Impairment in Walking Capacity and Myocardial Function in the Elderly: Is There a Role for Nonpharmacologic Therapy with Nutritional Amino Acid Supplements?

Roldano Scognamiglio, MD,[a,*] Amidio Testa, MD,[b] Roberto Aquilani, MD,[c] Francesco S. Dioguardi, MD,[d] and Evasio Pasini, MD[e]

Elderly persons have reduced muscular mass, with consequent deterioration of their daily activities and reduced quality of life. This is more pronounced in elderly patients affected by chronic diseases such as chronic heart failure (CHF). It has been demonstrated that oral amino acid (AA) supplementation improves muscle protein metabolism. A recent study shows that use of oral supplements with a special mixture of AAs for 12 weeks increases (1) 6-minute walk distance (from 212.5 ± 34 m to 268.8 ± 34.9 m; p <0.001), (2) maximal isometric muscular strength (from 14.6 ± 2.2 kg to 20.2 ± 2 kg; p <0.001), and (3) peak exercise left ventricular ejection fraction (LVEF 0.55 + 0.4 vs 0.67 + 0.7) (0.558 vs 0.67 ± 0.7; p <0.01). In a pilot observational study, we studied elderly patients with CHF who were clinically stable on standard therapy (age range, 68–76 years; New York Heart Association (NYHA) class II–III; LVEF <0.40; normal body mass index and arm muscle measurements; peak oxygen consumption <15 mL/kg per min). After basal assessment of (1) cardiac function (by 2-dimensional echocardiography), (2) 6-minute walk test, and (3) blood variables, an AA mixture (4 g × 2 die) was orally administered to the patients for 12 weeks in conjunction with standard therapies and a controlled diet. The AA supplements increased 6-minute walk distance significantly (201 ± 12 m vs 226 ± 9 m; p < 0.05). Interestingly, urea values were unchanged (31.3 ± 10.5 mg/dL vs 32.4 ± 8.1 mg/dL; p = NS). Our results suggest the potential role of a nonpharmacologic therapy with nutrients (ie, AAs) in an attempt to improve muscular metabolism and function in elderly subjects and in hypercatabolic syndromes such as CHF. **© 2008 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2008;101[suppl]:78E–81E)**

The elderly are a high-risk population with a very low level of physical activity that is significantly below the level recommended by public health guidelines.[1,2] This is a variable risk factor, and any therapy that can increase activity and exercise in the elderly could prevent health deterioration in later life. With advancing age, the main factors leading to inadequate physical activity and the correlated deterioration of daily life are (1) impaired protein synthesis in muscles[3] caused by reduced amino acid (AA)/protein intake in association with disturbances of insulin activities, and (2) the inability to increase cardiac function adequately during exercise.[4] These factors are more pronounced in the elderly with chronic diseases such as chronic heart failure (CHF).[5]

It has been demonstrated that use of oral AA supplements improves muscle protein metabolism[2] and significantly increases myocardial performance at rest and during exercise in patients with type 2 diabetes mellitus.[4] Subsequently, research regarding the clinical application of oral AA intake has focused on elderly persons in order to study the effects on walking capacities and myocardial function in healthy subjects with a sedentary lifestyle or with CHF. In a recent study,[6] we assessed the effects of oral AA supplements on walking capacity, maximal isometric muscular strength, and left ventricular (LV) function at rest and during exercise in healthy elderly subjects with reduced physical activity. In our study, patients were randomized to

[a]Metabolic Cardiology Unit, Department of Clinical and Experimental Medicine, University of Padua, Padua, Italy; [b]Rehabilitation Center, Foundation "E. Spalenza-Don Gnocchi," Rovato, Brescia, Italy; [c]Metabolic Service and Nutritional Pathophysiology, Foundation "S. Maugeri," IRCCS, Scientific Institute of Montescano, Pavia, Italy; [d]Department of Internal Medicine, University of Milan, Milan, Italy; and [e]Foundation "Salvatore Maugeri," IRCCS, Scientific Institute of Lumezzane, Brescia, Italy.

Statement of author disclosure: Please see the Author Disclosures section at the end of this article.

*Address for reprints: Roldano Scognamiglio, MD, Metabolic Cardiology Unit, Department of Clinical and Experimental Medicine, Polyclinic, via Giustiniani 2, 35100 Padua, Italy.

E-mail address: r.scognamiglio@unipd.it.

0002-9149/08/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjcard.2008.03.005

receive a special mixture of AAs (Big One; Professional Dietetics, Milan, Italy) or placebo for 12 weeks. This mixture contained all of the essential AAs and 2 nonessential AAs (tyrosine and cystene) in a complex ratio that was designed to match metabolic requirements under high demand. Here, we report preliminary data that provide some information on the effects of nutritional supplementation with AA on the walking capacities of elderly patients with stable CHF treated with standard therapy.

Amino Acid Supply Changes Ambulatory Capacity and Myocardial Function in Healthy Elderly Individuals

We recently studied the effects of AA supplements on the walking capacity and the LV function of healthy elderly individuals (for details, see our earlier published report[6]). In this study, after the basal evaluations, subjects (aged >65 years) were randomly assigned to either the AA group (n = 48) or the placebo group (n = 47). Subjects were reevaluated 12 weeks later. The following assessments were performed at baseline and after AA treatment: 6-minute walk test, Walking Impairment Questionnaire (WIQ) (to evaluate self-perceived ambulatory dysfunction), maximal isometric muscular strength of the right hand (by a dynamometer); LV systolic function at rest and during handgrip (by quantitative 2-dimensional [2D] echocardiography), and blood variables (including renal function).

In patients treated with AA supplements, the 6-minute walk distance increased from 212.5 ± 34 m to 268.8 ± 34.9 m ($p < 0.001$) but did not change after placebo (212 ± 36 m vs 212 ± 40 m; p = NS) (Figure 1). Moreover, the baseline scores on the 3 subscales of the WIQ changed significantly during AA supplementation: higher scores were obtained on the distance (54.2% ± 10.9% vs 68.3% ± 12%; $p < 0.001$), speed (52.2% ± 12% vs 72.2% ± 14.4%; $p < 0.001$), and stairs (72.4% ± 20.6% vs 98.2% ± 24%; $p < 0.001$) subscales of the questionnaire after AA treatment (Figure 1). Maximal isometric muscular strength also increased after oral AA supplementation, from 14.6 ± 2.2 kg to 20.2 ± 2 kg; $p < 0.001$) (data not shown).

Data on resting and exercise LV function are illustrated in Figure 2. All study subjects had a normal resting LV ejection fraction (LVEF) (>0.50). During AA treatment, neither resting LV end-diastolic volume nor LVEF changed significantly, but AA supply influenced LV performance during exercise. At the baseline examination, about 30% of subjects had LV dysfunction induced by isometric exercise. As a consequence, the LVEF at peak handgrip was significantly lower than the resting value (55% ± 9% vs 62% ± 8%; $p < 0.001$). After 3 months of oral intake of the AA mixture, the majority (75%) of subjects reversed this exercise LV dysfunction and values of peak exercise LVEF were higher than resting values (67% ± 7% vs 63% ± 6%; $p < 0.01$).

Effects in Elderly Patients with Chronic Heart Failure

In our pilot observational study, a group of 15 elderly patients with CHF (age range, 68–76 years; New York Heart Association [NYHA] class II–III) who were clinically stable and in therapy with angiotensin-converting enzyme (ACE) Inhibitors and diuretics were evaluated. The diagnosis of CHF was based on a history of exertional dyspnea or pulmonary edema and a reduced LVEF (<0.40). The underlying cause of CHF was ischemia in 92% and idiopathic dilated cardiomyopathy in 8%. These 15 patients were selected because they were normally nourished (normal body mass index and arm muscle area >10th percentile for age and sex) and had reduced exercise tolerance (peak oxygen consumption <15 mL/kg per minute in a bicycle ramp exercise test).

After basal assessment of cardiac function (by 2D echocardiography), 6-minute walk test, and blood variables, the AA mixture at a dosage of 4 g × 2 die was administered to patients in association with standard therapies and a controlled diet. The clinical evaluations were repeated 12 weeks later. Figure 3 shows the effects of AA supplementation on walking distance in elderly patients with CHF. At the basal evaluation, the 6-minute walk distance was 201 ± 12 m. At the end of AA treatment, the 6-minute walk distance significantly increased (226 ± 9.0 m; $p < 0.05$). Interestingly the urea values remained unchanged (31.3 ± 10.5 mg/dL vs 32.4 ± 8.1 mg/dL; p = NS) (data not shown).

Clinical Implications

In elderly persons without clinically evident cardiac disease, exercise LV dysfunction (despite a normal resting LV function) and a reduced ability of the muscle to work are important factors that can limit physical activity. The mixture of AAs tested improved walking capacity and maximal muscular strength without deleterious metabolic effects.[6] Notably, the increases in these parameters during AA supplementation were similar to those obtained through exercise training in elderly subjects.[7–10] Moreover, AA supplementation reversed exercise-induced LV dysfunction in most subjects. Thus, we can say that AA nutritional intervention may play a relevant role in improving and maintaining the advantageous effects of training. Indeed, it is well known that improvements obtained by exercise training are precarious and completely lost after a few months of detraining. In addition, interestingly, increased walking capacity and muscular strength may increase the capacity to perform everyday activities. Thus, the modified lifestyle could reduce the high risk of illness and disability in elderly subjects with a low physical activity.

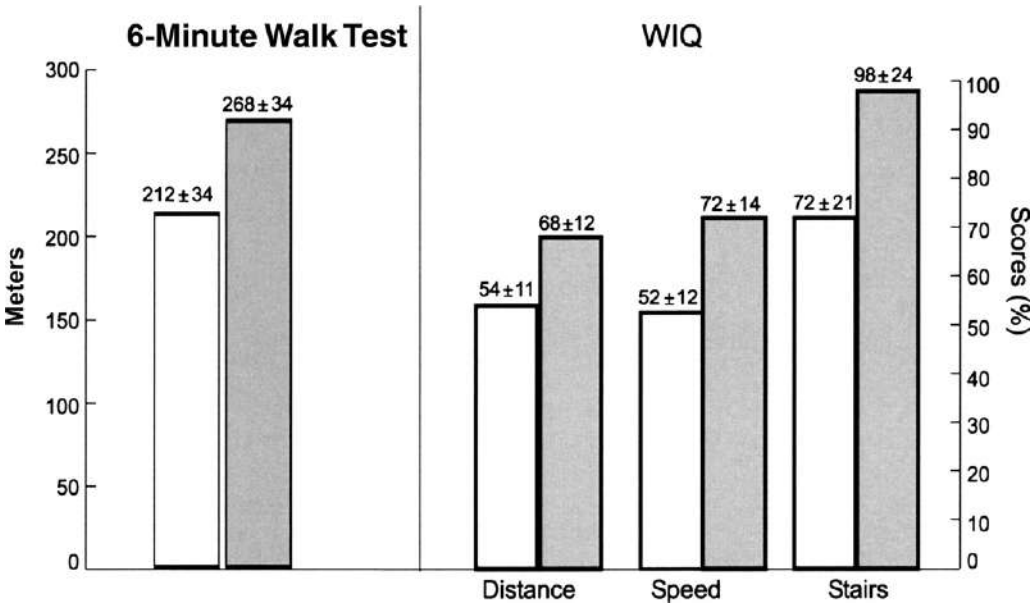

Figure 1. Changes at baseline (*white bars*) and after amino acid (AA) supplementation (*gray bars*) in the 6-minute walk test and self-perceived walking impairment induced by AA treatment. WIQ = Walking Impairment Questionnaire.

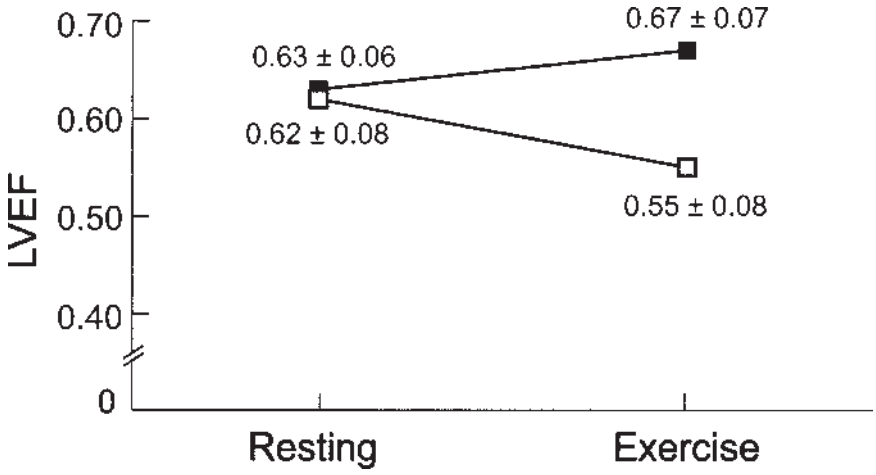

Figure 2. Left ventricular function, evaluated as left ventricular ejection fraction (LVEF), at rest and at peak exercise. Values are given for subjects at baseline (*white squares*) and after amino acid supplementation (*black squares*).

Finally, it is interesting to note that very preliminary data suggest that when associated with the standard therapy, AA supplementation may also improve the physical capacities of elderly patients with CHF.

Conclusion

Our observations must be confirmed in a randomized study with a large number of patients followed over a long period of time. Taken together, these results suggest the potential role of a nonpharmacologic therapy with nutrients (such as AAs) in an approach to improving muscular metabolism and function in elderly subjects with hypercatabolic syndromes.

Acknowledgment

We thank medical writer Dr. Robert Coates (Centro Linguistico, Bocconi University, Milan, Italy) for his linguistic revision.

Author Disclosures

The authors who contributed to this article have disclosed the following industry relationships:

Roldano Scognamiglio, MD, has no financial arrangement or affiliation with a corporate organization or a manufacturer of a product discussed in this article.

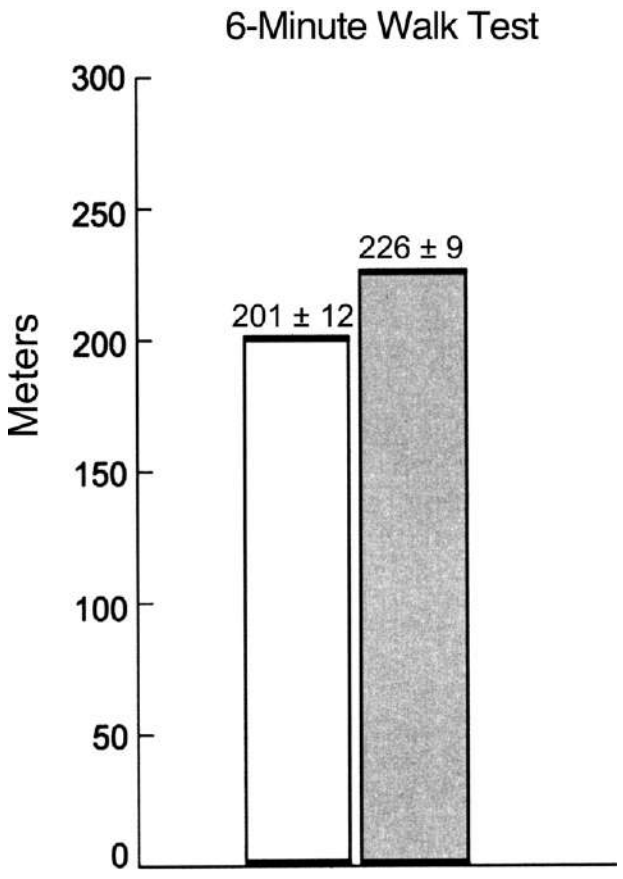

Figure 3. Changes in ambulatory capacity in patients with chronic heart failure at baseline (*white bars*) and after (*gray bars*) amino acid treatment.

Amidio Testa, MD, has no financial arrangement or affiliation with a corporate organization or a manufacturer of a product discussed in this article.

Roberto Aquilani, MD, has no financial arrangement or affiliation with a corporate organization or a manufacturer of a product discussed in this article.

Francesco S. Dioguardi, MD, serves as a consultant to Professional Dietetics s.r.l.

Evasio Pasini, MD, has no financial arrangement or affiliation with a corporate organization or a manufacturer of a product discussed in this article.

1. Berkman LF, Seeman TE, Albert M, Blazer D, Kahn R, Mohs R, Finch C, Schneider E, Cotman C, McClearn G. High, usual and impaired functioning in community-dwelling older men and women: findings from the MacArthur Foundation Research Network on Successful Aging. *J Clin Epidemiol* 1993;46:1129–1140.
2. Buchner DM. Physical activity and quality of life in older adults. *JAMA* 1997;277:64–66.
3. Volpi E, Ferrando AA, Yeckel CW, Tipton KD, Wolfe RR. Exogenous amino acids stimulate net muscle protein synthesis in the elderly. *J Clin Invest* 1998;101:2000–2007.
4. Scognamiglio R, Negut C, Piccoletto R, Dioguardi FS, Tiengo A, Avogaro A. Effects of oral amino acid supplementation on myocardial function in patients with type 2 diabetes mellitus. *Am Heart J* 2004; 147:1106–1112.
5. Aquilani R, Opasich C, Dossena M, Iadarola P, Gualco A, Arcidiaco P, Viglio S, Boschi F, Verri M, Pasini E. Increased skeletal muscle amino acid release with light exercise in deconditioned patients with heart failure. *J Am Coll Cardiol* 2005;45:158–159.
6. Scognamiglio R, Piccolotto R, Negut C, Tiengo A, Avogaro A. Oral amino acids in elderly subjects: effect on myocardial function and walking capacity. *Gerontology* 2005;51:302–308.
7. Binder EF, Schechtman KB, Ehsani AA, Stegen-May K, Brown M, Sinacore DR, Yarasheski KE, Holloszy JO. Effects of exercise training on frailty in community-dwelling older adults: results of a randomized, controlled trial. *J Am Geriatr Soc* 2002;50:1921–1928.
8. King AC, Rejeski WJ, Buchner DM. Physical activity interventions targeting older adults: a critical review and recommendation. *Am J Prev Med* 1998;15:316–333.
9. Stessman J, Hammerman-Rozenberg R, Maaravi Y, Cohen A. Effect of exercise on ease in performing activities of daily living and instrumental activities of daily living from age 70 to 77: the Jerusalem Longitudinal Study. *J Am Geriatr Soc* 2002;50:1934–1938.
10. Pickering GP, Fellmann N, Morio B, Ritz P, Amonchot A, Vermorel M, Boudert J. Effects of endurance training on the cardiovascular system and water compartments in elderly subjects. *J Appl Physiol* 1997;83:1300–1306.