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Rest and Exercise Left Ventricular Ejection Fraction Before and After Therapy in Young Adults with Hyperthyroidism and Hypothyroidism

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Thyroid hormone has numerous direct and indirect effects on cardiac function, and alterations in thyroid status may complicate preexisting cardiac disease.[1] Ikram[2] showed that cardiac failure may develop in thyrotoxic patients. Although clinical evidence of underlying cardiac disease was excluded, the mean age of his patients was 60 years. Several recent studies suggest that in middle-aged or older hyperthyroid[3-5] or hypothyroid[6] persons, cardiac reserve (determined by exercise radionuclide angiography) is impaired in the absence of underlying heart disease. The present study was performed to determine whether younger adult patients also had evidence of a thyroid cardiomyopathy.

Fifteen patients with untreated hyperthyroidism were studied. There were 10 women, mean age 30 years (range 19 to 39), and 5 men, mean age 24 years (range 19 to 31). All patients had at least moderate symptoms and signs of hyperthyroidism and diffuse goiters. Serum T_4 was elevated, at 19.2 ± 4.3 μg/dl (normal 5.1 to 10.8), serum T_3 was increased, at 413 ± 145 ng/dl (normal 115 to 220), and 24-hour radioactive iodine uptake was high, 35 to 90%, in all patients. Four patients received propranolol for brief periods before the initial study, but use of this drug was discontinued for at least 1 day. Seven subjects were restudied after at least 3 months of euthyroidism.

Five hypothyroid patients were studied. There were 2 women and 3 men, ages 20 to 48 years. Four had low serum T_4 and elevated thyrotropin levels; 1 patient had a normal T_4 level but a slightly increased basal thyrotropin and a markedly exaggerated thyrotropin response to thyrotropin releasing hormone. Three patients had at least moderate symptoms and signs of hypothyroidism. All but 1 patient were restudied when euthyroid, 10 to 18 months after treatment was initiated.

No patients had systemic hypertension or symptoms or signs of clinical heart disease. All subjects gave informed consent to participate in a protocol approved by the hospital human use committee.

Patients were exercised in a semisupine position. Workload was initially 200 kg-m/min, and this was increased every 3 minutes until fatigue developed.

Radionuclide gated blood pool ventriculography was performed at rest and during exercise after the patient's red blood cells were labeled with 20 to 25 mCi of technetium-99m pertechnetate. Ejection fractions were calculated on a computer by a single operator and wall motion was evaluated by a single observer. A normal study was defined as a rest ejection fraction greater than 50%, an exercise ejection fraction at least 5% higher than during rest and normal wall motion. Statistical methods used were Student t test for paired and unpaired data.

Hemodynamic measurements of the 15 untreated patients are listed in Table I. The results of the 7 patients studied before and after treatment of hyperthyroidism are also listed. As a group, the untreated patients had rest tachycardia, although the range was wide. All but 3 hyperthyroid patients reached the target heart rate during exercise, and all achieved a rate-pressure product greater than 23,000 beats mm Hg/min. Wall motion was determined visually to be normal at rest in all 15 patients.

In 4 hyperthyroid patients ejection fraction (EF) failed to increase by more than 5% during exercise. Compared with the 11 normal responders, these 4 patients had a higher serum T_4 (23.3 ± 4.0 vs 17.7 ± 3.4 μg/dl, $p < 0.02$) and rest heart rate (115 ± 11 vs 83 ± 12 beats/min, $p < 0.001$). Although the difference was not statistically significant, mean workload was 30% less (500 ± 141 kg-m/min vs 709 ± 247) in patients with abnormal EF responses, and mean exercise time was 26% less (8.2 ± 1.9 vs 11.0 ± 3.6 minutes). The rate-pressure products were equivalent. All 4 abnormal responders had a normal rest EF. Two had a small increase (from 60% to 63% and from 65% to 69%) and 2 a small decrease (from 67% to 63% and from 63% to 62%) with exercise; in all cases EF remained greater than 60%. One patient had some borderline hypokinesia of the inferior left ventricular (LV) wall with exercise, whereas all others had normal wall motion.

The effect of restoration of euthyroidism on cardiac function in 7 patients is shown in Table II. Exercise time improved in all but 1 subject, whereas maximal workload increased only in the abnormal responders. The 3 subjects who initially had a normal response to exercise maintained normal contractility when euthyroid; one showed an increase in contractile response as determined by the amount of change in EF. The 4 abnormal responders, in contrast, all had considerable improvement in exercise EF after therapy.

The hemodynamic measurements in 5 hypothyroid patients are listed in Table I. Four subjects were restudied after they were euthyroid. Three of 5 patients did not reach the target heart rate during exer-

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TABLE I Hemodynamic Measurements and Left Ventricular Ejection Fraction Before and After Exercise in Hyperthyroid and Hypothyroid Patients

	All Hyperthyroid (n = 15)	Treated Hyperthyroid (n = 7)		All Hypothyroid (n = 5)	Treated Hypothyroid (n = 4)	
		Before Therapy	After Therapy		Before Therapy	After Therapy
Heart rate (beats/min)						
Rest	92 ± 1*	98 ± 24	71 ± 9†	66 ± 28	55 ± 17	55 ± 10
Exercise	182 ± 20*	181 ± 23*	174 ± 19*	153 ± 22*	152 ± 25*	165 ± 11*
Blood pressure (mm Hg) (rest)						
Systolic	127 ± 18	133 ± 22	121 ± 12†	112 ± 11	108 ± 5	116 ± 18
Diastolic	75 ± 9	79 ± 7	83 ± 7	76 ± 4	75 ± 4	75 ± 10
Blood pressure (mm Hg) (exercise)						
Systolic	186 ± 26*	188 ± 26	184 ± 14*	181 ± 26*	184 ± 29*	175 ± 33*
Diastolic	83 ± 25	89 ± 11	95 ± 7*	80 ± 18	77 ± 20	82 ± 5
Double product (beats mm Hg/min)	33,828 ± 6,151	34,092 ± 7,371	32,202 ± 5,761	27,602 ± 4,412	27,745 ± 5,081	28,705 ± 4,466
Exercise time (min)	10.2 ± 3.4	8.9 ± 2.1	12.0 ± 2.7†	13.1 ± 2.7	13.4 ± 3.0	15.2 ± 6.4
Maximal work (kg-m/min)	653 ± 239	586 ± 212	743 ± 181†	900 ± 332	975 ± 330	1,000 ± 432
Ejection fraction (%)						
Rest	62 ± 5	65 ± 3	65 ± 6	64 ± 10	68 ± 8	69 ± 9
Exercise	70 ± 8*	72 ± 11	78 ± 7*†	69 ± 7	72 ± 2	76 ± 2†

*p <0.05 , rest vs exercise; †p <0.05, before vs after therapy.
Values are mean ± standard deviation.

TABLE II Hemodynamic Responses to Exercise in Seven Hyperthyroid and Four Hypothyroid Subjects Before and After Therapy

	Exercise Time (min)		Ejection Fraction (EF)							
			Max Work (kg-m/min)		Before Therapy (B)		After Therapy (A)		ΔEF	
Hyperthyroid	B	A	B	A	Rest	Exercise	Rest	Exercise	B	A
Normal responders										
1	8	12	600	600	67	75	66	84	8	18
2	9	8	500	500	62	76	73	82	14	9
3	13	16	1,000	1,000	70	93	70	87	23	17
Abnormal responders										
1	7	10	400	600	60	63	57	71	3	14
2	6	12	400	800	65	69	65	76	4	11
3	9	14	700	900	67	63	57	67	−4	10
4	10	12	500	800	63	62	69	76	−1	7
Hypothyroid										
1	16	21	1,200	1,400	60	73	59	77	13	18
2	9	6	500	400	77	74	75	77	−3	2
3	15	18	1,200	1,200	71	71	77	78	0	1
4	14	16	1,000	1,000	62	70	64	74	8	10

cise when hypothyroid, but these 3 all achieved their target rates when euthyroid. Rate-pressure products were more than 22,000 beats mm Hg/min. The effects of therapy in 4 patients are listed in Table II. Return to a euthyroid state improved the exercise time in 3 patients but maximal workload in only 1 patient. EF failed to increase by 5% in 2 patients, both when hypothyroid and later, after they became euthyroid. Rest EF was more than 70% in these 2 persons. All subjects had normal wall motion during exercise. Electrocardiograms were normal in every case.

We measured LVEF responses before and after therapy in young adults with thyroid abnormalities. Previous reports purport to show impaired LV reserve, taking this as evidence for an early thyroid "cardiomyopathy."[3-5] Eleven of our 15 hyperthyroid patients had a normal EF response. Four patients responded abnormally, that is, had less than a 5% increase in EF. These latter patients differed from the former by having higher T_4 levels, higher rest and exercise heart rates and shorter exercise time. This constellation of findings suggests that they were more hyperthyroid chemically and physiologically. Despite their relative exercise intolerance, the abnormal responders had generally preserved LV function, as evidenced by their high double product. Moreover, their exercise EF was at least 62%. Establishment of the euthyroid state in hyperthyroid patients improved exercise duration and maximal attainable EF. After therapy, 3 normal responders had an increase in exercise time but the maximal workloads were unchanged. After therapy, the 4 abnormal responders showed an increase in both exercise time and maximal workloads. Although the

rest EF was generally equivalent, exercise EF did increase after therapy.

Five hypothyroid patients were studied before and after therapy. Exercise duration was improved in all but 1 patient. Maximal workload was similar before and after therapy. Rest EF was not affected by thyroid hormone. Three of the 5 patients had a higher EF after exercise while hypothyroid. The other 2 patients, both with an EF of more than 70% at rest, either had no change or a slight decrease in EF with exercise. As a group, establishment of the euthyroid state appeared to increase exercise tolerance. These results differ from those of Forfar et al,[6] who reported a reduced rest and exercise EF in hypothyroidism. However, the mean age of his patients was 53 years. Given the wide range of normal exercise EF responses, the present findings fail to document a significant effect of thyroid hormone deficiency on EF response in a younger adult population.

In conclusion, this study of young hyperthyroid and hypothyroid patients documents essentially normal cardiac reserve. No patient had clinical evidence of cardiac dysfunction by history or physical examination. Patients complained of decreased exercise tolerance related to their thyroid abnormality. This was corrected with establishment of the euthyroid state. Radioangiography documented good overall cardiac function before and after therapy. Although a few hyperthyroid patients had a slight aberration in EF response, this was corrected with establishment of euthyroidism. Although our findings are at variance with those of previous studies, the disparities may be explained in part by methodologic differences. Moreover, mild changes in EF are believed to have low specificity. Consequently, the findings noted in these patients do not support there being a primary aberration in myocardial function.

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