Effects of Age and Gender on the Cardiovascular Responses to Isoproterenol

Michael J. Turner, Constance M. Mier, Robert J. Spina, Kenneth B. Schechtman, and Ali A. Ehsani

1Section of Applied Physiology, Division of Geriatrics and Gerontology and Washington University Claude D. Pepper Center, Cardiovascular Division, Department of Medicine, and 3Division of Biostatistics, Washington University School of Medicine, St. Louis, Missouri.

We studied the effects of age and gender on cardiovascular responses to β-adrenergic stimulation with the use of two-dimensional echocardiography in 16 young (aged 20–31) and 20 older (aged 60–75) healthy individuals. Following administration of atropine, each subject was given an infusion of isoproterenol at incremental doses from 0.010 to 0.030 μg kg⁻¹ min⁻¹. The slopes of the fractional shortening–end-systolic wall stress (FS–es) relationships were steeper in the young men (β = 0.87 ± 0.28, n = 8) compared to the older men (β = 0.41 ± 0.13, n = 10), and in the young women (β = 0.55 ± 0.14, n = 8) compared to the older women (β = 0.30 ± 0.13, n = 10). Furthermore, the magnitude of the age-associated differences in these slopes was larger in the men (old vs young) than in the women (old vs young) which, in the absence of changes in preload, suggests a greater decline in the contractile response to isoproterenol with advancing age in men compared to women. Furthermore, the men exhibited a greater attenuation of chronotropic response to isoproterenol than did the women. These observations suggest that gender plays a significant role in the age-associated decline in inotropic and chronotropic responses to β-adrenergic stimulation, with men exhibiting a greater decline with aging than women.

METHODS

Subjects
Sixteen young (20–31 years) and 20 older (60–75 years) adults participated in this study. There were 8 men and 8 women in the young group, and 10 men and 10 women in the older group. The ages of the older men and women were 64.7 ± 4.7 (mean ± SD) years and 64.8 ± 3.8 years, respectively; and the young men and women were 25.4 ± 3.1 years and 25.3 ± 3.4 years, respectively. The subjects’ characteristics for each group are summarized in Table 1. All participants were sedentary, and the older adults were screened for the presence of coronary risk factors and clinical coronary artery disease. All subjects were healthy, nonsmokers (>10 years), normotensive (BP ≤ 140/90 mm Hg), and asymptomatic. They had a normal cardiac examination and were not taking cardiovascular medications. A few subjects were taking multivitamins. None of the older subjects had evidence of myocardial ischemia, confirmed by a thallium-201 exercise stress test. None of the older women was on hormone replacement therapy. All subjects signed an informed written consent, and the study protocol was approved by the Human Studies Committee of the Washington University School of Medicine. All procedures were performed in accordance with Washington University School of Medicine guidelines.

Exercise Tests and Measurement of Maximal Oxygen Uptake (VO₂ max)
Initially, each older subject underwent a graded treadmill exercise test using the Bruce protocol (20). One to 2 weeks later, the subjects performed a maximal treadmill test to determine
The rationale for the use of atropine was to minimize the confounding effect of vagal tone, because earlier studies suggested that during β-adrenergic stimulation, it can have a significant negative inotropic effect (26,27). Therefore, we felt that atropine should be helpful to facilitate the interpretation of our findings. The reason for the selection of 1-mg dose of atropine for all the subjects was that a reasonably good vagal blockade is generally attainable with this regimen without a significant risk of urinary retention in older men with prostatic hypertrophy. Furthermore, Poller and colleagues (28) have shown that age-related changes in several cardiovascular variables (HR, systolic blood pressure [SBP], diastolic blood pressure [DBP], and estimates of contractility) in response to cardiac muscarinic blockade were independent of doses of atropine ranging from 0.93 to 1.89 mg in individuals of similar age to the current study. Therefore, it appears that the effect of the differences in body weight on the effectiveness of vagal blockade would be small in our subjects.

Infusion of isoproterenol was commenced approximately 3 minutes after the administration of atropine at successive doses of 0.010, 0.020, 0.025, and 0.030 μg kg⁻¹ min⁻¹ with the use of an infusion pump (Harvard Apparatus, Model 122: South Natick, MA) with simultaneous ECG and blood pressure (BP) monitoring. Each infusion stage lasted for 5 minutes. Repeat 2-D echocardiographic studies were performed 2 minutes following atropine administration and in the last 2 minutes of each stage of the isoproterenol infusion. BP was taken every 2 minutes with cuff sphygmomanometry simultaneously with echocardiographic recordings.

**Statistics**

The differences in variables between age groups and genders were compared with the use of a two-way analysis of variance. In response to vagal blockade, the effects of age and gender were analyzed by comparing the change in response for each variable from resting baseline to cholinergic muscarinic blockade with the use of a two-way analysis of variance. To assess the sensitivity of each variable to isoproterenol, the slopes of the linear portion of the dose-response curve for each subject across isoproterenol doses were analyzed with the use of a two-way analysis of variance.

### Table 1. Subject Characteristics at Rest and Maximal Exercise

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Older</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.3 ± 3.4</td>
<td>64.8 ± 3.8</td>
<td>64.7 ± 4.7</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.0 ± 7.1</td>
<td>66.0 ± 13.3</td>
<td>85.4 ± 10.4</td>
<td></td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.66 ± 0.09</td>
<td>1.71 ± 0.13</td>
<td>2.05 ± 0.13</td>
<td></td>
</tr>
<tr>
<td>EDD (mm)</td>
<td>47.2 ± 4.0</td>
<td>46.7 ± 3.5</td>
<td>52.4 ± 6.5</td>
<td></td>
</tr>
<tr>
<td>ESD (mm)</td>
<td>31.4 ± 2.5</td>
<td>28.8 ± 2.5</td>
<td>34.7 ± 4.1</td>
<td></td>
</tr>
<tr>
<td>LVmas/BSA (g/m²)</td>
<td>66.66 ± 12.25</td>
<td>63.60 ± 9.10</td>
<td>82.59 ± 20.9</td>
<td></td>
</tr>
<tr>
<td>h/lr</td>
<td>0.32 ± 0.085</td>
<td>0.34 ± 0.03</td>
<td>0.36 ± 0.06</td>
<td></td>
</tr>
<tr>
<td>V0₂max (L/min)</td>
<td>2.37 ± 0.23</td>
<td>1.44 ± 0.13</td>
<td>2.40 ± 0.55</td>
<td></td>
</tr>
<tr>
<td>V0₂max (ml/kg-min)</td>
<td>38.5 ± 3.96</td>
<td>46.7 ± 2.04</td>
<td>28.1 ± 2.8</td>
<td></td>
</tr>
<tr>
<td>HRmax (b/min)</td>
<td>198.8 ± 4.2</td>
<td>192.3 ± 9.6</td>
<td>166.3 ± 12.0</td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>109.9 ± 6.4</td>
<td>121.8 ± 10.7</td>
<td>112.1 ± 15.6</td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>71.3 ± 8.2</td>
<td>71.4 ± 8.2</td>
<td>66.2 ± 7.5</td>
<td></td>
</tr>
</tbody>
</table>

Note. Data are means ± SD. *Difference between genders (p < .05); †difference between age groups (p < .05). BSA: body surface area; EDD: end-diastolic diameter; ESD: end-systolic diameter; h/lr: left ventricular end-diastolic thickness-to-radius ratio; HRmax: maximal heart rate; LVmas: left ventricular mass; r: rest; V0₂max: maximal oxygen uptake.
way analysis of variance to compare the effects of age, gender, and the interaction between age and gender. Data are given as means ± SD.

RESULTS

Subject Characteristics
The subjects' characteristics are listed in Table 1. The men were heavier and taller compared to the women regardless of age (p < .05). Body surface area (BSA) was larger in the men than in the women regardless of age (Table 1). There were both age and gender effects for VO₂ max, with the young men having the highest and older women having the lowest VO₂ max (Table 1). The lower VO₂ max observed in the older subjects was in part due to a slower maximal heart rate (HRmax; Table 1).

Baseline Left Ventricular Size and Function

Age effects.—Baseline EDD, ESD, left ventricular mass, the wall thickness-to-radius (h/r) ratio (Table 1), and FS (Figure 1) did not differ (p > .05) between the older and younger subjects. Baseline HR (Figure 2), SBP, and DBP (Figure 3) were also not influenced by age (p > .05).

Gender effects.—Baseline EDD and ESD were significantly larger in the men than in the women (Table 1). In contrast, EDD normalized for BSA was larger in the women (p < .05). Baseline ESD normalized for BSA, the h/r ratio (Table 1), and FS (Figure 1) were not different (p > .05) between the men and women. The men had a greater LV mass than the women, expressed either in absolute values or normalized for BSA (p < .05, Table 1). Baseline HR (Figure 2), SBP, and DBP (Figure 3) were not influenced by gender.

Age × Gender Interaction Effects
The effect of age on FS in women was significantly (p < .05) different from the effect in men because baseline FS increased with age in the women, but did not in the men (Figure 1). All other baseline measures did not exhibit any significant Age × Gender interaction effects.

Cardiovascular Responses Following Cardiac Muscarinic Receptor Blockade

Age effects.—Age had no significant effect on the changes from baseline in EDD and ESD (see below) after vagal blockade. FS (Figure 1), HR (Figure 2), SBP, and DBP (Figure 3), and FS after atropine were not different between age groups. The increase in HR from rest to vagal blockade for all subjects was not influenced by body weight (r = .312, p > .05).

Gender effects.—The changes in EDD from baseline in response to vagal blockade were not different (p > .05) between the men (0.3 ± 2.5 mm and 1.8 ± 5.0 mm, young and older, respectively) and women (−1.3 ± 1.7 mm and −0.8 ± 2.8 mm, young and older, respectively). There were also no statistically significant differences (p > .05) in the change in ESD from rest to vagal blockade between the men (1.1 ± 2.0 mm and 2.0 ± 5.1 mm, young and older, respectively) and women (−0.4 ± 1.7 mm and 0.9 ± 1.6 mm, young and older, respectively). The changes in FS (Figure 1) and Dmax (Figure 4) were not different (p > .05) between men and women after atropine. The increase in HR in response to vagal blockade was greater in the women than in the men (Figure 2, p < .05), in part because of a greater degree of vagal blockade. The change in SBP and DBP in response to vagal blockade was not related to gender (Figure 3).

Age × Gender interaction effects.—There were no Age × Gender interaction effects in any of the variables following vagal blockade.

Cardiovascular Responses to β-Adrenergic Stimulation
We found that during the infusion of isoproterenol, all of the variables except for SBP and DBP increased rapidly in a linear fashion with the lower doses of isoproterenol. These variables reached a plateau during the final two infusion stages (i.e., 0.025 and 0.030 μg kg⁻¹ min⁻¹). It was, therefore, possible to as-
sess the sensitivity of each variable to isoproterenol by determining the slope of the linear portion of the dose-response curve for each subject.

**Age effects.**—EDD and ESD decreased in response to isoproterenol to similar extents in the young and older adults with no age-related effect (Table 2). The young subjects exhibited a greater increase in FS with a steeper slope of the dose-response relationship \( p < .01 \) than did the older subjects in response to isoproterenol, consistent with the age-associated diminished inotropic sensitivity to catecholamines (Table 2). Left ventricular \( \sigma_{es} \) decreased more in the young subjects \( p < .01 \) compared to the older subjects (Table 2). The FS-\( \sigma_{es} \) relationship was linear for both older men and women \( (r = .916 \pm .10 \text{ and } .920 \pm .095, \text{respectively}) \) and young men and women \( (r = .964 \pm .06 \text{ and } .984 \pm .01, \text{respectively}) \). The average slope of the FS-\( \sigma_{es} \) relationships was steeper in the young than the older subjects but the difference was not statistically significant (Figure 5). Each group exhibited a progressive increase in HR in response to increasing doses of isoproterenol (Figure 2) but the differences in the chronotropic sensitivity were insignificant between young and older adults (Table 2). There was no age-related difference in the SBP (Figure 3) responses to isoproterenol. Diastolic blood pressure (Figure 3) decreased throughout the incremental doses of isoproterenol in all groups \( (p < .001) \). The young subjects, however, showed a greater decrease in the DBP response, i.e., a steeper slope of the dose-response curve, than did the older subjects (Table 2).

**Gender effects.**—There were no gender-related differences in the EDD and ESD responses to isoproterenol (Table 2). The observed gender-related differences in either FS or \( \sigma_{es} \) responses to isoproterenol did not attain statistical significance (Table 2). The slopes of the FS-\( \sigma_{es} \) relationship were not different between the genders (Figure 5).

**VO**\(_{\text{max}}\) correlated significantly with the inotropic responses to \( \beta \)-adrenergic stimulation, i.e., the slope of the FS-\( \sigma_{es} \) relationship \( (r = -.701, p < .001) \). The slope of the relationship between \( \sigma_{es} \) and ISPr was steeper in the young than the older adults with no age-related effect (Table 2). There was no age-related difference in the SBP (Figure 3) responses to isoproterenol. Diastolic blood pressure (Figure 3) decreased throughout the incremental doses of isoproterenol in all groups \( (p < .001) \). The young subjects, however, showed a greater decrease in the DBP response, i.e., a steeper slope of the dose-response curve, than did the older subjects (Table 2).
EFFECTS OF AGE AND GENDER ON LEFT VENTRICULAR SYSTOLIC PERFORMANCE

Figure 5. The effects of age and gender on the fraction shortening vs. stress (FS-σes) relationship in response to isoproterenol (ISP) in the (A) young men (n = 8) and women (n = 8), and (B) older men (n = 10) and women (n = 10). There were significant Age × Gender interactions for the slope (p < 0.006) and the y-intercept (p < 0.001) of the FS-σes relationship, with men showing a greater age-related decline in inotropic responses to isoproterenol than women.

between VO2max and the inotropic response was different (p < .05) between the men (r = -.733, slope = -.23.22) and women (r = -.585, slope = -.33.66). However, there were no statistically significant differences in the y-intercept of this relationship attributable to gender. The differences in the chronotropic sensitivity to isoproterenol between the men and women did not attain statistical significance (Figure 2). Men had a greater increase in SBP in response to isoproterenol than women (Figure 3, p < .05). However, there was no gender-related difference in the DBP response to isoproterenol.

**Age × Gender interaction effects.**—There were no Age × Gender interaction effects in the EDD, ESD, FS, or σes responses to isoproterenol (Table 2). However, we found significant Age × Gender interactions both for the slope (p = .006) and y-intercept (p < .001) of the FS-σes relationship. The slope (Figure 5) was steeper in the young men (−0.87 ± 0.29) compared to the older men (−0.41 ± 0.13) and in the young women (−0.55 ± 0.14) compared to the older women (−0.38 ± 0.13), showing a greater increase in FS in the younger than in older subjects for a given decrease in σes. In addition, young subjects showed a significant gender-related difference in the slope of the FS-σes relationship, with the young men showing a steeper slope than the young women (Figure 5). In contrast, in the older groups the differences in the slope between the men and women were smaller and statistically insignificant (Figure 5). Therefore, the men exhibited a greater age-related decline in inotropic responses to isoproterenol than did the women (p = .006, Figure 5). The y-intercept was significantly higher for the young men (76.41 ± 6.5%) compared to the older men (57.99 ± 8.1%), suggestive of an age-associated decline in the contractile response to isoproterenol in men. In contrast, the y-intercept was virtually identical between the young and older women (63.74 ± 4.9% and 63.07 ± 5.8%, respectively). The age-associated changes in the y-intercept of the FS-σes relationship were significantly (p < .001) different between men and women.

The effect of age on the HR responses to isoproterenol in men was significantly different from that in women. The slope of the HR response to isoproterenol was less steep (p < .05) in the older men compared to the young men, suggestive of an age-associated decline in the chronotropic sensitivity to isoproterenol in men (Table 2, Figure 2). In contrast, there was no age-associated difference in the slope of heart rate responses to isoproterenol between the young and older women (Table 2, Figure 2). There was no Age × Gender interaction effects in the SBP and DBP responses to isoproterenol.

In order to examine the possible influence of different degrees of vagal blockade attributable to the dosage of atropine relative to body weight, we compared the cardiovascular responses between subgroups of subjects (three subjects per group) who received similar amounts of atropine relative to their body weight (young women = 14.5 ± 0.85 μg/kg; older women = 14.8 ± 0.68 μg/kg; young men = 14.4 ± 1.53 μg/kg; older men = 14.0 ± 1.2 μg/kg; p = .62) in a separate analysis. We found both age- and gender-related differences between the subgroups, with respect to FS and σes responses to isoproterenol, were similar to the entire groups, as outlined above. The HR response to vagal blockade was marginally different between the young women and young men (94.3 ± 7.7 bpm vs 78.7 ± 7.7 bpm, respectively; p = .07). In these subgroups who received similar doses of atropline relative to their body weight, the age- and gender-related differences in the contractile responses to isoproterenol were similar to those observed in the entire groups, as reflected in: (i) the slopes of the FS-σes relationship (young women = −0.46 ± 0.03, older women = −0.28 ± 0.12; young men = −0.96 ± 0.17, older men = −0.43 ± 0.05; young men different from young women and older men, p = .02; young women not different from older women); and (ii) the intercepts of the FS-σes relationship (young women = 60.5 ± 2.9%, older women = 60.2 ± 3.6%; young men = 80.8 ± 7.1%; older men = 62.1 ± 3.4%; young men different from older men, p = .01; young women not different from older women).

**Discussion**

The results of this study extend previous observations both in experimental animals (29,30) and in humans (15,17), showing that aging results in diminished inotropic responses to β-adrenergic stimulation, as evidenced by a decrease in the sensitivity of systolic shortening to isoproterenol and a less steep...
slop of the FS-$\sigma_m$ relationship in the absence of changes in preload observed in the older adults. We also found that the younger men exhibited significantly greater positive inotropic responses to $\beta$-adrenergic stimulation than did the younger women. Therefore, our observations suggest that gender should be taken into consideration in assessment of the age-associated decline in the contractile response to $\beta$-adrenergic stimulation because this effect appears to be more pronounced in men than in women. Unlike previous studies (7,28), we used the FS-$\sigma_m$ relationship because it is a reliable measure of LV contractile function, provided that preload and HR do not change significantly. In this study, the changes in EDD, used as an index of preload, in response to isoproterenol were small and not affected by either age or gender. The differences in chronotropic responses, which can affect the force-frequency relationship, may account for some of the differences in the LV contractile responses attributable to age and gender, because the increase in HR was smaller in the older men than in the young men.

One of the mechanisms underlying the age-related decrease in VO$_{2\text{max}}$ which begins after the age of 25 (31-33) is the decline in maximal cardiac output (13). Although cardiac output and stroke volume were not measured in the current study, the significant correlation that we found between the slope of the FS-$\sigma_m$ relationship and VO$_{2\text{max}}$ suggests that the age-associated decrease in $\beta$-adrenoreceptor-mediated LV contractile function can contribute to the lower maximal aerobic capacity in older adults by decreasing stroke volume, because changes in VO$_{2\text{max}}$ are influenced, in part, by alterations in cardiac output and stroke volume. The absence of a statistically significant larger LV mass in older subjects in this study may, in part, be due to a relatively low systolic blood pressure in these older men and women which could have prevented increased systolic loading.

Although studies in experimental animals (29,30,34) and humans (1,7,9) have documented the age-associated decreases in the chronotropic and inotropic responsiveness to $\beta$-adrenergic stimulation, only one has addressed the effect of gender (3). Even in that study, only chronotropic responses to isoproterenol were reported (3). Ford and James (35), using a larger dose of atropine, reported that the influence of age on the decrease in the chronotropic response to isoproterenol was lost with cardiac muscarinic receptor blockade (35). Although we did not use a dose of atropine sufficient to induce total vagal blockade, we also found that the age-related decline in HR response to isoproterenol was small following atropine ($p > .05$) when the effect of gender was not taken into consideration.

Previous studies in older sedentary men reported an age-related decrease in ejection fraction in response to dynamic exercise and isoproterenol (7,10,36). Our findings are consistent with those published by Stratton and colleagues who used a slightly larger dose of isoproterenol without atropine (7) and suggest that the diminished ejection fraction response to exercise in older men reported previously (10,36) may, at least in part, be mediated by the age-related decrease in the sensitivity to catecholamines because of the major role that the sympathetic nervous system plays in the circulatory adjustment during acute exercise. The new finding in this study is that gender can significantly modify the $\beta$-adrenergic-mediated increase in cardiac contractile function, with men showing a greater age-associated decrease in LV contractile function than women.

In vitro studies have reported a decrease in the contractile response to isoproterenol attributable to aging and the severity of heart disease (37,38). White and colleagues (39) assessed the $\beta$-receptors and postreceptor characteristics in explanted donor hearts of varying ages and found a substantial decrease in the $\beta_1$- but not in the $\beta_2$-receptor density with aging. The older hearts also exhibited a significant decrease in maximal tension in response to isoproterenol, which corresponded with the decrease in $\beta_2$-receptor density. These findings provide further evidence that one of the potential mechanisms underlying the age-associated decline in cardiac function in response to environmental challenges is a reduction in sensitivity to catecholamines. Furthermore, our data suggest that aging can induce an attenuation of $\beta_2$-mediated vasodilation, as reflected in a smaller decrease in DBP in older subjects.

The possible mechanism underlying the attenuation of the $\beta$-adrenergic-mediated cardiac responses in the older adults may involve changes in the myocardial adenosine levels and adenosine receptor $A_1$ function with advancing age. Adenosine has an antiadrenergic property with a direct negative chronotropic effect (34) and attenuation of $\beta$-adrenoreceptor-mediated contractile function (29,34). Aging induces the adenosine $A_1$ receptor-mediated reductions in both postsynaptic $\beta$-adrenergic responses (40) and the release of norepinephrine from the adrenergic nerve terminals in the myocardium (41). It is also associated with an increase in the interstitial concentration of adenosine in the myocardium (29). Therefore, it is plausible to expect that the age-related decreases in the $\beta$-adrenergic responses and adenylyl cyclase activity are due to the increased extracellular adenosine level (29,42). However, others have presented evidence that suggest the reductions in the $\beta$-adrenergic-mediated contractile reserve and adenylyl cyclase activity in senescence are associated with reduced capacity of adenosine to induce its antiadrenergic effect (34,43). It appears that the diminished $\beta$-adrenergic response with aging is mediated by a complex mechanism involving the age-associated reduction in coupling of adenosine $A_1$ receptors and their G proteins, and downregulation of the adenosine $A_1$ receptors (34,43). In view of these observations, it would be plausible to postulate that our findings could be due to the gender-related differences in alterations in myocardial adenosine $A_1$ receptor function with advancing age. Further studies are obviously needed to explore this possibility.

The limitations of our study include a relatively small sample size because we attempted to exclude individuals with coronary artery disease and hypertension in order to evaluate the effects of aging per se. Another limitation is the dosage of atropine used in this study. Because the men were larger than the women regardless of age, the dosage of atropine relative to body weight was smaller in the men than in the women. Therefore, it is possible that the gender-related differences in our findings could have been due to the differences in the dosage of atropine. However, we believe that this is unlikely for the following reasons: (i) in the older subjects, the slopes of the FS-$\sigma_m$ relationships were not significantly different between men and women even though the women received a larger dose of atropine which should induce a greater degree of vagal blockade and possibly a greater inotropic response to catecholamines because of the inhibitory effect of vagal tone on LV contractility (26,27,44); (ii) in the young subjects, the men who...
should have demonstrated a smaller increase in inotropic responses because of a smaller dose of atropine showed, in fact, a significantly greater inotropic response to isoproterenol, despite having a lesser vagal inhibition than women; (iii) there was no correlation between the increase in HR in response to atropine and body weight; and (iv) the gender-related differences in systolic contractile function were detectable even in those subjects who received similar doses of atropine per kilogram body weight. For these reasons, we believe it is unlikely that differences in the dose of atropine relative to the body weight can account for our findings.

In conclusion, the results of the present study provide evidence that older adults exhibit diminished inotropic responses to β-adrenergic stimulation, which may account, in part, for the age-associated decrease in aerobic exercise capacity. In addition, it appears that gender plays a major role in the age-related decline in cardiac responses to catecholamines, with men showing a greater age-associated decrease in the inotropic and chronotropic responses to catecholamines than women.

ACKNOWLEDGMENTS

Supported by NIA Grant, Claude D. Pepper Older Americans Independence Center AG-13629, RO1-AG 12233, and General Research Center Grant 5-M01 RR-00036. Michael Turner, Ph.D., was supported by Individual National Research Service Award 1-F32-AO05756-01.

Present address for Michael J. Turner, Ph.D., Department of Health Promotion & Kinesiology, University of North Carolina at Charlotte, 9201 University City Boulevard, Charlotte, NC 28223-0001. Present address for Constance M. Mier, PhD, Barry University, Department of Sport and Exercise Sciences, 11300 NE 2nd Avenue, Miami Shores, FL 33161-6695. Present address for Robert J. Spina, PhD, Department of Kinesiology and Health Education, The University of Texas at Austin, Bellmont Hall 222, Austin, TX 78712.

Address correspondence to Ali A. Ehsani, MD, Washington University School of Medicine, 4566 Scott Avenue, Campus Box 8113, St. Louis, MO 63110. E-mail: aehsani@imgate.wustl.edu

REFERENCES


Received April 24, 1998
Accepted March 24, 1999