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Range of Tricuspid Regurgitation Velocity at Rest and During Exercise in Normal Adult Men: Implications for the Diagnosis of Pulmonary Hypertension

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OBJECTIVES The aim of this study was to explore the full range of tricuspid valve regurgitation velocity (TRV) at rest and with exercise in disease free individuals. Additionally we examined the relationship of stroke volume (SV), cardiac output (CO) and TRV to exercise capacity.

BACKGROUND Doppler evaluation of TRV can be used to estimate pulmonary artery systolic pressure (PASP). Most studies have assumed TRV ≤2.5 m/s as the upper limits of normal. The full range of TRV with exercise has been incompletely defined.

METHODS Highly conditioned athletes (n = 26) and healthy, active, young male volunteers (n = 14) underwent standardized recumbent bicycle exercise. Exercise parameters included: TRV, SV, CO, systolic (SBP) and diastolic (DBP) systemic blood pressure.

RESULTS Tricuspid valve regurgitation, SV, HR and CO were significantly higher in athletes than in nonathletes over all workloads, including rest. Systolic blood pressure and DBP did not show significant differences between the two groups.

CONCLUSIONS This study defines the upper physiologic limits of TRV at rest and during exercise in normals and provides a noninvasive standard for the diagnosis of pulmonary hypertension. (J Am Coll Cardiol 1999;33:1662–6) © 1999 by the American College of Cardiology

Tricuspid regurgitation peak velocity (TRV) has been shown to correlate with pulmonary artery systolic pressure (PASP) at rest (1–3) and with exercise (3–7). By using the modified Bernoulli equation ($\Delta p = 4V^2$), the pressure gradient between the right ventricle and right atrium can be calculated. Right ventricular systolic pressure can be calculated as: right ventricular systolic pressure = 4 TRV^2 + right atrial pressure (RAP), where RAP equals estimated right atrial pressure. Right atrial pressure can be estimated from the jugular veins or from the inferior vena cava as imaged with two-dimensional echocardiography. Alternatively an empiric value can be utilized. There currently is no consensus among laboratories with respect to estimation of RAP for calculation of PASP. In the absence of obstruction to right ventricular outflow, right ventricular systolic pressure equals PASP. Traditionally it has been assumed that TRV ≤ 2.5 m/s. This corresponds to PASP ≤35 mm Hg (RAP assumed to be ≤10 mm Hg) and represents the upper limit in normals (1–3). The aim of this study was to explore the full spectrum of the physiologic TRV response during graded recumbent echo-Doppler bicycle exercise in young, highly conditioned male athletes and healthy, normal controls.

METHODS

Study population. We evaluated 26 NCAA Division I varsity male ice hockey players (mean age 20.26 ± 1.66 yr, range 18 to 23) with two-dimensional and Doppler echocardiography at rest and during recumbent bicycle exercise. For comparison we also evaluated 14 normally active (not competitive athletes) male volunteers (mean age 18.9 ± 0.9, range 18 to 21 years). Subject characteristics are outlined in Table 1. The study had been approved by the Human Subjects Review Committee at the University of Michigan.

2D echocardiography measurements. Standard two-dimensional measurements (left ventricular diastolic and systolic diameters, interventricular septum and posterior wall thickness, left atrium, aorta, left ventricular outflow tract) were obtained in the parasternal long axis view with

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Abbreviations and Acronyms

CO = cardiac output
DBP = diastolic blood pressure
EF = ejection fraction
PASP = pulmonary artery systolic pressure
RAP = right atrial pressure
SBP = systolic blood pressure
SV = stroke volume
TRV = tricuspid regurgitation velocity

the patient in the left lateral position (8). Left ventricular ejection fraction (EF) was calculated by Simpson's rule in the apical four chamber view (9). Left ventricular stroke volume was calculated as left ventricular outflow tract area × outflow tract time velocity integral. Cardiac output (CO) was calculated as SV × heart rate.

Echocardiography Doppler bicycle exercise. The athletes and the control subjects underwent a standardized echocardiography Doppler bicycle exercise study in the recumbent position; workload was increased by 40 watts every 2 min to a maximum of 240 watts. The protocol included both a low intensity "warm up" and a "cool-down" phase. Variables of systolic performance and TRV were analyzed at each stage (10,11). Pulmonary artery systolic pressure was estimated at rest and during exercise as $4TRV^2$ + 5 mm Hg (12). Agitated saline was injected intravenously to enhance the continuous-wave spectral Doppler signal of tricuspid regurgitation in all subjects. All studies were reviewed and analyzed off line by two observers.

Statistical analysis. Data for study population demographics and echocardiographic measurements (linear and volume) are presented as mean ± SD. Doppler data at the time of exercise are presented with 95% confidence intervals. Study population characteristics (age, weight, etc.) and left ventricular dimensions and volumes were compared based on Student *t* tests. For parameters measured during exercise (heart rate, blood pressure, Doppler parameters, PASP, etc.), athlete and nonathlete data were compared using repeated measures analysis of variance (SAS Proc Mixed software package, SAS Institute, Cary, North Carolina). An autoregressive covariance structure, which assumes a higher correlation for adjacent observations (i.e., sequential workloads), was employed in the analysis. For each variable of interest the effect for the athlete group was tested as well as the workload entered as a categorical variable. Because of the higher variance in the variable CO at higher workloads, a heterogeneous autoregressive covariance structure was used in the regression for CO. Interactions between workload and athlete group were tested but none was significant.

Table 1. Study Population Characteristics

Variable	Athletes n = 26	Controls n = 14	p Value
Age, yr	20.3 ± 1.7	18.9 ± 0.9	0.009
Height, cm	182.9 ± 4.7	180.9 ± 6.8	0.277
Weight, kg	85.4 ± 5.8	77.9 ± 8.8	0.007
BMI, kg/m^2	25.3 ± 1.3	23.9 ± 2.5	0.057
BSA, m^2	2.1 ± 0.1	2.0 ± 0.1	0.015
LVEDV, ml	129 ± 23	98 ± 19	0.002
LVEF, %	56 ± 4.6	59 ± 4.0	0.035

Values are given as mean ± SD. BMI = body mass index, calculated as WT/BSA; BSA = body surface area; LVEDV = left ventricular end diastolic volume; LVEF = left ventricular ejection fraction.

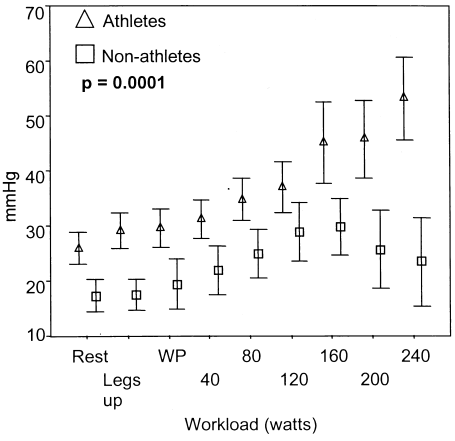

Figure 1. Calculated pulmonary artery systolic pressure response to exercise at each stage for athletes versus nonathletes. Mean value and 95% confidence intervals are given. Pulmonary artery systolic pressure was calculated using an assumed RA pressure of 5 mm Hg. Pulmonary artery systolic pressure was higher in athletes than in normals at each stage ($p < 0.0001$). WP = warm-up period.

RESULTS

Rest data. Subject demographics are shown in Table 1. Nonathletes were significantly younger than the athletes by 1.4 years, although the ranges overlapped considerably (athletes, 18–23 yr; nonathletes, 18–21 yr). Athletes were significantly heavier than nonathletes by 7.5 kg, had greater body mass index (BMI) by 1.4 and significantly greater body surface area (BSA) by 0.1 m^2. The two groups did not differ in height. Left ventricular end diastolic volume (LVEDV) was significantly higher and EF significantly lower in the athletes compared with normal healthy controls.

Exercise data. Pulmonary artery systolic pressure ($p = 0.0001$; Fig. 1), TRV ($p = 0.0001$; Fig. 2A and Table 2), HR ($p = 0.003$; Fig. 2D), SV ($p = 0.0003$; Fig. 2E) and CO ($p = 0.0267$; Fig. 2F) showed significant differences between athletes and nonathletes over all workloads, including rest. There were no significant differences in systolic blood pressure (SBP) ($p = 0.488$; Fig. 2B) and diastolic blood pressure (DBP) ($p = 0.469$; Fig. 2C) between the two groups.

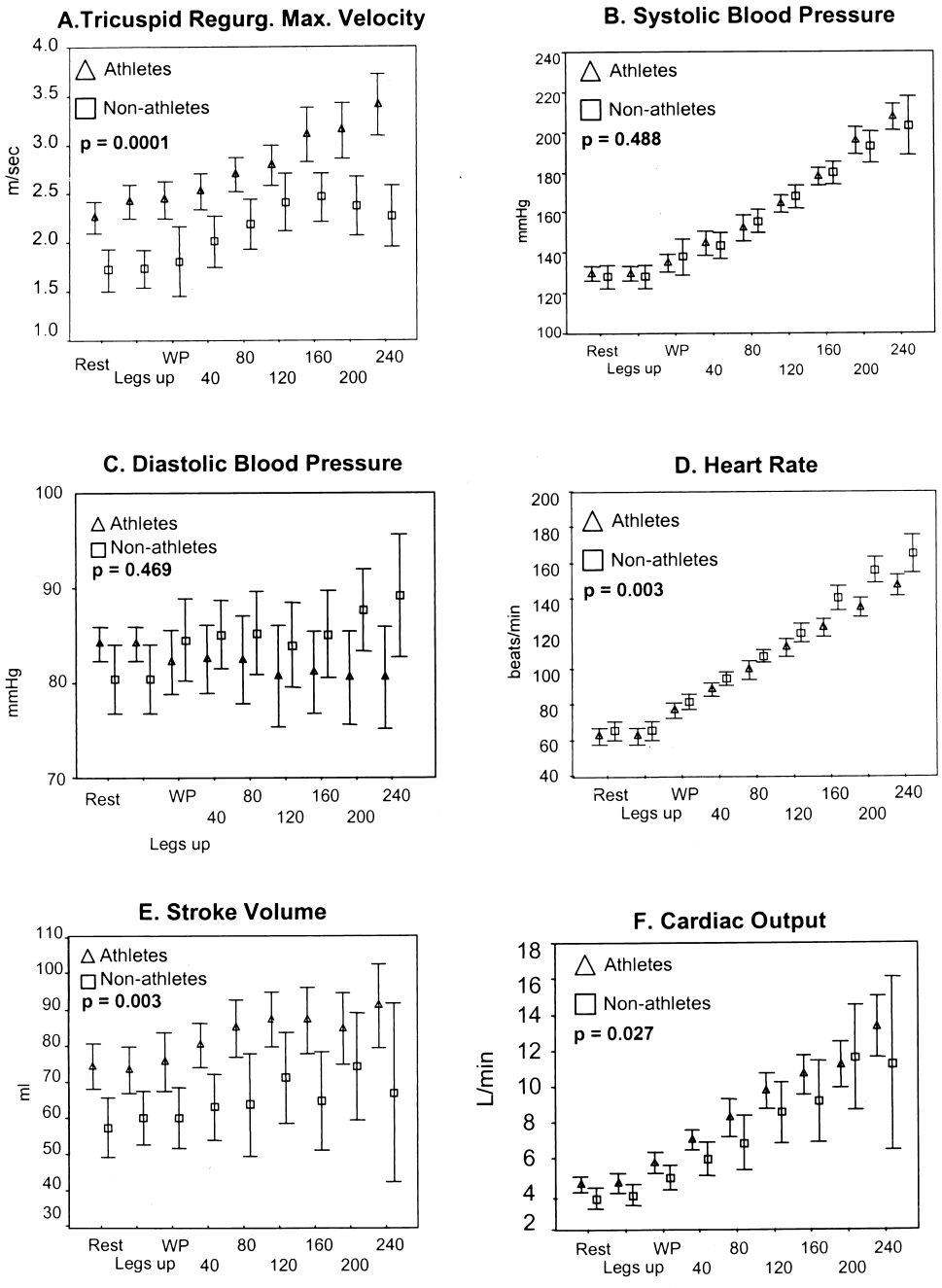

Figure 2. (Panel A–F). Mean value (with 95% confidence limits) for each measured parameter at each stage during exercise for athletes and nonathletes. WP = warm-up period.

In general, all measures except DBP increased with increasing workload; the rate of increase differed between the groups. Tricuspid regurgitation velocity and the derived variable PASP increased in both groups up to a workload of 160 watts after which the athlete group continued to increase while the nonathlete group decreased. Systolic blood pressure, HR and CO increased linearly with increasing workload in both groups. Stroke volume (SV) increased moderately with increasing workload in both groups.

DISCUSSION

Mechanisms of pressure elevation. Previous invasive studies have demonstrated mild increases in pulmonary pressure with exercise in the normal population and higher pressures in athletes (13,14). In our study we have confirmed this difference. The factors which result in an increase in PASP with exercise are not fully known. A partial explanation lies in the increase in SV with increasing

Table 2. Mean TRV with 95% Confidence Intervals for Athletes Versus Nonathletes by Workload

	Athletes			Nonathletes		
	TRV (m/s)			TRV (m/s)		
Workload (watts)	Mean	Lower 95% CI	Upper 95% CI	Mean	Lower 95% CI	Upper 95% CI
Rest	2.25	2.09	2.41	1.72	1.50	1.93
Legs up	2.42	2.25	2.59	1.73	1.54	1.92
Warm up	2.44	2.24	2.63	1.80	1.45	2.16
40	2.52	2.33	2.71	2.01	1.74	2.27
80	2.70	2.53	2.87	2.19	1.93	2.44
120	2.79	2.58	3.00	2.41	2.11	2.71
160	3.11	2.83	3.39	2.46	2.21	2.71
200	3.15	2.87	3.43	2.37	2.06	2.67
240	3.41	3.10	3.72	2.27	1.95	2.58

See also Figure 2A.

stress levels seen in both groups. The greater SV in athletes compared with normals would be in line with the greater increase in PASP. There was no significant difference between the two groups in SBP, suggesting that the mechanisms which regulate systemic arterial pressure with exercise are different and less flow dependent.

A second mechanism of increasing PASP is an increase in left atrial pressure with exercise (15–19). Both animal and clinical studies have demonstrated that left atrial pressure may increase to ≥20 mm Hg with maximal physical exertion. The relative contribution of increased flow and increased left atrial pressure to the increased PASP remains unclear. While not directly assessed in this study, prior studies have found that pulmonary vascular resistance does not rise with exercise and may even decline (16,17). As such, the elevation in PASP is most likely not related to primary changes in the pulmonary vasculature but is secondary to increases in flow and passive resistance due to an increase in left atrial pressure.

Clinical implications. This study delineates the full range of TRV and the derived variable PASP with exercise and, therefore, can serve as a reference standard for the diagnosis of rest or exercise induced pulmonary hypertension in symptomatic individuals. The range of TRV and PASP reported here is higher than generally recognized and in part is due to the levels of stress achieved. Well-conditioned athletes were capable of reaching PASP of 60 mm Hg with exercise. When evaluating patients it is crucial to integrate workload and cardiac output with the TRV and PASP response to determine if an increase in PASP is a pathologic phenomenon or within the range of normal physiologic responses.

Study limitations. It is important to underline a few limitations of this study. We evaluated the TRV response to exercise in a highly selected cohort of subjects with respect to gender, age and type of sport, all of which have been shown to impact cardiopulmonary performance. First, several prior studies have shown that age represents a major determinant in the physiologic variations of PASP (20–22). With increasing age there is a decrease in the pulmonary blood flow, an increase in the mean pulmonary pressure and an increase in pulmonary resistance, presumed related to reduced compliance of the pulmonary bed. Second, it has been demonstrated that physiologic cardiovascular adaptations to exercise are also dependent upon the type and magnitude of training (23–27). Greater increases in PASP are seen in individuals who engage in competitive sports requiring intermittent, intensive aerobic exercise as is the case with the athletes evaluated in this study (14).

In this study we have used a noninvasive technique to measure intracardiac pressures which is widely available and easily employed. In this study we did not attempt to measure RAP. Our results are reported as TRV and as PASP, using an assumed RAP of 5 mm Hg. This value of assumed RAP is consistent with previously known measured normals. While TRV is a quantifiable value which predictably increases with exercise, RAP may decrease or remain stable with exercise. Use of a fixed value for RAP may result in a mild systematic overestimation of PASP at higher workloads. By using a constant of 5 mm Hg, the degree of overestimation will be clinically insignificant.

Conclusions. Athletes have higher TRV compared with healthy control subjects both at rest and during exercise. Higher SV and CO are major contributors to this phenomenon. The range of TRV during stress is higher than previously recognized and in highly conditioned athletes may reach 60 mm Hg, a level traditionally considered pathologic.

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