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Hemodynamic Evaluation of Exercise Treadmill Test by a Computer-Aided Clinical Decision System

JOHN KABAL*,† and BRUCE K. LAGERMAN*

By applying a clinical decision system, introduced as the Noninvasive Hemodynamic Analyzer (NHA) system, to demonstrate its capability to compute the hemodynamic status of exercising patients. Retrospective study to use the average vital signs and anthropological data of a large clinical trial of exercise treadmill test. The NHA system computes the percent abnormal hemodynamic parameters and these results are compared to the percent clinical classification of coronary artery disease of the Seattle Heart Watch clinical study. Four groups of the clinical study (1) Healthy, (2) Hypertensive, (3) Angina Pectoris, and (4) Postmyocardial Infarction, were used and comprised the average data of several hundred patients. Each group had three subgroups according to the conducted exercise treadmill test, namely one upright and two exercise tests. In this study the statistical evaluation was not available because the average values did not permit it. Instead, we have chosen to compute the abnormal hemodynamic parameters according to the ideal values at the level of ±20%. Altogether 33 hemodynamic parameters were included and the abnormal values were expressed in percentage. The percent cumulative abnormal responses of each hemodynamic profile obtained by the Noninvasive Hemodynamic Analyzer system as compared to the published percent clinical classification of coronary artery disease of the Seattle Heart Watch clinical study was closely matched in all clinical groups. The results of this retrospective study prove that the hemodynamic computation of the NHA system is a valid approach to evaluate exercise treadmill tests.

Key words: exercise treadmill test; clinical decision system; hemodynamic evaluation; noninvasive cardiac output measurement.

*Reston Noninvasive Hemodynamic Center, Reston, Virginia.

†To whom correspondence should be addressed at Reston Noninvasive Hemodynamic Center, 1712 Clubhouse Road, Suite 103, Reston, Virginia 20190. E-mail: lagerman@attglobal.net

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death among American adults (Castelli, 1984). In recent years, more than 18 million Americans were diagnosed with angina pectoris (AP), myocardial infarction (MI) or both each year (American Heart Association, 2002). The total direct and indirect annual costs associated with CAD are approximately $100 billion (Krantz and Baker, 2003). The exercise treadmill test (ETT) is an important noninvasive diagnostic tool in evaluating CAD (Lee and Boucher, 1840–1845; Yamada *et al*., 1997). It is equally useful to classify patients with symptoms suggestive of AP or follow patients with evolution of known CAD. In addition to ETT, there are several sophisticated cardiopulmonary exercise tests (CET), which are essentially (but not exclusively) limited to the detection of obstructive coronary artery stenosis (Harrison *et al*., 1987; Mayo Clinic Cardiovascular Working Group on Stress Testing, 1996; Psirropoulus *et al*., 2002). The costs associated with these sophisticated imaging techniques is significantly higher, but more sensitive and specific than ETT. Nevertheless, in the hierarchy of the CETs, the standard noninvasive ETT can provide invaluable clinical information.

The primary goal of ETT is to demonstrate changes of the electrocardiograph (ECG) pattern (Desai *et al*., 2002; Sarullo *et al*., 2002). Its diagnostic and prognostic capabilities are further enhanced by different treadmill scores (Lipinski *et al*., 2002; Mark *et al*., 1991) which combines ST-segment deviation, treadmill time, and the degree of angina. ETT limitations are primarily linked to ECG alterations, such as, strain pattern of left ventricular hypertrophy, left bundle branch block, and

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Table 1. Summary of the "Seattle Heart Watch" Clinical Trial

Parameters	Healthy group			Hypertensive group			Angina pactoris group			Postmyocardial infarction group		
Number of participant	1275			193			306			97		
Age (years)	44.5 ± 7.4			49.3 ± 8.7			51.2 ± 8.4			50.3 ± 8.3		
Sex	Males			Males			Males			Males		
Height (cm)	178.3 ± 6.8			178.7 ± 6.0			176.3 ± 7.3			175.4 ± 7.4		
Weight (kg)	80.8 ± 9.8			84.0 ± 12.6			80.8 ± 12.1			77.8 ± 9.3		
	U	E-1	E-2	U	E-1	E-2	U	E-1	E	U	E-1	E-2
Systolic blood pressure	123 ± 13	155 ± 21	185 ± 22	141 ± 16	173 ± 25	197 ± 28	125 ± 17	151 ± 25	164 ± 30	121 ± 12	143 ± 21	159 ± 26
Diastolic blood pressure	77 ± 10	76 ± 11	71 ± 17	90 ± 11	90 ± 13	88 ± 15	80 ± 10	82 ± 12	82 ± 16	79 ± 8	80 ± 10	81 ± 13
Heart Rate	72 ± 11	108 ± 14	168 ± 15	77 ± 15	115 ± 18	167 ± 17	75 ± 12	116 ± 18	144 ± 24	76 ± 13	115 ± 16	150 ± 21
Est. VO_2max		35.3 ± 5.2			30.2 ± 8.0			21.3 ± 9.1			24.9 ± 8.1	
Clinical classification of heart disease		0%			8%			27%			75%	

others. However, two hemodynamic-related parameters are particularly important to enhancing the diagnostics accuracy: first, the absolute exercise tolerance, expressed as metabolic equivalents (MET) (Jette *et al.*, 1990); and second, the maximal exercise capacity as the single best clinical predictor of mortality (Myers *et al.*, 2002). Unfortunately, the hemodynamic aspects of ETT are generally limited because the capability of measuring cardiac output (CO) is not widely available. Without knowing the CO, calculating vascular resistance and other hemodynamic parameters is not possible.

In this paper, we introduce a clinical decision system, a novel Noninvasive Hemodynamic Analyzer (NHA), which is capable of computing CO and other hemodynamic parameters utilizing vital signs and anthropological data. We obtained the data from a large, well-known clinical study referred to as the Seattle Heart Watch (Bruce *et al.*, 1974). The evaluations of the Seattle Heart Watch clinical study were based on ECG of ETT and clinical signs. We selected data from four representative groups of the diagnosed patients according to their particular clinical status. Our primary research objective is to prove that the NHA system is capable of accurately computing and determining the same diagnosed groups (healthy, AP, MI, and hypertensive) as those in the Seattle Heart Watch study by calculating various hemodynamic parameters using the same underlying patient data.

METHODS

We introduce a clinical decision system, the Noninvasive Hemodynamic Analyzer (NHA), which is capable of computing CO and other important hemodynamic parameters. The data bank of a large clinical study from the cardiovascular literature was selected to compute the hemodynamic profile of the clinical groups of an original ETT study. This Seattle Heart Watch clinical study organized a network of 15 exercise testing facilities in four teaching hospitals and other clinics. Over an 18-month period, more than 2000 adult men were tested. A summary of the Seattle Heart Watch clinical study is shown in Table 1.

In the Seattle Heart Watch clinical study, a multistage, symptom-limited, submaximal exercise protocol was applied for different groups of cardiac conditions. For compilation only, the average data of each particular group, composed of several hundreds participants, were used. Patients were organized into four separate groups in accordance with the ECG results of ETT and clinical symptoms. The Seattle Heart Watch study did not include hemodynamic data, except the average vital signs changes were presented with the corresponding anthropological information. This patient information was used in our retrospective study.

The NHA is able to utilize the Seattle Heart Watch data independently of the ECG results and, by computing hemodynamic parameters, can reach the same conclusions as the clinical study. It is important to note that our retrospective study did not use statistical evaluations, but only a comparison of the NHA results to the end results of the Settle Heart Watch clinical study.

The Noninvasive Hemodynamic Analyzer (NHA) is capable of computing the hemodynamic status of exercising patients with scientific objectivity and accuracy. A flowchart of the NHA clinical decision system computing stroke volume (SV) and its related hemodynamic parameters is presented in Fig. 1.

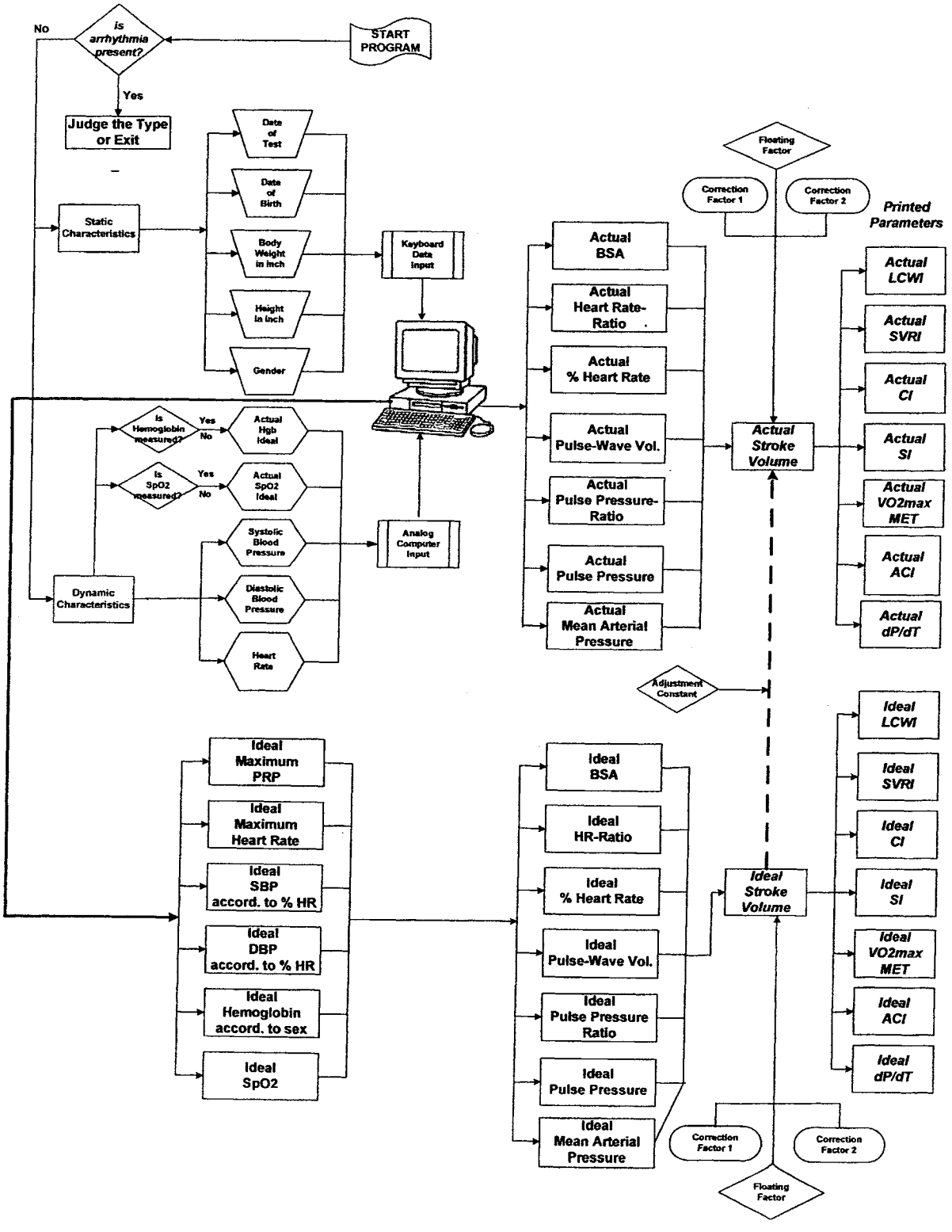


Figure 1. Cardiovascular clinical decision system: Flowchart of the noninvasive hemodynamic analyzer.

The calculations are initiated with the data inputs of five dynamic characteristics, namely, systolic and diastolic blood pressure, heart rate, arterial oxygen saturation, and hemoglobin. The static characteristics of patients include: date of test, date of birth, sex, height, and body weight. The computed hemodynamic parameters are divided by the patient body surface area (BSA), or "indexed" to be able to compare different patients.

The NHA software applies two unique algorithm cascades. Through the first cascade of algorithms, the ideal stroke volume is calculated. In the second cascade of algorithms, the actual stroke volume is computed by an adjustment constant relative to the corresponding ideal stroke volume.

To calculate the ideal stroke volume of a particular patient, the following physiological and/or mathematical equations are utilized:

(a) The Maximum Ideal Pressure Product (PRP) = Systolic Blood Pressure (SBP) × Heart Rate/100 is plotted against the % Maximum Heart Rate (Max. HR) (sex dependent: male = 333 and female = 294.)
(b) Max. HR can be obtained by using regression coefficients according to age and sex.
(c) Normal HR in resting state is assumed to be 40 ± 3% of Max. HR.
(d) From the Maximum Ideal PRP (sex dependent) the ideal SBP values can be calculated for any particular HR.

$$\text{PRP} = (\text{SBP} \times \text{HR})/100 \rightarrow \text{SBP}$$
$$= (\text{PRP} \times 100)/\text{HR}.$$

(e) To maintain a physiologically optimal oxygenated blood supply for the vital organs, such as the brain and heart, a constant opening blood pressure (mean arterial pressure or MAP) is required and this pressure is maintained by very sophisticated biofeedback mechanisms. Normal MAP is age dependent, according to the standard scales of males: 84–100 mmHg and females: 81–97 mmHg. Considering that MAP is the geometric average of pulse area between SBP and DBP (an approximate triangle): MAP = [(SBP − DBP)/3] + DBP.
(f) DBP = MAP − [(SBP − MAP)/2].
(g) Thus through steps (a)–(f) an Ideal SBP and DBP, including ideal pulse pressure (PP) (or curve for exercise study) can be computed according to the corresponding HR as ideal dynamic parameters.
(h) With the above obtained dynamic and static characteristics including; patient's age, height, body weight (frame), an ideal stroke volume can be computed by a series of equations.

The calculation of SV is based upon a theoretical model of pulse wave (PW) propagation. In the aorta and/or other blood vessels the manifestation of SBP as a pulse wave originates by the constriction of the left ventricle (systole). Although the values are different at the aortic level, the resulting MAP is practically the same at the cubital area to where a patient's blood pressure is actually measured.

The true SV can be measured only in the ascending aorta. However, that part of the blood volume which creates the PW in the major peripheral vessels is synchronous in time (pulse rate) with the bolus of the SV. The PW is the result of the oscillation of the SBP and DBP and their difference at the largest expansion is equal to Pulse Pressure (PP).

The calculated PP-Ratio (PP-R) = (SBP − DBP/(60/HR), is taken empirically as the largest circumferential extension of the blood vessel. If we assume that the PP-R is essentially the circumferential change of PW = $2r \times \pi$, we can calculate the area, equal to $r^2 \times \pi$, therefore:

$$r = \text{PP-R}/2 \times \pi \rightarrow [(\text{PP-R}/2 \times \pi)^2 \times \pi].$$

The goal is to calculate the pulse wave volume (PWV), so the approximate propagated bolus size (blood volume increase) will be equal to

$$\text{PWV} = [(\text{PPR}/2 \times \pi)^2 \times \pi]/(60/\text{HR}).$$

Multiplying the above equation by a floating factor and taking the square root value, the ideal SV is empirically computed, and as divided by the body surface area (BSA), and the ideal stroke index (SI) is obtained.

Finally, multiplying both parameters with the actual heart rate, CO and/or CI values are determined. The floating factor makes it possible to have a steady CI of approximately 3.5 L/min/m^2 irrespective of age or sex. The actual CO and/or SI is calculated in the same way, but is corrected by an adjustment constant.

The NHA Software Algorithms are Programmed to Calculate the Following Essential Hemodynamic Parameters as Ideal and Actual Values

(1) *Mean Arterial Pressure* (MAP, mm Hg). It is calculated as the geometric mean of systolic and diastolic blood pressure. It represents the "opening" blood

pressure which is steadily maintained in a healthy person.

(2) *Pulse Pressure* (PP, mm Hg). It represents the difference of SBP and DBP or propagation of left ventricular contraction (stroke) in the blood vessels.

(3) *Chronotropy*: It represents heart rate/min or actual heart rate in percent of the maximum heart rate.

(4) *Cardiac Index* (CI, L/min/m^2). This most important oxygen transport-related parameter describes the perfusion capability of the left ventricle.

(5) *Systemic Vacular Resistance Index* (SVRI, dyn·s·cm^5/m^2). A major component of afterload and its changes are inversely proportional to changes in oxygen demand.

(6) *Left Cardiac Work Index* (LCWI, kg·m/m^2).

$$\text{LCWI} = (\text{MAP} - \text{LVEDP}) \times \text{CI} \times 0.0144.$$

The value reflects the amount of physical work the left ventricle has to perform to eject CO and is proportional to the myocardial oxygen consumption.

(7) *Stroke Index* (SI, mL/beat/m^2). It is equivalent to the ejection performance of the left ventricle. The NHA computes first the stroke volume as follows: (square root of $3.14 \times B \times C \times L) \times (A/3.14 \times 2) \times (D/1000)$; where

A = Actual Pulse Pressure Ratio (PP-R)
PP-R = Actual Pulse Pressure/(60/Actual HR)
B = Actual Heart Rate Ratio (HR-R)
HR-R = (60/Actual HR)
C = Floating factor as ((100 − Actual %HR) × $E + F$
D = Actual HR
$E + F$ = Correction factors.

(8) *Acceleration Index* (ACI, s^2): Represents myocardial contractility (Inotropy): the peak acceleration of blood after the opening of the aortic valve.

$$\text{ACI} = \text{square root of } (((\text{PP-R} \times 20)/\text{HR-R})/1000) \times \text{Factor}$$

(9) *Total Body Oxygen Consumption*: (VO_2max, mL/kg/min). A valuable index of total body fitness at maximal exercise.

$$VO_2\text{max} = (((1.5/60) \times (60 - (100 - \%\text{HR})) + 4) \times \text{CO} \times 10)/\text{Lean Body Weight}$$

(10) *Metabolic Equivalent Unit* (MET): 3.5 ml of O_2/min/kg body weight. Generally accepted unitless parameter of ETT obtained as VO_2max/3.5.

(11) *Systolic Time Pressure* (STI, mmHg/s). This parameter is representing the force on the arterial wall during a unit time and correlated with the elasticity of the blood vessel walls (Belz, 1995).

(12) *Left Ventricular End Diastolic Pressure* (LVEDP, mmHg). This parameter was obtained by the following exponential equation using the NHA:

$$\text{LVEDP} = (\text{I-LCWI/A-LCWI}) - (10\text{^O},4342944819 \times \text{LVEDI}),$$

where I-LVCWI = Ideal Left Cardiac Work Index; A-LVCWI = Actual Left Cardiac Work Index; LVEDI = Left Ventricular End Diastolic Index.

The data of the Seattle Heart Watch clinical study were computed in three sequences (one in standing and two during treadmill stress testing) and the above listed 12 hemodynamic parameters were calculated for each sequence. For each actual hemodynamic parameter, the corresponding ideal hemodynamic parameters and percent differences were computed with the same heart rate. The differences from the ideal values were considered normal within ±20%. Most of the computed hemodynamic values were divided by the body surface area and expressed as an "indexed" form for individual comparisons.

Validity and Limitation of the NHA Clinical Decision System

The bias, precision and agreement of CO measurements by the NHA system were compared to the thermodilution CO technique applied to 203 ICU patients with different cardiac conditions (Kabal and Lagerman, 2004). The results of this previous retrospective study demonstrate the NHA system performs well over a wide range of CO values and within statistically accepted clinical accuracy. NHA clinical applications are limited to adults of both sexes over 18 years of age, provided that the input data are reliable and no significant arrhythmia is present.

RESULTS AND DISCUSSION

As a matter of study, the NHA belongs to the field of a composite scientific area comprising mathematics, applied computer science, and statistics to develop models

of complex problems. The application of this "combined" science approach is just beginning to enter into clinical medicine.

The NHA is essentially a clinical decision system which computes SV/CO and other related hemodynamic parameters. The NHA computation of SV has two segments. First, the ideal systolic and diastolic blood pressure values are calculated according to a given heart rate. Second, the pulse-wave volumes are calculated to obtain the ideal and actual stroke volumes. The NHA receives "typed-in" data for computation and can be used for multiple purposes, such as, prospective or retrospective studies and "what if . . ." research studies. In this paper, we describe a retrospective study utilizing the data of a large clinical study. Despite the fact that we were only able to use the average vital sign values and average anthropological data of Seattle Heart Watch clinical study, our objective was successfully achieved when the NHA results fell directly into the same diagnostic groups as the landmark clinical study.

Eleven actual and ideal parameters per subgroups (Upright-Rest, Exercise-1, and Exercise-2) are presented in Tables 2–5. Although the Seattle Heart Watch clinical study did not contain the calculated hemodynamic parameters, the ETT evaluation clearly designated four groups of cardiac conditions, namely, (a) Healthy (H), (b) Hypertensive (HT), (c) Angina Pectoris (AP), and (d) Postmyocardial Infarction (PMI). Our objective for conducting this research was to identify these cardiac condition groups using the NHA system.

From the tables of hemodynamic analysis, representative graphics are presented to view hemodynamic changes during ETT. Each table displays the ideal and actual values. The ideal parameters were calculated with the same heart rate as the actual parameters in each subgroup. The rise of the systolic blood pressure (SBP) and

Table 2. Hemodynamic Analysis of Exercise Performance in Healthy Group

Parameters	Standing			First exercise level			Second exercise level		
	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual
Tension Mean arterial BP (mmHg)	97	−4.7	92	97	5.7	102	97	12.5	109
Pulse pressure S–D arterial pressure diff. (mmHg)	53	−12.6	46	95	−17.2	79	127	−9.9	114
Chronotropy % Of maximum heart rate	40	0.0	40	60	0.0	60	93	0.0	93
Dynamia Cardiac index (L/min/m^2)	3.639	−12.6	3.180	10.516	−17.2	8.707	20.494	−9.9	18.465
Global resistance SVRI (dyn·s/cm^5/m^2)	2,040	9.7	2,238	649	30.6	848	291	28.6	374
Global capacity LCWI (kg·m/m^2)	4.7	−15.8	3.9	11.2	−7.9	10.3	15.4	10.0	17.0
Ejection Stroke index (mL/min/m^2)	51	−12.6	44	97	−17.2	81	122	−9.9	110
Inotropy Acceleration index (s^2)	1.09	−6.5	1.02	2.21	−9.0	2.01	3.96	−5.1	3.75
Oxygen consumption VO_2max/LEM (mL/kg/min)	5.0	−12.6	4.3	16.2	−17.2	13.4	37.8	−9.9	34.1
Metabolic equivalent unit METs (MaxVO_2/3.5)	1.4	−12.6	1.2	4.6	−17.2	3.8	10.8	−9.9	9.7
dP/dT Systolic time pressure (mmHg/s)	312	7.3	334	486	3.5	503	958	−2.1	938

Note. Ideal values are calculated at the corresponding actual heart rate.

Table 3. Hemodynamic Analysis of Exercise Performance in Hypertensive Group

Parameters	Standing			First exercise level			Second exercise level		
	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual
Tension Mean arterial BP (mmHg)	100	−7.3	92	100	18.2	118	100	24.9	124
Pulse pressure S–D arterial pressure diff. (mmHg)	67	−24.3	51	107	−22.1	83	131	−17.0	109
Chronotropy % Of maximum heart rate	44	0.0	44	65	0.0	65	95	0.0	95
Dynamia Cardiac index (L/min/m^2)	4.519	−19.1	3.656	11.904	−22.1	9.268	19.627	−17.0	16.290
Global resistance SVRI (dyn·s/cm^5/m^2)	1,673	34.1	2,244	581	56.9	911	318	57.5	500
Global capacity LCWI (kg·m/m^2)	5.8	−11.2	5.2	12.6	−0.7	12.5	16.0	17.1	18.7
Ejection Stroke index (mL/min/m^2)	59	−19.1	47	104	−22.1	81	118	−17.0	98
Inotropy Acceleration index (s^2)	1.31	−13.0	1.14	2.47	−11.8	2.18	3.98	−8.9	3.62
Oxygen consumption VO_2max/LEM (mL/kg/min)	6.5	−19.1	5.2	19.4	−22.1	15.1	37.3	−17.0	31.0
Metabolic equivalent unit METs (MaxVO_2/3.5)	1.8	−19.1	1.5	5.5	−22.1	4.3	10.7	−17.0	8.9
dP/dT Systolic time pressure (mmHg/s)	367	2.5	376	568	−1.4	560	1,009	−5.0	958

Note. Ideal values are calculated at the corresponding actual heart rate.

decline of diastolic blood pressure (DBP) during isometric exercise are characteristic responses of healthy adults regardless of gender, race, or exercise condition (Froelicher *et al*., 1993). These changes, shown in Graph 1, may induce only a slight increase in the mean arterial pressure (MAP) and widening of pulse pressure (PP) (Wolthuis *et al*., 1977).

The rise of SBP in healthy persons during exercise shows a logarithmic increase and reaches 25 mmHg or higher over the resting state (Froelicher *et al*., 1974). Hypertensive patients may reflect an increased SBP response to exercise (Lund-Johansen, 1988), as shown in the HT group. A recent study shows the exercise induced peak SBP of 200 mmHg or higher correlates independently with scintigraphic severity and extent of ischemia (Uehara *et al.,* 2000). Hypertension during exercise is also recognized as a poor prognosis and could lead to impairment of left ventricle function (Sanmarco *et al*., 1980). The SBP of AP and PMI groups showed a lower elevation, but without decline. In these groups, an elevation of DBP was also manifested, further decreasing the PP. Abnormal response, such as, increased DBP during exercise, always reflects deterioration of myocardial function and/or coronary artery disease (CAD) (Paraskevaidis *et al*., 1993).

The HR during ETT progressively increases to a sex and age dependent predetermined maximum level and normally cannot accelerate further (Filipovsky *et al*., 1992). An impaired heart rate response to graded exercise, called chronotropic incompetence (Lauer *et al*., 1996), is predictive of increased CAD incidence and increased mortality. Because the NHA system compares the actual and ideal hemodynamic changes at the actual heart rate, the blood pressure varies due to attenuated exercise HR responses can easily be detected.

A healthy person has an exercise HR-range (from rest to 60% maximal HR), regardless of exercise time or

workload (Hammond and Froelicher, 1985). Therefore, the resting HR is presented at 40% of the maximum HR (Karvonen *et al*., 1957). The resting HR is influenced by fever, endocrine conditions, environment, psychological state, and physical fitness. For example, the resting HR of trained athletes is significantly lower than 40% maximal HR (Saltin and Astrand, 1967), therefore, the exercise HR-range is larger then the normal 60% maximal HR. Thus, the corresponding maximum O_2 uptake or VO_2max could be comparably higher (Brawner *et al*., 2002; Cheng *et al*., 2002).

VO_2max increases linearly during ETT and is parallel with HR (Fairbarn *et al*., 1994). Their regression lines are close but not identical. Both parameters decline with age and are influenced by gender (Weisfeldt *et al*., 1995). It is now generally accepted that VO_2max levels during ETT are estimated by nomograms according to workload achieved (Lehmann *et al*., 1997). We computed the VO_2max by using our algorithms, in Graph 2, which resulted in uniform agreement to the results of the Seattle Heart Watch clinical study.

If VO_2max is divided by 3.5, the "Metabolic Equivalent" or MET is obtained (Jette *et al*., 1990). Under standard conditions, the quantity of oxygen consumed by a healthy person in a resting mode equals approximately 3.5 mL of O_2/kg/min. The use of MET as a representative value of exercise capacity (EC) is well established (Fletcher *et al*., 1990; Morris *et al*., 1991). EC is a convenient way to compare individual performance and appears as an independent factor in cardiovascular mortality (Buttrick and Scheuer, 1994). In this retrospective study, the four groups showed characteristic METs changes. In the healthy group, the METs were in close agreement with the ideal values. The HT group exhibited a 17% decrease at peak exercise level. The AP and PMI groups operated at significantly lowered peak values as

Table 4. Hemodynamic Analysis of Exercise Performance in Angina Pectoris Group

Parameters	Standing			First exercise level			Second exercise level		
	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual
Tension Mean arterial BP (mmHg)	101	−8.3	92	101	4.3	105	101	8.6	109
Pulse pressure S–D arterial pressure diff. (mmHg)	68	−33.9	45	110	−37.3	69	125	−34.4	82
Chronotropy % Of maximum heart rate	43	0.0	43	67	0.0	67	83	0.0	83
Dynamia Cardiac index (L/min/m^2)	4.404	−31.1	3.033	12.015	−37.3	7.533	16.455	−34.4	10.795
Global resistance SVRI (dyn·s/cm^5/m^2)	1,739	39.2	2,420	582	75.7	1,022	401	78.0	714
Global capacity LCWI (kg·m/m^2)	5.8	−32.9	3.9	12.8	−25.9	9.5	15.3	15.0	13.0
Ejection Stroke index (mL/min/m^2)	59	−31.1	40	104	−37.3	65	114	−34.4	75
Inotropy Acceleration index (s^2)	1.27	−18.7	1.03	2.50	−20.8	1.98	3.31	−19.0	2.68
Oxygen consumption VO_2max/LEM (mL/kg/min)	6.3	−31.1	4.3	19.8	−37.3	12.4	29.6	−34.4	19.4
Metabolic equivalent unit METs (MaxVO_2/3.5)	1.8	−31.1	1.2	5.7	−37.3	3.6	8.5	−34.4	5.5
dP/dT Systolic time pressure (mmHg/s)	322	16.8	376	499	15.3	576	673	12.2	755

Note. Ideal values are calculated at the corresponding actual heart rate.

Table 5. Hemodynamic Analysis of Exercise Performance in Postmyocardial Infarction Group

Parameters	Standing			First exercise level			Second exercise level		
	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual	Ideal	% Diff. of Ideal	Actual
Tension Mean arterial BP (mmHg)	100	−7.8	92	100	0.9	101	100	6.8	107
Pulse pressure S–D arterial pressure diff. (mmHg)	70	−39.6	42	109	−42.1	63	127	−38.4	78
Chronotropy % Of maximum heart rate	43	0.0	43	66	0.0	66	86	0.0	86
Dynamia Cardiac index (L/min/m^2)	4.402	−36.3	2.804	11.596	−42.1	6.717	17.115	−38.4	10.547
Global resistance SVRI (dyn·s/cm^5/m^2)	1,731	48.4	2,569	602	84.8	1,113	380	88.8	717
Global capacity LCWI (kg·m/m^2)	5.7	−38.5	3.5	12.5	−33.2	8.3	15.4	−18.9	12.5
Ejection Stroke index (mL/min/m^2)	58	−36.3	37	101	−42.1	58	114	−38.4	70
Inotropy Acceleration index (s^2)	1.29	−22.3	1.00	2.44	−23.9	1.85	3.43	−21.5	2.69
Oxygen consumption VO_2max/LEM (mL/kg/min)	6.3	−36.3	4.0	18.8	−42.1	10.9	30.9	−38.4	19.1
Metabolic equivalent unit METs (MaxVO_2/3.5)	1.8	−36.3	1.1	5.4	−42.1	3.1	8.8	−38.4	5.4
dP/dT Systolic time pressure (mmHg/s)	313	21.1	379	470	20.7	567	688	16.1	799

Note. Ideal values are calculated at the corresponding actual heart rate.

compared to the ideal levels with 34 and 45% decreases, respectively.

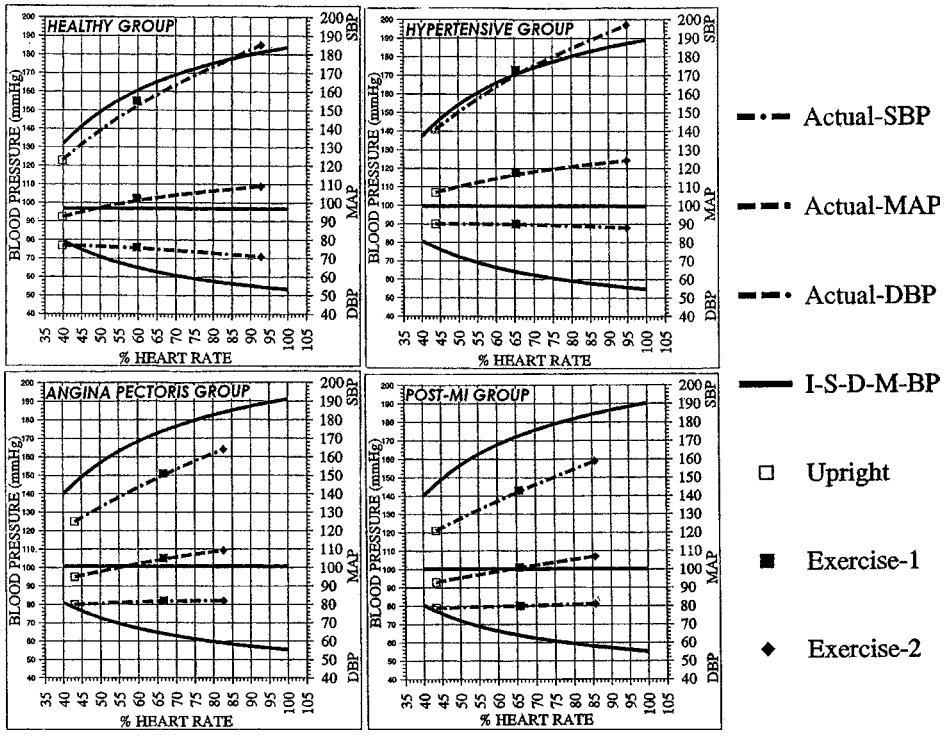
In healthy persons, the stroke index (SI) increases exponentially during ETT when plotted against the % HR (Graph 3).

At approximately 75% of the maximum HR, the SI does not increase further. Hence, the cardiac index (CI) at this level can only be augmented by elevating the HR to reach its peak CI (Higginbotham *et al.*, 1986). In elite athletes, SI could increase continuously over the full range of exercise (Zhou *et al.*, 2001). In elderly persons the exponential curve of SI is actually "curving back." However, this alteration is not completely irreversible. The age-associated decrease of left ventricular performance by moderate/intense endurance exercise training can be beneficially influenced. Cardiac adaptations contribute to an enhanced SI (with increased CI) in older endurance-trained men (Rodeheffer *et al.*, 1984).

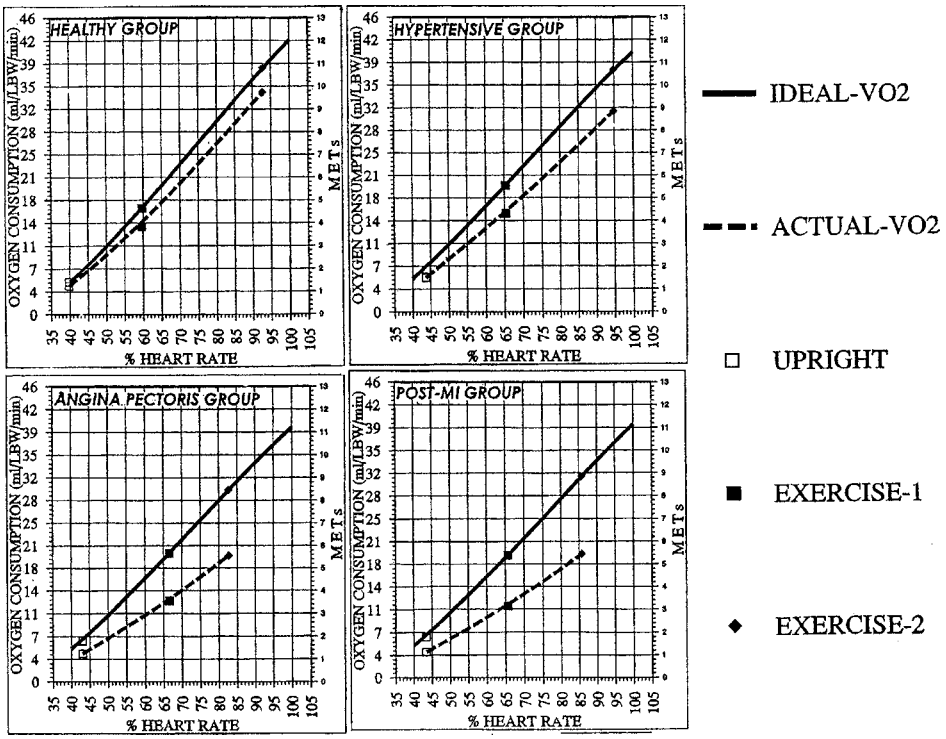
It is a convenient way to analyze the changes of the SV/SI curve plotted against the % maximum HR. The point where SI is not increasing, compared to the ideal SI curve, provides the opportunity to calculate the cardiac reserve (CR) during ETT. This observation supplies the scientific basis to determine the appropriate maximum cardiopulmonary exercise HR. In the groups of AP and PMI, a left shift of the SI curve demonstrates the inability of the left ventricle to perform adequately, thus demonstrating the lack of CR.

Myocardial contractility, or the inotropic state, represents the shortened capacity of the heart muscle at a certain workload (Rodeheffer *et al.*, 1984). The increased contractility during exercise (especially in younger patients) is attributed to acute catecholamine effect, as well as, to intrinsic cardiac adaptations.

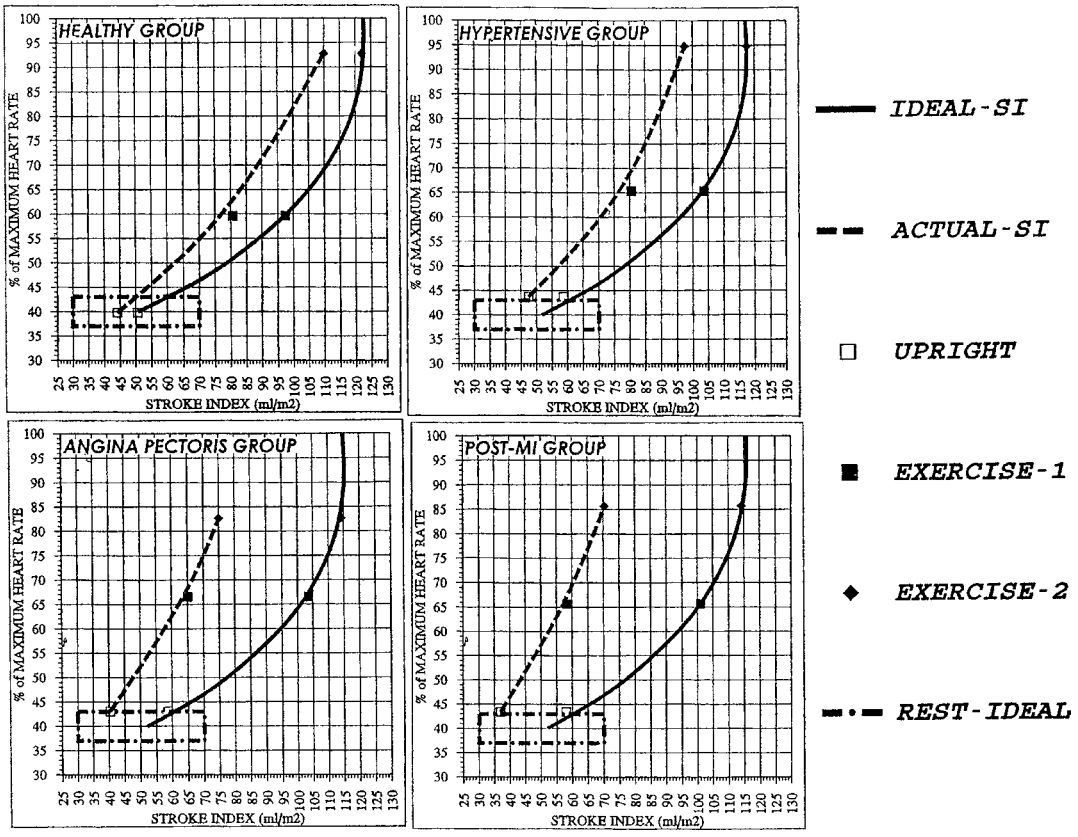
Clinically, the percent ejection fraction is accepted to approximate myocardial contractility, but this assumption is misleading. The acceleration index (ACI) provides



Graph 1. Blood pressure and heart responses in the four groups of the clinical trial.



Graph 2. VO_2max and/or METs in the four groups of the clinical trial.



Graph 3. Correlation between stroke index and % HR in the four groups of clinical trial.

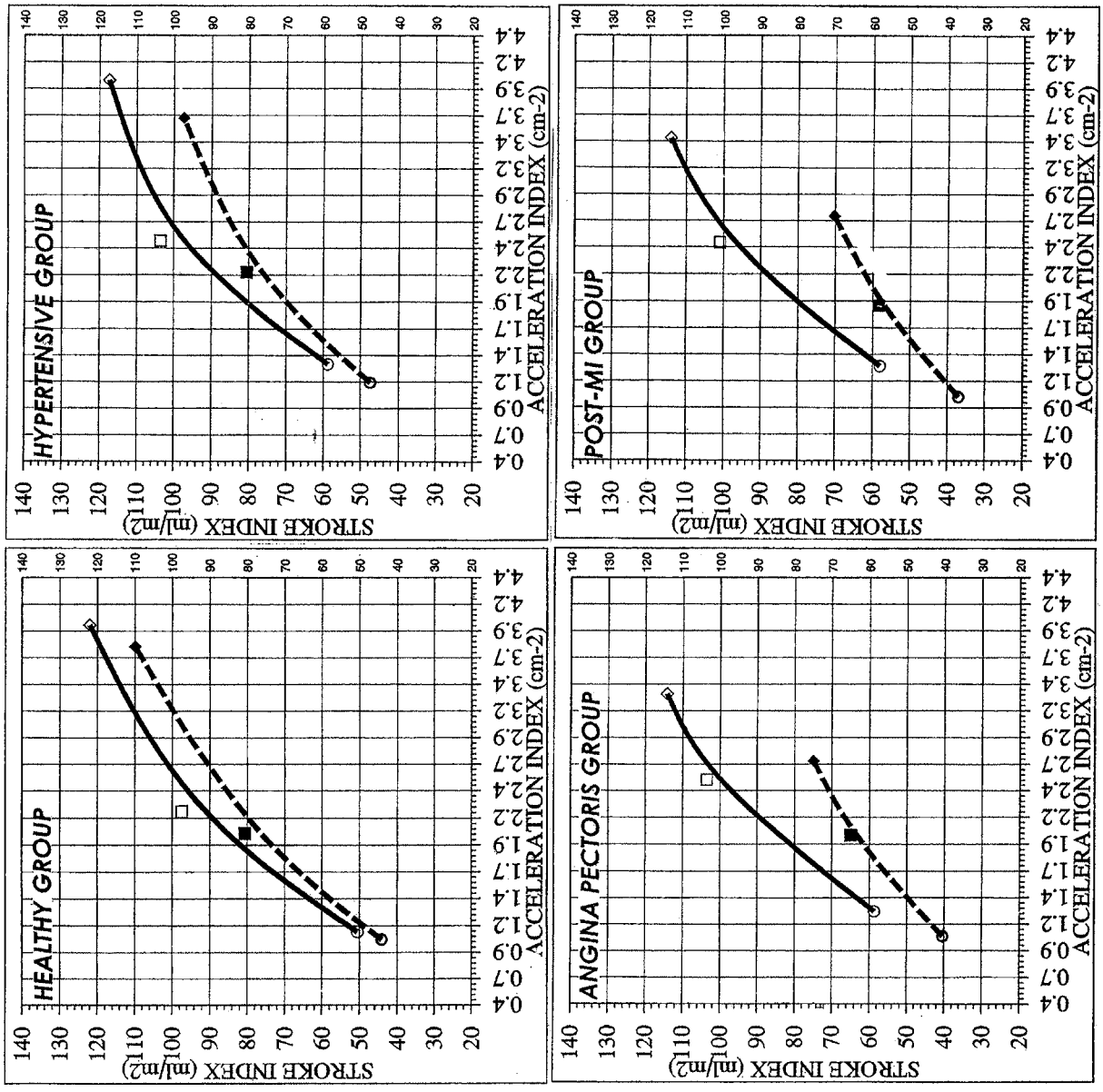
superior information regarding the speed of ejection (first 10–15 μs of systole) before other factors can interfere. Thus, the left ventricular function curve of SI/ACI can be a convenient and practical way to express and demonstrate myocardial contractility changes during ETT (Graph 4).

The H group demonstrated a normal ascending curve. However, the HT, AP, and PMI groups manifested a progressively increased deficit. The differences from the peak ideal ACI values were in the same line of -8.9 to -19% and 26.2%. These changes in ACI during ETT proved to be very useful evidence of left ventricular dysfunction.

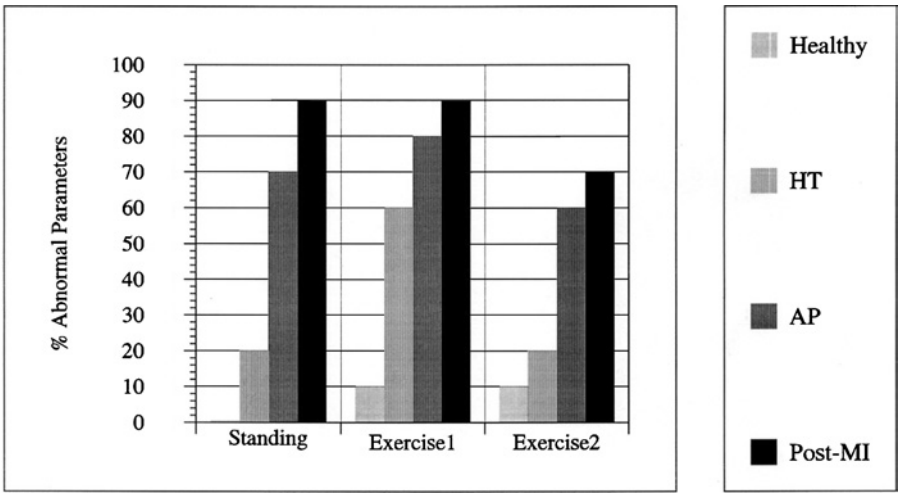
SUMMARY

The purpose of this retrospective study was to use the NHA system to reproduce the results of the Seattle Heart Watch clinical study. This well-known clinical study used conventional ETT to identify CAD and published the average data of the different groups with healthy, hypertensive, angina pectoris, and postmyocardial infarction participants. We used this same data and computed the hemodynamic profile of each groups. Because of the limited data published by the Seattle Heart Watch study, our research only deals with the application of the NHA system to select/identify the reported groups according to their hemodynamic parameters and not by the application of the typical statistical evaluation (Graph 5).

Graph 5 demonstrates the percent cumulative abnormal responses (% CAR) which were obtained by calculating the number of total abnormal parameters (with $\pm 20\%$ difference from the computed corresponding ideal parameters) in each subgroups: upright and during two exercise periods. The % CAR of the H group was zero in rest-standing and, during exercise, mildly changed. The HT group, which represented a mild hypertensive state, exhibited a higher % CAR response. However, the AP and PMI groups clearly presented incidences of % CAR in each subgroup. The first exercise subgroups reflected higher percent abnormal responses than the second



Graph 4. Myocardial contractility as related to SI in the four groups of the clinical trial.



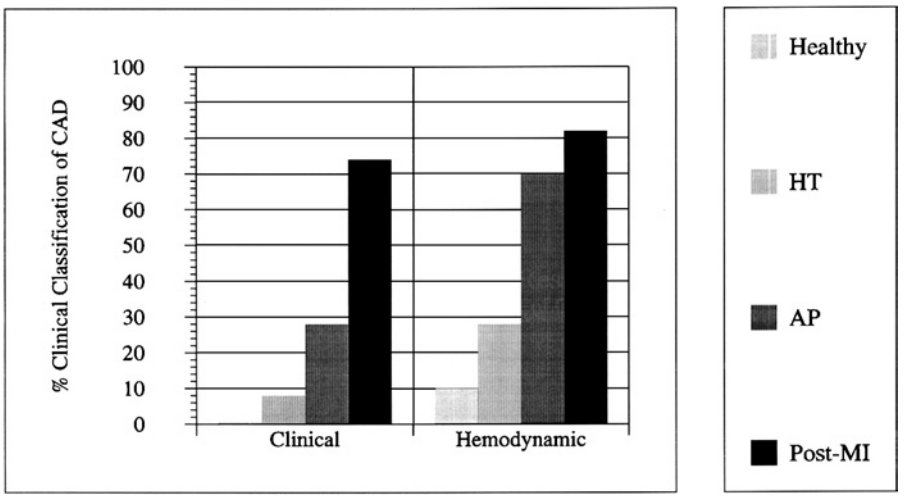
Graph 5. % Cumulative abnormal hemodynamic parameters of the four groups of the clinical trial.

exercise subgroups. Nevertheless, their change in the second subgroups reached 60 and 70% respectively.

Graph 6 presents the total group summaries of % CARs compared with the percent clinical classification of CAD during ETT according to cardiac diseases in each of the four groups.

In each of the three subgroups, 11 representative parameters, such as, MAP, PP, CI, SVRI, LCWI, SI, ACI, VO_2, METs, and STP (Tables 2–5) were taken into consideration. Altogether, 30 hemodynamic parameters were included. The % CAR was calculated using parameters within ±20% in each subgroup and their averages calculated. Heart rate differences were not involved because the calculated ideal HR was the same as the corresponding actual HR. The % CAR of each hemodynamic profile obtained by the NHA system, as compared to the published clinical classification of heart disease of the Seattle Heart Watch clinical study was closely matched in all clinical groups.

The results of this retrospective study prove the hemodynamic computation of the NHA system is a valid approach to evaluate ETT. We conclude that the NHA clinical decision system deserves further studies to fully determine its potential to the field of medical diagnostics.



Graph 6. % Cumulative abnormal hemodynamic responses compared with the % clinical classification of CAD of clinical trial.

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