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Preclinical abnormality of left ventricular function in chronic alcoholics

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Left ventricular function of a sample of subjects with chronic alcohol intake, in the form of wine, and without clinical or electrocardiographic signs of heart disease was compared with that of a sample of normal control subjects using non-invasive polygraphic recordings.

The statistical analysis has shown significant prolongation of PEP, PEPI, an increase in PEP/LVET, and a shortening of LVET and LVETI in the alcoholic subjects compared with the controls. All these abnormalities may be ascribed to left ventricular malfunction.

The role of chronic alcohol intake in the genesis of congestive cardiomyopathy has not been clarified; but alcoholic cardiomyopathy is a widely accepted clinical concept (Regan, 1971).

In a recent study (Demakis *et al.*, 1974), 57 subjects with cardiomyopathy associated with chronic alcohol ingestion were followed during an average period of 40·5 months: only a small group (26%) improved: these patients had an average duration of symptoms of only 4·2 months at the start of the study. A short duration of clinical symptoms before starting treatment is known to confer a better prognosis.

The measurement of systolic-time intervals by the simultaneous non-invasive recording of electrocardiogram, phonocardiogram, and carotid pulse wave is used in the assessment of cardiac function even in patients without clinical or electrocardiographic signs of heart disease (Spodick, Pigott, and Chirife, 1972; Levi *et al.*, 1976).

Spodick *et al.* (1972) investigated 26 ambulatory patients with high chronic alcohol intake but no clinical evidence of heart disease using the non-invasive measurement of systolic time intervals and comparing the results with those from normal control subjects and 12 patients with alcoholic cardiomyopathy. They found abnormalities of systolic time intervals in the 'normal' alcoholic patients that were in the same direction, but less marked, as those found reflecting depressed myocardial function in the cardiomyopathy group.

Unlike North America and the United Kingdom, wine, in Italy, represents more than 90 per cent of alcohol consumption. In order to determine whether wine has the same deleterious effects on the myocardium, we have investigated 43 chronic alcoholics by the same non-invasive technique as used by Spodick. With the aim of excluding from the sample, as far as possible, patients with preclinical arteriosclerotic heart disease, subjects over 40 years of age were not included in the study.

Subjects and methods

Forty-three subjects with a daily alcohol intake of more than 150 ml for a period of more than 5 years, and 34 normal controls matched for age, sex, and weight were examined. All patients with hypertension, diabetes, signs, or symptoms indicating heart disease, or who were over 40 years of age were excluded from the study.

Polygraphic recordings carried out 1 to 3 days after admission were made by standard methods, of lead II of the electrocardiogram, the heart sounds, and the right carotid pulse.

The heart sounds were recorded at the cardiac apex after securing the microphone (Battaglia-Rangoni, TM 1/102) with a rubber belt. The carotid pulse was recorded over the maximal external point of pulsation of the right carotid artery (Hellige microphone Mod. A Type Bouck-Brecht).

The electrocardiogram, phonocardiogram, and carotid pulse tracing were registered during relaxed mid-expiratory apnoea on a four-channel Battaglia-

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Rangoni oscillograph M10 at a paper speed of 100 mm per second.

The following systolic time intervals were obtained: heart rate in beats per minute; QS_2 (electromechanical systole of left ventricle); LVET (left ventricle ejection time); PEP (pre-ejection period); and PEP/LVET.

Heart rate was obtained from the cycle length (RR interval of the electrocardiogram). The QS_2 was measured from the beginning of Q wave (or R if the Q wave was absent) in lead II of the electrocardiogram, to the first high frequency deflection of the aortic component of the second heart sound. LVET was taken as the interval from the onset of the rapid upstroke of the carotid pulse to its incisura. PEP was derived as QS_2 minus LVET. Measurements from 5 consecutive beats were averaged.

Statistical analysis

Because of the relation between the systolic time intervals and heart rate, the groups of subjects (normal/alcoholics) were compared by means of the univariate analysis of covariance using the heart rate as covariate and QS_2, LVET, PEP, PEP/LVET as dependent variables.

In order to obtain a more comprehensive evaluation of the differences in myocardial performance between the two groups, a multivariate analysis of covariance was carried out by means of the systolic time intervals with the heart rate as covariate. Correlation coefficients were calculated for each pair of systolic time intervals and between each systolic time interval and heart rate.

The results we obtained have been compared with the results reached by means of the usual regression formula (Weissler *et al.*, 1968). Univariate and multivariate variance analyses were performed on systolic time intervals corrected for heart rate (QS_2I, LVETI, PEPI).

Results

There was no significant difference between the heart rates of the normal and alcoholic groups ($F=1{\cdot}14$) (Table 1).

The correlation coefficients for each pair of systolic time interval and between each systolic time interval and heart rate showed a different pattern in the normal subjects as compared with the alcoholics (Table 2).

Table 3 summarises the results obtained by means of the univariate analysis of covariance, using heart rate as covariate in comparing the two groups (normals-alcoholics): LVET, PEP, PEP/LVET were significantly different between the two groups of subjects.

These results are in agreement with the conclusions (Table 1) of a variance analysis performed on the systolic time intervals corrected (QS_2I, LVETI, PEPI) by means of Weissler's regression formula.

A significant difference ($P < 0{\cdot}01$) between normal

Table 1 *Systolic intervals: results in the two groups (normals/alcoholics), analysis of variance (STI corrected for heart rate by means Weissler's regression coefficients)*

Systolic time intervals	*Groups*	*Means*	*Standard deviations*	*F*
Heart rate	Normals	77	10·9	1·14
	Alcoholics	74	11·3	
QS_2I	Normals	540	16·3	1·61
	Alcoholics	533	23·1	
LVETI	Normals	414	12·9	12·9**
	Alcoholics	397	24·8	
PEPI	Normals	125	7·1	7·79**
	Alcoholics	134	17·7	

**P < 0·01.
QS_2I, LVETI, PEPI = values of QS_2, LVET, and PEP corrected for heart rate.

Table 2 *Pattern of correlation coefficients between systolic time intervals and heart rate in normals and alcoholics*

	QS_2	*LVET*	*PEP*
	Normals (alcoholics)	*Normals (alcoholics)*	*Normals (alcoholics)*
QS_2	—	—	—
LVET	0·96 (0·81)	—	—
PEP	0·65 (0·35)	0·44† (−0·26)	—
HR	−0·77 (−0·66)	−0·78 (−0·66)	−0·35 (−0·05)

†Note that r > 0 in normals.
r < 0 in alcoholics.

Table 3 *Systolic time intervals: results in two groups (normals/alcoholics), analysis of covariance (STI vs. HR)*

Systolic time intervals	*Groups*	*Means*	*Adjusted means*	*Regression coefficient (versus HR)*	*F*
QS_2	Normals	379	378·5	−0·0071	0·90
	Alcoholics	377	372·1		
LVET	Normals	285	284·6	−0·0150	6·74*
	Alcoholics	271	268·8		
PEP	Normals	94	94·5	0·0086	6·59*
	Alcoholics	104	103·0		
PEP/LVET	Normals	0·332	0·332	0·00004	12·22**
	Alcoholics	0·391	0·389		

Heart rate	Mean	(D.S.)
Normal individuals	77	(10·9)
Alcoholic individuals	74	(11·3)

*P < 0·05 **P < 0·01

Table 4 *Systolic intervals: results in two groups (normals/alcoholics): multivariate analysis*

	U-statistic	*Degrees of freedom*	*Approximate F-statistic*	*Degrees of freedom*
Multivariate analysis of covariance				
QS_2 +LVET +PEP vs. HR	0·803	(3, 1, 65)	5·15**	(3, 63)
Multivariate analysis of variance				
QS_2I +LVETI +PEPI	0·739	(3, 1, 66)	7·54**	(3, 64)

**P < 0·01.
QS_2I, LVETI, PEPI = QS_2, LVET, PEP corrected for heart rate by means of Weissler's linear regression in normal individuals.

subjects and the alcoholics was recorded even when performing a multivariate analysis of covariance by means of three STI (QS_2, LVET, PEP) with the heart rate as covariate (Table 4). The same results ($P < 0·01$) were obtained with a multivariate analysis of variance by means of corrected systolic time intervals (QS_2I, LVETI, PEPI).

Discussion

The importance of detecting as early as possible a deleterious influence of alcohol on the myocardium, especially before the appearance of clinical abnormalities or alterations of chest *x*-ray or electrocardiogram, is obvious. The study of Demakis *et al.* (1974) clearly showed that among the patients with cardiomyopathy associated with chronic alcohol ingestion, only those few with a shorter duration of symptoms can be expected to improve.

The importance of early diagnosis of cardiac malfunction has been confirmed by a recent study of Segel *et al.* (1974) on the effects of chronic ethanol consumption on metabolism, ultrastructure, and mechanics of the rat heart. After a period of 25 to 46 weeks of alcohol intake in well-nourished animals—electron microscopy already showed disordered mitochondrial cristae, swollen transverse tubules and sarcoplasmic reticulum, intercalated disc, and myofibril disruption. Concomitantly myofibrillar ATPase was depressed and isometric contraction of left ventricular papillary muscle was altered.

Similar conclusions were reached by Ettinger *et al.* (1976) in a study in which 11 male mongrel dogs were fed up to 36 per cent of their total daily caloric intake as ethanol for a mean period of 14·4 months while adequate nutrition was maintained. While resting left ventricular pressures, volumes, and stroke outputs remained within normal levels, prolonged ethanol intake resulted in intraventricular conduction abnormalities and morphological alterations, such as dilatation and localised swelling of the intercalated disc, which were related to duration of ingestion, consistent with a cumulative toxic effect of ethanol.

In agreement with Spodick's conclusions, the results we obtained by the univariate analysis of covariance using heart rate as covariate in comparing the two groups (normal-alcoholics), as well as by the analysis of variance using systolic time intervals corrected by means of Weissler's regression formula, showed a significant difference between the two groups. The same results were obtained by means of a multivariate analysis of covariance. In subjects with chronic alcohol intake, even in the absence of clinical, radiological, and electrocardiographic signs of heart disease, the prolongation of PEP, PEPI, the increase in PEP/LVET and the shortening of LVET and LVETI, may be interpreted as consistent with impaired myocardial performance. The regular intake of wine appears to be as deleterious in this respect as other forms of alcoholism.

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