

## PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) TUBE FEEDING OF NURSING HOME RESIDENTS IS NOT ASSOCIATED WITH IMPROVED BODY COMPOSITION PARAMETERS

S. KIMYAGAROV, D. TURGEMAN, Y. FLEISSIG, R. KLID, B. KOPEL, A. ADUNSKY

The "Gilad" Geriatric Center, Ramat-Gan, 52621, Israel. Corresponding author: Abraham Adunsky, adunger1@sheba.health.gov.il

**Abstract:** *Objectives:* To study differences in nutritional status and body composition, by feeding modality, among disabled nursing home residents. *Design:* A retrospective chart-review study. *Setting:* A nursing wing of a public urban geriatric center. *Participants:* Three groups of patients: non-dysphagic, orally-fed dysphagic and percutaneous endoscopic gastrostomy -fed dysphagic patients. *Intervention:* Standard nursing care. *Measurements:* Basal metabolic rate, total energy expenditure and nitrogen balance under oral or percutaneous endoscopic gastrostomy feeding. Dietary intake was assessed during a 3-days period by daily-food intake protocols and a 24-hours urinary creatinine excretion to detect nitrogen balance and calculate body composition parameters. *Results:* Data of 117 patients (55.5% females), mean age  $84.6 \pm 7.5$  (range 66-98 years) was analyzed. Dysphagic patients (60) differed from non-dysphagic patients (57) by lower body mass index ( $p=0.020$ ), fat mass index ( $p=0.017$ ), daily protein intake ( $p<0.0001$ ), daily energy intake ( $p<0.001$ ), protein related energy intake ( $p<0.001$ ) and a negative nitrogen balance ( $p<0.001$ ). In regression analyses, dysphagia was associated with increased risk of having a body mass index lower than  $22.0 \text{ kg/m}^2$  (OR=2.60, 95% CI 1.135-5.943), a negative nitrogen balance (OR=2.33, 95% CI 1.063-4.669), a low fat mass index (OR=2.53, 95% CI 1.066-6.007), and low daily protein and energy intakes per body weight (OR=2.87, 95% CI 1.316-6.268 and OR=2.99, 95% CI 1.297-6.880). Compared with orally-fed dysphagic patients (21pts.), percutaneous endoscopic gastrostomy -fed patients (39pts.) received an additional mean energy intake of 30.5% kcal per day and mean protein intake of 26.0%. This additional intake was not associated with improved body composition parameters (such as fat free mass, skeletal mass or body mass index). *Conclusion:* Dysphagic nursing home residents are characterized by worse nutritional, metabolic and body composition parameters, compared with non-dysphagic residents. Body composition parameters did not differ between orally-fed and percutaneous endoscopic gastrostomy-fed dysphagic patients, despite significantly better nutritional and metabolic parameters in PEG-fed patients. Other approaches (perhaps physical training, pharmacological etc.) should be sought to improve body composition of such patients.

**Key words:** Body composition, dietary protein, elderly, energy intake, nitrogen balance.

Dysphagia is common in patients with dementia, stroke, Parkinson and other neurodegenerative diseases, and is an important cause of weight loss in nursing home residents with a prevalence ranging between 40-60% (1-4). More than a half of all dysphagic patients are at high risk of malnutrition and dehydration due to low food intake that is strongly related to severity of dysphagia (5, 6). Between 43%–55% out of dysphagic patients suffer recurrent episodes of aspiration pneumonia and up to 50% will die within one year (7, 8). Inadequate protein and energy intake associated with impaired swallowing poses a challenge to caregivers with regards to optimizing disease management and nutritional support.

Recent reports of nutritional requirements for protein and energy, based on nitrogen balance studies, have suggested that intakes above the recommended dietary allowances (RDA) may prove beneficial for the healthy elderly population (9, 10). Due to low basal metabolic rates (BMR) and low energy requirements in the elderly, at any level of physical activity, protein/energy requirements ratio increases with age. Hence, the recommended daily amount of ingested protein of 0.86-1.0 g/kg body weight in healthy adult subjects and 1.25-1.5 g/kg in

frail elderly may be adequate (11). Caloric requirements may be up to 29% higher than basal metabolic rate, especially in demented nursing home residents (12-15).

Adjuvant feeding interventions by percutaneous endoscopic gastrostomy (PEG) technique is a common practice in cognitively impaired older patients who suffer eating or swallowing problems (16-18). Median PEG prevalence among nursing home residents varies between 5.6% in Germany and 34% in the USA (19-21). The prime purposes and hopes of tube feeding are avoiding hunger and thirst, improving nutritional status and preventing aspirations (22, 23), yet despite a vast use of PEG, data about protein-energy balance in such elderly institutionalized patients is scarce and largely unknown. A recent Cochrane review (24) has concluded that there was no evidence of increased survival in patients receiving enteral tube feeding. In addition, none of the studies included in this review showed benefits in terms of nutritional status and no reference was made as to body composition after PEG.

We hypothesized that controlled nutritional intake and improved nutritional parameters in PEG patients may result with better body composition parameters. Therefore, the

objective of this study was to look for possible differences in nutritional status and body composition among three groups of patients and to clarify the possible role of feeding modality on protein and energy intake of these patients and on body composition.

### Study participants

This is an observational retrospective chart-review study of 117 disabled demented elderly patients (65 females, 52 males) admitted to a nursing wing of a public urban geriatric center. All patients were 65 years and older (mean age 84.9±7.5, range 66–98 years). Patients were referred for permanent stays in the four nursing wards, after being considered as completely dependent patients in activities of daily living and mobility functions by certified geriatricians and a geriatric team comprising nurses, dietitians, physiotherapists, occupational therapist, social worker, etc. The study was approved by the local IRB of the hospital (no risk "exempt review" research). Data collection. We obtained data regarding age, gender, associated co-morbidities and anthropometric data. This included a routine BMI calculation (from weight and knee-ankle height) as well as fat free mass (FFM) and skeletal muscle mass (SMM) calculated by Forbe's and Heimsfield's equations (25, 26), respectively: FFM (kg) = 24.1×Urine Creatinine (g/24h)+20.7; SMM (kg) = 18.9×Urine Creatinine (g/24h)+4.1; We used a 24-hour creatinine excretion method to detect the status of skeletal mass because it specifically represents metabolically active muscle mass, in contrast to other types of investigation such as ultrasonography or computerized tomography which are difficult to perform in advanced nursing home populations. Additionally, this procedure is considered to be more sensitive than dual-energy X-ray absorptiometry or bioelectrical impedance analysis in detecting age-related changes in body mass, which may be due to changes in body water. BMR was calculated by Katch-McArdle equation (27) based upon FFM values, as follows: BMR (kcal)=370+(21.6×FFM, in kg). Functional status was evaluated according to the Functional Independence Measure (FIM) score (28) ranging between 18 (total functional dependence) to 126 (total functional independence).

Dietary intake was routinely assessed during a 3-days period (a. upon admission and under oral feeding; b. between 3-6 months after PEG insertion) by a daily food intake protocol, recording each component of consumed meals. Nitrogen balance (NB) in mg of nitrogen/kg/d was determined under usual (oral) or enteral (PEG) feeding. In each of these assessments we calculated dietary nitrogen intake, daily urinary nitrogen excretion and daily miscellaneous nitrogen losses (assumed to be as 20% of urinary nitrogen).

### Statistical analysis

All patients' data was used; no data were excluded from the analyses. Continuous data were compared using unpaired t-

tests, while binary data were compared using a Student t-test; all tests were two-sided, requiring  $p < 0.05$  to declare significance. In the multivariate model, we used a logistic regression analysis to assess associations between compared groups. All analyses were performed in a GCP-controlled environment using SAS version 8.2.

### Results

#### Patients' characteristics by dysphagia / no dysphagia

Overall, study population had a high prevalence of any dementia (92.8%), stroke (46.7%), Alzheimer's disease (31.7%) and Parkinson (21.6%). There were no differences between dysphagic and non-dysphagic patients regarding age or gender (Table 1). Dysphagic patients (60) differed from non-dysphagic patients (57) by lower values of BMI ( $p=0.020$ ), fat mass index ( $p=0.017$ ), daily protein intake ( $p<0.0001$ ), daily energy intake ( $p<0.0001$ ), protein related energy intake ( $p<0.0001$ ) and a negative nitrogen balance ( $p<0.001$ ). There were no differences between groups in BMR, FFM and SMM indexes. When analyzed by gender, dysphagic male patients had statistically significant more pronounced metabolic and nutritional derangements, compared with female patients (see Table 2).

**Table 1**

Baseline characteristics of study sample (117 pts.) by dysphagia / no dysphagia

	With dysphagia (57)	Without dysphagia (60)	p value
Age	85.0±7.5	85.0±5.3	NS
Male/Female ratio	1.0 : 1.19	1.0 : 1.11	NS
FIM score	46.5±24.8	30.4±17.2	<0.001
BMI (kg/m <sup>2</sup> )	25.7±4.0	23.8±4.3	0.020
Fat free mass index (kg/m <sup>2</sup> )	15.4±3.0	15.7±2.5	NS
Fat mass index (kg/m <sup>2</sup> )	10.2±4.5	8.2±4.5	0.017
Skeletal muscle mass index	7.41±1.91	7.59±1.42	NS
BMR(kcal/d)	1214±171		1218±145
NS			
Daily protein intake (g/d)	65.8±10.1	56.9±11.3	<0.001
Daily energy intake (kcal/d)	1596±405	1302±293	<0.001
Daily energy intake/BMR	1.31±0.70	1.07±0.20	0.012
Daily protein intake/BW	1.09±0.25	0.87±0.27	<0.001
Daily energy intake/ BW	25.8±5.6	22.5±6.2	<0.001
Protein related energy intake (%)	16.5±0.8	17.6±1.1	<0.001
Nitrogen balance	0.19±2.67	-1.47±2.59	<0.001

In regression analyses (Table 3), dysphagia was associated with increased risk of having a BMI<22.0kg/m<sup>2</sup> (OR=2.60, 95%CI 1.135-5.943,  $p=0.027$ ), being in a negative NB (OR=2.33, 95%CI 1.063–4.669,  $p=0.050$ ), and having a low fat mass index (OR=2.53, 95%CI 1.066–6.007,  $p=0.045$ ) as well as lower daily protein and energy intakes per body weight (OR=2.87, 95%CI 1.316–6.268,  $p=0.012$  and OR=2.99, 95%CI 1.297–6.880,  $p=0.016$ ).

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) TUBE FEEDING

**Table 2**

Descriptive Characteristics of dysphagic patients, by gender

Characteristic	Female (34)	Male (26)	p values
Age	85.7±5.5	84.1±4.9	NS
Body mass index (kg/m <sup>2</sup> )	25.6±5.4	21.9±2.8	0.002
Fat free mass index (kg/m <sup>2</sup> )	16.0±2.6	15.4±2.2	NS
Fat mass index (kg/m <sup>2</sup> )	9.6±5.3	6.5±2.4	0.007
Skeletal muscle mass index (kg/ m <sup>2</sup> )	7.3±1.2	7.9±1.8	NS
BMR (kcal/d)	1160±143	1291±110	NS
Daily protein intake (g/d)	60.9±10.7	50.9±12.0	0.001
Daily energy intake (kcal/d)	1376±283	1210±280	0.027
Daily energy intake/BMR	1.20±0.30	0.94±0.17	<0.001
Daily protein intake/BW (kg/d)	1.07±0.27	0.84±0.19	<0.001
Daily energy intake/BW (kcal/kg/d)	24.4±6.7	19.8±4.5	0.003
Protein related energy intake (%)	17.7±0.9	16.8±1.1	<0.001
Nitrogen balance	-0.66±1.97	-2.49±2.91	0.005

39 out of all 60 dysphagic patients underwent a PEG insertion procedure. In the other 21 patients, PEG insertion was rejected by care-giving guardians and patients went on with oral feeding. All patients were supplied with commonly used commercial isotonic formulas to provide an adequate total nutritional support. Table 4 shows that PEG-feeding was associated with additional energy intake of 30.5% kcal per day and increased protein intake of 26.0%. The daily energy intake/BMR, daily protein and energy intake/body weight ratios, compared with dysphagic oral-fed patients, were higher in PEG-fed patients. However, this was neither associated with improved BMI nor by body composition parameters (such as FFM index, fat mass index, skeletal mass index) or BMR.

**Table 3**

Regression analysis for nutritional and metabolic parameters associated with dysphagia

	Dysphagia (60pts.)	No Dysphagia (57pts.)	OR	95% CI		p
				Min	Max	
Body mass index <22.0 kg/m <sup>2</sup>	38.3%	19.3%	2.60	1.135	5.943	0.027
Low fat mass index	35.0%	17.5%	2.53	1.066	6.007	0.045
Daily protein intake/body weight <1.0g/kg/d	48.3%	24.6%	2.87	1.316	6.268	0.012
Daily energy intake/body weight <25.0 kcal/kg/d	41.7%	19.3%	2.99	1.297	6.880	0.016
Negative nitrogen balance	58.3%	38.6%	2.33	1.063	4.669	0.050

**Discussion**

Dysphagia is common in elderly institutionalized patients and is associated with weight loss, change of body composition and various nutritional deficiencies (4-6). The current approach to management of such patients favors early identification and subsequent attempts to prevent and treat potential complications, such as malnutrition (29,30). Despite extensive discussion about efficacy of PEG in demented people with inability to swallow or refusal to eat, use of PEG-feeding remains popular in this population.

**Table 4**

Body composition and nutrient intake, by feeding modality of dysphagic residents (60pts.)

Characteristics	Orally fed (21)	PEG-fed (39)	p
Age	84.6±6.9	84.1±8.5	NS
Body mass index (kg/m <sup>2</sup> )	23.5±3.7	24.2±3.1	NS
Fat free mass index (kg/m <sup>2</sup> )	15.8±2.7	15.7±3.0	NS
Fat mass index (kg/m <sup>2</sup> )	7.5±4.3	8.5±3.0	NS
Skeletal muscle mass index (kg/m <sup>2</sup> )	7.5±1.4	7.2±1.4	NS
Basal metabolic rate	1207±152	1198±161	NS
Daily protein intake	57.4±10.3	72.3±9.9	<0.001
Daily energy intake	1298±304	1585±329	<0.001
Daily energy intake/basal metabolic rate	1.0±0.2	1.3±0.4	0.012
Daily protein intake/body weight	0.9±0.2	1.2±0.3	0.002
Daily energy intake/body weight	23.1±6.9	31.8±9.4	<0.001
Protein related energy intake (%)	16.7±1.1	16.1±0.9	0.002
Nitrogen balance	-1.7±2.6	0.1±2.6	0.012

Our study shows that dysphagic institutionalized patients, compared with non-dysphagic patients, have lower values of BMI, fat mass index, daily protein and energy intake (both absolute and relative to body weight and to basal metabolic rate), as well as a more negative nitrogen balance. These findings are not surprising and are in accordance with previous studies (31, 32) showing that inadequate intakes have negative effects on energy-protein metabolism (particularly evident among males) and contribute to a more pronounced catabolic state in dysphagic patients (mean NB of -1.47±-2.59). The findings also support recent recommendations (11, 15) on the need to increase the amount of protein-caloric foods in frail elderly people who are high-risk due to co-existing morbidities and functional decline.

The literature regarding the effectiveness of enteral nutrition of elderly residents in long-term care facilities is controversial. Indeed, expert opinion has suggested that PEG-feeding may not be effective being unassociated with increased body weight or nutritional status improvement (33, 34). Clearly, PEG-insertion in dysphagic patients allows provision of nutrients and water, which resulted in our study in significant increases of daily caloric energy (by 30.5%), protein (by 26.0%) and conversion of a negative nitrogen balance into steady state equilibrium. This is in agreement with previous study (35) showings that mean protein intake needed to obtain a neutral nitrogen balance in elderly patients suffering from dysphagia must be higher than 1.28 g/kg per day (the RDA for healthy elderly people).

It has been previously shown (36, 37) that impaired body composition and specifically a low SMM index, increase the likelihood of death and may serve as a reliable predictor of 1-year survival in nursing home patients, compared with BMI or other body composition parameters. This is also supported by recent data showing that lower muscle mass is associated with similar trends in community-dwelling elderly (38). Taken altogether, these findings support the possibility that a low muscle mass has an independent effect on survival among nursing home residents and should be treated vigorously.

## JNHA: CLINICAL TRIALS AND AGING

Unfortunately, the nutritional and metabolic improvement in PEG-fed patients did not result in improved body composition parameters. One possible explanation for this observation may reflect the impaired modulation of myostatin pathway in circumstances such as inactivity, senescence and disease so common in demented and physically inactive elderly, resulting in up-regulation of myostatin and similar substances (39, 40). Still, it is possible that longer time periods of nutritional interventions are needed in order to affect body composition. Alternatively, this may suggest that strategies other than nutritional (e.g. pharmacological, physical therapy) should be sought in order to improve body composition, and consequently, improve survival.

Possible limitations in our study result from its retrospective nature and design, which does not allow for the establishment of a cause-effect relationship between enteral feeding and body composition parameters. In addition, despite adjustment made for important confounding variables, other may have not been considered. Finally, a longitudinal study with follow-up data of body composition and its interrelation with PEG feeding may provide information that could further clarify this issue. Despite these limitations, the present study is advantageous in the sense that it included a relatively large sample size of patients, all of whom underwent similar nursing and medical treatment programs, hence decreasing selection bias or a reduction in the validity of the study.

We conclude that understanding of the gap between nutritional parameters and body composition parameters is crucial and that other approaches, rather than nutritional, should be sought to improve body composition of these patients.

*Acknowledgements:* We give special thanks to all involved staff of the "Gilad Geriatric Center".

*Funding:* N/A

## References

1. Kayser-Jones J, Pengilly K. Dysphagia among nursing home residents. *Geriatr Nurs* 1999; 20:77-84.
2. O'Loughlin G, Shanley C. Swallowing problems in the nursing home: A novel training response. *Dysphagia* 1998; 13:172-83.
3. Ekberg O, Hamdy S, Woisard V, Wuttge-Hannig A, Ortega P. Social and physiological burden of dysphagia: its impact on diagnosis and treatment. *Dysphagia* 2002; 17:139-46.
4. Martineau J, Bauer JD, Isenring E, Cohen S. Malnutrition determined by the patient-generated subjective global assessment is associated with poor outcomes in acute stroke patients. *Clin Nutr* 2005; 24:1073-7.
5. Volkert D, Berner YN, Berry E, Cederholm T, Coti Bertrand P, Milne A et al. ESPEN guidelines on enteral nutrition: Geriatrics. *Clin Nutr* 2006; 25:330-60.
6. Leibovitz A, Baumoehl Y, Lubart E, Yaina A, Platinovitz N, Segal R. Dehydration among long-term care elderly patients with oropharyngeal dysphagia. *Gerontology* 2007; 53:179-83.
7. Marik PE, Kaplan D. Aspiration pneumonia and dysphagia in the elderly. *Chest* 2003; 124: 328-36.
8. Cabre M, Serra-Prat M, Palomera E, Almirall J, Pallares R, Clavé P. Prevalence and prognostic implications of dysphagia in elderly patients with pneumonia. *Age Ageing* 2009; 39:39-45.
9. Rand WM, Pellett PL, Young PR. Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. *Amer J Clin Nutr* 2003; 77:109-27.
10. Millward DJ. Sufficient protein for our elders? *Amer J Clin Nutr* 2008; 88:1187-8.
11. Wolfe RR, Miller SL, Miller KB. Optimal protein intake in the elderly. *Clin Nutr* 2008; 27: 675-84.
12. Wolf-Klein GP, Silverstone FA, Lansley SC, Tesi D, Ciampaglia C, O'Donnell M, et al. Energy requirements in Alzheimer's disease patients. *Nutrition* 1995; 11:264-8.
13. Poehlman ET, Dvorak RV. Energy expenditure, energy intake, and weight loss in Alzheimer disease. *Amer J Clin Nutr* 2000; 71:650S-5S.
14. Eastwood C, Davies GJ, Gardiner FK, Dettmar PW. Energy intakes of institutionalized and free-living older people. *J Nutr Health Aging* 2002; 6:91-2.
15. Alix E, Berrut G, Boré M, Bouthier-Quintard F, Buia JM, Chlala A et al. Energy requirements in hospitalized elderly people. *J Amer Geriatr Soc* 2007; 55:1085-9.
16. Freeman C, Ricevuto A, DeLegge MH. Enteral nutrition in patients with dementia and stroke. *Curr Opin Gastroenterol* 2010; 26:156-9. doi: 10.1186/1471-2318-7-22..
17. Shaikh AK, Hamilton EL, Bharadwaj P, Ward K. Revising the use of percutaneous endoscopic gastrostomy tubes in patients with advanced dementia. *Palliat Care Res Treat* 2009; 3:1-2.
18. Aita K, Takahashi M, Miyata H, Kai I, Finucane TE. Physicians' attitudes about artificial feeding in older patients with severe cognitive impairment in Japan: a qualitative study. *BMC Geriatr* 2007; 7:22.
19. Mitchell SL, Teno JM, Roy J, Kabumoto G, Mor V. Clinical and organizational factors associated with feeding tube use among nursing home residents with advanced cognitive impairment. *J Amer Med Assoc* 2003; 290: 73-80.
20. Clarfield AM, Monette J, Bergman H, Monett M, Ben-Israel Y, Caine Y, et al. Enteral feeding in end-stage dementia: a comparison of religious, ethnics and national differences in Canada and Israel. *J Gerontol* 2006; 61A: 621-7.
21. Wirth R, Bauer JM, Willschrei HP, Volkert D, Sieber CC. Prevalence of percutaneous endoscopic gastrostomy in nursing home residents. A nationwide survey in Germany. *Gerontology* 2010; 56: 371-7.
22. Jaul E, Singer P, Carderon-Margalit R. Tube feeding in the demented elderly with severe disabilities. *Isr Med Assoc J* 2006; 8:870-4.
23. Löser C, Aschl G, Hébuterne X, Mathus-Vliegen EM, Muscaritoli M, Niv Y et al. ESPEN guidelines on artificial enteral nutrition - Percutaneous endoscopic gastrostomy (PEG). *Clin Nutr* 2005; 24:848-61.
24. Candy B, Sampson EL, Jones L. Enteral tube feeding in older people with advanced dementia: findings from a Cochrane systematic review. *Int J Palliat Nurs* 2009; 15:396-404.
25. Forbes GB, Bruining GJ. Urinary creatinine excretion and lean body mass. *Amer J Clin Nutr* 1976; 29:1359-66.
26. Heymsfield SB, Arteaga C, McManus C, Smith J, Moffitt S. Measurement of muscle mass in humans: validity of the 24-hour urinary creatinine method. *Amer J Clin Nutr* 1983; 37:478-94.
27. McArdle W, Katch F, Katch V. 1996. *Exercise Physiology: Energy, Nutrition, and Human Performance*, 4th edition. Baltimore: Williams & Wilkins, p.850.
28. Linacre JM, Heinemann AW, Wright BD, Granger CV, Hamilton BB. The structure and stability of the Functional Independence Measure. *Arch Phys Med Rehabil* 1994; 75:127-32.
29. Berner YN, Stern F, Polyak Z, Dror Y. Dietary intake analysis in institutionalized elderly: a focus on nutrient density. *J Nutr Health Aging* 2002; 6:237-42.
30. Rofes L, Arreola V, Almiral A. Diagnosis and management of oropharyngeal dysphagia and its nutritional and respiratory complications in the elderly. *Gastroenterol Res Pract* 2011;818979. doi: 10.1155/2011/818979.
31. Millward DJ, Fereday A, Gibson N, Pacy PJ. Aging protein requirements and protein turnover. *Amer J Clin Nutr* 1997; 66:774-86.
32. Fukagawa NK, Young VR. Protein and amino acid metabolism and requirements in older persons. *Clin Geriatr Med* 1987; 3:329-41.
33. McCann R. Lack of evidence about tube feeding - food for thought. *J Amer Med Assoc* 1999; 1282: 1380-1.
34. Friedel DM, Ozick LA. Re-thinking the role of tube feeding in patients with advanced dementia. *N Engl J Med* 2000; 342(23):1756.
35. Gaillard C, Alix E, Boirie Y, Berrut G, Ritz P. Are elderly hospitalized patients getting enough protein? *J Am Geriatr Soc* 2008; 56:1045-9.
36. Kimyagarov S, Klid R, Levenkrohn S, Fleissig Y, Kopel B, Arad M., et al. Body mass index, body composition and mortality of nursing home elderly residents. *Arch Gerontol Geriatr* 2010; 51:227-30.
37. Landi F, Liperoti R, Fusco D, Mastropaolo S, Quattrociochi D, Proia A et al.. Sarcopenia and mortality among older nursing home residents. *J Am Med Dir Assoc* 2012; 13:121-6.
38. Wijnhoven HA, Snijder MB, van Bokhorst de van der Schueren MA, Deeg DJ, Visser M. Region-specific fat mass and muscle mass and mortality in community-dwelling older men and women. *Gerontology* 2012; 58:32-40.
39. Jespersen J, Kjaer M, Schjerling P. The possible role of myostatin in skeletal muscle atrophy and cachexia. *Scand J Med Sci Sports* 2006; 16:74-82.
40. Yarasheski KE, Bhasin S, Sinha-Hikim I, Pak-Loduca J, Gonzalez-Cadavid NF. Serum myostatin-immunoreactive protein is increased in 60-92 year old women and men with muscle wasting. *J Nutr Health Aging* 2002; 6:343-8.