Heart rate—left ventricular ejection time relations¹

Variations during postural change and cardiovascular challenges

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Regression equations for heart rate (HR)—ejection time (LVET) relations provide the appropriate factors for predicting or correcting left ventricular ejection time at any HR. We investigated HR-LVET regressions under different conditions common to both physiological and clinical studies of LVET which had been selected because of predictably different physiological responses. Ten normal subjects were studied during both supine and sitting rest and during isometric handgrip (IHG) in both supine and sitting postures and 10 during head-up tilt. Unexpectedly, as compared with pre-exercise rest on a bicycle ergometer, the slope for the resting state on a chair was slightly flatter, and LVET values were uniformly higher throughout the range of HRs measured.

Differences among HR-LVET slopes and intercepts appeared to reflect the established behaviour of stroke volume and ejection rate under the conditions studied. Differences observed among intercepts, especially in supine vs. upright postures, are substantial and require that the appropriate intercept be applied in predicting LVET at a given HR. Differences among slopes, while not statistically significant, may, under practical conditions, lead to unacceptable error if the appropriate slope factor is not used in correcting LVET for HR.

Left ventricular ejection time (LVET) is often measured to assess left ventricular performance under a variety of conditions (Kesteloot and Denef, 1970; Benchimol and Matsuo, 1971; Parisi, Salzman and Schechter, 1971; Takahashi and Moritz, 1972; Matsuura and Goodyer, 1973). Because LVET is dependent on heart rate (HR) (Braunwald, Sarnoff, and Stainsby, 1958; Jones and Foster, 1964) it is common practice to correct LVET for HR based on linear regression equations. The corrected value, the ejection time index (ETI), is calculated as follows: $ETI = LVET - b(HR)$, where b is the slope of the regression analysis of LVET on HR. By employing the intercept (a) of the regression equation, it is also possible to predict

LVET for a given HR using the formula $LVET = a + b(HR)$.

While LVET is HR dependent, the exact relation varies according to factors such as age, sex, and health status (Weissler, Harris, and White, 1963; Harris *et al.*, 1964; Spodick and Kumar, 1968; Kesteloot and Denef, 1970; Willems *et al.*, 1970; Takahashi and Moritz, 1972). Physiological challenges such as supine (Lindquist, Spangler, and Blount, 1973; Maher *et al.*, 1974) and upright (Lance and Spodick, 1976) bicycle exercise also effect differences in the HR-LVET relation. Demonstration of the HR-LVET relations under the different conditions in which LVET must be corrected for HR are of both theoretical and practical importance. They are of theoretical importance as an expression of the underlying physiology of these conditions. They are of practical importance as appropriate factors for correcting data.

To obtain a range of LVET behaviour, we chose

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postural changes, tilt, and isometric exercise because they are simply administered, common noninvasive challenges which evoke predictable cardiac responses (Stevens, 1966; Abelman and Fareeduddin, 1969; Helfant, DeVillas, and Meister, 1971; Spodick, Meyer, and St. Pierre, 1971; Siegel *et al.*, 1972; Fisher *et al.*, 1973). Though LVET has been measured during isometric exercise (Siegel *et al.*, 1972; Quarry and Spodick, 1974) and tilt (Stafford, Harris, and Weissler, 1970; Zambrano and Spodick, 1974) it has been corrected for HR by equations determined under other circumstances, owing to the absence of investigations of the actual HR-LVET regression analysis not only during these conditions but also during rest and stress testing in different postures.

The purpose of this study was to determine HR-LVET regression relations in different postures, including tilt, and during isometric exercise. We studied subjects in the resting state in supine and sitting positions, during isometric handgrip (IHG) in supine and sitting positions and during 70° head-up tilt.

Methods

All subjects were studied in the morning in the postabsorptive state and after a 30-minute rest period. Ten subjects were studied before and during isometric handgrip exercise in the supine and sitting positions and 10 during 70° head-up tilt. These two groups represented the same population, i.e. both comprised normally active healthy men, aged 22 to 32, none being a trained athlete or a hospital patient. All had a normal history, physical examination, 12-lead electrocardiogram, and chest x-ray film.

Recordings included a bipolar electrocardiogram and a right external carotid pulse curve using equipment previously described (Pigott *et al.*, 1971). The electrocardiogram and carotid pulse curve were simultaneously recorded on a Hewlett-Packard optical recorder No. 568-100A at a paper speed of 75 mm/s.

Recordings

Supine rest The supine controls were recorded after 15 to 30 minutes' rest in supine position, just before each of four levels of supine IHG. Thus, 4 supine resting recordings were taken for each of the 10 subjects.

Sitting rest The sitting controls were recorded after 15 to 30 minutes rest in a cushioned chair, just before each of 4 levels of sitting IHG. Thus, 4 sitting recordings were taken for each of the 10 subjects.

Supine IHG IHG was accomplished by having the subjects squeeze a rolled pressure cuff which had been inflated to 20 mmHg (Quarry and Spodick, 1974). The cuff was connected to a sphygmomanometer, the dial of which provided the feedback for subjects to maintain a constant level of contraction for the duration of each IHG. In order to obtain a wide range of HRs, four levels of IHG were studied. The four levels of IHG consisted of 15, 30, 50, and 100 per cent maximum voluntary contraction (MVC). MVC was established as the maximum pressure developed (as recorded on the sphygmomanometer) out of three trials in which each subject had been instructed to squeeze the rolled cuff as hard as possible. The 15 and 30 per cent MVC were held for 4 minutes with tracings recorded at 30-second intervals; 50 per cent MVC was held for a maximum duration up to 4 minutes, with tracings recorded at 30-second intervals; the maximal level was held for approximately 30 seconds with tracings recorded just before release.

Sitting IHG Recordings for sitting IHG were identical to those of supine isometric handgrip, with the single difference being that of posture.

Tilt Head-up tilt to an angle of 70° was recorded at 1, 4, and 7 minutes of tilt on a standard NASA tilt table (i.e. padded saddle without foot supports).

Measurements

HR was determined from the electrocardiogram by dividing 60 000 by the RR interval of the preceding cycle measured in milliseconds. LVET was measured as the time in milliseconds from the rapid upstroke to the incisura of the carotid pulse curve. Five LVETs with corresponding HRs were measured for each subject at each of the recording times indicated above. The mean LVET and HR values of these five beats were determined.

Statistical analyses

Regression analysis (including slope, intercept, and standard error of estimate) was carried out for each of the conditions under investigation. In order that each subject be used as the experimental unit, mean values within individuals were determined for each of the conditions under investigation, e.g. the mean value of the four supine resting recordings for each of the 10 subjects was determined. Thus, 10 points (one for each subject) were used in the regression analysis for supine rest, and formed the basis for comparisons with other regressions. Similarly, mean values within individuals were determined for sitting rest.

In a previous investigation (Spodick *et al.*, 1971) it was shown that HR and LVET did not vary

FIG. 1 Heart rate—left ventricular ejection time relation showing postural effects at rest. Slopes are virtually identical, but intercepts differ considerably. Equations represent regression analysis showing intercept, slope, and standard error of estimate. NB: sitting rest=sitting in cushioned chair (compare Fig. 5).

among 1, 4, and 7 minutes of tilt. The tilt data were, therefore, handled in the same way as the supine and sitting rest data, with a mean value determined within individuals. Thus, each of the 10 subjects investigated during tilt contributed one point in the regression analysis.

In order to obtain a wide range of HRs, four levels of IHG were studied in both supine and sitting positions. Without sacrificing information yet still having each subject contribute equally in the statistical analysis, the mean values within individuals were determined for (1) 15 per cent, (2) 30

TABLE HR-LVET regression equations for different conditions

	Intercept	Slope	Standard error of estimate
A. Supine rest	376.4	-1.16	± 9.76
B. Supine isometric handgrip	381.5	-1.20	± 9.49
C. Sitting rest in cushioned chair	354.5	-1.23	± 11.00
D. Sitting isometric handgrip	372.1	-1.32	± 10.10
E. Tilt	374.5	-1.68	± 12.20
F. Sitting rest on bicycle ergometer	353.6	-1.50	± 11.04

per cent, and (3) 50 and 100 per cent, combined. Regression analyses were performed on each of these levels of IHG. A pooled slope, intercept, and standard error of estimate were then determined for (1) supine IHG and (2) sitting IHG. These two IHG regressions then formed the basis for the comparison with other regressions.

Results

Results are summarized in the Table and illustrated in Fig. 1 to 5.

Supine rest

The HR-LVET relation for the 10 young adult males during supine rest (before IHG) is shown in Fig. 1. This relation had a slope of -1.16 ms/beat, an intercept at 376.4 ms and a standard error of estimate (SEE) ± 9.76.

Sitting rest The HR-LVET relation during sitting rest in a cushioned chair (before IHG) for the same 10 subjects as recorded during supine rest is also shown in Fig. 1. This relation had a slope of 1.23 ms/beat, an intercept at 354.5 ms, and SEE ± 11.00.

Supine IHG

The HR-LVET relation during supine IHG for the

FIG. 2 Heart rate—left ventricular ejection time relation during isometric handgrip (IHG) exercise in supine position. Measurements cover range of 15, 30, 50, and 100 per cent maximum voluntary contraction.

FIG. 3 Heart rate—left ventricular ejection time relation during isometric handgrip (IHG) exercise in sitting position. Measurements cover range of 15, 30, 50, and 100 per cent maximum voluntary contraction.

same 10 subjects as recorded during supine and sitting rest is shown in Fig. 2. This relation had a slope of -1.20 ms/beat, an intercept at 381.5 ms, and $SEE \pm 9.49$.

Sitting IHG

The HR-LVET relation during IHG in sitting position for the same 10 subjects as recorded during supine and sitting rest and supine handgrip is shown in Fig. 3. This relation had a slope of -1.32 ms/beat, an intercept at 372.1 ms, and $SEE \pm 10.10$.

Tilt

The HR-LVET relation for the other set of 10 young adult men during 70° head-up tilt is shown in Fig. 4. This relation had a slope of -1.68 ms/beat, an intercept at 374.5 ms, and $SEE \pm 12.20$.

Comparison of slopes

The t test for slopes showed no differences among any of the comparisons made. Even the largest difference between tilt (-1.68) and supine rest (-1.16) did not reach significance.

Discussion

We had previously investigated the HR-LVET relation during supine rest in normal men 21 to 35

years of age (Spodick and Kumar, 1968). The regression equation established at that time was $LVET = 375.7 - 1.22 HR$, while the supine rest equation determined in the present investigation for a smaller group of men of comparable age and health status, but entirely different subjects, showed $LVET = 376.4 - 1.15 HR$. In practice, with LVET expressed in milliseconds, investigators have rounded the slope to the nearest tenth to correct LVET for HR (Parisi *et al.*, 1971; Maher *et al.*, 1974; Quarry and Spodick, 1974). Both these slopes thus round to 1.2 ms/beat yielding, for practical purposes, virtually identical equations.

Supine rest vs. sitting rest

In comparing the resting HR-LVET relation in supine and sitting positions (Fig. 1; Table—A, C) it is apparent that the slopes are similar, with similar scatter around the regression line, as evidenced by the comparable standard errors of estimate. The single important difference is that the curve during sitting rest is uniformly lower and consequently has an intercept which lies lower on the ordinate than that of supine rest (a difference in intercepts of 21.9 ms). Since LVET varies directly with stroke volume (SV) this difference appears to reflect the known reduced SV with upright, as compared with supine posture (Bevegård, Holmgren, and Jonsson, 1963; Grimby, Nilsson, and Sanne, 1966; Astrand

FIG. 4 Heart rate—left ventricular ejection time relation during 70° head-up tilt.

and Rodahl, 1970). The fact that the two curves parallel one another suggests that if other variables affecting LVET are present, they must affect the LVET in a direction and magnitude which is similar for both supine and sitting rest.

Control vs. IHG

A statistical comparison of supine resting values with those of supine IHG shows no difference between slopes, while differences between intercepts and standard errors of estimate are small (Table—A, B). Likewise, a comparison of sitting rest with sitting IHG shows essentially the same similarities between curves (Table—C, D). The effects of IHG on SV have been reported and vary from small increases (Fisher *et al.*, 1973) to no change or even decreases at higher levels of contraction (Lind, 1970), while ejection rate has been shown to decrease in the presence of a high afterload (Braunwald *et al.*, 1958). Whether the changes in these variables during IHG were minimal or had opposing effects (e.g. reduced SV would shorten LVET, while reduced ejection rate would lengthen LVET) is not clear from our data. However, the important finding, to which this study is addressed, is that it appears that factors associated with IHG in either supine or sitting position do not alter the HR-LVET relation from that of the control state.

Supine IHG vs. sitting IHG

A comparison of postural effects on IHG yields similar findings to those of the postural differences during rest. Again, similar HR-LVET slopes occur during supine and sitting IHG (Table—B, D). As with supine vs. sitting rest, however, the curve during sitting IHG remains uniformly lower and thus has a lower intercept than that during supine IHG, a difference which again appears to reflect the smaller SV with upright posture noted previously. Since IHG was performed at identical stress levels in both sitting and supine positions, the data in both postures should represent comparable physiological challenges. Thus, once resting postural differences are taken into account, the increases over resting levels in variables such as cardiac output and adrenergic activity should be comparable during IHG for both supine and sitting postures. The similar HR-LVET slopes for both conditions support such comparability and suggest that determinants of LVET (such as SV and mean rate of ejection) do not act in a disproportionate fashion during IHG in supine as compared with sitting position.

Tilt vs. rest and IHG

The slope during tilt tended to be greater than the

slopes of the other four conditions studied in this investigation, but the differences between tilt vs. supine and sitting rest and supine and sitting IHG were not significant. The 95 per cent confidence interval of the slope for tilt is -1.168 ± 0.679 . Thus, the difference between tilt and the other slopes may be less or substantially greater with additional observations. An important consideration, however, should be the practical implications of this difference between slopes, e.g. if a slope factor of 1.2 (supine rest) rather than the observed tilt slope of 1.68 were multiplied by HRs recorded during tilt (range of 55 to 101 beats per minute), the resultant corrected ejection time would be substantially underestimated. Since ETI is determined in order to evaluate other factors (principally SV) affecting LVET, inappropriate conclusions regarding cardiac function may also be drawn. Thus, the importance of using appropriate correction factors is clear.

The regression line for LVET on HR during tilt was below that during rest and IHG within the range of HRs studied. This finding is consistent with the expected large reduction in SV in tilted normal subjects (Zambrano and Spodick, 1974). The sharper slope for tilt reflects a progressively larger reduction in LVET with higher HRs during tilt as compared with rest and IHG (Table). This could represent a disproportionate reduction in SV with increasing HRs during head-up tilt. Increased ejection rate via improved contractility or Starling effect would also explain decreased LVET (Braunwald *et al.*, 1958). However, tilt does not appear to change contractility (Paley *et al.*, 1971) and reduces preload (Abelmann and Fareeduddin, 1969). Improved ejection rate, therefore, does not seem to be a factor effecting the progressively greater shortening of LVET with increasing HR during tilt as compared with rest and IHG.

Sitting controls

In a previous investigation (Lance and Spodick, 1976) we studied the HR-LVET relation during rest, before bicycle exercise, with subjects seated on the bicycle ergometer and feet resting on the pedals. The subjects were entirely comparable to those in this study.

The slopes do not differ significantly; Fig. 5 shows the slope to be steeper and LVETs uniformly lower for subjects seated on the bicycle ergometer than that for subjects seated in a chair. The 95 per cent confidence interval for the slope for bicycle ergometer sitting is -1.50 ± 0.629 —again suggesting that the difference between slopes for sitting rest on a chair vs. on a bicycle ergometer may be less or substantially greater. The intercepts for the two

FIG. 5 Comparison of heart rate—left ventricular ejection time relations during upright rest: sitting in chair versus sitting on bicycle ergometer.

conditions are similar, but this is because of the steeper slope with bicycle sitting.

Data have been reported for 'sitting rest', but these have included not only chair but bicycle ergometer (Bevegård *et al.*, 1963) without accounting for or acknowledging potential differences between the two. As was pointed out in the discussion of tilt, if the slope factor is used to correct LVET for HR, even slope differences of the magnitude here observed can, in practice, lead to substantially different results—and conclusions. It, therefore, seemed important to point out these potential differences and the possibilities of errors if the two 'resting states' are used interchangeably.

Conclusions

Comparison of the heart rate-ejection time relation during supine and sitting rest on both a chair and a bicycle ergometer, during isometric handgrip in both supine and sitting postures, and during head-up tilt, reveal differences among the respective regression equations, which can be explained by the well-established differences in stroke volume and ejection rate among these states. These differences appear to account for the fact that under conditions in which stroke volume variations should be the major determinant, slopes will be similar, but intercepts will vary. Thus, our regression lines for supine

versus sitting rest in a chair, for example, have similar slopes, but the line for sitting rest remains uniformly below that for supine rest. Similar trends are also indicated for supine versus sitting isometric exercise; the curves parallel each other, but the curve for sitting IHG remains below that of supine IHG, apparently entirely because postural reduction of SV in the sitting position (Åstrand and Rodahl, 1970; Bevegård *et al.*, 1963; Grimby *et al.*, 1966). In contrast, during pre-exercise upright rest on the bicycle ergometer, there is a tendency toward a sharper decrease in LVET at increased heart rates and, hence, a somewhat steeper regression slope than for other resting conditions. It appears that when increases in HR accompany greater increases in stimuli which reduce SV or increase ejection rate, the HR-LVET slope becomes sharper.

Because of potential differences, it is suggested that clinicians and researchers use correction factors appropriate to the conditions being studied. Furthermore, since substantial differences among intercepts are presented, caution should be applied if the intercept factor is used to predict LVET for HR.

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