The Journal of Latin American

Geriatric Medicine

Volume 2 – Number 2 – 2016
Published Quarterly – ISSN: 2462-2958 – www.conameger.org

Official Journal of the COLEGIO NACIONAL DE MEDICINA GERIÁTRICA

PERMANYER MÉXICO
www.permanyer.com

The Journal of Latin American

Geriatric Medicine

Volume 2 – Number 2 – 2016
Published Quarterly – ISSN: 2462-2958 – www.conameger.org

Revista disponible íntegramente en versión electrónica en www.conameger.org

Official Journal of the COLEGIO NACIONAL DE MEDICINA GERIÁTRICA

PERMANYER MÉXICO
www.permanyer.com

THE JOURNAL OF LATIN AMERICAN GERIATRIC MEDICINE ORIGINAL ARTICLE

Systemic inflammatory response and mortality in hospitalized elderlies

Julio Alberto Díaz-Ramos[1]*, Carlos Adolfo Gazcón-Orozco[1], Adrián Camacho-Ortiz[2] and David Leal-Mora[1]

[1]Geriatrics Department, Benemérito Hospital Civil Fray Antonio Alcalde, Guadalara, Jal.; [2]Infectious Diseases Department, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey. Mexico

Abstract

Introduction: *Care for the elderly is increasing in emergency departments, and older patients present with complex medical conditions. Sepsis is one of the first causes of emergency department visits in the elderly. Existing data is contradictory, reporting that the elderly have enhanced or suppressed acute inflammation responses and these might contribute to death in hospitalized elderlies.* **Objectives:** *To determine whether the presence of systemic inflammatory response syndrome increases the risk of in-hospital mortality in adults over 60 years of age in the geriatric service of a university hospital.* **Patients and methods:** *Cross-sectional study of ≥ 60-year-old adults who had been admitted to the Geriatrics Service of a university tertiary hospital between August 2010 and December 2011. In-hospital mortality and mortality associated to the number of systemic inflammatory response syndrome components were analyzed. Odds ratio was determined in order to establish the risk between variables.* **Results:** *The in-hospital mortality rate was 15.8%. The systemic inflammatory response syndrome criteria were met in 30.9% of the patients. The odds ratio between the deceased systemic inflammatory response syndrome group and participants that survived was 1.4198 (95% CI: 0.813-2.4781; p = 0.2174.* **Conclusions:** *This study showed no risk relationship between the presence of systemic inflammatory response syndrome and in-hospital mortality in elderly patients.* (J Lat Am Geriat Med. 2016;2:45-50)

Key words: *Elderly. Mortality. Systemic inflammatory response.*

Corresponding author: *Julio Alberto Díaz-Ramos, julio.alberto.diaz.ramos.geriatra@gmail.com*

Resumen

Introducción: Los ancianos requieren cada vez más de los servicios de urgencias y se presentan con condiciones médicas complejas. La sepsis es una de las primeras causas de visitas a urgencias en los ancianos. Los datos existentes son contradictorios con respecto a si los adultos mayores tienen mayor o menor respuesta inflamatoria aguda y si esto contribuye a la muerte en ancianos hospitalizados. **Objetivos:** Determinar si la presencia del síndrome de respuesta inflamatoria sistémica (SRIS) aumenta la probabilidad de mortalidad hospitalaria en adultos mayores de 60 años en el Servicio de Geriatría de un hospital universitario. **Pacientes y métodos:** Estudio transversal en adultos mayores de 60 años admitidos en el Servicio de Geriatría de un hospital universitario de tercer nivel entre agosto de 2010 y diciembre de 2011. Se analizaron la mortalidad hospitalaria y la mortalidad en asociación con el número de componentes del SRIS. Se obtuvieron *odds ratio* (OR) con el fin de establecer el riesgo entre las variables. **Resultados:** La mortalidad global fue del 15.8%. El 30.9% de los pacientes cumplieron con los criterios de SRIS. La OR entre el grupo de participantes con SRIS que fallecieron y los que sobrevivieron fue de 1.4198, con un intervalo de confianza (IC) del 95% de 0.813-2.4781 (p = 0.2174). **Conclusiones:** Este estudio muestra una no relación de riesgo entre la presencia de SRIS y la mortalidad hospitalaria en pacientes ancianos.

Palabras clave: Respuesta inflamatoria sistémica. Mortalidad. Ancianos.

Correspondence to:
*Julio Alberto Díaz-Ramos
OPD Hospital Civil de Guadalajara
Unidad Hospitalaria Fray Antonio Alcalde
Calle Hospital, 278,
C.P. 44280, Guadalajara, Jal., México
E-mail: julio.alberto.diaz.ramos.geriatra@gmail.com

INTRODUCTION

Sepsis and inflammatory response in old age

Care for elderly people is increasingly in emergency departments (ED), and older patients typically present with complex medical conditions, stay longer for more-extensive diagnostic testing and treatment regimens and require special needs during their visit[1,2]. Up to 21% of visits to EDs are made by elderlies. Up to 50% of the elderly who attend an ED are hospitalized. This rate is 4.6 times higher than in young people[3]. Sepsis is one of the first causes of ED visits in older people. It is also the 10th cause of death in elderly people[4]. Sepsis represents a malignant generalized inflammation comprising the systemic inflammatory response syndrome (SIRS), which progresses through stages of increasing severity[5-8]. Existing data is contradictory regarding whether older adults have enhanced or suppressed acute inflammation and whether this contributes to the in-hospital mortality[9-12].

Twenty-five years after the definition of sepsis it has received a new revision. The task force defined sepsis as "life-threatening organ dysfunction due to a dysregulated host response to infection"[13]. In the absence of a gold-standard test for sepsis, several domains of validity and usefulness were used to assess potential clinical criteria to operationalize this definition. Among encounters with suspected infection, the Sequential (sepsis-related) Organ Failure Assessment (SOFA) and Logistic Organ Dysfunction System (LODS) scores have greater predictive validity compared with SIRS criteria[14]. The syndrome of systemic inflammatory response has been defined according to the presence of certain criteria: temperature > 38 or < 36 ºC, heart rate > 90 beats per minute, respiratory rate > 20 breaths per minute, or arterial carbon dioxide voltage < 32 mmHg, white blood cell count 10^9 > 12,000 or < 4,000 per mm^3 or bands > 10% (immature neutrophils)[15,16].

Blood stream infections can produce an immune response to bacterial endotoxins. Innate immune response stimulates macrophages to produce tumor necrosis factor (TNF), interleukin-1, and interleukin-6 (IL-1, IL-6). These three proinflammatory cytokines produce the inflammatory response, which is characteristic of early sepsis[17].

In severe sepsis, evidence of widespread organ dysfunction is also present, including multiorgan dysfunction (lung, liver, and/or kidney injury). The so-called "septic shock", in which patients suffer cardiovascular collapse unresponsive to fluid resuscitation and vasopressor therapy, is often the terminal event of severe sepsis[18].

SIRS with inappropriate vasodilatation is observed in many elderly patients and may contribute to the excessive mortality rate, and in this population it could be manifested by cognitive impairment, reduced functional capacity, and different inflammatory responses[19-21].

Immunosenescence

Inflammation is a key contributor to the pathophysiology of severe sepsis. While inflammation plays an important role in normal host defense, host responses become harmful during uncontrolled systemic activation[9,10,22]. Altered regulation of inflammation is postulated to be a central explanation as to why the elderly with infections have an exponentially higher risk of developing worse outcomes than younger adults[10,23-27].

Immunosenescence is characterized by an increased activity and different intensities in the immune system[28,29]. Excess comorbidity and poly-pathology could explain the inflammatory imbalance that the Anglo-Saxon literature has called from 15 years ago "inflammaging"[30,31]. We now know that this is a state of chronic inflammation, low grade, controlled, and asymptomatic; however, the increased serum levels of IL 6, 8, and 15, along with TNF-α favors organ damage at multiple levels and reduces responses to any aggressor event[32,33].

The role of the white cell count in the elderly with SIRS diagnosis remains unclear. Leukocytosis commonly accompanies SIRS; however, the white cell count may be within or even below the normal range in older people. Furthermore, the white cell count can be raised in inflammation with non-infectious causes, making it rarely helpful as a sole diagnostic parameter[9-12,23,34].

Age-related defects in the human immune system principally affect the adaptive immune response, as evidenced by major defects in cell-mediated immunity and significant impairment of humoral immune responses with age[23,34].

The presence of SIRS is one of the classic features of sepsis. However, it is not a typical finding in elderly patients. The evidence is inconclusive and often shows a considerable number of elderly patients without full features of SIRS. The aim of this study is

to determine whether the presence of SIRS increases the risk of in-hospital mortality in adults over 60 years old in the geriatric service of a university hospital.

METHODS

Design and patient selection

This was a cross-sectional study of ≥ 60-year-old adults admitted to the geriatrics ward. The criteria for SIRS were registered as the main variables.

We included all patients who were admitted between August 2010 and December 2011. The SIRS criteria for diagnoses were taken during the first record of vital signs and blood count registered during the hospitalization period. SIRS was defined as the presence of two or more of the following criteria: tachycardia, tachypnea or hypoxia; hypothermia or hypothermia; and leukocytosis, leukopenia, or bandemia. SIRS was defined as previously described[12,15,16]. We excluded all patients in which it was not possible to obtain full clinical records.

Table 1. Patient characteristics

Baseline characteristic	n (%)
Age (years)	
60-69	4 (0.9)
70-79	49 (12)
≥ 80	351 (87.1)
Gender	
Female	234 (58)
Male	170 (42)
SIRS criteria	
1	159 (39.4)
2	81 (20.0)
3	37 (9.2)
4	7 (1.7)
Causes of in-hospital mortality	
Community-acquired pneumonia	11 (17.2)
Healthcare-associated pneumonia	7 (10.9)
Urinary tract infection	6 (9.4)
Non-infectious causes	40 (62.5)

SIRS: systemic inflammatory response syndrome.

Setting

The study was performed at the Hospital Civil de Guadalajara Fray Antonio Alcalde, a 1000-bed teaching hospital in Mexico. The hospital has an average of 33,000 admissions per year and the geriatric service admits an average of 1,700 patients per year with an average length of hospital stay of seven days.

Statistical analysis

Frequencies and percentages were calculated. The chi-square or Fishers exact test were used for comparing percentages. Odds ratio (OR) was determined in order to establish the risk between variables. A P-value < 0.05 was considered statistically significant. In-hospital mortality and mortality in association with the number of SIRS components were analyzed.

RESULTS

A total of 404 patients were included. The mean age was 85 years old (SD ± 7) and 58% were women. The overall mortality rate was 15.8%. Baseline characteristic summary is shown in table 1.

Only 30.9% of patients met the criteria for SIRS, of whom 24 died, representing 37.5% of total deaths. A total of 101 patients with SIRS were discharged alive, representing 29.7% of outgoings. The prevalence of SIRS was 30.9%. A higher percentage of participants with two diagnostic criteria were identified in comparison to the group with four of them (20.0 vs. 1.7%). The most prevalent SIRS criteria diagnosed in the group of deceased elderly were respiratory rate (> 20/min) present in 48%, followed by leukocyte cell count (> 12,000 mm^3) present in 42.6%. In the group of deceased patients, the most prevalent SIRS criteria were respiratory rate (50%) and heart rate (HR) in 36%. The in-hospital mortality rate in those patients who did not meet the SIRS diagnosis was 62.5 vs. 37.5% in patients with SIRS. The difference between these two groups was 25% and did not reach significance (95% CI: −2.54 to 48.83; $x^2 = 3.706$; p = 0.0542). The in-hospital mortality rate in the presence of SIRS in patients ≥ 80 years old was not significantly different than that observed in the group of younger elderly (p = 0.1423). Mortality by age group can be seen in table 2.

The OR obtained between the ≥ 2 SIRS criteria groups (deceased and survivors) was 1.4198 with a 95% CI: 0.813-2.4781; p = 0.2174 (Table 3).

DISCUSSION

In this study no greater risk of in-hospital mortality was demonstrated in the presence of SIRS in elderly

Table 2. In-hospital mortality according to age group and systemic inflammatory response syndrome presence

Age (years)	Survivor % (n)	Mortality % (n)	OR	95% CI	P
60-69	33.3 (1)	0.0 (0)	0.5556	0.0126-24.5152	p = 0.7610
70-79	22.9 (8)	35.7 (5)	1.8750	0.4870-7.2197	p = 0.036
≥ 80	30.5 (92)	38.8 (19)	1.4457	0.7740-2.7001	p = 0.2476

Table 3. In-hospital mortality according to the number of systemic inflammatory response syndrome criteria

SIRS	Survivor % (n)	Mortality % (n)	Total % (n)
0	31.5 (107)	20.3 (13)	29.7 (120)
1	38.8 (132)	42.2 (27)	39.4 (159)
2	19.1 (65)	25.0 (16)	20.0 (81)
3	9.1 (31)	9.4 (6)	9.2 (37)
4	1.5 (5)	3.1 (2)	1.7 (7)
Total	(340)	(64)	(404)

SIRS: systemic inflammatory response syndrome.

patients. Our results partially replicate the results obtained in previous studies.

The prevalence of SIRS in our study was 30.9%, very similar to that reported in the elderly population by other authors. For example, in a study performed in over 3,000 patients diagnosed with sepsis, SIRS was identified in 29.2%. Of those patients, 44.2% presented changes in body temperature, 58.4% had tachycardia, 32.3% presented tachypnea, and 36.3% showed changes in white blood cell count[35]. Also, tachycardia and tachypnea prevalences in our study's population coincide with that reported in the previously mentioned analysis. Like them, a HR > 90 and respiratory rate > 20 were the signs most frequently found (50 and 48%, respectively). In another cohort of 11,988 patients with a mean age of 66 years, non-SIRS diagnostic criteria were met in 28%[36].

The link between poor outcomes and SIRS has been assessed without results supporting that the presence of SIRS increases the mortality risk in the elderly. It is undeniable that most of our study's population did not meet sufficient criteria to classify within the SIRS group. This finding is frequent in most studies performed in the elderly. For example, in a study in which the elderly showed a fivefold greater likelihood of severe sepsis than younger adults (6.5 vs. 1.3%), vital signs in the severe sepsis group were slightly different than those in the uninfected group and none achieved classifying within the definitions of SIRS[37]. Similarly, a prospective study performed in an emergency department of a university hospital, assessing a group of 56 patients, demonstrated bacterial infections in 39 of the subjects; the average age of this subgroup was 60 years old and the average SIRS criteria was 2[38].

The methodology of our study does not establish a causal relationship; however, the probability of risk (OR: 1.41; 95% CI: 0.813-2.4781; p = 0.2174) indicates no differences between the development or not of SIRS for the worst outcome in sepsis: death.

A study analyzed a mortality prognostic tool for the elderly, which compared laboratory variables between survivors and non-survivors. Heart rate and respiratory rate were related to increased mortality risk[39]. In another study of 23,114 subjects, characteristics of the elderly in the ED and 30-day mortality were analyzed. The prevalence of mortality was 20.7% in those > 75 years vs. 4.5% in participants < 75 years. This result is similar to the difference obtained in our study between groups of ≥ 80 vs. < 80 years old (12.0 and 3.7%, respectively; 95% CI: 5.29-12.85; p = 0.0001). The OR for 30-day mortality in older group adjusted to the severity of the disease was 2.9 (95% CI: 2.50-3.42). It is noteworthy that without adjustment for severity (which included white blood cell count), the OR increased to 5.21[40]. With all this, there are other studies that have found no relationship between the presence of SIRS and death[41-46].

As we have seen, the presence of SIRS and its association with sepsis in elderly patients remains an indecisive observation in most studies.

The cross-sectional design is the main limitation of this study because it is not possible to know the

direction of the correlations founded. Short data collection precluded a better analysis in this study. Our analysis did not consider other characteristics such as geriatric syndromes and comorbidity of participants. Despite this study's limitations, the analysis shows no risk probability between SIRS criteria and mortality.

CONCLUSION

Our study showed that there is no association between SIRS and in-hospital mortality in elderly patients with sepsis. We believe this may reflect the complexity of the phenomenon of inflammaging and how it interacts with the rest of the characteristic pathophysiological mechanisms of an aging population (Fig. 1; original scheme of the authors).

Until we have adequate biomarkers as predictors of risk levels, the assessment of elderly patients continues to be a challenge for health professionals in the acute-care context. However, we have the clinical tools called Comprehensive Geriatric Assessment (CGA). The CGA is a multidimensional and interdisciplinary diagnostic process to assess the functional capacity and health status of the elderly patient; through the CGA we are capable to develop a highly individualized therapeutic plan. The CGA requires considerable time and experience however that is not always available in the emergency wards. An alternative to CGA can be a risk-screening test. Loss of functionality is one of the risk factors that have proven to be a predictor of adverse outcomes in the context of ED. However, evidence of this strategy is inconclusive. Different strategies for elderly care in the ED are adaptations from the CGA. The integration of this type of evaluation within the medical approach in the ED has shown to reduce mortality and disability and even lower healthcare costs[48-51].

Given the particularly vulnerable situation of elderly patients, the most important recommendation in order to establish appropriate interventions and achieve better outcomes is promoting strategies for timely identification of elderly patients with high risk in the context of acute infections[3,52].

We believe that in the absence of reliable traditional prognostic markers, it is necessary to promote knowledge about the complexity of elderly patients and educate all members of the medical team about the most useful clinical approaches in elderly people. This strategy is essential to generate the sensitivity, knowledge, and skills to face the geriatric problems[3,53,54].

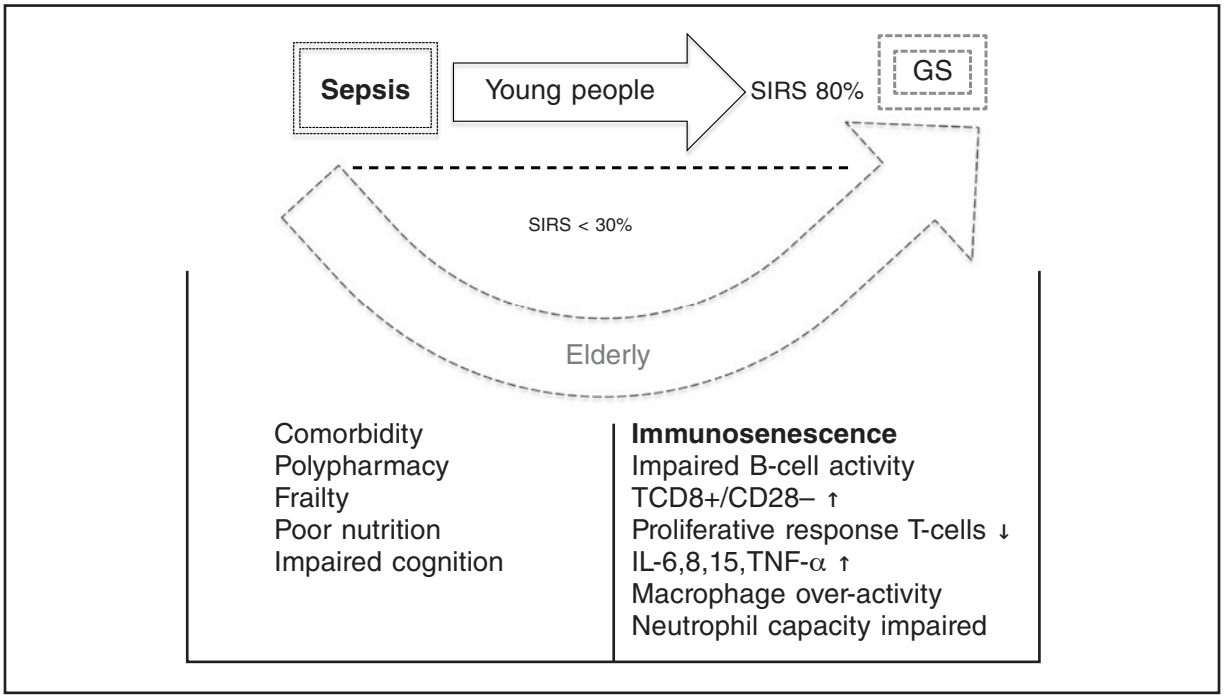


Figure 1. *Relation between sepsis, systemic inflammatory response syndrome and immunosenescence. GS: geriatric syndrome. IL: interleukin; SIRS: systemic inflammatory response syndrome; TNF: tumor necrosis factor. (Original scheme of the authors).*

REFERENCES

1. Wilber ST, Gerson LW, Terrel K, et al. Geriatric emergency medicine and the 2006 IOM reports on the future of emergency care. Acad Emer Med. 2006; 13:1345-51.
2. Hwang U, Morrison RS. The Geriatric Emergency Department. J Am Geriatr Soc. 2007;55:1873-6.
3. Aminzadeh F, Dalziel WB. Older adults in the emergency department: a systemic review of patterns of use, adverse outcomes, and effectiveness of interventions. Ann Emerg Med. 2002;39:238-47.
4. Angus DC, Wax RS. Epidemiology of sepsis: an update. Crit Care Med. 2001; 29(Suppl):109-16.
5. Muckart DJ, Bhagwanjee S. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference definitions of the systemic inflammatory response syndrome and allied disorders in relation to critically injured patients. Crit Care Med. 1997;25:1789-95.
6. Bossink AW, Groeneveld AB, Hack CE, Thies LG. Prediction of mortality in febrile medical patients. Chest. 1998;113:1533-41.
7. Alberti C, Brun-Buisson C, Goodman SV, et al. Influence of systemic inflammatory response syndrome and sepsis on outcome of critically ill infected patients. Am J Respir Crit Care Med. 2003;168:77-84.
8. Brun-Buisson C, Doyon F, Carlet J, et al. Incidence, risk factors, and outcome of severe sepsis and septic shock in adults. JAMA. 1995;275:968-74.
9. Leentjens J, Kox M, van der Hoeven JG, Netea MG, Pickkers P. Immunotherapy for the adjunctive treatment of sepsis: from immunosuppression to immunostimulation Time for a paradigm change? Am J Respir Crit Care Med. 2013;187: 1287-293.
10. Kale SS, Yende S. Effects of aging on inflammation and hemostasis through the continuum of critical illness. Aging Dis. 2011;2:501-11.
11. Marik PE, Zaloga GP. The effect of aging on circulating leveles of proinflamatory cytokines during septic shock. J Am Geriatr Soc. 2001;49:5-9.
12. American College of Physicians/Society of Critical Care Medicine Consensus Conference Commite. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992;20:864-74.
13. Shankar-Hari M, Phillips GS, Levy ML, et al. Sepsis Definitions Task Force. Developing a new definition and assessing new clinical criteria for septic shock: for the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:775-87.
14. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD. Assessment of Clinical Criteria for Sepsis For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:762-74.
15. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest. 1992;101:1644-55.
16. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. JAMA. 1995;273:117-23.
17. Henriquez-Camacho C, Losa J. Biomarkers for sepsis. BioMed Res Int. 2014;2014:547818.
18. Faix J. Biomarkers of sepsis. Crit Rev Clin Lab Sci. 2013;50:23-36.
19. Kohsaka S, Menon V, Lowe AM, et al. Systemic inflammatory response syndrome after acute myocardial infarction complicated by cardiogenic shock. Arch Intern Med. 2005;165:1643-50.
20. Grimble RF. Inflammatory response in the elderly. Curr Opin Clin Nutr Metab Care. 2003;6:21-9.
21. Thomas DR. The relationship between functional status and inflammatory disease in older adult. J Gerontol Biol Sci Med Sci. 2003;58A:995-8.
22. Seeley EJ, Matthay MA, Wolters PJ. Inflection points in sepsis biology: from local defense to systemic organ injury. Am J Physiol Lung Cell Moll Physiol. 2012;303:L355-63.
23. Opal SM, Girard TD, Ely EW. The immunopathogenesis of sepsis in elderly patients. Clin Infect Dis. 2005;41(Suppl 7):S504-12.
24. DeGaudio ER, Rinaldi S, Chelazzi C, Borracci T. Pathophysiology of sepsis in the elderly: clinical impact and therapeutic consideration. Curr Drug Targets. 2009;10:60-70.
25. Boyd AR, Orihuela CJ. Dysregulated inflammation as a risk factor for pneumonia in the elderly. Aging Dis. 2011;2:487-500.
26. Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. N Engl J Med. 2003;348:138-50.
27. Angus DC, van der Poll T. Severe Sepsis and septic schock. N Engl J Med. 2013;369:840-51.
28. Delves PJ, Roitt IM. The immune system (First of two parts). N Engl J Med. 2000;343:37-49.
29. Delves PJ, Roitt IM. The immune system (Second of two parts). N Engl J Med. 2000;343:108-17.
30. Franceschi C, Bonafe M, Valensin S, Olivieri F, De Luca M, Otta VE. Inflamm aging. An evolutionary perspective in immunosenescence. Ann NY Acad Sci. 2000;908:244-54.
31. Navarrete-Reyes AP, Montaña-Alvarez M. [Inflammaging. Aging inflammatory origin]. Rev Invest Clin. 2009;61:327-36.
32. Salminen A, Huuskonen J, Ojala J, Kauppinen A, Kaarniranta K, Suuronen T. Activation of innate immunity system during aging: NF kB signaling is the molecular culprit of inflamm aging. Ageing Res Rev. 2008;7:83-105.
33. Giunta S. Is inflammaging an auto(innate)immunity subclinical syndrome? Immun Ageing. 2006;3:12.
34. Shinkai S, Konishi M, Shephard RJ. Aging and immune response to exercise. Can J Physiol Pharmacol. 1998;76:562-72.
35. Shapiro N, Howell MD, Bates DW, Angus DC, Ngo L, Talmor D. The association of sepsis syndrome and organ dysfunction with mortality in emergency department patients with suspected infection. Ann Emerg Med. 2006;48:583-90.
36. Prier- Lindvig K, Pilsgaard-Herniksen D, Lonberg-Nielsen S, et al. How do bacteramic patients presents to the emergency department and what is the diagnostic validity of the clinical parameters; temperature, C-reactive protein and systemic inflamatory response syndrome? Scand J Trauma Resusc Emerg Med. 2014;221:39.
37. Ginde AA, Moss M, Shapiro NI, Schwartz RS. Impact of older age and nursing home residence on clinical outcomes of U.S. emergency department visits for severe sepsis. J Crit Care. 2013;28:606-11.
38. ten Oever J, Tromp M, Bleeker-Rovers CP, et al. Combination of biomarkers for the discrimination between bacterial and viral lower respiratory tract infections. J Infect. 2012;65:490-5.
39. Lee JS, Choi HS, Ko YG, Yun DH. Performance of the Geriatric Nutritional Risk Index in predicting 28-day hospital mortality in older adult patients with sepsis. Clin Nutr. 2013;32:843-8.
40. Byrne DG, Chung SL, Bennett K, Silke B. Age and outcome in acute emergency medical admissions. Age Ageing. 2010;39:694-8.
41. Hausfater P, Juillien G, Madonna-py B, Haroche J, Bernard M, Riou B. Serum procalcitonin measurement as diagnositic and prognostic marker in febrile adult patient presenting to the emergency department. Crit Care. 2007;11: R60.
42. Andrié RP, Ulrich MB, Ricarda F, Vedat T, Jan WS. Interleukin-6 is the estrongest predictor of 30-day mortality in patients with cardiogenic shock due to myocardial infarction. Crit Care. 2012;16:R152.
43. Nick- Hisamuddin NA, Azlan K. The use of laboratory and physiological parameters in predicting mortality in sepsis induced hypotension and septic shock patients attending the emergency department. Med J Malaysia. 2012;67: 259-64.
44. Wester AL, Dunlop O, Melby KK, Dahle UR, Wyller TB. Age-related differences in symptoms, diagnosis and prognosis of bacteremia. BMC Infect Dis. 2013; 13:346.
45. Wei C, Lei Z, Suping N, et al. The diagnostic value of different pro-inflammatory factor in early diagnosis of sepsis in patients with bloodstream infection. Chin Crit Care Med. 2014;26:165-70.
46. Ratzinger F, Schuardt M, Eichbichler K, Tsirkinidou I, Bauer M. Utility of sepsis biomarkers and the Infection Probability Score to discriminate sepsis and systemic inflammatory response syndrome in standard care patients. PLos One. 2013;8:e82946.
47. Buurmana BM, van den Berga W, Korevaarb JC, Milisend K, de Haanc RJ, de Rooij SE. Risk for poor outcomes in older patients discharged from an emergency department: feasibility of four screening instruments. Eur J Emerg Med. 2011;18:215-20.
48. McCusker J, Verdon J, Tousignant P, de Courval LP, Dendukuri N, Belzile E. Rapid emergency department intervention for older people reduces risk of functional decline. Results of a multicenter randomized trial. J Am Geriatr Soc. 2001;49:1272-81.
49. Lang PO, Zekry D, Michel JP, et al. Early markers of prolongued hospital stay in demented inpatients: a multicentre and prospective study. J Nutr Heath Aging. 2010;14:141-7.
50. Graf CE, Zekry D, Giannelli S, Michel JP, Chevalley T. Efficiency and applicability of the comprehensive geriatric assessment in the emergency department: a systematic review. Aging Clin Exp Res. 2011;23:244-54.
51. Graf CE, Zekry D, Giannelli S, Michel JP, Chevalley T. Comprehensive geriatric assesment in the emergency department. J Am Geriatr Soc. 2010;58:2032-3.
52. McCusker J, Cardin S, Bellavance F, Belzile E. Return of the emergency department among elders: patterns and preictors. Acad Emerg Med. 2000;7:249-59.
53. Jones JS, Rousseau EW, Schropp MA, Sanders AB. Geriatric training in emergency medicine residency programs. Ann Emerg Med. 1992;21:825-9.
54. Brymer C, Cavanagh P, Bawden M. Geriatric educational needs assessment of emergency department nurses. Gerontol Geriatr Educ. 1996;17:51-60.

THE JOURNAL OF LATIN AMERICAN GERIATRIC MEDICINE REVIEW ARTICLE

Nutritional issues in geriatric care: nutrition and HIV

Julio Alberto Díaz-Ramos[1]*, Luz Alicia González-Hernández[2], Claudia Fraga-Ávila[3], Gabriela Asencio-del Real[1], Alicia Piñeirúa-Menéndez[4], David Leal-Mora[1] and José Alberto Ávila-Funes[5]

[1]Department of Geriatrics and [2]HIV Unit, Hospital Civil Fray Antonio Alcalde; [3]Clinical and Geriatric Nutrition, Universidad Autónoma de Guadalajara. Guadalara, Jal.; [4]Specialst Clinic Condesa Iztapalapa; [5]Department of Geriatrics, Instituto Nacional de Ciencias Médicas Salvador Zubirán. Mexico City, Mexico

Abstract

The proportion of people over 50 years old living with HIV is increasing globally. The focus on HIV management must now include active surveillance of non-infectious and chronic comorbidities in a growing group of aging patients. In Mexico, there have been 22,150 HIV cases in adults older than 50 years, which represent 12% of the total affected population. Individuals at all stages of HIV disease are at risk of nutritional deficiency, and nutritional status is a strong predictor of disease progression, survival, and functional status during the course of the disease. HIV and malnutrition may cause severe immunodeficiency, which ultimately increases susceptibility to negative outcomes. Hence a cycle of frailty, malnutrition, and immunodeficiency is described. Weight loss and wasting syndrome are characteristic of advanced HIV disease and are strong predictors of mortality and morbidity in the ageing patient. Promoting a healthy nutritional state and avoiding weight loss can have multiple benefits in terms of improved response to antiretroviral therapy or in reducing morbidity and mortality. Nutritional assessment and dietary advice should be promoted as standards of quality of care of patients with HIV. The objective of this review is to present a detailed and exhaustive description of the current scientific evidence of nutritional aspects in the HIV population over 50 years old. (J Lat Am Geriat Med. 2016;2:51-62)

Key words: *Elderly. Frailty. HIV. Malnutrition.*

Corresponding author: *Julio Alberto Díaz-Ramos, julio.alberto.diaz.ramos.geriatra@gmail.com*

Resumen

La proporción de personas que viven con el VIH mayores de 50 años está aumentando a nivel mundial. El enfoque en la gestión del VIH debe incluir ahora una vigilancia activa de las comorbilidades no infecciosas y crónicas en un grupo cada vez mayor de pacientes de edad avanzada. En México, se han registrado 22,150 casos de VIH en adultos mayores de 50 años, que representan el 12% de la población total afectada. En todas las etapas de la enfermedad del VIH los pacientes están en riesgo de deficiencia nutricional, y el estado nutricional es un fuerte predictor de la progresión de la enfermedad, supervivencia y estado funcional durante el curso de la enfermedad. El VIH y la malnutrición pueden causar graves problemas de inmunodeficiencia, que en última instancia aumentan la susceptibilidad de desenlaces negativos. Por lo tanto, se describe un ciclo de fragilidad, desnutrición e inmunodeficiencia. La pérdida de peso y el síndrome de desgaste son características de la enfermedad avanzada por VIH, así como fuertes predictores de mortalidad y morbilidad en el paciente anciano. Promover un estado de nutrición saludable y evitar la pérdida de peso puede tener múltiples beneficios en términos de mejora de la respuesta a la terapia antirretroviral o en la reducción de la morbilidad y la mortalidad. En consecuencia, la evaluación nutricional y el asesoramiento dietético deben promoverse como estándares de calidad en la atención de los pacientes con VIH. El objetivo de esta revisión es presentar una descripción detallada y exhaustiva de la evidencia científica actual de los aspectos nutricionales en la población con VIH de más de 50 años de edad.

Palabras clave: VIH. Desnutrición. Ancianos. Fragilidad.

Correspondence to:
*Julio Alberto Díaz-Ramos
OPD Hospital Civil de Guadalajara
Unidad Hospitalaria Fray Antonio Alcalde
Calle Hospital, 278
C.P. 44280, Guadalajara, Jal., México
E-mail: julio.alberto.diaz.ramos.geriatra@gmail.com

INTRODUCTION

The proportion of people living with HIV (PLWH) over 50 years old is increasing globally[1-3]. Special interest has risen to better understand both their clinical behavior and the specific physiopathological aspects of HIV infection among the elderly. Moreover, PLWH have an increased risk of premature onset of age-associated chronic diseases that appeared to occur earlier among HIV-positive patients than HIV-negative subjects[4]. The focus on HIV management must now include, besides AIDS and acute complications, active surveillance of non-infectious and chronic comorbidities in a growing group of aging patients. The objective of this review is to present a detailed and exhaustive description of the current scientific evidence of nutritional aspects in the HIV population over 50 years old.

HIV INFECTION AMONG OLDER ADULTS: A REGIONAL PERSPECTIVE

Currently in developed countries almost 50% of PLWH are aged 50 years or older[5]. The increasing number of older adults living with HIV is in part due to the impact of highly active antiretroviral therapy (HAART), which has greatly improved the prognosis of HIV infection, allowing HIV-infected subjects to reach almost the same life expectancy as HIV-negative controls[6-8]. This benefit now poses new challenges for clinicians in order to adequately approach this growing population[9].

Also, according to the Centers for Prevention and Disease Control (CDC) in the USA, it was estimated that in 2010, 25% of newly diagnosed HIV/AIDS occurred in people aged 50 and older, while in the year 2000 they accounted for only 10%[10]. Here it is worth mentioning two things: some aging with HIV, and others diagnosed in old age. The two numbers have increased. This increase has been attributed to the lack of risk perception regarding HIV infection. This poor perception of risk is in both patient and health staff. Additionally, this specific population may be more vulnerable to HIV infection due to biological changes associated with the aging process (e.g. dryness of mucous membranes, more likely to have trauma, and susceptibility to virus). The introduction of drugs that enhance sexual performance and the establishment of a culture of aging in which it is allowed to have new and multiple sexual partners at older ages may have played a role in the increase of new sexual behaviors (e.g. non-protected sexual activity)[11].

Data regarding HIV infection in Latin American countries is limited and mainly comes from Brazil, Mexico, and Argentina[12,13]. In Mexico, the prevalence among the general population is around 0.2-0.3%, while prevalences among most at risk populations, such as men who have sex with men (MSM), transgender women, and male sex workers, can be as high as 20%. In MSM, prevalence varies across regions. In the study conducted by Bautista, the Midwestern region of Mexico has the lowest prevalence (9.9%) compared to the Northwest and East Central (20.0 and 20.4%, respectively). The same study reported an increase in the risk of acquiring HIV infection with age[14]. In Mexico, from 1983 to 2016, there have been 22,150 HIV cases in adults older than 50 years, which represents 12% of the total affected population, with an incidence of 12% in 2016[15]. Recently, in an analysis published by Avila-Funes, a sample of 184 adults over 50 with HIV was reported. The mean age in this study conducted in Mexico City was 59 years[16]. However, there is still limited data regarding the aging population living with HIV in Mexico.

AGING AND IMMUNOSENESCENCE

Aging is characterized by the acceleration of the rate of physiological damage and the accumulation of the resulting deficit in the body. Both mechanisms cause cellular damage as those trying to repair contribute to depletion of the cell and its regenerative capabilities[17].

Immunosenescence is characterized by an increase in activity in the immune system[18,19]. In biological aging, T-cells undergo deregulations in their proliferative capacity, and there is an increase in $CD8^+$ T/CD28 lymphocytes. On the other hand, it is likely that oxidative stress is the cause of a decrease in production of interleukin 2 (IL-2) and its receptors. The predominance of the Th2 response causes an increase in the activity of B-cells. There is also an increase in the number and activity of natural killer (NK) cells in improper compensation-specific cellular response[20,21]. Macrophages are over-activated, and neutrophils and antigen-presenting cells decrease their phagocytosis, thus hindering antigen presentation to lymphocytes[22].

There are different intracellular signaling pathways involved in the immune response, which are responsible for the characteristic biochemical profile of

immune senescence[23]. Some intracellular and nuclear systems responsible for promoting and suppressing the production of cytokines and their best-studied cell receptors are nuclear factor kappa B (NF-kB), sirtuins, and forkhead system box O (FoxO)[24-33]. The key to the aging of inflammatory origin is the way in which the senescent immune system converges with different wireless cell systems (NF-kB, sirtuins, FoxO) to produce deleterious effects by reactions that in previous stages of life favor survival while in older age predispose to degenerative diseases that cause the characteristic functional impairment[34].

AGING, IMMUNOSENESCENCE AND HIV

Some authors consider that HIV infection causes premature aging[35]. This is based on the fact that PLWH have multiple complications that are observed in HIV-negative populations as a consequence of aging, such as cognitive impairment, malnutrition, sarcopenia, osteoporosis and fractures, loss of physical abilities, falls, and frailty syndrome (FS)[36-49].

Most of these complications have been related to chronic immune activation, a characteristic feature of HIV infection, as well as to the numerical loss and dysfunction of $CD4^+$ cells in both clinical settings[50]. Ávila-Funes has previously published the biological similarities between aging, fragility, and HIV infection[51]. These include DNA damage, loss of DNA repair capacity, and altered apoptosis mechanisms of immune system cells[52,53].

Chronic exposure to antigens causes alterations in the immune response associated with both morbidity and mortality in old age. These changes have been grouped as "immunophenotype risk". This is characterized by (i) low levels of B-cells, (ii) increased levels of $CD8^+$ T-cells/$CD28^-$, (iii) poor proliferative response of T-cells, (iv) CD4/CD8 < 1, and (v) seropositivity to cytomegalovirus (CMV)[54,55]. Immunophenotype appears to be involved in the prevalence of comorbidity in older adults with HIV[56]. Compared to HIV-negative individuals, PLWH experience depletion of CD4 and high viral load and have high levels of inflammatory markers (IL-6), coagulation disorders, and activation of monocytes[57]. In the context of HIV infection, evidence suggests an inverse relationship between the use of antiretroviral therapy and these inflammatory markers[58]. There are observations that have confirmed the close relationship of the immune status of patients with HIV and the development of comorbidities typically observed in older age and the way in which HAART improves life expectancy and reduces developing disability risk[59-61]. Thus, it is clear that aging and HIV-1 infection are associated with similar immunological changes (Table 1).

Table 1. Immunosenescence and HIV

Immunological disorders common to aging and HIV infection
Risk immunophenotype:
1. Low levels of B-cells
2. B-cell activity increased and altered
3. Increased levels CD8+ T-cells/CD28–
4. Poor proliferative response of T-cells
5. Ratio CD4/CD8 < 1
6. CMV seropositivity
7. Elevated serum levels of IL-6, 8, 15, TNF-alpha
8. Decreased serum levels of IL-2 and their receptors
9. Predominance of Th2 response
10. Macrophages over-activated
11. Neutrophils and antigen-presenting cells with decrease in phagocytic capacity
12. Increased activity of NK cells

CMV: cytomegalovirus; IL: interleukin; NK: natural killer; TNF: tumor necrosis factor.

FRAILTY AND HIV

Frailty is a condition that increases vulnerability to stress; it is associated with a dysfunctional homeostatic response, and an increase in the likelihood of developing adverse outcomes (e.g. disability and death)[62,63]. Frailty syndrome can play more than a pathophysiologic role in older people with HIV[64-66]. It seems that FS occurs most often in the presence of low CD4 cell counts. It draws attention to the fact that to achieve an increase in CD4 using HAART, some pathological conditions (e.g. frailty, malnutrition) are reversed. Analyses show that there is no significant association between age and FS, when adjusted to CD4, but there is a significant association between age and CD4 count. As for HAART, prolonged use appears to be a protective factor against FS only if the CD4 count is at normal levels. For example, each year added on antiretroviral treatment, the risk of developing FS might decrease by up to 20%[67].

Chronic inflammation in old age is one of the factors that cause a state of vulnerability that is explained by the phenotype of frailty. The Cardiovascular Health Study found that frail patients had

C-reactive protein levels higher than non-frail participants[68]. Elevated levels of IL-6 in elderly women have also been associated with both loss of muscle strength, decreased speed, as well as increased disability for basic and instrumental activities of daily life[69,70]. Furthermore, high levels of IL-6 appear to predict the development of disability[71].

Sarcopenia is an essential component in the development of frailty phenotype[72]. Proteolytic and cytotoxic properties of tumor necrosis factor-alpha (TNF-a) and IL-6 generate cachexia and muscle wasting, which leads to loss of strength and muscle mass. Immobility also causes decreased muscle strength and endurance; this change has also been associated with increased serum levels of TNF-a and IL-6[73,74]. *In vitro*, high levels of IL-6 models cause suppression of the production of insulin growth factor (IGF)-1, and are predictors of handgrip strength and muscle power[75]. High levels of IL-6 with low levels of IGF-1 are also associated with an increased risk of disability and death in the aging population. In addition, levels of IGF-1 in the elderly relate to the status of body composition and intensity of loss of lean muscle mass with aging[76]. Functional skills are, for geriatrics, one of the most effective measures to understand the impact of aging through a range of different diseases such as HIV[77]. Functional complications of aging have been previously identified in both HIV and aging research after observations of the high prevalence of frailty phenotype in PLWH in the MACS study (Multicenter AIDS Cohort Study)[44].

NUTRITION AND AGING IN HIV INFECTION

The prevalence of malnutrition in the population with HIV has been previously described. Some studies have reported the nutritional characteristics of the population with HIV in Latin America. For example in Cuba, a descriptive study (which included populations with maximum age 41 years old) showed that the average weight of the study population was 66 kg with a body mass index (BMI) of 23 (SD ± 3.7). The classification of their nutritional status according to BMI was low for BMI < 18.5 (four patients). They also used the Subjective Global Assessment (SGA) where 12 out of 217 PLWH classified in malnutrition[78].

In Uganda, Mokori found a major prevalence of malnutrition (80%), but only 12% of participants had BMI values < 18.5[79]. In Latin America, Benavente described in Peru that 32.5% of HIV patients showed some degree of malnutrition[80]. Freijo explained that this variability was because malnutrition prevalence in PLWH depends on the diagnostic test used[81]. The prevalence of malnutrition in PLWH may also depend on the use of HAART and presence of coinfection. In a study conducted prior to antiretroviral therapy, and using the Chang algorithm for evaluation of nutritional status, malnutrition was found in 22% of HIV-positive asymptomatic individuals. However, this percentage varied depending on the disease progression: 42.7% of those classified as C2 were malnourished and 87.5% of those assigned to the C1 phase[82]. In a cross-sectional study of the health system in Brazil, they observed that older adults with HIV and coinfections had lower average weight versus young PLWH without hepatitis or tuberculosis[83]. In a cohort of more than 6,000 people with HIV in South Africa (54% aged 40 or older) the prevalence of malnutrition (BMI < 18.5) was 29 and 13% in rural and urban areas, respectively. Of participants who did not complete the study due to death, 45% had a BMI compatible with malnutrition. In this analysis, overweight and obesity were associated with lower mortality[84]. In another analysis of more than 400 participants, the average BMI was 24 and only 11% were classified as underweight (malnutrition)[85].

Treatment of HIV/AIDS and consequent patient survival can lead to overweight, obesity, and lipodystrophy. Accumulating evidence has shown that overweight and obesity are highly prevalent, even greater than weight loss[86]. Compared to the general population, the prevalence of obesity in adults with HIV has been reported as 46% lower in men and 17% higher in women[87]. In the VACS-VC cohort (Veterans Aging Cohort Study-Virtual Cohort), a prospective observational cohort of infected and noninfected veterans, BMI at baseline was 25[88]. In a cohort of minorities in North America (Hispanics and African Americans) 37.5% of the participants were classified as overweight at baseline and 22.1% as obese[89]. Still, in a cross-sectional and prospective study consisting of 140 newly diagnosed HIV-positive patients, 67% had normal weight according to BMI, 18.57% were considered as underweight, and only 1.43% were overweight; two patients (1.43%) were obese. The mean BMI was 21.59[90]. In all these studies the mean age ranged between 49 and 60 years.

It is undeniable that elderly patients with HIV are prone to malnutrition due to inadequate food intake, loss of appetite, nutritional loss, metabolic changes, and increases in the requirements of micro- and

macronutrients. To this must be added the other special factors of vulnerability in older people: socioeconomic factors, poverty, inability to feed themselves, and lack of social support[91]. Unintentional weight loss, changes in body composition, and metabolic changes associated with the use of antiretroviral therapy are common comorbidities in people aging with HIV. Individuals at all stages of HIV disease are at risk of nutritional deficiency, and nutritional status is a strong predictor of disease progression, survival, and functional status during the course of the disease[92].

NUTRITIONAL STATUS AND ITS ASSOCIATIONS IN HIV BASED ON EVIDENCE

Alterations in body weight have a negative influence on the health of PLWH. In the cohort of Nutrition For Healthy Life (NFHL), wasting syndrome (weight loss > 10%) was observed in 18%[4]. Other studies have reported a higher frequency of office visits and twice the costs in annual healthcare related to weight loss among PLWH[93]. An analysis of a cohort of veterans with HIV showed the importance of a healthy weight or even overweight, adjusted for duration of antiretroviral treatment. These weight ranges were associated with greater increases in CD4 cells compared with obese subjects or underweight patients[94].

It is well known that adherence is critical to achieve suppression of viral replication, reduce $CD4^+$ cell decrease, prevent viral resistance, promote immune reconstitution, and slow the progression of disease[95,96]. In a case control study looking at factors influencing HAART adherence, it was found that malnutrition (BMI < 18.5) in the group with adequate adherence was 8% compared to the non-adherent group where malnutrition was 42.5%. Also, the inability to obtain sufficient food and quality food was associated with poor adherence[97]. It has been reported that about 25% of patients on HAART who fail to achieve adequate levels of adherence also have nutritional disorders, and this may be for common causes such as poverty, poor support network, depression, etc.[98]. In an analysis in Africa, authors identified malnutrition (BMI < 18.5) and inadequate quantity and quality intake of food in 24 hours (< 3 meals/day) as an independent factor associated with non-adherence to HAART. It is noteworthy that the diagnosis of malnutrition was 10-times more frequent in participants without adherence than among adherent patients. Thus, eating a meal a day and dependence on food were both risk factors for a poor therapeutic adherence[99]. Food insecurity and malnutrition hinder adherence to HAART and are associated with negative outcomes related to HIV. In a study of educational intervention, adherence improved after systematically applying nutrition education[85]. Patients starting HAART who do not follow the nutritional recommendations are at increased risk of adverse drug effects, which can cause discomfort so intense as to lead to discontinuing or abandoning therapy. It is also known that poor nutritional status negatively affects the effectiveness of drug metabolism[100-104].

On the other hand, baseline BMI can be a predictor of recovery of $CD4^+$ cell counts in patients starting HAART. A high BMI is also associated with slow progression of HIV[105,106]. In a cohort in Tanzania, 27% had BMI < 18.5. In this group, any weight loss was associated with 5.4-fold increased risk of mortality compared to those who maintain or gain weight[107]. This analysis proved that a low BMI at the start of HAART and/or weight loss after the first month of treatment had an association with mortality. This means that malnutrition as measured by BMI may be an independent predictor of mortality[108-110]. The death risk appears to increase with increasing weight loss. Not surprisingly, malnutrition or severe emaciation are considered AIDS-defining entities[111]. In a different study, a group of adults living with HIV received nutritional supplements for six months (maximum age 43 years). The supplemented patients increased median CD4 (151 vs. 77 cells/mm^3 in controls) during the study period. Patients receiving supplementation also experienced a greater increase in body weight (12.7 vs. 4.9%; $p = 0.047$) and BMI (7.8 vs. 5.5%; $p = 0.007$). The BMI improved to 12 months (4.2 vs. 0.2; $p = 0.046$) as well as the absolute CD4 count (83.0 vs. 46.4%; $p = 0.002$)[112].

The association between nutritional status and immune performance is a constant result in multiple studies. In a study in patients with AIDS who were hospitalized in a university hospital and were receiving antiretroviral therapy, low BMI (18.5) had a significant association with decreased leukocytes and lymphocytes and lower hemoglobin and albumin levels compared to groups with BMI above the rank of malnutrition[113]. In cross-sectional study, longitudinal analyses data came from a sample of 864 HIV-infected MSM. Over time it was observed that overweight and obese PLWH possessed higher CD4 counts and lower

viral loads compared to normal weight HIV-infected men[114]. The lack of food security and poor nutritional status may accelerate the progression of HIV-related diseases (e.g. frailty) and undermine both adherence and treatment response to HAART[115]. The interaction between HIV/AIDS and malnutrition increases the burden of each condition alone. The PLWH require greater protein and micronutrient intake to support a weakened immune system. So in the assessment of nutritional status in HIV patients, especially those with infection, age becomes a health priority[116].

Therefore, the nutritional status prior to initiation of therapy and food security is not the only way that food and nutrition interact in PLWH. It is well known that some antiretroviral medications must be ingested with food. The elderly living with HIV are also more vulnerable to malnutrition since they may have impaired nutrient absorption (due to diarrhea/intestinal tract damage), reduced food intake (due to symptoms such as vomiting or pain on swallowing), food insecurity, and medication side effects such as loss of appetite or depression[117].

BIOLOGICAL PLAUSIBILITY BETWEEN HIV IN OLD AGE AND MALNUTRITION: A SHARED PATHOPHYSIOLOGY

The overlap between HIV and malnutrition has been recognized since the beginning of the AIDS epidemic, and poor nutritive states are observed frequently in patients without HAART with low $CD4^+$ cell counts or high levels of HIV-1 RNA cells. The relationship between nutritional status and HIV/AIDS, particularly those observed in immunological and clinical characteristics, were initially observed in 1992 in the MACS study. Eventually these data were used to create a phenotype related to FS, approximating four of the five domains of the Fried phenotype (in which are included unintended weight loss and decreased caloric intake). In this classic study, a strong association between HIV infection and the phenotype related to frailty was found in the MACS study[44]. In this respect, the studies of post-HAART era aimed to reinforce the theory that the presence of poor nutritional status, partially evaluated through the presence of FS, had a direct relationship with the immune status and the consequent viral load. By comparing the two eras of treatment, pre-HAART patients had a higher prevalence of FS than those post-HAART (24 vs. 10%)[43,45]. So, malnutrition is strongly associated with traditional markers of HIV disease, in particular $CD4^+$ cell count (current and nadir) and the detectable viral load[118-121]. The association between malnutrition, frailty, and low CD4 and/or presence of AIDS has been replicated previously[122]. Factors associated with malnutrition can lead to a greater understanding of the pathophysiology and development of potential interventions in HIV-infected populations. Malnutrition is commonly found in adults with HIV over 50 years old. A high $CD4^+$ cell count and decreased viral load are predictors of malnutrition in HIV[123,124]. Lack of essential micronutrients may not only contribute to the depletion and dysfunction of CD4 cells, but malnourished patients may have a suboptimal response to treatment when it is initiated. HIV and malnutrition may cause severe immunodeficiency, which ultimately increases susceptibility to negative outcomes. Hence, a cycle of frailty, malnutrition, and immunodeficiency is described[51]. Weight loss and wasting syndrome are characteristic of advanced HIV disease and are strong predictors of mortality and morbidity[125,126] (Fig. 1).

As noted in patients without HIV, the FS is detected more frequently in PLWH with the following characteristics: poorly educated, unemployed, with low income, presence of diabetes, kidney disease, symptoms of depression, and HCV coinfection. The FS is associated also with the nadir and current CD4 count and detectable RNA viral load[118-120,127].

In a descriptive study of body composition in African women of an urban population, participants were stratified according to baseline $CD4^+$ cell count. The analysis found that, compared with a group with cell count < 200 (median 175 cells/mm^3), weight and BMI in patients with better immune status (median 420) were higher (62.3 vs. 72 kg and 23.5 vs. 27.8 kg, respectively). The percentage of patients with malnutrition according to BMI was lower in patients with better immune status (1 vs. 11%)[128]. In the NFHL cohort, low $CD4^+$ cell counts were associated with low weights. In fact, for every decrease of 100 cell/mm^3 $CD4^+$ there was a decrease of 1.9 kg in weight[129]. In a study in West Africa that aimed to evaluate the impact of a nutritional intervention on the immune status, an increase in CD4 cell count 1.7 times higher (114 vs. 68 CD4 cells/mm^3) was found when comparing the nutritional support group versus the control. This finding shows how the nutritional status may influence treatment outcomes of HIV/AIDS[130].

Does HIV accelerated or accentuated aging? In some pathological processes in HIV there seems to

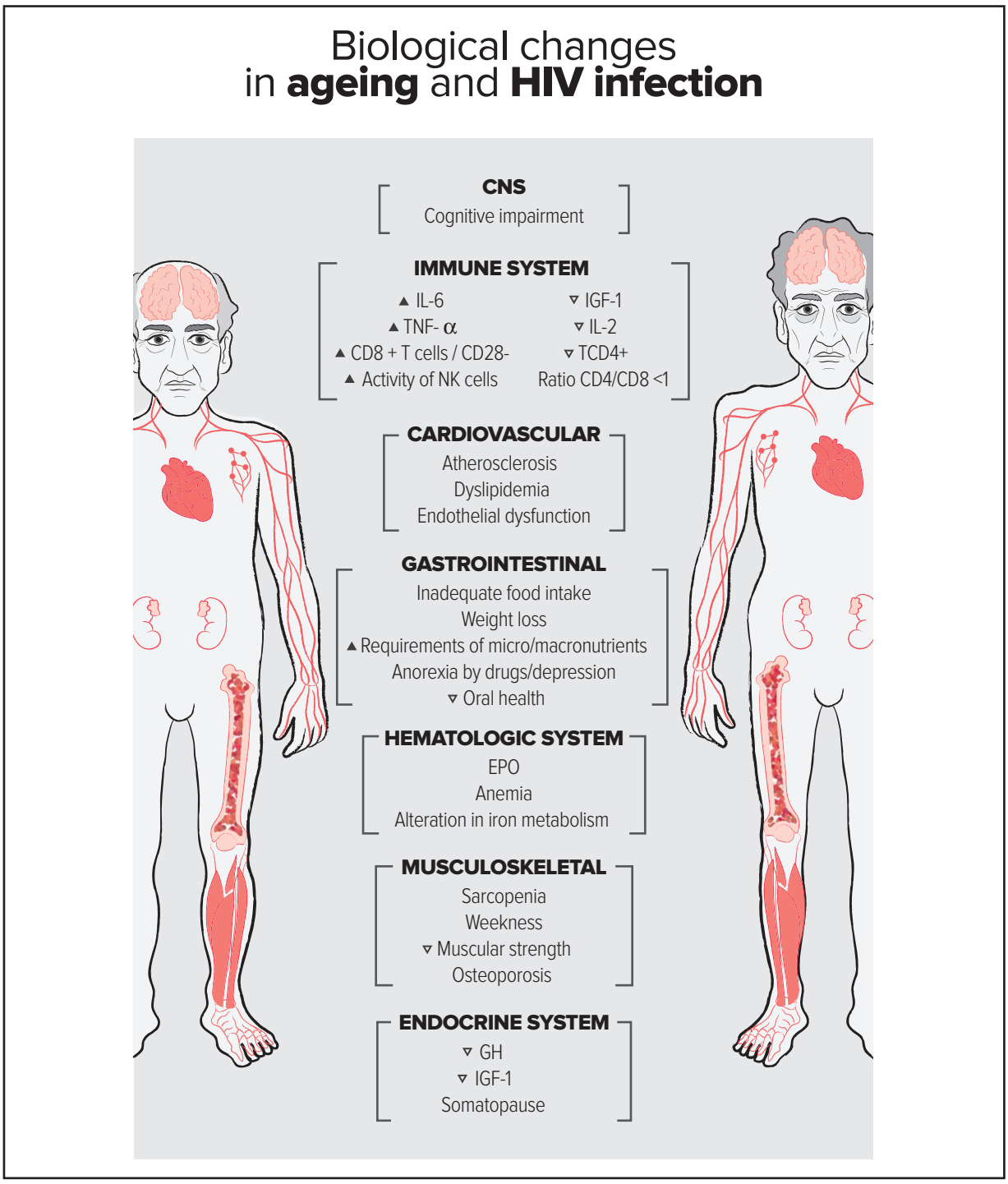


Figure 1. *Biological changes in ageing and HIV infection.*
CNS: central nervous system; EPO: erythropoietin; GH: growth hormone; IGF: insulin growth factor; IL: interleukin; NK: natural killer; TNF: tumor necrosis factor.

be a pattern of accelerated aging. This is clear in the immune system. Clinically, it is revealing that the prevalence of specific geriatric syndromes is greater in PLWH[16,51]. The underlying pathogenic processes involve alterations in caloric intake, nutrient absorption, and energy expenditure (Table 2).

Weight loss ultimately is a consequence of the negative caloric balance, regardless of the cause. The relative roles of altered energy intake and expenditure have been evaluated on several occasions. For example, Grunfeld, et al. showed that caloric intake was more important than the resting energy expen-

Table 2. Causes of malnutrition in HIV infection

Causes of nutritional deficiencies and food in HIV
Anorexia by drugs, malabsorption, systemic infections or tumors
Diffuse neurological disease that affects the feeling of hunger or the ability to eat (swallowing)
Focal neurological disease that affects food intake
Food insecurity caused by economic or psychosocial factors
Local pathological conditions affecting chewing, salivation, and gastrointestinal motility
Severe psychiatric illness

diture in predicting short-term changes in body weight in patients with HIV[8]. Not all studies have shown positive effects between high BMI and CD4 cell count after the start of HAART. A notable exception is the inconsistency of the protective association of weight in the group of women with HIV[94]. On the other hand, we must recognize that immune reconstitution is highly variable and a number of well-known factors predict an increase in CD4+ cell count in patients on HAART. Age, nadir CD4, coinfection with hepatitis C, residual viral replication, persistent immune activation, and thymus size are studied factors that influence the immune status. Possible explanations for the association between high BMI and gains in $CD4^+$ cell count include pleiotropic adipokine positive effects such as leptin, differences in thymus size, differences in the dynamics of the lymphocyte population in the gastrointestinal tract and other mucosa sites, and differences in apoptosis of T lymphocytes[131-140].

NUTRITIONAL ASSESSMENT IN ELDERLY POPULATIONS LIVING WITH HIV

As we mentioned before, aging people with HIV will be a constantly growing population and, as we have seen, the evidence suggests that proper nutrition promotes maintaining optimal immune function[141,142]. By contrast, the negative impact of HIV on nutritional status has been recognized since the beginning of the epidemic. Protein-calorie malnutrition with depleted lean muscle mass, adipose tissue, and micronutrients is a very common problem and causes a reduction in life expectancy and a decrease in quality of life[143]. Protein-calorie malnutrition (wasting) exacerbates the immune deficiency and causes weakness and dependence and reduced life expectancy[144]. In fact, malnutrition and nutritional deficiencies are potential risk factors for the development of frailty, and it is likely that the pathophysiology involves alterations in protein synthesis and energy metabolism described previously[97].

But, what is the proper way to measure the nutritional status of older people with HIV? Currently, although most subjects with HIV who have access to drug treatment undergo prolonged immune reconstitution and suppression of viral load, there is no consensus about which tool is best to assess the nutritional status in patients more than 50 years old with HIV. The best scale depends on the clinical context in which it is used, either as a screening tool or as part of a more comprehensive assessment. Perhaps the scales of assessment should include information such as the presence of chronic viral coinfections or some laboratory data, both known for their influence on HIV (e.g. viral load, $CD4^+$ cell count). Although it is well known that these factors contribute to vulnerability in older adults with HIV, they could represent something else in addition to the nutritional status. Measuring the risk of malnutrition in the clinical evaluation of the patient with HIV is invaluable for understanding the current needs and developing a medium-term forecast, especially at this historic moment when the infection has become a chronic disease and the largest group of PLWH is aged 50 years or more. Nutritional assessment requires adequate knowledge for interpretation so that the identification of the most effective tools for clinical use and research is critical to understanding and meeting the needs of older people with HIV. Tools to assess the nutritional status are used systematically in geriatrics and gerontology (Table 3).

Our proposal is that these tools should have a similar application in HIV care and research. The diagnosis of nutritional status in patients with HIV requires the integration of clinical, dietary, anthropometric, biochemical, and functional indicators[145]. In the same sense, given its importance it should be evaluated regularly and frequently as part of the comprehensive care of HIV patients over 50 years old. Initial clinical studies, performed mainly on inpatients, demonstrated the weakness of using weight-based measures to

Table 3. Comprehensive Geriatric Assessment suggested in patients with HIV

Comprehensive Geriatric Assessment
Physical health
Clinical history
Physical examination, laboratory and cabinet
List of problems
Specific indicators of severity
Functional status
Activities of daily living
Basic
Instrumented
Other functional scales
Mobility
Quality of life
Specific body segments
Muscular strength
Physical activity
Frailty
Nutritional status
Scales screening and diagnosis
Assessment of swallowing and gastrointestinal symptoms
Anthropometry
Mental health
Cognitive
Affective
Social and environmental factors
Networks and support
Adequacy of financial resources
Safety and environmental requirements
Structure and function of the household

Table 4. Negative effects of HIV on nutrients

Macronutrients	**Micronutrients**
Protein depletion (transferrin, albumin)	Low levels: Vitamins B12, B6,
Muscle loss (forearm circumference)	Water-soluble vitamins A and D
Lean mass depletion	Selenium and zinc
Body fat without significant condition	Negative caloric balance
Weight loss (men: lean mass, women: body fat)	

estimate nutritional status. Because of the wide ranges of premorbid body weights or BMI values as well as normal values, it may be difficult to detect wasting from a single measurement. The assessment of body weight provides no information about body composition; it cannot distinguish fat from muscle, it cannot distinguish lean mass from excess fluid, and it cannot detect micronutrient deficiencies at all (Table 4).

Body weight measurements were frequently difficult to interpret in patients with AIDS, especially hospitalized patients in whom wide swings in body weight resulted from diarrheal illnesses and from intravenous fluid administration. Quantitative measures of body composition had been developed more than 30 years earlier, but had few clinical applications other than in examining the changes that occur during critical illness, aging, and obesity. The focus of the Mini Nutritional Assessment (MNA) is useful in this complex context. The MNA is composed of different variables that assess the nutritional status in old age. We must say that there are no studies that have evaluated their use in aging people with HIV[145]. We consider there is a need for further research to identify measures of nutritional status to reach the highest levels of effectiveness and efficiency in the evaluation of older patients with HIV.

CONCLUSIONS

Undoubtedly, adequate nutritional status supports the proper performance of the immune system and improves physical performance. Weight loss caused by low intake, malabsorption, and altered metabolism is common in HIV infection. Identifying poor nutritional status can, therefore, improve clinical outcomes in patients with HIV by reducing the incidence of complications associated with HIV and malnutrition. Thus, it could slow the progression of HIV disease, improve quality of life, and ultimately reduce morbidity and mortality related to malnutrition in PLWH. A BMI between normal and overweight seems to have positive health benefits and a further reduction of immune reconstitution in HIV. Frailty is common in patients with HIV and is associated with low $CD4^+$ cell counts rather than with being older. It seems that the frailty of HIV patients is potentially reversible and/or transient, especially in those with adequate nutritional status. Promoting a healthy nutrition state and avoiding weight loss can have multiple benefits in terms of improved response to HAART or in reducing morbidity and mortality[146,147]. Poor nutritional status in the presence of HIV infection is a predictor of adverse outcomes, and patients with malnutrition develop more complications. However, malnutrition, rather than a vulnerable state, represents a continuum in the clinical spectrum of HIV infection and is also a pathological state in which converge, common to biological aging, immune se-

nescence pathophysiological pathways and frailty. Malnutrition can be the consequence of particular forms of aging and the confluence of HIV infection and the characteristic immune condition. Management needs a multilevel assessment of possible underlying causes: interventions focused on minimizing loss of weight and muscle mass, and improving the adverse conditions for adequate food (e.g. nutritional support, health education). It is worth noting that malnutrition may have social or environmental influences, such as access to food, physical inactivity, and depression. The Fried phenotype evaluates only the physical component of the construct of frailty; however, the negative effect of social factors, psycho-affective and cognitive, has been demonstrated and used by other detection tools[148-152].

The promotion of effective nutritional support is crucial to ensure adequate adherence to antiretroviral therapy. That is why nutritional assessment and dietary advice should be promoted as standards of quality of care of patients with HIV[153-155]. The sum of mortality and morbidity findings suggests that nutritional intervention at the beginning of HAART therapy could improve the survival and quality of life in patients with HIV. Finally, we consider that assessments of nutritional status need to be considered as an approximation of health status in elderly patients with HIV, and that should be part of routine screening in patients who are aging with HIV infection. The nutritional status at HIV diagnosis and before the initiation of HAART appear to be strong predictors of adherence and therapeutic success, as well as preventive for some other outcomes such as disability, loss of independence, and death. Our proposal is to include the patient who has aged with HIV in the approach used in geriatrics: Comprehensive Geriatric Assessment, which brings trans-disciplinary strategies at multiple levels, thus generating highly individualized interventions.

REFERENCES

1. Calcagnol A, Nozza S, Muss C, et al. Ageing with HIV: a multidisciplinary review. Infection. 2015;43:509-22.
2. World Health Organization. Definition of an older or elderly person. Definition. Geneva, Switzerland: WHO; 2011.
3. Ruttimann RW, Bonvehi PE, Vilar-Compte D. Influenza among the elderly in the Americas: a consensus statement. Rev Panam Salud Publica. 2013;33:446-52.
4. Schouten J, Wit FW, Stolte IG, van del Valk M, Geerlings SE. Comorbidity and ageing in HIV-1 infection: the AGEhIV Cohort Study. In XIX International AIDS conference; 2016; Washington DC.
5. Fletcher CV, Gebo K, Halter JB, Hazzard WR, Effros RB. Aging and Infectious diseases: workshop on HIV infection and aging: what is known and future research directions. Clin Infect Dis. 2008;47:542-53.
6. Perez JL, Moore RD. Greater effect of highly active antiretroviral therapy on survival in people aged 50 years compared with younger people in an urban observational cohort. Clin Infect Dis. 2003;36:212-18.
7. Sabin CA. Do people with HIV infection have a normal life expectancy in the era of combination antiretroviral therapy? BMC Med. 2013;11:251.
8. Guaraldi G, Cossarizza A, Franceschi C. Life expectancy in the immune recovery era: the evolving scenario of the HIV epidemic in northern Italy. J Acquir Immune Defic Syndr. 2014;65:175-81.
9. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet. 2013;382:1525-33.
10. Centers for Disease Control and Prevention. HIV/AIDS among persons aged 50 and older: CDC HIV/AIDS facts. Washington, DC, US Department of Health and Human Services; 2008.
11. Coleman CL. Revisiting HIV/AIDS. Men Nursing. 2006;1:20-7.
12. van Griensven F, de Lind van Wijngaarden JW, Baral S, Grulich A. The global epidemic of HIV infection among men who have sex with men. Curr Opin HIV AIDS. 2009;4:300-7.
13. Kerr LR, Mota RS, Kendall C, Pinho AD, Mello MB. High prevalence among men who have sex with men. AIDS. 2013;27:427-34.
14. Bautista-Arredondo S, Colchero MA, Romero M, Conde-Glez CJ, Sosa-Rubí S. Is the HIV epidemic stable among MSM in Mexico? HIV prevalence and risk behavior results from a nationally representative survey among men who have sex with men. PLOS One. 2013;8:e72616.
15. CENSIDA. Registro Nacional de Casos de SIDA. Actualización al 2o Trimestre del 2016. Registro Nacional. Ciudad de México: Dirección General de Epidemiología/Secretaría de Salud; 2016.
16. Ávila-Funes JA, Belaunzarán-Zamudio PF, Tamez-Rivera O, et al. Correlates of prevalent disability among HIV-infected elderly patients. AIDS Res Hum Retroviruses. 2016;32:155-62.
17. López-Otín C, Blasco MA, Partridge L. The hallmarks of aging. Cell. 2013;153:1194-217.
18. Delves PJ, Roitt IM. The immune system (First of two parts). N Engl J Med. 2000;343:37-49.
19. Delves PJ, Roitt IM. The immune system (Second of two parts). N Engl J Med. 2000;343:108-17.
20. Boren E, Gershwin ME. Inflamm aging; autoimmunity, and the immune risk phenotype. Autoimmun Rev. 2004;3:401-6.
21. Pawelec G. Immunosenescence comes of age. EMBO Rep. 2007;8:220-3.
22. Franceschi C, Bonafe M, Valensin S, et al. Inflamm-aging. An evolutionary perspective in immunosenescence. Ann NY Acad Sci. 2000;908:244-54.
23. Salminen A, Huuskonen J, Ojala J, Kauppinen A, Kaarniranta K, Suuronen T. Activation of innate immunity system during aging: NF-kB signaling is the molecular culprit of inflamm-aging. Ageing Res Rev. 2008;7:83-105.
24. Hayden MS, Gosh S. Shared principles in NF kB signaling. Cell. 2008;132:344-62.
25. Aggarwal, BB. Nuclear factor kB: The enemy within. Cancer Cell. 2004;6:203-8.
26. Abraham E. NF Kappa B activation. Crit Care Med. 2000;28:N100-4.
27. Burgering B. A brief introduction to FOXOlogy. Oncogene. 2008;27:2258-62.
28. Peng SL. FoxO in the immune system. Oncogene. 2008;27:2337-44.
29. Patridge L, Bruning JC. Forkhead transcription factors and ageing. Oncogene. 2008;27:2351-63.
30. North BJ, Verdin E. Sirtuins: Sir2 related NAD dependent protein deacetylases. Genome Biol. 2004;5:1-12.
31. Dali Youcef N, Lagouge M, Froelich S, Koehl C, Schoonjans K, Auwerx J. Sirtuins: Sir2 related NAD dependent protein deacetylases. Genome Biol. 2004;5:1-12.
32. Lagouge M, Froelich S, Koehl C, Schoonjans K, Auwerx J. Sirtuins: The "magnificent seven", function, metabolism and longevity. Ann Med. 2007;39:335-45.
33. Salminen A, Ojala J, Huuskonen J, Kauppinen A, Suuronen T, Kaarniranta K. Interaction of aging associated signaling cascades: Inhibition of NF kappa B signaling and longevity factors FoxOs and SIRT 1. Cell Mol Life Sci. 2008;65:1049-58.
34. Navarrete-Reyes AP. [Inflammaging. Aging inflammatory origin]. Rev Invest Clin. 2009;61:327-36.
35. Pathai S. Is HIV a model of accelerated or accentuated aging? J Gerontol A Biol Sci Med Sci. 2014;69:833-42.
36. Saktor N, Skolasky RL, Cox C, et al. Multicenter AIDS Cohort Study (MACS). Longitudinal psychomotor speed performance in human immunodeficiency virus-seropositive individuals: impact of age an serostatus. J Neurovirol. 2010;16:335-41.
37. Womack JA, Goulet JL, Gilbert C, et al. Increased risk of fragility fractures among HIV infected compared to uninfected male veterans. PLos One. 2011;6:e17217.
38. Young B, Dao CN, Buchacz K, Baker R, Brooks JT. Increased rates of bone fracture among HIV-infected persons in the HIV Outpatient Study (HOPS) compared with the US general population. Clin Infec Dis. 2011;52:1061-8.
39. Walker Harris V, Brown TT. Bone loss in the HIV-infected patient: evidence, clinical implications, and treatment strategies. J Infect Dis. 2012;205(Suppl 3):S391-8.
40. Erlandson KM, Allshouse AA, Jankowski CM, et al. Comparison of functional status instruments in HIV-infected adults on effective antiretroviral therapy. HIV Clin Trials. 2012;13:324-34.
41. Oursler KK, Sorkin JD, Smith BA, Katzel LI. Reduced aerobic capacity and physical functioning in older HIV-infected men. AIDS Res Hum Retroviruses. 2006;22:1113-21.
42. Richert L, Dehali P, Mercie P, et al. Groupe d'Epidémiologie Clinique du SIDA en Aquitaine (GECSA).High frequency of poor locomotor performance in HIV-infected patients. AIDS. 2011;25:797-805.

43. Desquilbet L, Jacobson LP, Fried LP, et al. A frailty related phenotype before HAART initiation as an independent risk factor for AIDS or death after HAART among HIV-infected men. J Gerontol A Biol Sci Med Sci. 2011;66:1030-8.
44. Desquilbet L, Jacobson LP, Fried LP, et al. HIV-1 infection is associated with an earlier ocurrence of a phenotype related to frailty. J Gerontol A Biol Sci Med Sci. 2007;62:1279-86.
45. Desquilbet L, Margolick JB, Fried LP, et al. Relationship between a frailty related phenotype and progressive deterioration of the immune system in HIV-infected men. J Acquir Immune Defic Syndr. 2009;50:299-306.
46. D'Souza G, Wiley DJ, Li X, et al. Incidence and epidemiology of anal cancer in the multicenter AIDS cohort study. J Acquir immune Defic Syndr. 2008;48:491-9.
47. Thomas J, Doherty SM. HIV infection a risk factor for osteoporosis. J Acquir Immune Defic Syndr. 2003;33:281-91.
48. Fausto A, Bongiovanni M, Menicagli L, et al. Potential predictive factors of osteoporosis in HIV-positive subjects. Bone. 2006;38:893-7.
49. Heaton RK, Franklin DR, Ellis RJ. HIV- associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. J Neurovirol. 2011;17:3-16.
50. Roederer M, Dubs JG. CD8 naive T cell counts decrease progressively in HIV-infected adults. J Clin Invest. 1995;95:2061-6.
51. Tamez-Rivera P, Martínez-Ayala P, Navarrete-Reyes AP, Amieva H, Avila-Funes JA. Molecular Crossroads of Frailty and HIV. J Frailty Aging. 2014;3:89-96.
52. Holmes GE, Bernstein C, Bernstein H. Oxidative and other DNA damage as the basis of aging: a review. Mutat Res. 1992;275:305-15.
53. Jaruga P, Jaruga B, Olczack. Oxidative DNA base damage in lymphocytes of HIV-infected drug user. Free Radic Res. 1999;31:197-200.
54. Olsson J, Wikby A, Johansson B, Lofgren S, Nilsson BO, Ferguson FG. Age related change in peripheral blood T lymphocyte subpopulations and cytomegalovirus infection in the very old: the Swedish longitudinal OCTO immune study. Mech Ageing Dev. 2000;121:187-201.
55. Wikby A, Johansson B, Olsson J, Lofrgen S, Nilsson BO, Ferguson F. Expansion of peripheral blood CD8T lymphocyte subpopulations and an association with cytomegalovirus seropositivity in the elderly: the Swedish NONA immune study. Exp Gerontol. 2002;37:445-53.
56. Deeks SG. HIV infection, inflammation, immunosenescence, and aging. Annu Rev Med. 2011;62:141-155.
57. Armah KA, McGinnis K, Baker J. HIV status, burden of comorbid disease, and biomarkers of inflammation, altered coagulation, and monocyte activation. Clin Infec Dis. 2012;55:126-36.
58. Erlandson KM, Schrack JA, Jankowski CM, Brown TT, Campbell TB. Functional impairment, disability, and frailty in adults aging with HIV-infection. Curr HIV/AIDS Rep. 2014;11:279-90.
59. Bergman H, Ferrucci L, Guralnik J. Frailty: an emerging research and clinical paradigm-issues and controversies. J Gerontol A Biol Sci Med Sci. 2007;62:731-7.
60. Wilson JF. Frailty -and its dangerous effects- might be preventable. Ann Intern Med. 2004;141:489-92.
61. Martin CP, Fain MJ, Klotz SA. The older HIV-positive adult: a critical review of the medical literature. Am J Med. 2008;12:1032-7.
62. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:M146-56.
63. Avila-Funes JA, Amieva H. Frailty: an overused term among the elderly even in gastroenterology. J Clin Gastroenterol. 2009;43:199.
64. Engels EA, Pfeiffer RM, Landgren O, Moore RD. Immunologic and virologic predictors of AIDS related non-Hodgkin lymphoma in the highly active antiretroviral therapy era. J Acquir Immune Defic Syndr. 2010;54:78-84.
65. Terzian AS, Holman S, Nathwani N. Factors associated with preclinical disability and frailty among HIV uninfected women in the era of cART. J Womens Health. 2009;18:1965-74.
66. Bandeen-Roche K, Xue QL, Ferrucci L. Phenotype of frailty: characterization in the women's health and aging studies. J Gerontol A Biol Sci Med Sci. 2006;61:262-6.
67. Ianas V, Berg E, Mohler MJ, Wendel C, Klotz SA. Antiretroviral therapy protects against frailty in HIV-1 infection. J Int Assoc Provid AIDS Care. 2013;1:62-6.
68. Walston J, McBurnie MA, Newman A, et al. Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities. Arch Intern Med. 2002;162:2333-41.
69. Ferrucci L, Penninx BW, Volpato S, et al. Change in muscle strength explains accelerated decline of physical function in older women with high interleukin 6 serum levels. J Am Geriatr Soc. 2002;50:1947-54.
70. Leng SX, Xue QL, Tian J, Walston JD, Fried LP. Inflammation and frailty in older women. J Am Geriatr Soc. 2007;55:864-71.
71. Ferruci L, Harris TB. Serum IL-6 level and the development of disability in older person. J Am Geriatr Soci. 1999;47:639-46.
72. Morley JE. Frailty. Med Clin N Am. 2006;90:837-47.
73. Bautmans I, Njemini R, Predom H, Lemper JC, Mets T. Muscle endurance in elderly nursing home residents is related to fatigue perception, mobility and circulating tumor necrosis factor alpha, interleukin 6, and heat perception, mobility and circulating tumor necrosis factor alpha, interleukin 6, and heat shock protein 70. J Am Geriatr Soc. 2008;56:389-96.
74. Florez H, Troen BR. Fat and inflammaging: a dual path to unfit ness in elderly people? J Am Geriatr Soc. 2008;56:558-60.
75. De Martinis M, Franceschi C, Monti D, Ginaldi L. Inflammation markers predicting frailty and mortality in the elderly. Exp Mol Pathol. 2006;80: 219-27.
76. Payette H, Roubenoff R, Jacques PF, et al. Insulin like growth factor 1 and interleukin 6 predict sarcopenia in very old community living men and women: The Framingham Heart Study. J Am Geriatr Soc. 2003;51:1237-43.
77. Bierman AS. Functional status: the six vital sign. J Gen Intern Med. 2001;16: 785-6.
78. Linares-Guerra EM, Santana-Porbén S, Carrillo-Fornés O, et al. [Nutritional status of the persons living with HIV/AIDS; its relationship with T CD4+ cells counts]. Nutr Hosp. 2013;28:2197-207.
79. Mokotori A, Kabehenda MK, Nabiryo C, Wamuyu MG. Reliability of scored patient generated subjective global assessment for nutritional status among HIV infected adults in TASO Kampala. Afr Health Sci. 2011;11(Suppl 1):S86-92.
80. Benavente GB. Estado Nutricional y hábitos alimentarios de pacientes con VIH. Rev Peruana Epidemiol. 2011;15:113-17.
81. Freijo S, Mengoni A. Estado nutricional al ingreso de los pacientes internados con VIH. Diaeta. 2010;28:37-44.
82. Linares M, Bencomo J, Santana S, Barreto J, Ruiz M. Aplicación del método Chang en la evaluación nutricional de indiviudos VIH/SIDA. J Bras Doencas Sex Transm. 2005;17:259-64.
83. Bassichetto KC, Bergamaschil DP, Schlickmamn-Frainer DE, Salles-Garcia VR, Tramarin-Trovoes EA. Weight and height of people living with HIV/AIDS attended by the Brazilian national health system. Red Bras Epidemiol. 2013; 16:622-32.
84. Otwombel KN, Petzold M, Modisenyane T, Martinson NA, Chirwa T. Factors associated with mortality in HIV-infected people in rural and urban South Africa. Glob Health Action. 2014;7:25488.
85. Martínez H, Palar K, Linnemayr S, et al. Tailored nutrition education and food assistance improve adherence to HIV antiretroviral therapy: Evidence from Honduras. AIDS Behav. 2014;18:S566-77.
86. Mankal PK, Kotler DP. From wasting to obesity, changes in nutritional concerns in HIV/AIDS. Endocrinol Metab Clin N Am. 2014;43:647-63.
87. Thompson-Paul AM, Wei SC, Mattson CL, et al. Obesity among HIV-infected adults receiving medical care in the United States: Data From the Cross-Sectional Medical Monitoring Project and National Health and Nutrition Examination Survey. Medicine. 2015;94:1-10.
88. Womack JA, Goulet JL, Gibert C, et al. Physiologic and fragility fracture in HIV-Infected male veterans. HIV/AIDS. 2013;56:1498-504.
89. Taylor BS, Lian Y, Garduño LS, et al. High risk of obesity and weight gain for HIV-infected of uninsured minorities. J Acquired Immune Defic Syndr. 2014;65: 33-40.
90. Wanke CA, Silva M, Knox TA, Forrester J, Speigelman D. Weight loss and wasting remain common complications in individuals infected with human immunodeficiency virus in the era of highly active antiretroviral therapy. Clin Infect Dis. 2000;31:803-5.
91. Louise C, Ivers LC, Cullen KA, et al. HIV/AIDS, Undernutrition and Food Insecurity. Clin Infect Dis. 2009;49:1096-102.
92. Swaminathan S, Padmapriyadarsini C, Sukumar B, et al. Nutritional status of persons with HIV infection, persons with HIV infection and tuberculosis and HIV-negative individuals from southern India. Clin Infect Dis. 2008;46: 946-9.
93. Siddiqui J, Phillips AL, Freedland ES, Sklar AR, Darkow T. Prevalence and cost of HIV-associated weight loss in managed care population. Curr Med Res Opin. 2009;25:1307-17.
94. Crum-Cianflone NF, Roediger M, Elberly LE, Vyas K, Landrum ML. Obesity among HIV-infected persons: impact of weight on CD4 cell count. AIDS. 2010;24:1069-72.
95. Steel G, Nwokike J, Joshi MP. Development of a multi-method tool to measure ART adherence in resource-constrained settings: The South Africa experience. RPM Plus. 2007;6.
96. Weiser S, Tuller D, Frongillo E. Food Insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. PloS One. 2010;5:357-66.
97. Berhe N, Tegabu D, Alemayehu M. Effect of nutritional factors on adherence to antiretroviral therapy among HIV-infected adults: a case control study in Northern Ethiopia. BMC Infect Dis. 2013;13:233.
98. Hardon AP, Akurut D, Comoro C, et al. Hunger, waiting time and transport costs: Time to confront challenges to ART adherence in Africa. AIDS Care. 2007;19:658-65.
99. Olupot-Olupot P, Katawera A, Cooper C, Small W, Anema A, Mills E. Adherence to antiretroviral therapy among a conflict-affected population in Northeastern Uganda: a qualitative study. AIDS. 2008;22:1882-4.
100. Deribe K, Hailekeros F, Biadgilign S, Amberbir A, Beyene B. Defaulters from antiretroviral treatment in Jimma University Specialized Hospital, Southwest Ethiopia. Trop Med Int Health. 2008;13:328-33.
101. Franke M, Murray M, Muñoz M. Food insufficiency is a risk factor for suboptimal antiretroviral therapy adherence among HIV-infected adults in urban Peru. AIDS Behav. 2011;15:1483-9.
102. Marcellin F, Boyer S, Protopopescu C. Determinants of unplanned antiretroviral treatment interruptions among people living with HIV in Yaounde', Cameroon (EVAL survey). Trop Med Int Health. 2008;13:1470-8.
103. Martin A, Palar K, Derose K, Adams J. Food insecurity and nutritional barriers to antiretroviral therapy: lessons from Latin America and the Caribbean. J HIV AIDS Soc Serv. 2011;10:194-214.

104. Raiten D, Grinspoon S, Arpandi S. Nutritional considerations in the use of ART in resource limited settings. Report. Durban, South Africa: World Health Organization, Department of Nutrition for Health and Development; 2005.
105. Shor-Posner G, Campa A, Zhang G. When obesity its desirable: a longitudinal study of the Miami HIV-1-infected drug users (MIDAS) cohort. J Acquir Immune Defic Syndr. 2000;23:81-8.
106. Jones CY, Hogan JW, Snyder B. Overweight and human immunodeficiency virus (HIV) progression in women: associations HIV disease progression and changes in body mass index in women in the HIV Epidemiology Research Study cohort. Clin Infect Dis. 2003;37:69-80.
107. Sudfeld CR, Isanaka S, Mugusi FM, et al. Weight change at 1 month of antiretroviral therapy and its association with subsequent mortality, morbidity, and CD4 T cell reconstitution in a Tanzanian HIV infected adult cohort. Am J Clin Nutr. 2013;97:1278-87.
108. Koethe JR, Lukusa A, Giganti MJ, et al. Association between weight gain and clinical outcomes among malnourished adults initiating antiretroviral therapy in Lusaka, Zambia. J Acquir Immune Defic Syndr. 2010;53:507-13.
109. Madec Y, Szumulin E, Genevier C, et al. Weight gain at 3 month of antiretroviral therapy is strongly associated with survival: evidence from two developing countries. AIDS. 2009;23:853-61.
110. Liu E, Spiegelman D, Semu H, et al. Nutritional status and mortality among HIV-infected patients receiving antiretroviral therapy in Tanzania. J Infect Dis. 2011;204:282-90.
111. CDC. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults. Report. National Center for Infectious Diseases Division of HIV/AIDS, Division of HIV/AIDS; 1992.
112. Evans D, McNamara L, Maskew M, et al. Impact of nutritional supplementation on immune response, body mass index and bioelectrical impedance in HIV-positive starting antiretroviral therapy. Nutr J. 2013;12:111.
113. Santos AC, Almeida AM. Nutritional status and CD4 cell counts in patients with HIV/AIDS receiving antiretroviral therapy. Rev Soc Bras Med Trop. 2013;46:698-703.
114. Aaron JB, Keneth HM, Heidi MC, Chris GM, Steven AS. Body mass index, immune status and biological control in HIV infected men who have sex with men. J Int Assoc Provid AIDS Care. 2013;12:319-24.
115. United Stated Agency for International Development. HIV, Food Security and Nutrition. Policy Brief. UNAIDS; 2008.
116. Kalofonos IP. All I Eat is ARVs: The paradox of AIDS treatment in central Mozambique. Med Antropol Q. 2010;24:363-80.
117. Oketch JA, Paterson M, Maunder EW, Rollins NC. Too little, too late: Comparison of nutritional status and quality of life of nutrition care and support recipient and non-recipient among HIV-positive adults in KwaZulu-Natal. South Africa. Health Policy. 2011;99:267-76.
118. Onen NF, Agbebi A, Shacham E. Frailty among HIV-infected persons in an urban outpatient care setting. J Infec. 2009;59:346-52.
119. Piggott DA, Muzaale AD, Mehta SH. Frailty, HIV infection, and mortality in an aging cohort of injection drug users. PLos One. 2013;8:e:54910.
120. Althoff KN, Jacobson LP, Cranston RD. Age, comorbidities, and AIDS predict a frailty phenotype in men who have sex with men. J Gerontol A Biol Sci Med Sci. 2014;69:189-98.
121. Justice AC, Freiberg MS, Tracy R. Does an index composed of clinical data reflects of inflammation, coagulation, and monocyte activation on mortality among those aging with HIV? Clin Infec Dis. 2012;54:984-94.
122. Vlahov D, Anthony JC, Munosz A, et al. The ALIVE study, a longitudinal study of HIV-1 infection in intravenous drug user: description of methods and characteristics of participants. NIDA Res Monogr. 1991;109:75-100.
123. Cuzin L, Delpierre C, Gerard S. Immunologic and clinical responses to highly active antiretroviral therapy in patients with HIV infection aged >50 years. Clin Infect Dis. 2007;45:654-7.
124. Nguyen N, Holodniy M. HIV infection in the elderly. Clin Interven Aging. 2008;3:453-72.
125. Meynell J, Barroso J. Bioimpedance analysis and HIV-related fatigue. J Assoc Nurses AIDS Care. 2005;162:13-22.
126. Argemi X, Dara S, You S, et al. Impact of malnutrition and social determinants on survival of HIV-infected adults starting antiretroviral therapy in resource-limited settings. AIDS. 2012;26:1161-6.
127. Adeyemi O, Livak B. Higher Veterans Aging Cohort Study (VACS) index scores in HIV-positive adults with CD4 counts <200 cells/mm3 despite viral suppression. J Acquir Immune Defic Syndr. 2013;63:e78-81.
128. Hamill MM, Ward KA, Pettifor JM, Norris SA, Prentice A. Bone mass, body composition and vitamin D status of ARV-naive, urban, black South African women with HIV infection, stratified by CD4 count. Osteoporos Int. 2013;24:2855-61.
129. Mangili A, Murman DH, Zampini AM, Wanke CA, Mayer KH. Nutrition and HIV infection: Review of weight loss and wasting in the era of highly active antiretroviral therapy from the Nutrition for Healthy Living Cohort. Clin Infect Dis. 2006;426:836-42.
130. Serrano C, Laporte R, Ide M, et al. Family nutritional support improves survival, immune restoration and adherence in HIV patients receiving ART in developing country. Asia Pac J Clin Nutr. 2010;191:68-75.
131. Grunfeld C, Pang M, Schimuzu L. Resting energy expenditure, caloric intake, and short-term weight change in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. Am J Clin Nutr. 1992;55:455-60.
132. Bosch RJ, Collier AC, Zackin R, Benson CA. Pretreatment factors associated with 3 year (144-week) virologic and immunologic responses to potent antiretroviral therapy. J Acquir Immune Defic Syndr. 2007;44:268-77.
133. Smurzynskai M, Collier AC, Koletar SL, et al. Trials Group longitudinal linked randomized trials (ALLRT): rationale, design and baseline characteristics. HIV Clin Trials. 2008;9:268-82.
134. Lederman M, McKinnis R, Kelleher D. Cellular restoration in HIV infected person treated with abacavir and a PI: age inversely predicts naive CD4 cell count increase. AIDS. 2000;14:2635-42.
135. Kaufmann D, Bloch M, Finlayson R, Zaunders J, Smith D, Cooper D. The extent of HIV-1 related immunodeficiency and age predict the long-term CD4 T lymphocyte response to potent antiretroviral therapy. AIDS. 2002;16:359-67.
136. Grabar S, Le Moing V, Goujard L. Clinical outcome of patients with HIV-1 infection according to immunologic and virologic response after 6 months of HAART. Ann Intern Med. 2000;133:401-10.
137. Kaufman G, Perrin L, Pantaleo G. CD4 T-lymphocyte recovery in individuals with advance HIV-1 infection receiving potent antiretroviral therapy for 4 years: the Swiss HIV Cohort Study. Arch Intern Med. 2003;163:2187-95.
138. Greub G, Ledergerber B, Bategay M, et al. Clinical progression, survival, and immune recovery during antiretroviral therapy in patients with HIV-1 and HCV coinfection: the Swiss HIV Cohort Study. Lancet. 2000;356:1800-5.
139. Ostrowski S, Katzenstein T, Thim P, Pedersen BK, Gerstoft J, Ullum H. Low-level viremia and proviral DNA impede immune reconstitution in HIV-1 infected patient receiving HAART. J Infec Dis. 2005;191:348-57.
140. Smith KY, Valdes H, Landay A. Thymic size and lymphocyte restoration in HIV infected patients following 48 weeks of therapy with zidovudine, lamivudine and ritonavir. J Infect Dis. 2000;181:141-7.
141. de Pee S, Semba RD. Role of nutrition in HIV infection: review of evidence for more effective programming in resource-limited settings. Food Nutr Bull. 2010;31:S313-44.
142. Mahlungulu S, Grobler LA, Visser ME, Volmink J. Nutritional interventions for reducing morbidity and mortality in people with HIV. Cochrane Database Syst Rev. 2007;18:CD004536.
143. Kotler DP, Wang J, Pierson RN. Body composition studies in patients with the acquired immunodeficiency syndrome. Am J Clin Nutr. 1985;42:1255-65.
144. Kotler DP, Tierney AR, Wang J. Magnitude of body-cell-mass depletion and the timing of death from wasting in AIDS. Am J Clin Nutr. 1989;50:444-7.
145. Robles-González L, Beas-Ibarra A, Cano-Saldaña YM, Martínez-Saucedo MG. Estado nutricio de pacientes VIH positivos. Revista Médica MD. 2011;3:92-8.
146. Cobb G, Bland RM. Nutritional supplementation: the additional costs of managing children infected with HIV in resource-constrained settings. Trop Med Int Health. 2013;18:45-52.
147. Koethe JR, Chi BH, Megazzini KM, Heimburger DC, Stringer JS. Macronutrient supplementation for malnourished HIV-infected adults: a review of the evidence in resource-adequate and resource-constrained settings. Clin Infect Dis. 2009;49:787-98.
148. Guerrero-Escobedo P, Tamez-Rivera O, Amieva H, Avila-Funes JA. Frailty is associated with low self-esteem in elderly adults. J Am Geriatr Soc. 2014;62:396-8.
149. Sánchez-García S, Sánchez-Arenas R, García-Peña C, Rosas-Carrasco O, Avila-Funes A. Frailty among community-dwelling elderly Mexican people: prevalence and association with sociodemographic characteristics, health state and the use of health services. Geriatr Gerontol Int. 2014;14:395-402.
150. Bernal-López C, Potvin O, Avila-Funes JA. Frailty is associated with anxiety in community-dwelling elderly adults. 2012;60:2373-4.
151. Kawano-Soto CA, García-Lara JM, Avila-Funes JA. A poor social network is not associated with frailty in Mexican community-dwelling elderly adults. J Am Geriatr Soc. 2012;60:2360-2.
152. Casale-Martínez RI, Navarrete-Reyes AP, Avila-Funes JA. Social determinants of frailty in elderly Mexican community-dwelling adults. J Am Geriatr Soc. 2012;60:800-2.
153. World Health Organization. Essential prevention and care intervention for adults and adolescents living with HIV in resource-limited settings. Report. Geneva: WHO; 2008.
154. Academy for Educational Development. FANTA. HIV/AIDS: a guide for nutritional care and support. Guide. Washington, DC: Academy for Educational Development; 2004.
155. World Bank. HIV/AIDS, nutrition and food security: what we can do a synthesis of international guidance. Guide. Washington, DC: World Bank; 2007.

THE JOURNAL OF LATIN AMERICAN GERIATRIC MEDICINE REVIEW ARTICLE

Cardiopulmonary resuscitation in the elderly: a review

Juan Carlos Viveros-García*, Jorge Luis Torres-Gutiérrez and Nallely Sandoval-García

Department of Geriatrics, Hospital Regional del ISSSTE, León, Guanajuato, Gto., Mexico

Abstract

Increased life expectancy has led us to an aged society. Mexico will have 28% of its population over 65 years old in 2050. The elderly die the most, so they are more exposed to receive cardiopulmonary resuscitation compared to a younger population. Our knowledge of cardiopulmonary resuscitation in the elderly is still insufficient, so clinicians make decisions based on poor or none of evidence. The main objective of this review is to present the reader with the most important issues about cardiopulmonary resuscitation in the elderly. We made an online search of papers published between 2000 and 2016 in three important databases with the keywords: "elderly" and "CPR". We found that cardiac arrest in the elderly has a high mortality rate, particularly in vulnerable populations such as frail patients. The older patient may benefit from a short-lasting cardiopulmonary resuscitation, with neurological and functional outcomes similar to younger populations. The main factors associated to mortality after cardiopulmonary resuscitation are dependence, frailty, comorbidity, and previous cognitive status, and not age by itself. Special considerations must be taken in bioethical controversies, trying to respect dignity and autonomy. (J Lat Am Geriat Med. 2016;2:63-6)

Key words: *CPR. Elderly.*

Corresponding author: *Juan Carlos Viveros-García, drviveros.geriatria@gmail.com*

Resumen

El aumento de la esperanza de vida nos ha llevado a una sociedad envejecida. Para el 2050 la proporción de adultos mayores de 65 años en México será del 28%. La muerte entre las personas ancianas es más común, por lo tanto están más expuestas a recibir reanimación cardiopulmonar (RCP) en comparación con sujetos más jóvenes. A pesar de esto nuestro conocimiento sobre la RCP en ancianos es aún insuficiente, por lo que los clínicos tomamos decisiones basadas en evidencia débil. El principal objetivo de esta revisión es proveer al lector de información sobre los puntos más importantes de la RCP en ancianos. Se realizó una búsqueda en bases de datos en línea sobre los trabajos publicados entre 2000 y 2016 con las palabras clave: ancianos y RCP. Encontramos que el paro cardíaco en ancianos tiene una mortalidad alta, particularmente en los más vulnerables, como los ancianos frágiles. El anciano se puede beneficiar de una RCP de corta duración, con un pronóstico neurológico similar al de población más joven que sobrevive a la RCP. Los principales factores asociados a mortalidad tras la RCP son la dependencia, la fragilidad, la comorbilidad y el estado cognitivo previo, y no la edad en sí misma. Se deben tomar en cuenta consideraciones bioéticas especiales en este grupo poblacional, tratando de mantener la dignidad y la autonomía.

Palabras clave: RCP. Ancianos.

INTRODUCTION

Demographic and epidemiologic changes in the last decades have resulted in an aged society. Life expectancy has increased dramatically, especially in the last 50 years[1]. In Mexico the aged population (over 65 years of age) has increased as well, and it is expected to represent 28% of the total population by 2050[2].

Considering that the elderly have the highest mortality rates, they are more likely to receive cardiopulmonary resuscitation (CPR)[3]. As in many other areas of geriatric medicine, the published material on CPR

Correspondence to:
*Juan Carlos Viveros-García
Av. Pradera, 1101
Col. Azteca, León
C.P. 37520, Guanajuato, Gto., México
E-mail: drviveros.geriatria@gmail.com

in the elderly is limited, and as a consequence, knowledge about the characteristics of this subject is poor.

The main objective of our article is to give the reader a general review of the most important issues about CPR in the elderly, and to help the healthcare professionals in their own decision making model in clinical practice.

We searched the online databases PubMed, ProQuest, and, Cochrane database of systematic reviews for papers (original articles, reviews, editorials and meta-analyses) with the keywords (MeSH Medical Subject Headings) "CPR", "cardiopulmonary resuscitation", and "elderly" published between 2000 and 2016. We included one paper published in 1993 and another published in 1999 because of its content.

HISTORY OF CARDIOPULMONARY RESUSCITATION

Mouth-to-mouth resuscitation was first mentioned in France in 1740, when the Paris Academy of Science suggested giving artificial ventilation to drowning victims. It was not until 1891 that the first chest compression took place; 25 years later the first case of successful chest compressions was described[4].

Later, in the 20th century, the American military adopted mouth-to-mouth ventilation for non-responsive victims. In 1960 the American Heart Association (AHA) developed a formal CPR training program, with a periodic release of guidelines[4]. Two decades later, the first successful defibrillation took place in 1980[5]. Nevertheless, mortality after cardiac arrest has not improved in the last 20 years[6].

EPIDEMIOLOGY OF CARDIOPULMONARY RESUSCITATION IN THE ELDERLY

Most of the publications on CPR are not centered in the elderly, despite the fact that the average age of patients with cardiac arrest is reported as between 67.3 to 79.0 years old[7,8]. These same reports are very heterogeneous on the outcome after surviving CPR, with an average of return to spontaneous circulation of 15%. However, in frail elderlies the survival rate is 0-2%[8], very low compared with younger people who received short-lasting CPR which is 26%[6,9]. In patients with cognitive impairment, survivals are three times lower[10] than the average elderly population.

Another important factor worth mentioning is the discharge rate in CPR survivors. Only 3.8-24.0% of patients with spontaneous circulation after CPR are discharged[8]. Furthermore, the probability of discharge is inversely proportional to age. In a study of CPR survivors, only 22.6% of patients 65 years or older were discharged. This rate decreased to 12% in nonagenarian patients, and was associated with an increased risk of institutionalization[6].

THE ELDERLY IN THE INTENSIVE CARE UNIT

The number of elderlies in the intensive care units (ICU) has increased in the last years. Currently, almost 10% of patients in the ICU are aged 80 years or older, and this rate continues to increase annually by 5.6%[11].

Critically ill patients have a greater risk of cardiac arrest, which can be anticipated in 85.5% of the cases with programs like Rapid Response Teams (RRT)[10]. The RRT were designed to decrease in-hospital cardiac arrest, and have shown positive results, even in special populations like pediatric patients[12]. The elderly, however, seldom fulfill the criteria for activation of RRT, even though they have life-threatening conditions. This lack of RRT activation is a result of age-related changes such as a decreased response to catecholamine, immunosenescence, frailty, polypharmacy, and use of β blockers, among others. All of these contribute to conditions with few symptoms and accompanied by hidden hypoperfusion[13,14]. In addition to the issues previously mentioned, the elderly in critical conditions receive less vital life support, including mechanical ventilation and renal replacement therapy[15]. The greater the comorbidity, the greater the risk of in-hospital cardiac arrest, and therefore the risk of receiving CPR[6].

Geriatric patients may benefit from a short-lasting CPR, particularly in the context of witnessed cardiac arrest, presentation of defibrillate rhythms like ventricular fibrillation or pulseless ventricular tachycardia, or in cases of cardiac arrest due to hypoxia[16]. Nevertheless, the most frequent rhythms of cardiac arrest in the elderly are asystolia and pulseless electrical activity[8].

DO NOT RESUSCITATE ORDERS AND PRINCIPLE OF PATIENT AUTONOMY

Do not resuscitate orders (DNR) are beginning to spread worldwide, especially in the elderly and healthcare providers[3]. Despite the increased use of DNRs, only 25% of hospitalized patients discuss with

their physician the decision making model in case of developing cardiac arrest. In most cases the decision of initiating CPR or not relies on family members, without considering the principle of autonomy of the patient[8,10]. These situations arise due to lack of communication from both sides of the patient-physician relationship and the imminent possibility of death[18].

Most elderlies prefer full control of their healthcare decisions; in reality fact, they usually lack or autonomy on decision making[17]. In a hypothetic scenario, a clinical trial calculated an expected CPR survival rate of 75%[8]. This overestimation is based in information that lacks scientific evidence, or in common beliefs[3,19]. In Mexico, in a real case of cardiac arrest without DNR or anticipated will, physicians have the legal obligation of performing CPR[20].

BIOETHICS AND FUTILITY

One of the fundamental medical ethics principles when facing "end of life" scenarios, are good practice, palliative care, and avoidance of futile actions[21]. Defining futility, however, is an extremely difficult task.

Any intervention with a very low possibility of success, survival, or recovery is considered futile and frequently leads to disability, dependence, or death[22]. More accurate estimations report the rate of success after the intervention at below 5%, or three successful cases out of 100 cases[10].

In most Latin American countries, denying an intervention is extremely rare because of the legal bases relevant to futility. In Mexico "Declaration of an Anticipated Will" was introduced in 2008. Through this legal action, any patient with a chronic condition and life expectancy of six months or less has the right to withhold advanced life support, without denying ordinary care[20]. In conclusion, the most appropriate strategy is to face cardiac arrest and end-of-life situations with ethics, humanism, supported by evidence, and trying to include the patient in the decision-making model.

POST CARDIOPULMONARY RESUSCITATION FUNCTIONALITY, COGNITION AND INSTITUTIONALIZATION

The main objective of CPR is to save lives; nevertheless, we cannot lose sight of the long-term outcomes once the patient has returned to spontaneous circulation.

The long-term prognosis after CPR is controversial. For example, in one trial of CPR survivors, older age was related to poor neurological prognosis after hospital discharge, with only 6% of elderlies recovering their prior functional status[8]. In another study, patients aged 70 years and older had a poor prognosis after non-cardiovascular cause of cardiac arrest, with greater risk of cognitive impairment and functional limitation after CPR[23].

On the other hand, in more recent studies of CPR survivors, the neurologic prognosis was not modified by age. More specifically, octogenarians who were discharged after CPR had a good neurological prognosis, similar to that of a younger population[24]. Another series of patients in an ICU reported a good survival with a satisfactory neurological outcome[25].

In out of hospital cardiac arrest (OHCA), in a study with patients 70 years and older who received CPR, the 30-day survival rate was: 6.7% in patients aged 70-79 years, 4.4% in 80-89 years, and 2.4% in those aged 90 years and older. When the cardiac arrest rhythm is shockable, the mortality was lower in all age groups. In a multivariate analysis, the following factors were associated with increased 30-day survival: younger age, OHCA not at home, witnessed OHCA, CPR before arrival of emergency medical services (EMS), first-recorded defibrillating rhythm, and short response EMS time. The study found age as a specific mortality predictor, but in those who survived, functional status and neurological prognosis was not modified by age[26].

The use of controlled hypothermia as an intervention to improve neurological outcome has been described in recent years. However, there is lack of evidence in controlled trials to recommend or avoid its usage in the elderly[27].

CARDIOPULMONARY RESUSCITATION IN FRAIL ELDERLIES

There is a lack of publications of frail elderlies who received CPR; despite this, most clinicians think that these patients will not survive. Even though only half of the physicians give recommendations, when they give it, the information is not clear[28].

The participation of geriatricians in informing family members and frail patients at risk of cardiac arrest has made decisions easier[29]. This discussion should be included in the patient-physician relationship, especially in the institutionalized patient where the prevalence of frail elderlies is higher[30].

We should consider the low frail survival rate after CPR, reported from 0-2%, with a mean of 1.7%[8,31], when advising patients. So, CPR in frail elderlies has become more an ethical problem, with an increasing number of editorials which question whether to give or withhold CPR in those patients[32].

CONCLUSIONS

Cardiac arrest in the elderly has been associated with a high mortality, particularly in vulnerable populations such as frail patients. The main risk factors that contribute to mortality are dependence, frailty, comorbidity, and preexisting cognitive impairment. Even in the critically ill geriatric patient, age should not be considered in the decision-making process about CPR. It appears that survival depends also on hospital resources, including the number of trained staff available, cause of cardiac arrest, and the length of CPR. We consider that the elderly without multiple comorbidities, severe cognitive impairment, or terminally ill should receive a short-lasting CPR, particularly if it is a witnessed cardiac arrest, of defibrillating cardiac arrest rhythm. We still lack evidence regarding this issue, so we suggest increasing the research on CPR in the elderly.

REFERENCES

1. World report on Ageing and Health, World Health Organization, Luxembourg, September 2015.
2. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, et al. Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. Cuernavaca, México: Instituto Nacional de Salud Pública (MX), 2012.
3. Cherniack E. Increasing use of DNR orders in the elderly worldwide: whose choice is it? J Med Ethics. 2002;28:303-7.
4. American Heart Association (AHA). History of CPR. Available at: cpr.heart.org/AHAECC/CPRAndECC/AboutCPRFirstAid/HistoryofCPR/UCM_475751_History-of-CPR.jsp
5. Eisenberg M. Contemporary Cardiology: Cardiopulmonary Resuscitation. Chapter 1: History of Cardiopulmonary Resuscitation. 2009, pp 1-9. Humana Press Inc., New Jersey, USA.
6. Ehenbach W, Barnato A, Randal J, et al. Epidemiologic study of in hospital cardiopulmonary resuscitation in elderly. N Engl J Med. 2009;361:23.
7. Adams B, Zeiler K, Jackson W, Hughes B. Emergency medicine residents effectively direct inhospital cardiac arrest teams. Am J Emerg Med. 2005;23: 304-10.
8. Cadogan M. CPR decision making in older adults. J Gerontol Nurs. 2010;36: 10-15.
9. Rosenberg M, Wang C, Hoffman-Wilde S, Hickam D, Hickham D. Results of cardiopulmonary resuscitation. Failure to predict survival in two community hospitals. Arch Intern Med. 1993;153:1370-5.
10. Kite S, Wilkinson W. Beyond Futility: to what extent is the concept of futility useful in clinical decision-making about CPR?. Lancet Oncol. 2002;3:638-42.
11. Su Y, Jung H, Rim T, Guy D, Myeon S. Mortality and outcomes in very elderly patients 90 years of age or older admitted to ICU. Respir Care. 2014;60:347.
12. Marx J. Pediatric Rapid Response Team Reduces Deaths and Codes. Journal Watch Emergency Medicine. 2007.
13. Demetriades D, Karaiskakis M, Belmahos G, et al. Effect on outcome of early intensive management of geriatric trauma patients. Br J Surg. 2002;80: 1319-22.
14. Retamar P, Lopez-Prieto MD, Rodríguez-Lopez M, et al. Predictors of early mortality in very elderly patients with bacteriemia: a Prospective Multicenter Cohort. Int J Infect Dis. 2014;26:83-7.
15. Fuchs L, Chronaki C, Park S, Novack V, Baumfeld Y. ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Med. 2012;38:1654-61.
16. Elshove-Bolk j, Guttormsen AB, Austlid I. In-hospital resuscitation of the elderly: Characteristics and outcome. Resuscitation. 2007;74:372-6.
17. Fassier T, Valour E, Colin C, Danet F. Who am I to decide whether this person is to die today? Physicians' life-or-death decisions for elderly critically ill patients at the emergency department–ICU interface: A qualitative study. Ann Emerg Med. 2016;68:29-39.
18. Chiu C, Feuz M, McMahan R, Miao Y, Sudore R. "Doctor, make my decisions": Decision control preferences, advance care planning, and satisfaction with communication among diverse older adults. J Pain Symptom Manage. 2016; 51:33e40.
19. Perry F, Jennings B. CPR in hospice. Hastings Cent Rep. 2003;33:3-9.
20. Asamblea Legislativa del Distrito Federal IV Legislatura. Ley de Voluntad Anticipada para el Distrito Federal. Available at: http://www.aldf.gob.mx/archivo077346ece61525438e126242a37d313e. [Accessed 5 August 2016].
21. Delgado Fontaneda AJ, López Sainz MI. [Ethical and legal problems in severe dementia. The right to die in peace]. Rev Esp Geriatr Gerontol. 2009;44:43-7.
22. Marco CA, Larkin GL, Moskop JC, et al. Determination of ''futility'' in emergency medicine. Ann Emerg Med. 2000;35:604-12.
23. De Vos R, de Haes HM, Koster RW, de Haan RJ. Quality of survival after cardiopulmonary resuscitation. Arch Intern Med. 1999;159:249-54.
24. Winther M, Pellis T, Kuiper M, et al. Mortality and neurological outcome in the elderly after target temperature management for out-of-hospital cardiac arrest. Resuscitation. 2015;91:92-8.
25. Grimaldi D, Dumas F, Perier M, et al. Short- and long-term outcome in elderly patients after out-of-hospital cardiac arrest: A Cohort Study. Crit Care Med. 2014;42:2350-7.
26. Libungan B, Lindqvist J, Strömsoe A, et al. Out-of-hospital cardiac arrest in the elderly: A large-scale population-based study. Resuscitation. 2015;94:28-32.
27. Howes D, Gray S, Brooks S, et al. Canadian Guidelines for the use of targeted temperature management (therapeutic hypothermia) after cardiac arrest: A joint statement from The Canadian Critical Care Society (CCCS), Canadian Neurocritical Care Society (CNCCS), and the Canadian Critical Care Trials Group (CCCTG). Resuscitation. 2016;98:48-63.
28. Mallery L, Hubbard R, Moorhouse P, Koller K, Eamonn E. Specialist physician approaches to discussing cardiopulmonary resuscitation for frail older adults: A qualitative study. J Palliat Care. 2011;27:12-19.
29. Harkness M, Wanklyn P. Cardiopulmonary resuscitation: capacity, discussion and documentation. QJM. 2006;99:683-90.
30. Fabricio-Wehbe S, Partezai R, Vanderlei J, Silva J, Aleixo M. Association of Frailty in hospitalized and institutionalized elderly in the community-dwelling. Rev Bras Enfer. 2016;69:691-6.
31. Edin MG. Cardiopulmonary resuscitation in the frail elderly: clinical, ethical and halakhic issues. Isr Med Assoc J. 2007;9:177:9.
32. Gordon M. Ethical and clinical Issues in Cardiopulmonary Resuscitation (CPR) in the Frail Elderly with Dementia: A Jewish Perspective. JEMH. 2006;1:1-4.

THE JOURNAL OF LATIN AMERICAN GERIATRIC MEDICINE REVIEW ARTICLE

Body mass index in older adults: controversial issues

Ana Cecilia Rios-Márquez[1], Mario Ulises Pérez-Zepeda[2] and Mariana González-Lara[3]*

[1]Juarez Autonomous University of Tabasco, Villahermosa, Tab.; [2]Geriatric Epidemiologic Research Department, National Institute of Geriatrics , Mexico City; [3]Postgraduate Division, Faculty of Medicine, Mexican National Autonomous University, Mexico City. Mexico

Abstract

It has been found by investigators that decreased muscle strength and muscle mass leads to decreased gait speed, increased risk of falls, and reduced ability to carry out activities of daily living. The body mass index is a simple index that is frequently used to classify people as underweight, overweight, or obese. However, despite using cut-off values proposed by the World Health Organization, these could misclassify according to the older adults' body composition. In fact, not only must anthropometric aspects be considered, but clinical and dietary characteristics also influence better nutritional status. Estimation of maximum height by knee height is one of the most used surrogates, since it is not affected by height loss resulting from degenerative changes. Therefore, knee height shows a strong correlation with body height with little error and it is the best predictor of body height. The aim of this manuscript is to address, in a comprehensive review, some recent controversial issues regarding the use of body mass index in older adults. (J Lat Am Geriat Med. 2016;2:67-71)

Key words: *Body mass index. Knee height. Older adults.*

Corresponding author: *Mariana González-Lara, mariana.glara@gmail.com*

Resumen

Se ha investigado que la disminución en la masa y fuerza muscular conlleva una disminución de la velocidad de la marcha, incremento en el riesgo de caídas y también disminución en la habilidad para realizar actividades de la vida diaria. El índice de masa corporal (IMC) es un índice sencillo que se usa frecuentemente para clasificar a las personas en bajo peso, sobrepeso u obesidad. Sin embargo, a pesar del uso de los puntos de corte propuestos por la Organización Mundial de la Salud, éstos podrían malclasificar de acuerdo a la composición corporal de los adultos mayores. De hecho, no sólo hay que considerar los aspectos antropométricos, sino que las características clínicas y dietéticas también influyen en un mejor estado nutricional. La estimación de la estatura máxima mediante la altura de rodilla es un sustituto comúnmente usado, ya que no está afectado por la pérdida de estatura debida a cambios degenerativos. Por lo que la altura de rodilla muestra una fuerte correlación con la estatura y con un mínimo error, lo que puede ser el mejor predictor para estimar la estatura. El objetivo de este texto es abordar, a partir de una revisión de la literatura, algunos tópicos controversiales en torno a la utilización del IMC en los adultos mayores.

Palabras clave: Índice de masa corporal. Altura de rodilla. Adultos mayores.

Correspondence to:
*Mariana González-Lara
Geriatric Epidemiology Research Department
National Institute of Geriatrics
Periférico Sur, 2767
Col. San Jerónimo Lídice, Del. Magdalena Contreras
C.P. 10200, Ciudad de México, México
E-mail: mariana.glara@gmail.com

INTRODUCTION

Aging is associated with a loss of neuromuscular function and performance, partly related to decreased muscle strength caused by a loss of skeletal muscle mass and particularly by changes in muscle architecture. This decrease in muscle strength, along with other factors such as aging of somatosensory and motor nervous systems, leads to decreased gait speed, increased risk of falls, and a reduced ability to carry out activities of daily living[1]. Body mass index (BMI) is the most commonly used tool to correlate risk of health problems with the body composition at the population level and is a simple index commonly used to classify a person as underweight, overweight and obese. It was first described by Quetelet, et al.[2], and nowadays is one of the tools readily available worldwide for the clinician that helps to discriminate between someone at risk of cardiovascular adverse outcomes (obesity) or death (under-nutrition). It is obtained as the weight in kilograms divided by the square of the height in meters (kg/m^2)[3]. Although there is currently enough evidence on how to categorize adults by this index, this is still unclear for older adults. The World Health Organization (WHO) had recommended the following cut-off values for this population, regarded as normal: greater than 23 kg/m^2 and less than 28 kg/m^2; however, this is ambiguous and difficult to apply in a clinical setting in which subjects such as older adults have lost height. Some evidence has rather pointed to a U-shaped association between BMI and overall health status (e.g. in obese or in underweight older adults)[4].

AGING AND BODY MASS INDEX

Aging is frequently associated with height loss, and this phenomenon occurs since early adulthood; maximum height is estimated to be reached at around 20-years of age[2]. Various factors contribute to height loss. The most important cause would be vertebral compression fracture caused by osteoporosis, among other less common or less well described factors[5]. A study recently reported that the cumulative average of height loss from age 30-70 was 3 cm for men and 5 cm for women, and that from age 30-80 was 5 cm for men and 8 cm for women[6]. Such height loss presents serious problems for the validity of BMI as the weight-height ratio in the elderly, and there is the potential for an overestimation of BMI because of shortened height[5]. For example, according to data reported by the National Health and Nutrition Survey (Table 1) these surveys are based with BMI categorization for the adult population suggested by the WHO, not taking into account the height decrease of the elderly mentioned above[7]. Generally, BMI is an indicator that, according to the WHO classification (regardless of age and sex), allows evaluating if the subject has problems of underweight, overweight, or obesity, and is not so useful in older adults who have markedly decreased their height with age, since the interrelation based on current height is problematic. On the other hand, depending on the degree of changes at the spinal level, height may be a measure of questionable value in some elderly, although its determination may be more reliable if estimated through knee height. Moreover, because of multiple factors such as physiologic changes associated with aging, chronic diseases, polypharmacy, and psychosocial changes, older adults have an increased risk of under-nutrition, which is associated both with increased mortality and morbidity. Malnutrition often goes unrecognized because nutrition assessment is limited to one measure of BMI or weight. In western countries, it is estimated that more than two-thirds of adults aged > 65 years have a BMI > 25[8]. A more precise estimation of an older adult's height could lead to a better assessment of the nutritional status in this group. Since the length of the long bones of arms and legs remain constant with age, arm length and knee height have been used as proxy measures for height estimation in older adults. Estimation of maximum height by knee height is one of the most used surrogates, since it is not affected by height loss resulting from degenerative changes[9]. Knee height shows a strong correlation with body height with little error and is the best predictor of body height[10].

Table 1. Report by the National Health and Nutrition Survey in Mexicans aged between 60 to 69 years

	Men 60-69 years	Women 60-69 years
Underweight	1.0%	1.3%
Normal weight	25.6%	18.8%
Overweight	49.8%	36.2%
Obesity	23.6%	43.7%

Several international studies have shown that height estimation formulas through knee height measurement are easily conducted among individuals aged 60 or older[11-14]. To measure knee height, an adjustable measuring stick is used. The subject may be in a sitting or supine position with the knee bent at a 90° angle. Various researchers have proposed predictive knee height equations in different countries for different groups of people[10].

ALTERNATIVES TO ASSESS BODY COMPOSITION

The first formulas that were carried out to calculate height by measuring knee height were only for white and black American elderly conducted by Chumlea, et al. in 1992[12]. Although the study was conducted in older adults in Ohio, USA, the formula for white Americans have shown satisfactory results for Italians[10]. But this formula does not apply to all populations; this is why various equations have been developed to predict height using knee height, for example for the French and Chinese elderly population[13]. In Mexico, formulas for Mexican men and women were created in 2002 by Mendoza[14] (Table 2).

Anthropometric measures are necessary to determine the nutritional status of a patient, mainly to assess body composition: weight, height, BMI, body circumferences (mid arm, waist, hip and calf), waist-to-hip ratio, elbow amplitude, knee-height, and skinfold thickness[15]. There are other tools that complement the nutritional assessment. One of these is the Mini Nutritional Assessment (MNA), which consists of a scale (score 0-14) that covers global behavior, subjective factors, weight and height. The MNA is fast, describes the main features, but does not give a complete assessment of nutritional status. However, this tool was complemented by the work of Toulouse University, The Medical School in New Mexico, and the Nestle Research Centre (Switzerland). In this second part of the MNA, the scale comprises 12 items covering anthropometric measurements, dietary behavior, global and subjective factors. It takes 10-15 minutes and the score range is 0-30. A score of 24-30 indicates no nutritional risk, 17.0-23.5 is nutritional risk, and less than 17 high nutritional risk or likely malnutrition. Other tools are the creatinine height index (CHI, reflecting muscle mass and therefore declining with age) and the change in intracellular water as estimated from total body potassium decline with age and have been used as a parameter of nutritional assessment.

Nutritional assessment in the elderly should be supplemented with functional ability, physical and mental health, and the socio-environmental situation. The functional ability is estimated with measures of Activities of Daily Living and Instrumental Activities of Daily Living. The Mini-Mental State Examination assesses most of the major aspects of cognitive function and the Geriatric Depression Scale is easy to use and is widely accepted[16]. All these are necessary for a proper assessment of the elderly and not only anthropometric data such as height or weight.

During aging, besides the physiological changes mentioned above, there exists a condition typical of the elderly: sarcopenia. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of

Table 2. Equations developed to predict height using knee height

	Men	Women
White Americans Chumlea, et al. 1992[12]	59.01 + (2.08 x knee height)	75.00 + (1.91 x knee height) – (0.17 x age)
Black Americans Chumlea, et al. 1992[12]	95.79 + (1.37 x knee height)	58.72 + (1.96 x knee height)
French elderly Zhang, et al. 1998[13]	74.69 + (2.07 x knee height) – (0.21 x age)	67 + (2.20 x knee height) – (0.251 x age)
Chinese elderly Zhang, et al. 1998[13]	67.78 + (2.01 x knee height)	71.70 + (1.98 x knee height) – (0.044 x age)
Mexicans Mendoza, et al. 2002[14]	52.6 + (2.17 x knee height)	73.7 + (1.99 x knee height) – (0.23 x age)

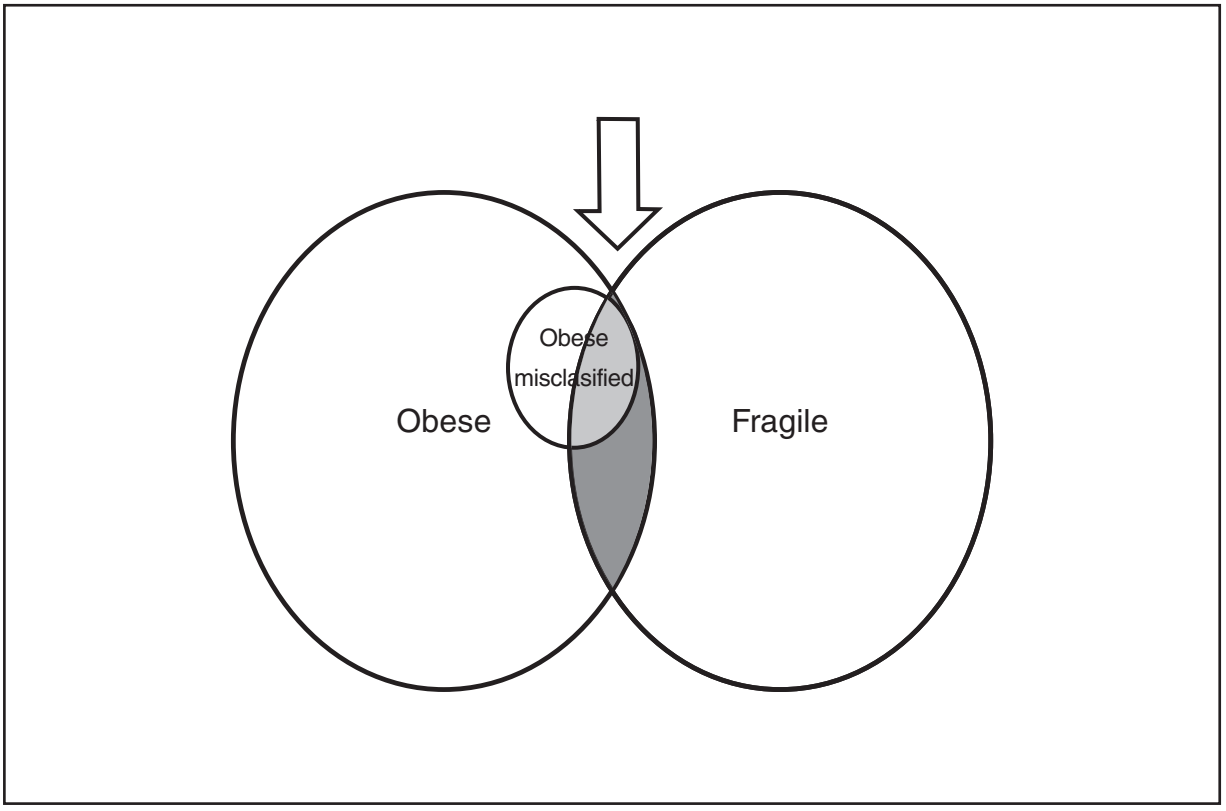


Figure 1. *Scope of obesity and frailty misclassification.*

adverse outcomes such as physical disability, poor quality of life and death[17]. Sarcopenia goes hand-in-hand with frailty. Frailty is a geriatric syndrome resulting from age-related cumulative declines across multiple physiologic systems, with impaired homeostatic reserve and a reduced capacity of the organism to withstand stress, besides including cognitive status, social support, and other environmental factors, thus increasing vulnerability to increased risk of disability, mortality of all causes, and greater need for healthcare[17-19]. Frail older people exhibit sarcopenia, and some older people with sarcopenia are also frail[17]. Obesity in older persons negatively affects physical functioning, particularly when it is accompanied by low muscle strength; this is "sarcopenic obesity". Poor muscle strength relative to excessively high body mass impedes the weight-bearing activities that are vital for maintaining independence in daily life[20].

As mentioned at the beginning, BMI is used to classify low weight, underweight and obesity[3], but using the values for the young adult population as it has been reported by the National Health and Nutrition Survey in Mexico[7], these cut-off values are badly sorting a portion of older adults, the obese mainly, and as has been said, frailty and sarcopenia are present (Fig. 1). This group of elderly is erroneously indicated to follow strict diets to lose weight, and this is often more deleterious than in younger subjects. Although BMI is the most frequently used measure to evaluate overweight and obesity, the method does not allow for true body adiposity.

The BMI has some limitations in people with decreased muscle mass and elevated body fat, and in individuals with increased body fat who are classified as having a normal BMI. Because elderly persons lose muscle mass[21], imposing restrictions purely on the basis of an elevated BMI is potentially detrimental[8].

CONCLUSIONS

Geriatric syndromes such as frailty, falls, functional decline, and hospitalization[17,22] could lead to disability and do not allow a part of the population of older adults to be in a standing position. Therefore, conventional height measurement can not be performed, and here knee height measurement is useful. Sarcopenic obesity should not be missed, which as men-

tioned above, can indicate unnecessary diets; indeed, to maintain weight in the elderly may be a protective factor[21].

In 2010 in Mexico, about 400 specialists served a population of eight million older adults[23], an insufficient number, and now, despite the fact that the number of geriatricians is increasing, the older population is increasing even more. Of the population aged 65 years or more, 69.3% live in low socioeconomic status[24], with little access to specialized services such as geriatrics and nutrition.

As primary care is essential for older adults, it is appropriate to use knee height for the measurement of height in the formula for BMI for the elderly population, thus avoiding bad assessments changing the course of health in older people.

REFERENCES

1. Landinez Parra NS, Contreras Valencia K, Castro Villamil A. [Aging, exercising and physical therapy]. Rev Cubana Salud Pública. 2012;38:562-80.
2. Caponi S. [Quetelet, the average man and medical knowledge]. Hist Cienc Saude Manguinhos. 2013;20:831-47.
3. World Health Organization. Obesity: preventing and managing the global epidemic. Geneva, Switzerland; 1999.
4. Organización Panamericana de la Salud. Valoración Nutricional del Adulto Mayor. In: Guía Clínica para Atención Primaria a las Personas Adultas Mayores. Primera. Washington, DC: Organización Panamericana de la Salud; 2002. p. 58-70.
5. Kuwabara A, Ogawa-Shimokawa Y, Tanaka K. Body weight divided by squared knee height as an alternative to body mass index (A). Med Hypotheses. 2011; 76:336-8.
6. Sorkin JD, Muller DC, Andres R. Longitudinal change in height of men and women: Implications for interpretation of the body mass index. Am J Epidemiol. 1999;150:969-77.
7. Gutiérrez JP, Rivera JA, Shamah-Levy T, Oropeza C, Hernández-Avila M. Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. México; 2012.
8. Winter JE, Macinnis RJ, Wattanapenpaiboon N, Nowson CA. BMI and all-cause mortality in older adults : a meta-analysis. Am J Clin Nutr. 201499: 875-90.
9. Marais D, Marais ML, Labadarios D, Chb MB. Use of knee height as a surrogate measure of height in older South Africans. S Afr J Clin Nutr. 2007;20: 39-44.
10. Pini R, Tonon E, Cavallini MC, et al. Accuracy of equations for predicting stature from knee height, and assessment of statural loss in an older Italian population. J Gerontol A Biol Sci Med Sci. 2001;56:3-7.
11. Fogal AS, Castro C, Priore SE, Cotta RMM, Ribeiro AQ. Stature estimation using the knee height measurement amongst Brazilian elderly. Nutr Hosp. 2015;31: 829.34.
12. Chumlea WC, Guo S. Equations for predicting stature in white and black elderly individuals. J Genentol. 1992;47:197-203.
13. Zhang H, Hsu-Hage BH-H, Wahlqvist ML. The use of knee height to estimate maximum stature in elderly Chinese. J Nutr Health Aging. 1998;2:84-7.
14. Mendoza-Núñez VM, Sánchez-Rodríguez MA, Cervantes-Sandoval A, Correa-Muñoz E. Equations for predicting height for elderly Mexican Americans are not applicable for elderly Mexicans. Am J Hum Biol. 2002;355:351-5.
15. Sánchez-García S, García-Peña C, Duque- MX, et al. Anthropometric measures and nutritional status in a healthy elderly population. BMC Public Health. 2007;9:1-9.
16. Stanga Z. Basics in clinical nutrition: Nutrition in the elderly. E Spen Eur E J Clin Nutr Metab. 2009;4:e289-99.
17. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia : European consensus on definition and diagnosis Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;39:412-23.
18. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults : Evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:146-56.
19. Landi F, Cruz-Jentoft AJ, Liperoti R, et al. Sarcopenia and mortality risk in frail older persons aged 80 years and older: results from ilSIRENTE study. Age Ageing. 2013;42:203-9.
20. Stenholm S, Alley D, Bandinelli S, Griswold M, Koskinen S, Rantanen T, et al. The effect of obesity combined with low muscle strength on decline in mobility in older persons: results from the InCHIANTI Study. Int J Obes (Lond). 2010; 33:635-44.
21. Zeanandin G, Molato O, Le F, Guérin O, Hébuterne X, Schneider SM. Impact of restrictive diets on the risk of undernutrition in a free-living elderly population. Clin Nutr. 2012;31:69-73.
22. Carlson C, Merel SE, Yukawa M. Geriatric syndromes and geriatric assessment for the generalist. Med Clin N Am. 2015;99:263-79.
23. Gutiérrez-Robledo LM, D'Hyver de los Deses C. [Geriatrics]. Aten Fam. 2010;17: 24-5.
24. Gutiérrez-Robledo LM, Ávila-Fematt FM, Montaña-Álvarez M. [Geriatrics in Mexico]. El Resid. 2010;V:43-8.

THE JOURNAL OF LATIN AMERICAN GERIATRIC MEDICINE CLINICAL CASES

Gait disorders in the elderly: current perspectives around two cases

Julio Alberto Díaz-Ramos[1]*, Iris Janet Martínez-Lemus[1], Olga Berenice González-Hernández[2], David Leal-Mora[1], Jazmín Teresa Pozos-López[3] and Sergio Iván Valdés-Ferrer[4]

[1]Geriatrics Department, Hospital Civil Fray Antonio Alcalde; [2]Geriatrics Department, Hospital General Regional Nº 46, IMSS. Guadalajara, Jal.; [3]Geriatric Neurology Department, Hospital General Dr. Manuel Gea González, Mexico City; [4]Department of Neurology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City. Mexico

Abstract

Gait disorders are one of the most feared geriatric syndromes due to the negative outcomes. Their prevalence increases with age and represent a diagnostic challenge for most doctors. Gait in old age has adaptive features that are still considered normal. However, not all forms of walking observed in elderly people are normal. Because of the complexity of the act of walking, its evaluation requires a comprehensive examination. The intervention will depend on the integration of an interdisciplinary team to assess systematically the changes in walking and make a timely diagnosis through appropriate tools. We present two clinical cases that serve as an introduction to the assessment of gait disorders in old age through an approach that combines elements of both the Compressive Geriatric Assessment and a through neurological examination. (J Lat Am Geriat Med. 2016;2:72-8)

Key words: *Gait disorders. Geriatric assessment. Elderly.*

Corresponding author: *Julio Alberto Díaz-Ramos, julio.alberto.diaz.ramos.geriatra@gmail.com*

Resumen

El trastorno de la marcha es uno de los síndromes geriátricos más temidos por sus desenlaces negativos. Su prevalencia se incrementa con la edad y su diagnóstico representa un reto para la mayoría de los médicos. La marcha en el adulto mayor posee características que siguen considerándose normales; sin embargo, no todas las formas de caminar observadas en las personas mayores son normales. La complejidad inherente a la marcha requiere una evaluación integral. La intervención dependerá de la integración de un equipo transdisciplinario que evalúe sistemáticamente las alteraciones en el caminar y realice un diagnóstico oportuno a través de las herramientas apropiadas.

A continuación, presentamos dos casos clínicos que sirven de introducción a la evaluación de la marcha en la vejez a través de un abordaje que combina elementos tanto de la evaluación geriátrica integral (EGI) como de la neurología clínica.

Palabras clave: Trastornos de la marcha. Evaluación geriátrica. Adulto mayor.

Correspondence to:
*Julio Alberto Díaz-Ramos
OPD Hospital Civil de Guadalajara
Unidad Hospitalaria Fray Antonio Alcalde
Calle Hospital, 278
C.P. 44280, Guadalajara, Jal., México
E-mail: julio.alberto.diaz.ramos.geriatra@gmail.com

INTRODUCTION

The human ability of bipedal locomotion, given by coordination of the central nervous system and hind limbs, is one of the most dramatic features achieved through evolutionary forces. Not surprisingly, this is also one of the fundamental differences between humans and other species capable of locomotion. The difficulties that hinder the ability to walk (gait disturbances) can cause serious health complications, ranging from falls to immobility. Gait disorders are some of the most feared geriatric syndromes due to the negative outcomes such as functional decline, institutionalization, hospitalization, disability, dependence, and even death. The prevalence increases with age; thus, while at 60 years of age it is 15%, prevalence rises to 50% beyond 85 years[1-3].

Despite their high prevalence, gait disorders represent a diagnostic challenge for most inexperienced physicians or those without specific training for assessing locomotion. Due to its inherent complexity, a comprehensive assessment is required, which involves various healthcare professionals (physical therapists, nutritionists, neurologists, and geriatricians, among others), in order to achieve a thorough diagnostic and therapeutic strategy. Timely intervention will depend on the integration of a multi-disciplinary team and proper assessment of changes in walking in elderly patients, and diagnosis through clinical expertise and appropriate tools. Here we present two cases of gait disorders seen at a tertiary care University Hospital, and use these real-life scenarios to introduce the combined elements and components of the Comprehensive Geriatric Assessment (CGA) as well as the clinical neurological assessment.

CASE 1

A 71-year-old man with a 25-year history of type 2 diabetes and hypertension and a gastrointestinal stromal tumor resected without complications 10 years ago. For the past three years he has dealt with difficulties in episodic memory and inability to concentrate and subsequent spontaneous recovery of information. In the last six months he noticed difficulty in separating the feet of the ground surface, urinary incontinence, and moderate headache; also, in this period he had three falls. Three months before his evaluation, emotional liability and anhedonia appeared. Physical examination revealed mild weakness (4/5) in all four limbs. The functionality is affected in relation to the difficulties in mobilizing and by the presence of mild symptoms of depression (Table 1).

Gait evaluation

The patient struggled to lift and move the feet forward, the so-called magnetic gait. The initial contact with the ground was with the toes, short shuffling step heels apart, and imbalance at the beginning of ambulation. The position was otherwise normal, but with reduced balance of the arm and slow turning.

Magnetic resonance imaging

This showed supratentorial ventricular system dilation associated with remodeling contours of lateral ventricles and sub-ependymal hyperintensity on T2-weighted images. Evans index was 0.45 (Fig. 1).

CASE 2

A 73-year-old man with a past medical history of hypertension and prostatic hyperplasia diagnosed five years prior to the current event. His chief complaint was a two-year history of intermittent, diffuse, non-oppressive headache of moderate intensity, presenting on average five days per week. The clinical feature began after a fall with head trauma in the frontal region. Six months before presenting to the clinic, episodic memory problems began. A month before being evaluated, insomnia, nocturnal hallucinations, disorientation, and decreased mood appeared. In the previous year he had at least four falls. Simultaneously, he presented urinary incontinence, decreased visual acuity and hearing loss, and unintentional weight loss associated with hyporexia. On physical examination, we found normal strength and reflexes in all four limbs. Functionality was deeply affected and difficulties in mobilizing caused by ataxic gait caused the presence of several affective symptoms, which reached the cutoff point for the diagnosis of depression (Table 1).

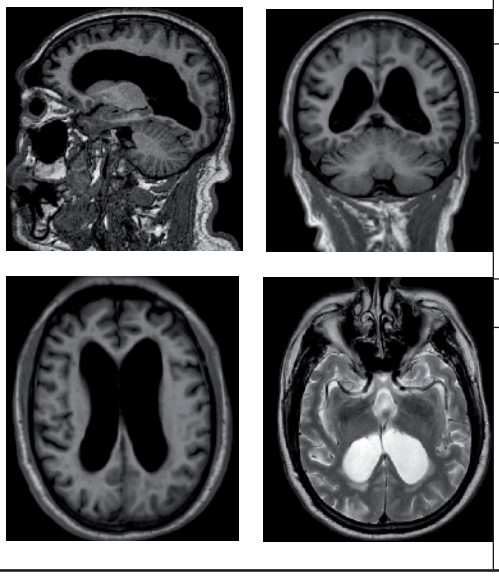
Gait evaluation

The patient had a complex gait disorder characterized by trunk instability, starting each step rolling from heel to toes, leading to a drumroll sound. Gait support base was wide, and walking revealed an

Table 1. Results obtained through the Comprehensive Geriatric Assessment

CGA	Case 1	Case 2
MMSE (30)	25	26
CAM (0)	0	0
Clock (10)	8	9
MoCA (30)	27	19
Yesavage (0-15)	3	6
Rosow-Breaslow (3)	3-2	3 -3
Nagi (5)	5-4	5-4
Katz (A)	B	B
Barthel (100)	100-100-95	95-90-80
Lawton-Brody (8)	8-6-6	8-8-5
Get Up and Go (≥ 3)	Magnetic gait (5)	Ataxic gait (3)
ICIQ-SF (0)	14	13
Tinetti (balance, 0-16)	7	9
Tinetti (gait, 0-12)	6	6

Time occurred in between the different functional assessments scores in Nagi, Barthel, and Lawton-Brody scale was about six months. This is consistent with the evolution of the symptoms, particularly with the onset of gait disorders in both cases.
CAM: Confusion Assessment Method; CGA: Comprehensive Geriatric Assessment; ICIQF-SF: International Consultation on Incontinence Questionnaire-Short Form; MMSE: Mini-Mental State Evaluation; MoCA: Montreal-Cognitive Assessment.



Gait	Case
Imbalance	✔
Abnormal postural	✗
Short steps	✔
Steps dragged	✔
Slow steps	✔

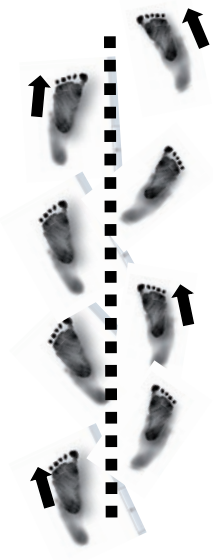


Figure 1. *Clinical and radiological features in gait disorder of Case 1.*
Normal pressure hydrocephalus (NPH) refers to a condition of pathologically enlarged ventricular size with normal opening pressures on lumbar puncture. NPH is associated with a classic triad of cognitive impairment, gait disturbance, and urinary incontinence. Idiopathic NPH is more common in elderly individuals. Brain magnetic resonance imaging is an essential test in a patient with NPH and demonstrates ventriculomegaly out of proportion to sulcal enlargement and no evidence of cerebrospinal fluid flow obstruction. Up to two-thirds of patients can expect some degree of benefit after shunting. In half of these, however, the benefit will not be sustained.

obvious deviation to the left side, making tandem walking impossible due to postural instability. We noticed a stooped position, and the patient kept his eyes focused on the floor as he walked. Arm swinging was reduced and, to make turns in either direction, one foot was anchored and used as the axis of rotation, while the other made wide, small and broken down steps in order to turn around.

Computed tomography scan

This showed the presence of an extra-axial space-occupying lesion in the right frontal lobe, with significant mass effect and perilesional edema (Fig. 2).

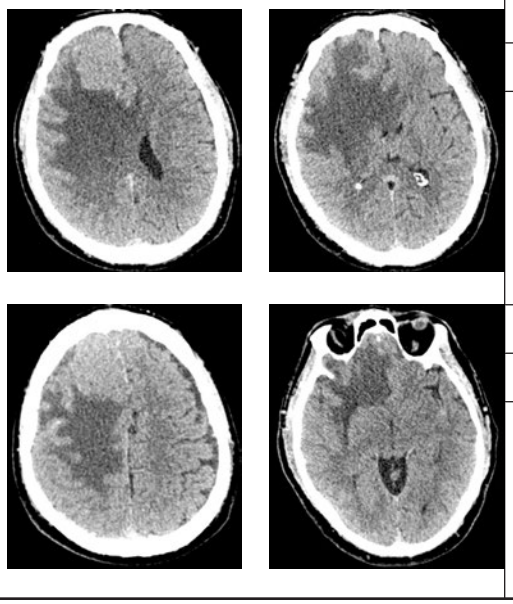
DISCUSSION

The way we walk defines us. Gait characteristics are as specific as fingerprints, to the extent that gait problems can first reveal the presence of underlying medical problems. Some diseases have features that prompt a profound gait investigation.

The CGA is a diagnostic strategy that qualifies tools for an optimal evaluation of gait disorders. The CGA can identify a variety of potentially correctable health problems and promote positive health outcomes in older people[4,5]. Examples of this include gait disorders and falls. The term "geriatric syndrome" is used to refer to common conditions in the elderly that do not fit into specific categories based on organic diseases. Gait disorders and falls are part of the spectrum of geriatric syndrome. Both have a negative impact on quality of life and functionality of the older patient, and can be identified through the CGA (Table 1).

Assessment of gait and falls

The ability of older adults to perform activities of daily living depends on their mobility, meaning the ability to move safely and effectively. Mobility is an important component of physical function. Both gait and balance represent different aspects of mobility. It is well known that deterioration of these functions is associated with increased risk of falls and injuries. Walking speed, for instance, is a strong predictor of disability and mortality in the elderly[6].



Gait	Case
Wide-based	✔
Unable to tandem	✔
Unstable trunk	✔
Heel-toe	✔
Deviation	✔

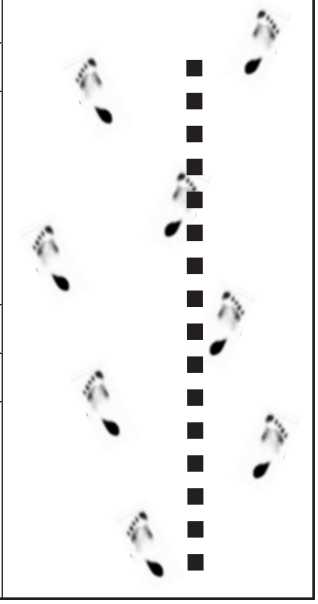


Figure 2. *Clinical and radiological features in gait disorder of Case 2.*
Brain tumors can produce symptoms and signs by local brain invasion, compression of adjacent structures, and increased intracranial pressure. In addition to the histology of the tumor, the clinical manifestations are determined by the function of the involved areas of brain. The proper evaluation of the patient with a suspected brain tumor requires a detailed history, a comprehensive neurologic examination, and appropriate diagnostic neuroimaging studies. Patients with primary or metastatic brain tumors may present with either generalized or focal signs and/or symptoms.

Assessment of gait speed can help identify patients who require further evaluation (e.g. those at risk of falls) and is useful in diagnosing frailty syndrome[7].

A third of community dwelling people older than 65 years of age and up to 50% of those over 80 fall each year. Elderly persons with a past history of falling, and those with gait and balance disorders, are at high risk of loss of independence[1,8].

Gait disorder evaluation should be integrated into the clinical history and physical examination in all geriatric patients. In order to achieve normal gait, older people must have adequate joint mobility, optimal muscle performance, and preserved proprioception. In the presence of pathological changes at any of those levels, elderly people develop gait changes that lead to balance problems, muscle weakness, and falls.

Gait assessment instruments

There are several tools to evaluate the walking process; for instance, the timed test Get Up and Go. This test is easy to apply and is useful in assessing the main features of gait: fast walking, stride length, base of support, regularity of steps, and the ratio between time supported by both feet versus time supported on only one foot[9,10].

The Tinetti test or Performance Oriented Mobility Assessment (POMA), which provides a structured context in which very specific components are evaluated, is also useful. Dr. Mary Tinetti, a leading scholar in the study of falls and independence in the elderly, proposed the scale two decades ago in 1986. The scale has two domains: gait and balance. Its main purpose is to detect those elderly at risk of falling. It consists of nine balance items and seven gait items. Items are scored as 0 (i.e. patient does not maintain stability during changes in position, or has a pattern of inappropriate gait); 1, indicating changes in position or gait patterns with certain postural compensation (called adaptive condition); and a rating of 2, given to people without difficulty implementing the various tasks of the scale. The maximum balance score is 16 points and 12 points for gait, tallying up to a total maximum of 28. For instance, 19-24 is considered as minimal risk. More than 24 points is considered safe, and less than 19 points is equal to very high risk[11].

Another tool is The Short Physical Performance Battery (SPPB), which characterizes lower-extremity function. It includes measures of standing balance (timing of tandem, semi-tandem, and side-by-side stands; four-meter walking speed and ability; and time to rise from a chair five times). The SPPB captures a wide range of functional abilities, and summary scores < 9 have independently predicted disability in activities of daily living. Some components of the SPPB are also predictive of falls[12,13].

Gait types

We have already mentioned that gait disorders increase with age, and that they predict negative outcomes (e.g. cardiovascular disease, cognitive impairment, reduced survival)[1,8,14-17].

However, we should emphasize that gait in old age has unique characteristics that are still considered normal. Overall, gait tends to be slow, shuffling, and tends to be cautious[18] (Table 2).

Using the same argument, not all forms of walking observed in old people are normal (Table 3). For example, a feature associated with frontal lobe

Table 2. Normal gait changes associated with aging

Age effects on the walk
Posture projected discretely forward (head, torso, hips, knees)
Upper extremities balancing decreased
Vertical displacement of trunk reduced
Dorsal and plantar flexion of the ankle and hip extension reduced
Step length decreased and width increased
Reduction in swing phase at expense of double support phase
Speed reduced (15-20% per decade)
Cadence decreased
Angle of the foot with the ground decreased
Bipedal phase prolonged
Rolling time/time support shortened
Pelvic rotations reduced
Propulsive force decreased

Table 3. Comparison between normal gait in old age and in neurological diseases

Clinical features	Normal aging	Normal pressure hydrocephalus	Cerebellar ataxia	Vestibular dysfunction	Extrapyramidal
Imbalance	✗	✔	✔	✔	✔
Abnormal posture	✗	✔	✗	✗	✗
Freezing	✗	✗	✗	✗	✗
Short walk	✔	✔	✔	✔	✔
Slowness	✔	✔	✔	✗	✔
Signs of Parkinsonism (akinesia, plastic hypertonia, tremor)	✗	✗	✗	✗	✔
Signs of ataxia (dysmetria, dyssynergia, slow speech)	✗	✗	✔	✗	✗
Nystagmus	✗	✗	✗	✔	✗

pathology is walking difficulty, with persistent imbalance and constant falls. The presence of other signs and symptoms may lead to suspect frontal lobe dysfunction including depression, release signs, and impaired executive function[19].

CONCLUSIONS

Gait disorders are highly prevalent in old age. These are also some of the most feared geriatric syndromes due to their potential negative outcomes: falls, disability, and death.

It is essential to assess gait routinely as part of the systematic approach of the elderly. A strategy that has proven useful is performing the CGA. A diagnostic approach based on clinical data obtained from a detailed neurological evaluation coincides with the basic principles of geriatrics. We consider it important to emphasize this fact with the purpose of promoting multidisciplinary teamwork, and cement the idea that clinical information is a cornerstone during the process of medical diagnosis. A diagnostic approach based on clinical findings obtained after a thorough neurological exam concur with the basic principles of geriatric evaluation. We want to emphatically remind the reader of how relevant a multidisciplinary approach is during the diagnostic process of gait disorders, highlighting the obvious: a thorough questioning and clinical exam are cornerstones for an accurate diagnosis.

Deliberate search for gait disorders, through tests like Tinetti and Get Up and Go, and integrating the said information with a thorough neurological exam are effective for early detection of pathologies associated with gait disorders of the elderly.

ETHICAL RESPONSIBILITIES

Protection of people and animals: The authors state that for this investigation, experiments have not been performed on humans or animals.

Confidentiality of data and right to privacy and informed consent: The authors declare that in this article, patient personal data does not appear.

DECLARATION OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Verghese J, Levalley A, Hall CB, Katz MJ, Ambrose AF, Lipton RB. Epidemiology of gait disorders in community-residing older adults. J Am Geriatr Soc. 2006; 54:255-61.
2. Sudarsky L. Gait disorders: prevalence, morbidity, and etiology. Adv Neurol. 2001;87:111-7.

3. Jahn K, Zwergal A, Schniepp R. Gait disturbances in old age: classification, diagnosis, and treatment from a neurological perspective. Dtsch Arztebl Int. 2010;107:306-15.
4. Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet. 1993;342: 1032-6.
5. Devons CA. Comprehensive geriatric assessment: making the most of the aging years. Curr Opin Clin Nutr Metab Care. 2002;5:19-24.
6. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. JAMA. 2011;305:50-8.
7. Gross AL, Xue QL, Bandeen-Roche K, et al. Declines and impairment in executive function predict onset of physical frailty. J Gerontol A Biol Sci Med Sci. 2016;7:1624-30.
8. Verghese J, Lipton RB, Hall CB, Kuslansky G, Katz MJ, Buschke H. Abnormality of gait as a predictor of non-Alzheimer's dementia. N Engl J Med. 2002;347:1761-8.
9. Ensberg M, Gerstenlauer C. Incremental Geriatric Assessment. Prim Care Clin Office Pract. 2005;35:619-43.
10. Mathias S, Maual IS, Osaacs B. Balance in elderly patients: the "get-up and go" test. Arch Phys Med Rehabil. 1986;67:387-9.
11. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. J Am Geriatr Soc. 1986;34:119-26.
12. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med. 1995;332:556-61.
13. de Rekeneire N, Visser M, Peila R, et al. Is a fall just a fall: correlates of falling in healthy older persons. The Health, Aging and Body Composition Study. J Am Geriatr Soc. 2003;51:841-6.
14. Bloem BR, Gussekloo J, Lagaay AM, Remarque EJ, Haan J, Westendroop RG. Idiopathic senile gait disorders are signs of subclinical disease. J Am Geriatr Soc. 2000;48:1098-101.
15. Marquis S, Moore MM, Howieson DB, et al. Independent predictors of cognitive decline in healthy elderly persons. Arch Neurol. 2002;59:601-6.
16. Wilson RS, Schneider JA, Beckett LA, Evans DA, Benett DA. Progression of gait disorder and rigidity and risk of death in older persons. Neurology. 2002; 58:1815-19.
17. Scarmeas N, Albert M, Brandt J, et al. Motor signs predict poor outcomes in Alzheimer disease. Neurology. 2005;64:1696-703.
18. Bloem BR, Haan J, Lagaay AM, van Beek W, Wintzen AR, Roos RA. Investigation of gait in elderly subjects over 88 years of age. J Geriatr Psychiatry Neurol. 1992;5:78-84.
19. Ambrose A, Levalley A, Verghese JA. A comparison of community residing older adults with frontal and parkinsonism gaits. J Neurol Sci. 2006;248: 215-18.
20. Snijders AH, van de Warrenburg BP, Giladi N, Bloem BR. Neurological gait disorders in elderly people: clinical approach and classification. Lancet Neurol. 2007;6:63-74.
21. Factor SA, Higgins DS, Qian J. Primary progressive freezing gait: a syndrome with many causes. Neurology. 2006;66:411-14.

INFORMACIÓN A LOS AUTORES

The Journal Latin American Geriatric Medicine es el organo oficial de difusión del Colegio Nacional de Medicina Geriatrica en México, es una publicación periodica que responde a las necesidades actuales de la geriatría a nivel Latinoamerica. Representa un esfuerzo conjunto para hacer de la geriatría una especialidad de vanguardia con la importancia científica que merece. Publica textos, en español y en inglés sobre temas relacionados con la geriatría en forma de editoriales, artículos originales, de revisión, breves y actualizaciones, clásicos, indicadores, noticias, reseñas bibliográficas y cartas al editor. Conviene recordar que esta revista es un espacio abierto a todas las instituciones médicas y a contribuciones de investigadores nacionales y extranjeros, en especial a médicos e investigadores en el área clínica y epidemiológica en problemas relacionados con el envejecimiento. Puesto que el inglés es por excelencia el idioma de comunicación científica, se aceptarán artículos en este idioma. El número máximo de autores para artículos de revisión es de seis y tres para trabajos breves. La extensión debe de ser de 5 a 8 cuartillas (desde la hoja frontal hasta las referencias bibliográficas), más dos cuadros y una figura.

Estilo y formato

Todos los manuscritos deben de apegarse a las normas del Comité Internacional de Editores de Revistas Médicas. La hoja frontal debe llevar únicamente el título del trabajo (en español y en inglés que no exceda 90 caracteres), los nombres completos de los autores, sus grados académicos y su adscripción institucional; además, debe indicarse el responsable de la correspondencia, así como su dirección, teléfono, fax y dirección electrónica.

El resumen y el abstrac debe tener una extensión máxima de 150 palabras y estructurarse con los subtítulos: objetivo, material y métodos, resultados y conclusiones; en los artículos breves no deben de ser mayores de 100 palabras. También se tienen que incluir de tres a seis palabras clave.

El texto del escrito deberá contener las secciones correspondientes a introducción, material y métodos, resultados y discusión.

Los autores tienen la responsabilidad de enviar las referencias bibliográficas completas y de su correcta citación en el texto. Estas se deben numerar por orden consecutivo, de acuerdo con el sistema de Vancouver. Las de revistas incluyen: a)apellido(s) e inicial(es) de todos los autores (mencionarlos todos cuando sean seis o menos; cuando sean siete o más, señale sólo los seis primeros y añada "et al"); b) título completo del artículo, utilizando mayúscula sólo para la primera letra de la palabra inicial (y para nombres propios); c) abreviatura de la revista como esta indizada en index Medicus; d) año de publicación; e)volumen, en números arábigos; f) números completos de las páginas (inicial y final), separados por un guión. Para libros: a) apellido(s) e inicial(es) de todos los autores; b) título del libro; c) número de la edición, sólo si no es la primera d) ciudad en la que la obra fue publicada; e) nombre de la editorial; f) año de la publicación (de la última edición citada si hay más de una edición); g) número del volumen si hay más de uno, antecedido de la abreviatura "vol" ; h) número de la página citada; en caso de que la cita se refiera al capítulo de un libro, indicar la primera y la última página del capítulo, separadas por un guión.

Las unidades de medida deben de corresponder al Sistema Internacional de Unidades.

Cada cuadro se debe de enviar en una hoja por separado; han de contener título y se designarán con números romanos: cuadro I, cuadro II, etcétera, en el mismo orden en el que se mencionan en el texto. Las ilustraciones serán gráficas, fotografías o esquemas y se designarán con números arábigos: figura 1, figura 2, etcétera; también se enviarán en hojas separadas, cada una con su título. Si las figuras incluyen gráficas, éstas deberán incorporar los datos con los que fueron construidas (impresas o en archivo).

Todos los manuscritos se someten a una revisión preliminar en la que se determina si se apegan a la línea editorial y a las normas *The Journal Latin American Geriatric Medicine* en caso afirmativo, se encomienda una segunda evaluación a dos especialistas. Para asegurar la confidencialidad, los trabajos se envían de forma anónima y los autores tampoco conocen la identidad de los revisores.

Envío de artículos

Los manuscritos, deben enviarse por correo a: *The Journal Latin American Geriatric Medicine*. Vasco de Quiroga No. 15. Colonia Sección XVI. Tlalpan DF. 7to. Piso Servicio de Geriatría, INCMNSZ. C.P. 14420 México D.F. correo electrónico: sgan30@hotmail.com .

Todo trabajo enviado se acompañará de una carta firmada por todos los autores, cuyo contenido incluya lo siguiente; a) la aprobación del contenido del trabajo (incluyendo cuadros y figuras) y el orden de aparición de los autores (que se considerará definitivo sin excepción alguna); b) la transferencia de los derechos de autor a *The Journal Latin American Geriatric,* en caso de que el trabajo sea aceptado, c) descripción de la participación específica de los autores firmada de manera individual; y, d) mención de que se trata de un trabajo original que no ha sido publicado, total o parcialmente, ni sometido para su publicación por ellos mismos u otros autores, a otra revista nacional o extranjera. *The Journal Latin American Geriatric Medicine* se reserva el derecho de aceptar o rechazar, de acuerdo con las recomendaciones del Comité editorial, cada uno de los trabajos recibidos, así como de realizar cualquier corrección editorial que estime necesaria.

Se enviarán sobretiros del artículo publicado al autor responsable de la correspondencia.

Editor en Jefe:
Dra. Sara G. Aguilar Navarro
sgan30@hotmail.com

Co-editores:
Dr. J. Alberto Avila Funes
avilafunes@live.com.mx

Dr. Jorge Torres Gutierrez
drjorgeluistorresgutierrez@hotmail.com

Dra. Ivonne Becerra Laparra
ibecerra@medicasur.org.mx

www.conameger.org

Ejemplos de referencias

1. Reichenbach J, Schubert R, Horváth R, et al. Fatal neonatal-onset mitochondrial respiratory chain disease with T cell immunodeficiency. Pediatr Res. 2006;60:321-6.
2. Espinosa G, Bucciarelli S, Cervera R, et al. Thrombotic microangiopathic haemolytic anemia and antiphospholipid antibodies. Ann Rheum Dis. 2004;63:730-6.

PERMANYER MÉXICO
www.permanyer.com

© 2016 Permanyer México
Temístocles, 315
Col. Polanco, Del. Miguel Hidalgo
11560 Ciudad de México
Tel.: (044) 55 2728 5183
mexico@permanyer.com

www.permanyer.com

TCF Impreso en papel totalmente libre de cloro

Este papel cumple los requisitos de ANSI/NISO Z39.48-1992 (R 1997) (Papel Permanente)

Edición impresa en México

ISSN: 2462-2958
Dep. Legal: B-21.964-2016
Ref.: 3576AX161