### II. Clinical problems

# LEFT VENTRICULAR RELAXATION AND RAPID FILLING IN PATIENTS WITH ESSENTIAL HYPERTENSION AND UNSTABLE ANGINA PECTORIS

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Our studies during the period from 1970 till 1984 proved that there were-considerable abnormalities of left ventricular relaxation and filling in essential hypertension (H), ischemic heart disease (IHD) and in left ventricular hypertrophy due to other reasons (2, 3). A concept is being formed that slow and incomplete relaxation is a frequent and early sign of disturbed left ventricular function in hypertrophy and ischemia (1, 10—12, 15).

The aim of the present work is to continue the investigations started and towork out the details of the changes of left ventricular relaxation and rapid filling

in essential hypertension and unstable angina pectoris (UAP).

#### Material and methods

A total of 60 patients were studied — 30 (26 males and 4 females) with H aged between 19 and 56 years (mean age of 39.0 years) and 30 (27 males and 3 females) with UAP aged between 35 and 69 years (mean age of 52.9 years) prior to administration of an active antihypertensive and antianginal treatment. H patients were of stage 2 after WHO and with echocardiographically proved left ventricular hypertrophy (13, 16). UAP patients were dlagnosed after WHO modified criteria (4). Of them, 20 patients had an old myocardial infarction and 22 — hypertension, too. Left ventricular systolic function of the patients evaluated according to the ejection fraction and  $V_{\rm cf}$ , demonstrated abnormal values only in 2 patients with H and in 5 with UAP. The results from these two patients groups were compared with those from 33 healthy males aged between 20 and 45 years (mean age of 30.1 years). Normal ranges were determined by two standard deviations of the corresponding mean rates in healthy individuals.

We measured (in ms) the time intervals of early diastole after the method of Alvares and Goodwin (7) from the simultaneous recording of M-mode echocardiography of the mitral valve, AGG, PCG and ECG after a method introduced

in our Clinic (3).

1. Isovolumetric relaxation period (IVRP) — from the onset of the aortic component  $(A_2)$  of the second sound of PCG till point D of the mitral echocardiogram.

2. Active suction period (ASP) — from point D of the mitral echocardio-

gram till point 0 of the ACG.

3. Rapid relaxation period (RRP) — from  $A_2$  of the second sound of PCG. till point 0 of ACG.

4. Slow relaxation period during the rapid filling (SRPRF) — from point 0 till point F of ACG.

5. Rapid filling period (RFP) — from point D of the mitral echocardiogram

till point F of ACG.

We assessed by using semiautomated computerized analysis (Echocomputer

NIEMT — MA Sofia) of the left ventricular echogram (5):

a) Rapid filling fraction (RFF - %) — relation between the blood volume entered left ventricle during the rapid filling and the stroke volume in percentage;

b) mean rapid filling rate  $(MRFR - ml.s^{-1})$  — blood volume entered the left ventricle during the rapid filling related to the time required for rapid fil-

ling.

#### Results and discussion

Time intervals of early diastole showed considerable differences between the patients studied and the control persons (table 1). IVRP and total RRP were sta-

Table 1
Indexes of relaxation and rapid filling  $(\bar{x}\pm s)$ 

Indexes	Healthy n=33	H patients n=30	UAP patients n=30
IVRP p p'	43.4±6.6	70.4±12.3 0.0001	81.2±12.7 0.0001 0.001
ASP	$64.8 \pm 8.9$	$51.8 \pm 10.8$ 0.0001	$52.4 \pm 17.9$ $0.001$ $0.32$
RRP p,	$108.3 \pm 12.3$	$122.2 \pm 17.7$ $0.001$	133.6±23.1 0.0001 0.045
ŜRPRF p	$75.8 \pm 12.3$	$78.8 \pm 13.9$ $0.32$	$80.3 \pm 14.3$ $0.10$ $0.32$
p' RFP p	140.0±15.8	$130.7 \pm 20.2$ $0.045$	$132.9 \pm 20.8$ $0.10$ $0.32$
RFF	72.4±7.8	$54.0 \pm 9.8$ 0.0001	$46.9 \pm 12.4$ $0.0001$ $0.02$
MRFR P P'	488.6±103.9	399.4±137.8 0.0001	304.0±76.0 0.0001 0.10

Note: p — compares patients with healthy persons p' — compares H patients with UAP ones

tistically reliably prolonged, more expressed in UAP patients. ASP was shortened without any difference between both patients' groups. SRPRF did not differ from that in healthy controls.

IVRP was abnormally prolonged in all the UAP patients and in 27 (90 per cent) patients with H (p < 0.02) while RRP was increased in 16 UAP patients (53.3 per cent) and in 7 cases with H (23.3 per cent) (p < 0.05). ASP was subnor-

mal in 12 UAP patients (40.0 per cent) and in 11 cases with H (36.7 per cent) (p > 0.32). In the rest patients these time intervals were in normal ranges. SRPRF was abnormally increased in 2 H and one UAP patient. Although total RPP mean values were significantly shortened in H and insignificantly in UAP patients, it was subnormal in 3 H and 2 UAP patients only.

Mean values of both RFF and MRFR decreased in patients as compared with these of the healthy controls statistically significantly to a greater extent for RFF in UAP patients. According to the individual data analysis, RFF was subnormal in 24 UAP patients (80.0 per cent) and in 19 patients with H (63.3 per cent) (p>0.10) but MRFR — in 17 (56.7 per cent) and 13 (43.3 per cent) (p>0.10),

respectively. The rest patients demonstrated normal RFF and MRFR.

The prolonged time of isovolumetric relaxation in H and UAP is of complex genesis. On the one hand, the cause is the greater afterload of the left ventricle because of higher arterial pressure in the patients than in the healthy controls, and the earlier closure of the aortic valve, respectively (mean arterial pressure in healthy persons 87.9 ± 5.6 mm Hg, in arterlal hypertension 121.1 ± 7.1 mm Hg, and in UAP  $111.7 \pm 19.3$  mm Hg; p<0.0001) (2, 8, 14). On the other hand, it is determined by the reduced speed of decrease of the left ventricular pressure, and the later opening of the mitral valve, respectively, due to reduced compliance of the myocardium as a consequence of hypertrophy (5, 14), ischemia and focal fibrosis (10). These functional and morhological factors are differently manifested in the two diseases. This explains the difference in IVRP duration between the two patients' groups. IVRP is prolonged in all the UAP patients although arterial pressure is normal in 11 ones (36.7 per cent) at the moment of assessment. At the same time, 3 H patients have IVRP of normal duration with an increased arterial pressure. These facts indicate that reduced speed of decrease of left ventricular pressure due to changes in the myocardium is more important for IVRP prolongation than the increased afterload of the ventricle.

The shortened time of active suction in patients as compared to that of healthy persons suggests a reduced relaxation speed. It is proved that in this period relaxation velocity is greater than the filling one. That is why a suction effect by the left ventricle is formed. The end of ASP (point 0 of ACG) denotes the mo-

ment of balance between these two velocities (7).

In 1958, Weissler et al. (18) established that «isovolumetric relaxation» (denominated as RRP after introduction of echocardiography) prolonged with H patients and was inversely related with protodiastole duration, left atrial pressure and velocity of left ventricular relaxation. Our data in previous investigations are like these, too (2).

We specify in the present study that prolonged time of total period of rapid relaxation (RRP) in both UAP and H patients as compared with that in healthy persons is on the account of strongly prolonged IVRP with shortened ASP and, therefore, also reflects the reduced relaxation speed and decrease of left ventri-

cular pressure (7).

During SRPRF filling rate prevails already over that of relaxation and both of them progressively decrease (7). Our results (normal SRPRF duration) allow us to assume that the interrelation between the velocities of relaxation and filling during this period does not show any principal difference between UAP and H patients and healthy individuals. These data confirm our findings in previous investigations (2) that this interval does not change with stage one and two of H as well as with IHD.

RFP shortening in UAP and H patients established in our present study is determined by the shortened ASP and by reduced relaxation speed, respec-

tively.

The duration of IVRP, ASP and RRP does not depend on heart rate (7). Though heart rate does not differ between patients and healthy persons (p>0.10) time duration of these three intervals in the patients differs reliably from that

of the healthy controls.

The reduction of both RFF and MRFR reflects the restriction of the ventricular filling in the period of early diastole. The greater decrease of these parameters in UAP patients is parallel to the greater prolongation of IVRP and suggests more expressed disturbances of left ventricular compliance in IHD. The decreased RFP in both patients' groups expresses dislocation of left ventricular fil-

ling towards diastasis and atrial contraction.

The prolonged IVRP and RRP, the shortened ASP and RFP as well as the reduced RFF and MRFR form a non-invasive echoapexphonocardiographic constellation characteristic for the decreased left ventricular compliance. According to our results and to literary data available, disturbances of diastolic function in UAP and H patients are frequent and precede the changes of the systolic one (2, 10—12, 15, 17). The functional pathology during the early diastole in UAP and H patients is unidirectional but differs in quantitative aspect. This confirms the view of other authors that disturbances of diastolic function do not possess any specific diagnostic importance (1, 6, 9, 17). However, they enable the evaluation of the degree of the pathological process in myocardial hypertrophy, ischemia, and fibrosis. In relation to this fact one can determine the necessity and dosage of drugs improving the diastolic function in single patients.

We can conclude that the changes of the early diastole in UAP and H patients are not specific but frequent and early. That is why they enable the individual

adaptation of the necessary medical treatment.

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## ЛЕВОЖЕЛУДОЧКОВАЯ РЕЛАКСАЦИЯ И БЫСТРОЕ НАПОЛНЕНИЕ У БОЛЬНЫХ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ И НЕСТАБИЛЬНОЙ СТЕНОКАРДИЕЙ

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#### РЕЗЮМЕ

Исследовано 60 больных — 30 больных гипертонической болезнью с гипертрофией левого желудочка и 30 больных нестабильной стенокардией. Исследование проводилось до начала активного лечения. При помощи симультанной записи на эхокардиограмме М-типа, АКГ и ФКГ исследованы интервалы времени ранней диастолы, средняя скорость и фракция быстрого наполнения левого желудочка. Результаты проведенного исследования были сопоставлены с соответствующими данными 33 здоровых лиц.

Период изоволуметрической релаксации и суммарный период быстрой релаксации показывают достоверное удлинение, причем степень удлинения больше при нестабильной стенокардии. Период активного присывания укорочен, притом различий между обеими группами не устанавливается. Средняя скорость и фракция быстрого наполнения у больных понижены по сравнению со здоровыми. Наибольшее понижение устанавливается при фракт

ции быстрого наполнения у больных нестабильной стенокардией.

Оформляется неинвазивная эхо-апекс-фонокардиографская констеляция, характерная при пониженной растяжимости левого желудочка в результате гипертрофии, ишемии и фиброзе миокарда. Изменения ранней диастолы нозологически не являются специфичными, но они довольно часты, возникают рано, в связи с чем возникает возможность индивидуального адаптирования необходимой медикаментозной терапии.