

THE ASSOCIATION BETWEEN
EXERCISE BLOOD PRESSURE AND THE
PREVALENCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES

by Barbara J. Naimark

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Department of Physiology

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ABSTRACT

Of the factors associated with an increased risk of cardiovascular disease, hypertension emerges as a potent contributor to cardiovascular mortality. Detection of individuals at risk of developing hypertension has the obvious benefit of providing more time for applying measures to prevent or delay the onset of cardiovascular complications.

Ambulatory blood pressure is strongly associated with the presence of cardiac abnormalities, such as left ventricular hypertrophy, and it has been postulated that hypertensive cardiac changes may occur despite a normal (<140 mmHg systolic: <90 mmHg diastolic) or borderline hypertensive (140-159 mmHg and/or 90-104 mmHg diastolic) casual blood pressure at rest. It has also been postulated that an exaggerated systolic blood pressure (SBP) response to exercise (≥ 200 mmHg) may be a marker for left atrial enlargement and/or left ventricular hypertrophy in those considered to be normotensive or borderline hypertensive by conventional criteria. In order to test the latter hypothesis 429 subjects (353 normotensives and 76 borderline hypertensives) attending a preventive fitness program were studied to determine the relative prevalence of electrocardiographic atrial and ventricular abnormalities among those who had a normal exercise SBP and those with an exaggerated exercise SBP.

Three electrocardiographic indices of left atrial enlargement were analyzed, namely the Macruz Index (the P/PR segment

ratio), the P terminal force in lead V_1 (PTFV₁), and the Root Sum Square (RSS) of the initial and terminal portions of the P-wave in lead V_1 . The electrocardiographic indices of left ventricular hypertrophy examined were the wave amplitude of: R in AVL, R in V_5 or V_6 (whichever is larger), R in Lead I plus S in Lead III, and R in V_5 or V_6 (whichever is larger) plus S in V_1 .

The prevalence of left ventricular hypertrophy, as indicated by an abnormality in one or more of the ventricular electrocardiographic indices, was significantly greater among normotensive subjects with abnormal exercise SBP than among those with normal exercise SBP for both males and females ($p < 0.001$). In the borderline hypertensive subjects the corresponding differences in prevalence were not significant.

The prevalence of left atrial abnormality, as indicated by PTFV₁, was significantly greater among normotensives with exaggerated exercise SBP than among those with normal exercise SBP for both males and females ($p < 0.05$ and $p < 0.01$, respectively). The corresponding differences in prevalence for the Macruz Index and the RSS were not significant. In the case of borderline hypertensives the corresponding differences in prevalence were only significant for the Macruz Index in females ($p < 0.05$) and for PTFV₁ in males ($p < 0.05$).

Simple correlation and analysis of the linear regression of various electrocardiographic indices on exercise SBP showed significant relationships for both males and females in the case of

PTFV₁ and the Macruz Index and for male subjects in the case of RSS, RV₅/RV₆ and RV₅/RV₆+SV₁.

In view of the demonstration of a significant association between exercise SBP and sex, age and resting blood pressure, a multivariate analysis of the association between exercise SBP and the various electrocardiographic indices was carried out. A significant effect of exercise SBP independent of sex, age and resting SBP was found in the case of PTFV₁, RV₅/RV₆, RV₅/RV₆+SV₁, but not for the other indices of atrial abnormality or left ventricular hypertrophy. These results suggest that PTFV₁, RV₅/RV₆ and RV₅/RV₆+SV₁ are more sensitive than the other atrial and ventricular electrocardiographic indices to the changes in atrial and ventricular function which appear to be associated with an exaggerated SBP response to exercise.

The findings of the present study support the hypothesis that an abnormally high SBP on exercise is associated with an increased prevalence of atrial abnormality and left ventricular hypertrophy among subjects who are normotensive at rest. Further investigation involving larger numbers of borderline hypertensive subjects will be necessary to clarify the situation in this category of subjects. In future studies of the predictive value of exercise SBP with respect to the presence of atrial and ventricular abnormalities the significant effects of sex, age and resting SBP must be taken into account in the experimental design.

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LIST OF ABBREVIATIONSUnits of measure

cm	centimeter
g/dl	grams per deciliter
kg	kilogram
Km/h	kilometers per hour
mg/dl	milligrams per deciliter
mmHg	millimeters of mercury
mV	millivolt
sd	standard deviation
sec	second
b/m	beats per minute

Miscellaneous

BP	blood pressure
CHD	coronary heart disease
DBP	diastolic blood pressure
EKG	electrocardiograph
FEV ₁	forced expiratory volume in one second
FVC ₁	forced vital capacity
HR	heart rate
HT	hypertension
LAE	left atrial enlargement
LVH	left ventricular hypertrophy
MCI	Manitoba Cardiac Institute
PTFV ₁	P terminal force in lead V ₁
PWA ₁	P-wave abnormalities
RSS	root sum square
SBP	systolic blood pressure

1. INTRODUCTION

Hypertension (HT) is a term applied to a state in which the systemic arterial blood pressure is elevated above a certain arbitrary designated value. Systolic and diastolic pressures above 160 mmHg and 104 mmHg respectively are considered to be clearly abnormal; pressures below 140 mmHg systolic and 90 mmHg diastolic are considered to be clearly normal (Kannel, W.B. 1974). The significance attributed to blood pressures between these limits has varied from study to study (Julius, S. and Schork, M. 1971). Accordingly, for the purposes of the present study, systolic blood pressures between 140 and 159 mmHg and diastolic pressures between 90 and 104 mmHg shall be regarded as borderline abnormal and shall be referred to as "borderline hypertensive."

HT is one of the most important factors predisposing to cardiovascular disease and the treatment and control of HT among other measures has been credited with the decline of mortality from cardiovascular disease over the past two decades (Kannel, W.B. and Thom, T. 1984). The identification and control of even mild degrees of HT may be clinically important (Hypertension Detection and Follow-up Program, 1982). It has also been suggested that if it were possible to identify individuals who are normotensive but at increased risk for the development of HT, measures might be applied which could prevent the onset of HT.

It has been postulated that the blood pressure (BP) response to exercise may be helpful in refining the classification of

hypertensive subjects and moreover may be a means of identifying individuals who are at risk for HT (Naughton, J. 1982; Wilson, N. and Meyer, B. 1981; Olin, R. A. et al., 1983). It also might reasonably be postulated that if the BP response to exercise in normotensives is a prognostic indicator of subsequent HT, one might expect to see an association between the BP response to exercise and variables known to be associated with HT (Criqui, M. H. et al., 1983) such as electrocardiographic (EKG) left ventricular hypertrophy (LVH) and P-wave abnormalities (PWA). It therefore seemed appropriate to determine if there is an association between the BP response to exercise and the prevalence of EKG abnormalities.

The general objective of the work described in this thesis is to document selected EKG changes of subjects at rest and to relate these changes to the attained level of BP during exercise.

In order to determine if normotensive subjects ($< 140/90$ mmHg) or subjects with borderline blood pressures (140-159 mmHg SBP and/or 90-104 mmHg DBP) with an exaggerated BP response to exercise (SBP \geq 200 mmHg) have a higher prevalence* of EKG abnormalities, indicating target organ damage, the following specific objectives were pursued:

*Prevalence (or "point prevalence") refers to a static picture or "snapshot" of the number of persons who have a disease or a characteristic under study in a population at one point in time (Freidman, G. D. 1976).

3.

- i. comparison of the prevalence of PWA and EKG evidence of LVH in normotensive subjects whose resting BP does not exceed 139/89 mmHg and whose exercise systolic pressure is ≥ 200 mmHg systolic, with those subjects who have normal resting blood pressures but whose systolic pressures are < 200 mmHg during exercise.
- ii. determination of the prevalence of PWA and LVH in subjects with resting BP in the range 140-159 mmHg systolic and/or 90-104 mmHg diastolic (who had not received antihypertensive medication) and whose exercise systolic BP is ≥ 200 mmHg, and to compare them to untreated subjects with resting blood pressures in the same range whose exercise systolic pressures are < 200 mmHg.
- iii. determination of the relationship between age, sex, resting blood pressure and electrocardiographic indices of PWA and LVH both in terms of the independent effects of these factors as well as their joint relationship.

2. LITERATURE REVIEW

Among the identified precursors of cardiovascular disease, hypertension plays a dominant role (Kannel, W.B., 1974; Hofman, O. et al., 1974; Paul, O. 1971; Page, L. B. et al., 1972). Indeed of all the risk factors which include serum cholesterol level, diabetes and the cigarette habit, HT emerges as a potent and

independent contributor to coronary heart disease (CHD), cerebral vascular disorders (both hemorrhagic and others) - thrombotic, aortic aneurysm and peripheral vascular disease (Kannel, W. B. et al., 1961; Gordon, T. 1972). Although blood pressure generally rises with age, there is no indication that elevated pressure is any less of a risk factor in the older individual than in a younger person (Kannel, W. B. and Thom, T. 1984).

In the twenty years between 1963 and 1983, the overall death rate for all cardiovascular diseases declined by 36% in the United States (Kannel, W. B. and Thom, T. 1984). In Canada, where the coronary trends are similar to those in the United States, apparent parallel changes in cardiovascular mortality have occurred (Health and Welfare Canada, 1981). It is still essentially unknown, however, whether this decline in mortality is occurring as a result of a decline in the incidence of new cases or if there has been a change in the prognosis, severity, case fatality, and survivorship after development of cardiovascular disease. These major gaps in knowledge stand in the way of determining causes of the decline in cardiovascular mortality. Even if such information can be obtained, determining causation would still be difficult if the declines were due to factors or behavior not specific to the cardiovascular diseases, e.g., a better standard of living, greater awareness of health hazards, healthier life styles, better nutrition, or better and wider use of medical care. Indeed a strong case can be made for general influence on health operating

on the entire population since the decline in cardiovascular mortality has occurred in both sexes, and in all age groups. The fact that rates for non-cardiovascular causes of death are also declining reinforces the suggestion that there are general health-promoting factors at work (Kannel, W. B. and Thom, T. 1984).

It has been reported and widely accepted that the decline in mortality from accelerated malignant forms of HT is attributable to use of potent antihypertensive agents. The efficacy of controlling even mild degrees of HT has been reviewed (Kaplan, N. 1983). The findings of two controlled clinical trials (the Hypertension Detection and Follow-up Program [HDFP] of the National Institutes of Health - 1979 and the Australian Therapeutic Trial - 1980) indicated that controlling mild HT (defined as DBP 90-104 mmHg and DBP 95-109 mmHg in the two studies respectively) is beneficial with respect to reducing cardiovascular morbidity and mortality. However, no reduction in mortality in treated mild hypertensives was found in two other studies (the Veteran's Administration Study - 1970; and the United States Public Service Trial [USPHS]). In the latter two trials mild HT was defined as DBP between 90 and 104 mmHg and DBP between 90 and 114 mmHg, respectively. In the USPHS trial there was a beneficial effect of therapy on hypertensive morbidity, particularly LVH.

In a large British project (the Medical Research Council [MRC] Working Party Trial - 1985) it was concluded that "if 850 mildly hypertensive patients (DBP 90-109 mmHg) are treated for one

year about one stroke will be prevented...an important but infrequent benefit."

An unexpected outcome of therapy in mild hypertensives (DBP \geq 90 mmHg) was found in the Multiple Risk Factor Intervention Trial (MRFIT - 1982). At entry, subjects were randomly assigned to either a Special Intervention (SI) program or to their usual sources of care in the community (UC). After seven years of follow-up, for the 70 percent of subjects who were free of resting EKG abnormalities at entry the SI group had CHD and all-cause mortality rates which were significantly lower than those of the UC group. This was consistent with findings of HDFP. However, in the 30 percent of subjects who had abnormal resting EKG's at entry, CHD and all-cause mortality rates were higher in the SI group. The MRFIT findings suggest that the diuretic component of the SI regimen, particularly high dose diuretic therapy, may have been responsible for the excess mortality. Given the foregoing complexities, it is not surprising that the question of whether and how to treat mild HT has not been resolved (Freis, E. 1982; Smith, W. 1977).

In a critical review of borderline HT (defined as "below 160/100 and above 140/90 for average or single readings"), it was determined that the risk of development of sustained HT (defined as "blood pressure always above 160 mmHg systolic and 100 mmHg diastolic) in a patient with borderline HT was double that in normotensives (Julius, S. et al., 1971). Other investigators

(Koopstein, S. I. et al., 1962) followed normotensive (systolic BP <150 mmHg; diastolic <90 mmHg) and borderline hypertensive (systolic BP 150-160 mmHg; diastolic 90-94 mmHg) males, aged 20-30 years, for periods of 10 and 15 years. The percentages of normotensives who developed HT (i.e., ≥ 160 mmHg and/or ≥ 95 mmHg) were 4.5 and 9.5, respectively. By contrast, the percentage of subjects with borderline pressures who developed HT were 21.2 and 24.6, respectively. Early detection of persons with HT has the obvious benefit of providing more time for applying measures to prevent or delay the onset of cardiovascular complications.

It may also be important to identify individuals who are normotensive at rest but who are at increased risk for the development of HT, because it may be possible to apply measures which will prevent the development of HT. It had been earlier suggested (Thomas, C. B. 1952) and more recently (Wilson, N. and Mayer, B. 1981; Olin, R. A. et al., 1983) that an exaggerated BP response to exercise indicates such an increased risk. Specifically, Wilson and Mayer and Olin et al. state that individuals with a resting BP $\leq 140/90$ mmHg but with SBPs during exercise in excess of 225 mmHg - are at increased risk for developing HT. Wilson and Mayer contend that even with statistical control in the analysis of factors such as family history of cardiovascular disease, weight at first visit, weight change, hypercholesterolemia, alcohol consumption and smoking, the "hyper-responders" had a "point estimate of relative risk well

over unity when compared with controls." In a report assessing borderline hypertensives (SBP at rest 140-150 mmHg) (Franz, I. W. 1982) it was found that after 3.8 years 97% of "ergometric-positive" subjects, i.e., those whose exercising BP exceeded 200/100 mmHg at 100 watts developed HT (SBP >150 mmHg). Conversely, only 32% of those with "ergometric-negative" borderline HT developed HT (SBP >150 mmHg).

The definition of normotension at rest and of normal and exaggerated BP response to exercise, varies from study to study. In the case of exercise BP the definition is usually based on SBP because sphygmomanometric measurement of DBP is unreliable due to background noise interfering with auscultation of the 4th and 5th Korotkoff sounds (Erikssen, J. 1980; Comess, K. A. and Fenster, P. E. 1981). For this reason several investigators did not include exercising diastolic blood pressure in their analyses (Irving, J. B. et al., 1977; Erikssen, J. 1980; Comess K. A. and Fenster, P. E. 1981). In a study of 22 subjects (8 normals, 8 "benign phase" hypertensives and 5 "malignant phase" hypertensives) it was found that DBP measured directly increased on average during exercise by 6 mmHg (Bevan, A. T. 1969). In other studies using indirect BP measurement DBP increases of 2 to 11 mmHg were found (Astrand, I. 1986; Bruce, R. A. et al., 1974; Irving, J. B. et al., 1977).

Although systolic pressures obtained by cuff auscultation may differ from intra-arterial values, they are nonetheless clinically

useful. The reported results of one study (Comess, K. A. and Fenster, P. E. 1981) demonstrated that when subjects were standing or walking at various speeds and grades the auscultation method consistently underestimated the intra-arterial BP by 5.1 - 10.3% (8 - 15 mmHg); however, the changes in systolic pressures recorded by the two methods paralleled each other. In a second study (Irving, J. B. et al., 1977) it was confirmed that there is a small but consistent discrepancy between the direct and indirect measurement of exercising systolic BP. Two maximal treadmill tests were performed on the same day, the first using a BP cuff and the second using intra-arterial monitoring. Fifteen of 20 of paired maximal SBP measurements agreed within 20% over a range of 100 - 240 mmHg. The correlation coefficient (r) was 0.721 reflecting the effect of a few values showing marked differences. In another study (Clausen, J. P. and Trap-Jensen, J. 1976) there was no statistically significant difference between the SBPs measured directly and indirectly during bicycle exercise. At maximum exercise intra-arterial pressure was 174 ± 5.72 mmHg and cuff pressure was 170 ± 5.33 mmHg.

In a study of normal men and women 48-63 years old, during exercise at various workloads, using bicycle ergometry, it was found that average exercise systolic BP in the normotensive subjects (<170 mmHg systolic and <100 mmHg diastolic) was 196 ± 22 (mean \pm sd) mmHg in women and 212 ± 23 mmHg in men, at a heart rate (HR) of about 150 beats per minute (Astrand, I. 1965). In

a study using treadmill exercise, it was found that, in normotensive (<140/90 mmHg) middle aged males, the mean increase in systolic pressure from rest to near maximal exercise was 60 (± 20) mmHg (Bruce, R. A. et al., 1973). In a later study (Bruce, R. A. et al., 1974) it was found that the mean value of systolic pressure during maximal exercise, in 1275 healthy men with a mean age of 44.5 years, was 185 (± 22) mmHg. In an attempt to standardize normal BP response during near maximal exercise, 1678 males with a mean age of 48.1 years were studied using bicycle ergometry (Erikssen, J. et al., 1980). The mean BP at rest was found to be 130 mmHg systolic and 91 mmHg diastolic and the mean systolic pressure during maximal exercise was found to be 213 mmHg. An earlier study (Walthuis, R. A. et al., 1977) also attempted to establish a complete set of reference values for BP response of men to maximal exercise. The investigators studied 704 men of median age 37 years by means of treadmill ergometry and found the median systolic pressure at maximal exercise to be 200 mmHg and the median BP at rest to be 130 mmHg systolic and 80 mmHg diastolic.

Franz, I. W. (1982) used a standard ergometric procedure to study 173 normotensive males and 150 normotensive females (SBP <140 mmHg) aged 20 to 50 years (mean 35.5 ± 7.3 years and 34.7 ± 8 years, respectively). It was demonstrated that there was no significant difference in mean SBP between males and females at "relatively equal workloads independent of different body weights of the subjects." The females reached mean SBP values of 186 ± 7

mmHg, and the males 188 ± 14 mmHg at 100 watts. There was no significant difference in the levels of SBP or HR attained during bicycle ergometric work or during recovery among the age groups 20 to 30, 30-40, and 40-50.

Studies of BP responses to exercise in hypertensives have also yielded variable results. Astrand, I. (1965) found that hypertensive subjects ($> 170/100$ mmHg) had mean exercise SBP, at a HR of 150 beats, of $228 (\pm 18)$ mmHg in females and $242 (\pm 33)$ mmHg in males. Eight of the 38 hypertensive subjects had exercise pressures within one standard deviation of the exercise BP of normotensive (SBP < 170 mmHg and DBP < 100 mmHg) subjects. Bruce, R. A. et al., (1974) reported values in hypertensives (> 140 mmHg systolic and > 90 mmHg diastolic) at maximal exercise of $197 (\pm 28)$ mmHg. Franz, I. W. (1982) evaluated 57 hypertensive subjects with a mean resting BP of 164 ± 6 mmHg systolic and/or 105 ± 5 mmHg diastolic (Group 1), 52 "borderline hypertensive" subjects with a mean resting BP of 150 ± 5 mmHg systolic and/or 92 ± 5 mmHg diastolic (Group 2), and 173 normotensive subjects with a mean resting BP of 134 mmHg systolic ± 11 and/or 85 ± 1.8 diastolic (Group 3). Two distinct exercise BP profiles were found in Group 2: 57.7% of subjects in Group 2 had an exercise BP which was not significantly different from Group 1 (211 ± 20 mmHg), and the remaining 42.3% of Group 2 subjects were found to have an exercise BP (183 ± 14 mmHg) which did not differ significantly from Group 3 (mean exercise BP of 188 ± 20 mmHg).

Another report (Amery, A. et al., 1967) documented the influence of blood pressure on the hemodynamic response to exercise in 61 asymptomatic patients aged 19 to 68 years. SBP during exercise increased as a function of age. These findings were similar to those observed in normal subjects (DBP \leq 90 mmHg). In general, however, hypertensive patients (DBP $>$ 90 mmHg) demonstrated a greater rise in systolic pressure with exercise than normal subjects, but in the youngest group this was not apparent. It was concluded, therefore, that the BP response in the youngest group was not sufficiently characteristic to be used as a test for hypertensive disease. Extensive reviews have been written on the hemodynamic responses of hypertensive subjects to exercise and findings have been reported which indicate that subjects in the early stages of HT may have normal exercise BPs (mean 194.9 mmHg systolic) while those in later stages have consistently elevated exercise BPs (mean 229.5 mmHg systolic) (Sannerstedt, R. et al., 1966; Lund-Johansen, P., 1967).

In studies of blood pressure at rest or during exercise the question of reproducibility and the validity of single measurements of BP arises. According to the Canadian Hypertensive Society and others (Canadian Hypertensive Society Report, 1984; Folkow, B. 1971; Julius S. and Schork, A. 1971), the variability of blood pressure is such that measurement of it on any one occasion is inadequate to provide a reliable estimate of an individual's usual BP. On the other hand, some have indicated that even single casual

BP measurements are strongly predictive of the subsequent development of hypertensive and atherosclerotic disease (Kannel, W. B. et al., 1980; Koch-Weser, J. 1973).

In a study of exercise BP variability in 156 middle-aged subjects during a treadmill exercise test performed on average 9 months (range 1 to 30 months) after the initial stress test, it was found that exercise SBP values were within 10% of the first determination in two-thirds of the subjects. The overall mean pressure difference between the two treadmill tests was 8.6 mmHg which was thought to be "unimportant" (Irving, J. B. et al., 1977). Data obtained using exercise on a bicycle ergometer on 19 young male subjects on two occasions, separated by a mean interval of 9.8 days, showed that BP and HR readings were not only reproducible but were even more so as exercise progressed (Caen, J. L. et al., [quoted by Comess, K. A. and Fenster, P. E. 1981]).

We can suggest that although a single casual elevated BP measurement is subject to variability, it should not be ignored. Exercising SBPs have been shown to be less variable and may therefore be a more reliable measure of subject BP.

It is apparent that knowledge of exercise BP is limited at present. It is clear that identification of additional prognostic indicators is needed to clarify the clinical significance of elevated exercise SBPs, particularly in the normotensive ($\leq 139/89$ mmHg) and the borderline hypertensive (140-159/90-104 mmHg) subjects.

Electrocardiographic indices of left ventricular and atrial abnormalities have been used in evaluating the clinical significance of resting BP levels.

In a review of studies on the sensitivity and specificity of electrocardiographic indices of LVH in detecting LVH, determined by measurement of left ventricular wall thickness at autopsy, it was found that, depending on which voltage criterion was used, the percentage of false positive diagnosis of LVH ranged from 0.5% to 6.0% and the percentage of false negatives from 59% to 90%, indicating a high level of specificity and a low level of sensitivity (Kilty, S.E. and Lepeschkin, E., 1965). There is a high correlation between left ventricular wall thickness (the sum of the thickness of the ventricular septum and the posterior wall) and the precordial voltage index RV_5 plus SV_1 ($r = 0.85$) (Toshima, H. et al., 1977).

The Manitoba Follow-up Study using three criteria for LVH (R in V_5 or $V_6 > 26$ mm; R in $AVL > 11$ mm; R in V_5 or $V_6 + S$ in $V_1 > 35$ mm) reported that in normotensive males ($SBP \leq 139$ mmHg $DBP \leq 89$ mmHg) in the age range 30-60 the prevalence of LVH varied between 1% and 2.4% (depending on which one of the three criteria was used) and not on the age of the subject. In subjects with $SBP 140-159$ mmHg and/or $DBP 90-104$ mmHg the frequency of LVH varied between 1.6% and 6.3%, the highest frequency being present in the oldest subjects (Mathewson, F., Manfreda, J. and Mymin, D., unpublished data, 1985).

In the Framingham study, incidence of both CHD and EKG-LVH increased in proportion to antecedent BP (Kannel, W. B. 1983). At systolic pressures exceeding 180 mmHg, EKG-LVH developed in 50% of subjects. In addition to drastic curtailment of life expectancy, EKG-LVH was a harbinger of serious cardiovascular disease (Kannel, W. B. 1970).

Sokolow, M. et al. (1967) compared BP measured during daily activity (using a portable monitor which recorded BP every 1/2 hour) with casual clinic BP (BP measured at rest once during each of three successive clinic visits). They found that EKG-LVH related more closely to the average BP during daily activity than to the casual clinic BP. This finding has been supported in more recent studies (Rowlands, D. B. et al., 1982; Devereux, R. B. et al., 1983; Pickering, T. G. et al., 1985; Rowlands, R. B. et al., 1981; Drayer, J. M. et al., 1983) which showed that LVH in patients with HT is more closely related to BP during activity or stress than to casual BP. These findings were obtained using both direct (intra-arterial) and indirect (sphygmomanometric) BP measurement. Further supportive findings were obtained in an echocardiographic study which demonstrated that left ventricular mass index was weakly associated to resting BP and that correlation was better with SBP during exercise than during rest (Ren, J. 1985). Hypertensive patients with an exercise SBP of 190 mmHg or greater tended to have an increased left ventricular mass. None of the normotensive controls reached an exercise SBP of 190 mmHg. Their

mean exercise SBP was 154 ± 15 mmHg.

It has been demonstrated that LVH, appraised by echocardiography, is more strongly related to both exercise test (blood pressure) profile and to BP during daily activity (ambulatory blood pressure) than to a single casual BP measurement at rest. Subjects whose exercise test BP profile and/or ambulatory BP record was "pathologic" had average values of intraventricular septum thickness and diastolic-posterior wall thickness significantly higher ($P < 0.05$) than subjects who were not in the "pathological" group (de Gaudemaris, R. et al., 1985). A recent abstract (Brown, J. et al, 1986) reported on normotensive individuals (no HT definition given) without known cardiac disease and with a hypertensive response on exercise tolerance testing ($BP > 200$ mmHg). Using echocardiography, and predicted values based on body surface area, it was found that posterior wall thickness, ventricular septal thickness and LV mass exceed 95% confidence limits in 89%, 65% and 88%, respectively. The authors concluded that hypertensive cardiac end-organ changes may occur despite normal BP at rest and that exaggerated SBP response in exercise tolerance testing may be a marker for LVH in those considered to be normotensive by conventional criteria.

Changes in the EKG pattern of atrial depolarization have long been recognized as reflecting hemodynamic or anatomical changes affecting the atria (Macruz, R. et al., 1958; Morris, J. et al.,

1964; Kasser, I. and Kennedy, J. W. 1969; Josephson, M. E. et al., 1977; Di Bianco, R. et al., 1979).

The clinical significance of PWA in HT has been studied by several groups of investigators (Thomas, P. and De Jong, D. 1954; Macruz, R. et al., 1958; Morris, J. et al., 1964; Tarazi, R. et al., 1966; Guyton A. and Coleman, T. 1969; Truett, J. and Sorlie, P. 1971; Frolich, E. et al., 1971; Julius, S. and Schork, M. 1978, Fodor, G. et al., 1983). In a study using the P/PR segment ratio in Lead II (the Macruz Index), a mean value of 1.2 (range 1.0 to 1.6) was found in normal subjects (Macruz, R. et al., 1958). It was found that the Macruz Index correctly identified 74% of patients with acquired and congenital left heart disease who had LAE as determined by cardiac catheterization, X-ray and fluoroscopy.

In the mid-sixties a series of normal subjects and patients with precisely defined valvular abnormalities were studied (Morris, J. et al., 1964). The hemodynamic evaluation in all patients included catheterization of all four cardiac chambers. Thirteen patients free of disease were included in the normal subject population. As a result of these observations a new EKG measure to detect left-sided disease was proposed, P-terminal force in Lead V_1 (PTFV₁). P-wave measurements were made with calipers and a hand magnifying lens. The P-wave in lead V_1 was divided into initial and terminal portions by noting the point of change in morphology. The second portion of the P-wave represented

electrical depolarization of the left atrium. The product of duration and amplitude of the terminal element (PTFV₁) was calculated and values more negative than -0.03 mm sec were defined as abnormal.

Of the 87 patients with left-sided valvular disease, 75 were found to have an abnormal P-terminal force. Of the 12 cases with normal P-terminal force, 9 were classified as minimal valvular disease and 3 as severe. Other investigators noted similar PWAs in the presence of hypertension (Sodi-Pallares and Calder, R. [quoted by Morris, J. et al., 1964]).

In another study (Di Bianco, R. et al., 1979) atrial pressure and size were associated with the following electrocardiographic measurements:

- PTFV₁ (abnormal < -0.03 mm sec)
- P-wave duration in lead II (abnormal > 0.12 sec)
- P-wave duration in simultaneous leads I, II and III

(definition of abnormal not given).

The PTFV₁ was found to correlate best with pulmonary capillary wedge pressure (PCW) ($r=0.67$, $n=57$). For PCW values greater than 14 mmHg the sensitivity of PTFV₁ for predicting PCW was 85% and the specificity was 79%. No significant correlation between P-wave duration in lead II or simultaneous leads I, II and III and pulmonary wedge pressures were found. The mean left atrial dimension in patients with an abnormal PTFV₁ was 4.4 ± 0.6 cm, whereas in patients with a normal PTFV₁ the mean was 3.7 ± 0.8 cm.

The correlation ($r = 0.41$) was significant and is consistent with the findings of others where correlations were also significant (Termini, B.A. and Lee, Y., 1975; Rubler, S. et al., 1978).

In an earlier study, left atrial volume and pressure measurements in 23 normal subjects and 117 patients with cardiovascular disease were related to P-wave characteristics measured with the aid of calipers and a magnifying lens. The Macruz Index (P/PR segment ratio) was measured in lead II, the V_1 P-terminal force was calculated as previously described. The duration and amplitude of the P-wave was measured in leads I, II and V_1 . $PTFV_1$ showed a highly significant correlation ($r = 0.56$; $p < 0.001$) with changes in left atrial volume but was stated to be less well correlated to increases in left atrial pressure (correlation coefficient not reported). The $PTFV_1$ was abnormal in 66% of subjects with left atrial pressure abnormalities. The P-wave duration in Leads I and II and the Macruz Index, were abnormal in 57% and 53% of these subjects, respectively. (Kasser, I. and Kennedy, J. W. 1969).

In a recent study, the sensitivity and specificity of electrocardiographic criteria for LAE were assessed (Manuswamy, K. et al, 1984). Left atrial dimensions were determined by M-mode echocardiography. The following results were obtained:

- criterion: duration of the negative phase of the P-wave in lead $V_1 > .04$ sec: sensitivity 83%, specificity 80%.

- criterion: $PTFV_1 < -0.04$ mm sec: sensitivity 69%, specificity 93%.
- criterion: Macruz Index, i.e., P-wave duration/P-R segment greater than 1.6: sensitivity 31%, specificity 64%.

The study was deficient in that patients taking drugs which might alter the P-R interval were not excluded and there were no assessments made of atrial pressure and atrial conduction.

In a comparison of P-wave measurements with left atrial diameters determined by echocardiography in 48 patients the following statistically significant correlations were found: P-wave duration ($r = 0.75$, $p < 0.00001$); $PTFV_1$ ($r = 0.49$; $p < 0.0004$); Macruz Index ($r = 0.48$, $p < 0.0006$) (Cherife, R. et al., 1975).

Determination of the specificity and sensitivity of abnormal P-wave duration in lead II (> 0.12 sec) and $PTFV_1$ (< -0.03 mm sec), in relation to left atrial size documented by echocardiography, demonstrated a specificity of 80% and a sensitivity of 67% in subjects with left atrial transverse dimension greater than 4.0 cm (Waggoner, A. D. et al., 1976).

Electrocardiographic criteria for LAE were evaluated in a group of 100 patients with a wide spectrum of cardiovascular diseases and compared with the echocardiographic measurement of LAE. The specificity of $PTFV_1$ was 88 percent, while the specificity of the Macruz Index was 50 percent; the corresponding

sensitivities were 77 percent and 50 percent, respectively (Termini, B. A. and Yu-Chin Lee, 1975).

Similar findings were demonstrated in a group of subjects with valvular or hypertensive heart disease. Linear regression analysis showed a significant correlation between EKG PTFV₁ and LAE measured by electrocardiography ($r = 0.32$, $p < 0.01$) (Ikram, H. et al., 1977).

In a recent publication (Fodor, G. et al., 1986) the total area (in mm²) of the P-wave in lead V₁ was measured by means of the Carl Zeiss Model planimeter. The rationale for measuring the total wave, rather than only the terminal portion of the wave, was that division of the P-wave into right and left components is arbitrary and there is a partial temporal overlap between right and left atrial potentials. In order to express the total electromotive force of the P-wave in a uniform manner, the total area was measured.

The results demonstrated that the total area (in mm²) of the P-wave in V₁ was significantly larger in middle-aged (mean age 51.8 ± 1.3 years for males, 52.4 ± 1.4 years for females) hypertensives than in middle-aged (mean age 48.6 ± 1.5 years for males, 48.7 ± 1.3 years for females) normotensive controls, i.e., total area for males 0.59mm² vs 0.31mm² ($p < 0.0001$); and for females 0.55mm² vs 0.26mm² ($p < 0.0001$).

Although the literature provides an ample basis for postulating an association between high exercise SBP and increased

increased prevalence of LVH and PWA, the rationale for which is elaborated below, the literature provides relatively little evidence as to the effect of such factors as age and sex on the electrocardiographic indices of LVH and PWA.

3. RATIONALE

The rationale which underlies the postulated association between the SBP response to exercise and EKG abnormalities may be formulated as follows:

If an exaggerated SBP response to exercise is an indicator of an increased risk of hypertensive disease, and if EKG abnormalities (LVH and PWA) are indicators of hypertensive disease, then one may postulate that subjects with an exaggerated response will exhibit increased prevalence of LVH and PWA. The relationship between exercise SBP response in normotensives and borderline hypertensives and EKG abnormalities has not been investigated. Such an investigation would seem to be a logical step in the search for prognostic indicators of early impairment of cardiac function.

It has been demonstrated that ambulatory BP is a better predictor of the risk for the development of cardiovascular complications than is casual resting BP (Sokolow, M., 1961). However, the technique of ambulatory BP monitoring is cumbersome and expensive. Since it has also been shown that exercise SBP correlates more strongly with ambulatory SBP than with casual clinical measurements, it would suggest that the SBP response to

exercise is a better tool for assessing the risk of HT, and its associated cardiovascular abnormalities, than is casual resting BP (Miller-Craig, M.W. et al., 1980). Among these associated abnormalities are changes in the electrocardiogram; in particular, abnormalities related to the P-wave and QRS complexes.

The abnormalities in the SBP response to exercise and in the electrocardiogram in HT may have a common pathophysiological basis. The hemodynamic abnormalities are present in the early stages of HT including an increased cardiac output, an increased peripheral resistance, and in some cases high levels of plasma renin. The hemodynamic abnormalities appear to be neurogenic in that they can be abolished with pharmacological blockade. In some borderline hypertensives elevated pressures appear to be primarily related to elevated cardiac output associated with parasympathetic inhibition. In others, elevated pressures are associated with increased peripheral resistance which could be reduced to normal with alpha-adrenergic blockade.

Plasma renin levels were determined in a subgroup of borderline HT. Thirty-five percent of these subjects had high plasma renin levels and also demonstrated larger falls in BP after autonomic blockade, than the other subjects in this subgroup. This may be regarded as further evidence of a generalized increase of sympathetic activity in these subjects. The widespread distribution of altered autonomic activity suggests an aberration in the function of the integrative centres of cardiovascular

control (Julius, S. et al., 1975).

It has thus been postulated that HT represents a response to increased cardiac output due to excessive adrenergic activity and an associated reduction in parasympathetic activity. In functional terms the result of the increased adrenergic input to the heart is a shift in the Frank-Starling curve "upward and to the left" (Frolich, E.D. et al., 1970; Julius, S. et al., 1971). This in turn results, both in man and in spontaneously hypertensive rats (SHR), in a hyperkinetic circulation manifested by tachycardia, increased cardiac output and increased myocardial contractility (Frohlich, E.D. 1971). Increased total peripheral resistance due to arteriolar constriction is accompanied by venoconstriction which shifts blood to the central circulation and adds to the central "hyperfunction" of the heart (Freis, E.D. 1960). Such "hyperfunction" may affect the left atrium even before signs of LVH appear (Frolich, E.D. et al., 1975). It has also been indicated that in early HT impaired diastolic filling of the left ventricle due to reduced compliance leads to impaired atrial emptying, left atrial enlargement (LAE) and associated EKG abnormalities (Dreslinski, G.R. et al., 1981).

On the basis of the foregoing considerations it is plausible to suggest that a propensity to high cardiac output and excessive adrenergic activity could, on the one hand, lead to EKG abnormalities and, on the other, could also lead to excessive increases in SBP on exercise. It is therefore reasonable to

postulate that there is an association between excessive SBP response to exercise and the presence of LVH and PWA.

4. OBJECTIVES

4.1 Specific objective one

To determine the prevalence of PWA and LVH in normotensive subjects (resting BP less than 140/90 mmHg) whose SBP on exercise is ≥ 200 mmHg, and to compare the prevalence to that in subjects with resting blood pressures in the same range whose SBP on exercise is < 200 mmHg systolic.

4.1.1 Hypothesis 1 Subjects who are normotensive at rest and who have an exaggerated SBP response to exercise will have a higher prevalence of PWA than subjects without an exaggerated SBP response.

(Ho: there is no association between an exaggerated exercise SBP and PWA.)

4.1.2 Hypothesis 2 Subjects who are normotensive at rest and have an exaggerated BP response to exercise will have a higher prevalence of LVH than those subjects who are normotensive at rest and do not have an exaggerated SBP response to exercise.

(Ho: there is no association between an exaggerated exercise SBP and voltage of QRS complexes in normotensive subjects.)

4.2 Specific objective two

To determine the prevalence of PWA and LVH in untreated, borderline hypertensive subjects whose resting SBP is 140-159 mmHg systolic and/or 90 - 104 mmHg diastolic but whose exercising SBP is ≥ 200 mmHg, and to compare them to untreated borderline hypertensive subjects with resting BPs in the same range whose exercise SBP is < 200 mmHg.

4.2.1 Hypothesis 3 Untreated borderline hypertensive subjects who have an exaggerated SBP response to exercise will have a higher prevalence of PWA than untreated borderline hypertensive subjects who do not have an exaggerated BP response to exercise.

(Ho: there is no association between an exaggerated exercise SBP and PWA in untreated borderline hypertensive subjects.)

4.2.2 Hypothesis 4 Untreated borderline hypertensive subjects who have an exaggerated SBP response to exercise will have a higher prevalence of LVH than untreated borderline hypertensives who do not have an exaggerated BP response to exercise.

(Ho: there is no association between an exaggerated exercise SBP and LVH in untreated borderline hypertensive subjects.)

4.3 Specific objective three

To determine the influence of age, sex and resting SBP on the values of the electrocardiographic indices of PWA and LVH both in terms of the independent effects of these factors and their joint

relationships (interaction) with the level of exercise SBP.

4.3.1 Hypothesis 5 There is an effect by exercise SBP, which is independent of the effects of age, sex and resting SBP, on the electrocardiographic indices of LVH and PWA.

(Ho: there is no independent effect of the level of exercise SBP on the EKG indices of PWA and LVH.)

5. METHODS AND MATERIALS

5.1 Background Information

The study design was cross sectional, defined as an examination of the relationship between diseases and other characteristics or variables of interest as they exist in a defined population at one particular time (Freidman, G. D. 1974). The population source was participants in a preventive fitness program (Pre-fit) open to the general public. The purpose of the program is to promote cardiovascular health through exercise and the modification of cardiovascular risk factors such as smoking, hypercholesteremia and obesity. On entry into the program each new member, with the assistance of a staff member as required, completed a questionnaire designed to elicit information on current health status and medical history. Information was also obtained concerning age, occupation and marital status. Specific information was sought concerning cardiovascular status, family history of cardiovascular disease, smoking habits and medications.

The program is conducted in the Reh-Fit Centre, a facility

owned and operated by the Manitoba Cardiac Institute (MCI), a non-profit corporation.

The Centre consists of a 40,000 sq. ft. field house, including: i) a 200 metre running track; ii) a variety of exercise facilities and equipment; iii) an exercise laboratory; iv) a staff of doctors, nurses, technicians and physical educators.

In addition to the Pre-fit program, MCI has a cardiac rehabilitation program (Reh-fit) conducted in a similar fashion to the Pre-fit program. Members of the Reh-fit program are individuals with established coronary artery disease and/or peripheral arterial insufficiency who are referred to the Centre by their family physician or cardiologist.

5.2 Subjects

The subjects were selected from the 629 male and female Pre-fit members who joined the program between 1979 and 1981. The data used in the study were obtained from examinations and tests conducted on first entering the program.

5.2.1 Criteria for inclusion in the study are listed below

- a) The subjects were free of clinical evidence of coronary artery disease, peripheral disease, and cerebrovascular disease.
- b) The subjects were not on any antihypertensive therapy.

- c) The subjects did not have any resting systolic or diastolic blood pressures in excess of 160 mmHg and 104 mmHg, respectively.
- d) The subjects did not have a positive stress test, defined as chest tightness, or pain on exertion accompanied by 1 mm or more horizontal ST segment depression or horizontal ST segment depression of greater than 2.0 mm in the absence of symptoms.
- e) The subjects achieved an exercise HR of at least 80% of age predicted maximum.

These criteria were used in order to exclude subjects whose blood pressure response to exercise, ability to exercise and EKG characteristics were not impaired by overt disease or medication.

5.3 Study Protocols

5.3.1 Questionnaire

The questionnaire was designed to be self-administered. The information elicited and its categorization is described below.

- a) Subjects recorded whether they were male or female.
- b) Subjects recorded their occupations and these were coded in 9 categories using the Standard Occupation Classification (Statistics Canada, 1980).
- c) Subjects recorded their marital status according to the categories: married, single, widowed or divorced.

- d) Subjects recorded their current smoking habit. They reported if they were currently smokers and if so, how much they smoked each day. If they did not currently smoke they reported how long ago they had stopped smoking.
- e) Subjects recorded any family history of myocardial infarction, diabetes, or hypertension in a parent or sibling who was at or under the age of 55 years at the time of diagnosis of the disease.
- f) Subjects listed current medications and any known disease or disability.

5.3.2 Clinical data

Clinical data obtained included age (yrs), height (cm), weight (kg), serum cholesterol (mg/dl) and triglycerides (mg/dl), glucose (mg/dl), hemoglobin (mg/dl), FEV_1/FVC (FEV_1 defined as the volume of air expired in 1.0 second during a maximum forced expiratory effort beginning at full inspiration (Folkow, B. 1971). FVC (forced vital capacity) is an index of the distensibility of the lungs and thoracic cage. The subject makes a forceful maximum expiration after a forceful maximal inspiration (Cherniack, R.M. et al., 1972). BP (mmHg), HR (b/m) were measured. Exercise work load was expressed in METS. METS refers to resting oxygen uptake during work \div resting metabolic rate. One MET is the basal oxygen requirement of the body in a post-absorptive inactive state, sitting quietly (average normal value 3.5 ml O_2 /Kg/min American

Heart Association, 1972).

5.3.3 Resting Blood Pressure

Supine and seated BP measurements were recorded using a mercury sphygmomanometer. The protocol used was similar to that recommended by the Canadian Hypertensive Society (1984). The subject rested five minutes with arm bared and well supported. A cuff of appropriate size for the mid-upper arm circumference, namely 15 x 23 cm for adult arm size less than 33 cm, and 15 cm x 33 cm for adult arm size 33 to 41 cm, was applied snugly with the lower edge approximately 3 cm above the crease of the elbow and the bladder centered over the brachial artery. The radial pulse was palpated while the cuff was inflated to 30 mmHg above the level at which the radial pulse disappeared. The systolic and diastolic pressures were identified as the first and last Korotkoff sounds, respectively. Three successive BP readings, with at least one minute intervals between readings, were taken in the right arm, and the mean of the second and third readings were used to determine the final BP for recording and statistical purposes.

5.3.4 Modified Balke Treadmill Test:

Exercise testing was performed on a treadmill using a modification of the Balke procedure (Balke, B. and Ware, R.W. 1959).

- a) The subject was "warmed-up" on the treadmill by walking for two minutes at 2.4 Km/h and 0° elevation, then 3.2 Km/h at 0° elevation for one minute.

- b) The speed was then increased to 5.4 Km/h with elevation increased by 2° after each minute of exercise.
- c) Exercise was continued until the subject experienced moderately severe fatigue or dyspnea unless other symptoms (e.g., chest pain) or signs (e.g., significant arrhythmias) occurred.
- d) During recovery the speed was reduced to 2.4 Km/h and elevation reduced to 0° for 30 seconds to one minute.
- e) The subject then remained seated at rest for an additional six minutes after exercise.
- f) The Marquette Electronics Inc. EKG Computer-Assisted System for Exercise - Series 3510, number IF 360120, 2.5 amp, 60 Hz, 115 Volts, was used to monitor the EKG and HR at rest, during exercise and recovery. Leads V₃, V₅ and AVF were monitored during exercise, and, just prior to exercise, BP, HR and a 12 lead resting EKG at a paper speed of 25 mm/sec and at a sensitivity of 1mV/cm was recorded.
- g) HR was measured every minute throughout exercise and during the six minute post-exercise recovery period.
- h) BP was measured every two minutes during exercise and for six minutes after exercise ceased. It has been our experience and the experience of others (American Heart Association, 1972) that after a six

minute post-exercise rest period BP and HR have returned to pre-exercise levels and the electrocardiogram has reverted to a pre-exercise pattern.

5.3.5 EKG Measurements

5.3.5.1 P-wave Measurements

The three methods of measurement used to identify PWA are described below (see Figure 1 and Figure 2).

- a) Using a magnifying lens and calipers the P-wave duration and the PR interval were measured in Lead II according to the Minnesota Code (Prineas, R.J. et al., 1982). The PR interval was measured from the onset of the P-wave to the onset of the QRS complex. The width of the P-wave was measured from the onset of the P-wave to the onset of the PR segment (Figure 1). The PR segment is the segment between the end of the P-wave and the onset of the QRS complex. The P/PR segment ratio was calculated as P duration divided by the PR segment (Macruz, R. et al., 1958).
- b) Using a magnifying lens the duration (sec) and amplitude (mm) of the negative portion of the P-wave in Lead V_1 was measured. The depth of the negative deflection of the P-wave was measured from the isoelectric line (defined as the straight line from the onset of the P-wave in one cycle to the onset of the P-wave in the next cycle) to the point where the

greatest deflection occurred. The duration of the negative deflection was measured between the points of intersection of the leading edge of the trace with the isoelectric line (Figure 2). The product of duration and amplitude gave the P-terminal force in Lead V_1 (PTFV₁) (Ikram, H. et al., 1977).

- c) For measurement of the area of the P-wave deflection in Lead V_1 the EKGs were photocopied onto transparencies and projected in order to magnify the complexes. The magnification was 14.2 times. Two complexes were traced for each subject. The positive and/or negative areas were measured on the tracings. The areas of the initial and terminal portions of the P-wave deflection were determined in relation to the isoelectric line defined as a straight line from the onset of the P-wave in one cycle to the onset of the P-wave in the next cycle (Figure 2) (Cromwell, L. et al., 1980). In cases of a biphasic P-wave the rising limb of the dominant wave was extrapolated to the P-P baseline. The tracing was then placed on a digitized magnetic board and a transducer (cursor) (Microplan II Image Analysis System - Laboratory Computer Systems, Inc., Cambridge, MA) was moved around the contours of the P-wave deflections. The transducer automatically switched

off as soon as it returned to the point of origin. The size of the area was then automatically computed. Each complex was measured three times. The first measurement was a practice tracing and was discarded. The final two measurements were averaged and if the coefficient of variation was less than 5% the average was used for the analysis.

If the coefficient of variation was greater than 5%, the process was repeated.

Intra-rater reproducibility of area measurements was examined in 50 subjects. A discrepancy of 1% was found in 85% of the sample, between 1 and 2% in 13% of the sample, and greater than 2% in 2% of the sample.

In order to assess inter-rater reliability, a second observer measured the EKGs of 25 subjects independently. Two complexes were measured in each subject. The difference in measured areas between the investigator and the second observer was less than 2% in all cases.

In order to express the total electromotive force of the P-wave in a uniform manner, the root sum square (RSS) area of the P-wave was calculated as follows:

$$\text{RSS area} = \sqrt{(\text{positive area})^2 + (\text{negative area})^2}$$

P-wave measurements were obtained on all subjects with the following exceptions:

- a) P-waves in Lead II in 8 males and 7 females
- b) P-waves in Lead V_1 in 4 males and 4 females.

5.3.5.2 QRS Measurements

The measurements used in the identification of LVH were the voltage of the R-wave in precordial Leads V_5 and V_6 , in the standard limb Lead I and in the augmented limb lead AVL; and the voltage of the S-wave in precordial Lead V_1 and in the standard limb Lead III.

All voltages were recorded in millimeters, with upward deflections measured from the top of the baseline to the top of the peak and downward deflections from the bottom of the baseline to the bottom of the peak (Figure 2). Two complexes in each lead were measured and averaged.

Measurements were obtained on all subjects with the following exceptions:

- a) RAVL in 8 males and 3 females.
- b) RV_5/RV_6 in 2 males and 5 females.
- c) $RV_5/RV_6 + SV_1$ in 4 males and 4 females.
- d) R_1+S_3 in 3 males and 5 females.

5.4 Variable definitions

5.4.1 Independent variables

- a) Sex: In the analysis of results subjects were divided into males and females.

- b) Age: The subjects were classified according to age. Five age categories were used, viz., 20-29, 30-39, 40-49, 50-59, >60 years.
- c) Resting blood pressure: Resting SBP was analyzed both as a continuous and categorical variable. In the latter case the subjects were classified in 4 categories, viz., SBP <120, 120-129, 130-139, 140-159 mmHg for descriptive purposes and for certain statistical analyses (ANOVA and log-linear modelling). For univariate and statistical modelling subjects were classified into 2 categories, viz., SBP <140 mmHg and SBP 140-159 mmHg.
- d) Exercise blood pressure. Exercise SBP was analyzed both as a continuous and categorical variable. In the latter case the subjects were classified into 3 categories, viz., SBP <180, 180-199, \geq 200 mmHg for descriptive purposes and for statistical modelling. In subsequent analyses subjects were classified into 2 categories of exercise SBP, viz., <200 mmHg and \geq 200 mmHg.
- e) Exercise/resting blood pressure ratio. The exercise/resting SBP ratio was analyzed both as a continuous and categorical variable. In the latter case the subjects were classified into four categories, viz., exercise/resting SBP $\times 100$ <135, 135-146, 147-158, 159-211.

5.4.2 Dependent variables

5.4.2.1 Atrial variables

- a) P/PR segment ratio (Macruz Index). The Macruz Index was analyzed both as a continuous and as a categorical variable. In the latter case the upper limit of normal used in the present study was that reported by Macruz, R. et al. (1958), viz., 1.6.
- b) The P-terminal force in Lead V_1 (PTFV₁). When present PTFV₁ was analyzed both as a continuous and as a categorical variable. In the latter case the lower limit of normal used in the present study was that reported by Morris, J. et al. (1964), viz., -0.03 mm sec. PTFV₁ was also analyzed by categorizing it as present or absent.
- c) Root Sum of Squares of P-wave areas in Lead V_1 (RSS) was analyzed as a continuous variable. Normal values for this index have not been established.

5.4.2.2 Ventricular variables

- a) The voltage of the R-wave in Leads V_5 or V_6 , (RV_5/RV_6) whichever is larger, was analyzed as a continuous variable.

- b) The voltage of the R-wave in Lead AVL (RAVL) was analyzed as a continuous variable.
- c) The voltage of the R-wave in Lead V_5 or V_6 (whichever is larger) plus the voltage of the S-wave in Lead V_1 (RV_5/RV_6+SV_1) was analyzed as a continuous variable.
- d) The voltage of the R-wave in Lead I plus the voltage of the S-wave in Lead III (R_1+S_3) was analyzed as a continuous variable.
- e) For the purpose of categorical analysis electrocardiographic LVH was defined as being present when one or more of the foregoing measurements exceeded the upper limit of normal, viz., $RV_5/RV_6 = 26$ mm; RAVL = 11 mm; $RV_5/RV_6+SV_1 = 35$ mm; $R_1+S_3 = 24$ mm.

The normal limits referred to are those reported by Kannel, W.B. (1970); Sokolow, M. and McIlroy, M., (1986); and Prineas, R.J. et al. (1982).

5.5 Statistical Analysis

All data in the study were analyzed using the Statistical Analysis System (SAS) (1982) software on an Amdahl 5870 computer located at the Fort Garry Campus of The University of Manitoba.

Summary statistics for each variable were expressed as the mean \pm standard deviation (sd). A probability level (p-value) of less than 0.05 was considered significant for hypothesis testing.

The Chi-square test was used to test the hypothesis of no difference between the prevalence of EKG abnormalities between subjects with normal exercise SBP and subjects with abnormal SBP within various categories of resting SBP. Relationships between the attained level of the exercise SBP (independent variable) and each EKG index (dependent variable) was determined using linear regression analysis for each sex.

Analysis of variance (fixed effect ANOVA Model) was used to assess the significance of the effects of the independent variables age, sex, resting SBP and exercise SBP on the electrocardiographic dependent) variables. Logarithmic and square root transformations were applied to positively skewed variables for analysis in ANOVA models.

Pairs of means of the dependent variables within categories of significant main effects and interactions found in ANOVA models were compared with multiple t-tests. The levels of significance for the multiple tests were adjusted using Bonferroni's correction (Miller, R., 1981).

Log-linear modelling was used to examine relationships among categorically scaled variables, i.e., absent/present and normal/abnormal categorization of the electrocardiographic variables.

PTFV₁ was analyzed using three approaches. PTFV₁ was analyzed on a continuous scale as the dependent variable in ANOVA models with all cases for which PTFV₁ was absent having been

excluded. $PTFV_1$ was treated as a categorical variable when dichotomized in log-linear modelling. Dichotomization was achieved in two ways: 1) $PTFV_1$ present or absent; 2) $PTFV_1$ "abnormal" (<-0.03 mm sec) or "normal" (≥-0.03 mm sec).

6. RESULTS

6.1 Social, Economic, Family and Health History

There were 429 subjects who met the criteria for inclusion in the study, 68% of all potential study subjects (Section 5.2.1). The age range of the selected population was 20 to 75 years, with a mean age (\pm sd) 43.7 ± 12.1 for males and 45.3 ± 12.5 for females. Fifty-three percent of the males and 48% of the females were between the ages of 40 and 59 and 8% of the males vs 15% of the females are over the age of 60 (Table 1).

As shown in Table 2, 96% of males were employed, 4% were retired, 52% were in managerial or administrative occupations. One half of the female population did not work outside the home and those who did were primarily teachers or in social sciences and related fields. Eight-three percent of males and 79% of females were married (Table 3). Thirteen percent of males and 18% of females were smokers (Table 4). Sixteen percent of males and 17% of females had family histories of early myocardial infarction, 13% and 21% of males and females, respectively, had family histories of HT, and 10% of the males and 9% of the females had a family history of diabetes (Table 5).

6.2 Clinical Data

As depicted in Table 6, the mean weight (\pm sd) was 81.3 ± 11.3 Kg in males and 63.7 ± 12.1 Kg in females. Both values are greater than "desirable" for adults over 25 years of age according to the data of the Build and Blood Pressure Study (Krupp, M. A. et al., 1976). The SBP on exercise was on the average 20 mmHg greater in males than in females, while there was little difference in exercise DBP. The SBP during recovery was on average 15 mmHg greater in males than in females, while there was little difference in DBP.

The MET level achieved during exercise was on average 3 units higher in males than in females, while there was little difference in heart rate.

The triglyceride level was on average 38 mg/dl higher in males than in females, while there was little difference in cholesterol, glucose and hemoglobin levels.

There was also little difference between males and females in FEV_1/FVC .

The mean \pm sd values of EKG variables are depicted in Table 7. There was, on average, little or no difference between males and females in the values of P, PR segment, and PR interval durations. The Macruz Index, RSS, RV_5 , RV_6 , R_1+S_3 , RV_5/RV_6+SV_1 and RAVL were on average greater in males than in females, while $PTFV_1$ was more negative in males than in females. Frequency histograms of the atrial and ventricular EKG variables are shown in Figures 3-10 for

males and females. The values of the Macruz Index (Fig. 3), RV_5 (Fig. 8), R_1+S_3 (Fig. 9), RV_5+SV_1 (Fig. 10) approach a normal distribution. The values of RSS (Fig. 6) and RAVL (Fig. 7) are positively skewed. If all values of $PTFV_1$, including zeros, are considered (Fig. 5), the frequency histogram is positively skewed. A normal distribution is approached if only non-zero values are considered (Fig. 4). The difference in frequency distribution was the basis for the different approaches used in the statistical analysis of $PTFV_1$ described earlier (Sec. 5.5).

6.3 Distribution of Subjects According to Resting and Exercise SBP

Subjects were divided into four categories of resting SBP (<120, 120-129, 130-139 and 140-159 mmHg), and three categories of exercise SBP (<180, 180-199 and ≥ 200 mmHg) were defined. The frequency distribution of all subjects, and of males and females separately, among combinations of resting/exercise SBP categories, is depicted in Tables 8, 9 and 10.

Twenty percent of the males and 15% of the females had resting SBP above the normal range, i.e., ≥ 140 mmHg. Forty percent of males and 13% of females had exercise SBP ≥ 200 mmHg.

Thirty-four percent (67/197) of males with normal resting SBP had exercise SBP ≥ 200 mmHg. By contrast, only 6% (10/156) of females fell into this category.

Sixty-three percent (31/49) of males with abnormal resting SBP had SBP ≥ 200 mmHg and 52% (14/27) of females fell into this category.

6.4 The Macruz Index by Resting and Exercise SBP and Sex

As shown in Table 11, the mean Macruz Index, for the total group, increased with exercise SBP in each category of resting SBP (except for 120-129 mmHg). This was most pronounced in the resting SBP category 140-159 mmHg.

In males, the mean Macruz Index increased with exercise SBP in each category of resting SBP (except for the category <120 mmHg). This was most pronounced in the resting SBP category 140-159 mmHg. Within the exercise SBP category ≥ 200 mmHg the mean Macruz Index increased with resting SBP

In females, the mean Macruz Index increased with exercise SBP in the categories of resting SBP 130-139 and 140-159 mmHg. A trend was absent in the two lowest resting SBP categories. Within the exercise SBP category ≥ 200 mmHg, the mean Macruz Index increased with resting SBP. The differences were much greater than those observed in the male subjects.

For both males and females, the highest mean Macruz Index was found in the category resting SBP 140-159 mmHg and exercise SBP ≥ 200 mmHg.

6.5 PTFV₁ by Resting and Exercise SBP and Sex

Mean PTFV₁ was calculated for all subjects with a measurable terminal P-wave component. As shown in Table 12, mean PTFV₁ tends to increase both with increasing level of resting SBP and increasing level of exercise SBP. The trend is most apparent at levels beyond 140 mmHg resting SBP and ≥ 200 mmHg exercise SBP.

In males, mean $PTFV_1$ increased with exercise SBP in the three highest resting SBP categories. In females, such a trend was less apparent.

6.6 RSS by Resting and Exercise SBP

As shown in Table 13, the mean RSS for the total group tends to increase with increasing levels of exercise SBP in the resting SBP categories 120 and 130-139 mmHg.

Within the exercise category <180 mmHg the mean RSS increased with resting SBP.

In males, the highest mean RSS was in the category SBP 140-159 mmHg and exercise SBP ≥ 200 mmHg.

In females, it was only in the resting SBP category 120 mmHg that mean RSS tended to increase with exercise SBP.

6.7 RAVL by Resting and Exercise SBP and Sex

As shown in Table 14, the relationship between RAVL and exercise SBP was not consistent for all levels of resting SBP. The relationships within sex categories were also not consistent. It is possible that the non-normal distribution of RAVL is responsible for these inconsistencies.

6.8 RV_5/RV_6 According to Resting and Exercise SBP and Sex

As shown in Table 15, the mean RV_5/RV_6 for the total group tends to increase with exercise SBP. Within the exercise SBP category <180 mmHg, the mean RV_5/RV_6 increased with resting SBP.

The relationship of RV_5/RV_6 to resting and exercise SBP within sex categories were not consistent.

6.9 R_1+S_3 by Resting and Exercise SBP and Sex

As shown in Table 16, for the total group the mean R_1+S_3 tends to increase both with increasing level of SBP and increasing level of exercise SBP. The trend with exercise SBP is most apparent at levels beyond 180 mmHg.

In males, the mean R_1+S_3 increased with exercise SBP in the resting SBP category 140-159 mmHg. In females, there is no increase of mean R_1+S_3 with exercise blood pressure in any of the categories of resting blood pressure.

6.10 RV_5/RV_6 by Resting and Exercise SBP and Sex

As shown in Table 17, for the total group there was an increase in mean RV_5/RV_6+SV_1 with exercise SBP in all categories of resting SBP but 140-159 mmHg. There was an increase in mean RV_5/RV_6+SV_1 with resting SBP in exercise SBP category <180 mmHg.

The relationship of RV_5/RV_6+SV_1 to resting and exercise SBP within sex categories was not consistent.

6.11 Relationship between Exercise SBP and Age and Sex and Resting BP

Since the subjects in the present study varied by age, sex and resting SBP, analysis of variance was carried out to determine the effects of these variables on the attained level of SBP during exercise. It was found that all four variables had a significant effect on exercise SBP (<0.001). Accordingly, a variety of statistical analyses were carried out to examine the independent and joint effects of age, sex, resting SBP and exercise SBP on the

electrocardiographic variables. The results of these analyses are displayed in Tables 18 to 25 and are described in detail below.

6.12 Relationship between EKG Variables and Age and Sex

The relationship between the EKG variables and age and sex is shown in Table 18. The relationship between age and sex and EKG variables was examined by an ANOVA Model and, in the case of $PTFV_1$, the relationship was also examined by log-linear modelling.

Mean values of the Macruz Index and RSS were significantly greater for males than for females. Neither the Macruz Index nor RSS was associated with age. Presence or absence of $PTFV_1$ was not related to sex and in subjects in whom it was present its magnitude was not related to sex. Presence of $PTFV_1$ was more likely with increasing age; however, in subjects in whom it was present its magnitude did not increase with age.

For all 4 QRS variables ($RAVL$, RV_5/RV_6 , R_1+S_3 and RV_5/RV_6+SV_1) there was a significant difference between the sexes and the values for males were greater than for females. For all 4 variables there was a significant association with age, i.e., $RAVL$, R_1+S_3 , RV_5/RV_6+SV_1 increased with age and RV_5/RV_6 decreased with age. The relationship with age was not significantly different for males and females.

The distribution of $RAVL$ was observed to be positively skewed. Using logarithmic and square root, transformations of $RAVL$ in ANOVA models demonstrated the same age and sex effects as for untransformed $RAVL$ (i.e., the sex and age effects were significant

at the $p < 0.0001$ level). The results reported were therefore restricted to the untransformed values of RAVL.

No significant ($p < 0.05$) joint effects between age and sex were detected for any of the EKG variables.

6.13 Relationship Between EKG Variables and Resting SBP

The relationship of resting SBP to the EKG variables is shown in Table 19. The relationship was examined by determining the additional contribution of resting SBP to the ANOVA Model with age and sex (Section 6.21). RV_5/RV_6+SV_1 is the only variable which was related to resting SBP when controlled for the effects of age and sex. This relationship was not significantly different for males and females.

6.14 Relationship Between EKG Variables and Exercise SBP

The relationship of exercise SBP to the EKG variables is shown in Table 20. The relationship was examined by determining the contribution to ANOVA models provided by exercise SBP over and above that of age, sex and resting SBP. The relationship was also examined by determining the contribution of exercise SBP to ANOVA models when exercise SBP was dichotomized into categories (< 200 mmHg and ≥ 200 mmHg).

For the Macruz Index there was a relationship to exercise SBP which was significantly influenced by sex and age. Table 20 suggests that the relationship is limited to females. RSS was not related to exercise SBP. The presence or absence of $PTFV_1$ in relation to exercise SBP is significantly different for males and

females. Table 20 suggests that although, stronger for females than for males, the presence of $PTFV_1$ increases in both sexes with exercise SBP. In those with $PTFV_1$ present, the magnitude of $PTFV_1$ increased with exercise SBP independent of sex.

RV_5/RV_6 and RV_5/RV_6+SV_1 increase with exercise SBP, and the relationship is independent of sex. There were no significant joint effects between sex and exercise or age and exercise for any of the ventricular variables. The same relationship as those described above were observed when exercise SBP was dichotomized into categories (<200 mmHg and ≥ 200 mmHg).

The relationship between EKG abnormalities and exercise SBP was first examined by linear regression of EKG values on exercise SBP. Because there were differences between the sexes this was done separately for males and females. The scatter plots of the EKG variables against exercise SBP are shown in Figure 11 to 24. Significant relationships were observed for both males and females between exercise SBP and both $PTFV_1$ and the Macruz Index; and for male subjects between exercise SBP and each of RSS, RV_5/RV_6 and RV_5/RV_6+SV_1 . Correlations and linear regression coefficients and p-values for all relationships examined are given in Table 21.

6.15 Relationship Between EKG Variables and the Exercise/Resting SBP Ratio

In order to determine if the association between EKG variables and the absolute level of SBP on exercise is different than the association between EKG variables and the ratio of exercise SBP

pressure to resting SBP, a multivariate analysis using ANOVA models was undertaken. The results are shown in Table 22.

With regard to the significance (determined by ANOVA) of the effects of sex, age and exercise blood pressure category, and joint effects, the findings using the exercise/resting blood pressure ratio as the independent variable (Table 22) differed from the findings using the absolute level of blood pressure (Table 20) as described below.

- a) There was no 3 factor interaction for the Macruz Index although the relationship approached significance ($p = 0.135$).
- b) There was no independent exercise effect for $PTFV_1$ (present and analyzed as a continuous variable) although the relationship approached significance ($p = 0.087$).
- c) There was no independent exercise effect for RV_5/RV_6+SV_1 .

6.16 Log-Linear Modelling Relating the Dichotomization of $PTFV_1$, Macruz and LVH to Age (5 categories), Sex, Resting SBP (4 categories), and Exercise SBP (3 categories)

Only EKG variables which could be dichotomized (normal/abnormal or present/absent) are included in this analysis. Log-linear modelling can be considered the counterpart to the linear models in ANOVA methods for categorical data. As shown in Table 23, $PTFV_1$ was categorized in two ways: (1) $PTFV_1$ present or absent; (2) $PTFV_1$ normal (≥ -0.03 mm sec) or abnormal (< -0.03 mm sec). The Macruz Index was categorized as normal or abnormal

(>1.6) and LVH was categorized as absent or present (abnormal values in one or more of the variables RV_5/RV_6 , $RAVL$, R_1+S_3 , RV_5/RV_6+SV_1).

In all four models there was a significant two factor interaction between sex-age, resting SBP - age and resting SBP - exercise SBP independent of relationship with the dependent variables. $PTFV_1$ (definition (1)) exhibited an interaction of sex and exercise SBP independent of relationships with the dependent variables.

For $PTFV_1$ (definition (1) and definition (2)), a significant association was found with exercise SBP ($p < 0.0001$). For LVH, a significant association was also found with exercise SBP ($p < 0.01$). Macruz Index was not associated with exercise SBP; however, a significant association was found with sex and resting SBP combinations ($p < 0.03$). For $PTFV_1$ (definition (1) and definition (2)) a significant association was found with age ($p < 0.0001$) ($p < 0.05$), respectively. For LVH, a significant association was found with sex ($p < 0.0002$).

6.17 Prevalence of Abnormal Electrocardiographic Indices According to Exercise SBP

Table 24 shows the prevalence of EKG abnormalities for subsets of subjects defined by sex, resting and exercise SBP.

In normotensive males and females the prevalence of electrocardiographic LVH was significantly greater in those with exercise SBP ≥ 200 mmHg than in those with exercise SBP < 200 mmHg.

A significant difference in prevalence was also observed in normotensives in the case of $PTFV_1$. Insignificant differences in prevalence were observed for the abnormal Macruz Index among normotensives.

Among borderline hypertensives, the differences in prevalence rates between those subjects with exercise SBP ≥ 200 mmHg and those with exercise SBP < 200 mmHg were significant for females for the Macruz Index and for males for $PTFV_1$ but were not significant for either sex for LVH.

6.18 Log-Linear Modelling Relating the Dichotomization of $PTFV_1$, Macruz and LVH to Age (5 categories), Sex, Resting SBP (2 categories), and Exercise SBP (2 categories).

In view of the effects of age, sex and resting SBP on the EKG variables described earlier, the univariate analysis shown in Table 24 was supplemented by a multivariate analysis shown below.

Results of the log-linear analysis are shown in Table 25. $PTFV_1$ was categorized as normal (≥ -0.03 mm sec) or abnormal (< -0.03 mm sec).

In all three models there was a significant two factor interacting term involving age - resting SBP, independent of relationships with the dependent variables. The three factor interaction describing the relationship between sex - resting SBP - exercise SBP was also significant in all models. In the model for $PTFV_1$ the two factor interaction between sex and age was significant independently of relationships with the dependent variables.

For abnormal $PTFV_1$, a significant association was found with exercise ($p < 0.0001$) and resting SBP ($p < 0.009$). For abnormal Macruz Index, a significant association was found with sex ($p < 0.0001$) and exercise ($p < 0.03$). For LVH, a significant association was found with sex ($p < 0.0001$) and exercise ($p < 0.02$). The difference between models in Tables 23 and 25 is the following:

In the Log-Linear Modelling Analysis relating the dichotomization of $PTFV_1$ (normal/abnormal) to 4 categories of resting SBP (Table 23) and to 2 categories of resting SBP (Table 25), there was a significant association for $PTFV_1$ with resting SBP in the latter, but not in the former.

The difference in results may be related to the fact that the proportion of abnormal values of $PTFV_1$ (< -0.03) was similar in the three lower categories of resting SBP but increased in the SBP category 140-159 mmHg. When the SBP was dichotomized (< 140 and 140-159 mmHg) a significant association for $PTFV_1$ and resting SBP was revealed.

Similar reasoning explained the significant association for Macruz Index and exercise BP in Table 25, but not in Table 21.

7. DISCUSSION

As indicated in the Introduction to this thesis, there have been several studies indicating that the blood pressure response to exercise may be a more useful indicator of the presence of cardiac abnormalities associated with the hypertensive or pre-hypertensive

state than is the level of resting blood pressure (Sokolow, M. et al., 1967; Rowlands, D.B. et al., 1982; Devereux, R.B. et al., 1983; Pickering, T.G. et al., 1985; Drayer, J.M. et al., 1983). The findings of these earlier studies formed the basis of the hypotheses underlying the present investigations; namely, that subjects with an exaggerated SBP response to exercise would exhibit a higher prevalence of electrocardiographic abnormalities than subjects whose exercise SBPs were normal; and that this difference in prevalence would hold true for subjects who were normotensive at rest as well as those whose resting SBPs were in the borderline hypertensive range.

7.1 The Study Population

The present study has several characteristics which distinguish it from previous studies in the field. First of all, it is the largest study in terms of the numbers of subjects investigated. Second, it is the most comprehensive study in terms of the range of subject age investigated. Third, it is one of only a few studies in which cardiologic abnormalities have been related to exercise SBP. Moreover, in the latter connection, the other studies relating cardiologic abnormalities to exercise blood pressure have dealt with echocardiographic variables rather than electrocardiographic variables as in the present study.

The study population is characterized by a nearly equal representation of men and women. Subjects with clinical or laboratory manifestations of heart disease were excluded as were

subjects who were receiving, or had received, antihypertensive medication, including diuretics. Exercise tolerance was similar to that in a middle aged population reported by Pollock, M.L. et al., in 1976 and 1982. This is perhaps not surprising given the fact that although the study group covered a range of ages from 20 to 75 years the largest number of subjects were middle aged.

Although the foregoing characteristics suggest that the study population was similar to the general population, it must be remembered that it is not fully representative. First, it is a population which is self-selected; that is, it comprises individuals who are motivated towards improving their physical fitness to the extent of seeking out, enrolling in and paying for a preventive fitness program. Second, the study population is made up of individuals who are predominantly white, in the middle and upper middle economic classes and who are employed or self-employed. The final study population included sufficient numbers of subjects to allow the hypotheses to be tested. That is to say, there were enough subjects (122 of 429) who had abnormal exercise SBP, who were either normotensive (77 of 122) or hypertensive (45 of 122) at rest, to permit meaningful analyses of the prevalence of electrocardiographic abnormalities to be carried out. The relative frequency of subjects with exercise SBPs ≥ 200 mmHg increased progressively with the level of resting blood pressure. However, the relative frequency of subjects with exercise SBP ≥ 200 mmHg was higher in males than in females. The

explanation for this finding is not certain but it is worth noting that the levels of exercise intensity achieved by the males was on average greater than that achieved by females. Thus there may be, in the study population, females who are potential hyperresponders, in terms of exercise SBP, who did not achieve the level of exercise intensity required to make their hyperresponsiveness manifest. The discrepancy between males and females, in the relative frequency of blood pressures ≥ 200 mmHg, was much less among subjects who were borderline at rest than among those who were normotensive.

7.2 The Relationship of the Experimental Findings to the Hypotheses

In the univariate analysis of the prevalence rates of EKG abnormalities, subjects who are normotensive at rest and who have an exaggerated SBP response to exercise have a higher prevalence of PWA than subjects without an exaggerated response (Hypothesis 1); and subjects who are normotensive at rest and who have an exaggerated SBP response to exercise have a higher prevalence of abnormalities in voltages of QRS complexes than subjects without an exaggerated response (Hypothesis 2).

However, with respect to the analogous hypotheses for the borderline subjects, no significant difference was seen in the prevalence of QRS abnormalities between those with an exaggerated response to exercise and those without, and equivocal differences were observed in the prevalence of PWA. The lack of significance

for relatively large differences in percentage frequency in certain categories is related to the small number of subjects in these categories. On the other hand, it is possible that once hypertension develops the functional differences between hyperresponders and normal responders are reduced. The effects of age, sex and resting SBP on the level of exercise SBP prompted an analysis of the independent and joint effects of these factors on the values of the atrial and ventricular electrocardiographic indices. The implications of the results of these analyses are described below.

7.2.1 Atrial Electrocardiographic Indices

Three atrial electrocardiographic indices were used in the present study: the Macruz Index (the P/PR segment ratio), the P-terminal force in Lead V_1 , and a new index introduced by Fodor et al. (1986), the Root Sum Square (the square root of the sum of the squares of the positive and the negatives areas of the P-wave).

As reported in the literature review, assessment of the functional and diagnostic significance of these atrial electrocardiographic indices has yielded variable results (Kasser, I. and Kennedy, J.W., 1969; Termini, B.A. and Yu-Chin Lee, 1977). Overall these studies suggest that $PTFV_1$ is a more sensitive indicator of atrial abnormality than is the Macruz Index, although in one study the Macruz Index was said to be superior to $PTFV_1$ (Tarazi, R.C. et al., 1966). The only study using the Root Sum

Square is that reported by Fodor, J. et al. (1986) These authors made no attempt to validate this index against an independent measure of atrial function.

The mean values for the Macruz Index for the subjects in the present study are higher than the mean values reported for normal subjects in the literature (Macruz, R. et al., 1958; Morris, J. et al., 1964; Fodor, G. et al., 1986). However, in all but one study in the literature, in which Macruz Index values are reported, mean values for male and female subjects are not reported separately. The observation in the present study of significantly greater values of the Macruz Index in males than in females, when examined in relation to resting SBP, suggests that future studies employing this index should take this sex difference into account. Although the mean values for the Index were higher in the borderline subjects than in the normotensive subjects in the present study, the difference was not statistically significant. Similar findings have been reported by Fodor et al. (1986). Although the independent association between the SBP response to exercise and the Macruz Index was not significant, a significant 3 factor interaction of age, sex and exercise SBP was observed implying the relationship between age and exercise SBP was different for males and females. Log-linear modelling suggested that the abnormal Macruz Index (>1.6) varied significantly with sex, resting blood pressure and exercise blood pressure groupings. These findings indicate the necessity of controlling

for age, sex and resting SBP when studying the blood pressure response to exercise.

A difference in mean values from ANOVA between males and females was not observed for $PTFV_1$ (Table 20). The mean value of $PTFV_1$, when examined in relation to the resting SBP, was greater in borderline subjects than in normal subjects but the difference was not statistically significant. A statistically significant association between the SBP response to exercise and $PTFV_1$, which was independent of both age and sex, was observed. This is the first study in which such an association has been demonstrated. Log-linear modelling involving dichotomization of $PTFV_1$ according to two definitions revealed significant differences in age, sex, resting and exercise SBP.

The mean values of the RSS index were greater for both males and females in the present study than those reported by Fodor et al. (1986). The nature of this difference is not clear. There were differences in the two study populations. Fodor et al. studied 106 middle-aged subjects of whom 51 were hypertensives. In the present study the age range was broader, the number of subjects four times as great, the mean resting blood pressures of borderline hypertensives were 148/93 mmHg in males and 146/92 mmHg in females, whereas the mean values were 172/104 mmHg in males and 170/107 mmHg in females in the study by Fodor et al. Methodological differences may also account for differences in mean RSS values between the two studies. In the present study P-wave areas were

measured in relation to the P-P baseline as described under Methods. Fodor et al. measured P-wave areas in relation to the P-PR segment baseline. The two methods yield comparable results except in cases where there is a "wandering" baseline when the Fodor method yields lower values than the method used in the present study.

In the present study the male subjects had significantly higher values of RSS than did the female subjects. Fodor, J. et al. (1986) also observed a difference between males and females but this was not significant. Fodor, J. et al. found that the values for RSS were significantly greater in hypertensives than in normotensives of the same age and sex. The mean values for RSS in the borderline subjects included in the present study were higher than those found in the normotensives but the difference was not statistically significant. Male subjects with an exercise SBP equal to or greater than 200 mmHg had a significantly higher mean value for RSS than those whose exercise SBP was <180 mmHg. In the intermediate exercise SBP category (180-199 mmHg) the mean value of RSS was significantly higher than in the category of exercise SBP <180 mmHg. No association was observed between RSS values and exercise SBP in females.

7.2.2 Ventricular Electrocardiographic Indices

The electrocardiogram is the most specific non-invasive method of establishing the presence of left ventricular

hypertrophy. Electrocardiographic evidence of left ventricular hypertrophy is often present in the absence of overt clinical signs such as left ventricular heave and radiographic enlargement of the left ventricle (McIlroy and Sokolow, 1986). Left ventricular echocardiography is the most sensitive of the non-invasive methods for detecting left ventricular hypertrophy. It has been demonstrated that left ventricular thickness (the sum of the thickness of the ventricular septum and the posterior wall) correlates well with the spatial maximum QRS voltage ($r= 0.67$) and the sum of RV_5 and SV_1 ($r= 0.85$) (Toshima, H. et al., 1977).

Four ventricular electrocardiographic indices were used in the present study: the amplitude of the R wave in the unipolar limb Lead AVL; the amplitude of the R wave in either precordial lead V_5 or V_6 (whichever is the greatest); the amplitude of the R wave in standard limb Lead I plus the amplitude of the S wave in the standard limb Lead III (R_1+S_3); the amplitude of the R wave in either V_5 or V_6 (whichever is greatest) plus the amplitude of the S wave in V_1 .

The mean values for R_1+S_3 , RV_5/RV_6 and RV_5/RV_6+SV_1 for male subjects in the present study are similar to the values for these indices reported in a study of normal limits of QRS voltages in male subjects (Kilty, S.E. et al., 1985). In the present study there is a significant effect of age, in both male and female subjects, on the values for the ventricular electrocardiographic indices. Moreover, the mean values of the indices are

significantly greater in males than in females. These findings are in accord with reports in the literature which show that electrocardiographic left ventricular hypertrophy increases in prevalence with increasing age and that the prevalence in males is greater than in females (Kannel, W.B. 1983). Unpublished data from the Manitoba Follow-Up Study (1985) demonstrated a similar age effect in male subjects aged 30 to 60 years with systolic blood pressures in the range 140-159 mmHg. The frequency of left ventricular hypertrophy varied between 1.6 and 6.3 percent, the highest frequency being present in the oldest subjects. The prevalence in normotensive subjects of similar ages varied between 1 and 2.37 percent and was independent of age. The prevalence of abnormal values for the electrocardiographic indices were 1% for RAVL, 0.9% for R_1+S_3 , 6% for RV_5/RV_6 , and 12% for RV_5/RV_6+SV_1 in the present study.

A statistically significant association is demonstrated between resting SBP and RV_5 or RV_6+SV_1 , and between exercise SBP and RV_5/RV_6+SV_1 , and between exercise SBP and RV_5/RV_6 , which is independent of age and sex. Log-linear modelling demonstrated that LVH varied significantly with sex and exercise SBP groupings.

Voltage abnormalities are the earliest signs of LVH (Sokolow, M. and McIlroy, M.B., 1986). As LVH progresses other EKG changes (ST depression and T-wave abnormalities) appear. In selecting subjects for the present study those with the latter abnormalities were excluded and the examination for EKG evidence of

LVH was confined to measurement of QRS voltages in leads RAVL, V_1 , V_5 , and V_6 . It would be of some interest to study other groups of subjects which include individuals with ST segment and T-wave changes in order to determine if there is an association between such changes and the SBP response to exercise.

7.3 The Blood Pressure Response to Exercise and Electrocardiographic Indices of Atrial and Ventricular Abnormality

The log-linear statistical modelling analysis of the results of the present study indicates that the prevalence of certain atrial and ventricular electrocardiographic abnormalities is significantly influenced by the level of the exercise SBP irrespective of the resting blood pressure. These findings support the hypotheses, elaborated earlier in this thesis; namely, that the prevalence of atrial and ventricular abnormalities is greater among subjects who are normotensive at rest, and who have an exaggerated SBP response to exercise, than in subjects without an exaggerated response.

Analysis of the association between exercise SBP and the values of the various electrocardiographic indices, without dichotomization into normal and abnormal values based on normal limits published in the literature, indicates that an effect of exercise, independent of sex, age and resting SBP, was significant in the case of $PTFV_1$, RV_5/RV_6 and RV_5/RV_6+SV_1 but not for the other indices. The explanation for this difference is not

apparent from the data. It is possible that $PTFV_1$, RV_5/RV_6 and RV_5/RV_6+SV_1 are more sensitive than the other atrial and ventricular electrocardiographic indices to the changes in atrial and ventricular function which appear to be associated with blood pressure hyper-responsiveness on exercise. This in turn may reflect the possibility that the association between the values of $PTFV_1$, RV_5/RV_6 and RV_5/RV_6+SV_1 and exercise SBP is not obscured by the influence of other factors, such as age, sex and resting blood pressure, whereas the association is obscured in the case of the other atrial and ventricular indices.

The presence of significant independent effects of age and sex on several of the indices, and the presence of significant three-factor interactions suggests that in using the SBP response to exercise for predictive purposes the influence of age and sex should be taken into account. In evaluating the differences between males and females with respect to the association between exercise SBP and the values of certain electrocardiographic indices the effects of spurious influences should be considered. As noted earlier, the female subjects in the present study, on average, achieved lower levels of work intensity during exercise than did the male subjects, as reflected in MET levels although the average heart rate on exercise was the same in males and females. This is in accord with the observations of others that the heart rate of females is higher than that of males at a given level of work intensity (Astrand, I., 1965). The difference in

mean MET level between males and females in the present study is greater than that reported by Pollock in a study using a similar protocol and age group. In that report active men and women achieved 12.6 ± 1.2 METS and 11.0 ± 1.8 METS, respectively, while inactive men and women reached 10.3 ± 1.3 METS and 10.1 ± 1.5 METS (Pollock, M. L. et al., 1976; Pollock, M. L. et al., 1982). Since there is an association between MET level and exercise SBP, some women with electrocardiographic abnormalities may have been placed in an inappropriately low exercise SBP category because they did not exercise intensively enough to manifest their "hyper-responsiveness."

When the SBP response to exercise was expressed relative to the level of resting SBP (i.e., as the exercise/resting blood pressure ratio) the trends in the relationship between the EKG variables and the exercise/resting blood pressure ratio were similar to those observed with the absolute level of exercise SBP except that there was no independent effect of exercise on RV_5/RV_6+SV_1 . In the case of Macruz and $PTFV_1$, the relationships with the exercise/resting blood pressure ratio approached, but did not reach, significance.

The demonstration of an association between exercise SBP and electrocardiographic abnormalities, which is independent of the level of the resting blood pressure, is consistent with the contention that an excessive SBP response to exercise may be one of the early manifestations of the hypertensive state and may also

be a means of identifying individuals who are at increased risk for the development of the cardiac sequelae of hypertension. Convincing evidence on these questions must come from carefully controlled prospective studies of the clinical outcomes of normotensive and borderline hypertensive individuals who have an abnormal SBP response to exercise but are otherwise normal.

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TABLES 1 - 25

TABLE 1 Distribution of Study Subjects by Age and Sex

Age (years)	Males		Females		Total	
	N	%	N	%	N	%
20 - 29	21	9	17	9	38	8
30 - 39	74	30	51	28	125	29
40 - 49	72	29	39	21	111	26
50 - 59	57	24	48	27	105	25
60+	22	8	28	15	50	12
TOTAL	246	100	183	100	429	100

TABLE 2 Distribution of Subjects by Occupation and Sex

Occupation	Males		Females		Total	
	N	%	N	%	N	%
Managerial, administrative	128	52	18	10	146	34
Social and natural sciences, engineering, mathematics, religion, teaching	52	21	37	20	89	20
Medicine and health, sports, recreation	22	9	13	7	45	11
Clerical	5	2	18	10	23	5
Sales	12	5	5	3	17	4
Service	5	2	-	-	5	1
Housewife	-	-	90	49	90	21
Farming, forestry, logging	2	1	-	-	2	0
Processing	5	2	-	-	5	1
Transportation, equipment operators	5	2	-	-	5	1
Retired	10	4	2	1	12	2
TOTAL	246	100	183	100	429	100

TABLE 3 Distribution of Subjects by Marital Status and Sex

Marital status	Males		Females		Total	
	N	%	N	%	N	%
Married	203	83	144	79	347	81
Single	27	11	23	12	50	12
Widowed	8	3	9	5	17	4
Divorced	8	3	7	4	15	3
TOTAL	246	100	183	100	429	100

TABLE 4 Distribution of Subjects by Smoking Habit and Sex

Smoking Habit	Males		Females		Totals	
	N	%	N	%	N	%
Current	33	13	33	18	66	15
Past	103	42	52	28	155	36
Never	110	45	98	54	208	49
TOTAL	246	100	183	100	429	100

TABLE 5 Proportion of Subjects with Family History
of Disease by Sex

	Males		Females		Totals	
	N	%	N	%	N	%
	246	100	183	100	429	100
History in Family Member* Age \leq 55 years						
Myocardial infarction	39	16	34	17	73	17
Diabetes	24	10	17	9	41	9
Hypertension	31	13	38	21	69	16

*Family member is defined as mother or father, or siblings, or any combination thereof.

TABLE 6 Mean and Standard Deviation of Clinical Data by Sex

Clinical data N = 429	Males N = 246	Females N = 183
Age (yr)	48.6 ± 11.6	49.7 ± 13.6
Height (cms)	176.0 ± 4.5	162.1 ± 5.1
Weight (Kg)	81.3 ± 11.3	63.7 ± 12.1
Cholesterol (mg/dl)	228.0 ± 47.7	221.7 ± 46.9
Triglyceride (mg/dl)	133.7 ± 96.6	95.7 ± 51.9
Glucose (mg/dl)	90.3 ± 21.0	89.9 ± 15.0
Hemoglobin (g/dL)	15.5 ± 1.0	13.8 ± 1.1
FEV ₁ /FVC	78.5 ± 8.0	81.0 ± 8.1
BP supine syst (mmHg)	131.0 ± 18.0	126.7 ± 17.1
BP supine diast (mmHg)	83.2 ± 9.0	77.8 ± 9.2
BP sitting syst (mmHg)	127.5 ± 13.9	122.4 ± 14.8
BP sitting diast (mmHg)	81.5 ± 9.3	78.3 ± 8.3
BP max exercise syst (mmHg)	192.9 ± 22.0	172.9 ± 23.4
BP max exercise diast (mmHg)	90.1 ± 10.6	87.3 ± 11.0
BP recovery syst (mmHg)	181.6 ± 23.3	166.9 ± 22.7
BP recovery diast (mmHg)	86.5 ± 11.0	82.8 ± 10.5
HR rest (b/m)	72.1 ± 14.0	75.4 ± 13.8
HR exercise (b/m)	175.9 ± 15.3	171.8 ± 14.0
MET	11.4 ± 2.6	8.5 ± 1.9

TABLE 7 Mean and Standard Deviation of Electrocardiographic Variables by Sex

EKG Variables	Males	Females
P Lead II (sec)	.10 ± .01 (238)	.09 ± .01 (176)
PR segment (sec)	.06 ± .01 (238)	.06 ± .01 (176)
PR interval (sec)	.16 ± .01 (238)	.15 ± .01 (176)
Macruz Index	1.64 ± .47 (238)	1.48 ± .65 (176)
PTFV ₁ (mm sec)	-.030 ± .019 (158)	-.026 ± .016 (92)
RSS (mm ²)	.817 ± .385 (241)	.649 ± .256 (175)
RV ₅ /RV ₆ (mm)	16.84 ± 6.32 (244)	13.92 ± 4.92 (180)
R ₁ +S ₃ (mm)	9.17 ± 5.04 (243)	6.50 ± 3.00 (178)
RV ₅ /RV ₆ +SV ₁ (mm)	27.10 ± 8.88 (242)	22.93 ± 6.92 (179)
RAVL (mm)	3.35 ± 3.11 (238)	1.99 ± 1.93 (180)

The figures in parentheses represent the number of subjects in each category.

TABLE 8 Distribution of Male and Female Subjects by Exercise SBP and Resting SBP

EXERCISE SBP (mmHg)	RESTING SBP (mmHg)				Total
	<120	120-129	130-139	140-159	
	80*	57	26	11	174
<180	45.9**	32.7	14.9	6.3	
	59.7***	47.9	26.0	14.4	40.5
	37	40	36	20	133
180 - 199	27.8	30.0	27.0	15.0	
	27.6	33.6	36.0	26.3	31.0
	17	22	38	45	122
>200	13.9	18.0	31.1	36.8	
	12.6	18.4	38.0	59.2	28.4
TOTAL	134	119	100	76	429
	31.2	27.7	23.3	17.7	100

The figures in each cell are:

*FREQUENCY

**PERCENT OF ROW TOTAL

***PERCENT OF COLUMN TOTAL

TABLE 9 Distribution of Male Subjects by Exercise SBP and Resting SBP

EXERCISE SBP (mmHg)	RESTING SBP (mmHg)				Total
	<120	120-129	130-139	140-159	
	26*	19	12	7	64
<180	40.6**	29.6	18.7	10.9	
	41.2***	28.3	17.9	14.2	26.0
	23	28	22	11	84
180 - 199	27.3	33.3	26.1	13.1	
	36.5	41.7	32.8	22.4	34.1
	14	20	33	31	98
≥ 200	14.2	20.4	33.6	31.6	
	22.2	29.8	49.2	63.2	39.8
TOTAL	63	67	67	49	246
	25.6	27.2	27.2	19.9	100

The figures in each cell are:

*FREQUENCY

**PERCENT OF ROW TOTAL

***PERCENT OF COLUMN TOTAL

TABLE 10 Distribution of Female Subjects by Exercise SBP and Resting SBP

EXERCISE SBP (mmHg)	RESTING SBP (mmHg)				Total
	<120	120-129	130-139	140-159	
	54*	38	14	4	110
<180	49.0**	34.5	12.7	3.6	
	76.0***	73.0	42.4	14.81	60.1
	14	12	14	9	49
180-199	28.5	24.4	28.5	18.3	
	19.7	23.0	42.4	33.3	26.7
	3	2	5	14	24
≥200	12.5	8.3	20.8	58.3	
	4.2	3.8	15.1	51.8	13.1
TOTAL	71	52	33	27	183
	38.8	28.4	18.0	14.7	100

The figures in each cell are:

*FREQUENCY

**PERCENT OF ROW TOTAL

***PERCENT OF COLUMN TOTAL

TABLE 11 Macruz Index According to Resting and Exercising SBP and Sex

EXERCISE SBP (mmHg)		MACRUZ INDEX (mean ± sd)				Totals
		<120	120-129	130-139	140-159	
Males	<180	1.70 ± .60	1.40 ± .42	1.57 ± .35	1.38 ± .25	1.56 ± .49
	180-199	1.52 ± .44	1.65 ± .48	1.64 ± .34	1.73 ± .58	1.62 ± .45
	≥200	1.65 ± .21	1.67 ± .45	1.68 ± .49	1.78 ± .52	1.70 ± .46
	Total	1.62 ± .47	1.60 ± .46	1.65 ± .42	1.72 ± .52	1.64 ± .47
Females	<180	1.41 ± .43	1.36 ± .28	1.27 ± .20	1.31 ± .22	1.36 ± .35
	180-199	1.61 ± .41	1.83 ± .82	1.37 ± .22	1.50 ± .19	1.57 ± .51
	≥200	1.43 ± .51	1.58 ± *	1.73 ± .49	2.04 ± 1.8	1.86 ± 1.4
	Total	1.43 ± .43	1.48 ± .50	1.38 ± .30	1.75 ± .33	1.48 ± .65
Total	<180	1.50 ± .51	1.37 ± .37	1.40 ± .30	1.35 ± .23	1.43 ± .42
	180-199	1.56 ± .42	1.71 ± .60	1.54 ± .32	1.63 ± .46	1.61 ± .47
	≥200	1.61 ± .27	1.66 ± .44	1.69 ± .49	1.86 ± .97	1.73 ± .73
	Total	1.53 ± .46	1.54 ± .48	1.56 ± .41	1.73 ± .88	1.57 ± .55

*This mean was based on only 2 subjects.

TABLE 12 PTFV₁ by Resting and Exercising SBP and Sex*

		PTFV ₁ (mean ± sd)				
		EXERCISE SBP (mmHg)	RESTING SBP (mmHg)			Totals
		<120	120-129	130-139	140-159	
Males	<180	-.024 ± .010	-.024 ± .008	-.019 ± .016	-.024 ± .001	-.023 ± .009
	180-199	-.023 ± .008	-.025 ± .015	-.024 ± .011	-.031 ± .012	-.025 ± .012
	≥ 200	-.038 ± .013	-.030 ± .017	-.033 ± .017	-.041 ± .020	-.036 ± .011
	Total	-.027 ± .012	-.026 ± .014	-.029 ± .016	-.037 ± .019	-.030 ± .016
Females	<180	-.019 ± .009	-.024 ± .013	-.025 ± .007	-.026 ± .020	-.022 ± .010
	180-199	-.028 ± .013	-.019 ± .009	-.017 ± .008	-.039 ± .019	-.026 ± .015
	≥ 200	-.033 ± .031	-.027 ± .002	-.032 ± .006	-.033 ± .019	-.032 ± .016
	Total	-.023 ± .012	-.023 ± .012	-.024 ± .009	-.034 ± .019	-.026 ± .014
Total	<180	-.022 ± .009	-.024 ± .011	-.023 ± .009	-.025 ± .010	-.023 ± .010
	180-199	-.025 ± .011	-.024 ± .014	-.022 ± .011	-.035 ± .016	-.026 ± .013
	≥ 200	-.027 ± .015	-.029 ± .016	-.033 ± .016	-.038 ± .020	-.035 ± .018
	Total	-.025 ± .012	-.025 ± .013	-.027 ± .014	-.036 ± .019	-.028 ± .015

* Subjects with no measureable PTFV₁ excluded.

TABLE 13 RSS According to Resting and Exercising SBP and Sex

EXERCISE SBP (mmHg)		RSS (mean ± sd)				Totals
		<120	120-129	130-139	140-159	
Male	<180	.688 ± .31	.587 ± .17	.800 ± .41	.779 ± .26	.689 ± .30
	180-199	.881 ± .56	.823 ± .30	.811 ± .41	.746 ± .26	.825 ± .40
	≥ 200	.919 ± .45	.797 ± .32	.873 ± .42	.975 ± .38	.897 ± .39
	Total	.807 ± .45	.746 ± .29	.840 ± .41	.894 ± .35	.817 ± .38
Female	<180	.573 ± .19	.701 ± .30	.648 ± .31	.844 ± .19	.639 ± .26
	180-199	.607 ± .19	.729 ± .31	.597 ± .17	.843 ± .33	.676 ± .26
	≥ 200	.766 ± .34	.630 ± .10	.606 ± .08	.624 ± .25	.639 ± .22
	Total	.589 ± .20	.705 ± .20	.619 ± .22	.725 ± .28	.649 ± .26
Total	<180	.631 ± .24	.660 ± .27	.724 ± .37	.803 ± .23	.658 ± .27
	180-199	.775 ± .47	.795 ± .24	.731 ± .34	.787 ± .29	.771 ± .36
	≥ 200	.890 ± .42	.781 ± .31	.838 ± .40	.863 ± .38	.844 ± .38
	Total	.693 ± .36	.728 ± .29	.771 ± .37	.835 ± .34	.746 ± .34

TABLE 14 RAWL According to Resting and Exercising SBP and Sex

EXERCISE SBP (mmHg)	RAWL (mean ± sd)				Totals
	≤120	120-129	RESTING SBP (mmHg) 130-139	140-159	
Males <180	3.44 ± 3.14	4.42 ± 3.17	5.51 ± 4.76	1.82 ± 1.84	3.83 ± 3.51
180-199	2.40 ± 2.12	2.48 ± 2.28	3.73 ± 3.30	3.93 ± 2.32	2.98 ± 2.62
≥ 200	3.00 ± 2.84	2.51 ± 2.03	3.36 ± 3.37	4.18 ± 3.67	3.37 ± 3.20
Total	2.96 ± 2.81	3.04 ± 2.62	3.78 ± 3.63	3.76 ± 3.20	3.35 ± 3.11
Females <180	1.26 ± 1.21	2.45 ± 2.07	3.32 ± 3.45	1.91 ± 2.00	1.97 ± 2.00
180-199	2.70 ± 2.46	1.22 ± 0.83	2.01 ± 1.67	1.82 ± 1.72	2.00 ± 1.80
≥ 200	1.08 ± 0.38	1.12 ± 0.17	1.50 ± 0.96	2.57 ± 1.70	2.02 ± 1.40
Total	1.54 ± 1.60	2.14 ± 1.91	2.48 ± 2.56	2.22 ± 1.70	1.99 ± 1.93
Total <180	2.02 ± 2.44	3.12 ± 2.64	4.11 ± 4.08	1.85 ± 1.78	2.68 ± 2.80
180-199	2.51 ± 2.22	2.14 ± 2.06	3.10 ± 2.90	2.98 ± 2.29	2.63 ± 2.40
≥ 200	2.66 ± 2.67	2.38 ± 1.98	3.10 ± 3.39	3.67 ± 3.24	3.10 ± 3.00
Total	2.24 ± 2.41	2.66 ± 2.37	3.35 ± 3.39	3.22 ± 2.87	2.67 ± 2.52

TABLE 15 RV_5/RV_6 According to Resting and Exercising SBP and Sex

EXERCISE SBP (mmHg)		RV_5/RV_6 (mean \pm sd)				Totals
		≤ 120	120-129	RESTING SBP (mmHg) 130-139 140-159		
Male	<180	12.97 \pm 6.11	13.11 \pm 5.81	13.95 \pm 4.73	14.70 \pm 3.22	13.38 \pm 5.46
	180-199	18.63 \pm 6.23	18.36 \pm 6.46	16.84 \pm 5.95	15.99 \pm 5.68	17.72 \pm 6.16
	≥ 200	17.60 \pm 8.47	18.25 \pm 5.44	18.28 \pm 5.55	18.77 \pm 6.48	18.33 \pm 6.28
	Total	16.07 \pm 7.13	16.83 \pm 6.33	17.10 \pm 5.62	17.54 \pm 6.16	16.84 \pm 6.33
Female	<180	13.60 \pm 4.11	13.62 \pm 5.62	14.53 \pm 3.99	13.66 \pm 9.90	13.43 \pm 4.72
	180-199	11.50 \pm 3.47	14.79 \pm 3.93	14.87 \pm 5.42	16.11 \pm 3.31	14.11 \pm 4.41
	≥ 200	16.25 \pm 2.81	8.75 \pm 0.35	19.05 \pm 6.93	13.11 \pm 6.47	14.43 \pm 6.44
	Total	13.30 \pm 4.04	13.70 \pm 5.24	15.36 \pm 5.19	14.26 \pm 5.90	13.92 \pm 4.92
Total	<180	13.39 \pm 4.81	13.45 \pm 5.62	14.28 \pm 4.21	14.40 \pm 5.32	13.60 \pm 5.01
	180-199	15.93 \pm 6.33	17.29 \pm 6.04	16.07 \pm 5.72	16.04 \pm 4.61	16.39 \pm 5.81
	≥ 200	17.39 \pm 7.72	17.36 \pm 5.81	18.30 \pm 5.63	17.06 \pm 6.92	17.58 \pm 6.42
	Total	14.61 \pm 5.86	15.46 \pm 6.07	16.51 \pm 5.56	16.42 \pm 6.17	15.60 \pm 5.91

TABLE 16 $R_1 + S_3$ According to Resting and Exercising SBP and Sex

EXERCISE SBP (mmHg)		$R_1 + S_3$ (mean \pm sd)				Totals
		<120	120-129	RESTING SBP (mmHg)		
				130-139	140-159	
Males	<180	8.36 \pm 5.05	9.63 \pm 5.51	10.43 \pm 7.75	6.17 \pm 1.99	8.86 \pm 5.52
	180-199	7.37 \pm 3.71	8.50 \pm 3.55	10.88 \pm 6.50	9.27 \pm 3.54	8.92 \pm 4.61
	≥ 200	8.98 \pm 4.31	8.60 \pm 3.20	8.67 \pm 5.34	11.55 \pm 5.60	9.59 \pm 5.04
	Total	8.14 \pm 4.41	8.85 \pm 4.09	9.70 \pm 6.17	10.24 \pm 5.13	9.17 \pm 5.02
Females	<180	5.28 \pm 2.51	7.18 \pm 3.24	8.19 \pm 3.97	6.66 \pm 0.28	6.36 \pm 3.13
	180-199	7.05 \pm 2.94	5.43 \pm 2.36	6.07 \pm 2.88	9.09 \pm 3.17	6.71 \pm 3.03
	≥ 200	5.50 \pm 0.50	5.87 \pm 0.17	7.50 \pm 2.00	6.76 \pm 2.77	6.68 \pm 2.31
	Total	5.65 \pm 2.62	6.72 \pm 3.07	7.22 \pm 3.37	7.53 \pm 2.89	6.50 \pm 3.02
Total	<180	6.30 \pm 3.81	7.99 \pm 4.22	9.18 \pm 5.91	6.32 \pm 1.63	7.28 \pm 4.32
	180-199	7.25 \pm 3.43	7.55 \pm 3.53	9.10 \pm 5.83	9.18 \pm 3.32	8.12 \pm 4.21
	≥ 200	8.35 \pm 4.16	8.36 \pm 3.21	8.52 \pm 5.01	10.10 \pm 5.31	9.03 \pm 4.70
	Total	6.82 \pm 3.78	7.91 \pm 3.81	8.89 \pm 5.52	9.34 \pm 4.66	8.04 \pm 4.40

TABLE 17 RV_5/RV_6+SV_1 According to Resting and Exercising SBP and Sex

	EXERCISE SBP (mmHg)	RV_5/RV_6+SV_1 (mean \pm sd)				Totals
		<120	120-129	RESTING SBP (mmHg) 130-139	140-159	
Males	<180	20.89 \pm 7.40	20.88 \pm 7.01	22.95 \pm 6.70	33.14 \pm 8.72	22.59 \pm 8.12
	180-199	28.68 \pm 9.26	29.46 \pm 7.73	28.31 \pm 7.63	25.54 \pm 9.02	28.43 \pm 8.21
	\geq 200	26.39 \pm 12.72	28.70 \pm 7.08	29.50 \pm 7.07	29.39 \pm 9.99	28.85 \pm 8.94
	Total	24.95 \pm 9.95	26.82 \pm 8.15	28.07 \pm 7.46	29.05 \pm 9.69	27.10 \pm 8.85
Females	<180	22.42 \pm 5.42	22.60 \pm 8.23	24.87 \pm 7.02	23.66 \pm 9.56	22.84 \pm 6.85
	180-199	19.12 \pm 5.23	23.14 \pm 5.25	24.60 \pm 7.41	26.50 \pm 7.16	23.03 \pm 6.63
	\geq 200	24.58 \pm 5.13	19.12 \pm 1.59	29.40 \pm 9.09	21.01 \pm 8.17	23.14 \pm 8.21
	Total	21.85 \pm 5.49	22.59 \pm 7.46	25.44 \pm 7.45	23.31 \pm 8.05	22.93 \pm 6.93
Total	<180	21.90 \pm 6.12	22.02 \pm 7.83	24.07 \pm 6.83	30.30 \pm 9.51	22.75 \pm 7.23
	180-199	25.06 \pm 9.16	27.57 \pm 7.64	26.80 \pm 7.62	25.97 \pm 8.02	26.44 \pm 8.12
	\geq 200	26.07 \pm 11.6	27.88 \pm 7.31	29.40 \pm 7.21	26.86 \pm 10.10	27.75 \pm 9.01
	Total	23.33 \pm 8.06	24.97 \pm 8.11	27.17 \pm 7.52	27.18 \pm 9.51	25.33 \pm 8.32

TABLE 18 Relationship Between EKG Variables (mean \pm sd) and Age and Sex

EKG Variables	Sex*	AGE (Years)					Totals	p**
		20-29	30-39	40-49	50-59	60+		
Macruz	M	1.60 \pm .48	1.61 \pm .38	1.57 \pm .40	1.75 \pm .55	1.76 \pm .64	1.64 \pm .47	S(0.001)
	F	1.34 \pm .35	1.52 \pm .55	1.45 \pm .41	1.59 \pm .99	1.37 \pm .28	1.48 \pm .65	
	T	1.48 \pm .44	1.57 \pm .40	1.53 \pm .40	1.68 \pm .80	1.54 \pm .51	1.50 \pm .55	
PTFV ₁ (mm Sec)	M	-.020 \pm .009 10/21***	-.025 \pm .016 40/74	-.021 \pm .008 46/72	-.027 \pm .010 45/57	-.024 \pm .010 16/22	-.025 \pm .016 158/246	A(0.0001)†
	F	-.019 \pm .012 4/17	-.019 \pm .009 18/51	-.018 \pm .009 18/39	-.022 \pm .013 30/48	-.026 \pm .011 22/28	-.022 \pm .014 92/183	
	T	-.020 \pm .009 14/38	-.024 \pm .014 58/125	-.020 \pm .009 64/111	-.025 \pm .014 75/105	-.026 \pm .011 38/50	-.023 \pm .015 250/429	
RSS	M	-.841 \pm .34	-.698 \pm .35	-.642 \pm .28	-.656 \pm .33	-.603 \pm .20	-.676 \pm .31	S(0.0001)
	F	-.522 \pm .15	-.671 \pm .26	-.504 \pm .19	-.512 \pm .19	-.573 \pm .20	-.538 \pm .20	
	T	-.698 \pm .32	-.645 \pm .32	-.597 \pm .26	-.591 \pm .29	-.586 \pm .20	-.607 \pm .27	

Contd.

TABLE 18 (Contd.) Relationship Between EKG Variables (mean \pm sd) and Age and Sex

EKG Variable	Sex	AGE (Years)					Totals	p**
		20-29	30-39	40-49	50-59	60+		
RAVL (mm)	M	1.92 \pm 1.6	2.45 \pm 2.5	3.50 \pm 3.3	4.25 \pm 2.8	4.92 \pm 4.2	3.35 \pm 3.11	S(0.0001)
	F	1.36 \pm 1.3	1.62 \pm 1.6	1.79 \pm 2.1	2.20 \pm 2.0	2.92 \pm 2.0	1.99 \pm 1.93	A(0.0001)
	T	1.65 \pm 1.6	2.12 \pm 2.2	2.90 \pm 3.0	3.39 \pm 2.7	3.80 \pm 3.3	2.67 \pm 2.52	
RV ₅ /RV ₆ (mm)	M	21.26 \pm 5.3	17.69 \pm 6.1	15.50 \pm 6.3	16.60 \pm 6.4	14.70 \pm 5.1	16.84 \pm 6.32	S(0.0001)
	F	14.44 \pm 2.9	14.19 \pm 5.6	13.77 \pm 4.8	14.11 \pm 4.6	13.05 \pm 5.3	13.92 \pm 4.92	A(0.01)
	T	18.12 \pm 5.5	16.29 \pm 6.1	14.89 \pm 5.9	15.48 \pm 5.8	13.78 \pm 5.2	15.60 \pm 5.94	
R ₁ +S ₃ (mm)	M	7.16 \pm 2.7	7.72 \pm 4.2	9.43 \pm 5.4	10.45 \pm 4.5	11.63 \pm 7.1	9.17 \pm 5.04	S(0.0001)
	F	6.16 \pm 2.7	5.72 \pm 2.7	6.35 \pm 2.7	6.67 \pm 3.1	8.03 \pm 3.2	6.50 \pm 3.00	A(0.0001)
	T	6.70 \pm 2.7	6.92 \pm 3.8	8.33 \pm 4.8	8.76 \pm 4.4	9.65 \pm 5.5	8.04 \pm 4.49	
RV ₅ /RV ₆ + SV ₁ (mm)	M	32.30 \pm 8.3	28.62 \pm 8.8	25.12 \pm 8.6	26.72 \pm 9.1	24.12 \pm 7.1	27.10 \pm 8.88	S(0.0001)
	F	24.33 \pm 5.3	23.63 \pm 8.4	22.44 \pm 6.7	22.70 \pm 5.6	21.89 \pm 7.1	22.93 \pm 6.92	A(0.007)
	T	28.64 \pm 8.1	26.62 \pm 9.0	24.28 \pm 8.0	24.89 \pm 7.8	22.86 \pm 7.1	25.33 \pm 8.35	

* M = Male

F = Female

T = Total

** P = the figures in parentheses are the level of significance (P values) for tests of the effects of sex (S) and age (A) from ANOVA models. If not mentioned then effect is not significant at $p < .05$.

*** Not all subjects had a measurable PTFV₁. The number of subjects with measurable PTFV₁ over the total number of subjects is shown for each category.

† = Level of significance based on presence/absence of PTFV₁ analyzed in a log-linear model.

TABLE 19 Relationship Between EKG Variables (mean ± sd) and Resting SBP and Sex

Dependent Variable	Sex*	RESTING SBP (mmHg)				Totals	P**
		120	120-129	130-139	140-149		
Macruz	M	1.62 ± .479	1.60 ± .468	1.65 ± .425	1.72 ± .521	1.64 ± .47	S(0.01)
	F	1.44 ± .439	1.48 ± .503	1.38 ± .302	1.75 ± 1.34	1.48 ± .65	
	T	1.53 ± .465	1.54 ± .485	1.56 ± .408	1.73 ± .889	1.57 ± .55	
PTFV ₁ (mm sec)	M	-.023 ± .010 35/63***	-.022 ± .012 45/67	-.024 ± .013 43/67	-.031 ± .015 35/49	-.025 ± .016 158/246	A(0.0001)†
	F	-.019 ± .010 29/71	-.019 ± .010 22/52	-.020 ± .007 19/33	-.028 ± .015 22/27	-.022 ± .014 92/183	
	T	.021 ± .010 64/134	.021 ± .011 67/119	.022 ± .011 62/100	.030 ± .015 57/76	.023 ± .015 250/429	
RSS ₂ (mm ²)	M	.688 ± .37	.618 ± .24	.696 ± .34	.740 ± .29	.676 ± .31	S(0.001)
	F	.487 ± .16	.585 ± .25	.512 ± .19	.603 ± .23	.538 ± .20	
	T	.574 ± .30	.574 ± .30	.603 ± .24	.639 ± .31	.607 ± .27	

Contd.

TABLE 19 (Contd.) Relationship Between EKG Variables (mean \pm sd) and Resting SBP and Sex

Dependent Variable	Sex*	RESTING SBP (mmHg)				Totals	p**
		120	120-129	130-139	140-149		
RAVL (mm)	M	2.96 \pm 2.86	3.04 \pm 2.61	3.78 \pm 3.68	3.76 \pm 3.23	3.35 \pm 3.11	S(0.0001)
	F	1.54 \pm 1.60	2.14 \pm 1.91	2.48 \pm 2.56	2.22 \pm 1.70	1.99 \pm 1.93	A(0.0009)
	T	2.24 \pm 2.41	2.66 \pm 2.37	3.35 \pm 3.39	3.22 \pm 2.87	2.67 \pm 2.52	
RV ₅ /RV ₆ (mm)	M	16.07 \pm 7.13	16.83 \pm 6.35	17.08 \pm 5.69	17.54 \pm 6.07	16.84 \pm 6.32	S(0.0001)
	F	13.30 \pm 4.04	13.70 \pm 5.24	15.36 \pm 5.19	14.26 \pm 5.90	13.92 \pm 4.92	A(0.01)
	T	14.61 \pm 5.86	15.46 \pm 6.07	16.51 \pm 5.56	16.42 \pm 6.17	15.60 \pm 5.94	
R ₁ +S ₃ (mm) ³	M	8.14 \pm 4.41	8.85 \pm 4.09	9.70 \pm 6.17	10.24 \pm 5.13	9.17 \pm 5.04	S(0.0001)
	F	5.65 \pm 2.62	6.72 \pm 3.07	7.22 \pm 3.37	7.53 \pm 2.89	6.50 \pm 3.00	A(0.002)
	T	6.82 \pm 3.78	7.91 \pm 3.81	8.89 \pm 5.52	9.34 \pm 4.66	8.04 \pm 4.49	
RV ₅ /RV ₆ +SV ₁ (mm)	M	24.95 \pm 9.95	26.82 \pm 8.15	28.07 \pm 7.46	29.05 \pm 9.69	27.10 \pm 8.88	S(0.0004)
	F	21.85 \pm 5.49	22.59 \pm 7.46	25.44 \pm 7.45	23.31 \pm 8.05	22.93 \pm 6.92	A(0.0011)
	T	23.33 \pm 8.06	24.97 \pm 8.11	27.17 \pm 7.52	27.18 \pm 9.51	25.33 \pm 8.35	R(0.003)

* M = Male

F = Female

T = Total

** P = The figures in parentheses are the level of significance (P values) of the effect of Sex (S), Age (A) and resting blood pressure (R) from ANOVA models. If not mentioned then effect is not significant at $p < 0.05$

*** See legend Table 11.

† = Level of significance based on presence/absence of PTFV₁ analyzed in a log-linear model.

TABLE 20 Relationship Between EKG Variables (mean \pm sd) and Exercise SBP and Sex

EKG Variable	Sex*	EXERCISE SBP (mmHg)				Totals	p**
		180	180-199	200			
Macruz	M	1.56 \pm .49	1.62 \pm .45	1.70 \pm .46	1.64 \pm .47	SAE(0.001)	
	F	1.36 \pm .35	1.57 \pm .52	1.86 \pm 1.40	1.48 \pm .65		
	T	1.43 \pm .42	1.61 \pm .47	1.73 \pm .73	1.57 \pm .55		
PTFV ₁ (mm ² Sec)	M	-.019 \pm .007 37/64***	-.021 \pm .010 48/84	-.030 \pm .015 73/98	-.025 \pm .016 158/246	E(0.01) A(0.0001)†	
	F	-.018 \pm .009 43/110	-.022 \pm .012 27/49	-.027 \pm .013 22/24	-.022 \pm .014 92/183		
	T	-.019 \pm .008 80/174	-.021 \pm .011 75/133	-.029 \pm .015 95/122	-.023 \pm .015 250/429		
RSS ₂ (mm ²)	M	.571 \pm .25	.683 \pm .33	.743 \pm .32	.676 \pm .31	S(0.0003)	
	F	.529 \pm .21	.559 \pm .21	.534 \pm .18	.538 \pm .20		
	T	.545 \pm .23	.638 \pm .31	.701 \pm .31	.607 \pm .27		

Contd.

TABLE 20 (Contd.) Relationship Between EKG Variables (mean \pm sd) and Exercise SBP and Sex

EKG Variable	Sex*	EXERCISE SBP (mmHg)			Totals	P**
		180	180-199	200		
RAVL (mm)	M	3.38 \pm 3.5	2.98 \pm 2.6	3.37 \pm 3.2	3.35 \pm 3.11	S(0.0001)
	F	1.97 \pm 2.0	2.00 \pm 1.8	2.02 \pm 1.4	1.99 \pm 1.93	A(0.002)
	T	2.68 \pm 2.8	2.63 \pm 2.4	3.10 \pm 3.0	2.67 \pm 2.52	
RV ₅ /RV ₆ (mm)	M	13.38 \pm 5.4	17.72 \pm 6.1	18.83 \pm 6.2	16.84 \pm 6.32	S(0.003)
	F	13.43 \pm 4.7	14.11 \pm 4.4	14.43 \pm 6.4	13.92 \pm 4.92	A(0.03)
	T	13.60 \pm 5.0	16.39 \pm 5.8	17.58 \pm 6.4	15.60 \pm 5.94	E(0.01)
R ₁ +S ₃ (mm)	M	8.86 \pm 5.5	8.92 \pm 4.6	9.59 \pm 5.0	9.17 \pm 5.04	S(0.0001)
	F	6.36 \pm 3.1	6.71 \pm 3.0	6.68 \pm 2.3	6.50 \pm 3.00	A(0.005)
	T	7.28 \pm 4.3	8.12 \pm 4.2	9.03 \pm 4.7	8.04 \pm 4.49	
RV ₅ /RV ₆ + SV ₁ (mm)	M	22.59 \pm 8.1	28.43 \pm 8.2	28.85 \pm 8.9	27.10 \pm 8.88	S(0.002)
	F	22.84 \pm 6.8	23.03 \pm 6.6	23.14 \pm 8.2	22.93 \pm 6.92	A(0.01)
	T	22.75 \pm 7.2	26.44 \pm 8.1	27.75 \pm 9.0	25.33 \pm 8.35	E(0.0009)

* M = Male

F = Female

T = Total

** P = The figures in parentheses are the level of significance (P value) of Sex (S); Age (A); exercise blood pressure (E); 2 factor interaction (sex and exercise blood pressure) (SE); 3 factor interaction (sex, age and exercise blood pressure) (SAE) from ANOVA models. If not mentioned then effect is not significant at $p < 0.05$.

*** See legend Table 11.

† = Level of significance based on presence/absence of PTFV₁ analyzed in a log-linear model.

TABLE 21 Linear Regression Coefficients (Correlation) for
EKG Variables and Exercise SBP

EKG Variable	Sex*	Regression Coefficient	Correlation Coefficient	p**
Macruz	M	0.003	0.14	0.03
	F	0.007	0.22	0.002
PTFV ₁	M	0.0002	0.37	0.0001
	F	0.0001	0.26	0.001
RSS	M	0.003	0.23	0.0004
	F	0.0005	0.06	0.433
RAVL	M	-0.006	0.04	0.534
	F	0.002	0.02	0.791
RV ₅ /RV ₆	M	0.091	0.32	0.0001
	F	0.023	0.11	0.136
R ₁ +S ₃	M	0.017	0.07	0.250
	F	0.014	0.11	0.148
RV ₅ /RV ₆ +SV ₁	M	0.128	0.32	0.0001
	F	0.027	0.09	0.221

*M = Male

F = Female

**p = The figures in the column are the level of significance (p values) for the test of zero correlation between the EKG variables and the exercise blood pressure.

TABLE 22 Relationship Between EKG Variables (mean ± sd) and Exercise/Resting SBP Ratio and Sex

EKG Variables	Sex*	SBP RATIO				Totals	p**
		<135	135-146	147-158	159-211		
Macruz	M	1.61 ± .54	1.59 ± .45	1.66 ± .47	1.67 ± .45	1.64 ± .47	
	F	1.28 ± .25	1.57 ± .95	1.61 ± .56	1.58 ± .55	1.48 ± .65	
	T	1.41 ± .41	1.58 ± .74	1.64 ± .51	1.65 ± .46	1.57 ± .55	
PTFV ₁ (mm sec)	M	-.024 ± .010 23/43***	-.027 ± .015 37/56	-.033 ± .019 46/64	-.032 ± .015 52/83	-.030 ± .015 158/246	
	F	-.026 ± .013 30/64	-.025 ± .016 26/53	-.023 ± .014 21/41	-.030 ± .011 15/25	-.026 ± .014 92/183	
	T	-.025 ± .012 53/107	-.026 ± .015 73/109	-.030 ± .018 67/105	-.031 ± .015 67/108	-.028 ± .015 250/429	
RSS ₂ (mm ²)	M	.760 ± .39	.747 ± .31	.874 ± .39	.851 ± .40	.817 ± .38	
	F	.684 ± .26	.640 ± .29	.623 ± .23	.625 ± .18	.645 ± .25	S(0.02)
	T	.716 ± .32	.695 ± .31	.777 ± .36	.796 ± .37	.766 ± .34	

Contd.

TABLE 22 (Contd.) Relationship Between EKG Variables (mean \pm sd) and Exercise/Resting SBP Ratio and Sex

EKG Variables	Sex*	SBP RATIO				Totals	P**
		< 135	135-146	147-158	159-211		
RAVL (mm)	M	4.66 \pm .374	3.78 \pm 3.17	3.21 \pm 3.18	2.55 \pm 2.41	3.35 \pm 3.11	S(0.0001)
	F	2.22 \pm 2.18	1.98 \pm 2.00	1.75 \pm 1.45	1.77 \pm 1.83	1.99 \pm 1.93	A(0.001)
	T	3.19 \pm 3.12	2.92 \pm 2.82	2.67 \pm 2.75	2.37 \pm 2.31	2.67 \pm 2.52	
RV ₅ /RV ₆ (mm)	M	14.17 \pm 5.00	15.49 \pm 6.18	17.72 \pm 6.31	18.40 \pm 6.50	16.48 \pm 6.32	S(0.0006)
	F	13.60 \pm 4.41	14.83 \pm 6.04	13.55 \pm 4.48	13.43 \pm 4.06	13.92 \pm 4.92	E [†] (0.006)
	T	13.80 \pm 4.64	15.16 \pm 6.09	16.12 \pm 6.01	17.25 \pm 6.36	15.60 \pm 5.94	
R ₁ +S ₃ (mm)	M	10.12 \pm 6.17	9.99 \pm 5.60	9.46 \pm 5.13	7.92 \pm 3.61	9.17 \pm 5.04	S(0.0001)
	F	7.21 \pm 3.11	6.55 \pm 3.17	5.28 \pm 2.58	6.62 \pm 2.49	6.50 \pm 3.00	A(0.002)
	T	8.38 \pm 4.78	8.33 \pm 4.89	7.84 \pm 4.77	7.62 \pm 3.42	8.04 \pm 4.49	
RV ₅ /RV ₆ +SV ₁ (mm)	M	24.64 \pm 8.75	25.10 \pm 8.48	28.30 \pm 8.68	28.74 \pm 8.97	27.10 \pm 8.88	S(0.002)
	F	23.11 \pm 6.60	23.72 \pm 8.49	21.77 \pm 6.02	22.67 \pm 5.26	22.93 \pm 6.92	A(0.001)
	T	23.72 \pm 7.52	24.43 \pm 8.47	25.79 \pm 8.37	27.32 \pm 8.63	25.33 \pm 8.35	

* M = males

F = females

T = total

**P = The figures in parentheses are the level of significance (P value) of sex (S), age (A) exercise/
resting blood pressure ratio (E[†]); from ANOVA models. If not mentioned, then effect is not significant at
p < 0.05.

*** See legend Table 12.

TABLE 23 Results of Log Linear Modelling Relating the Dichotomization of PTFV₁, Macruz and LVH to Age (5 categories), Sex, Resting SBP (4 categories) and Exercise SBP (3 categories)

Dependent Variable	Final Model	Likelihood Ratio X ² (df)	Level of Significance For Test of Fit
PTFV ₁ +	Definition (1) AR, RE, SA (<0.05) PA (<0.0001) PSE (<0.0001)	188 (195)	0.61
	Definition (2) AR, RE, SA, SE (<0.05) PA (<0.05) PE (<0.0001)	171 (198)	0.92
Macruz	AR, RE, SA, SE (<0.05) MSR (<0.03)	206 (196)	0.27
LVH	AR, RE, SA, SE (<0.05) LS (<0.0002), LE (<0.01)	191 (201)	0.67

+ = Two definitions of PTFV₁ categories:

(1) P=PTFV₁ present/absent

(2) P=PTFV₁ abnormal <-0.03/normal ≥-0.03

M = normal/abnormal (>1.6) Macruz

L = LVH presence or absence as defined by abnormal values in 1 or more of the variables

RV₅/RV₆, RAVL, R₁+S₃ and

RV₅/RV₆+SV₁

A = 5 age categories (20-29, 30-39, 40-49, 50-59, 60+ years)

S = 2 sex categories (males, females)

R = 4 resting blood pressure categories (<120, 120-129, 130-139, 140-159 mmHg)

E = 3 exercise blood pressure categories (<180, 180-199, ≥200 mmHg)

TABLE 24 Prevalence Rate (%) of Abnormal Electrocardiographic Indices

Electro- cardio- graphic Indices	RESTING SBP (mmHg)	Sex*	EXERCISE SBP		P***
			(mmHg) 200	(mmHg) 200	
Presence					
LVH	<140	M	19.2(130)**	32.8(67)	<0.05
		F	4.8(146)	20.0(10)	<0.05
	140-159	M	16.6(18)	29.0(31)	
		F	15.3(13)	7.1(14)	
Macruz >1.6					
	<140	M	49.2(130)	53.7(67)	
		F	33.5(146)	40.0(10)	
	140-159	M	55.5(18)	63.3(30)	
		F	23.0(13)	64.2(14)	<0.05
PTFV ₁ <-0.03					
	140	M	16.9(130)	37.3(67)	<0.01
		F	8.2(146)	40.0(10)	<0.01
	140-159	M	16.6(18)	60.0(30)	<0.01
		F	46.1(13)	43.0(14)	

* M = male

F = female

** Figures in parentheses are numbers of subjects in the category.

*** P = The figures are the level of significance (P-value) determined by chi-square test for each row of table. When numbers in body of table were small (< 5) Fisher's exact test for 2 by 2 tables was used.

TABLE 25 Results of Log-Linear Modelling Relating the Dichotomization of PTFV₁, Macruz and LVH to Age (5 categories), Sex, Resting SBP (2 categories), and Exercise SBP (2 categories)

Dependent Variable	Final Model*	Likelihood Ratio (x ² df)	Level of Significance for the Test of Fit
PTFV ₁	AR, SA, SRE (<0.05) PE (<0.0001) PR (<0.009)	50 (57)	0.74
Macruz	AR, SRE (<0.05) MS (<0.0001) ME (<0.03)	66 (61)	0.32
LVH	AR, SRE (<0.05) LS (<0.0001) LE (<0.02)	70 (61)	0.20

*Definitions

P = Normal/abnormal (<-0.03 mm sec) PTFV₁.

M = Normal/abnormal (>1.6) Macruz.

L = LVH presence or absence as defined by abnormal values in 1 or more of the variables RAVL, RV₅/RV₆, R₁+S₃ and RV₅/RV₆+SV₁.

A = 5 age categories (20-29, 30-39, 40-49, 50-59, 60+ years).

S = 2 sex categories (males, females).

R = 2 resting BP categories (<140, 140-159 mmHg).

E = 2 exercise BP categories (<200, ≥200 mmHg).

FIGURES 1 - 24

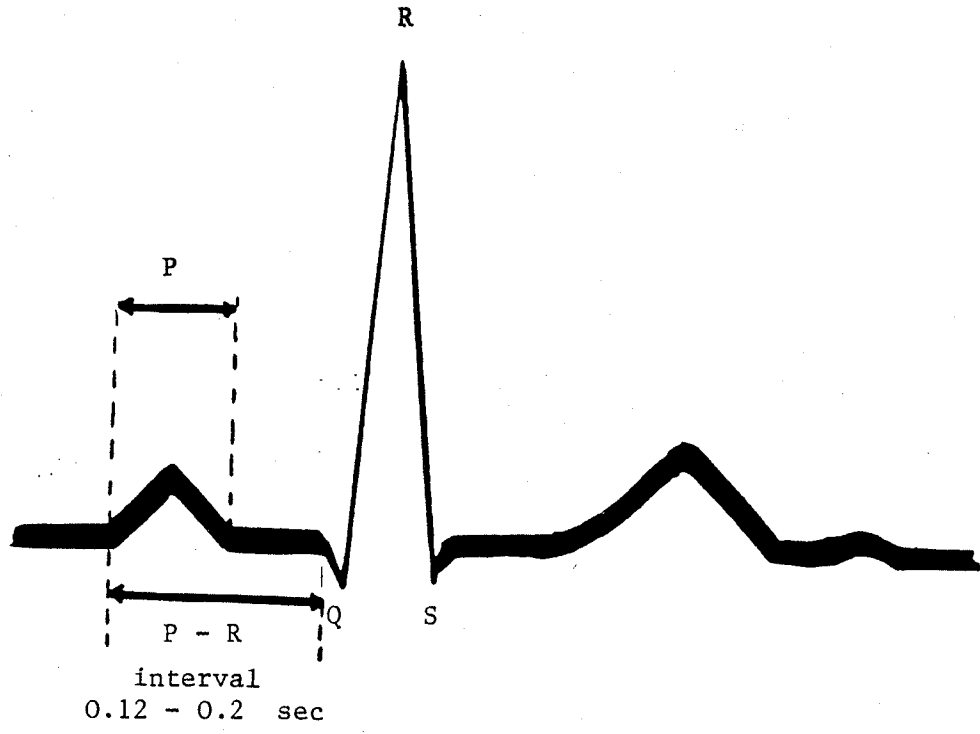


Figure 1 Measurement of P wave duration and P-R interval in Lead II

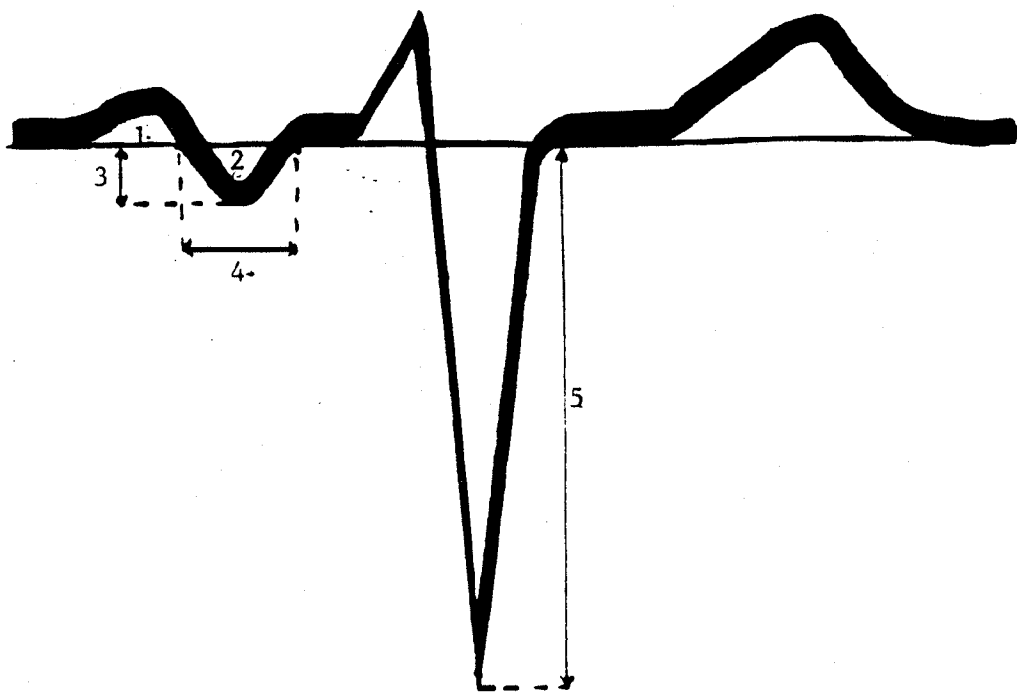


Figure 2 Measurement of P wave and S wave in Lead V_1

- 1 area of positive component of P wave
- 2 area of negative component of P wave
- 3 amplitude of negative component of P wave
- 4 duration of negative component of P wave
- 5 amplitude of S wave

DISTRIBUTION OF MACRUZ INDEX BY SEX

FIGURE 3

PERCENTAGE

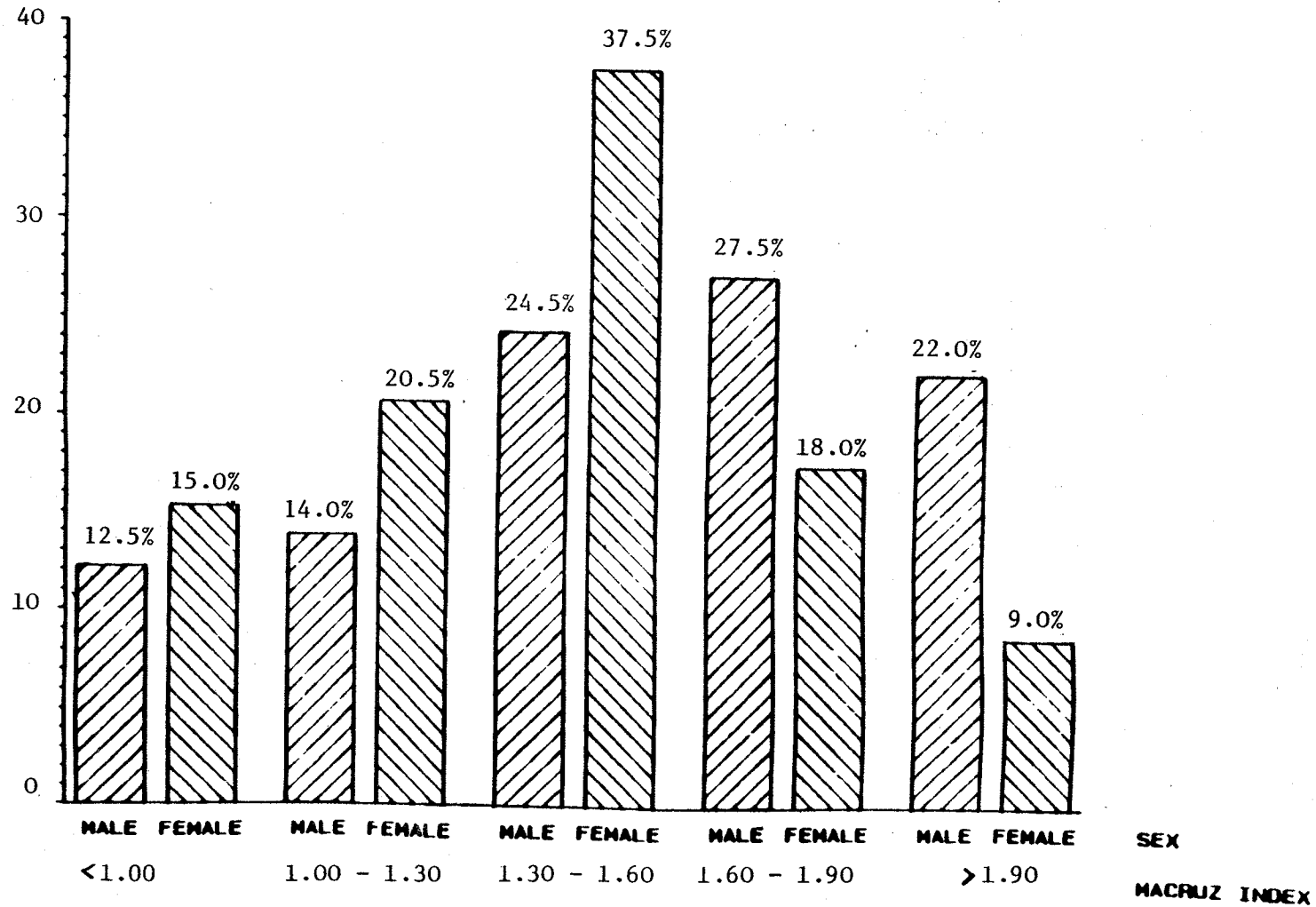


FIGURE 4

DISTRIBUTION OF PTFV1 BY SEX

PERCENTAGE

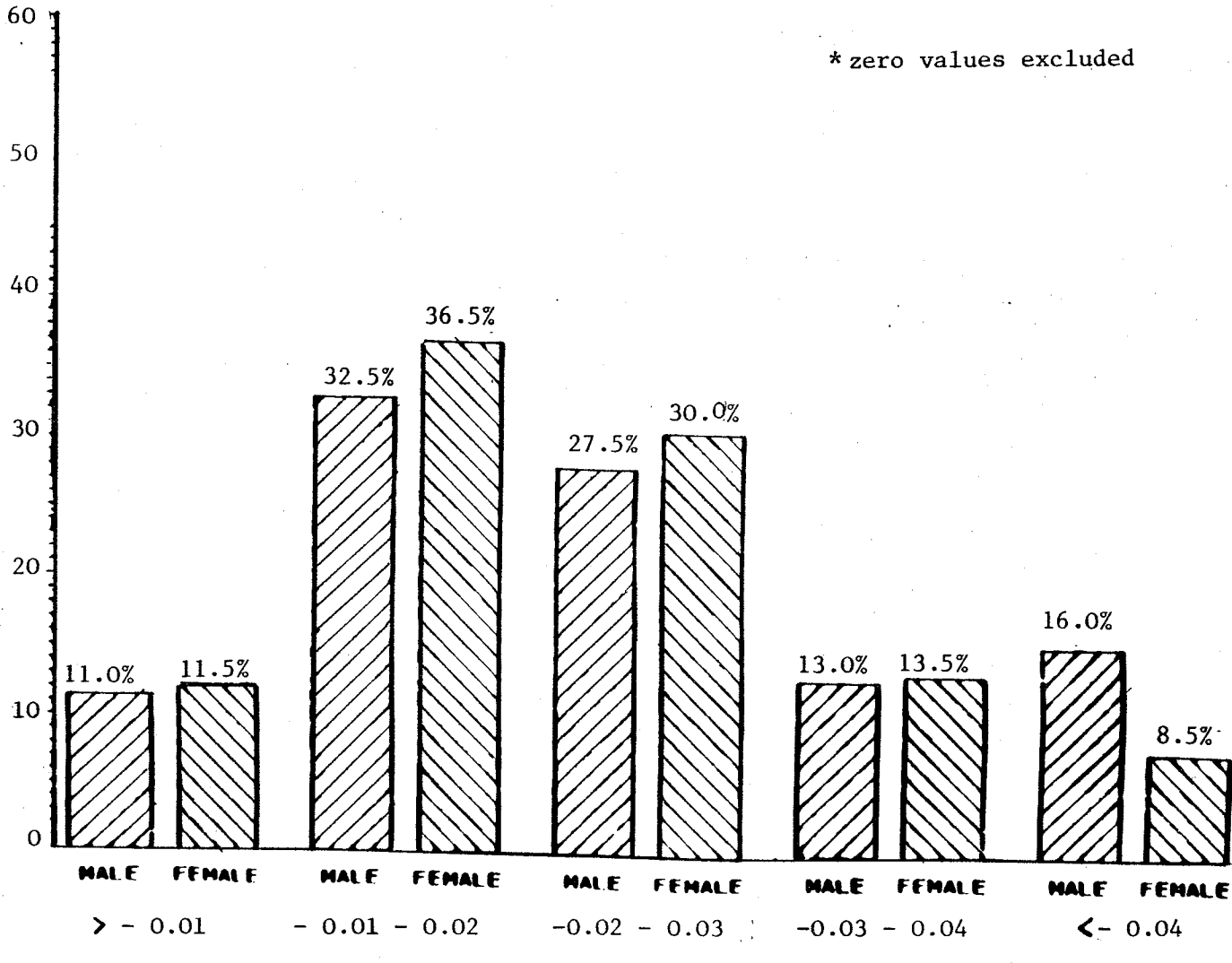


FIGURE 5 **DISTRIBUTION OF PTFV₁ BY SEX**

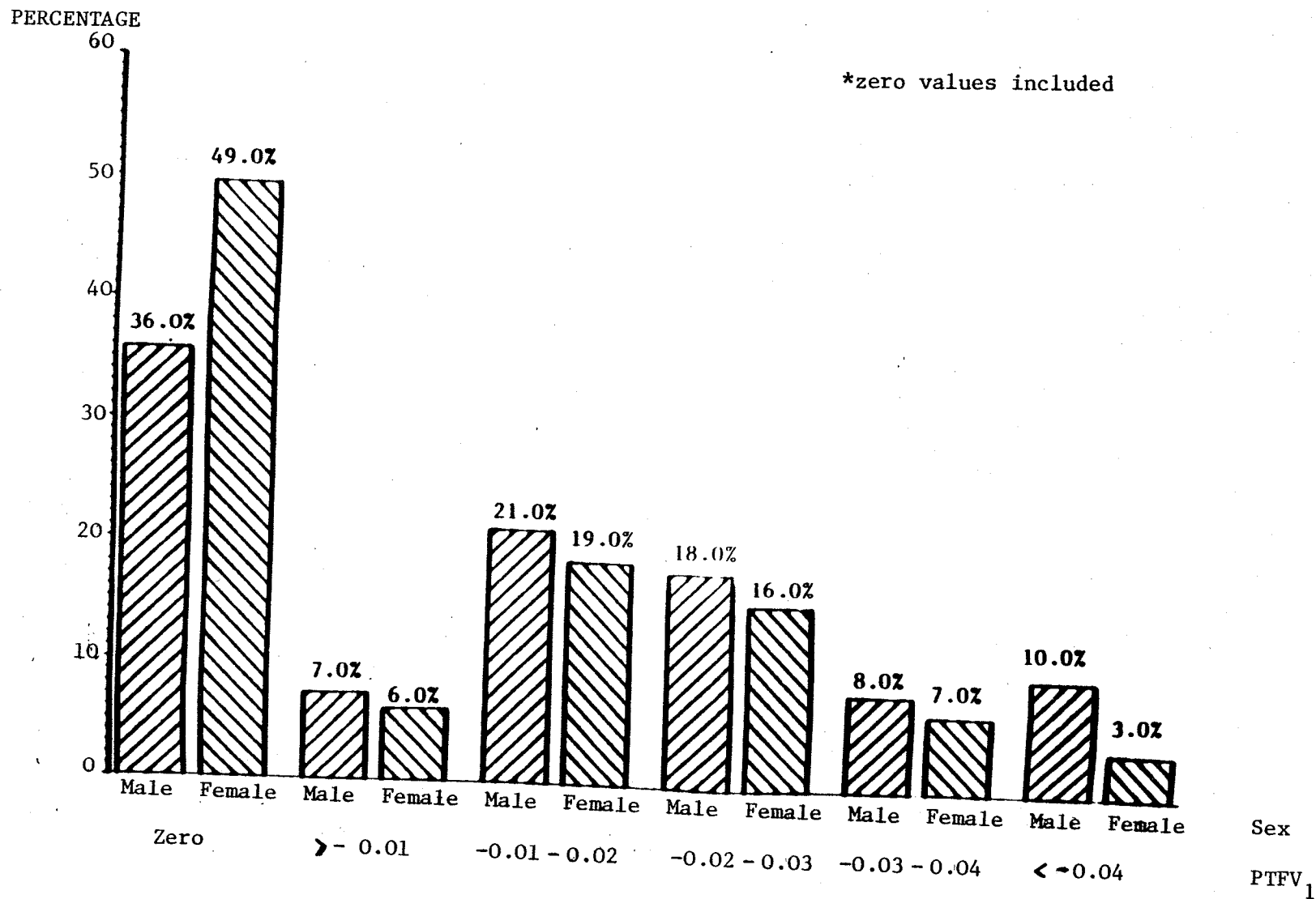


FIGURE 6 **DISTRIBUTION OF RSS BY SEX**

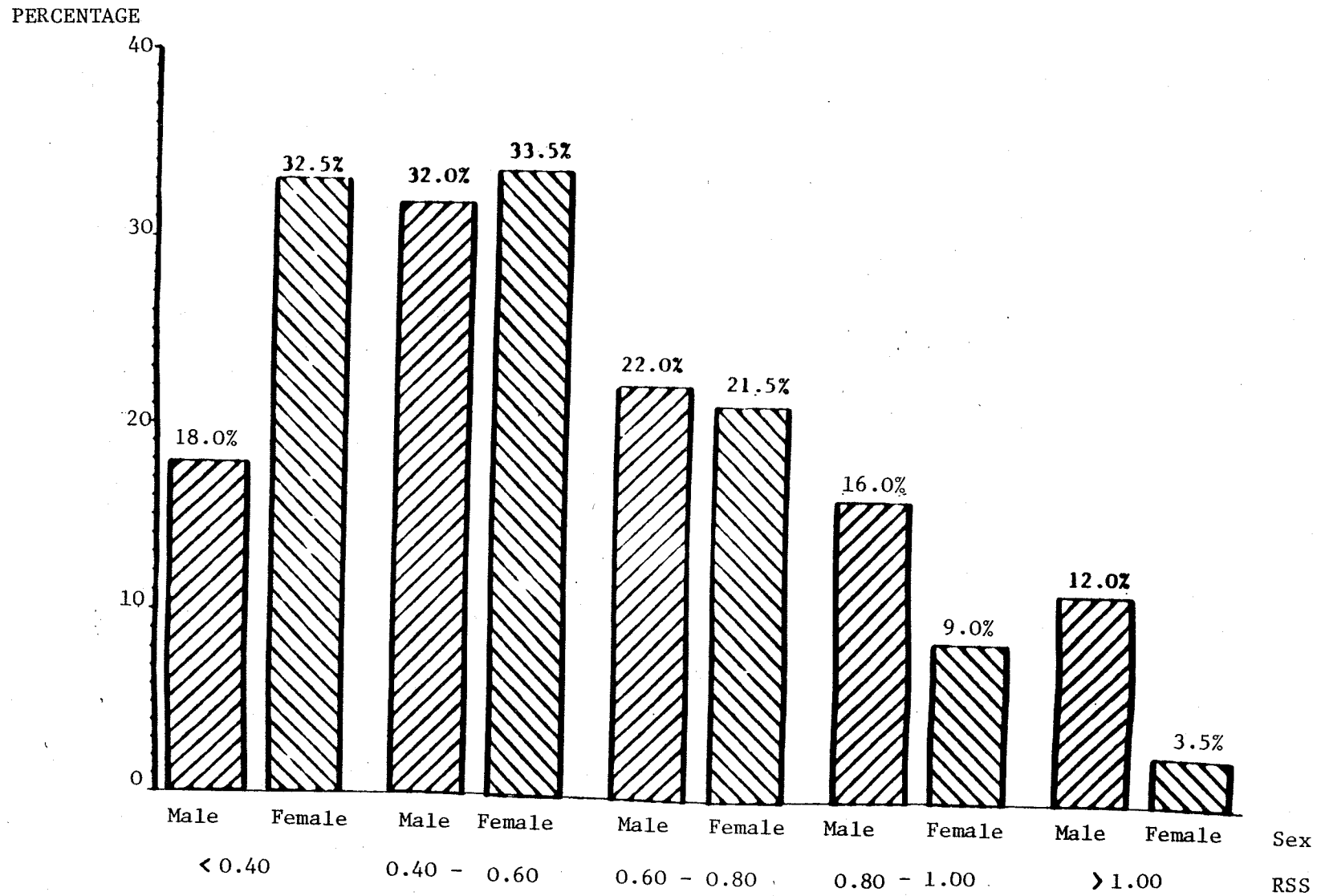


FIGURE 7 DISTRIBUTION OF RAVL BY SEX

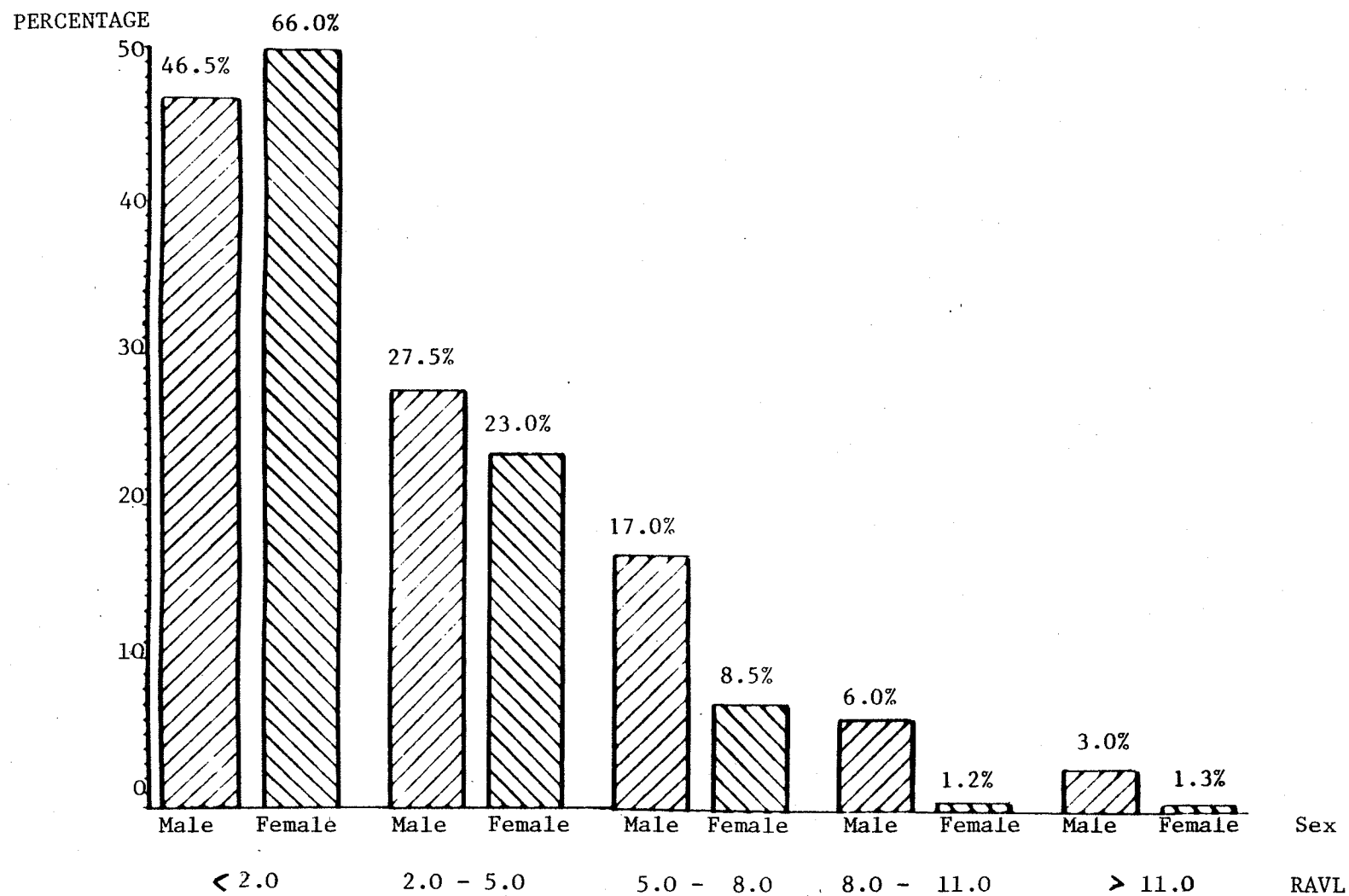


FIGURE 8 **DISTRIBUTION OF RV5 BY SEX**

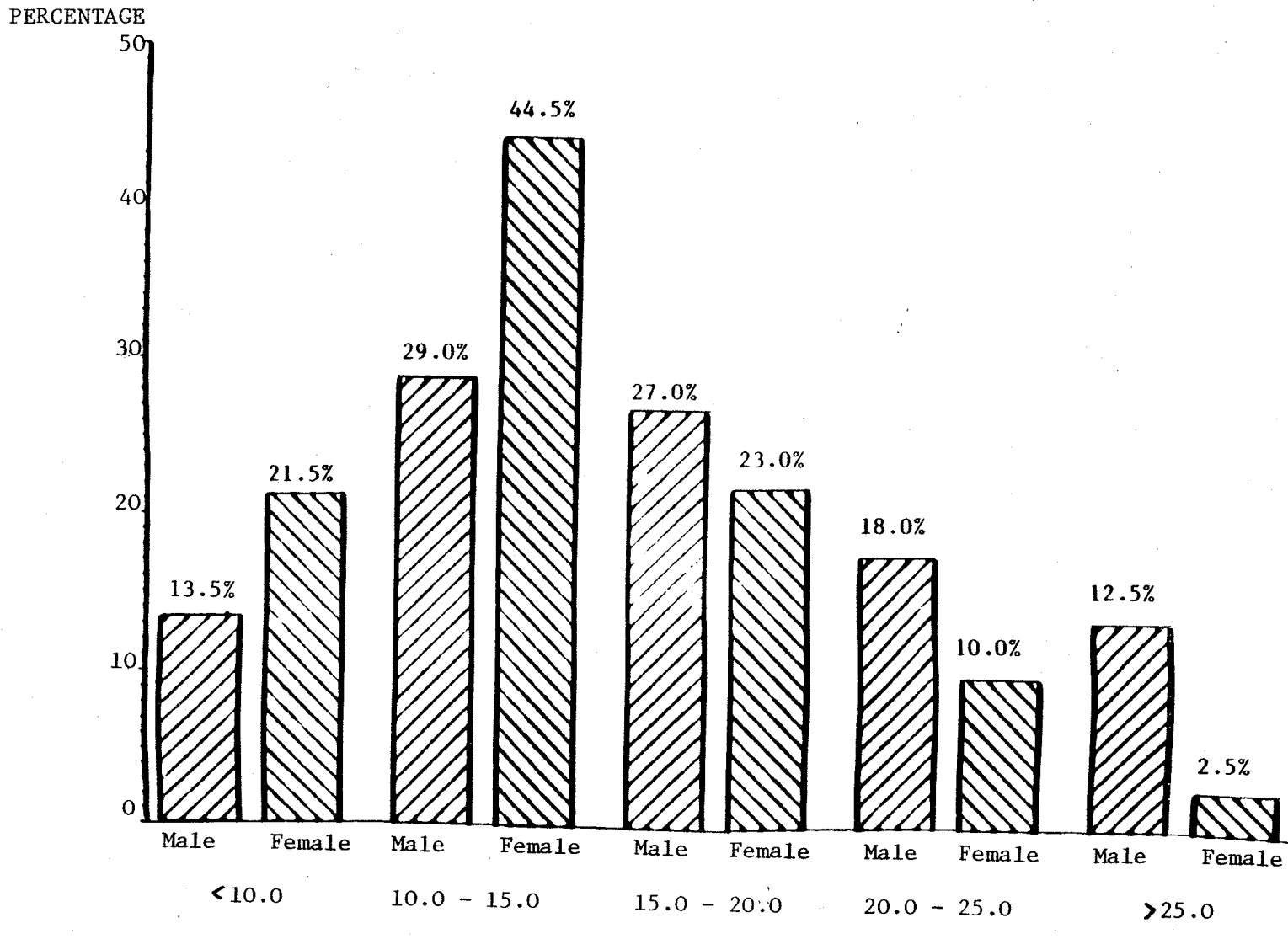


FIGURE 9 **DISTRIBUTION OF R₁+S₃ BY SEX**

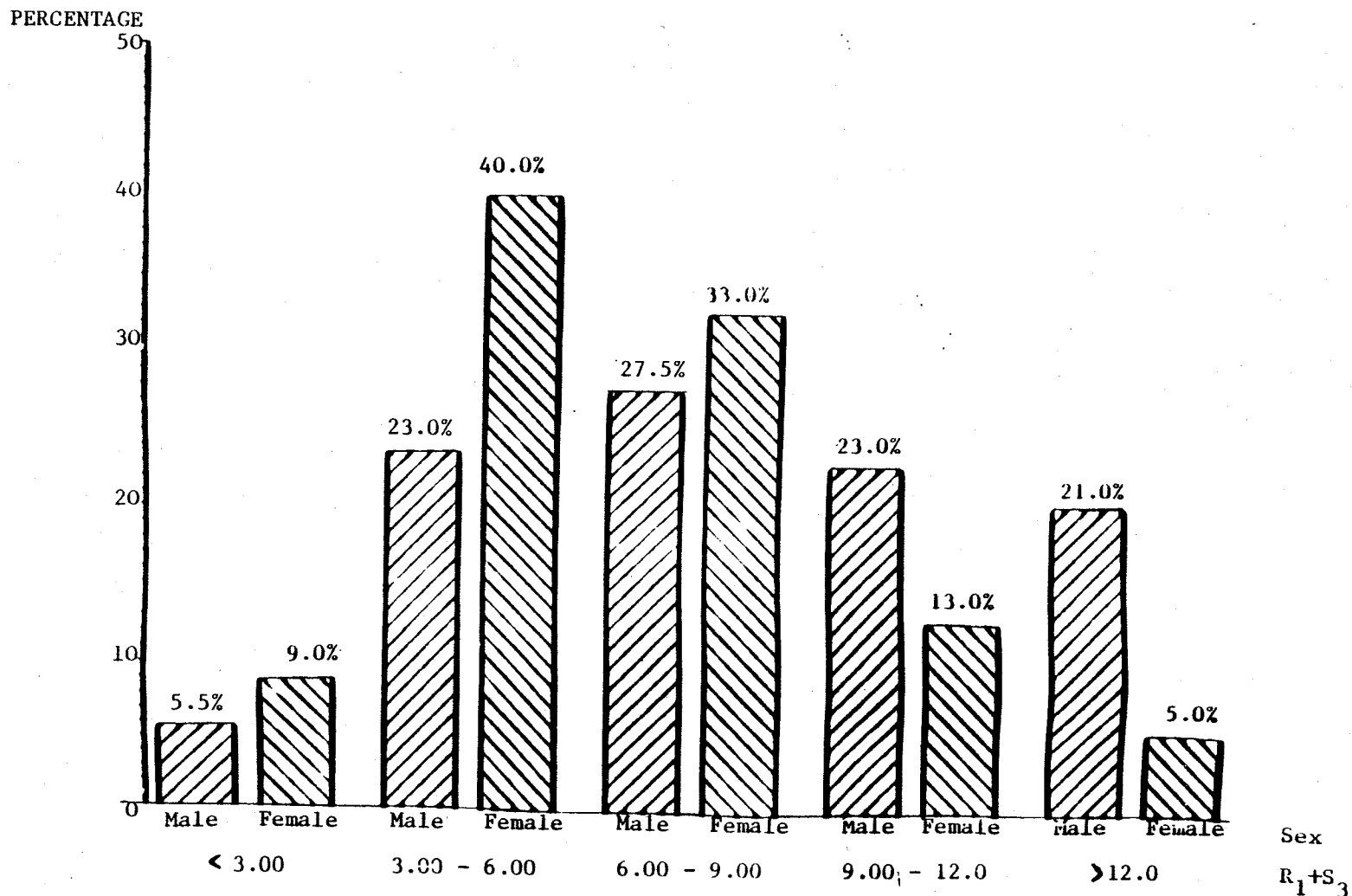


FIGURE 10 DISTRIBUTION OF RV5 + SV1 BY SEX

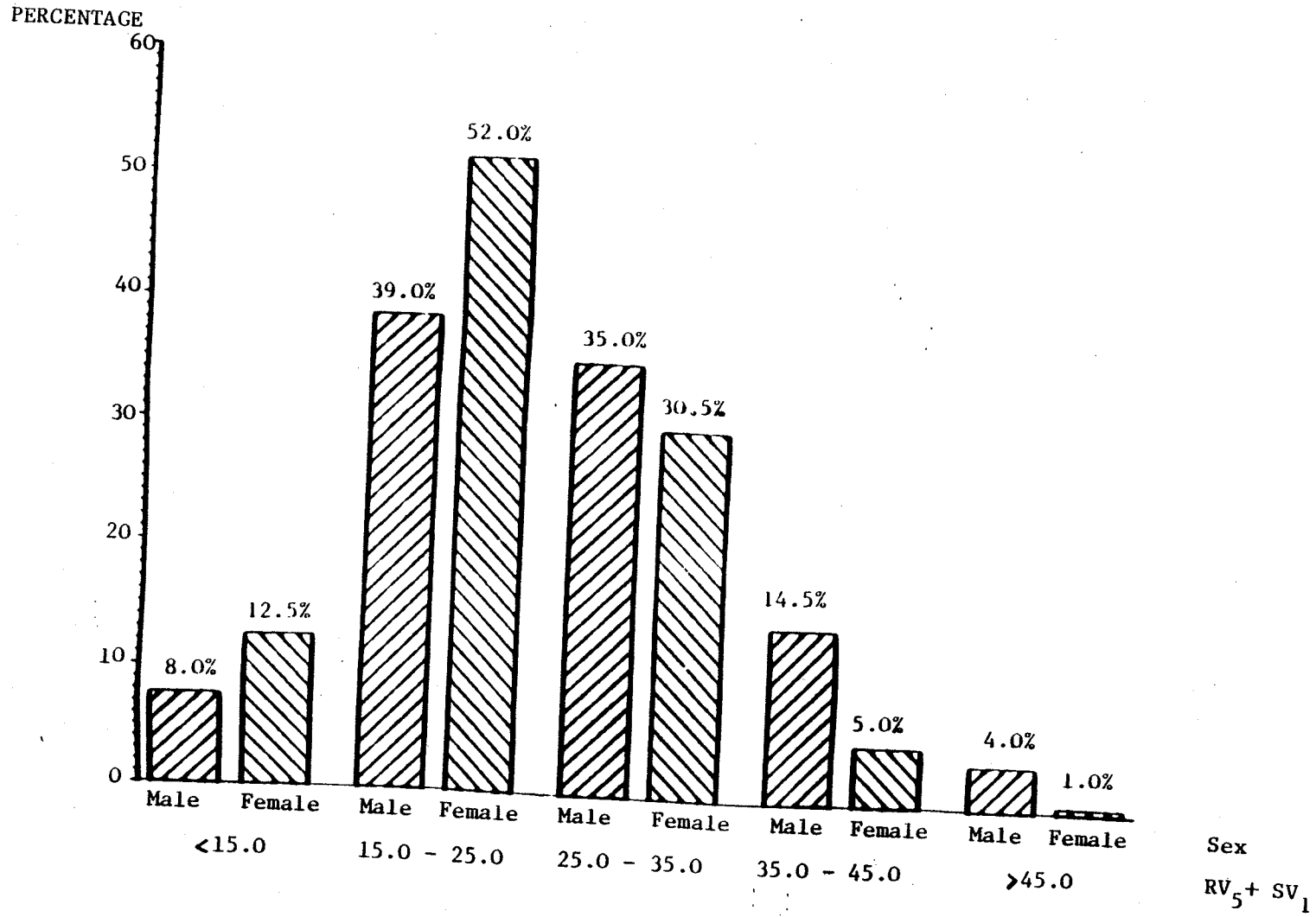
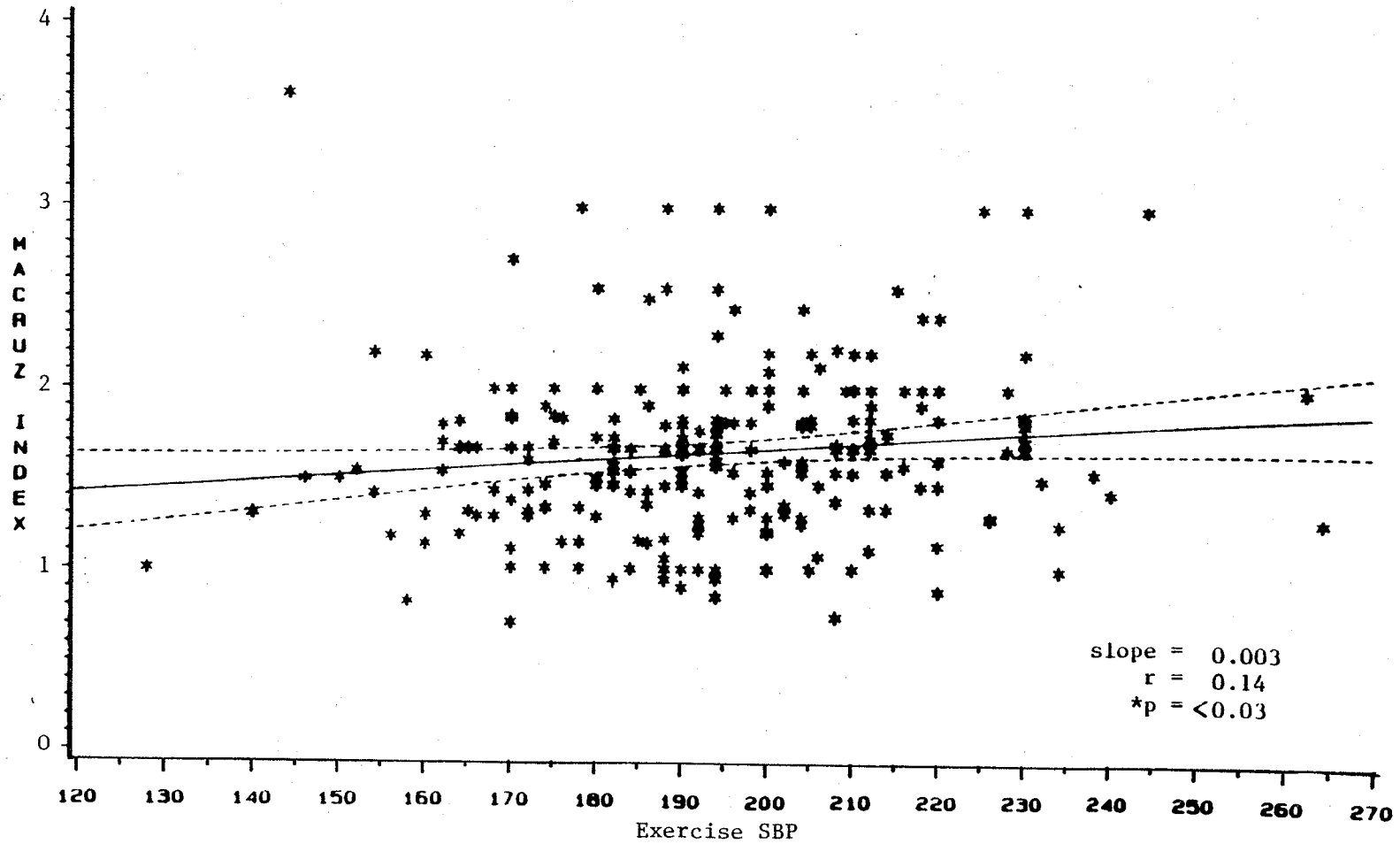


FIGURE 11

LINEAR REGRESSION OF MACRUZ INDEX ON EXERCISE SBP FOR MALE SUBJECTS



*p values are the same for slope and correlation coefficient.

FIGURE 12

LINEAR REGRESSION OF MACRUZ INDEX ON EXERCISE SBP FOR FEMALE SUBJECTS

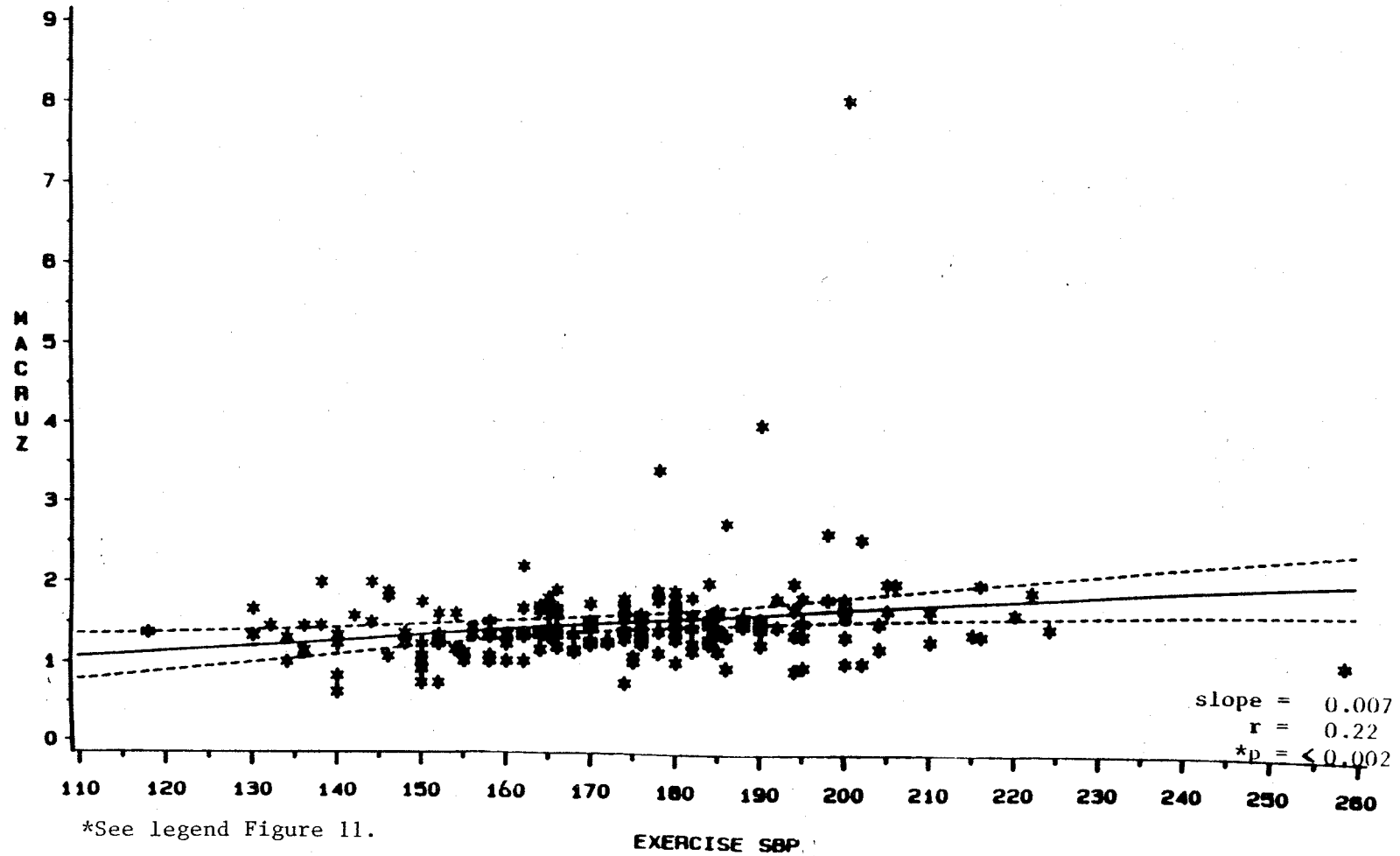


FIGURE 13

LINEAR REGRESSION OF PTFV1 ON EXERCISE SBP FOR MALE SUBJECTS

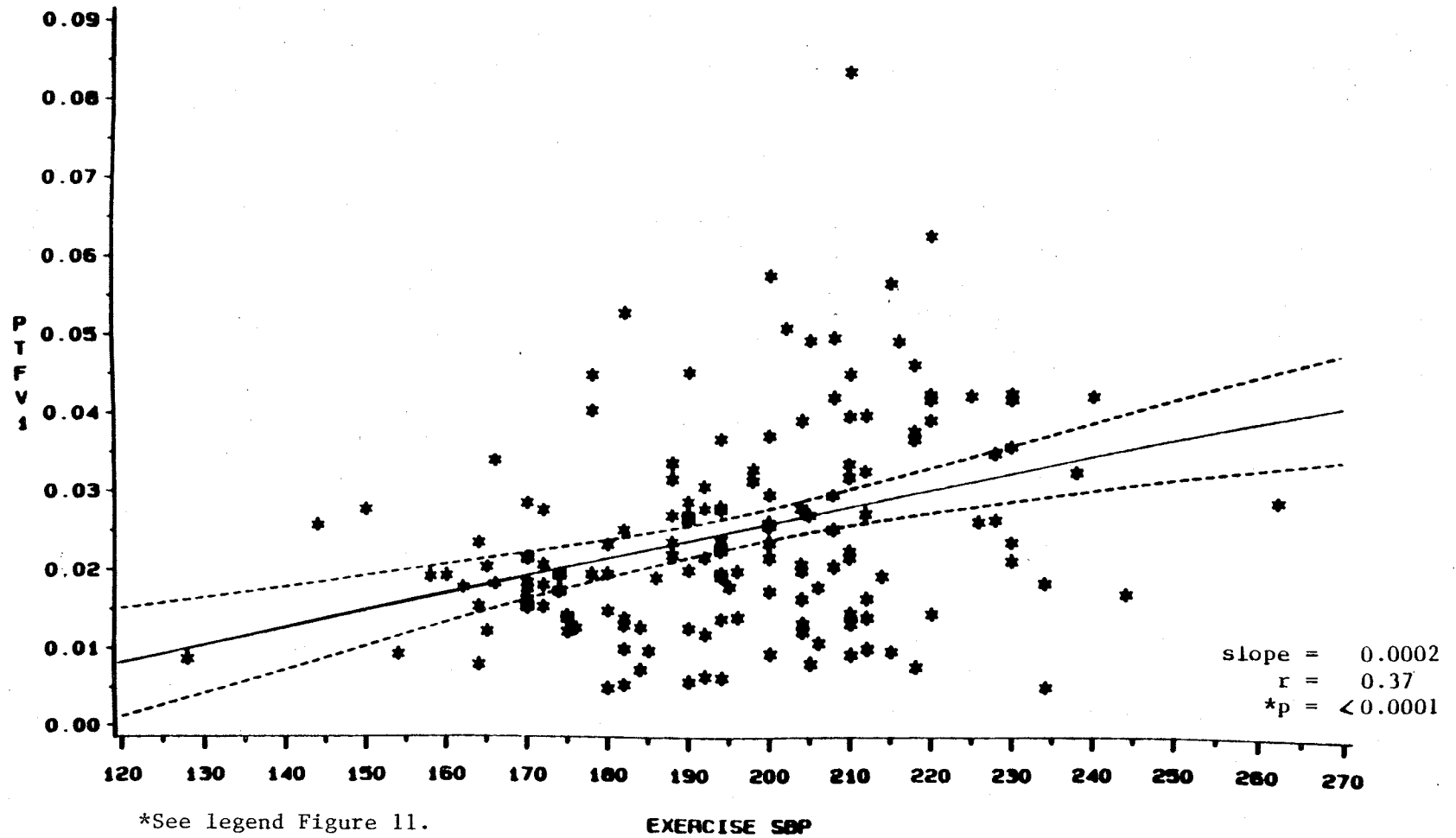


FIGURE 14

LINEAR REGRESSION OF PTFV1 ON EXERCISE SBP FOR FEMALE SUBJECTS

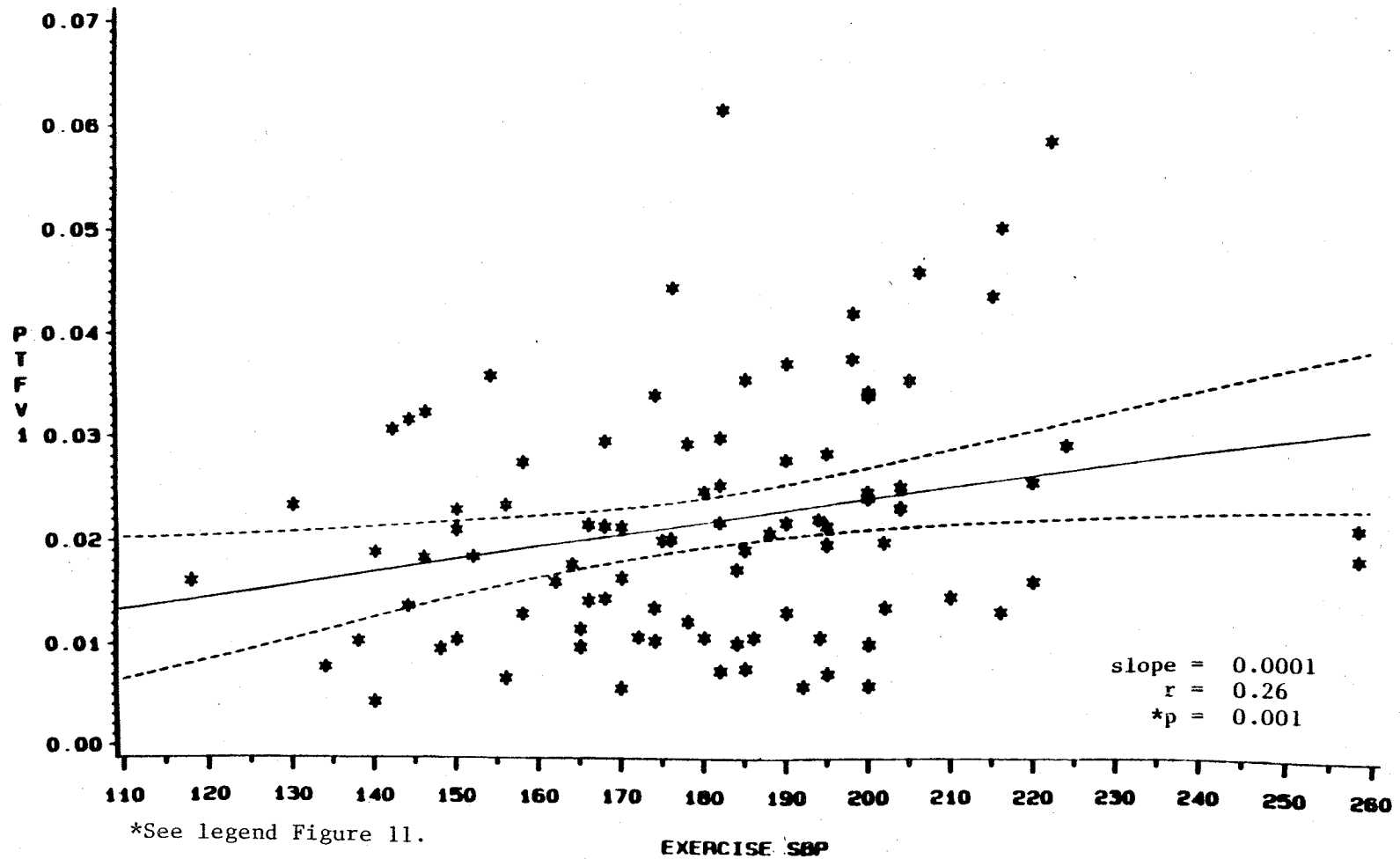
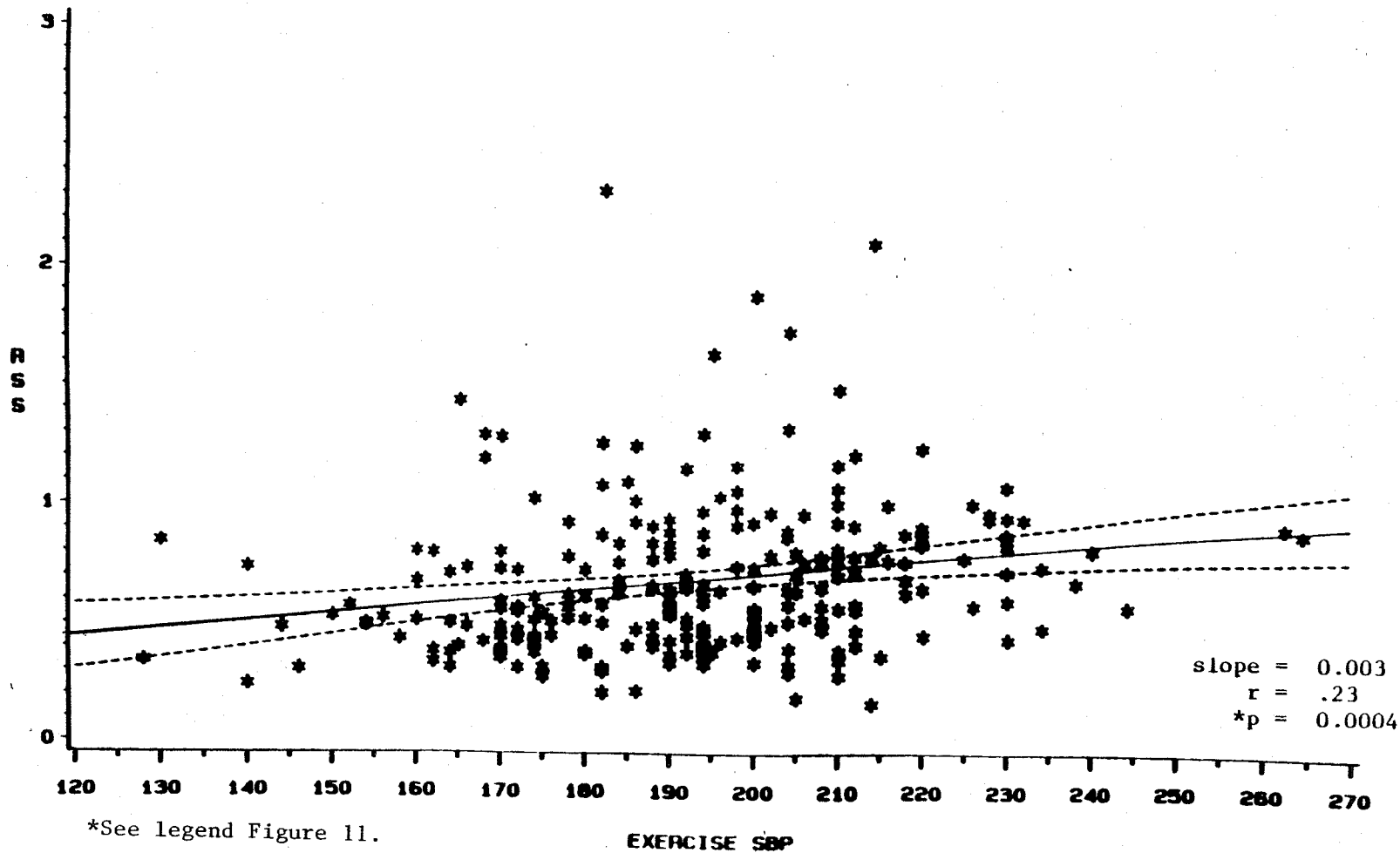


FIGURE 15

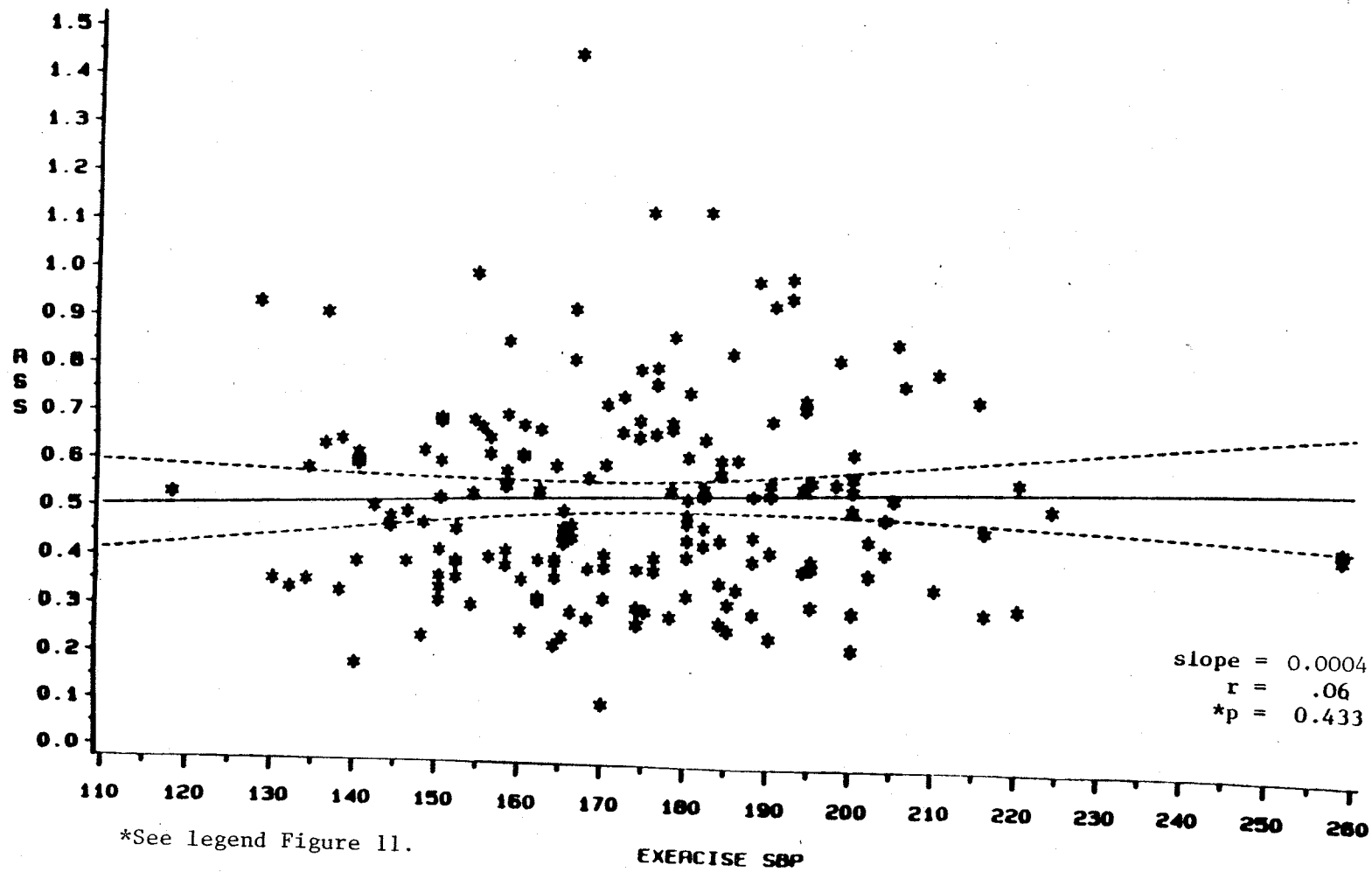
LINEAR REGRESSION OF RSS ON EXERCISE SBP FOR MALE SUBJECTS



*See legend Figure 11.

FIGURE 16

LINEAR REGRESSION OF RSS ON EXERCISE SBP FOR FEMALE SUBJECTS



*See legend Figure 11.

FIGURE 17

LINEAR REGRESSION OF RAVL ON EXERCISE SBP FOR MALE SUBJECTS

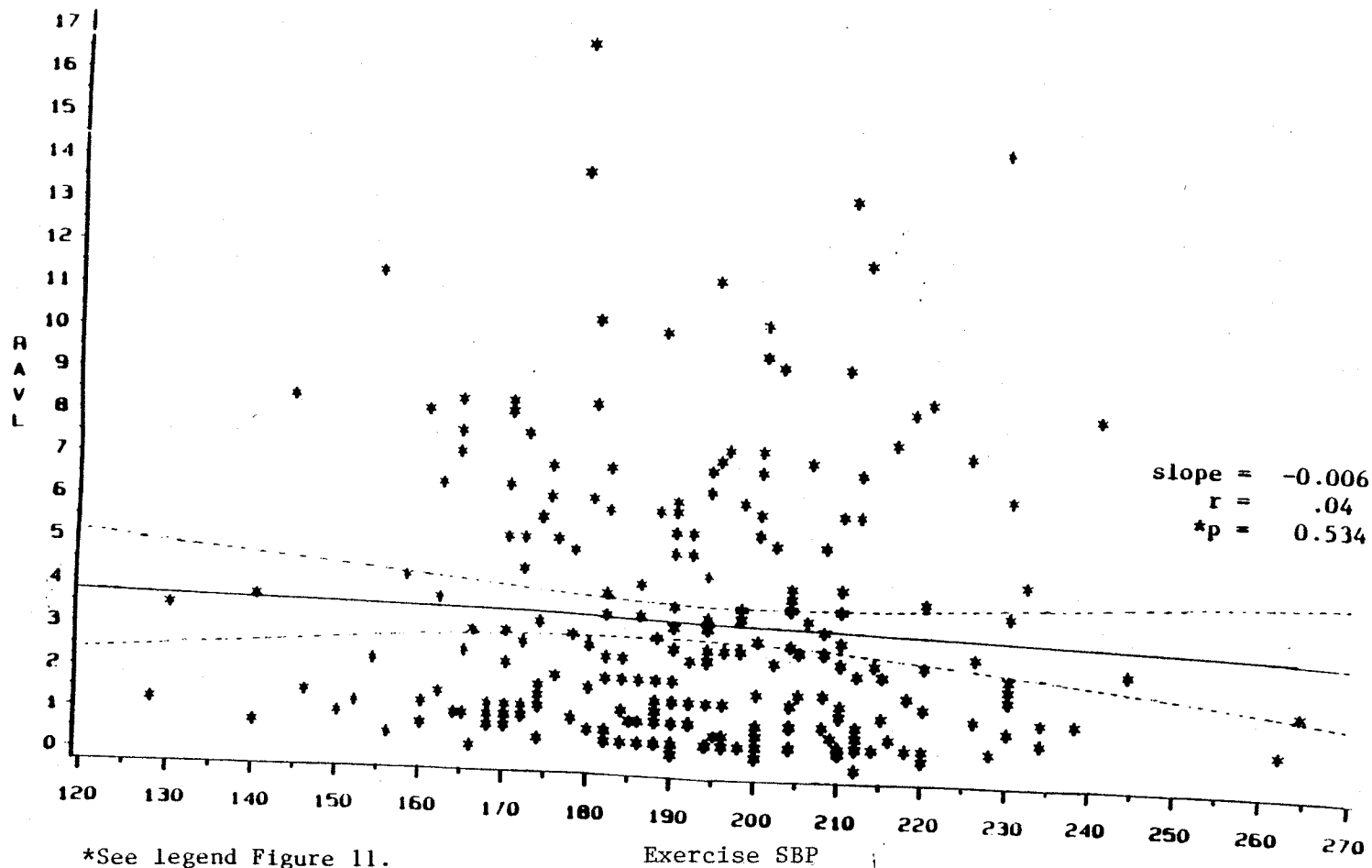


FIGURE 18

LINEAR REGRESSION OF RAVL ON EXERCISE SBP FOR FEMALE SUBJECTS

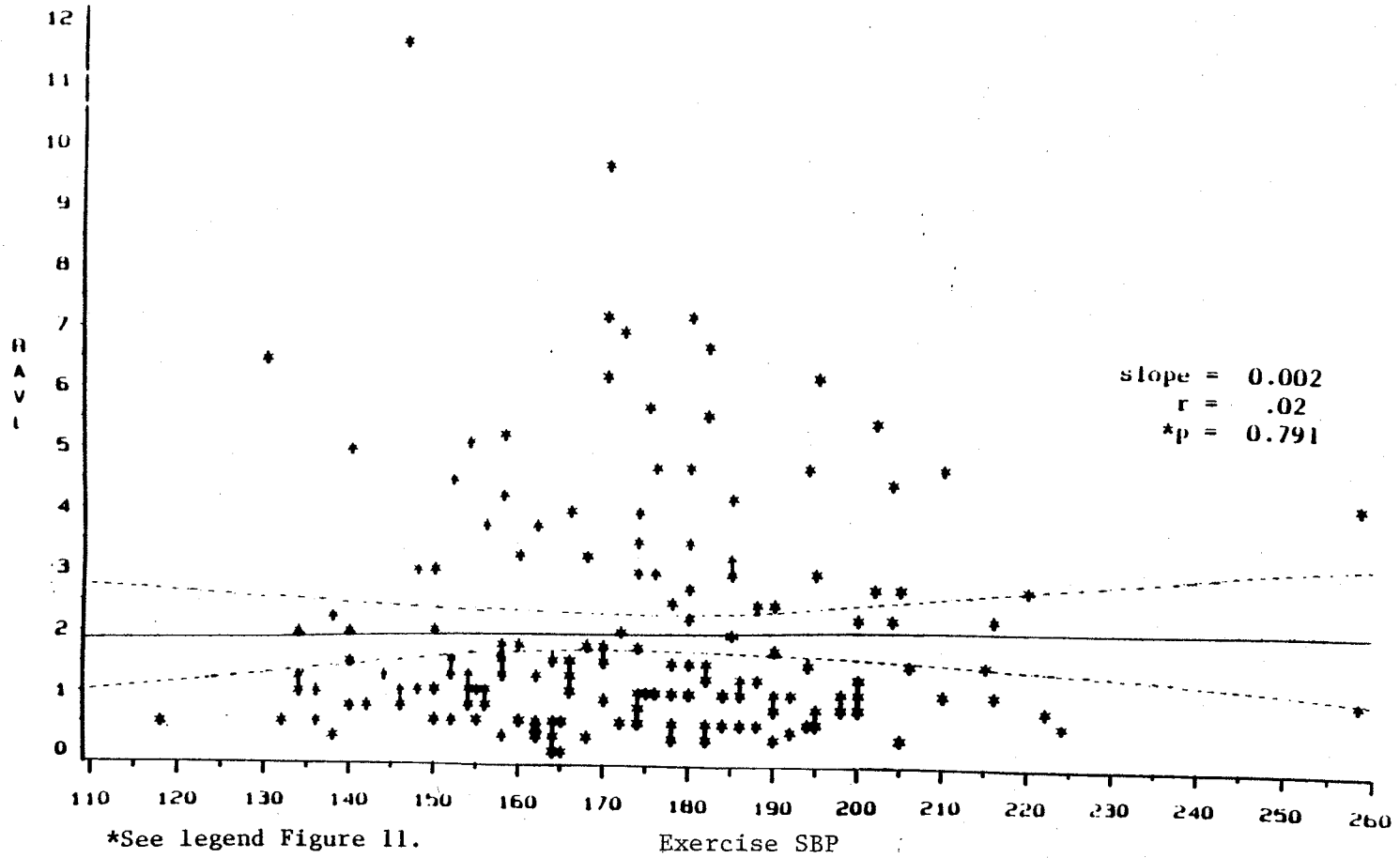


FIGURE 19

LINEAR REGRESSION OF RV5 ON EXERCISE SBP FOR MALE SUBJECTS

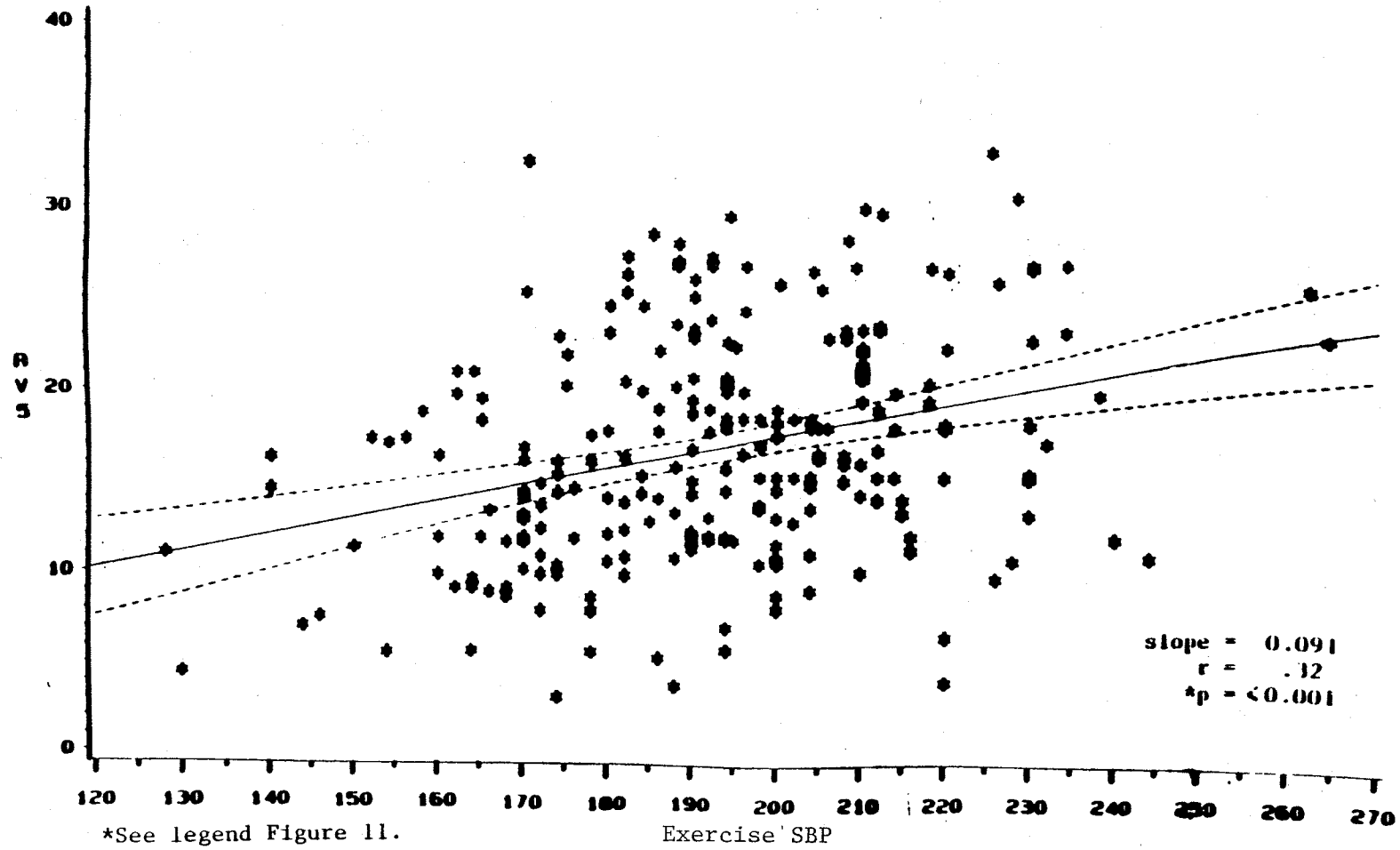


FIGURE 20

LINEAR REGRESSION OF RV5 ON EXERCISE SBP FOR FEMALE SUBJECTS

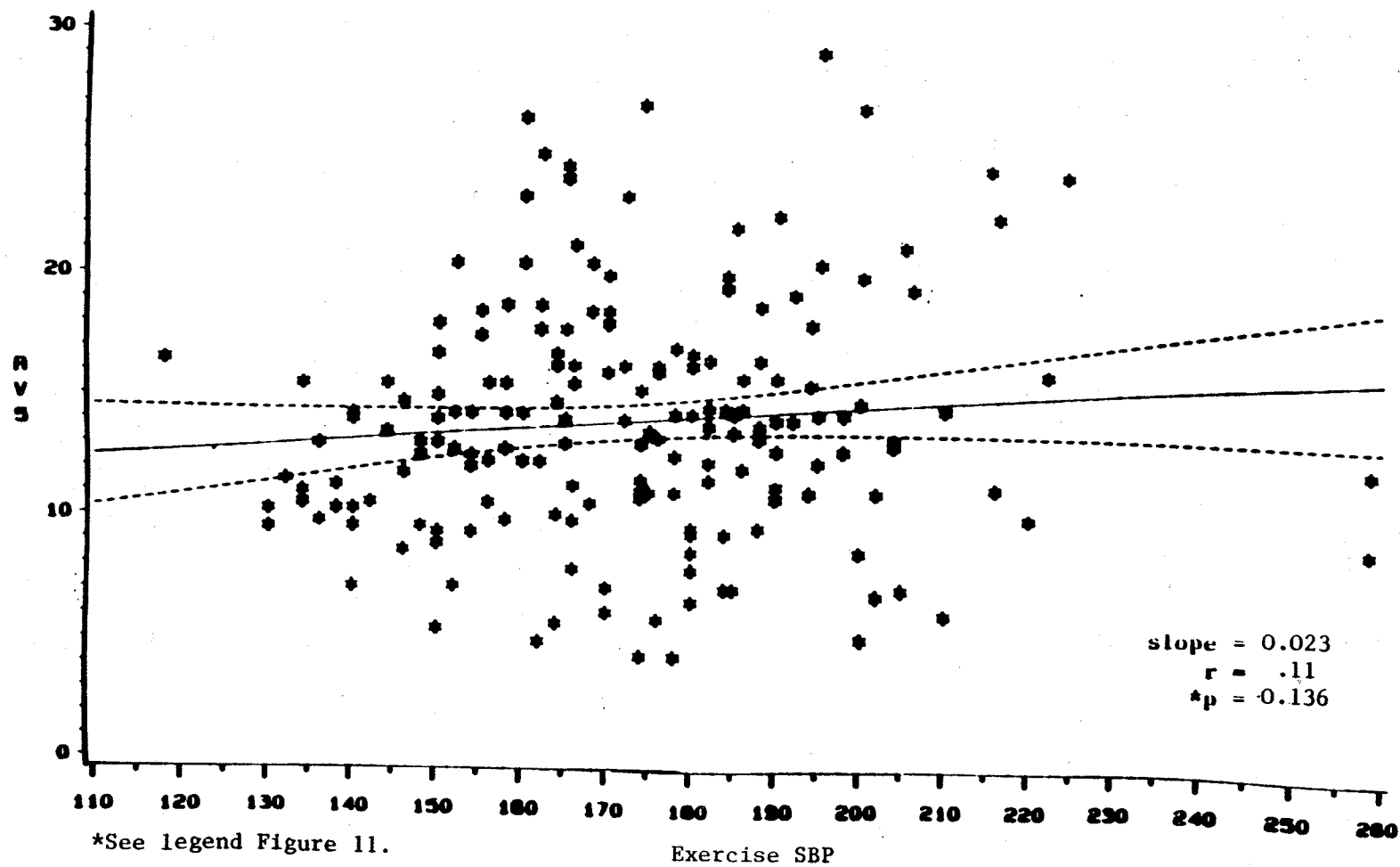


FIGURE 21

LINEAR REGRESSION OF R1S3 ON EXERCISE SBP FOR MALE SUBJECTS

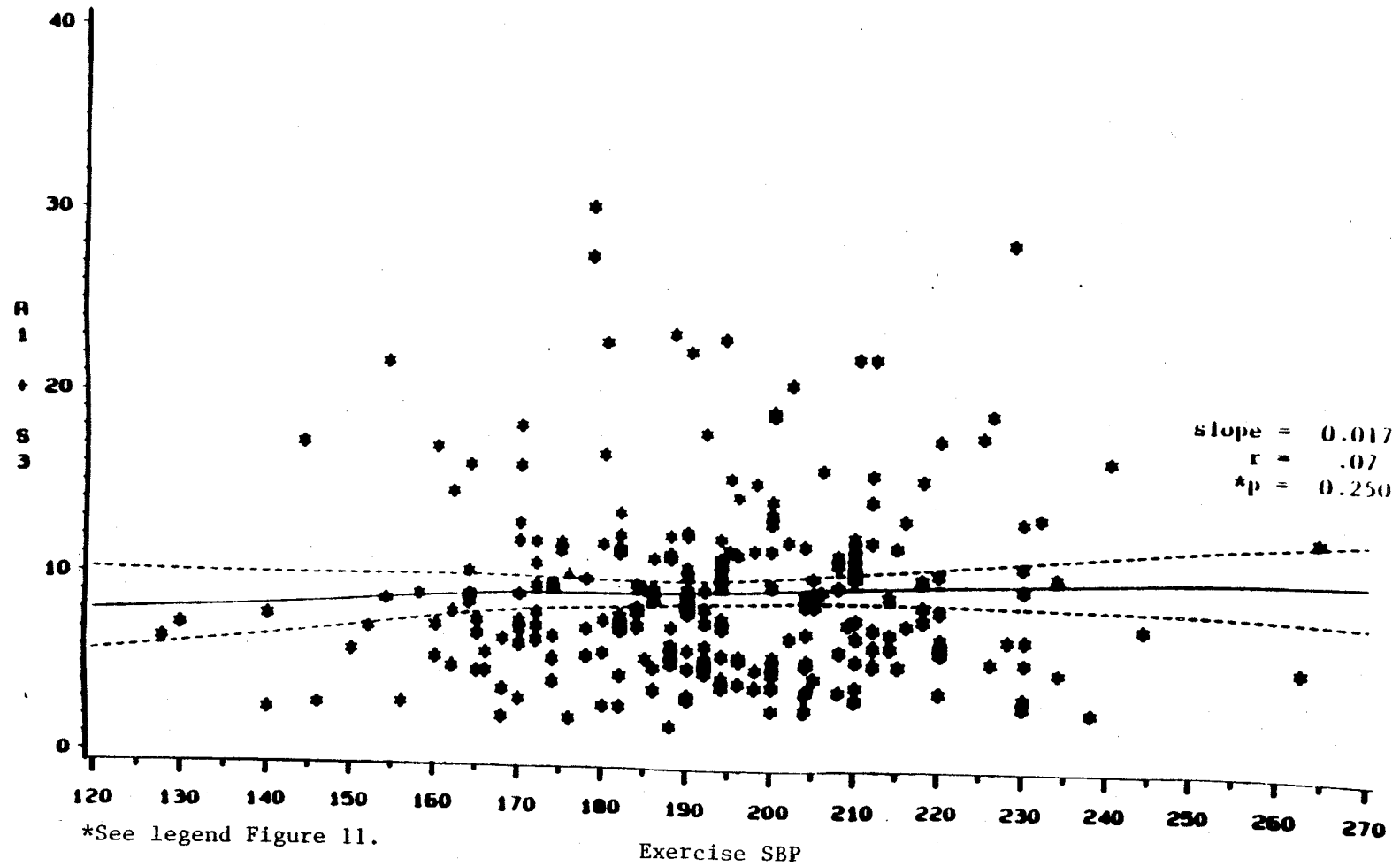


FIGURE 22

LINEAR REGRESSION OF R1S3 ON EXERCISE SBP FOR FEMALE SUBJECTS

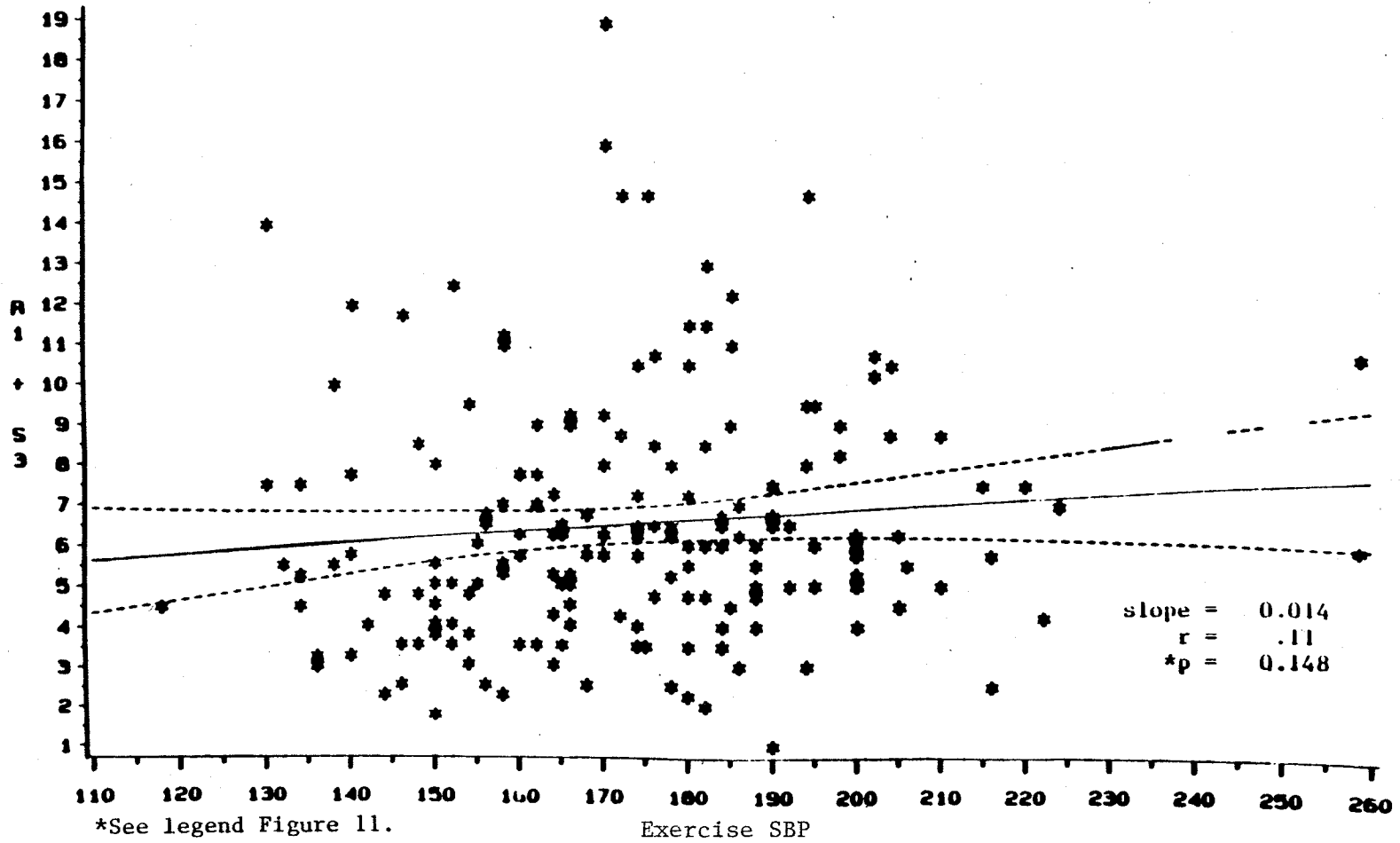


FIGURE 23

LINEAR REGRESSION OF RV5 + SV1 ON EXERCISE SBP FOR MALE SUBJECTS

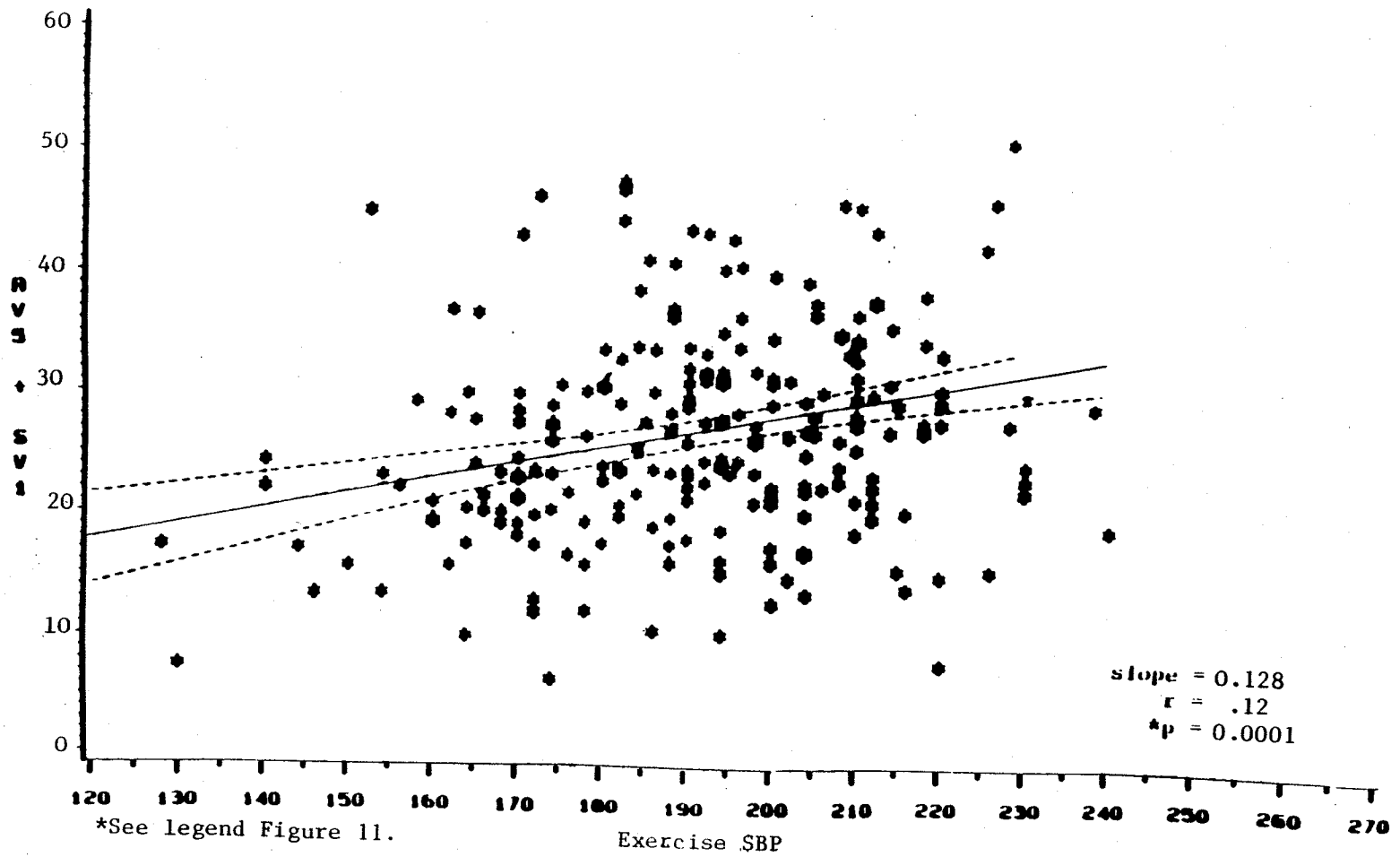


FIGURE 24

LINEAR REGRESSION OF RV5 + SV1 ON EXERCISE SBP FOR FEMALE SUBJECTS

