INFLUENCE OF ANGIOTENSIN CONVERTING ENZYME INHIBITION TO SEGMENTAL WALL MOTİON ABNORMALITIES DUE TO CORONARY ARTERY DISEASE

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Between August 1990-January 1991, patients with significant left ventricular dilatation included in our study group. There were 18 male patients with a mean age of 50±12 years (range:22-65). Selection was done among patients suffered from myocardial infarction at least 4 months ago (mean:5.1±8 months). All patients were in NHYA class III-IV.

We started enalapril (mean:20 mgr/day) to randomly selected 9 patients (Group A). Mean fallow-up period was 4.7±0.8 months. Pre and post treatment cardiac catheterization was performed to all patients. Ventriculographies of all patients recorded at 30° right anterior oblique position were evaluated by centerline method and compared with a control group. In both groups pre and post treatment circumfrential extent of akinesis or hypokinesis were 3 standart deviations (SDs) from normal for anterolateral segment and 2 standart deviations from normal for apikal segment.

In spite of continuation of post-treatment segmental wall motion abnormalities in group A; with respect to control group, post-treatment anterolateral (p< 0.001) and apical (p< 0.05) wall motion was significantly better than pre-treatment.

We conclude that ACE inhibitors must be used in chronic congestive heart failure due to coronary artery disease.

Key words: Angiotensin converting enzyme, segmental wall motion abnormalities

It is established that the renin —angiotensin— aldosterone system has an important role in congestive heart failure physiopathology[1]. Over activity of renine - angiotensin- aldosterone system cause maintanence and deterioration of congestive heart failure[2,3].

Therefore, ACE inhibitors became established in congestive heart failure treatment beside conventional therapy (Diuretic, digitalis, salt restriction and rest).

ACE inhibitors improve cardiac pump function by decreasing left ventricular afterload via arterial and venous dilatation. Thereby, improvement in life expectancy[4,5], exercise capacity and clinical situation can be expected. It was shown that left ventricular dilatation after acute myocardial infarction can be regressed by decreasing left ventricular load[5,6].

Ventricular remodeling ensue in either normal or ischemic myocardial territory in patients with diffuse transmural myocardial infarction[7, 8,9]. Reduction of ventricular wall stress is one of the main factor affecting ventricular dilatation rate[10,11]. The operative mechanism are the same for the patients with chronic congestive heart failure. In the present study, we aimed to evaluate the effect of ACE inhibition on segmental wall motion abnormalities in chronic heart failure due to coronary artery disease.

Methods

18 patients with significant left ventricular dilatation were included in this study. All of them were male with a mean age of 50±12 years (range: 22-65).

Selection was done among patients suffered from myocardial infarction at least 4 months ago (mean: 5,1±0.8 months).

All patients were in NYHA class III-IV. Patients with diabetes mellitus, hypertension, chronic renal failure, and patients with myocardial infarction less than 4 months were excluded from the study. The medication that have been given before (digitalis, diüretic, antianginal and antiarrytmic) was continued throughout the study. All patients were taking digitalis. 8 of the patients were taking long acting nitrate, 9 of them diüretic and 2 of them antiarrytmic agents (Group III antiarrytmic)

The patients were numbered from 1 to 18.

Enalapril was started to patients with odd numbers (Group A). Initial dose of enalapril was 2.5 mg/day and it was increased gradually to a maximum of 30 mg/day (mean: 20 mg/day).

5 of the Group B patients (Digitalis group) were taking long acting nitrate, 6 of them diüretic, and 3 of them antiarrytmic agents (Group III antiarrytmic).

After recording enddiastolic pressures, left ventriculography was performed. Cine-angiographic recording was done at 30° right anterior oblique position, and left ventricular volume was calculated according to single-plane method[12,13]. Magnification correction was done. Followup examination was done weekly in the first month afterwards montly for 5 months (4.7±0.8 months).

After the follow-up period, all patients underwent repeat catheterisation. Their left ventriculography was done, and end diastolic pressure was recorded again.

Control group included 50 normal cases with normal coronary arteriography and ventriculography to whom coronary arteriography was performed because of their anginal complaints. These cases (control group) were free of valvular heart disease, their ECG were normal and their left ventricular end diastolic pressure were less than 12 mmHg.

Measurment of wall motion by the centerline method:

Motion was measured along 100 chords drawn perpendicular to a centerline constructed midway between the end-diastolic and end-systolic contours (Figure 1). The measured motion of the 100 chords was normalized for heart size by dividing the length of the end-diastolic perimeter. This results in a dimension less shortening fraction, a linear equivalent of the volume ejection fraction. Since normal motion varies from chord to chord, the normalized motion (Mi) at each chord i is converted into units of normal standart deviations (SDi): Zi=(Mi-Ni)/SDi. This standardization allows comparison of the motion of different regions of the ventricle.

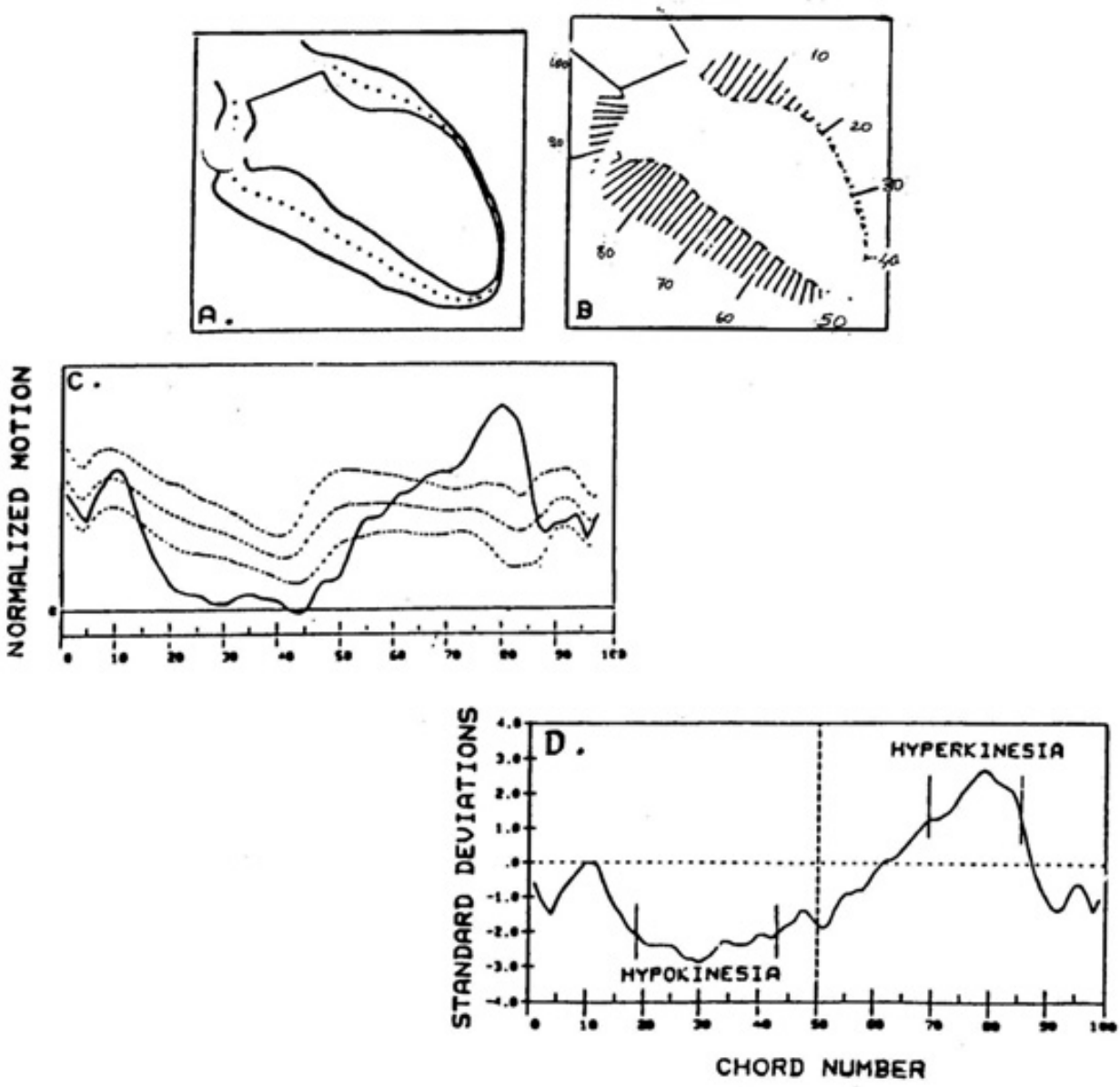

Figure 1. Centerline method of regional wall motion analysis: A, End-diastolic and end-systolic left ventricular endocardial contours and centerline (A) constructed by the computer midway between the two contours. B, Motion is measured along 100 chords constructed perpendicular to the centerline. C, Motion at each chord is normalized by the enddiastolic perimeter to yield a shortening fraction. Motion along each chord is plotted for the patient (solid line). The mean motion in the normal ventriculogram group (dashed line) and one standard deviation above and below the mean (dotted lines) are shown for comparison. D, Standardized motion. The wall motion of the patient is nowplotted in units of standart deviations from the normal mean (dotted line). The normal ventriculogram group mean is represented by the horizontal zero line. Vertical lines delimit the most hyperkinetic (HYPER) and most hypokinetic (HYPO) parts of the anterior and inferior regions.

Positive values indicate hyperkinesis; negative values, hypokinesis.

The location of wall motion abnormality is expressed as the chord number at the beginning and end of the abnormal region. Wall motion in each of five regions of the left ventricular contour and mitral valve was determined by averaging the motion abnormality, expressed in SD, of chords 1 to 16, 17 to 32, 33 to 48, 49 to 64, and 65 to 80, corresponding to the anterobasal, anterolateral, apical, inferior and posterobasal regions and the mitral valve, respectively. The severity of hypokinesis in this segment was measured and compared with

motion in the predetermined regions by paired t test.

Results

Of the 18 consenting eligible patients, 9 were randomly assigned to enalapril and 9 to medication that have given previously. The mean age of the two groups were similar (49.4±13.6 and 56.5±3.5 years).

Initial mean systolic and diastolic blood pressure were similar in two groups. Mean systolic and diastolic blood pressure were 131±19 and 83±14 mmHg in group A. These values were 134±6 and 82±7 mmHg in group B respectively. Mean systolic and diastolic blood pressure were 127±10 and 77±9 mmHg in Group A after treatment and the difference was not significant (p=NS).

Mean systolic and diastolic blood pressure were 130±11 and 78±6 mmHg in group B after treatment and the difference was not significant (p=NS).

Mean left ventricular end diastolic pressure was 25±8 and 26.5±6.5 mmHg respectively for group A and B (p=NS).

After treatment, left ventricular end-diastolic pressure was 18.2±6.7 mmHg and 22.6±5.7 mmHg respectively for group A and B. The reduction of left ventricular end diastolic pressure was significant in group A ($p< 0.05$) and the reduction in group B was not significant (p=NS). Pre and post treatment ejection fraction values didn't change significantly in two groups (P=NS) (Group A: %30±9, %32±19, Group B: %35±8, %32±6).

The mean age of control group was 48±7 years. Segmental wall motion by centerline method of control group is shown in Figure 2.

Pre-treatment, anterolateral, apikal, inferior and posterobasal segmental wall motion in both groups were significantly poorer than control group ($p< 0.001$). In respect to control group, there was no statistically significant improvement in post-treatment segmental wall

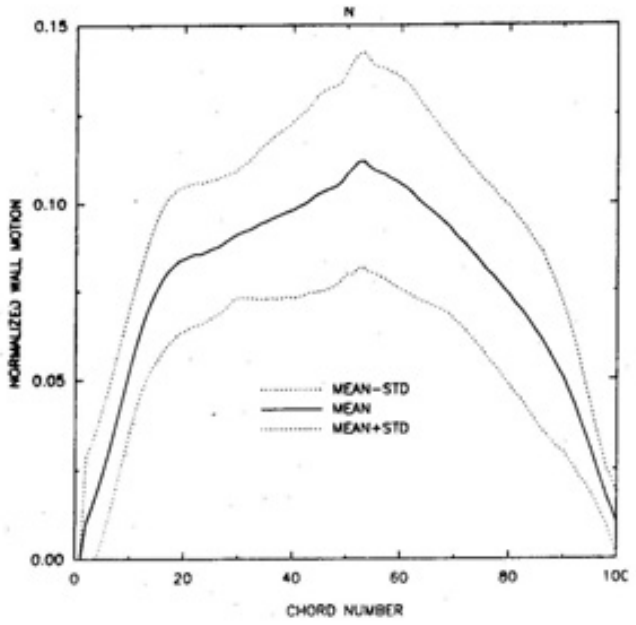

Figure 2. Measurment of wall motion in 30 degree RAO projection in normal cases.

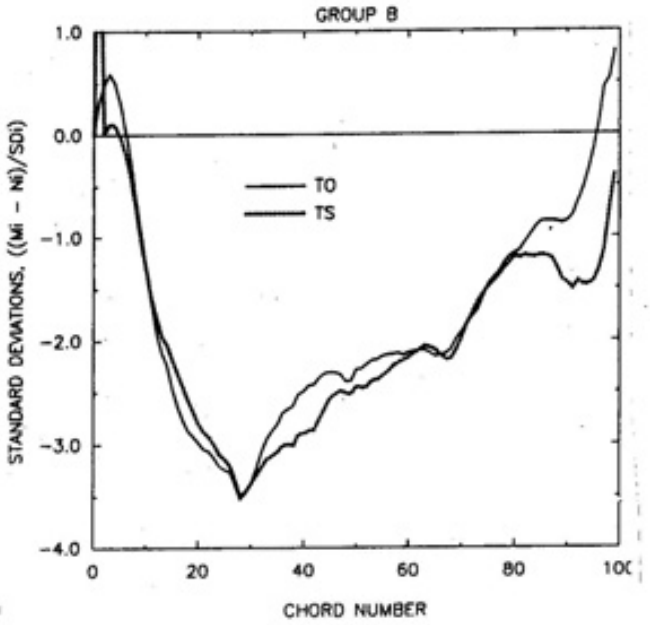

Figure 3. Determination of the circumferential extent of akinesis and hypokinesis more than 1,2 and 3 SDs from normal in group B (TO: preatreatment, TS post-treatment)

motion abnormalities in two groups and wall motion abnormalities in both groups were still significantly poorer than control group ($p< 0.001$). Pre-treatment anterolateral, apical, inferior, posterobasal segmental wall motion abnormalities were comparable in group A and B (p=NS). There was no statistically significant difference between pre and post-treatment segmental wall motion abnormalities in group B (P= NS, Figure 3).

In spite of continuation of post treatment segmental wall motion abnormalities in group A with respect to control group; post treatment anterolateral ($p< 0.001$) and apical ($p< 0.05$) segmental motion was significantly better than pretreatment (Figure 4).

When post treatment segmental wall motion of group A and B was compared, anterolateral and apical segmental wall motion improved significantly in group A ($p< 0.01$, Figure 5).

Discussion

Ventricular dilatation is an important expression of systolic dysfunction of diverse causes. Left ventricule begins to dilate soon after myocardial infarction and in the acute phase, such chamber enlargement is caused primarily by expansion of the infarct. When contractile myocardium is lost; in order to restore stroke volume, ventricular dilatation must occur[15]. Recently, data from both clinical and experimental studies, such as that the region of myocardium without an infarct is also involved in the overall pattern of enlargement of the left ventricular chamber[16,17]. The eventual volume of the ventricle with an infarct has been shown to be related to the size of the infarct as assessed by the proportion of the ventricular silhoutte that is either akinetic or dyskinetic[16]. Progressive dilatation and wall motion abnormalities of left ventricule is inversly correlated with life expectancy[18]. Unloading of the heart by ACE inhibition causes reduction of ventricular

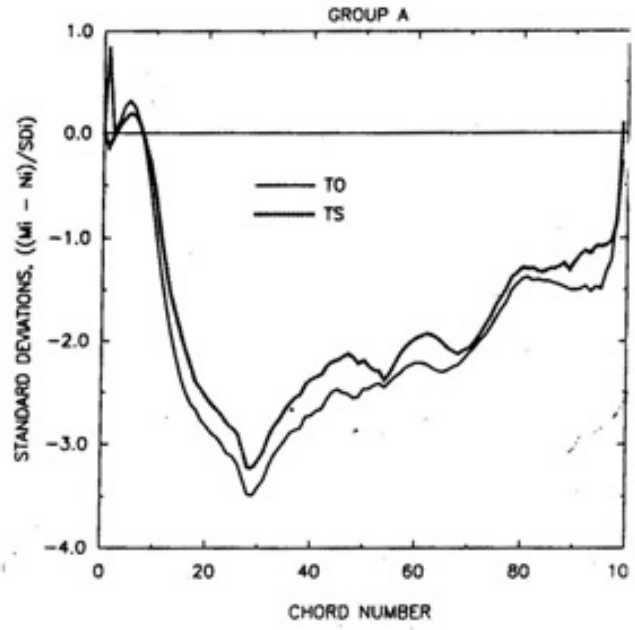

Figure 4. Determination of the circumferential extent of akinesis and hypokinesis more than 1, 2 and 3 SDs from normal in group A (TO: pretreatment, TS:post treatment)

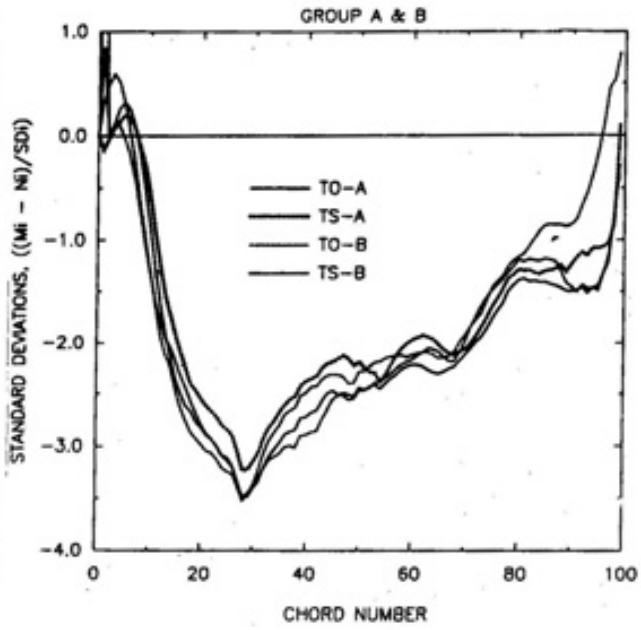

Figure 5. Determination of the circumferential extent of akinesis and hypokinesis in two groups more than 1,2,3 SDs from normal

dilatation rate or regression of ventricular dilatation soon after acute myocardial infarction[5,6,11,19,20].

It was shown that ACE inhibitors cause unloading of left ventricule in chronic stage as in acute stage[21,22].

The effect of ACE inhibition is not only hemodynamic but also reduction of collagen content and considerable change in the ratio of type I and type III collagen due to reduced angiotensin II blood consentration[20,23,24] (Remodeling of left ventricule).

In our study, we found that segmental wall motion abnormalities were improved in enalapril group. But, statistically significant improvement is found only in anterolateral and apical segments. Maybe, segmental wall motion improvement in this group depends on reduction of afterload and left ventricular wall stress which causes restriction of hibernating myocardial territory. As quoted before, remodeling of the heart will occur only if the heart is unloaded while the plasma consantrations of angiotensin II are simultaneously reduced. In an experimental study, treatment with a vasodilator that unloads the heart but activates the renin angiotensin aldosterone system did not reduce heart size[25].

It was shown that evaluation of segmental wall motion is a better indicator than ejection fraction for survival.

We conclude that ACE inhibitors must be used in chronic congestive heart failure due to coronary artery disease and it is not surprizing to expect improved life quality and longer survival in these patients.

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