{R_2 - R_1 \times 100\%}{R_2}$	Significance	$\frac{R_1 \times 100\%}{R_2}$	$\frac{R_2 - R_1 \times 100}{R_2}$	Significance
Total	63.8	36.2	$X^2 = 7.6$ $p < 0.01$	59.1	40.9	$X^2 = 3.3$ N.S.
Akinesis + Paradox	50.8	49.2	N.S.	40.3	59.7	$X^2 = 3.8$ N.S.
Paradox Only	69.6	30.4	$X^2 = 15.3$ $p < 0.005$	65.4	34.6	$X^2 = 9.4$ $p < 0.005$
Mean	61.4 ± 5.6	38.6 ± 5.6	$X^2 = 5.2$ $p < 0.01$	54.1 ± 7.5	45.9 ± 7.5	$X^2 = 0.67$ N.S.

Where R_1 = Mean value for all views in Reproducibflity 1 Study.

R_2 = Mean value for all views in Reproducibility 2 Study.

Figure 1

Representation of Echocardiographic Views

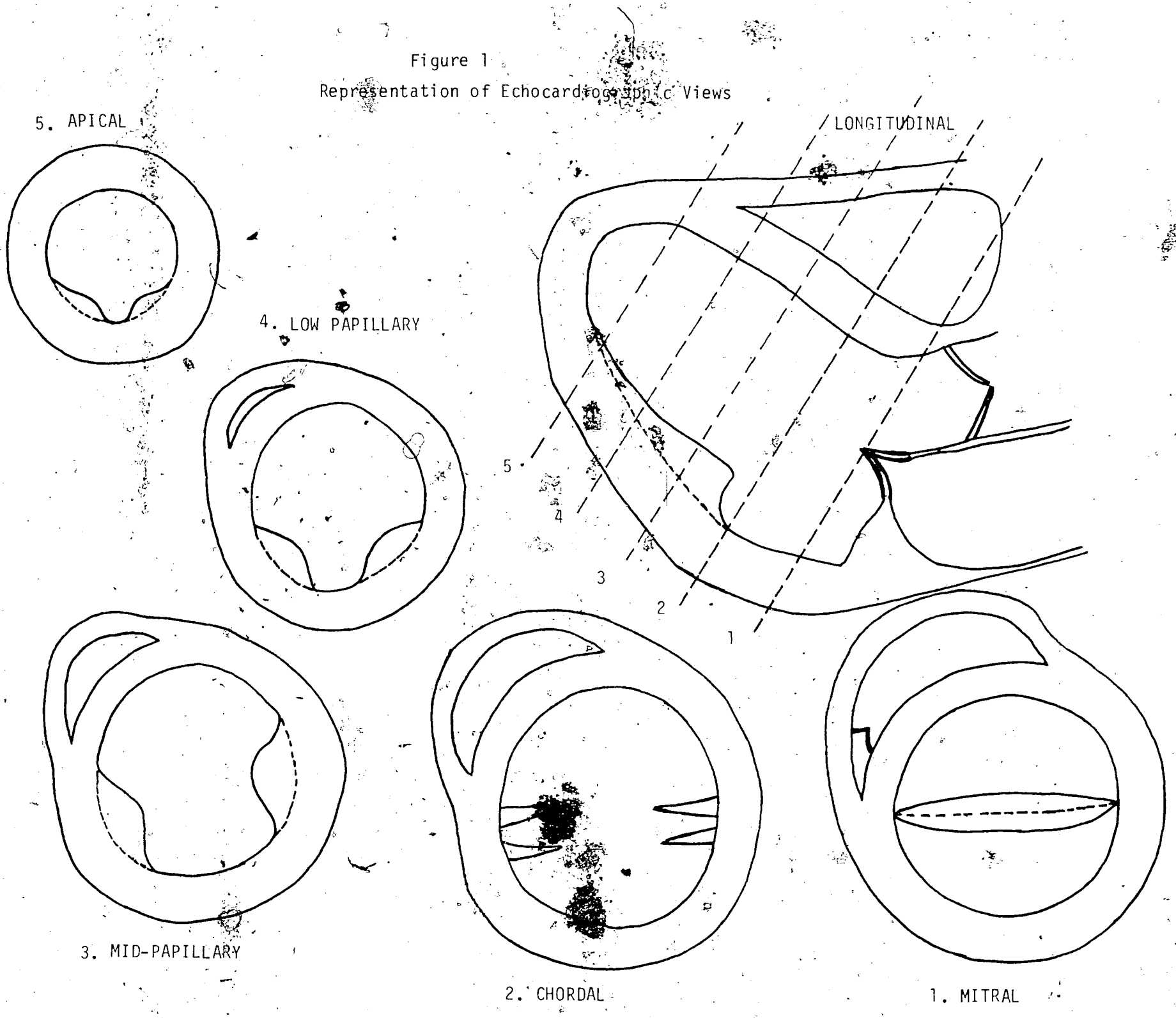
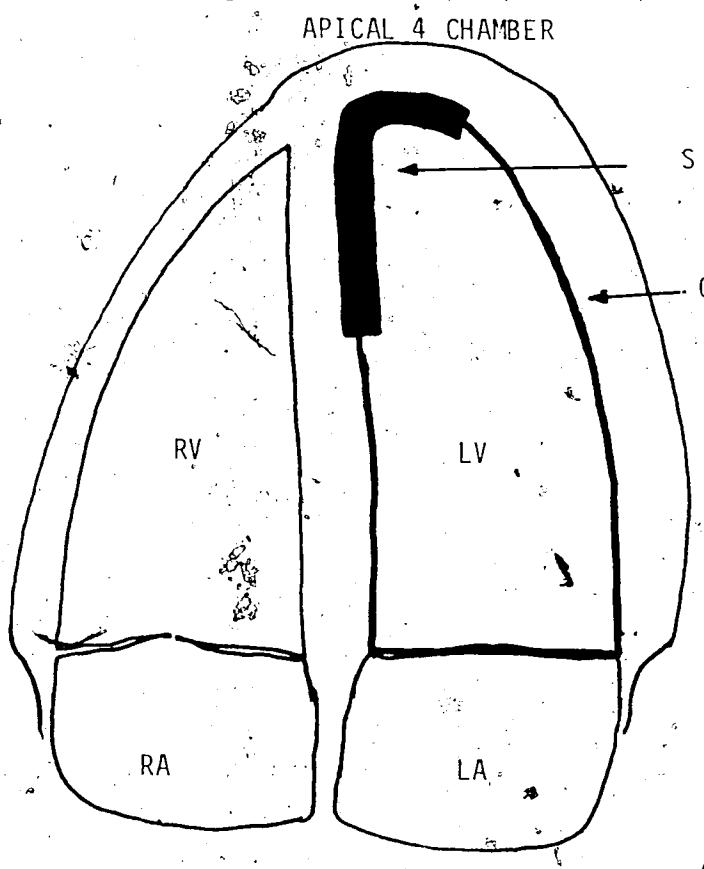
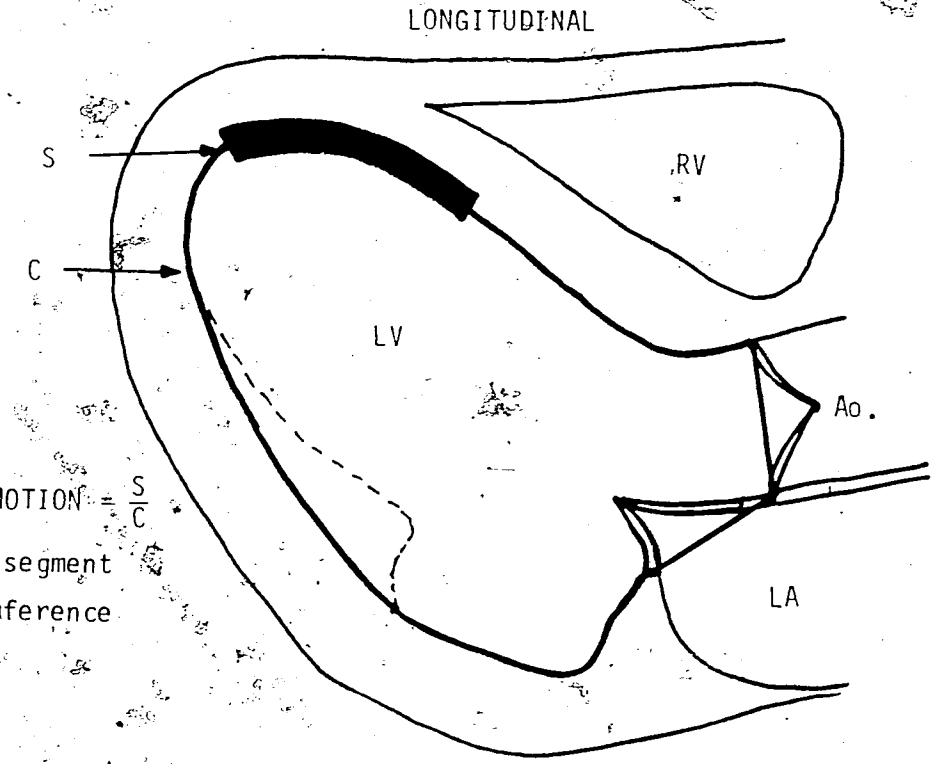


Figure 2

Method of Calculation of Abnormal Wall Motion.





$$\% \text{ LV ABNORMAL WALL MOTION} = \frac{S}{C}$$

where S = abnormal segment

C = LV circumference

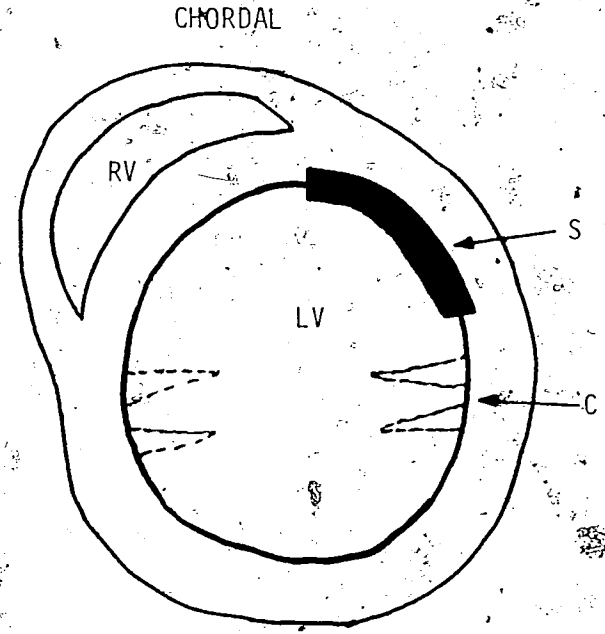


FIGURE 3

2 D ECHOCARDIOGRAPHIC CROSS-SECTIONAL VIEWS

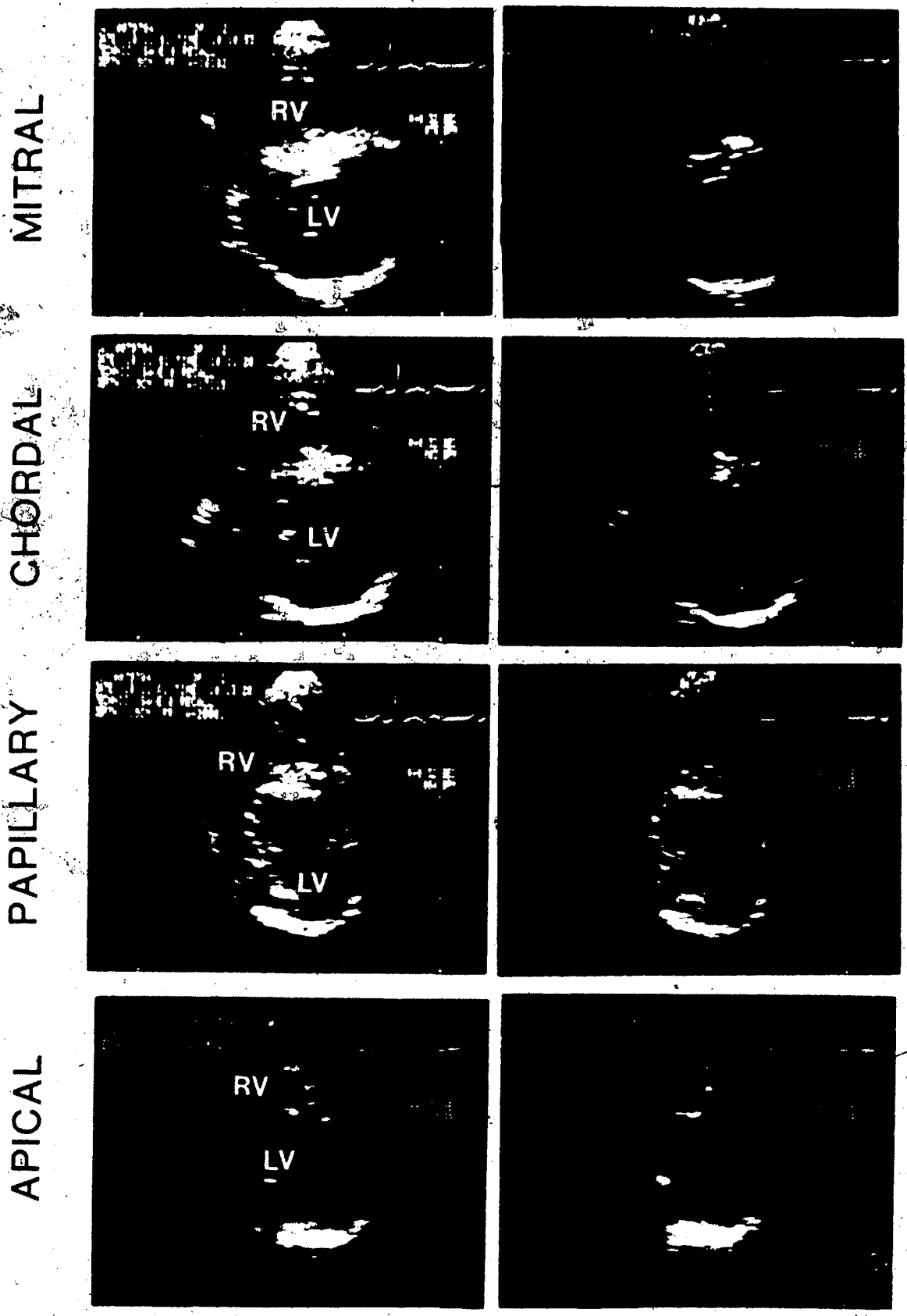


Figure 4
Mid Papillary Cross-section

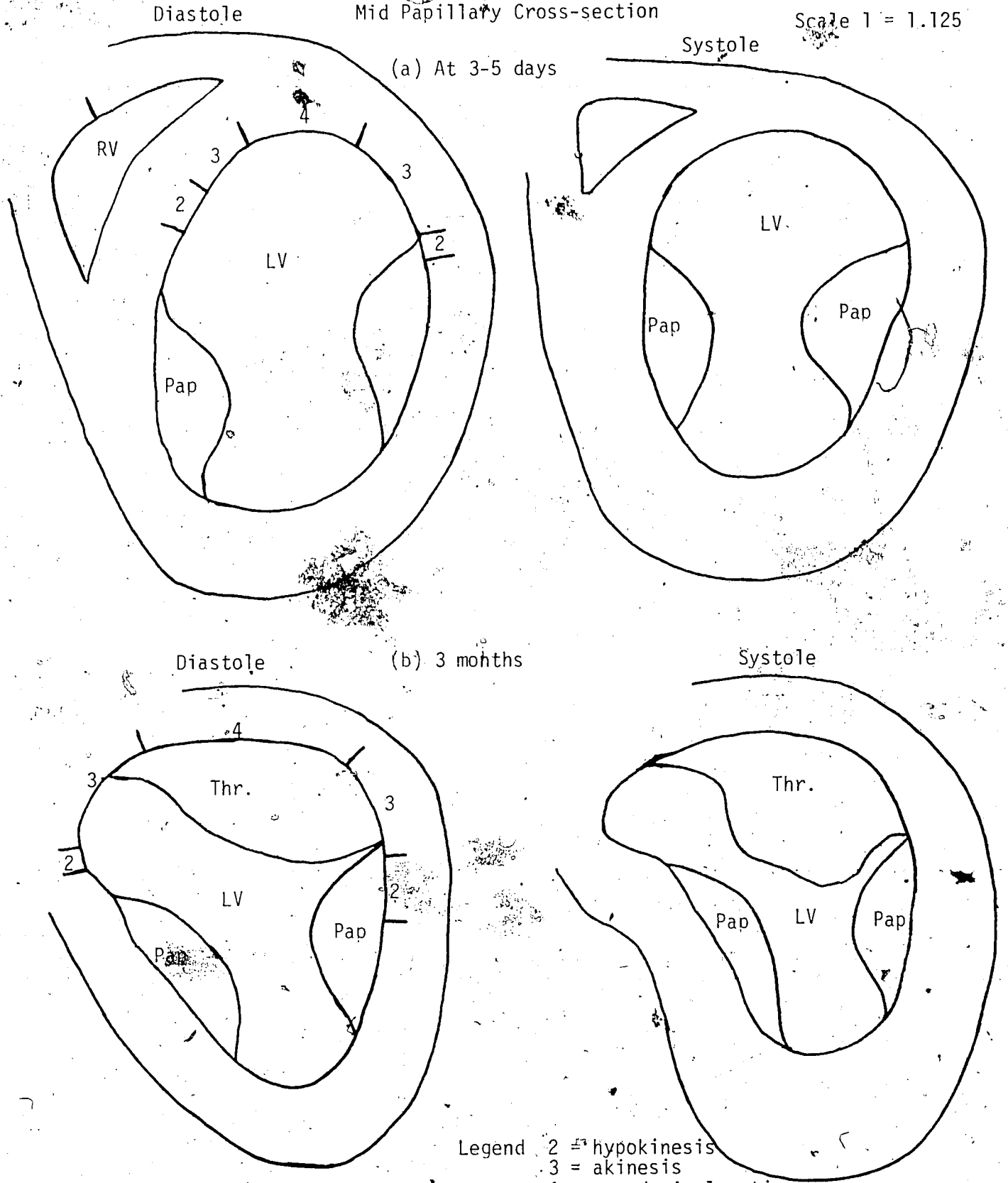
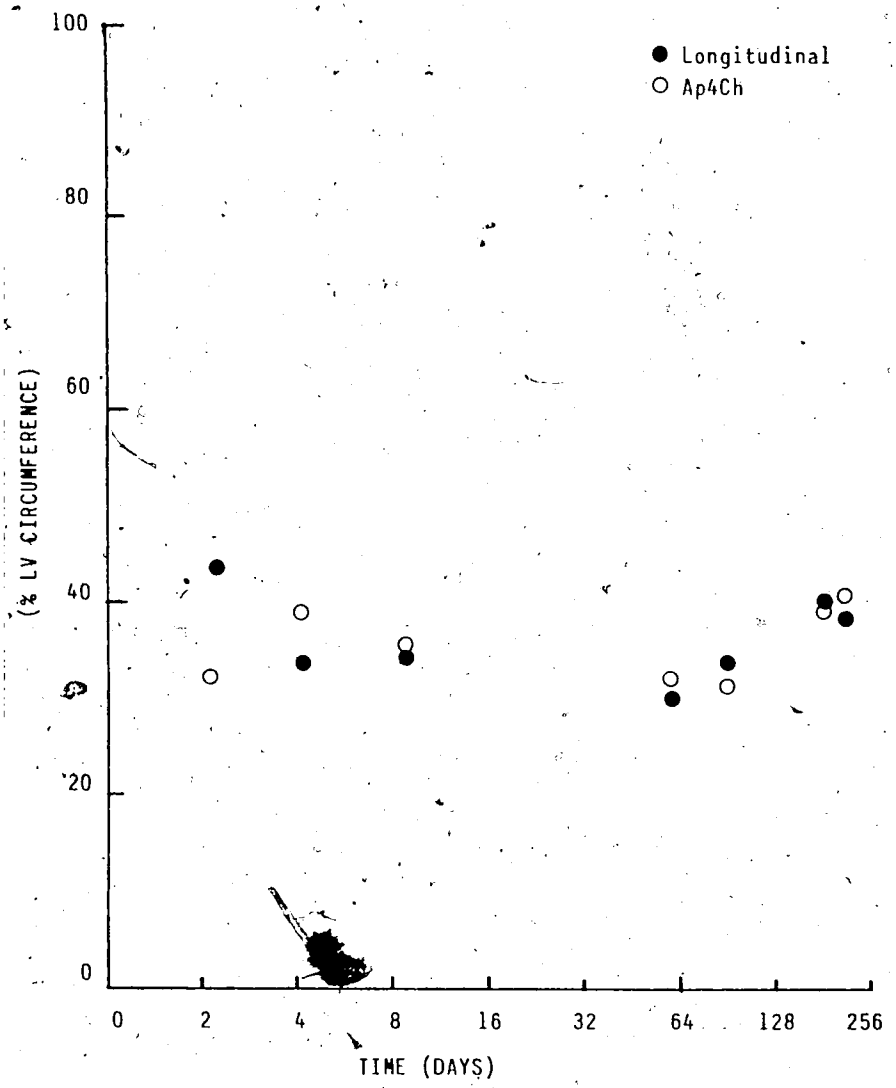
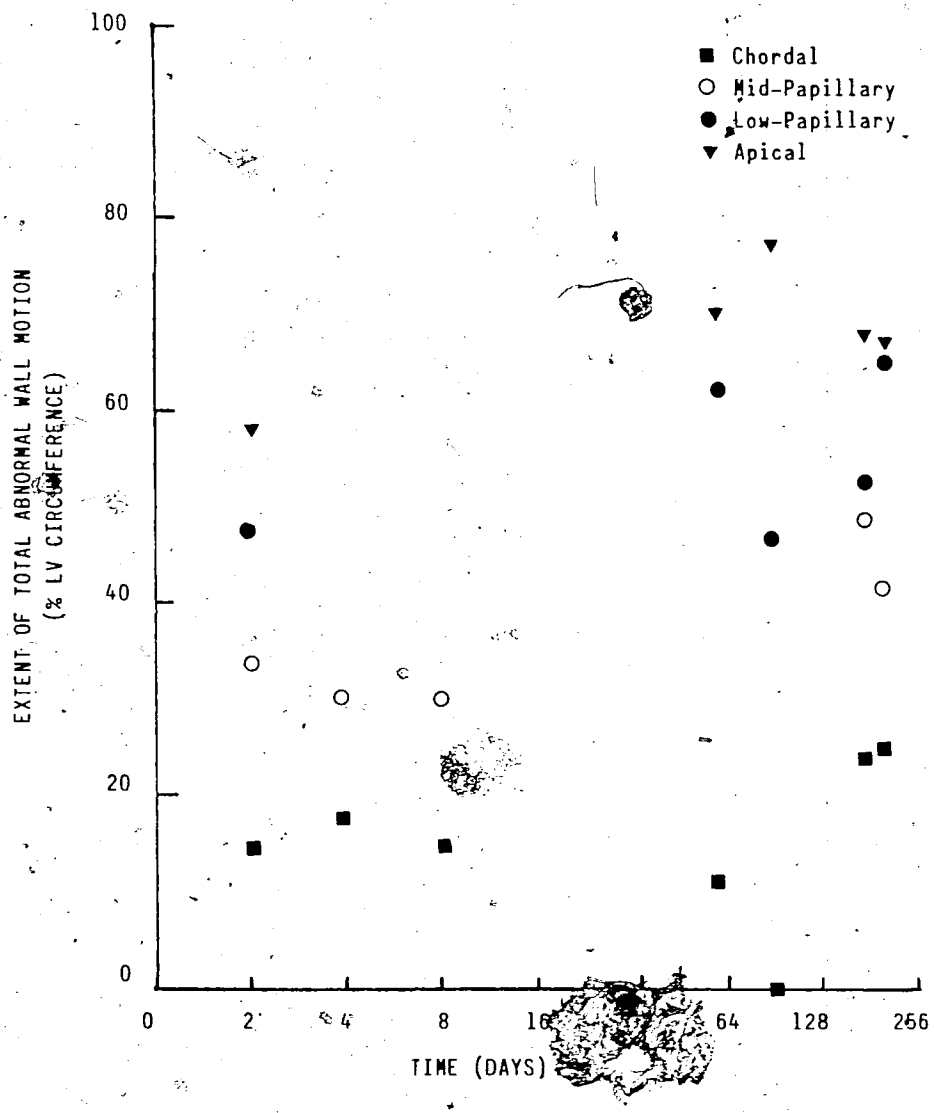


FIGURE 5(a)
EXTENT OF TOTAL ABNORMAL WALL MOTION
WITH TIME IN ONE PATIENT





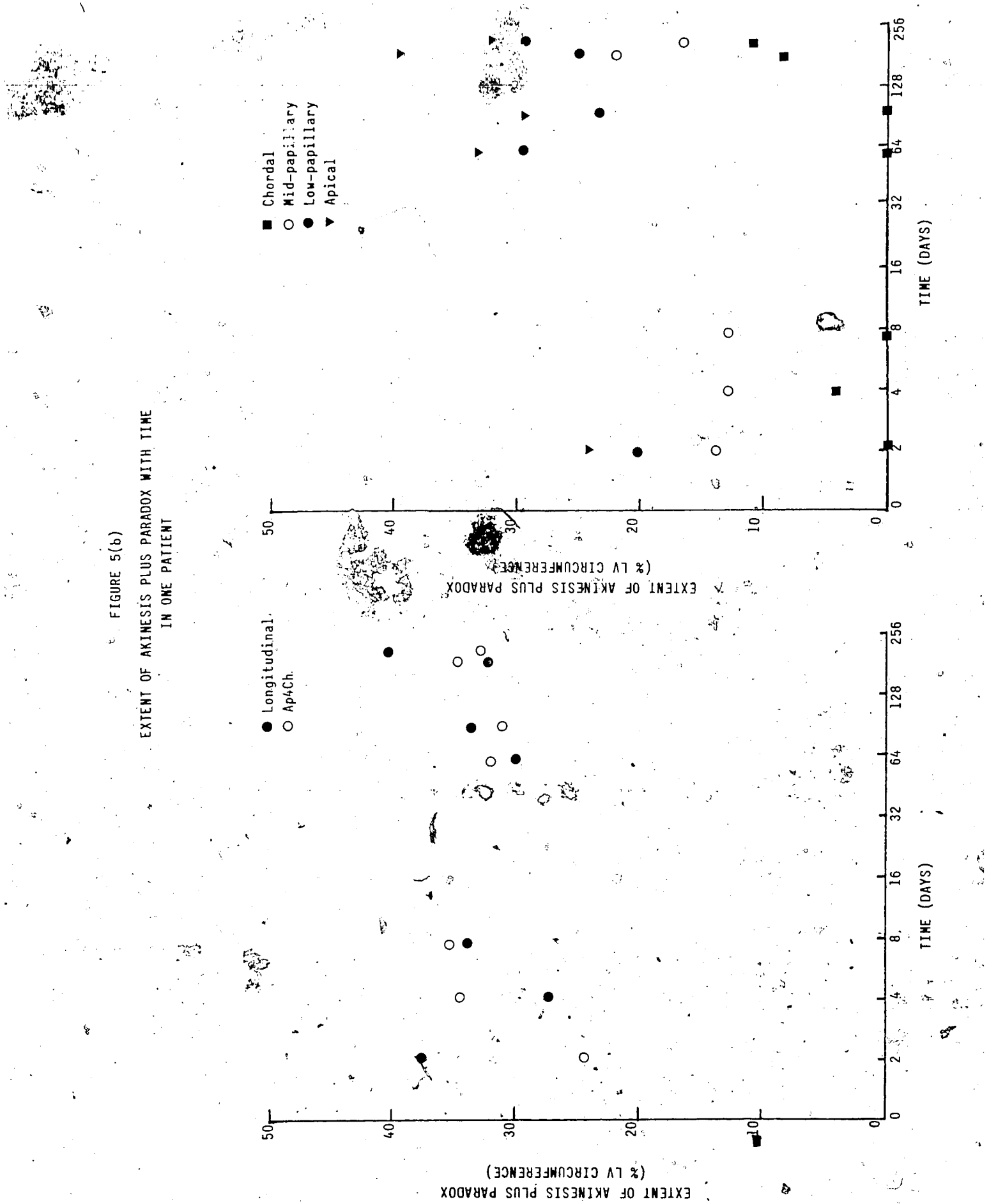


FIGURE 5(b)

EXTENT OF AKINESIS PLUS PARADOX WITH TIME IN ONE PATIENT

FIGURE 5(c)

EXTENT OF PARADOX WITH TIME
IN ONE PATIENT*

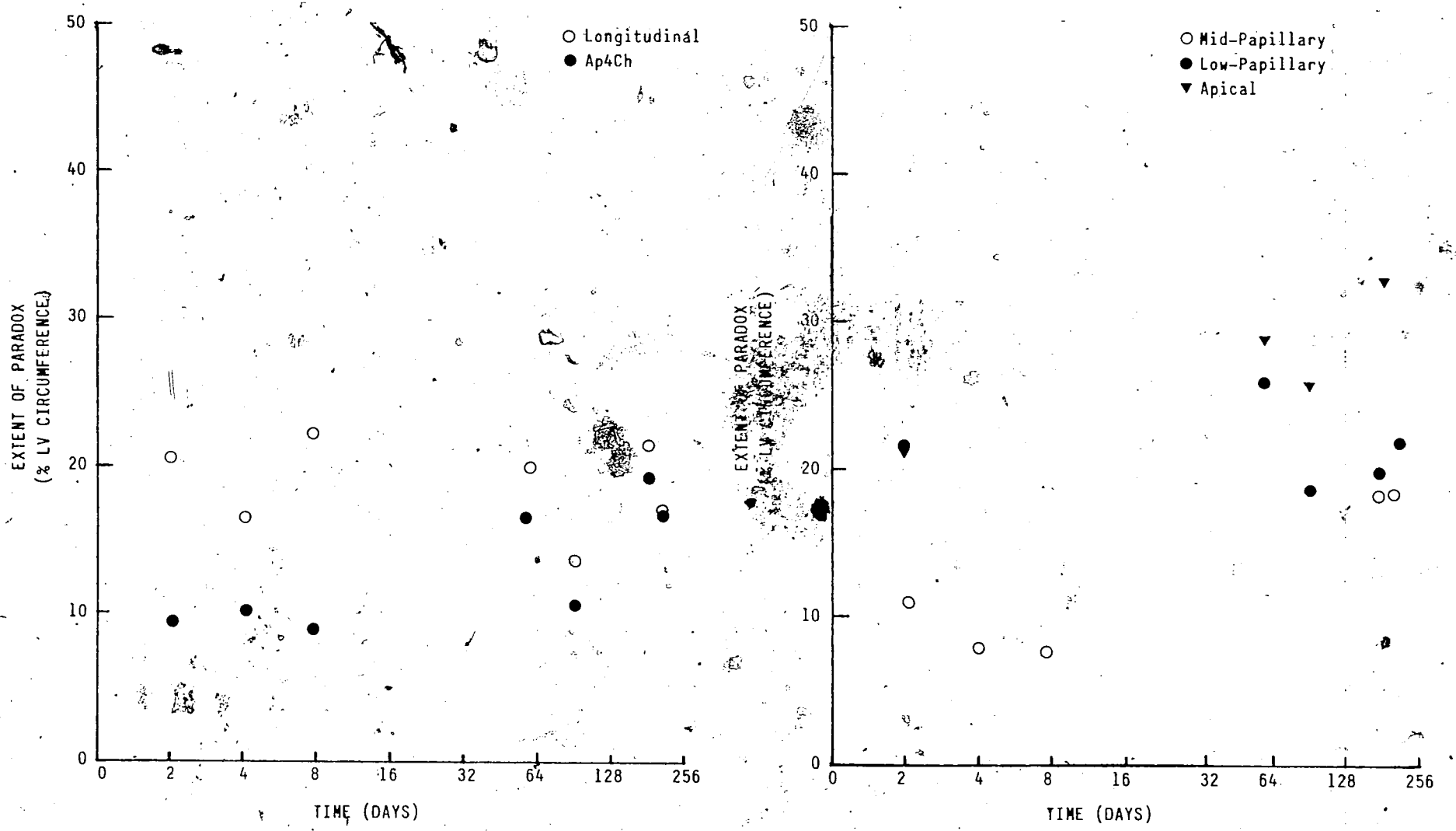


FIGURE 6(a): LONGITUDINAL VIEW

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

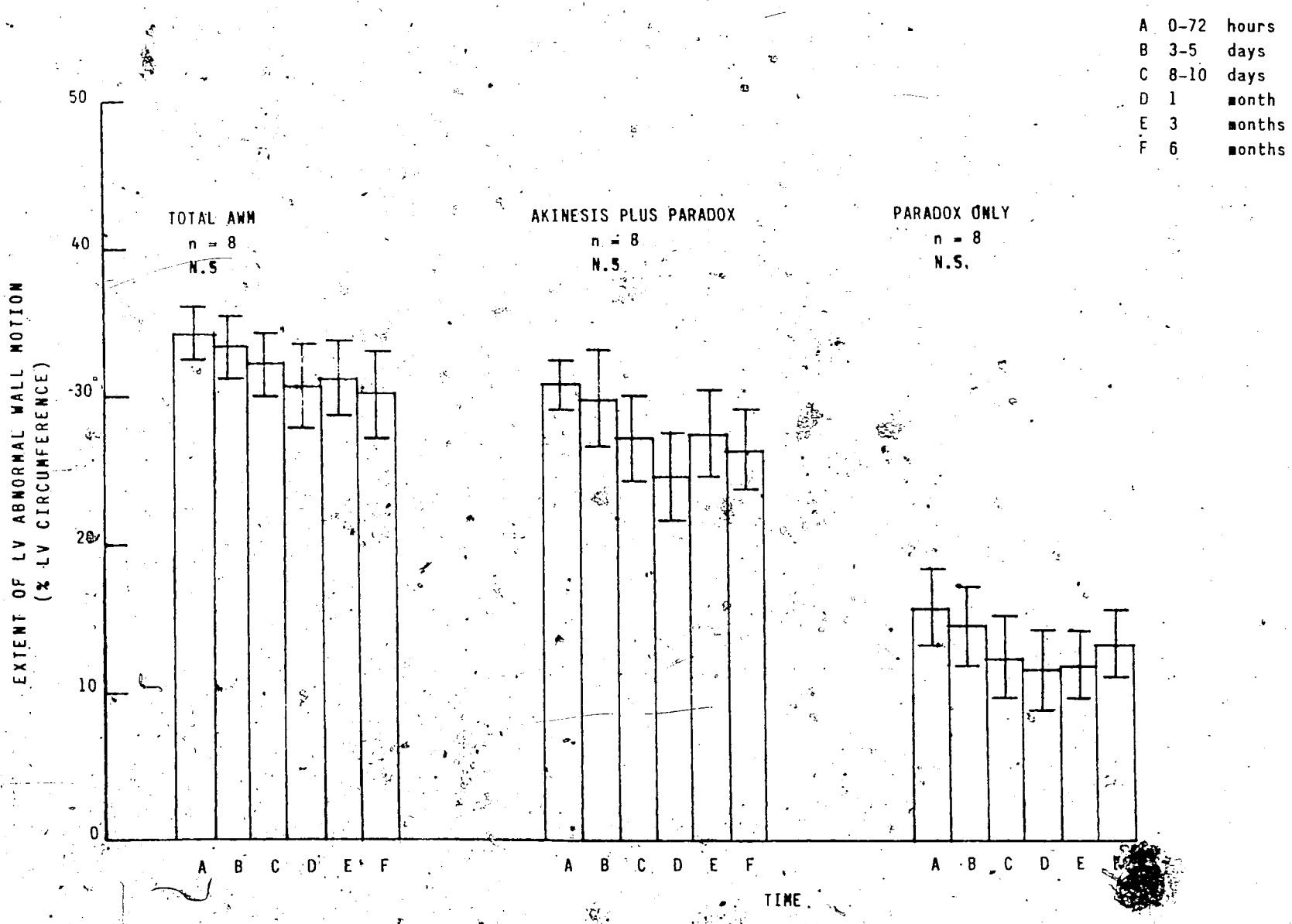


FIGURE 6(b): [illegible] 4 CHAMBER VIEW

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

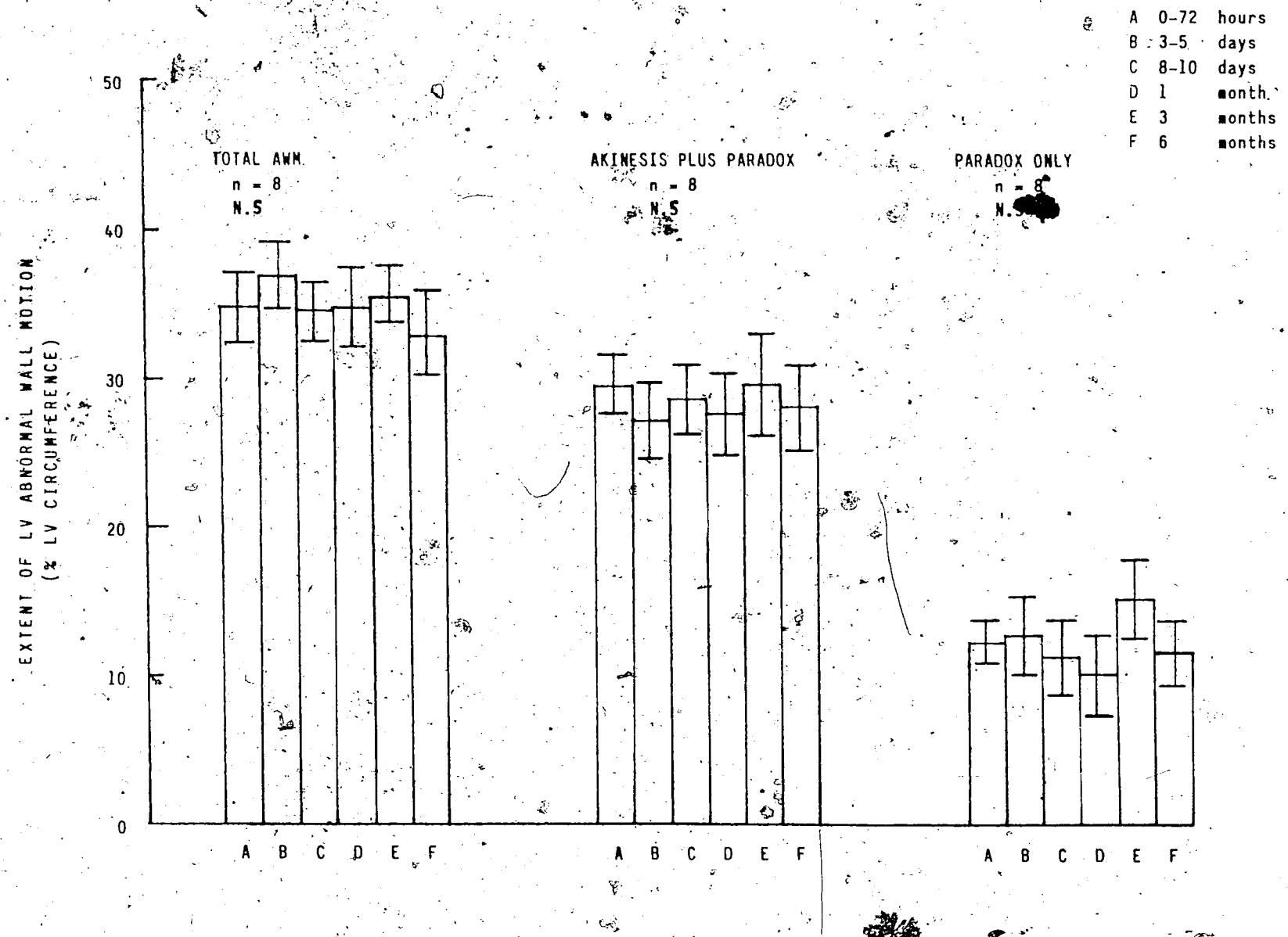


FIGURE 6(c): LONG AXIS COMPOSITE

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

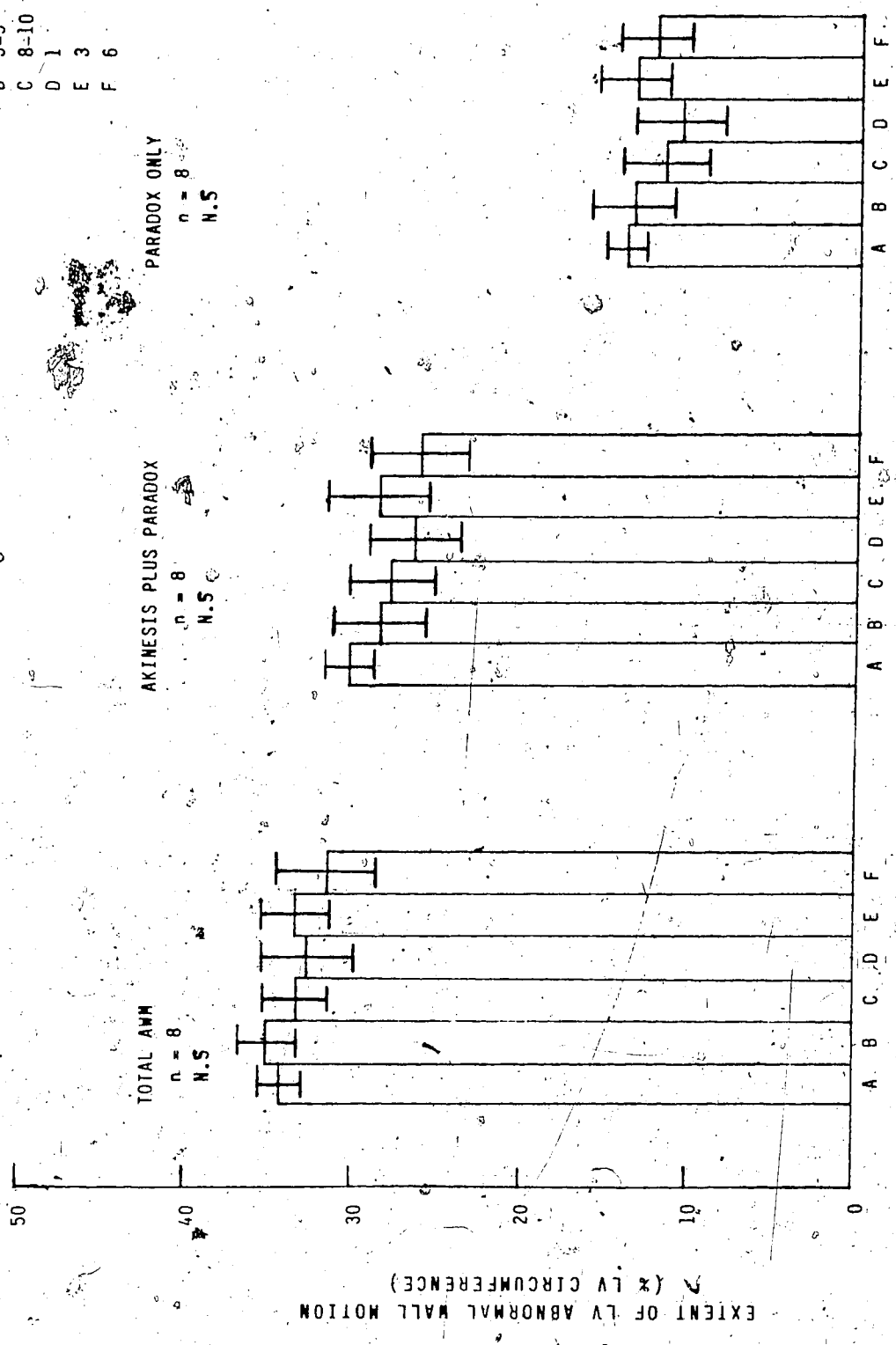


FIGURE 7(a): LONGITUDINAL VIEW

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

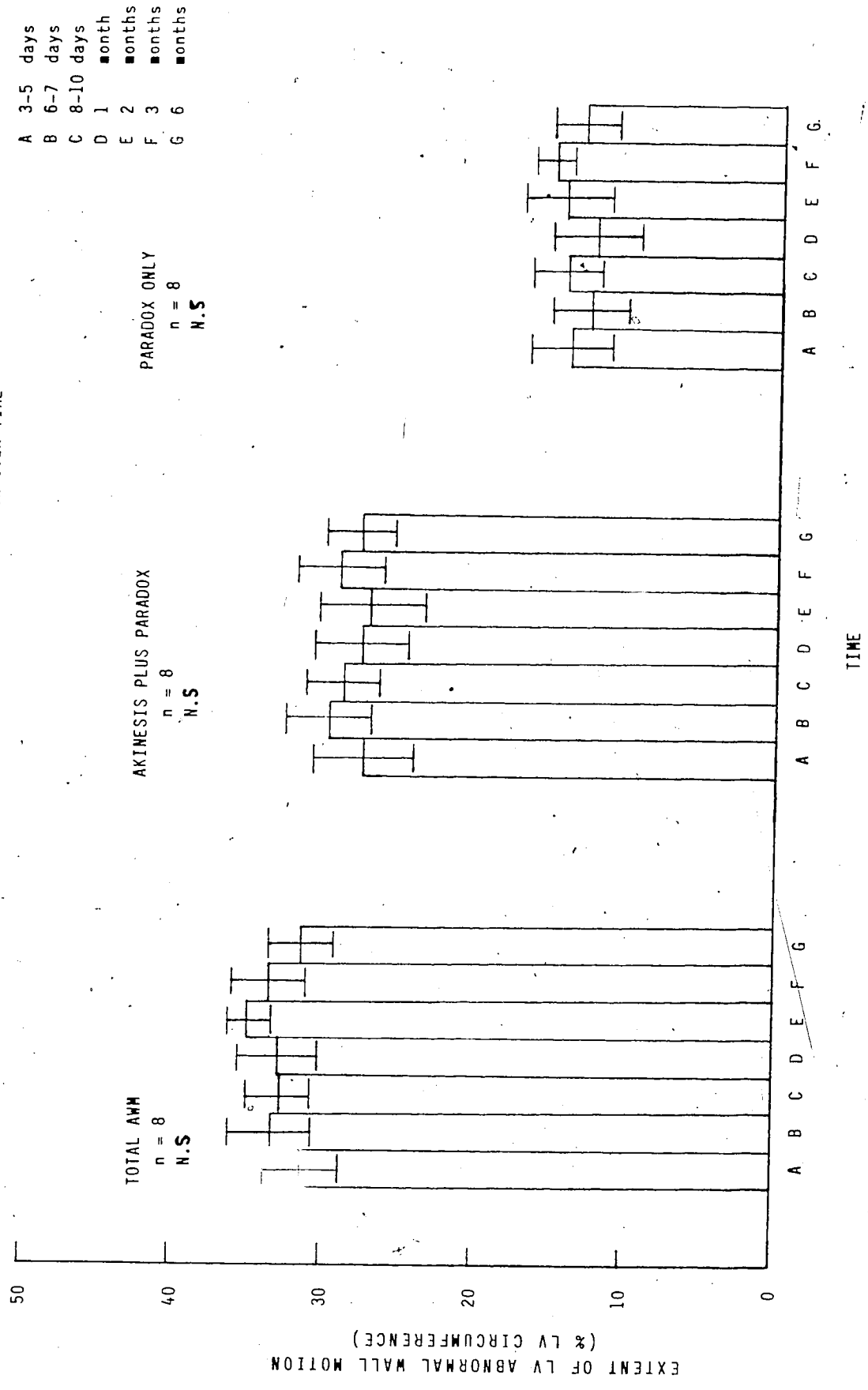


FIGURE 7(b): APICAL 4 CHAMBER VIEW

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

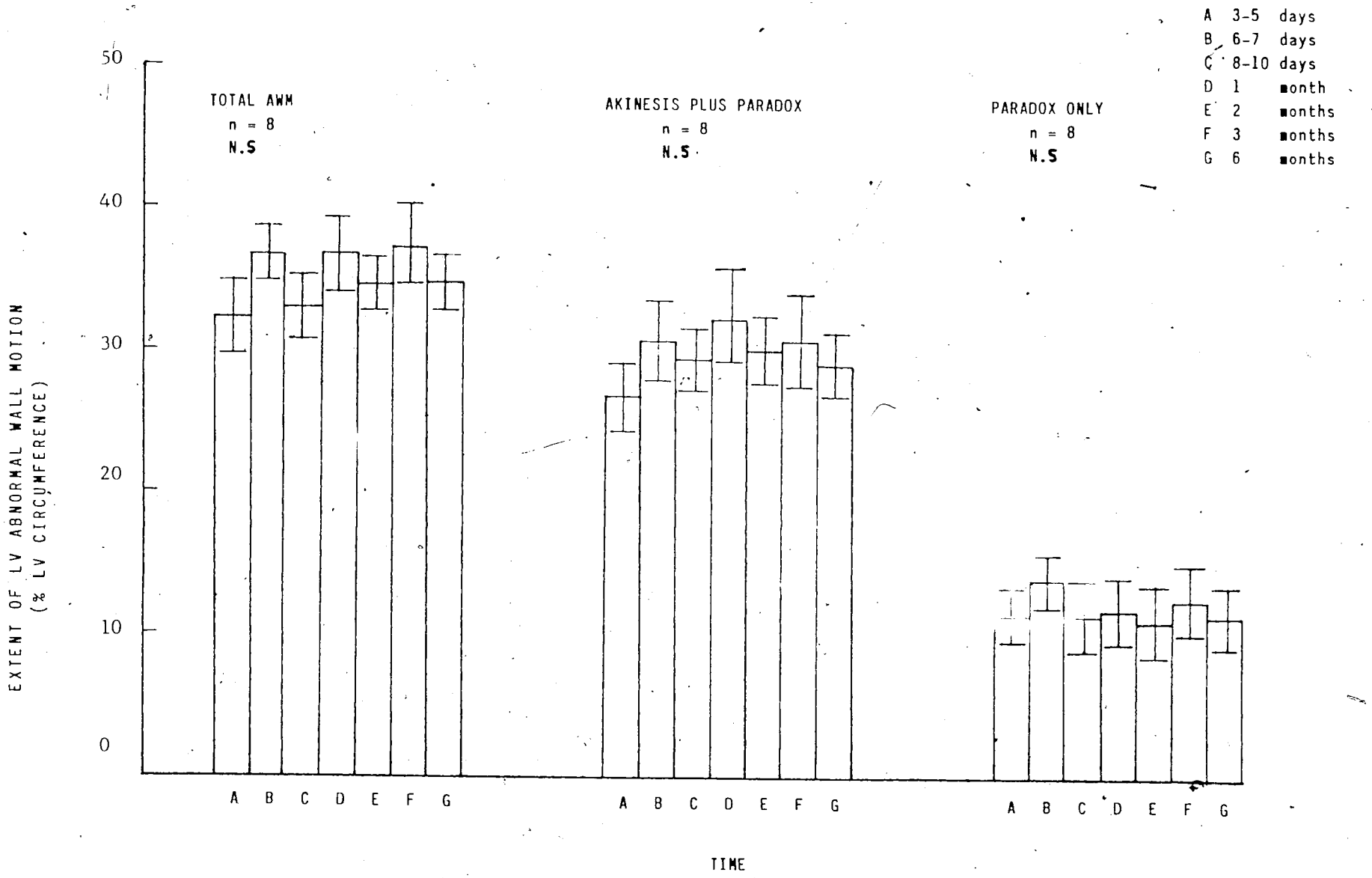


FIGURE 7(c): LONG AXIS COMPOSITE

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

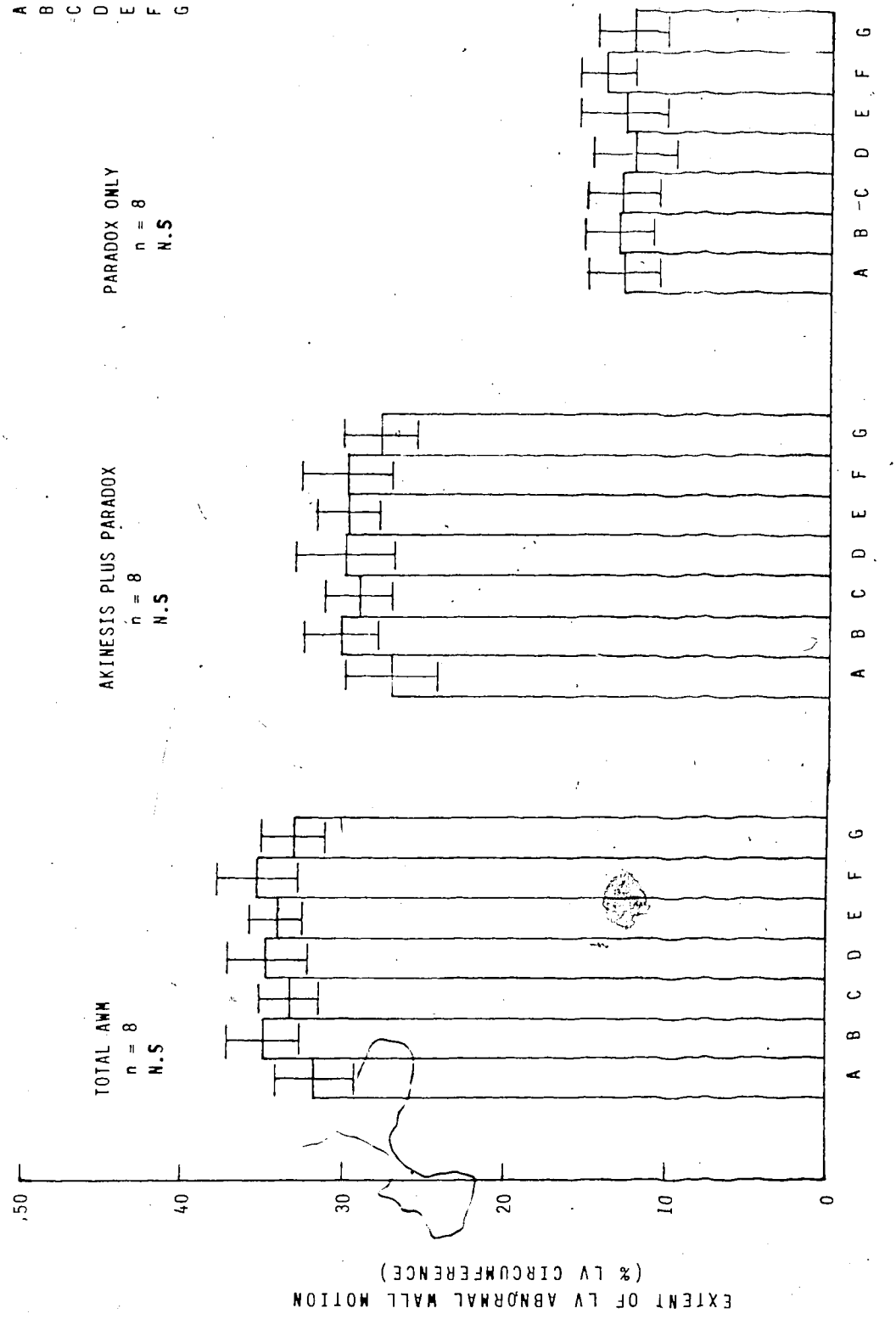


FIGURE 8(a): LONGITUDINAL VIEW

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

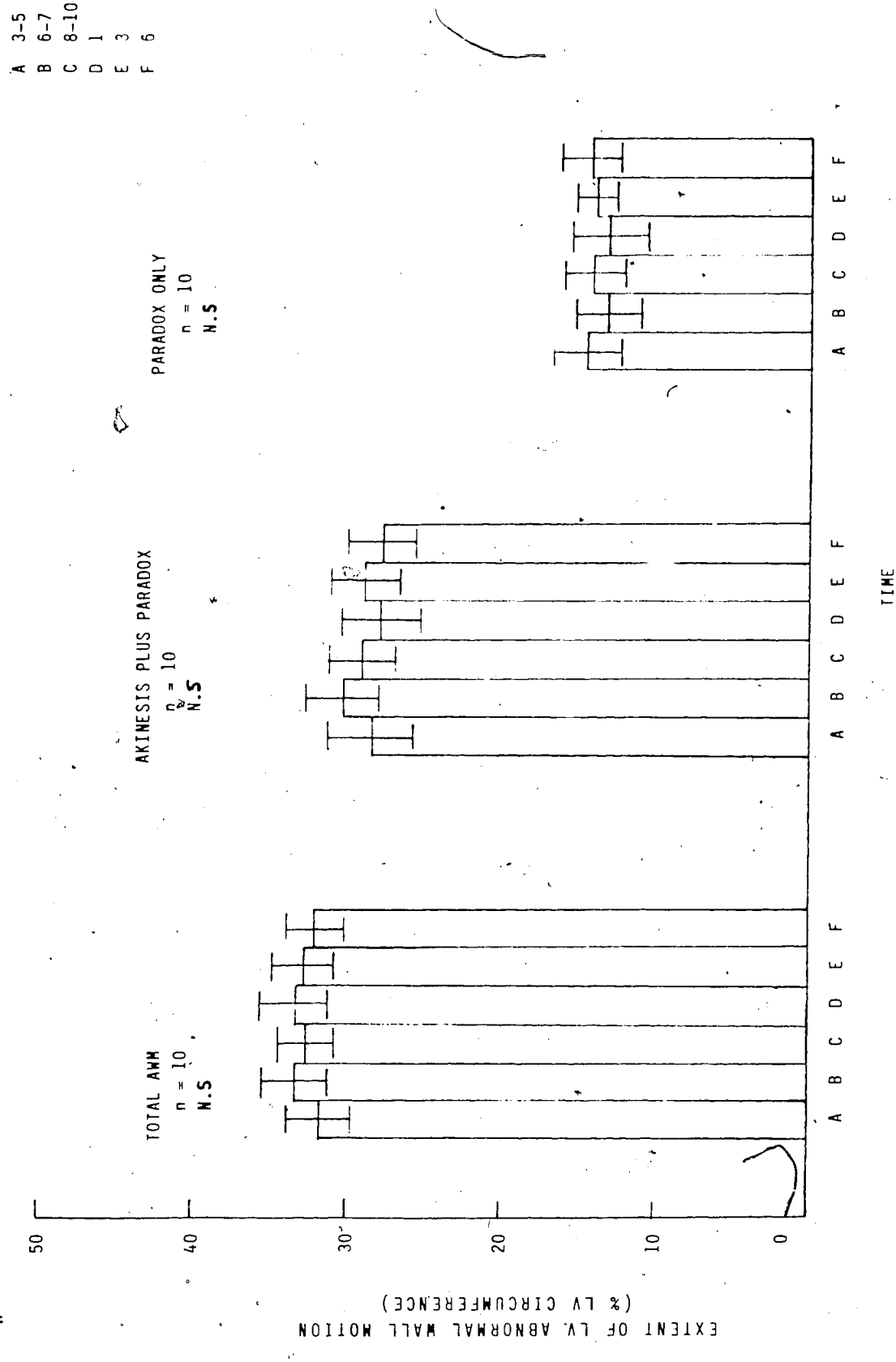


FIGURE 8(b): APICAL 4 CHAMBER VIEW

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

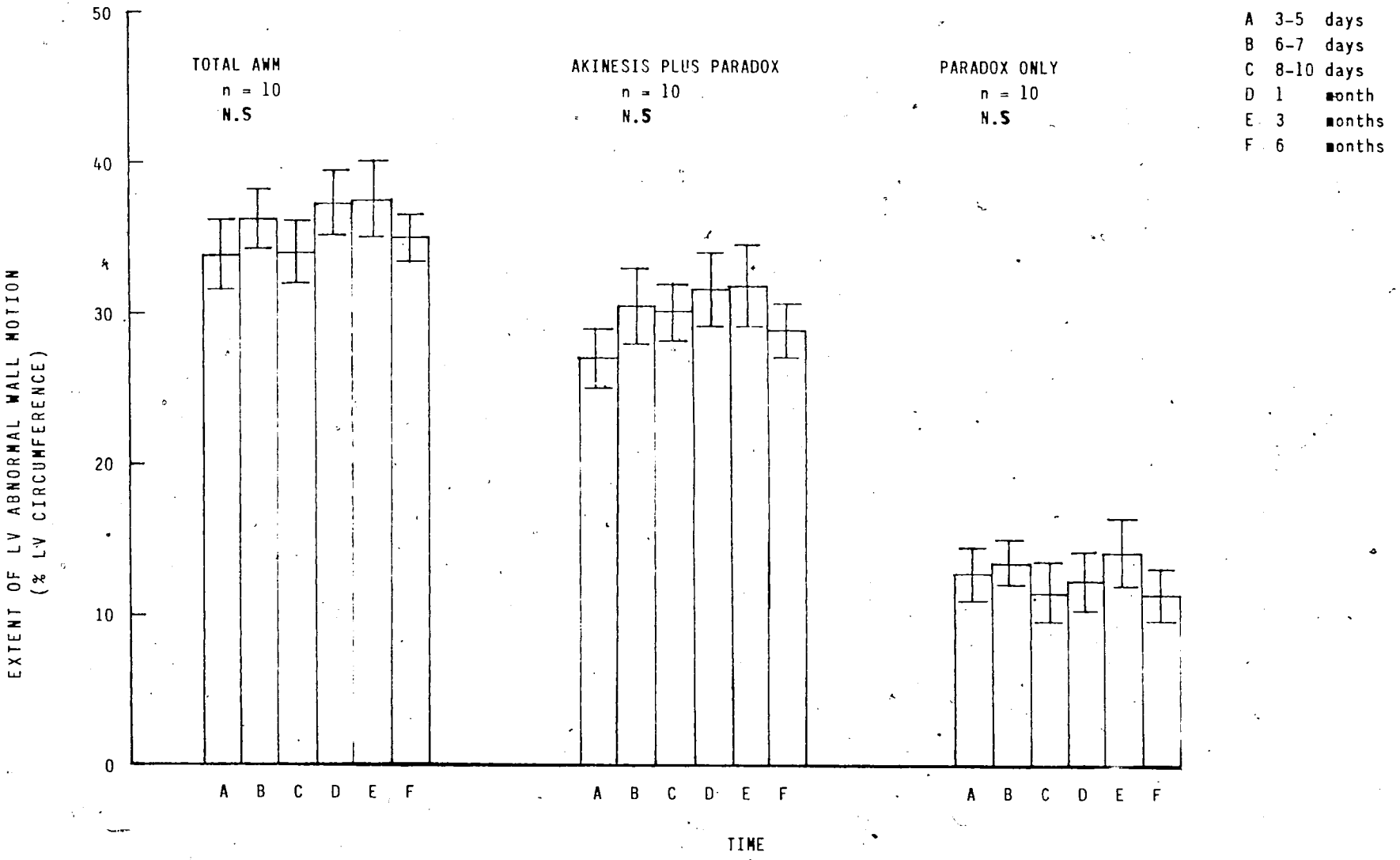
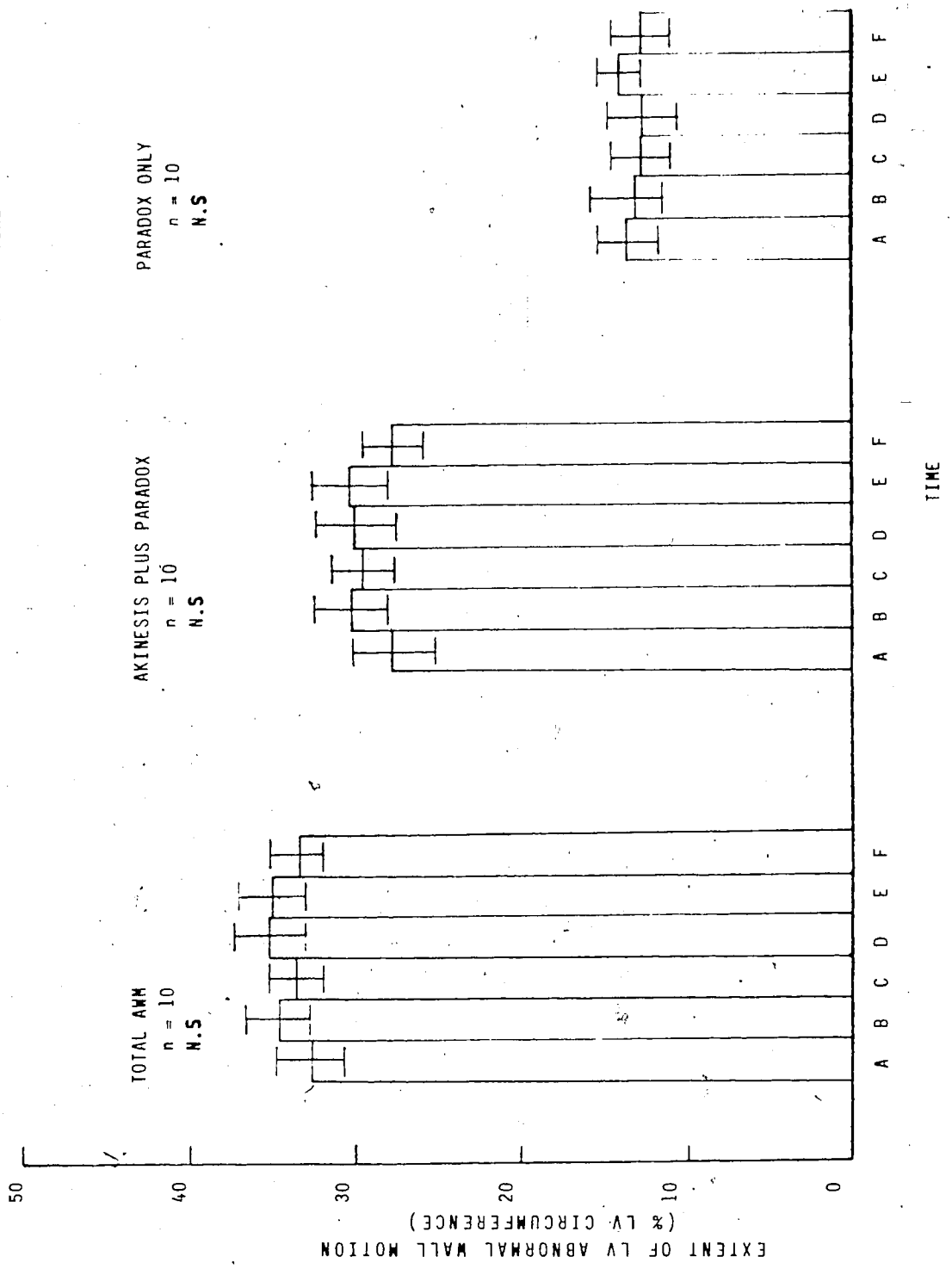


FIGURE 8(c): LONG AXIS COMPOSITE

CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME



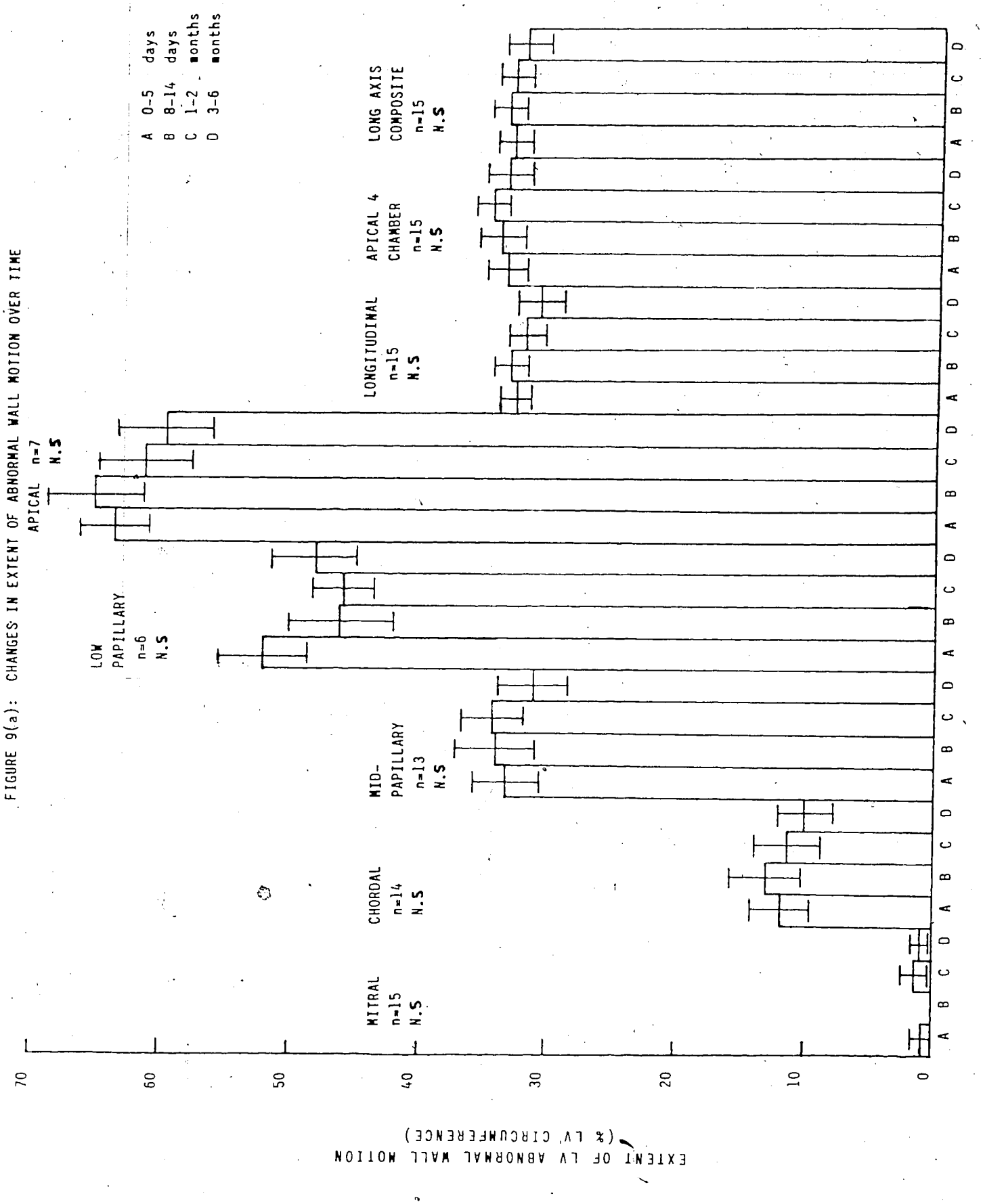


FIGURE 9(a): CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

FIGURE 9(b): CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

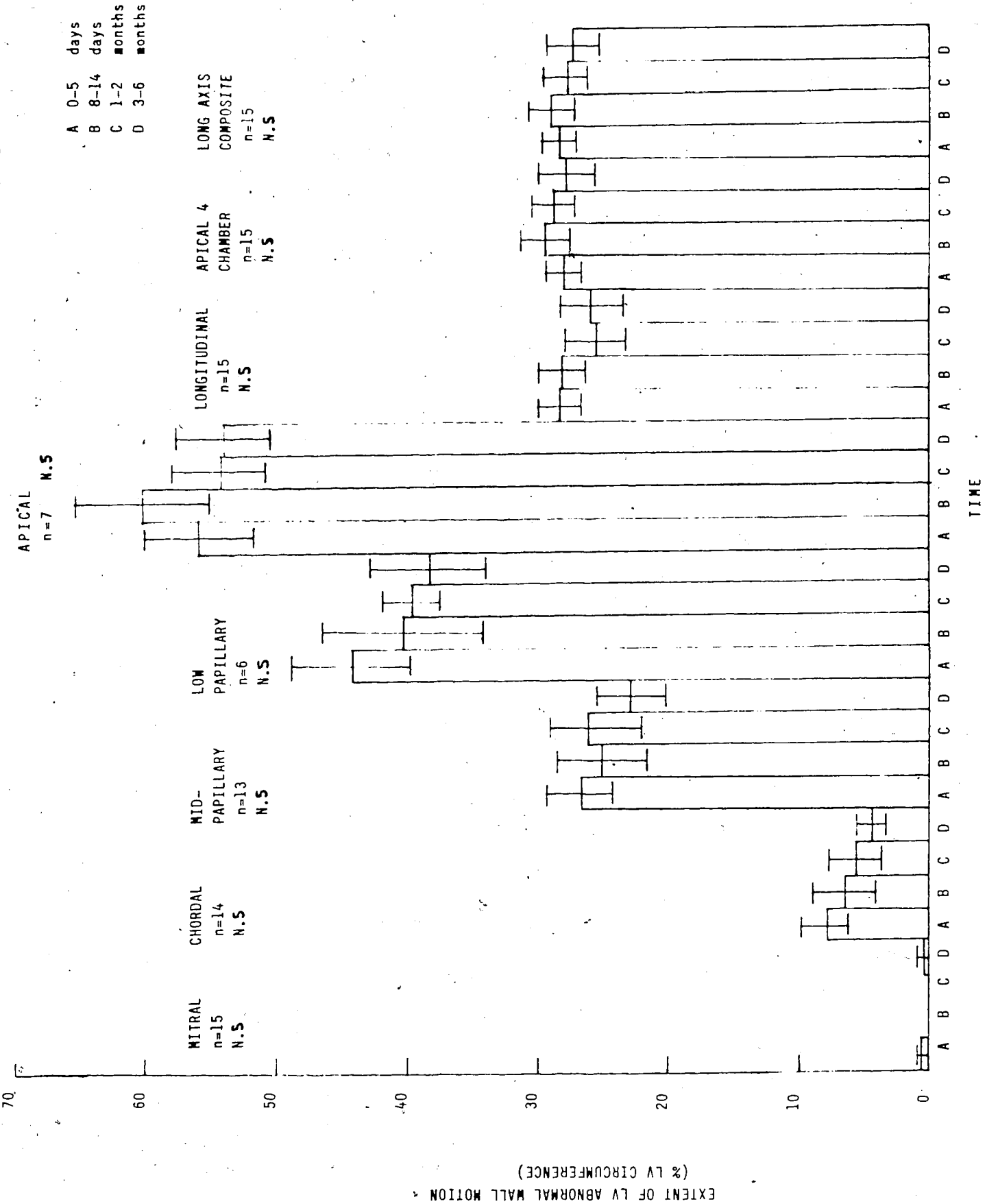


FIGURE 9(c): CHANGES IN EXTENT OF ABNORMAL WALL MOTION OVER TIME

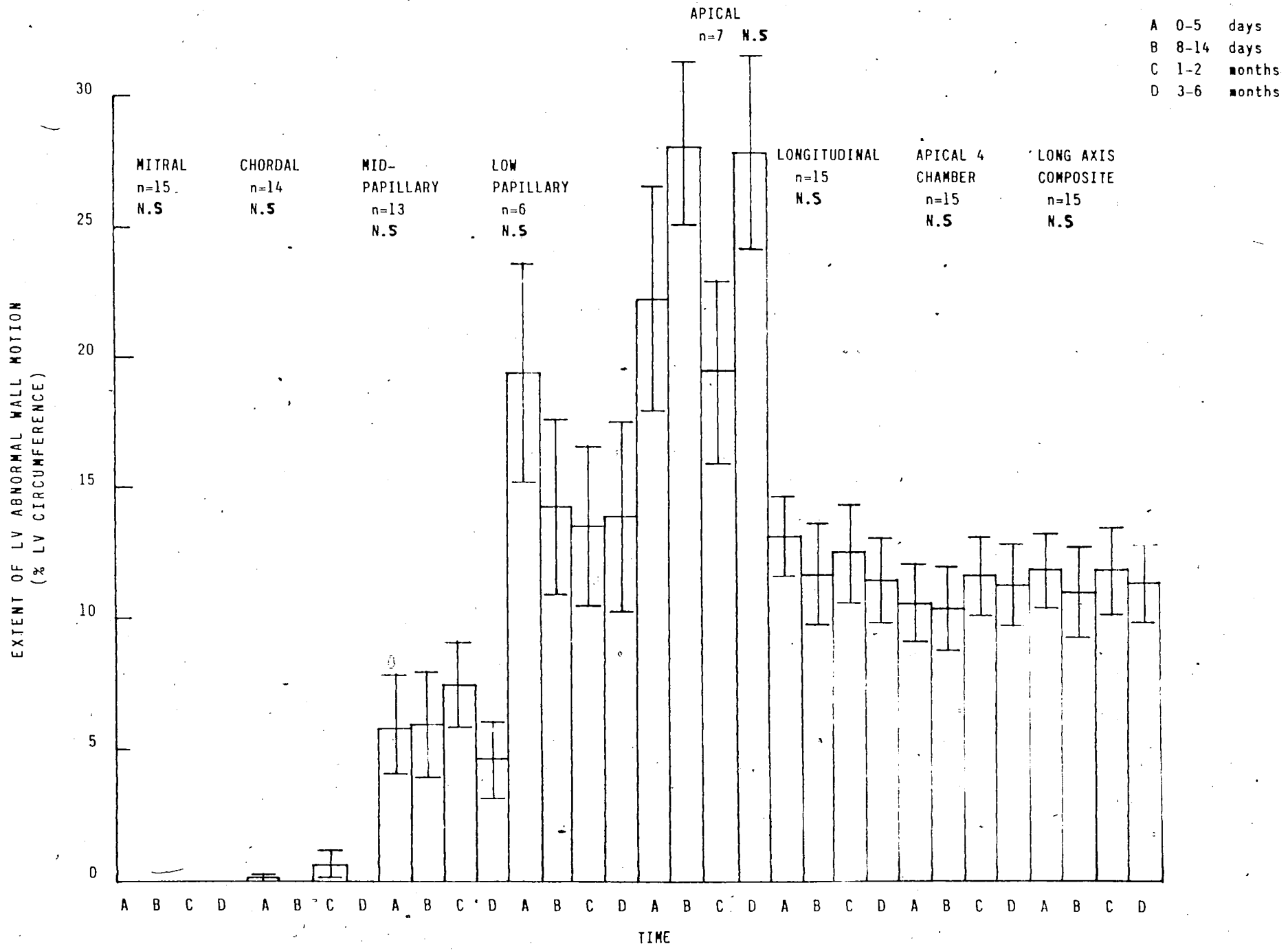


FIGURE 10(a):- LONGITUDINAL VIEW

EFFECT OF INFARCT SIZE ON EXTENT OF ABNORMAL WALL MOTION AFTER INFARCTION

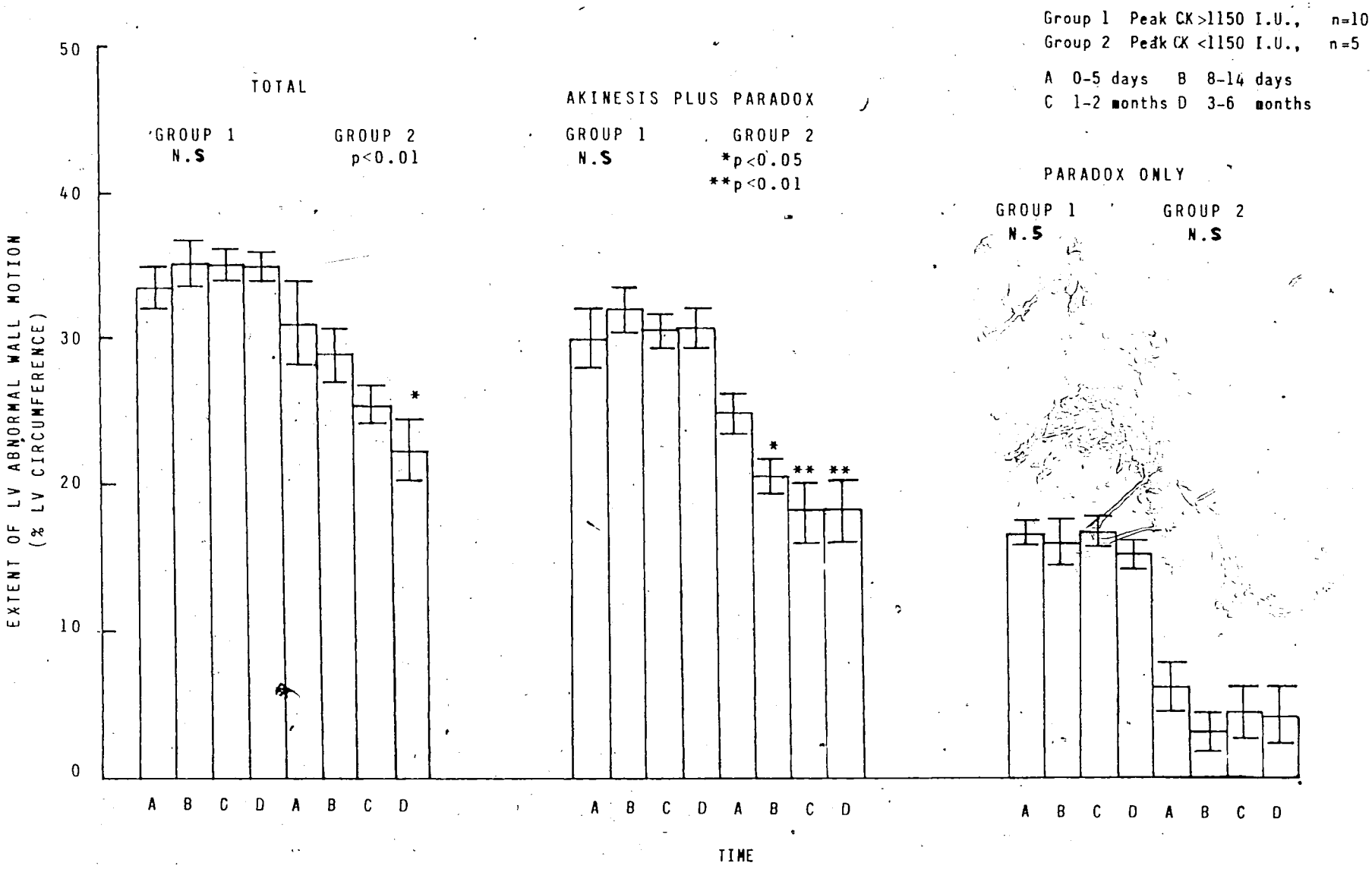


FIGURE 10(b): APICAL 4 CHAMBER VIEW

EFFECT OF INFARCT SIZE ON CHANGES IN ABNORMAL WAL MOTION AFTER INFARCTION

Group 1 Peak CK > 1150 I.U., n=10
Group 2 Peak CK < 1150 I.U., n=5
A 0-5 days B 8-14 days
C 1-2 months D 3-6 months

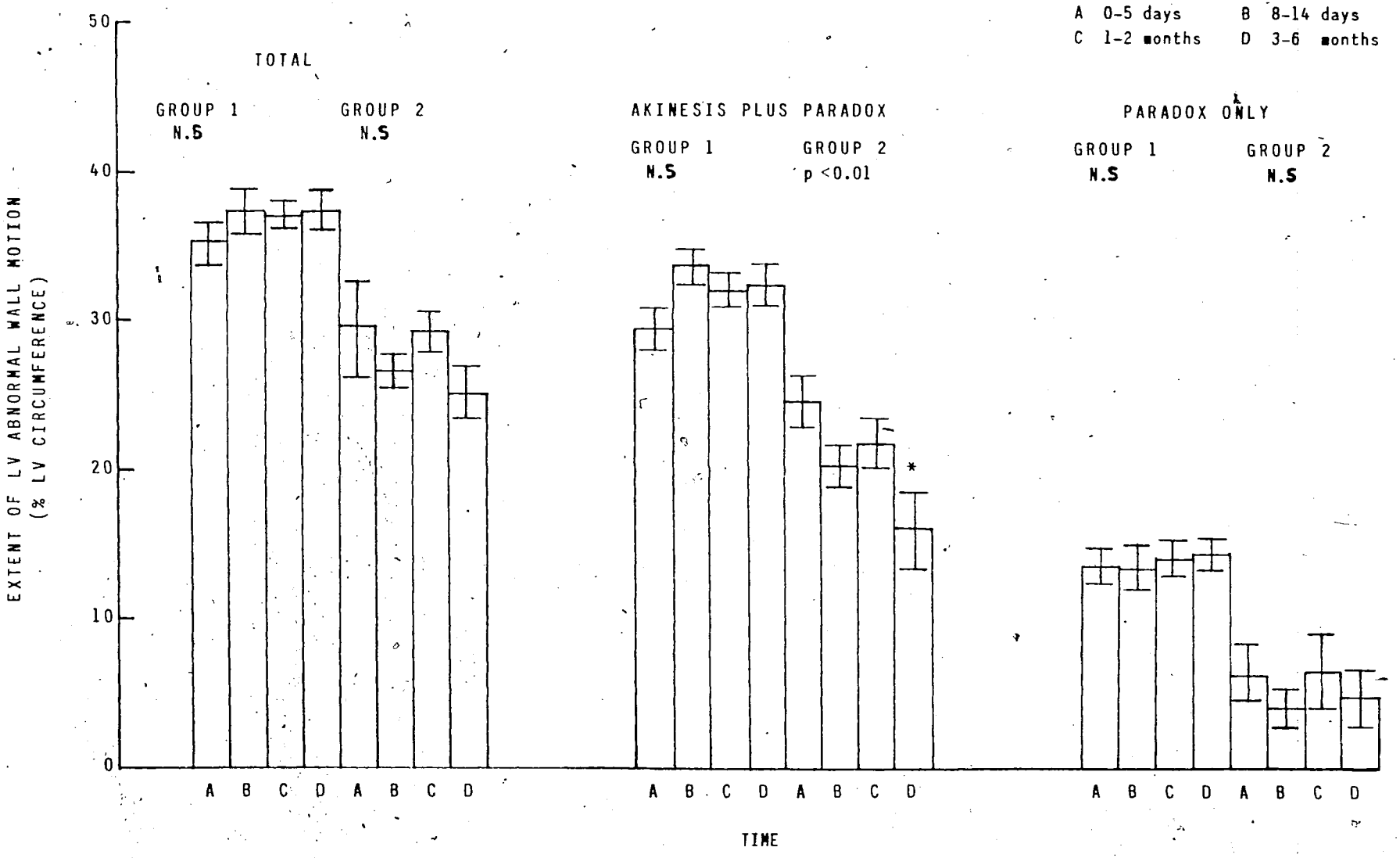


FIGURE 10(c): LONG AXIS COMPOSITE

EFFECT OF INFARCT SIZE ON CHANGES IN ABNORMAL WALL MOTION AFTER INFARCTION

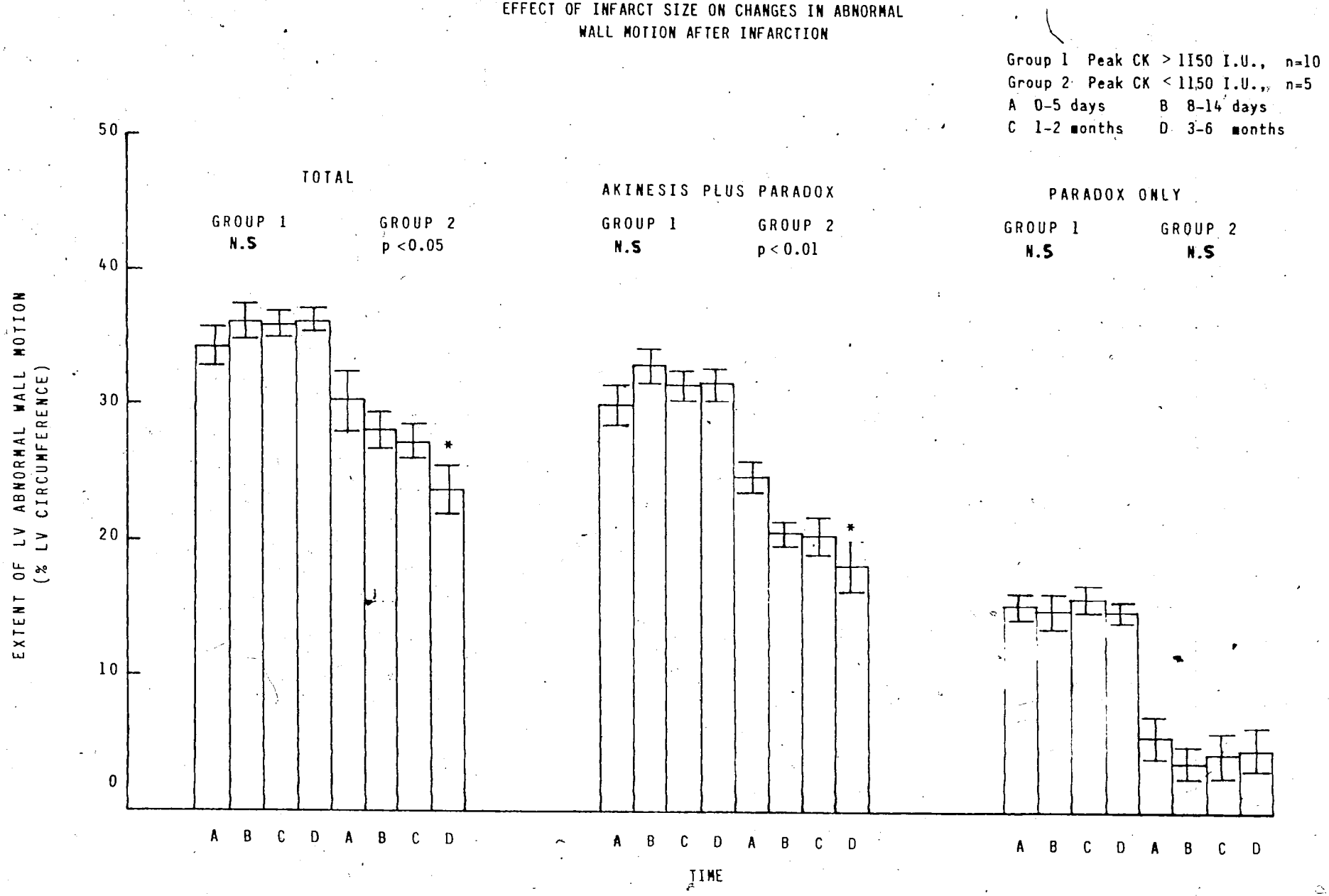


FIGURE 10(d): CHORDAL CROSS-SECTION

EFFECT OF INFARCT SIZE ON CHANGES IN ABNORMAL WALL MOTION FOLLOWING INFORMATION

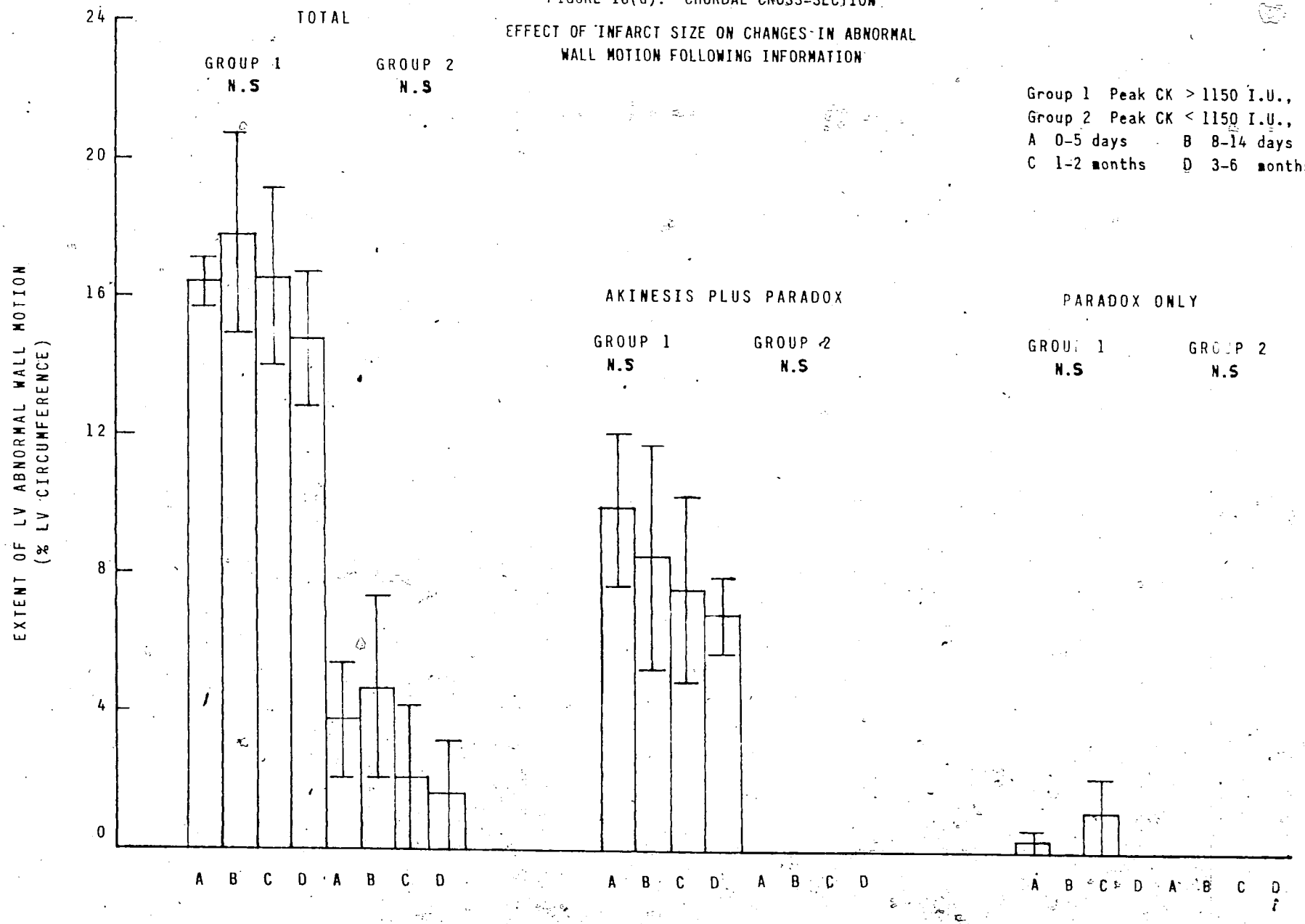


FIGURE 10(e): MID-PAPILLARY CROSS-SECTION

EFFECT OF INFARCT SIZE ON CHANGES IN
ABNORMAL WALL MOTION FOLLOWING INFARCTION

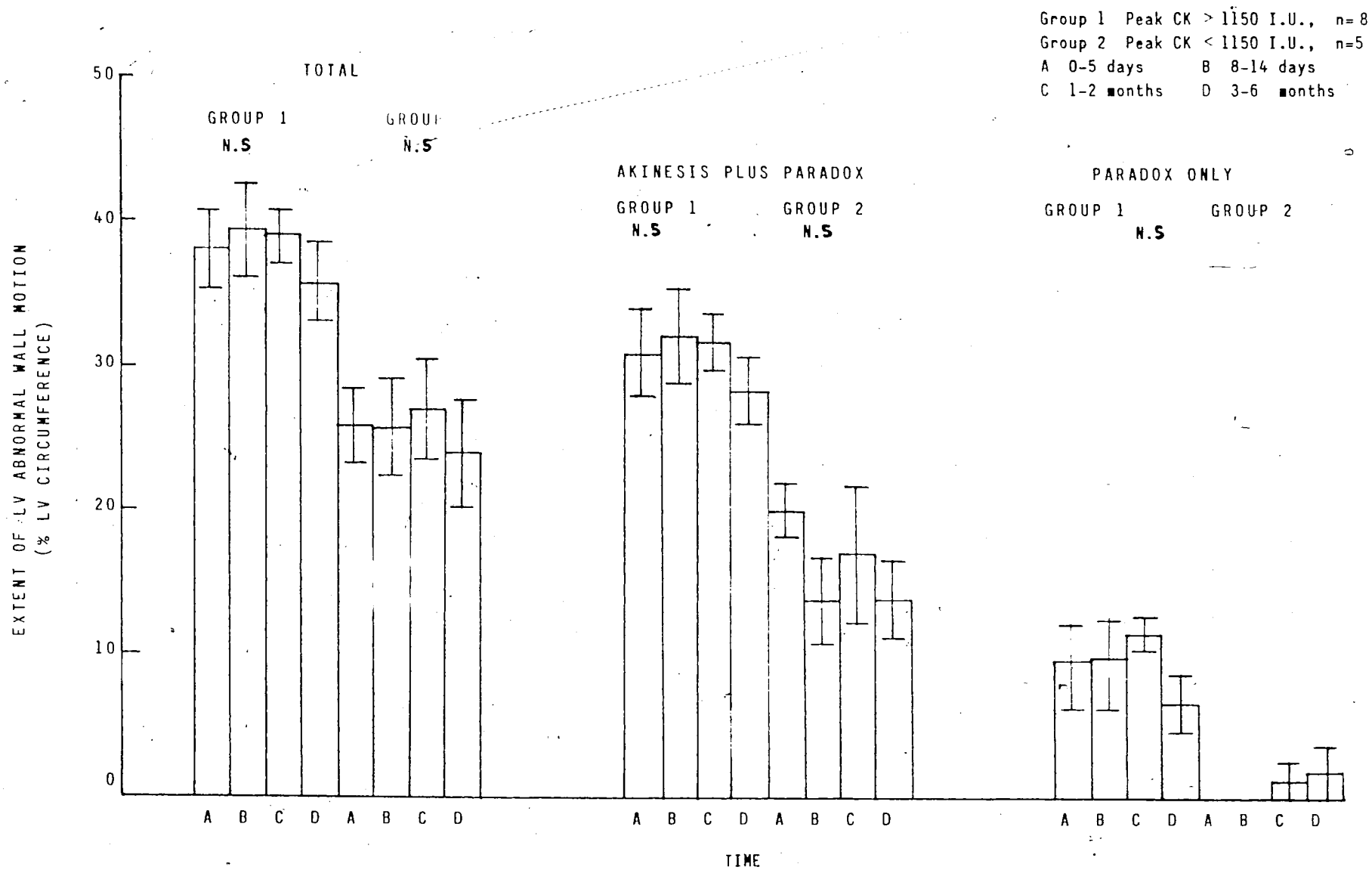


FIGURE 11(a) LONGITUDINAL VIEW

SIZE OF INFARCTION AS A DETERMINANT OF
CHANGES OVER TIME IN EXTENT OF ABNORMAL WALL MOTION

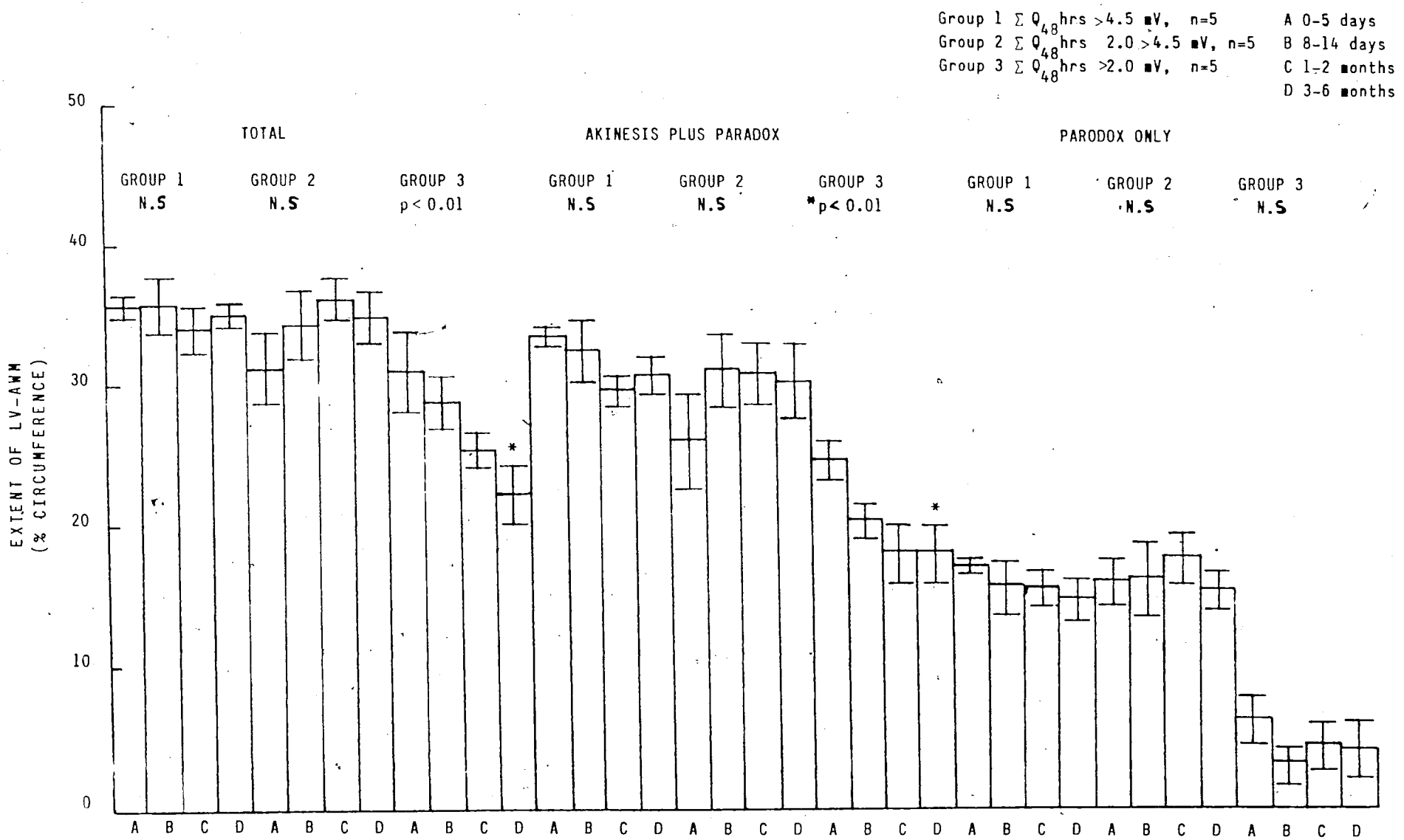


FIGURE 11(b) APICAL 4 CAHMBER VIEW

SIZE OF INFARCTION AS A DETERMINANT OF CHANGES OVER TIME IN EXTENT OF ABNORMAL WALL MOTION

Group 1 ΣQ hrs >4.5 mV, n=5
Group 2 ΣQ hrs, $2.0 > 4.5$ mV, n=5
Group 3 ΣQ hrs < 2.0 mV, n=5

A 0-5 days
B 8-14 days
C 1-2 months
D 3-6 months

TOTAL			AKENISIS PLUS PARADOX			PARADOX ONLY		
Group 1	Group 2	Group 3	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
N.S	*p < 0.05	N.S	N.S	*p < 0.05	** p <0.01	N.S	N.S	N.S

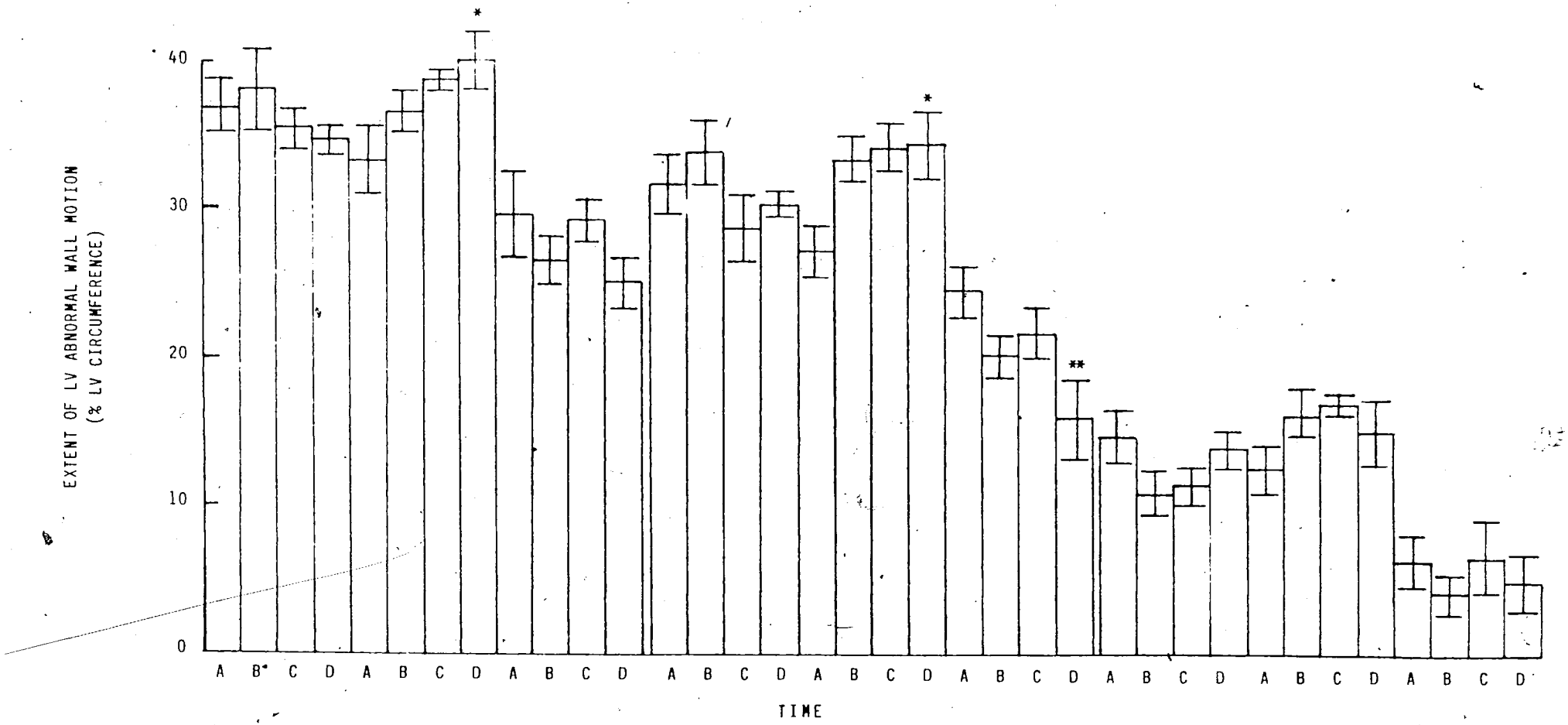


FIGURE 11(c): LONG AXIS COMPOSITE

EFFECT OF INFARCT SIZE ON CHANGES IN ABNORMAL WALL MOTION AFTER INFARCTION

Group 1 ΣQ hrs >4.5 mV, n=5
Group 2 ΣQ hrs <2.0 4.5 mV, n=5
Group 3 ΣQ hrs >2.0 mV, n=5

A 0-5 days
B 8-14 days
C 1-2 months
D 3-6 months

TOTAL AWM			AKINESIS PLUS PARADOX			PARADOX ONLY		
Group 1	Group 2	Group 3	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
N.S	*p <0.05	*p <0.05	N.S	*p< 0.05	**p <0.01	N.S	N.S	N.S

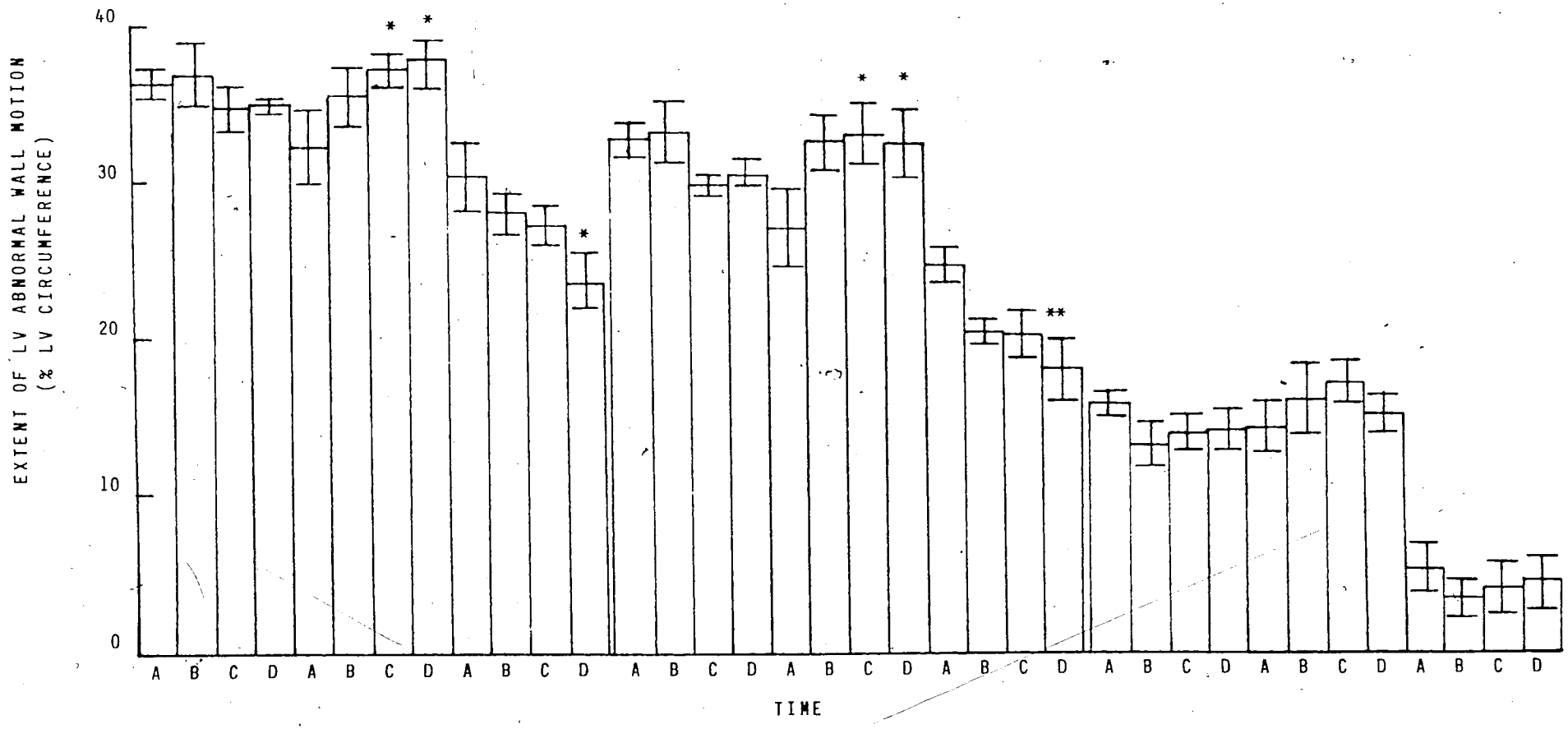


FIGURE 12: LONG AXIS COMPOSITE

EFFECT OF INFARCT SIZE ON CHANGES IN ABNORMAL WALL MOTION AFTER INFARCTION

Group 1 Extent of paradox alone (3-5 days) >15%, n=4
Group 2 Extent of paradox alone (3-5 days) 8 <15%, n=7
Group 3 Extent of paradox alone (3-5 days) <8, n=4

A 3-5 days
B 8-14 days
C 1-2 months
D 3-6 months

TOTAL AWM			AKINESIS PLUS PARADOX			PARADOX ONLY		
GROUP 1	GROUP 2	GROUP 3	GROUP 1	GROUP 2	GROUP 3	GROUP 1	GROUP 2	GROUP 3
N.S	*p <0.05	*p <0.05	N.S	*p< 0.05	*p < 0.05 **p < 0.01	N.S	N.S	N.S

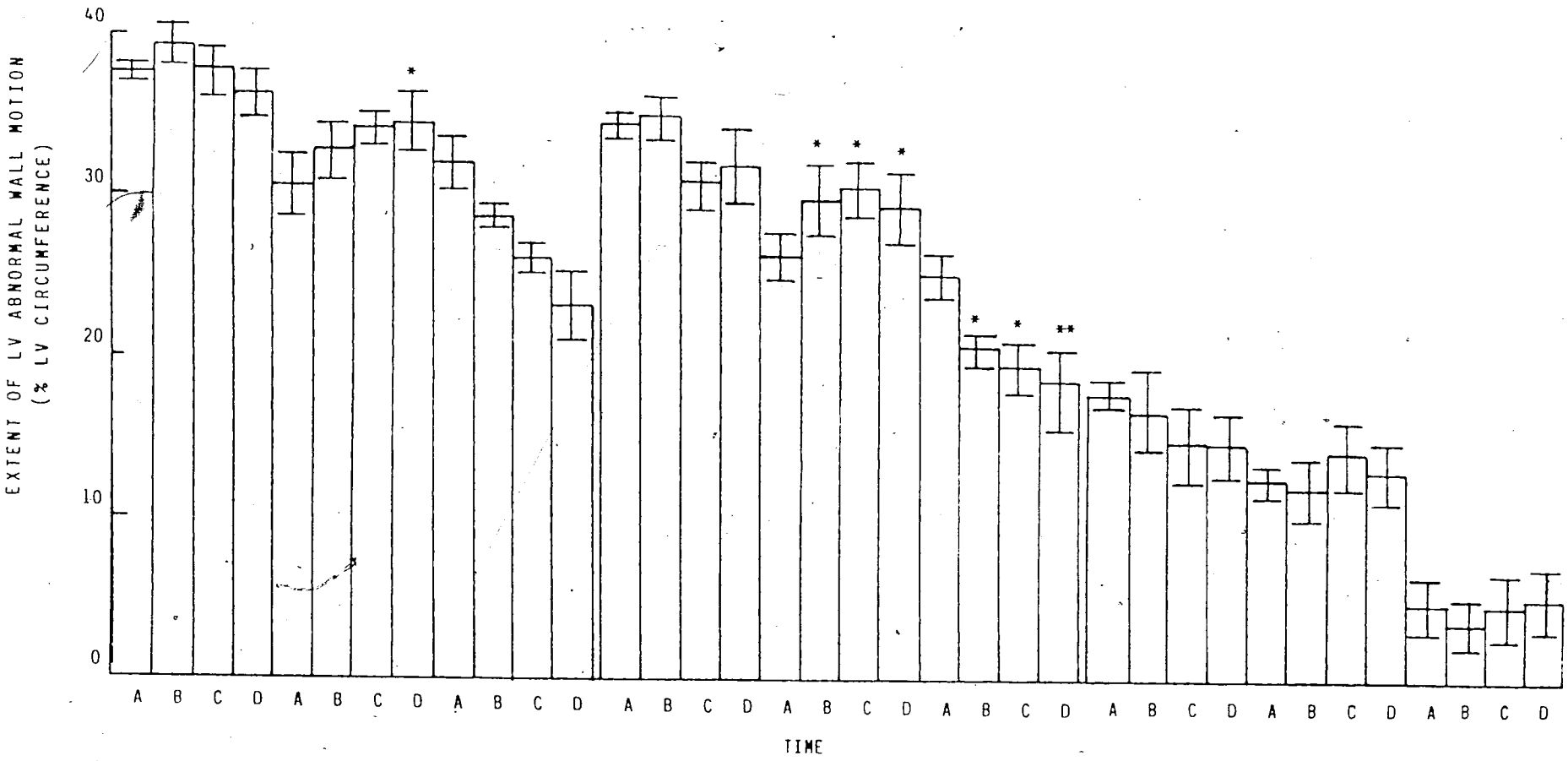


FIGURE 13

RELATIONSHIP BETWEEN PEAK CK AND LV-AWM

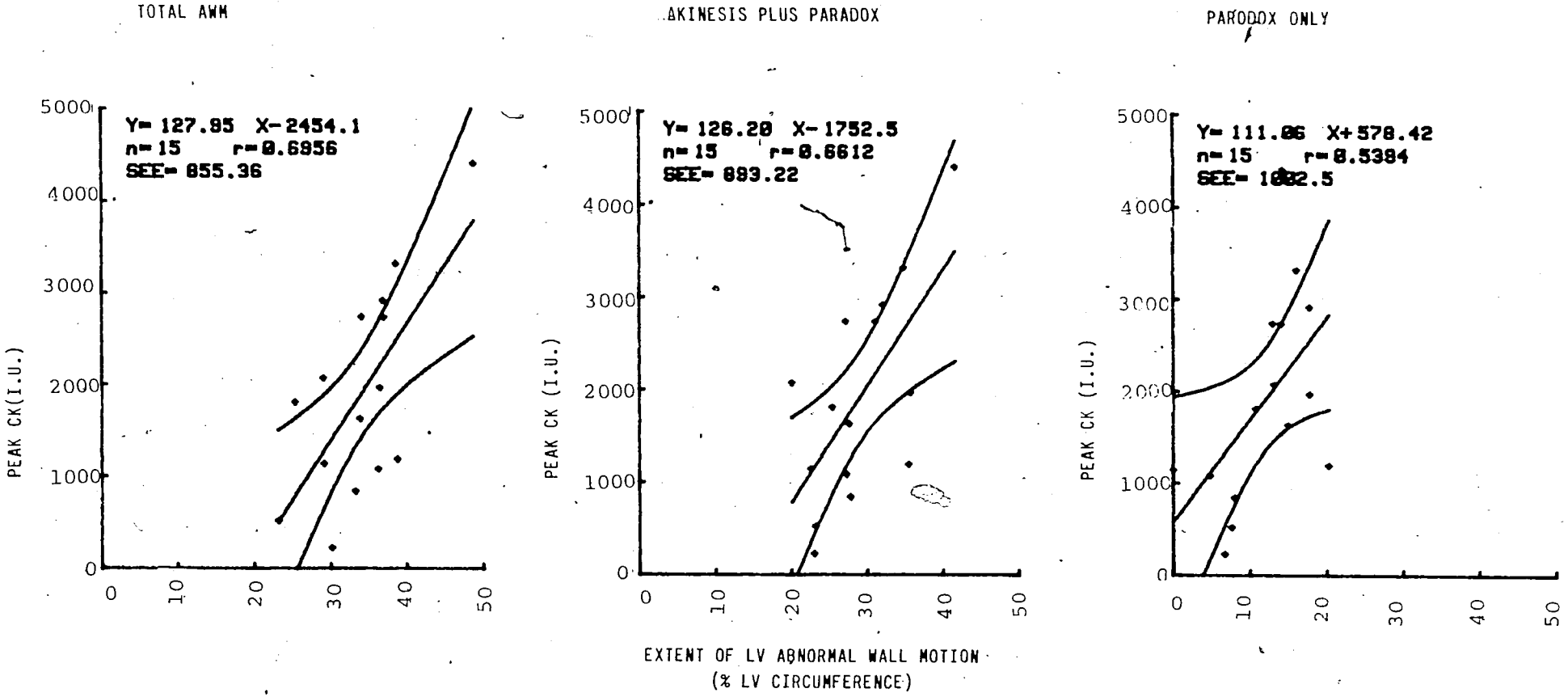
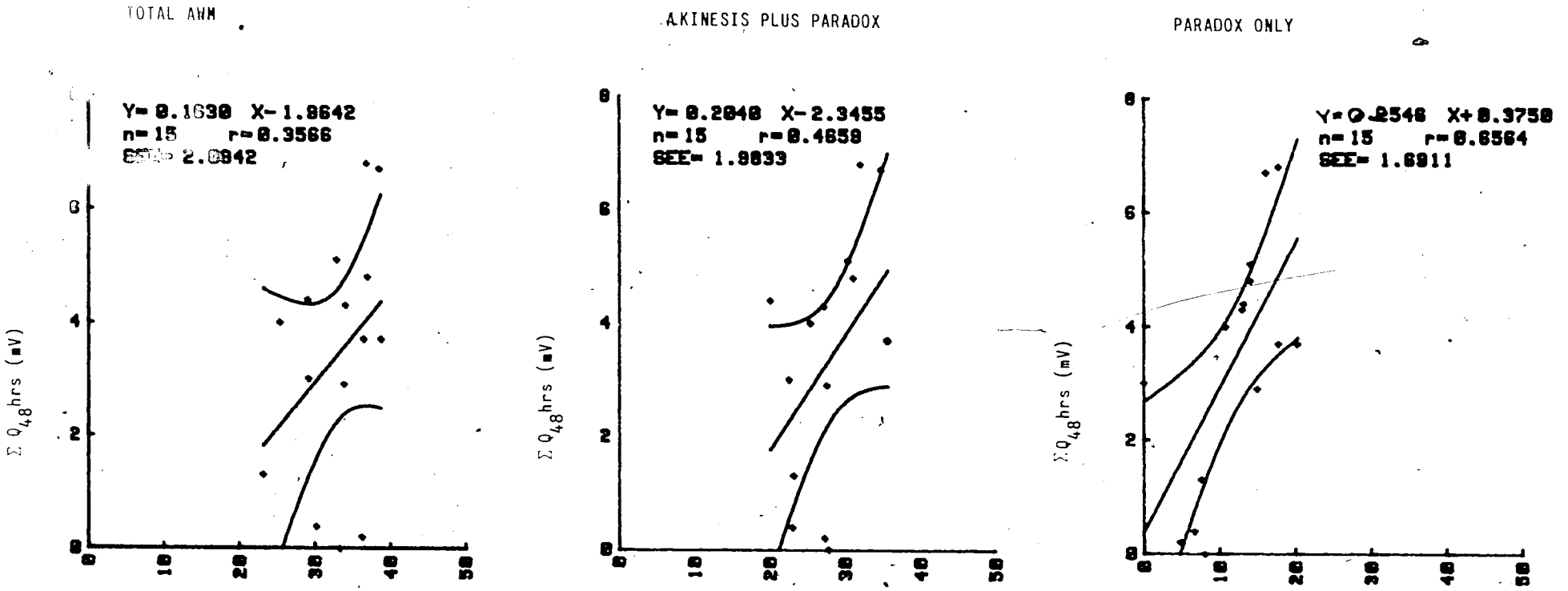


FIGURE 14

RELATIONSHIP BETWEEN ΣQ_{48}hrs AND LV-AWM



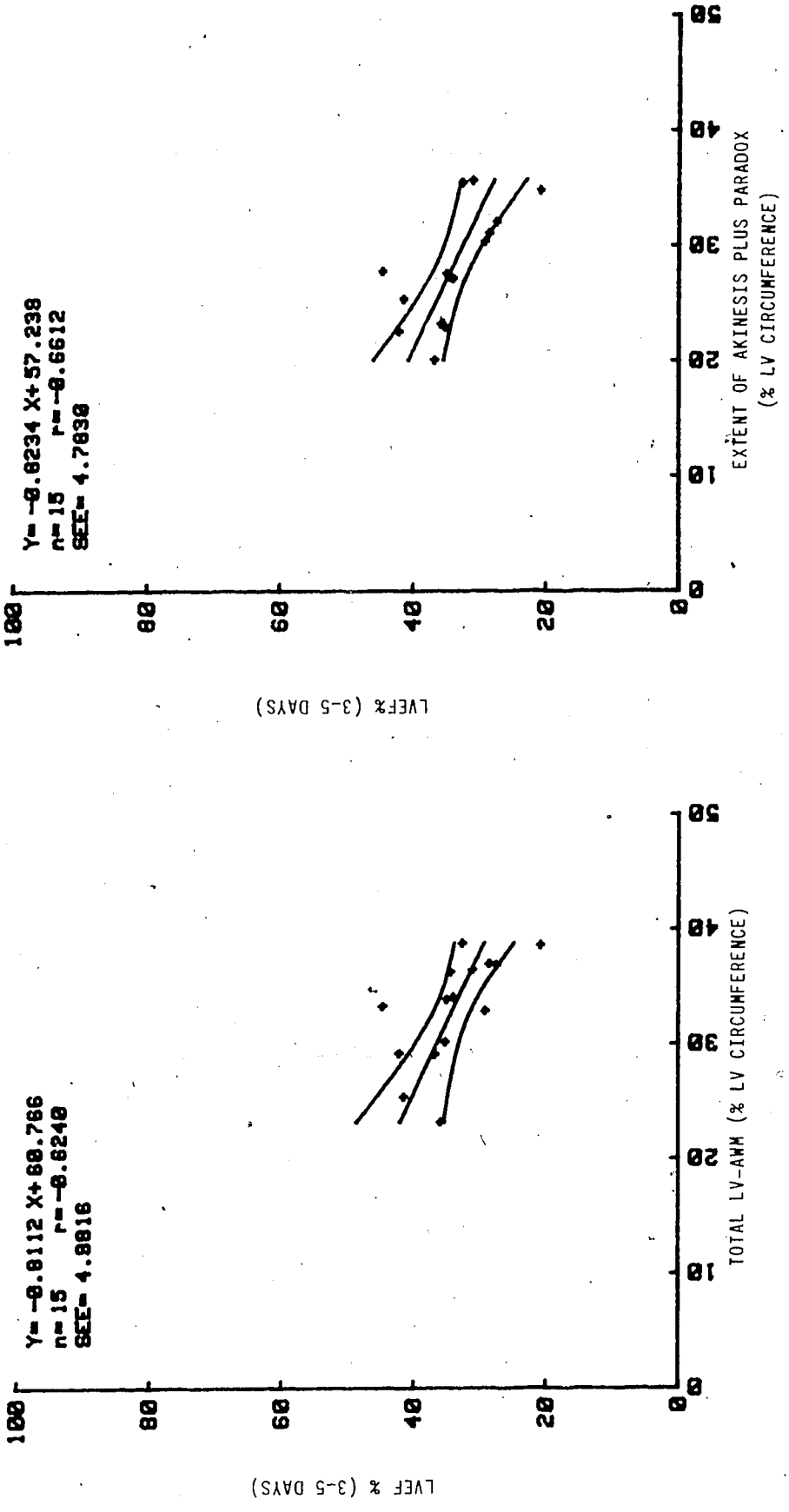


FIGURE 15

RELATIONSHIP BETWEEN LVEF AND EXTENT
OF LV-AWM at 3-5 DAYS POST MI

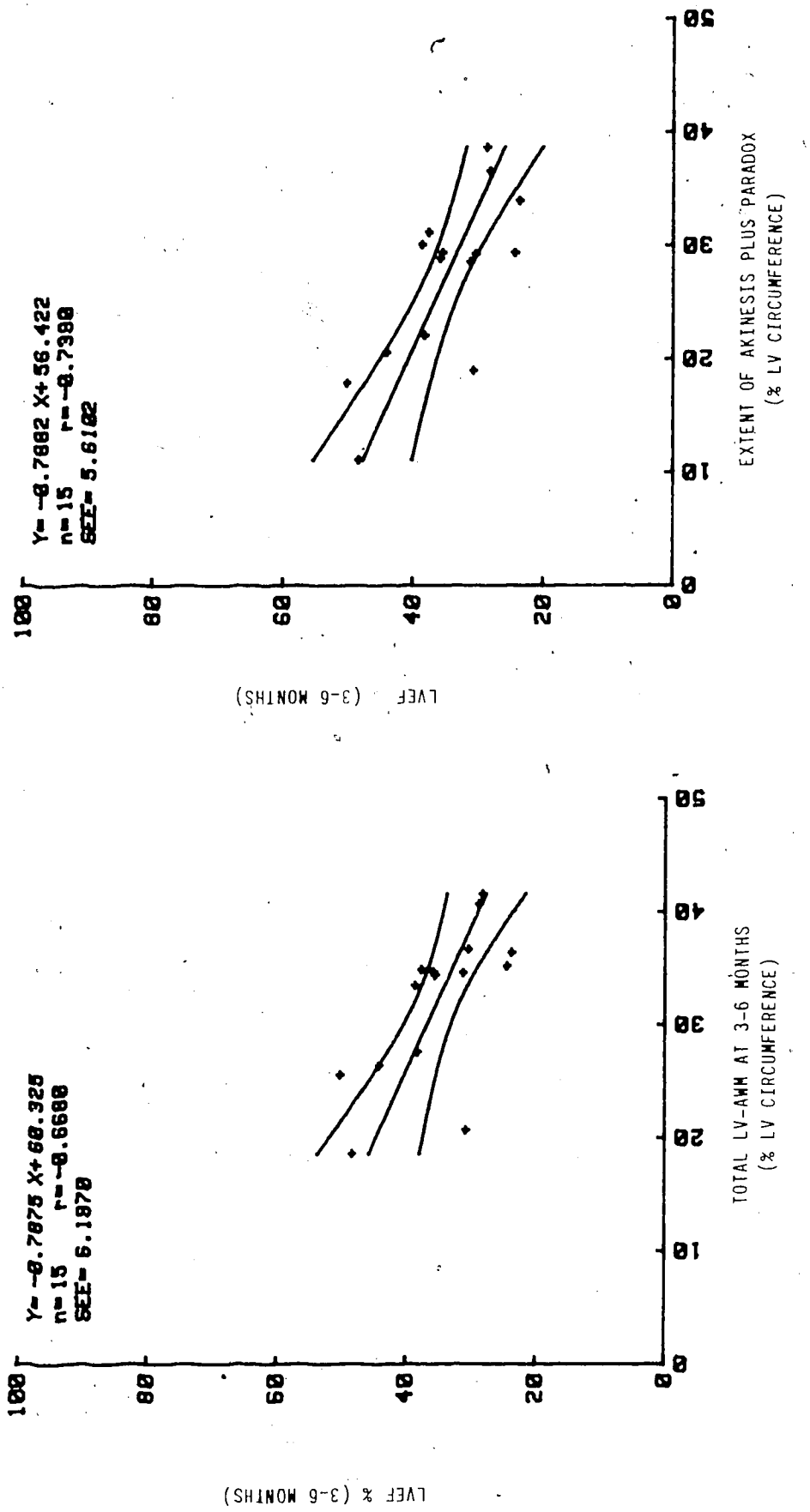


FIGURE 16

RELATIONSHIPS BETWEEN LVEF AND EXTENT OF LV-AWM AT 3-6 MONTHS POST MI

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