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CASE REPORT

A Royal Jelly Mixture with Berberine for Dressing Change on a Refractory Skin Ulcer: A Case Report

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ABSTRACT

It has been reported that a 92-year-old female had got a bruise superficial wound on her right leg one and a half years ago, developing into refractory skin ulcer due to improper management before. A prepared cream, mixed royal jelly with berberine for dressing change, was made on the scene through the crush of berberine tablets, working with fresh royal jelly. Topical dressing change with the cream was done every 3 days, and two months later, such the ulcer became clean and was covered fully with fresh granulation tissue. This kind of cream consists of the ingredients of TCM purely, free of antibiotic, and being quite effective clinically, also helpful for proper use of antibiotic.

1. Introduction

This is a 92-year-old female patient with a bruise superficial wound on her right leg over one and a half years, which developed into a refractory skin ulcer because of improper management prior to the latest admission. A prepared cream was made on the scene for the topical dressing change, consisting of fresh royal jelly and berberine, and then applied to the wound surface after cleaning once every 3 days, lasting for two months. The wound surface became clean, and covered fully with fresh granulation tissue. The skin ulcer healed pretty well, and its vibrant effect for refractory skin ulcer was impressive.

2. Case Report

This is a 92-year-old female, who sustained a bruise superficial wound by a hard object on her right leg from a fall at home one and a half years ago. The wound was about 2cm long and without obvious bleeding. The patient and her families didn't pay more attention to it; thenceforward, the wound gradually widened and deepened, then applied erythromycin ointment to the wounded part by herself; however, it was no better, but rather grew worse. Two months later, the wound measuring 6×4 cm, and the purulent secretion on the surface was increased. So far, the patient at home was

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admitted to one hospital for this skin ulcer, resulting from the neglect by this patient. The wound infection was treated with systemic use of antibiotics, associated with topical dressing change for such an ulcer by mupirocin and erythromycin ointments. About 3 months passed before she was admitted to our hospital, and no significant improvement had been achieved during the course.

The patient on admission presented with an ulcer in the heel of her right foot measuring 4×3 cm, above the level of lateral malleolus, and having a wide communication with the Achilles tendon. The wound revealed a small blood oozing and fluid oozing, and peripheral soft tissue edema (Figure 1). The doctor concerned made a deep cleaning of the wound surface at first, and then, a specific cream consisting of fresh royal jelly and berberine, named Mi Lian Cream (MLC) for topical dressing change, was prefabricated on the scene. We applied it to topical dressing change once every 3 days, together with a careful observation of the healing. And over the duration of two months, the wound surface became clean, and covered fully with fresh granulation tissue (Figure 2). No allergy to the jelly preparation was found here.

Figure 1. the skin ulcer on admission

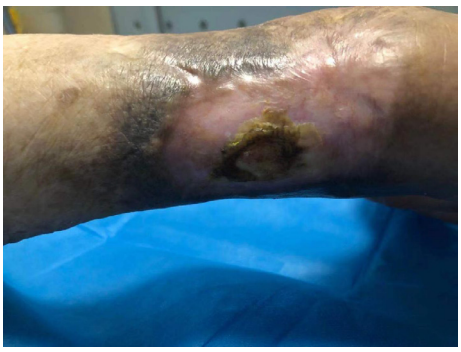

Figure 2. the wound healing through MLC for 2 months

Reasons for composition: (1) Fresh royal jelly is animal-derived, safe completely in medication, from the secretion of worker bee, in which lysozyme and epidermal growth factor are contained to kill germs and promote healing for a refractory skin ulcer. (2) Berberine is vegetable-derived, a kind of alkaloid in Coptis, which can be applied to suppress a variety of pathogenic microorganisms in wound tissues. In addition, the hyperosmotic environment made with the mixture of animal-vegetable components in the nature, free of antibiotics, also restrain the bacterial growth in skin ulcers; thus, a less induction to multiple drug resistance (MDR) in bacteria was obtained.

Formula of MLC 5 tablets of berberine (500 mg) once, was grinded into powder, and then mixed thoroughly with 10 grams of fresh royal jelly. A yellowish cream, 5% royal jelly mixture with berberine, turned out as a consequence, ready-made for topical dressing change.

3. Discussion

Royal jelly, secreted from pharyngeal gland by apis cerana, has its pharmacological effect in medication as well as tonic, both in antiseptic therapy and promoting tissue regeneration [1]. The properties of fresh jelly, safe completely in its application [2], could be applied to topical dressing change of ulcer healing, especially for refractory skin ulcer in lower extremities (a poor blood supply); with which, E. Coli, S. aureus, Strep. haemolyticus and Tinea epidermidis can be covered in its antibacterial spectrum [3]. In addition, several kinds of nutrients and epidermal growth factor (EGF) contained in fresh jelly can repair injured tissue and promote epidermis regeneration [4]. Superoxide dismutase(SOD) in the jelly has an antioxidant effect on dermis to facilitate its cellular regeneration [5].

Berberine originates from vegetable medicine--Coptis Chinensis, characteristic of antiseptic effect on bacterial infection in gut. It was mainly used to treat dysentery in the past [6]; and now, berberine has been proved to restrain the growth of S. aureus, Strep. haemolyticus, N. gonorrhoeae in vitro and boost the leukocytic phagocytosis in vivo [7].

The refractory skin ulcer on her right leg resulted from a bruise superficial wound one and a half years ago, which made progress due to improper management before. During the course, the old lady got doctors for a cure around the city, and many attempts were already made to try to control it, including both systemic medication and topical dressing change, together with the bacteriostasis lotion for skin health from the folk, finally evolving into the present condition. The medical team thought divergently for the sake of a better healing and tried to seek for the inspiration from the vegetable treasury of TCM. Mi Lian Cream (MLC), 5% mixed jelly with berberine, turned out as a consequence, which is reasonable in its composition. Fortunately, this kind of dressing cream has succeeded in the topical dressing change of this case. Compared with its previous condition, the present one was clean and vibrant in skin healing; and

the patient was fully satisfied with such a healing.

This is also a dressing preparation composed of natural components of TCM purely, free of any kinds of antibiotics used now in a surgical ward. Nursing homes will benefit from the less exposure to antibiotics in chronically hospitalized patients with the help of such a preparation, which would improve the rational use of antibiotic by means of the less induction to MDR in bacteria clinically [8]. Considering the significance mentioned above, we reported this case based on the efficacy of MLC (a jelly mixture with berberine) for the first time. No matter how a drug of TCM or western medicine it is, we think, its effective ingredients exist in the manner of one chemical compound or several ones, and it should be proven clinically effective on the basis of supportive evidence. We conducted the initial exploration in its application of MLC, and look forward to the following results applied to more inpatient patients and deeper research for its mechanism.

4. Conclusions

A specifically-used cream, consisting of fresh royal jelly and berberine (free of antibiotic), was prepared on the scene for an aged patient with a fractory skin ulcer on her right leg; with which, the wound surface healed quite well through the careful dressing changes, being also helpful for rational use of antibiotic clinically.

Acknowledgement

We are grateful to Mr Xinping Wang, a nursing worker, who took care of the aged patient with a refractory skin ulcer carefully over the duration of 2 months.

References

[1] Fratini F, Cilia G, Mancini S(2016) Royal Jelly: An ancient remedy with remarkable antibacterial properties. Microbiol Res 192:130-141.

[2] AM Ali, H Kunugi(2020) Apitherapy for age-related skeletal muscle disfunction(sarcopenia): A review on the effects of royal jell, propolis, and bee pollen. Foods 9:1362-1365.

[3] Butler E, Oien R F, Lindholm C(2016) A pilot study investigating lactic acid bacterial symbionts from the honeybee in inhibiting human chronic wound pathogens. Int Wound J 13:729-737.

[4] Daniele G, Casabianca H(2012) Sugar composition of French royal jelly for comparison with commercial and artificial sugar samples. Food Chem 134:1025-1029.

[5] Alvarez-Suarez J M, Giampieri F, Battino M(2013) Honey as a source of dietary antioxidants: structures, bioavailability and evidence of protective effects against human chronic diseases. Curr Med Chem, 20:621-638.

[6] Wang Y, Wen B, Yu H(2018) Berberine Hydrochloride-Loaded Chitosan Nanoparticles Effectively Targets and Suppresses Human Nasopharyngeal Carcinoma. Journal of Biomedical Nanotechnology 14:512-517.

[7] Dan Y, Xiaohe X, Cheng J(2008) Microcalorimetric investigation of the effect of berberine alkaloids from Coptis chinensis Franch on Staphylococcus aureus growth. Science in China Series B: Chemistry 51:1026-1030.

[8] Kwakman P H, de Boer L, Ruyter-Spira C P(2011) Medical-grade honey enriched with antimicrobial peptides has enhanced activity against antibiotic-resistant pathogens. Eur J Clin Microbiol Infect Dis, 30:251-257.

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ARTICLE

Neuropsychological and Physical Trajectories in Neurotypical and High-cognitive Performing Older Adults

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ABSTRACT

The maintenance of high cognitive performance in old age has increasingly become a public health interest due to associations between cognition, well-being, longevity, and autonomy. The objective of the research is to investigate cognitive, physical, and psychological trajectories of neurotypical older adults (NOAs) and high performing older adults (HPOAs). An exploratory study to investigate 21 NOAs and six HPOAs (mean age 71, SD = ± 3.59), followed up for one year. The older adults were submitted to physical fitness, quality of life, anxiety, depression, RAVLT, ACE-R, and Stroop tests, being assessed at three moments: baseline, six months after the cognitive (MEMO) or stimulation (Stimullus) interventions, and six months after the multimodal interventions, which could be physical or psychopedagogical interventions (health education lectures). Nonparametric statistical tests (Mann-Whitney and Wilcoxon) were performed with $p \leq 0.05$. The results demonstrated that the cognitive measures were good predictors of cognitive performance and we observed positive correlations between cognitive and mood measures. The older adults with high performance had a lower prevalence of depressive symptoms. There were gains in global cognitive performance, mood, and in physical fitness variables associated with multimodal interventions, evident in the neurotypical group.

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1. Introduction

The maintenance of high cognitive performance in old age has increasingly become a public health interest due to associations between cognition, well-being, longevity, and autonomy. However, according to Randolph [1], most studies published in this field still focus on cognitive decline and only a minority focus on investigating normal or increased cognitive performance in old age [2].

Over the last two decades, a better understanding of the profile of high-performing older adults (HPOAs) generated a growing interest in the field of aging neuroscience, being proposed the term SuperAgers which was originally operationalized in the Northwestern Program, based on the following criteria: individuals over 80 years old; episodic memory performance equal to or above that of cognitively typical individuals between 50-60 years old; performance in cognitive domains of non-mnemonic functions at least on the average for their age [3,4].

Theoretical constructs about older adults with a greater resilience proposed the description of these individuals as resilient agers [5], cognitively elite [6], optimal memory performers [7], using validated psychometric criteria. In an original study, Harrison et al. [3] demonstrated that HPOAs did not have significant cortical atrophy and presented thickening of the anterior cingulate cortex compared to the individuals in the control group.

The term HPOAs, first mentioned by Cabeza [8] and indicated by Borelli et al. [2], promotes an expanded concept, which may vary according to local cultural and sociodemographic characteristics. Additionally, they may have biological, neurocognitive and image aspects that can differentiate them from other NOAs, providing resilient brain structure [9].

Neuropsychological models indicate that cognitive decline is a consequence of aging, becoming more pronounced after the sixth decade of life in Neurotypical Older Adults (NOAs) [10,11]. However, there is variability in cognitive trajectories, and it increases with age, indicating that individual differences grow with advancing age [12]. Some of these differences have been explained by effects, such as preclinical neurodegenerative disease, Alzheimer's disease in samples of older individuals [13], as well as the presence of NOAs or HPOAs.

Some proposed cognitive theories, such as cognitive reserve and brain maintenance [14,15], have sought to explain the variability in cognitive trajectories, with some older individuals starting to decline earlier and others maintaining their independence and well-being. Studies in neurosciences and neuroimaging have led to advances in understanding the neural mechanisms related to cognitive outcomes already described by Cabeza et al. [16], who proposed the contribution of reserve, maintenance, and compensation mechanisms in the individual variability of cognitive trajectories.

In Brazil, given the variability of the educational and socio-cultural profile of the older population, studies are needed to document the profile of these HPOAs, as well as the effectiveness of interventions that promote cognitive health. The objective of the research is to investigate the associations between cognitive, physical, and psychological measures in NOAs and HPOAs and their relationship with physical and psychological measures, as well as to characterize the profile of HPOAs in psychological and physical measures.

2. Materials and Methods

This is a quantitative, exploratory, and quasi experimental study that used a longitudinal design, being approved, as well as its Informed Consent Form, by the Research Ethics Committee of the university, *Certificado de Apresentação para Apreciação Ética* (CAAE, Presentation Certificate for Ethical Appreciation) number *information suppressed for evaluation* and opinion number *information suppressed for evaluation*. Data collection was performed between June 2017 and July 2018.

Sample

The convenience sample consisted of 27 older adults with a mean age of 71 years (SD = ± 3.59) from the (*information suppressed for evaluation*) group. In the sample, 21 were characterized as NOAs and six as HPOAs. The study started with the participation of 85 individuals and continued with 51 individuals, after the baseline assessment, from which they were distributed in mnemonic strategies (MEMO) or cognitive stimulation (*Stimullus*), and again distributed to a physical training program (aerobic training associated with a systematic and personalized exercise program) or psychoeducational intervention (health education lectures). A total of 17 participants made up the sample loss after one year, and seven did not participate in any of the assessments. We allocated the participants so that they could be compared to a memory intervention group and a physical training or psychoeducational intervention program.

Instruments

In addition to the Anamnesis, composed of sociodemographic, health and lifestyle data, participants were assessed by physical, psychological, and cognitive measures, detailed below:

Physical measures: a) the muscle strength control test (handgrip strength), respecting the criteria described by Shiratori et al. [17], three attempts alternating the limbs, with an interval of 60 seconds and being instructed to the maximum isometric contraction after the verbal command; b) the cardiorespiratory capacity test (CRC) with continuous monitoring of the electrocardiogram, added to serial blood pressure measurements, in order to determine V02 max; c) the Dual Energy X-ray Absorptiometry body composition measure to quantify lean mass, fat mass and bone component (DPX-L) with full body assessment, using the LUNAR software, v1.2, for this analysis.

Psychological measures: a) the questionnaire of the World Health Organization Quality of Life Group (WHOQOL-OLD), according to Fleck et al. [18]; b) the Beck Anxiety Inventory (BAI) to measure levels of anxiety, according to the guidelines of Beck and Steer [19]; c) the 15-item Geriatric Depression Scale (GDS) adapted for the Brazilian population by Almeida and Almeida [20].

Cognitive measures: a) the Addenbrooke Cognitive Exam – Revised. The ACE-R is used to assess five cognitive domains, offering a total and partial score for each domain, adapted and validated for Brazil as a cognitive screening test by Carvalho and Caramelli [21]; b) the Rey Auditory-Verbal Learning Test - Using the adapted version of the RAVLT for the older population of Brazil [22]; c) the Victoria Stroop Test [23].

Methodological procedures

In the present study, data referring to 12 months of follow-up will be presented, including four stages: 1) selection and recruitment, 2) assessment 1 (baseline), 3) assessment 2 (six months later) and 4) assessment 3 (one year later).

For Assessment 1, all participants were assessed individually through Anamnesis and psychological, physical, and cognitive measures. For each of these steps, a researcher was responsible for the respective area with the help of assistants, and each assessment lasted about 60 minutes.

Assessments 2 and 3 followed the same procedures as in Assessment 1, with a six-month period for each assessment. In the first six months, the participants were subdivided into two groups of cognitive interventions consisting of eight weekly sessions: training based on mnemonic strategies (MEMO) or the cognitive stimulation program (*Stimullus*). The *Stimullus* program sessions comprised cognitive stimulation activities, based on the discrimination of visual and auditory stimuli, and the MEMO program sessions focused on the use and training of mnemonic strategies of categorization, the place association method, verbal association, and reading method, according Chariglione, Janczura e Belleville [24].

Subsequently, for the next six months, the participants were divided according to age, sex, and educational level in two groups with the following activities: a physical training program (aerobic training associated with a systematic and personalized workout program) or a psychopedagogical health intervention, based on 60-to-90-minute lectures with topics related to the well-being and health in aging.

Data analysis

Initially, the descriptive data of the sample were analyzed by mean, standard deviation and frequencies. Normality was tested for all variables, investigated by the Shapiro-Wilk test. As most of the data did not follow a normal distribution, the analyzes were performed using the non-parametric statistical Mann-Whitney tests, to compare the performance of the groups, and the Wilcoxon test, to compare the effects of the interventions comparing the initial performance to the assessment performed after six months and one year. The R software, version 3.4.3, and the SPSS software, version 20, were used for the analyzes - both with a significance level of $p \leq 0.05$.

3. Results

Descriptive analysis

An analysis of sociodemographic variables showed 23 older women (85.19%) and 04 older men (14.81%), with a higher frequency of individuals aged from 67 to 72 years (N = 16; 59.26%), followed by individuals from 61 to 66 (N=5; 18.52%), and 73 to 78 years (N = 5; 18.52%) for each interval, with only one individual (3.70%) aged between 79 and 84 years. As for their educational level, the individuals were evenly distributed in the groups ranging from incomplete elementary education and complete higher education. Regarding marital status, 11 were married (40.74%), 2 were single (7.41%), 6 were separated/divorced (22.22%), 1 was widowed (3.70%) and 7 were in the "others" category (25.93%).

Physical, psychological, and cognitive measures of the sample are shown in Table 1. The participants' handgrip strength of the dominant hand average was 24.11 Kgf/cm^2 (SD = ± 6.52). According to Shephard's criteria [25], handgrip strength at 55 years old is 34 Kgf/cm^2 and that, at 75 years old, it drops to 22 Kgf/cm^2, and that the handgrip strength measures of these individuals are directly proportional to their overall muscular strength. Regarding body composition, most of the sample was overweight (BMI greater than 25.8kg/m^2 and with fat mass of 35.4%).

Regarding bone mineral density, the average obtained was 1.128 kg (SD = ± 102). The minimum value between the predicted and assessed maximum oxygen consumption (VO_2max) levels was 48% with an average of 82%. The maximum value was 29.41 ml-kg.min. The VO_2max/PV ratio had the following results: 20 ml/pulse (maximum) and 6.5 ml/pulse (minimum).

According to Table 1, the domains of WHOQOL OLD (such as sensory functions, death, and dying) had a mean lower than 3.5 (2.35 and 2.17), respectively. Regarding the presence of symptoms of anxiety and depression, the sample scores demonstrated low levels of anxiety and/or depression (BAI: 4.52 SD = ± 4.24; GDS: 2.59 SD = ± 2.15). In cognitive measures, such as Stroop (time), 75%

Table 1. Description of the Physical, Psychological and Cognitive Variables (N=27), Brasília, DF, 2019.

Variable	Min	1stQ	Med	Mean	3rdQ	Max	SD
Physical measures							
Handgrip strength of the dominant hand (Kgf/cm^2)	14.00	19.00	25.00	24.11	29.00	38.00	6.52
Cardiorespiratory Capacity (ml/kg/min)	48%	64%	81%	82%	97%	136%	22%
DMO (gl/cm^2)	962	1048	1112	1128	1188	1311	102
DXA (%G)	14.90	32.10	36.70	35.40	40.50	53.30	8.69
Fat mass (Kg)	9.30	19.20	23.80	25.20	31.20	56.90	9.98
Lean mass (Kg)	30.30	38.50	42.90	44.60	48.70	65.40	8.17
BMI (Kg/m^2)	21.20	25.80	28.00	28.90	31.70	45.40	5.11
Psychological measures							
Whoqol old - Sensory Functions	1.75	2.00	2.25	2.35	2.50	3.50	0.46
Whoqol old - Autonomy	2.75	3.38	3.50	3.70	4.00	4.75	0.51
Whoqol old - Past, present and future activities	2.75	3.50	3.75	3.90	4.25	5.00	0.60
Whoqol old - Social Participation	2.75	3.50	3.75	3.90	4.25	5.00	0.60
Whoqol old - Death and dying	1.0	1.75	2.00	2.17	2.38	4.00	0.73
Whoqol old - Intimacy	1.0	3.25	3.50	3.46	4.00	4.75	0.94
Beck's anxiety inventory	0.00	1.00	3.00	4.52	7.00	16.00	4.24
Geriatric Depression Scale	1.00	1.00	2.00	2.59	3.50	8.00	2.15
Cognitive measures							
Stroop (time)	13.00	23.80	27.00	28.00	31.70	61.30	8.52
ACE-R	44.00	73.00	80.00	78.26	89.50	96.00	13.49
ACE-A	11.00	14.00	17.00	15.60	17.50	18.00	2.24
ACE-M	10.00	14.50	19.00	18.60	23.00	26.00	4.96
ACE-F	3.00	8.00	10.00	9.44	11.00	13.00	2.74
ACE-L	9.00	20.50	24.00	22.00	25.00	26.00	4.10
ACE-V	8.00	12.00	14.00	13.20	15.50	16.00	2.65
Learning curve (RAVLT)	26.00	34.50	41.00	42.50	48.00	71.00	10.70
Forgetting speed (RAVLT)	0.78	0.93	1.00	1.09	1.13	2.50	0.32
Proactive interference (RAVLT)	0.20	0.67	0.80	0.84	1.00	1.75	0.35
Retroactive interference (RAVLT)	0.29	0.71	0.80	0.78	0.88	1.00	0.18

Note: ACE-R = Addenbrooke's Cognitive Examination – Revised; ACE-A = Attention and orientation, ACE-M= Memory; ACE-F = Fluency; ACE-L = Language; ACE-V = Visuospatial; RAVLT = Rey Auditory Verbal Learning Test Learning; Min= Minimum; 1stQ = 1st Quartile; Med = Median, 3rdQ = 3rd Quartile; Max = Maximum; SD = Standard Deviation.

of individuals taking less than or equal to 31.70 seconds. On the ACE-R, memory test was the domain with the greatest variability.

Among the assessments that make up the Rey Auditory-Verbal Learning Test (RAVLT), namely, learning curve, forgetting speed, proactive interference (PI) and retroactive interference (RI) indices, the mean values were, respectively, 48, 1.13, 1 and 0.88. The learning curve showed a relatively high SD (10.70) and the proactive and retroactive interference indices had mean values equal to 0.8.

Classification of high-performing older adults

Individuals were classified as HPOAs using their performance in the RAVLT - Learning Curve (sum of A1 to A5) [22]. According to the positive correlation (Spearman's Correlation Coefficient: 0.604, p = 0.001) between educational level and the performance in the RAVLT - Learning Curve (A1-A5), we chose to consider the mnemonic performance according to the educational level. Thus, to compose the HPOA group, a performance higher than the 75th percentile on the RAVLT Learning Curve at baseline (first assessment) was considered for the groups ranging from "Incomplete Elementary School and Incomplete High School" or 5 to 10 years (>34 points) of education, and "Complete High School to Higher Education" or 11 years or over of education (> 50 points) (refer to Table 2). Based on this criterion, six individuals were classified as HPOAs, three of whom having between 5 and 10 years of education, and three having 11 years or over.

Neurotypical Older Adults vs. High Performing Older Adults

As shown in Table 3, there were statistically significant differences between the group of individuals with typical performance and the HPOA group at baseline regarding their performance in the RAVLT (Recovery 1 to Recovery 5, and Recovery 7) and number of depressive symptoms, indicating that the HPOA group had a superior memory performance and a lower prevalence of depressive symptoms than the NOA group. There were no differences between groups regarding age, ACE-R performance, Stroop and WHOQOL-OLD scores.

Regarding physical performance measures, for the purposes of homogenization, we excluded four older men who composed the NOA group and, thus, the analyzes were carried out with 17 older women in the typical group and six older women in the HPOA group. As shown in Table 4, at baseline, the groups were similar in terms of body composition and physical fitness. However, there is a tendency for the group with better mnemonic performance to present lower waist circumference (p=0.06).

Table 2. Score on the Rey Auditory Verbal Learning Test Learning Curve according to the educational level and classification of High Performing Older Adults (N=27), Brasília, DF, 2019.

	N	Mean	SD	Med	Min	Max	P-25	P-75
General sample (N=27)								
5 to 10 years	13	31,77	9,66	32,00	17	48	25	34
11 years or over	14	40,71	8,77	38,50	27	55	36	50
5 to 10 years (N=13)								
Neurotypical older adults	10	27,70	6,53	30,50	17	34	23	33
High-cognitive performing older adults	3	45,33	3,06	46,00	42	48	42	48
11 years or over (N=14)								
Neurotypical older adults	11	37,18	5,95	37,00	27	50	35	40
High-cognitive performing older adults	3	53,67	1,53	54,00	52	55	52	55

Note: N = Number of subjects; SD = Standard Deviation; Min= Minimum; Max =Maximum; P-25= Percentile 25; P-75= Percentile 75.

Table 3. Cognitive and psychological performance in Neurotypical Older Adults and in High Performing Older Adults (N=27), Brasília, DF, 2019.

		Neurotypical Older Adults (N=21)		High Performing Older Adults (N=6)		
		Mean	**SD**	**Mean**	**SD**	**P value**
Age		70.19	5.48	69.83	3.60	0.93
SEX	Female	N=17	81%	N=6	100.0%	0.54
	Male	N=4	19%	N=0	0.0%	
STROOP_TIME STROOP 1		25.24	11.81	19.67	5.65	0.26
STROOP_ERROR 1		1.71	1.93	1.50	1.38	0.89
STROOP_TIME STROOP 2		29.62	7.07	27.17	10.21	0.19
STROOP_ERROR 2		3.14	3.69	1.83	1.33	0.71
STROOP_TIME STROOP 3		46.29	34.38	34.83	8.08	0.32
STROOP_ERROR 3		5.48	3.66	4.50	3.89	0.51
STROOP_INTERFERENCE		21.05	26.19	15.17	7.73	0.63
RAVLT_A1		3.43	1.40	6.17	2.93	**0.02***
RAVLT_A2		6.19	1.72	9.00	1.41	**0.00***
RAVLT_A3		7.19	1.97	10.83	.75	**0.00***
RAVLT_A4		7.62	1.96	11.83	.75	**0.00***
RAVLT_A5		8.24	2.34	11.67	1.37	**0.00***
RAVLT_A6		5.57	2.58	8.67	3.50	0.06
RAVLT_A7		5.48	2.27	9.33	2.16	**0.00***
RAVLT_RECOGNITION		12.19	2.06	13.33	2.73	**0.01***
RAVLT_V_FORGETTING		1.19	.75	1.33	.52	0.50
PI		1.29	.96	.83	.41	0.29
RI		.71	.46	.67	.52	0.89
ACE-A		15.24	2.64	15.50	2.35	0.89
ACE-M		15.95	5.83	18.67	5.61	0.41
ACE-F		8.90	3.25	10.50	1.22	0.24
ACE-L		20.10	4.90	24.00	2.37	0.12
ACE-V		12.62	2.44	13.83	2.40	0.24
ACE-R		72.81	14.70	82.50	10.60	0.14
MMSE		24.10	3.70	26.17	2.79	0.22
GDS		3.33	2.27	2.17	1.72	**0.01***
Whoqol old - Sensory Functions		9.81	2.64	9.33	2.80	0.72
Whoqol old - Autonomy		14.05	2.52	15.67	2.16	0.24
Whoqol old - Past, present and future activities		15.19	2.73	16.00	2.19	0.41
Whoqol old - Social Participation		15.19	2.84	15.33	3.01	1.00
Whoqol old - Death and dying		10.24	4.28	7.33	2.25	0.08
Whoqol old - Intimacy		15.00	3.89	16.17	2.32	0.55
Whoqol old - overall		79.48	11.12	79.83	8.42	1.00

Note: N = Number of subjects; SD = Standard Deviation; RAVLT= Rey Auditory-Verbal Learning Test; RAVLT_REC = Forgetting speed; PI= proactive interference index; RI= retroactive interference index; MMSE = Mini Mental State Examination; GDS = Geriatric Depression Scale; *p≤0,01.

Table 4. Anthropometric and physical fitness variables among Neurotypical Older Adults and High Performing Older Adults (N=27), Brasília, DF, 2019.

	Neurotypical Older Adults (N=17)		High Performing Older Adults (N=6)		
	Mean	**SD**	**Mean**	**SD**	**P value**
Weight (Kg)	70.88	10.87	71.33	23.36	0.47
Height (m)	1.94	.24	2.00	.00	0.86
BMI	28.53	3.62	29.33	10.17	0.35
RSP	128.00	21.65	127.33	23.65	0.92
RDP	74.47	9.45	74.17	8.47	0.92
Bpm	77.12	13.01	77.33	7.61	1.00
Waist circumference	97.65	6.65	93.17	14.80	0.06
Hip circumference	104.29	7.86	106.83	18.54	0.61
DHM (Pounds/F)	41956.76	5857.87	42758.17	6346.88	0.47
NDHM (Pounds/F)	44.53	9.96	44.83	7.99	1.00
BMD g/cm²	922.41	445.30	1124.83	67.60	0.47
DEXA (%G)	38.82	5.05	34.67	12.29	0.61
VO² ml/kg.min	19.65	4.36	19.83	5.34	0.29
HR max (bpm)	135.71	21.09	142.67	13.09	0.71
VO²/FC max (ml/b)	10.35	2.83	9.17	1.17	0.81
PV max (l/min)	51.47	15.46	44.17	13.41	0.23

Note: SD = Standard Deviation; BMI= Body Mass Index; RSP= Resting systolic pressure. RDP= Resting diastolic pressure. Bpm= Beats per minute. DHM= Dominant Hand Mean. NDHM= Non-Dominant Hand Mean. BMD= Bone mineral density; DEXA= Dual-energy X-ray absorptiometry bone mineral density; VO_2max = maximum oxygen consumption; HR=Heart rate; PV= Pulmonary ventilation.

Follow-up

Regarding the follow-up assessment (after six months and one year), we observed that NOAs had a higher performance in the ACE-R Total in the assessment performed after six months and a reduction in the number of depressive symptoms after one year, when compared to the number of depressive symptoms in the initial assessment. In the assessment performed after one year, they were also slower in the Stroop test condition 3.

As for the parameters of physical fitness, this group also showed an increase in Bone Mineral Density in their subsequent assessments, and variation in their DEXA, with an increase in fat mass in the assessment performed after six months and a reduction in the assessment performed after one year, which may be associated with type of intervention to which they were engaged: in the first semester they performed only cognitive interventions and, in the second semester, part of this group performed physical stimulation activities (resistance and aerobic training). According to Table 5, the same changes were not observed in the HPOA group, however it is necessary to consider that the reduced number of participants may have reduced the statistical power of the analyzes. The general sample had similar gains to the typical performance group.

Table 5. Follow-up measures in multimodal interventions in Neurotypical Older Adults, High Performing Older Adults, highly cognitive older adults, and general sample (N=27), Brasília, DF, 2019.

	Neurotypical Older Adults (N=21)			High Performing Older Adults (N=6)			General sample (N=27)		
	Mean	**SD**	**P**	**Mean**	**SD**	**P**	**Mean**	**SD**	**P**
RAVLT_IP									
IA	1.28	.95		.83	.40		1.18	0.87	
6M	1.00	.63	0.29	.83	.40	0.75	0.96	0.58	0.26
1Y	.95	.38	0.19	.66	.51	0.50	0.88	0.42	0.12
ACE_R									
IA	72.80	14.70		82.50	10.59		74.96	14.30	
6M	76.38	15.44	**0.04**	81.16	15.48	0.94	77.44	15.28	0.09
1Y	76.80	13.02	0.05	83.33	15.12	0.62	78.25	13.49	**0.04**
S_T3									
IA	46.28	34.38		34.83	8.08		43.74	30.75	
6M	42.30	24.63	0.33	36.66	14.90	0.92	41.11	22.70	0.34
1Y	36.65	13.94	**0.01**	34.33	10.55	0.49	36.29	13.12	**0.01**
GDS									
IA	4.04	2.31		1.66	1.21		3.51	2.32	
6M	3.33	2.26	0.15	2.16	1.72	1.00	3.07	2.18	0.24
1Y	3.04	2.24	**0.02**	1.00	.00	0.37	2.59	2.15	**0.01**
OQL									
IA	79.47	11.12		79.83	8.42		79.55	10.43	
6M	80.80	10.44	0.46	81.16	4.35	0.65	80.88	9.36	0.37
1Y	76.80	5.82	0.29	80.50	4.72	0.87	77.62	5.73	0.42
WC									
IA	99.61	8.08		93.16	14.79		98.18	9.99	
6M	99.90	7.75	0.56	95.66	16.48	0.25	98.96	10.08	0.28
1Y	100.00	9.07	0.35	98.50	19.48	0.12	99.66	11.69	0.42
BMD(g/cm²)									
IA	978.38	416.85		1124.83	67.60		1010.92	372.018	
6M	1105.15	105.24	0.36	1135.66	69.34	0.44	1112.19	97.73	1.00
1Y	1127.04	106.94	**0.01**	1131.00	88.99	1.00	1127.92	101.60	**0.04**
DEXA (%G)									
IA	37.09	6.45		34.66	12.29		36.55	7.88	
6M	42.80	9.07	**0.00**	39.33	17.00	0.12	42	11.07	**0.00**
1Y	35.57	7.74	**0.03**	35.00	12.37	0.81	35.44	8.69	0.08

Note: SD = Standard Deviation; P= P Value; IA= Initial assessment; 6M= 6 months; 1Y= 1 year; RAVLT_IP = proactive interference index; S_T3= Stroop_Time3; GDS= Geriatric depression scale; OQL= Overall quality of life; WC= Waist circumference; BMD= Bone mineral density; DEXA= Dual-energy X-ray absorptiometry bone mineral density.

4. Discussion

In the present study, HPOAs had a lower prevalence of depressive symptoms than NOAs at baseline and there were gains in global cognitive performance, mood, and physical fitness variables associated with multimodal interventions, evident in the NOA group. Thus, the NOA group presents higher benefits than the HPOA one, but it could be tested in the next studies due to our reduced sample.

In this study's sample, we observed that the HPOA group was composed by six older women. Previous studies indicated that higher prevalence of HPOAs was observed in women than in men [26]. Maccora et al. [27] observed a higher prevalence of female HPOAs (85.19%) and no association between most factors previously associated with cognitive decline. For women, the associated factors were a higher number of years of education and a higher frequency of investigative activities. Modern studies corroborate the role of educational level in the cognitive and cerebral reserve and the association of years of education with a higher-than-average episodic memory [28].

Regarding physical aspects, specifically muscle strength, the results presented here coincide with previous studies [29,30] and demonstrate that the average muscle strength is above the cutoff point in relation to what is necessary for daily life activities. About cardiovascular performance, as demonstrated by other authors [31,32], this may be associated with a reduction in the risk of cognitive decline in older individuals. Stability of cardiorespiratory capacity was observed in relation to the follow-up period.

However, physical measures did not differ between HPOAs and NOAs. Only waist circumference had statistical significance, with lower circumferences in the HPOA group than in the NOA group at baseline. Concerning the psychological variables, the presence of above-average values in aspects related to quality of life (WHOQOL-OLD) and the absence or low levels of anxiety and/or depression (BAI and GDS) stands out. The results of a number of studies suggest that some mechanisms could be involved in this correlation, such as the association of depression and anxiety with high levels of glucocorticoids and subsequent neuronal damage, as well as greater activation of the limbic system to the detriment of cortical areas [34].

As for cognitive aspects, the results obtained in the ACE-R are like those described by Carvalho and Caramelli [21]. Regarding the RAVLT scores, which assesses recent memory, learning, interference, and recognition memory, as expected, a better performance was observed in the HPOA group. Nitrini et al. [35] studied the influence of age and education in neuropsychological tests and observed differences in memory performance, considering literate and illiterate individuals. Regarding the Stroop test, which assesses attention and executive functions, the results related to the measurement of time indicated an average value of 28s, with the minimum and maximum values being 13 and 61.3, respectively.

In summary, the data on stability and increase in cognitive functions over time, when analyzed longitudinally, have implications in the context of aging and in the HPOA study, with the prospect of a successful aging necessarily linked to cognition.

Although the findings are promising, this is an exploratory study, in which we intended to verify differences and the trajectory of HPOAs and NOAs in physical, cognitive, and psychological measures after participating in multimodal interventions. A high research dropout rate out of 50% of the sample, and this could be associated with the number of assessments and interventions. In addition, the small sample (HPOA group n=6; NOA group n=21) did not allow us to perform multiple comparisons and more sophisticated statistical analysis. Due to these limitations, these findings could not be generalized, and other studies need to test the efficacy of each intervention.

5. Conclusions

A higher mnemonic performance in older adults was associated with emotional health variables, while multimodal interventions proved to be beneficial in the context of Brazilians older adults. This is a new branch of research in Gerontology and neurosciences and the cooperation of different research programs is necessary to understand the impact of multimodal interventions in different cognitive profiles.

Author Contributions

Alessandro Amorim AITA - Investigation (Lead), Conceptualization (Lead), Formal analysis (Equal), Project administration (Equal), Writing-original draft (Equal), Writing-review & editing (Equal).

Corina SATLER - Methodology (Lead), Formal analysis (Equal), Writing-original draft (Equal), Writing-review & editing (Equal).

Henrique Salmazo da SILVA - Formal analysis (Lead), Methodology (Equal), Writing-original draft (Equal), Writing-review & editing (Equal).

Isabelle Patriciá Freitas Soares CHARIGLIONE - Funding acquisition (Lead), Project administration (Lead), Supervision (Lead), Investigation (Equal), Writing-

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Conflict of Interest

The authors report no conflicts of interest.

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References

[1] Randolph JJ. Positive neuropsychology: The Science and practice of promoting cognitive health. Applied Neuropsychology: Adult 2018 July; 25(4):287-294. Available from: https://doi.org/10.1080/23279095.2018.1457465.

[2] Borelli WV, Carmona KC, Studart-Neto A, Nitrini R, Caramelli P, da Costa JC. Operationalized definition of older adults with high cognitive performance. Dement Neuropsychol 2018b; 12(3): 221-227. Available from: https://doi.org/10.1590/1980-57642018dn12-030001.

[3] Harrison TM, Weintraub S, Mesulam MM, Rogalski E. Superior memory and higher cortical volume in usually successful cognitive aging. J Int Neuropsychol Soc. 2012 Nov;18(6):1081-1085. Available from: https://doi.org/10.1017/S1355617712000847.

[4] Rogalski E, Gefen T, Mao Q, Connelly M, Weintraub S, Geula C, et al. Cognitive trajectories and spectrum of neuropathology in superagers: the first ten cases. Hippocampus 2019; 29(5): 458-467. Available from: https://doi.org/10.1002/hipo.22828.

[5] Bott NT, Bettcher BM, Yokoyama JS, Frazier DT, Wynn M, Karydas A, et al. Youthful processing speed in older adults: Genetic, Biological and Behavioral Predictors of Cognitive Processing Speed Trajectories in Aging. Front Aging Neurosci. 2017 Mar 10(9): 55. Available from: https://doi.org/10.3389/fnagi.2017.00055.

[6] Lin Y, Mutz J, Clough PJ, Papageorgiou KA. Mental Toughness and Individual Differences in Learning, Educational and Work Performance, Psychological Well-being, and Personality: A Systematic Review. Front Psychol. 2017 Aug 11;8:1345. Available from: https://doi.org/10.3389/fpsyg.2017.01345.

[7] Dekhtyar M, Papp KV, Buckley R, Jacobs HIL, Schultz AP, Johnson KA, et al. Neuroimaging markers associates with maintenance of optimal memory performance in late-life. Neuropsychologia. 2017 Jun; 100:164-170. Available from: https://doi.org/10.1016/j.neuropsychologia.2017.04.037.

[8] Cabeza R. Hemispheric asymmetry reduction in older adults: the HAROLD model. Psychol Aging. 2002 Mar;17(1):85-100. Available from: https://doi.org/10.1037//0882-7974.17.1.85.

[9] Yu J, Collinson SL, Liew TM, Ng TP, Mahendran R, Kua EH, et al. 2019. Supercognition in aging: cognitive profiles and lifestyle factors. Appl Neuropsychol Adult. 2019; Feb 22:1-7. Available from: https://doi.org/10.1080/23279095.2019.1570928.

[10] Harada CN, Love MCN, Triebel K. Normal cognitive aging. Clin Geriatr Med. 2013 Nov; 29(4): 737–752. Available from: https://doi.org/10.1016/j.cger.2013.07.002.

[11] Salthouse TA. When does age-related cognitive decline begin. Neurobiol Aging. 2009 Apr;30(4):507-514. Available from: https://doi.org/10.1016/j.neurobiolaging.2008.09.023.

[12] Dang C, Harrington KD, Lim YY, Ames D, Hassenstab J, Laws SM, et al. Superior Memory reduces 8-year risk of mild cognitive impairment and Dementia but not amyloid b-associated cognitive decline in older adults. Arch Clin Neuropsychol. 2019 Jul 26;34(5):585-598. Available from: https://doi.org/10.1093/arclin/acy078.

[13] Harrington KD, Lim YY, Ames D, Hassenstab J, Laws SM, Martins RN, et al. Amyloid b-associated cognitive decline in the absence of clinical disease progression and systemic illness. Alzheimers Dement (Amst). 2017 Jun 9; 8:156-164. Available from: https://doi.org/10.1016/j.dadm.2017.05.006.

[14] Stern Y. Cognitive reserve in ageing and Alzheimer´s disease. Lancet Neurol. 2012 Nov;11(11):1006-1012. Available from: https://doi.org/10.1016/S1474-4422(12)70191-6.

[15] Nyberg L, Lövdén M, Riklund K, Lindenberger U, Bäckman L. Memory aging and brain maintenance. Trends Cogn Sci. 2012 May;16(5):292-305. Available from: https://doi.org/10.1016/j.tics.2012.04.005.

[16] Cabeza R, Albert M, Belleville S, Craik FIM, Duarte A, Grady CL, et al. Maintenance, reserve and compensation: the cognitive neuroscience of heatlhy aging. Nat Rev Neurosci. 2018 Nov;19(11):701-710. Available from: https://doi.org/10.1038/s41583-018-0068-2.

[17]. Shiratori AP, Iop RR, Borges Júnior NG, Domenech SC, Gevaerd MS. Protocolos de avaliação da força de preensão manual em indivíduos com artrite reumatoide: uma revisão sistemática. Rev. Bras. Reumatol. 2014 Apr; 54(2):140-147. Available from: https://doi.

org/10.1016/j.rbr.2014.03.009.

[18] Fleck MPA, Chachamovich E, Trentini CM. Projeto WHOQOL-OLD: método e resultados de grupos focais no Brasil. Rev. Saúde Pública 2003 Dec; 37(6): 793-799. https://doi.org/10.1590/S0034-89102003000600016.

[19] Beck AT, Steer RA. Manual for the Beck Anxiety Inventory. San Antonio, TX: Psychological Corporation, 1990.

[20] Almeida OP, Almeida SA. Confiabilidade da versão brasileira da Escala de Depressão em Geriatria (GDS) versão reduzida. Arq. Neuro-Psiquiatr. 1999 June; 57(2B):421-426. https://doi.org/10.1590/S0004-282X1999000300013.

[21] Carvalho VA, Caramelli P. Brazilian adaptation of the Addenbrooke's Cognitive Examination-Revised (ACE-R). Dement. neuropsychol. [Internet]. 2007 June [acesso em 7 jun. 2019];1(2):212-216. Available from: https://doi.org/10.1590/S1980-57642008DN10200015.

[22] Malloy-Diniz LF, Lasmar VAP, Gazinelli LSR, Fuentes D, Salgado JV. The Rey Auditory-Verbal Learning Test: applicability for the Brazilian elderly population. Rev. Bras. Psiquiatr. 2007 Dec; 29(4):324-329. Available from: https://doi.org/10.1590/S1516-44462006005000053.

[23] Spreen O, Strauss E. A Compendium of Neuropsychological tests: administration, norms, and commentary. 2nd ed. New York: Oxford University Press; 1998.

[24] Chariglione IPFS, Janczura GA, BELLEVILLE S.Cognitive interventions to improve memory in healthy older adults: the use of Canadian (MEMO) and Brazilian (Stimullus) approaches. Estudos de psicologia (natal. Online. 2018; 21: 02-13. Available from: http://dx.doi.org/10.22491/1678-4669.20180002.

[25] Shephard RJ. Envelhecimento, atividade física e saúde. São Paulo: Phorte; 2003.

[26] Nicodemo D, Godoi M. Juventude dos anos 60-70 e envelhecimento: estudo de casos sobre feminização e direitos de mulheres idosas. Rev. Ciênc. Ext. 2010;6(1): 40-53. Available from: https://ojs.unesp.br/index.php/revista_proex/article/view/324.

[27] Maccora J, Peters R, Anstey KJ. Gender differences in superior-memory SuperAgers and associated factors in an Australian cohort. Journal of Applied Gerontology, 2020; 40(4): 433-442. Available from: https://doi.org/10.1177/0733464820902943.

[28] Josefsson M, de Luna X, Pudas S, Nilsson LG, Nyberg L. Genetic and lifestyle predictors of 15-year longitudinal change in episodic memory. J Am Geriatr Soc. 2012 Dec;60(12):2308-2312. Available from: https://doi.org/10.1111/jgs.12000.

[29] Moura PMLS. Estudo da força de preensão palmar em diferentes faixas etárias do desenvolvimento humano. Brasília. Tese [Mestrado em Ciências da Saúde] - Universidade de Brasília; 2008. Available from: https://repositorio.unb.br/handle/10482/1699.

[30] Vilaça KHC, Ferriolli E, Lima NKC, Paula FJA, Marchini JS, Moriguti JC. Força muscular e densidade mineral óssea em idosos eutróficos e desnutridos. Rev. Nutr. 2011 Dez; 24(6): 845-852. Available from: https://doi.org/10.1590/S1415-52732011000600005.

[31] Wendell CR, Gunstad J, Waldstein SR, Wright JG, Ferrucci L, Zonderman AB. Cardiorespiratory Fitness and accelerated cognitive decline with aging. J. Gerontol. A Biol. Sci. Med. Sci. 2014 Apr; 69(4):455-462. Available from: https://doi.org/10.1093/gerona/glt144.

[32] Hörder H, Johansson L, Guo X, Grimby G, Kern S, Östling S, Skoog I. Midlife cardiovascular fitness and dementia: A 44-year longitudinal population study in women. Neurology. 2018 Apr 10;90(15):e1298-e1305. Available from: https://doi.org/10.1212/WNL.0000000000005290.

[33] Chariglione IPFS, Silva HS, Silva AA, Sacramento AM. Cognitive performance and physical fitness in the health of Brazilian elderly women. Rev. bras. psicol. esporte, 2018;8(2). Available from: https://doi.org/10.31501/rbpe.v8i2.9875.

[34] Tonga JB, Eilertsen DE, Solem IKL, Arnevik EA, Korsnes MS, Ulstein ID. Effect of Self-Efficacy on Quality of Life in People With Mild Cognitive Impairment and Mild Dementia: The Mediating Roles of Depression and Anxiety. Am J Alzheimers Dis Other Demen. 2020 Jan-Dec; 35:1533317519885264. Available from: https://doi.org/10.1177/1533317519885264.

[35] Nitrini R, Caramelli P, Herrera Júnior E, Porto CS, Charchat-Fichman H, Carthery MT, et al. Performance of illiterate and literate nondemented elderly subjects in two tests of long-term memory. J Int Neuropsychol Soc. 2004;10(4):634-638. Available from: https://doi.org/10.1017/S1355617704104062.

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EDITORIAL

The Necessity of Community Connectedness in Iranian Older Adults during the COVID-19 Pandemic

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In the last decade, COVID-19 outbreak was one of the major crises encountered the world [1]. During the COVID-19 pandemic, Iranian people have been advised to stay at home and far away others. If it is essential to leave their residence, people have been urged to avoid gathering and maintain physical distance from others. Community disconnectedness for older adults was primary prevention specially for elders with comorbidities [2]. For the first time, most of Iranian older adults were experiencing an unwanted and prolonged separation from others.

In the Middle East, Iran has one of the largest ageing populations. Regarding the importance of the mental health in older adults, more attention needs to be paid to them as a vulnerable group when a crisis emerges [3]. Health system decisions not only should be focused on reducing the spread of the disease but also mental health issues of older adults like depression should be considered.

In fact, the root of depression which can lead to suicide is loneliness. Perceived community disconnectedness or loneliness is a major risk factor for physical and mental health in older adults. Community connectedness is important for promoting mental health and protecting from the development and progression of physical diseases. Community connectedness is a significant contributing factor in deducing morbidity and mortality in older adults.

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The perceived absence of community connectedness has been linked to diminished longevity, especially between older adults in whom decreasing economic resources, illness, widowhood, and impaired mobility.

Loneliness in older adults is associated with multiple undesirable outcomes, including depression, cognitive dysfunction, disability, cardiovascular disease, psychological distress, impaired immune system functioning and increased mortality rates [4].

In recent years, the internet has revolutionized people communication. Nowadays, the internet is an appropriate option which facilitate communication with families, friends and society for older adults then for overcoming loneliness, community connectedness with the aid of internet can be appropriate selection which should be considered [5].

Encouraging older adults to begin using the Internet to communicate with others could help to improve social contacts and decline loneliness. The result of a study indicated that the internet use was associated with lower levels of loneliness among elderly. Loneliness among the elderly is associated with a higher chance for metabolic syndrome [6] and an increased risk of death. The maintenance of personal relationships through the Internet could be critical to well-being for older adults. Moreover, among the general population, using the Internet to maintain communication with family and friends has been associated with well-being [7], further providing support for the idea that going online could be beneficial for older adults.

Care, love and support are the natural responses to individuals who are sick then at the time of social isolation. The importance of community connections, especially for vulnerable groups or those who are sick is undeniable. Loneliness and social isolation are realties that influence many aspects of life. In time of crisis, for addressing all physical and mental health issues, an integrated holistic care should be developed.

In conclusion, the Internet use has a significant effect on decreased perceived loneliness. In fact, online activities may be an effective tool for reducing loneliness among older people by maintaining the levels of social contact.

References

[1] Tian T, Meng F, Pan W, Zhang S, Cheung T, Ng CH, et al. Mental health burden of frontline health professionals treating imported patients with COVID-19 in China during the pandemic. Psychological medicine. 2020:1-2.

[2] Shahid Z, Kalayanamitra R, McClafferty B, Kepko D, Ramgobin D, Patel R, et al. COVID-19 and older adults: what we know. Journal of the American Geriatrics Society. 2020;68(5):926-9.

[3] Kang C, Tong J, Meng F, Feng Q, Ma H, Shi C, et al. The role of mental health services during the COVID-19 outbreak in China. Asian Journal of Psychiatry. 2020;52:102176.

[4] Wu B. Social isolation and loneliness among older adults in the context of COVID-19: a global challenge. Global health research and policy. 2020;5(1):1-3.

[5] Yu K, Wu S, Chi I. Internet use and loneliness of older adults over time: The mediating effect of social contact. The Journals of Gerontology: Series B. 2021;76(3):541-50.

[6] Whisman MA. Loneliness and the metabolic syndrome in a population-based sample of middle-aged and older adults. Health Psychology. 2010;29(5):550.

[7] Bessière K, Pressman S, Kiesler S, Kraut R. Effects of internet use on health and depression: a longitudinal study. Journal of medical Internet research. 2010;12(1):e1149.

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ARTICLE

Does Locomotive Syndrome, Associated with Sarcopenia or otherwise, Influence Quality of Life in Individuals Aged over 80 years? Third Wave of the LOCOMOV Project

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ABSTRACT

Introduction: Locomotion is a determinant of intrinsic capacity of older people and can be limited by dysfunction in locomotory organs, characterizing Locomotive Syndrome (LoS). Knowledge on locomotive problems and sarcopenia, and their interface with quality of life, in the oldest old in the literature is scarce.

Objective: To evaluate the correlation between LoS and sarcopenia and their influence on quality of life in oldest old.

Methods: A cross-sectional study of an observational, descriptive and analytical epidemiological survey in independent older adults aged 80 and over from São Paulo, Brazil and who participated in the third wave of the LOCOMOV Project, was carried out. Sociodemographic data, comorbidities, functioning in activities of daily living, physical functioning, quality of life, and presence of sarcopenia and LoS were assessed. The statistical analyses included the Test-for-Comparing-Two-Proportions, Pearson's Correlation Coefficient, the chi-Square test and Student´s *t*-test.

Results: Thirty oldest old with a mean age of 89.1 years were evaluated. The prevalence of LoS was high (53.3%) and correlated significantly with chronic pain (p-value 0.024), worse performance on the SPPB and Gait speed (p-value <0.001). Sarcopenia was not correlated with LoS, but worse quality of life on the physical domain was significantly associated with LoS (p-value <0.001) regardless of the presence of sarcopenia.

Conclusions: LoS was highly prevalent among the oldest old studied and negatively impacted their quality of life, regardless of the presence of sarcopenia.

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1. Introduction

According to the 2015 Aging and Health Report by the World Health Organization (WHO), for the first time in history, the majority of the population can expect to live to 60 years or older [1]. However, these extra years of life are highly heterogeneous due to factors such as genetics and the physical and social environments to which the older person is exposed. Functional capacity represents a combination of an individual´s intrinsic capacity and their relationship and interaction with the environment [1].

In 2019, Beard et al. outlined five determinants that define an individual's intrinsic capacity: cognition, locomotion, sensory and psychological determinants and vitality. Since then, an assessment model that correlates these factors has been proposed as an alternative to the fragmented view of independent factors. Mobility is associated with vitality and both are, therefore, closely related to healthy aging and quality of life in older people [2].

Thus, identifying the factors that influence locomotory independence in older individuals is an essential element of health care and promotion. The concept of Locomotive Syndrome (LoS) was first proposed in 2007 by the Japanese, and can be defined as reduced mobility due to dysfunction of locomotory organs, such as bones, muscles, joints, tendons or nerves, and its consequent risk of dependence for locomotion. Musculoskeletal pathologies that can lead to this condition including osteoarthritis, osteoporosis, fractures, spinal canal stenosis and sarcopenia [3,4]. A Japanese study carried out in 2011 estimated that 21.5% of patients who were dependent on others for basic activities of daily living had locomotory dysfunction as the main cause of dependence [5]. In order to identify these patients and help diagnose LoS, a questionnaire called the 25-Question Geriatric Locomotive Function Scale (GLFS-25) was developed in 2008 [6]. The instrument was later translated, cross-culturally adapted and validated for use in the Brazilian population (GLFS-25P) [7,8].

Sarcopenia is another major cause of dependence for locomotion in older people and the syndrome assessment algorithm was recently updated by the European Working Group on Sarcopenia in Older People (EWGSOP). The SARC-F questionnaire is designed for initial screening of cases [9,10]. During its Brazilian validation, the questionnaire, when used in association with Calf Circumference (CC) measurement, proved more sensitive for detecting patients diagnosed with sarcopenia [11].

Quality of life reflects personal opinions and conceptions, based on beliefs, experiences and sensations. These perceptions and feelings should be evaluated multidimensionally, including physical, psychological and social domains, level of dependence, environmental influences and aspects of spirituality and religiosity [12]. The term quality of life includes, but is not limited to, health status and medical interventions [13], highlighting the relevance of a comprehensive view of the patient that encompasses their personal, socioeconomic, educational and cultural background. In order to provide this multidimensional approach, several quality of life questionnaires are used in the literature.

The older population, especially the oldest old, often exhibit comorbidities that lead to functional decline. Thus, strategies for screening and controlling comorbidities are vital, starting with the recognition of possible causes of functional deficits and their consequent impact on quality of life. For this purpose, simple screening methods are available, such as questionnaires and tests of functioning [14].

Currently, knowledge about quality of life and its correlations with locomotion problems in the literature is scarce. The aim of the present study was to assess the influence of LoS and sarcopenia on quality of life in independent oldest old living in the community.

2. Materials and Methods

A cross-sectional study of the 2016 observational, longitudinal survey, called the LOCOMOV Project, which included independent older people aged 80 years or over living in the community in the city of São Paulo, Brazil [8] was conducted. This study was approved by the Research Ethics Committee of the Federal University of São Paulo (CAAE permit no. 42336720.1.0000.5505).

2.1 Sample

Individuals participating in the third wave of the LOCOMOV Project were assessed in the period spanning from February 2020 to February 2021. Exclusion criteria included presence of dementia syndrome, severe acute or decompensated chronic illness, limiting sensory deficit, and fracture in the last six months [15].

2.2 Data Collection

Sociodemographic data and disease history were collected and functioning scales applied. Participants then answered the GLFS-25P, SARC-F and WHOQOL-Bref questionnaires. Finally, physical tests were carried out to assess strength, gait, balance and physical performance. The questionnaires applied, although designed to be self-administered, were completed by the interviewer in the presence of the participant while heeding the recommendations to refrain from providing additional explanations about the questions, considering age and

possible visual, motor and educational limitations of the study participants. For comorbidity data, a personal history of chronic pain, nutritional status (malnutrition or obesity), osteoarthritis, falls in the last year and use of walking device were checked. Chronic pain was defined as pain lasting more than six months. Regarding nutritional status, the classification of World Health Organization (WHO) and Pan American Health Organization (PAHO) was used according to BMI, with score <23 classed as malnutrition and ≥ 30 as obesity [16,17]. The diagnosis of osteoarthritis was made by reviewing the medical record. Participants were probed directly about use of walking devices and number of falls in the last year.

2.3 Assessment Instruments

Functioning in daily life

The Katz and Lawton scales were applied, measuring the ability to perform basic Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs), respectively. The Katz scale is widely used among health professionals for the assessment of functional independence and the performance of six functions - bathing, dressing, going to the bathroom, transferring, continence and the ability to feed. For each item, the individual is considered independent if he or she can perform the activity without help [18]. The Lawton scale assesses the ability to perform instrumental activities such as using a telephone, doing laundry, and handling finances. The scale measures nine domains, each rated from 1 to 3 (1 denoting unable, 2 need assistance, and 3 independent). The score ranges from 9 to 27 where the higher the score, the greater the person's abilities [19,20,14].

GLFS-25P

Comprising 25 questions with answers scored from 0 to 4 points.. Total score ranges from 0 to 100 points, where the higher the score, the greater the locomotive limitation of the patient [6]. The cutoff point of ≥19 was established for the diagnosis of LoS in the Brazilian population, with 86% sensitivity and 67% specificity [8].

SARC-F + CC

Five questions are asked about the ability to carry weight, walk unassisted, transfer from chair or bed, climb stairs, and number of falls in the last year. Each item is scored from 0 to 2, with 0 denoting no difficulty, 1 some difficulty and 2 failure. The scores on the 5 questions are added to the measure of calf circumference (CC) and, if this is abnormal (> 33cm for women and >34cm for men), the individual receives 10 more points. The total score ranges from 0 to 20, with values >11 indicating risk of sarcopenia [21].

Quality of life

Defined by the WHO as an individual´s "perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns", serves to help understand the influence of these limitations on every aspect of life. This information is essential in the decision-making process aimed at well-being and healthy aging. The WHOQOL-Bref is a tool devised by the WHO for assessing quality of life in adults. This is a 26-item reduced version of the World Health Organization Quality of Life Instrument 100 (WHOQOL-100), comprising 2 general questions and 24 representing each of the 24 facets that make up the original instrument. The WHOQOL-Bref is composed of the domains physical capacity (PHYS), psychological well-being (PSYCH), social relationships (SOCIAL) and the environment (ENVIR) of the individual. Each domain comprises questions with answers ranging from 1 to 5 evaluated separately [22,23].

Physical Functioning Assessment

Hand Grip (HG): Muscle strength was measured in the study by HG. The individual is asked to remain in a sitting position with shoulders adducted in neutral rotation, without supporting arms on any surface. The subject is then asked to flex the elbow at 90°, with the forearm in a neutral position and the wrist ranging from 0 to 30° of extension. Three measurements of the dominant arm, with an interval of one minute between them, are taken using the Jamar dynamometer instrument, selecting the highest value obtained [24]. Values <16 kg for women and <27 kg for men were considered impaired, according to cutoff values stipulated in the 2019 sarcopenia algorithm update [9].

Five Times Sit-to-Stand Test (5xSST): For this test, a pre-test is first performed in which the individual is asked to cross their arms across their chest and get up from a chair. If the patient is able to get up from the chair safely and thinks he or she is capable of performing the test, it is continued, whereas if the individual does not perform the pre-test correctly and safely, the test is ended. For older people aged 80 years or more, the cutoff of 14.8 seconds is used where those who perform the test in ≥ 14.9 seconds have worse performance and greater impairment in lower limb mobility, and more susceptible to falls and morbidity. If the individual is not able to get up five times from the chair, no score is given [25,26].

Gait Speed (GS): For this test, the individual is asked to walk in a straight line at their usual gait speed. The time the individual takes to walk 4 meters is measured, with total distance increased in order to allow the initial and final periods of deceleration/acceleration to be disregarded. The test is considered abnormal for GS < 0.8 m/s [27].

Short Physical Performance Battery (SPPB): The test initially assesses balance in three different positions: patient in orthostasis, without any support point (including walking devices), initially with feet positioned side by side, later in semi-tandem and finally in tandem position. In each of the positions, the patient is expected to be able to remain still for 10 seconds. The first two positions score 1 if the individual manages to hold for 10 seconds and 0 if they do not. In the tandem position, the individual receives 2 points for maintaining 10 seconds, 1 point for managing to remain in the position for 3-9 seconds, and 0 for <3 seconds. Gait speed is then evaluated, as described in the specific item. The score for this step ranges from 0 to 4 points (0 if unable; 1 for time > 8.70 seconds; 2 for6.21-8.69 seconds; 3 for4.82-6.20 seconds; and 4 for < 4.82 seconds). Finally, the 5xSST test, outlined above is evaluated with score ranging from 0 to 4 (0 if unable; 1 for time > 16.70 seconds; 2 for 13.70-16.69 seconds; 3 for 11.20-13.69 seconds; and 4 points for ≤ 11.19 seconds). The final score on the battery ranges from 0 to 12 and a cutoff point of ≤8 was established for patients with poor physical performance, according to the updated 2019 sarcopenia algorithm [28,9].

2.4 Statistical Analysis

The data obtained was double keyed into the Excel Office 2010 program and then treated using the Statistical Package for Social Sciences - SPSS for Windows (SPSS V20) and Minitab 16. Initially, a complete descriptive analysis of the quantitative variables was performed, expressed as mean, median, quartiles (Q1, Q3), minimum, maximum, standard deviation, coefficient of variation (CV) and confidence interval (CI), representing the variation of the mean according to statistical probability. To characterize the distribution of the relative frequency of qualitative covariates, the Equality of Two Proportions Test was used. Subsequently, Pearson's Correlation Coefficient was used for quantitative bivariate analyses. The qualitative analysis of the instruments was performed using the chi-square test, expressed as absolute values and their percentages. Finally, the comparison of means for two or more groups was performed using Student´s *t*-test. A significance level of 0.05 (5%) was defined, with confidence intervals constructed with 95% statistical confidence.

3. Results

The initial sample of the LOCOMOV Project comprised 102 older adults with several losses thereafter. Regarding losses in the third wave of the study in 2020, there were 16 deaths, exclusion of 12 participants due to dementia diagnosis, 2 for decompensated chronic disease and 41 because of irregular follow-up (due to coronavirus pandemic, and others). Thus, a final sample of only 30 participants was assessed (Figure 1).

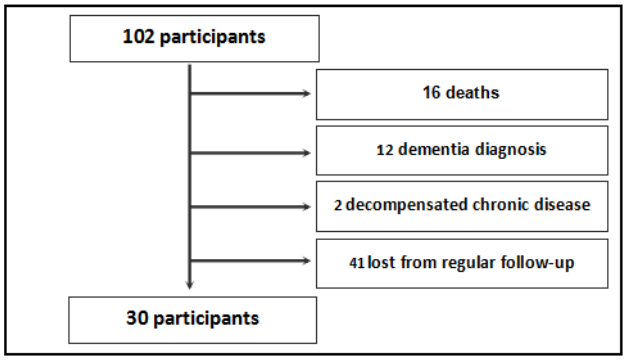

Figure 1. Study Flowchart

Regarding the sample, most participants were female (80%) and widowed (80%). The mean age of participants was of 89.1 ± 1.5 years and mean education was 3.48 years. For tests of functioning, most participants performed well, i.e. above the cutoff (Table 1).

The percentage of participants reporting chronic pain (76.7%) and LoS (53.3%) was high, while the rate of sarcopenia (26.7%) was lower (Table 2).

LoS was statistically significantly correlated with quality of life according to physical (r=-0.598, p <0.001) and environmental (r = -0.370, p 0.044) domains, and exhibited a tendency towards significance for the psychological domain (r= - 0.335, p 0.071). Los also correlated positively with sarcopenia (r= 0.563, p <0.001) and negatively with physical performance as measured by the SPPB (r= -0.752, p<0.001), muscle strength (r= -0.450, p 0.013) and gait speed (r= -0.707, p <0.001).

For qualitative variables, there was no statistically significant association between LoS and sarcopenia (p = 0.272). LoS showed a positive statistically significant association with the presence of chronic pain (93.8%; p = 0.024) (Table 4).

Individuals diagnosed with LoS had a mean of 48.4 on the physical domain of quality of life compared to 69.4 for those without LoS (p-value = 0.002) (Table 5). In individuals with LoS, the physical domain of quality of life did not differ significantly for presence or absence of sarcopenia (p 0.452) (Table 6).

Table 1. Sample characteristics according to quantitative variables

		Mean	Median	Standard Deviation	CV	Q1	Q3	Min	Max	N	CI
Age		89.1	88	4.3	5%	86	92	83	101	30	1.5
Education (years)		3.48	4	3.28	94%	1	4	0	11	29	1.19
Falls (nº)		0.37	0	0.61	168%	0	1	0	2	30	0.22
Physical Tests	HG	21.9	22	7.1	32%	19	24	2	38	30	2.5
	GS	0.73	0.75	0.29	40%	0.49	0.96	0.02	1.33	30	0.10
	5xSST	12.5	11	5.1	41%	9	13	8	31	25	2.0
	SPPB	8.40	9	3.29	39%	6	12	1	12	30	1.18
LoS	GLFS-25P	23.3	20	18.6	80%	10	33	2	81	30	6.6
Sarcopenia	SARC-F + CC	6.20	5	5.59	90%	1	11	0	17	30	2.00
WHOQOL- Bref	PHYS	58.2	61	19.6	34%	54	71	14	100	30	7.0
	PSYCH	67.2	67	16.0	24%	55	79	29	88	30	5.7
	SOCIAL	79.9	83	15.9	20%	75	92	33	100	30	5.7
	ENVIR	70.2	72	15.6	22%	63	80	22	94	30	5.6

Table 2. Sample characteristics according to qualitative variables

			N	%	P-value
Comorbidities	Malnutrition	No	26	86.7%	<0.001
		Yes	4	13.3%	
	Chronic pain	No	7	23.3%	<0.001
		Yes	23	76.7%	
	Osteoarthritis	No	25	83.3%	<0.001
		Yes	5	16.7%	
	Osteoarthritis	No	6	20.0%	<0.001
		Yes	24	80.0%	
Demography	Civil status	Married	4	13.3%	<0.001
		Divorced	1	3.3%	<0.001
		Single	1	3.3%	<0.001
		Widowed	24	80.0%	Ref.
	Gender	Female	24	80.0%	<0.001
		Male	6	20.0%	
Functioning	ADL	Independence	28	93.3%	<0.001
		Part. Dependence	2	6.7%	
	IADL	Independence	11	36.7%	Ref.
		Mild dependence	10	33.3%	0.787
		Moderate dependence	6	20.0%	0.152
		Severe dependence	2	6.7%	0.005
		Total dependence	1	3.3%	0.001
Walking device		No	17	56.7%	0.302
		Yes	13	43.3%	
LoS	GLFS-25P	Yes	16	53.3%	0.606
		No	14	46.7%	
Strength	HG	Normal	23	76.7%	<0.001
		Impaired	7	23.3%	
Sarcopenia	SARC-F + CC	Yes	8	26.7%	<0.001
		No	22	73.3%	
Physical tests	5xSST	< 14.8s	20	66.7%	<0.001
		≥14.8s	5	16.7%	
	SPPB	Impaired	13	43.3%	0.302
		Normal	17	56.7%	
	GS	<0.8m/s	17	56.7%	0.302
		≥0.8m/s	13	43.3%	

Table 3. Correlation of Quantitative Variable

		Age	Education (years)	Falls	HG	GS	5xSST	SPPB	GLFS 25-P	SARC-F + CC	PHYS	PSYCH	SOCIAL
Education (years)	Corr (r)	-0.275											
	P-value	0.141											
Falls	Corr (r)	0.330	-0.195										
	P-value	0.075	0.301										
HG	Corr (r)	-0.154	0.092	-0.112									
	P-value	0.417	0.630	0.554									
GS	Corr (r)	-0.424	0.047	0.039	0.291								
	P-value	0.020	0.806	0.836	0.119								
5xSST	Corr (r)	0.309	-0.051	-0.165	-0.108	-0.433							
	P-value	0.133	0.809	0.431	0.607	0.031							
SPPB	Corr (r)	-0.420	0.049	0.078	0.348	0.857	-0.645						
	P-value	0.021	0.797	0.680	0.059	<0.001	0.001						
GLFS-25P	Corr (r)	0.236	0.001	0.091	-0.450	-0.707	0.052	-0.752					
	P-value	0.210	0.995	0.633	0.013	<0.001	0.807	<0.001					
SARC-F + CC	Corr (r)	0.199	0.117	0.179	-0.466	-0.327	-0.164	-0.446	0.563				
	P-value	0.291	0.537	0.345	0.009	0.078	0.435	0.014	0.001				
PHYS	Corr (r)	0.021	-0.259	0.117	0.081	0.369	-0.050	0.325	-0.598	-0.205			
	P-value	0.913	0.167	0.537	0.672	0.045	0.814	0.080	<0.001	0.278			
PSYCH	Corr (r)	0.123	-0.415	-0.167	0.092	0.160	0.129	0.261	-0.335	-0.405	0.376		
	P-value	0.516	0.023	0.377	0.629	0.398	0.537	0.164	0.071	0.026	0.040		
SOCIAL	Corr (r)	0.327	-0.370	0.061	-0.299	-0.038	-0.030	-0.011	-0.031	-0.087	0.320	0.701	
	P-value	0.077	0.044	0.749	0.109	0.843	0.889	0.953	0.872	0.648	0.085	<0.001	
ENVIR	Corr (r)	0.208	-0.473	-0.091	0.168	0.120	0.052	0.218	-0.370	-0.408	0.497	0.842	0.674
	P-value	0.271	0.008	0.633	0.374	0.529	0.805	0.248	0.044	0.025	0.005	<0.001	<0.001

Table 4. Association between LoS and others covariates

		Normal		Impaired		Total		P-value
		N	%	N	%	N	%	
ADLs	Independence	14	87.5%	14	100%	28	93.3%	0.276
	Part. Dependence	2	12.5%	0	0.0%	2	6.7%	
IADLs	Independence	3	18.8%	8	57.1%	11	36.7%	0.149
	Mild dependence	7	43.8%	3	21.4%	10	33.3%	
	Moderate dependence	3	18.8%	3	21.4%	6	20.0%	
	Severe dependence	2	12.5%	0	0.0%	2	6.7%	
	Total dependence	1	6.3%	0	0.0%	1	3.3%	
Civil Status	Married	2	12.5%	2	14.3%	4	13.3%	0.564
	Divorced	0	0.0%	1	7.1%	1	3.3%	
	Single	1	6.3%	0	0.0%	1	3.3%	
	Widowed	13	81.3%	11	78.6%	24	80.0%	
Gender	Female	14	87.5%	10	71.4%	24	80.0%	0.202
	Male	2	12.5%	4	28.6%	6	20.0%	
Malnutrition	No	15	93.8%	11	78.6%	26	86.7%	0.213
	Yes	1	6.3%	3	21.4%	4	13.3%	
Walking device	No	7	43.8%	10	71.4%	17	56.7%	0.096
	Yes	9	56.3%	4	28.6%	13	43.3%	
Chronic pain	No	1	6.3%	6	42.9%	7	23.3%	0.024
	Yes	15	93.8%	8	57.1%	23	76.7%	
Obesity	No	12	75.0%	13	92.9%	25	83.3%	0.179
	Yes	4	25.0%	1	7.1%	5	16.7%	
Osteoarthritis	No	3	18.8%	3	21.4%	6	20.0%	0.343
	Yes	13	81.3%	11	78.6%	24	80.0%	
HG	Normal	13	81.3%	10	71.4%	23	76.7%	0.275
	Impaired	3	18.8%	4	28.6%	7	23.3%	
5xSST	< 14.8seg	8	72.7%	12	85.7%	20	80.0%	0.283
	≥14.8seg	3	27.3%	2	14.3%	5	20.0%	
SPPB	Inappropriate	9	56.3%	4	28.6%	13	43.3%	0.096
	Appropriate	7	43.8%	10	71.4%	17	56.7%	
GS	<0.8m/s	11	68.8%	6	42.9%	17	56.7%	0.110
	≥0.8m/s	5	31.3%	8	57.1%	13	43.3%	

Table 5. Association between LoS and quality of life

WHOQOL-Bref	LoS	Mean	Median	Standard Deviation	CV	Min	Max	N	CI	P-value
PHYS	Yes	48.4	53.6	19.0	39%	14.3	75.0	16	9.3	0.002
	No	69.4	67.9	13.8	20%	53.6	100.0	14	7.2	
PSYCH	Yes	64.1	62.5	17.3	27%	29.2	87.5	16	8.5	0.254
	No	70.8	79.2	14.2	20%	45.8	87.5	14	7.4	
SOCIAL	Yes	77.9	79.2	14.0	18%	41.7	100.0	16	6.9	0.472
	No	82.1	87.5	18.2	22%	33.3	100.0	14	9.5	
ENVIR	Yes	67.2	67.2	17.0	25%	21.9	93.8	16	8.3	0.264
	No	73.7	78.1	13.6	19%	46.9	90.6	14	7.1	

Table 6. Association between LoS, in presence or absence of sarcopenia, and physical domain of quality of life

WHOQOL-Bref	Sarcopenia	Mean	Median	Standard Deviation	CV	Min	Max	N	CI	P-value
PHYS	Yes	42.9	39.3	26.4	62%	14.3	75.0	5	23.1	0.452
	No	50.9	53.6	15.4	30%	25.0	75.0	11	9.1	

4. Discussion

In the present study, mean age was 89.1 years in the clinically compensated individuals with no cognitive impairments impacting functioning. In the oldest old assessed, many variables had high coefficients of variation, such as education, number of falls in the last year, and LoS and sarcopenia screening questionnaires, revealing heterogeneity among the participants.

Regarding LoS, 53.3% of the sample had an established diagnosis according to the GLFS-25P. A statistically significant relationship between LoS and chronic pain was found. This data is essential to draw attention to a diagnosis that is often neglected in health care. Appropriate treatment of chronic pain can improve performance and intrinsic capacity of older individuals.

The study results confirmed a correlation between LoS and worse performance on the short physical performance battery (SPPB) and in gait speed (GS), an expected finding, given the impact of LoS on patient functioning and independence for locomotion, as previously described in the literature [5].

There are few studies investigating the impact of this syndrome on the perception of quality of life. In the second wave of the Locomov project, conducted by Arbex et al. in 2020, LoS was correlated with worse scores in physical, psychological and environmental domains of quality of life on the WHOQOL-Bref [8]. Although the present study was based on the initial sample of the second wave, there was a regular correlation between LoS and the physical domain only. However, this difference might be explained by the reduced current sample population, in that the patients who remained in the project were probably those with better physical performance and less locomotive limitations in the previous study.

The association between LoS and worse quality of life scores implies that physical limitation has a deleterious effect on the quality of aging of the oldest old studied. Preserved ability to move around, climb stairs and carry weight, i.e., maintain some locomotive independence, is associated with better perceived quality of life by older adults [8].

Sarcopenia was present in only 26.7% of the sample and was not associated with LoS. This lack of association may have occurred due to the low prevalence of sarcopenia and small sample size. LoS was associated with worse quality of life regardless of the presence of sarcopenia.

Promoting musculoskeletal health during aging is believed to be beneficial by ensuring longer functional independence, control of comorbidities that impact locomotion such as chronic pain, and consequently better intrinsic capacity of the individual and enhanced quality of life.

Study limitations

The high rate of death and other outcomes, such as dementia syndrome, observed in the longitudinal LOCOMOV Project led to a small sample size. Another factor further limiting the sample size was the COVID-19 pandemic. The older population is a risk group for the virus and, from the outset of the pandemic, recommendations emphasize that this group avoids unnecessary exposure and remain in contact only with family members they live with. Thus, many patients failed to attend routine geriatric appointments, largely justifying the follow-up losses observed in the study, since data collection was concomitant with outpatient consultations and started a month prior to the pandemic restrictions in Brazil.

5. Conclusions

Despite the small sample, the present study suggested a statistically significant association between LoS and chronic pain and also worse performance by participants with LoS on test of functioning such as gait speed and physical performance. LoS was associated with worse health-related quality of life regardless of the presence of sarcopenia. Recognizing the characteristics of the oldest old in relation to their musculoskeletal limitations is important to guide effective prevention and rehabilitation actions for functional dependence, contributing to the quality of life and healthy aging of this population.

Author Contributions

All authors were involved in the data collection, results evaluation and article writing of the study.

Conflict of Interest

The authors declare they have no relationships/conditions/circumstances that present a potential conflict of interest.

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References

[1] World Health Organization. (2015). World report on ageing and health. Geneva, Switzerland: World Health Organization.

[2] Beard JR, Jotheeswaran AT, Cesari M, et al. The structure and predictive value of intrinsic capacity in a longitudinal study of ageing. BMJ Open 2019;9:e026119. DOI: 10.1136/bmjopen-2018-026119.

[3] Nakamura K, Yoshimura N, Akune T, Ogata T, Tanaka S. [The concept and definition of locomotive syndrome in a super-aged society]. Nihon Rinsho. 2014 Oct;72(10):1715-20. Japanese.

[4] Ishibashi H. Locomotive syndrome in Japan. Osteoporosis Sarcopenia. 2018 Sep;4(3):86-94. DOI: 10.1016/j.afos.2018.09.004.

[5] Nakamura K. The concept and treatment of locomotive syndrome: its acceptance and spread in Japan. Journal of Orthopaedic Science. 2011; 16(5):489-491. DOI: 10.1007/s00776-011-0108-5.

[6] Seichi A. Hoshino, Y. Doi, T. Akai, M. Tobimatsu, Y. Iwaya, T. Development of a screening tool for risk of locomotive syndrome in the elderly: the 25-question Geriatric Locomotive Function Scale. J Orthop Sci, 17 (2) (2012), pp. 163-172.

[7] Tavares DRB, Santos FC. Síndrome locomotora em idosos: tradução, adaptação cultural e validação brasileira do instrumento 25-Question Geriatric Locomotive Function Scale. Rev Bras Reumatol. 2017; 57 (1): 56-63.

[8] Arbex MCFB, Okazaki JEF, Tavares DRB, Figueiredo Bersani AL, Santos FC. Locomotive Syndrome is associated with chronic pain and poor quality of life in Brazilian oldest old: LOCOMOV Project. J Orthop Sci. 2020 Mar 12:S0949-2658(20)30057-9. DOI: 10.1016/j.jos.2020.02.007.

[9] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16-31. DOI: 10.1093/ageing/afy169. Erratum in: Age Ageing. 2019 Jul 1;48(4):601.

[10] Malmstrom TK, Morley JE. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. J Am Med Dir Assoc. 2013 Aug;14(8):531-2. DOI: 10.1016/j.jamda.2013.05.018. Epub 2013 Jun 25.

[11] Barbosa-Silva, T. G., Menezes, A. M. B., Bielemann, R. M., Malmstrom, T. K., & Gonzalez, M. C. (2016). Enhancing SARC-F: Improving Sarcopenia Screening in the Clinical Practice. Journal of the American Medical Directors Association, 17(12), 1136-1141. DOI: 10.1016/j.jamda.2016.08.004.

[12] Almeida, MABD. Gonçalves, A.; Vilarta, R. (org.).

Qualidade de vida e atividade física: explorando teoria e prática. Barueri: Manole, 2004. Conexões, Campinas, SP, v. 2, n. 2, p. 105-108, 2007. DOI: 10.20396/conex.v2i2.8637950.

[13] Bullinger, M., Anderson, R., Cella, D., & Aaronson, N. (1993). Developing and evaluating cross-cultural instruments from minimum requirements to optimal models. Quality of life research: an international journal of quality of life aspects of treatment, care and rehabilitation, 2(6), 451-459.

[14] Freitas, EV, Py, Lígia. Tratado de geriatria e gerontologia, 4. ed., Rio de Janeiro: Guanabara Koogan, 2017.

[15] Carmo SN, Santos FC. Locomoção em idosos longevos: um estudo de coorte prospectiva. Dissertação (Mestrado Profissional) - Universidade Federal de São Paulo, Escola Paulista de Medicina. Programa de Pós-Graduação em Tecnologias e Atenção à Saúde. São Paulo, 2019.

[16] World Health Organization (WHO). Obesity: preventing and managing the global epidemic. Geneva: Program of Nutrition, Family and Reproductive Health; 1998.

[17] Organização Pan-Americana (OPAS). XXXVI Reunion del Comite Asesor de Investigaciones en Salud - Encuestra Multicentrica - Salud Bienestar y Envejecimiento.(SABE) en America Latina e el Caribe - Informe preliminar [Internet]. [cited Mar. 2002]. Available from: http://www.opas.org/program/sabe.htm.

[18] Lino, V. T. S., Pereira, S. R. M., Camacho, L. A. B., Ribeiro Filho, S. T., & Buksman, S. (2008). Adaptação transcultural da Escala de Independência em Atividades da Vida Diária (Escala de Katz). Cadernos de Saúde Pública, 24(1), 103-112. DOI: 10.1590/s0102-311x2008000100010.

[19] Lawton MP, Brody E. Assessment of older people: self-maintaining and Instrumental Activities of Daily Living. Gerontologist. 1969; 9:179-86.

[20] Lawton MP. The functional assessment of elderly people. J Am Geriatr Soc. 1971; 19:465-81.

[21] Barbosa-Silva TG, Menezes AM, Bielemann RM, Malmstrom TK, Gonzalez MC; Grupo de Estudos em Composição Corporal e Nutrição (COCONUT). Enhancing SARC-F: Improving Sarcopenia Screening in the Clinical Practice. J Am Med Dir Assoc. 2016 Dec 1;17(12):1136-1141. DOI: 10.1016/j.jamda.2016.08.004.

[22] The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment (1998). Psychological medicine, 28(3), 551-558.

[23] Fleck, Marcelo PA, Louzada, Sérgio, Xavier, Marta, Chachamovich, Eduardo, Vieira, Guilherme, Santos, Lyssandra, & Pinzon, Vanessa. (2000). Aplicação da versão em português do instrumento abreviado de avaliação da qualidade de vida "WHOQOL-bref". Revista de Saúde Pública, 34(2), 178-183.

[24] Figueiredo IM, Sampaio RS,Mancini MC, Silva FCM,Souza MAP. Teste de força de preensão utilizando o dinamômetro Jamar. ACTA FISIATR 2007; 14(2): 104 - 110.

[25] Bohannon RW. Reference values for the five-repetition sit-to-stand test: a descriptive metaanalysis of data from elders. Percept Mot Skills 2006; 103(1):215-222.

[26] Buatois S, Miljkovic D, Manckoundia P, Gueguen R, Miget P, Vancon G et al. Five times sit to stand test is a predictor of recurrent falls in healthy community-living subjects aged 65 and older. J Am Geriatr Soc 2008; 56(8):1575-1577.

[27] Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. JAMA 2011;305(1):50-8.

[28] Nakano, MM. Versão brasileira da Short Physical Performance Battery SPPB: adaptação cultural e estudo da confiabilidade. 2007. Dissertação (mestrado) - Universidade Estadual de Campinas, Faculdade de Educação, Campinas, SP. Available from: http://www.repositorio.unicamp.br/handle/REPOSIP/252485.

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CASE REPORT

An Introduction of the Vaporized Therapy with Tea Herb Drink for Relieving Agitation due to Pulmonary Encephalopathy

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ABSTRACT

What methods would you choose apart from increasing sedatives for agitation in an advanced patient with hypercapnic encephalopathy due to AECOPD? This is a 94-year-old female who suffered from COPD for over 30 years, occurred with an accelerated episode of cough, productive sputum and a dropping down to 86% in SatO□ due to a cold weather. A diagnosis of pulmonary encephalopathy (PE) was made on the basis of the subsequent agitation and delirium, and the sedatives, such as quatiepine and haloperidol, had to be given for her mental excitation respectively, but she still pulled out indwelling needle herself and refused to any infusion therapy. As an alternative, a vaporized therapy integrated with tea herb drinking had to be applied to relieving her agitation, being designed as the vaporization of the inhaled oxygenation by means of high-flow oxygenation device (HFOD), with an ampoule of ambroxol mixed into the inhaler and simultaneous drinking of TCM tea herb for reducing sputum, helping dissolve the mucoid bolts inside her terminal bronchioles when being infected. We thought that a better efficacy would be achieved for hypercapnic encephalopathy due to AECOPD if we concentrate on a good ventilation of small airway through the vaporized therapy.

1. Introduction

This is a case of chronic obstructive pulmonary disease (COPD) occurred in a 94-year-old female who complained of recurrent cough and expectoration for over 30 years, with an accelerated episode over the past week. Recently, an aggravated episode of cough emerged with lots of purulent sputum due to a cold weather, and her $SatO_2$ dropped once a time down to 86%. A diagnosis of lower respiratory tract infection (LRTI) and secondary pulmonary encephalopathy (PE) was reasonably made according to her nocturnal agitation; and sedatives were given for her mental excitation. She refused to any infusion therapy, and a vaporized therapy integrated with TCM tea herb was designed, as an alternative, to help her expectoration for a better ventilation. Two days after realizing it, an easier expectoration came with a slight percussion, and she fell asleep easily without injecting any

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sedatives; her total situation also improved steadily since then.

2. Case Report

2.1 General Material

This was a 94-year-old female with a complain of recurrent cough with productive sputum for over 30 years, being admitted to hospital again with an accelerated episode of COPD. She had a 10-year history of Alzheimer's disease, being under good control in agitation regardless of memory loss and delirium sometimes. During the hospitalization, another aggravated episode of cough with purulent sputum came to her due to a cold weather, manifesting as a fever (38.4°C), apathetic, along with a poor appetite for eating and malaise in her body. She looked a bit emaciated, with a barrel chest, retention of her jungular veins, and finer moist rales were heard, in auscultation, on the bases of her lungs, especially on the right. CBC showed: WBC 8.2×10^9/L, N 76%;C-reactive protein 17.7 mg/L. Blood gas analysis: pH 7.45, pO_2 45 mmHg, pCO_2 37 mmHg, Lac 1.86 mmol/L. Thus a clinical diagnosis of low respiratory tract infection (LRTI) was made according to the patchy focus demonstrated in her lower lobe on the right on iconography (Figure 1).

As a response to LRTI, an cephalosporin compound, consisting of cefoperazone and sulbactam, 2 grams of which were given intravenously, every 8 hours; but the nocturnal excitation emerged with delirium, and 25 mg of quatiepine was applied firstly to dealing with her agitation. Furthermore, 5 mg of haloperidol mixed with 0.3 mg of scopolamine had to be injected intramuscularly to help fall asleep lasting for a week. The patient pulled out indwelling needle herself during the hospitalization and refused to any infusion therapy because of agitation. Increasing the dose of quatiepine to 500 mg a day gradually, her $SatO_2$ was dropped, once a time, down to 86%. As an alternative, a vaporized therapy integrated with TCM tea herb was applied to her phlegm obstruction, twice a day, to help with an easy expectoration for her.

2.2 A Composition of the Vaporized Therapy Integrated with Tea Herb Drinking and its Efficacy

A vaporization of the inhaled oxygenation integrated with TCM tea herb for expectoration was elaborately designed for the purpose of reducing sputum. We used a set of HFOD (Spirry®, Figure 2) to vaporize the inhaled oxygenation (Temp: 32°C, Oxygen Flow: 35 L/min, Oxygen %: 40%);and an ampoule of ambroxol was added to the inhaler every time to dissolve the mucoid bolts. Simultaneously, having TCM tea herb, consisting of adenophora, gypsum, licorice etc., can help reduce sputum, given twice a day, seven days for one course.

Prior to the vaporized therapy, several doses of haloperidol and scopolamine were forced to be injected intramuscularly to suppress her agitation. Two days after realizing it, the patient fell asleep at night without the help of any sedative injections, accompanied by easier expectoration with a slight percussion (Figure 2). It was showed on her repetitive blood gas analysis: pH 7.45, pO_2 88 mmHg, pCO_2 33 mmHg, Lac 1.34 mmol/L, much better than before; and so did the CT-scan for her lungs (Figure 1).

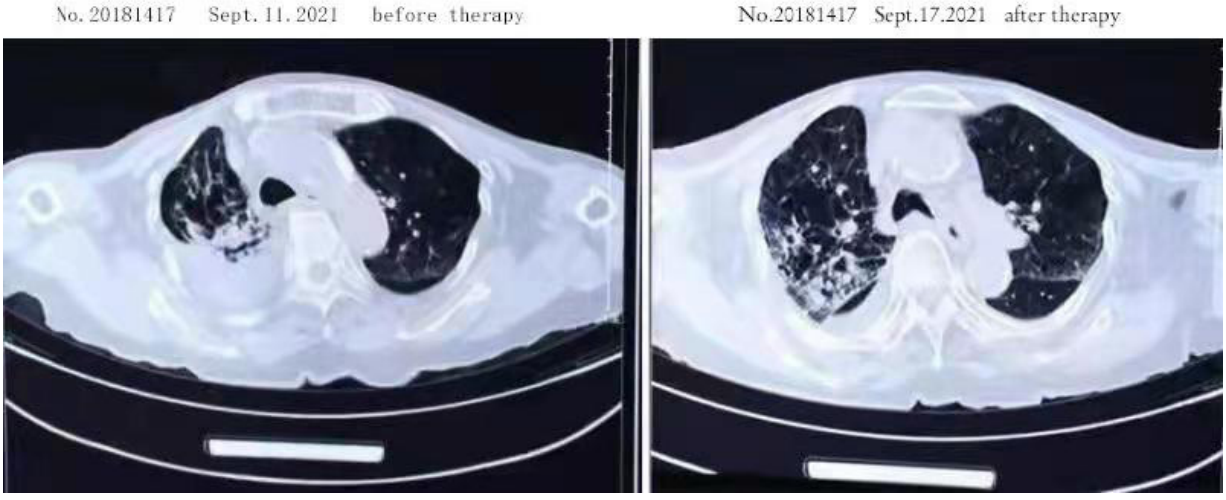

Figure 1. chest CT-scans before and after the vaporized therapy with TCM tea herb

Figure 2. high-flow oxygenation device and the subsequent expectoration

3. Discussion

3.1 Reasons for a Combination of the Vaporized Oxygenation Helped with TCM Tea Herb

The mucoid bolts caused by AECOPD inside the terminal bronchioles would result in symptomatic pulmonary encephalopathy by blocking the tiny airway [1], together with the concomitant endotoxinemia from gram-negative bacilli (MDR) hidden inside muci, which should be tried to clear up from the airway [2]. The combined therapy for expectoration occurred to realize it,characteristic of the vaporization of the inhaled oxygenation (mixed with 35% oxygen).

As a key step, it was designed elaborately to reduce the sputum with a higher viscosity, which reached to "throwing out" the mucoid sputum by means of High-Flow Oxygenation Device with a humidifier (Spirry®, HFOD). The inhaled gas had been vaporized with a temperature of 32°C and some moisture to dissolve the tiny sputum bolts inside.

During the process, an ampoule of ambroxol was mixed into the absorber. And the acidglycoprotein (AAG) in mucoid bolts, produced by Goblet Cell in the wall of bronchiole, can be restrained or broken up to lower the viscosity [3].

The tea herb of TCM, consisting mainly of ephedra and almond, had been regarded for a long time as reducing sputum in ancient China. Nowadays, we added adenophora to the tea herb instead of ephedra and almond, aiming at Nourishing-Yin and reducing sputum based on the TCM theory [4]. And being accompanied by gypsum and licorice,the composition of tea herb here will help expectorate the mucoid sputum with the both lungs working well.

3.2 Comparison with Classic Antibiotic Therapy

One type of powerful antibiotic therapy or combination of two types of antibiotics has always been chosen to treat the infection in lower respiratory tract (LRTI) for killing the pathogenic bacteria (MDR), but the side effects of them would emerge, as a consequence, about 3-5 days later in the aged, including the loss of appetite, antibiotic-associated diarrhea (AAD), and mental excitation provoked by carbapenams [5]. Recently, we focused on the tiny mucoid bolts inside the terminal bronchioles in patients with LRTI (AECOPD), which was key to pathogenesis of pulmonary encephalopathy. A rational integration of the vaporized oxygenation with the drinking of revised TCM tea herb was carefully designed to promote reducing sputum. Thus, the agitation due to being short of oxygen subsided in a shorter time.

The advantages of combined therapy were fully showed here: (1) Reducing sputum can throw away any kinds of germs no matter how they are gram-negative bacilli, fungi or germs resistant to antibiotics (MDR) [2]. (2) The vaporized therapy can decrease the exposure to powerful antibiotics by lowering the dose of antibiotics, which benefits from the proper use of antibiotics [6], and helps control the total costs of medication with a better outcome.

This aged female suffered from AECOPD, associated with mental excitation from pulmonary encephalopathy. She refused to any infusion therapy in spite of advice. As

a compensation, the vaporized therapy with TCM tea herb had to be applied to relieving her symptoms. Two days after realizing it, the patient fell asleep without injecting any sedatives, and her total situation improved steadily since then. To verify its efficacy, the repetitive blood gas analysis and chest CT-scan were done, and the results showed a much better improvement than before.

4. Conclusions

We thought that a key to dealing with the agitation due to LRTI concerns about breaking down the tiny mucoid bolts in it, and a much better efficacy would be achieved if we concentrate on a good ventilation of small airway through the vaporized therapy.

References

[1] Gupta H, Alrohimi A, Nathuo N, et al. (2020) Posterior reversible encephalopathy syndrome due to chronic obstructive pulmonary disease. Canadian journal of neurological sciences, 47: 569-571.

[2] Wang J, Cui Z, Liu S, et al.(2017) Early use of noninvasive techniques for clearing respiratory secretions during noninvasive positive-pressure ventilation in patients with acute exacerbation of chronic obstructive pulmonary disease and hypercapnic encephalopathy: A prospective cohort study. Medicine, 96: e6371.

[3] Paleari D, Rossi GA, Nicolini G, et al.(2011) Ambroxol: a multifaceted molecule with additional therapeutic potentials in respiratory disorders of childhood. Expert Opin Drug Discov, 6:1203-1214.

[4] Abiba.(1978) Effects of sublingual administration of Ephedra herba aqueous extracts on respiratory resistance in dogs. Annu Rep Tohoku Coll Pharm, 25: 23-25.

[5] Wilcox N, Minton J.(2001) Role of antibody response in outcome of antibiotic associated diarrhea. Lancet, 357:158-159.

[6] Clift C, Salisbury DM.(2017) Enhancing the role of vaccines in combatting antimicrobial resistance. Vaccine, 35: 6591-6593.

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