Journal of Frailty, Sarcopenia and Falls

Original Article

The mortality determinants of sarcopenia and comorbidities in hospitalized geriatric patients

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Abstract

Objectives: Determine the influence of muscle mass, muscle strength, physical performance, nutritional status and certain comorbidities on the four years mortality risk of hospitalized geriatric patients. **Design:** Retrospective cohort study. **Setting:** During hospitalization of the included geriatric patients, the determinants of sarcopenia and nutritional status were obtained. **Participants:** A total of 302 patients hospitalized at the geriatric department of the Saint-Elisabeth hospital in Antwerp (Belgium) from 01/08/2012 until 31/01/2013. **Measurements:** Muscle mass was measured using a CT scan. The muscle strength was obtained by measuring the handgrip strength using a Jamar dynamometer. The physical performance was measured by performing the SPPB. The nutritional status was surveyed by using the MNA-SF. Comorbidities were obtained through medical records. **Results:** The variables gender (HR= 0.609; 95% CI 0.442-0.838), nutritional status (HR= 2.953; 95% CI 1.924-4.531), muscle mass (HR= 0.443; 95% CI 0.251-0.780), muscle strength (HR= 0.215; CI 95% 0.079-0.587), physical performance (HR= 0.407; 95% CI 0.237-0.702) and heart failure (HR= 1.440; 95% CI 1.022-2.029) have been shown to be significant. **Conclusion:** The determinants gender, nutritional status and physical performance have the greatest prognostic value.

Keywords: Sarcopenia, Definition, Geriatrics, Hospitalization, Mortality

Introduction

Initially, sarcopenia was described as an age-related loss of skeletal muscle mass. This geriatric syndrome gives rise to a diminished ability to resist against external stressors[1,2]. Later research however, demonstrated that, besides skeletal muscle mass, also muscle strength and/or physical performance were important in the clinical specification of sarcopenia. Since then, a revolution in the concept of the definition of sarcopenia had been set[3-5]. Several international research groups, including the European Working Group on Sarcopenia in Older People (EWGSOP), use these three determinants to present their clinical definition for the diagnosis of sarcopenia[6,7]. Unfortunately, these groups all use their own diagnostic criteria and cut off values. As a result, nowadays, there is still no universal operational definition of sarcopenia[8-10].

Sarcopenia is known to be associated with an increased risk for several adverse outcomes such as frailty, hospitalization, disability and mortality[4,13,14]. Especially the determinants muscle mass, muscle strength and physical performance have been found to play a major part in the increased risk of these adverse outcomes[4,5]. Also, sarcopenic patients with a diminished nutritional status have been shown to be at greater risk of dying in the short-term[15]. In addition, comorbidities such as heart failure and orthopedic surgery can induce worse outcomes in these patients. In this matter, chronic heart failure can provoke additional loss of muscle mass and strength[16]. On the other hand, orthopedic surgery can imply a significant risk of postoperative morbidity and mortality[3].

The authors have no conflict of interest.

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Edited by: *Yannis Dionyssiotis*

Accepted *28 October 2017*

Since little is known in literature about the long-term effect of certain determinants on the mortality risk in hospitalized geriatric patients, this study sought to determine which parameters of sarcopenia and comorbidities increase the mortality risk in these patients. This study especially aimed to define which of these determinants have the greatest prognostic value in predicting the mortality risk. It also wanted to compare the magnitude of this risk between the different subclasses in each class variable (nutritional status, muscle mass, muscle strength, physical performance, heart failure, orthopedic surgery).

Materials and method

Design

A retrospective cohort study was conducted to determine the long-term effect of determinants of sarcopenia, nutritional status and several comorbidities on the mortality risk in hospitalized geriatric patients.

Setting

During hospitalization of the included geriatric patients, determinants of sarcopenia were measured and the nutritional status was surveyed in order to screen for associations with the risk of mortality.

Subjects

All patients hospitalized at the geriatric department of the Saint-Elisabeth hospital in Antwerp (Belgium) during the period 01/08/2012-31/01/2013 were included. No patients were excluded. A total of 302 subjects was obtained.

Measurements

The following determinants were used: muscle mass, muscle strength, physical performance, nutritional status, and the presence of the comorbidities heart failure and/or a history of orthopedic surgery.

The muscle mass was measured by a computed tomography (CT) scan (Siemens Somatom Balance, Siemens, Erlangen, Germany) of both upper legs. The muscle volume obtained was multiplied by 1.055 g/mm^3, assumed to be the constant density of skeletal muscles[17]. The mean of both legs was used in subsequent statistical analysis. The subjects were subdivided into 2 groups (Low Muscle Mass, and Normal Muscle Mass) with a cut-off value of 0.893 kg for men and 0.630 kg for women, calculated by taking the mean value plus one standard deviation (SD).

The muscle strength was obtained by measuring the handgrip strength using a Jamar dynamometer (Lafayette Instrument, IN, USA). The patient was positioned with the shoulders in neutral position and elbows in 90° flexion. The best of 3 observations in each hand was noted. The mean value of both hands was used in the statistical analysis[12]. The subjects were again divided in two categories with cut-off values of 30 kg (male) or 20 kg (female) based on the EWGSOP criteria[7].

The physical performance was measured by performing the Short Physical Performance Battery (SPPB). This test consists of the following 3 subtests: a balance test, repeated chair stand test and gait speed test. Each subtest was rated on a scale from 0 to 4, with a maximum score of 12. The subjects were divided into three categories: 'Low SPPB-scores' (scores 0-4), 'Intermediate SPPB-scores' (scores 5-7) and 'High SPPB-scores' (scores 8-12)[7,11,18].

The nutritional risk status was surveyed by using a questionnaire, i.e. the Mini-Nutritional Assessment - Short Form (MNA-SF)[19]. This questionnaire was taken on the first working day after the day of admission. The subjects were divided in three groups: 'Malnourished' (score 0-7), 'Risk of Malnutrition' (scores 8-11) and 'Normal nutritional status' (scores 12-14)[10].

The comorbidities were obtained later through research of medical records. The presence of heart failure was defined as the presence of reduced ejection fraction (<50%) and/or a diastolic dysfunction[20]. The history of orthopedic surgery was defined as whether or not the patient had an open orthopedic surgery (e.g. Open reduction internal fixation (ORIF), prosthesis surgery or amputation) in the period of 2012 up to and including 2016[3].

Statistical analysis

Statistical analysis was done with SPSS 24 (SPPS Inc., Chicago, IL, USA). The determinants were subdivided into categories for all the statistical analyses, as described in the previous section. Descriptive analyses were used to determine the demographic and clinical properties. Multiple cox proportional hazard regressions were used to determine hazard ratios (HR), each time adjusted for the confounding variables age and gender. A Kolmogorov-Smirnov test and Shapiro-Wilk test were used to verify the normal distribution of the different variables. Student's t-tests were used to test for differences in the distribution of continuous variables. A chi-square test was used for testing the significance of associations with categorical variables. P-values<0.05 were considered statistically significant. Correlations were calculated using the Pearson correlation coefficient (PCC).

Ethics

Oral informed consent was obtained from all patients at the beginning of hospitalization regarding all the necessary tests and follow up. Almost all of these tests were routinely performed in normal clinical practice. Sixty patients did not give their informed consent for muscle mass measurements with a CT-scan. All further information was obtained through the medical records and the Civil Affairs Office. There were no detrimental effects for the subjects.

Parameter	N	Missing data	Mean	SD	Min	Max
Patient characteristics						
Age (y)	302	0	85.94	6.38	65	102
Follow-up time (d)	302	0	949.98	533.93	2	1540
Determinants						
MNA-SF	301	1	9.23	3.08	0	14
Muscle mass (kg)	203	99	0.52	0.21	0.13	1.29
SPPB scores	276	26	3.69	3.18	0	12
Muscle strength (kg)	272	30	13.09	8.36	0	50

SD= Standard deviation; MNA-SF= Mini Nutritional Assessment-Short form; SPPB= Short Physical Performance Battery.

Table 1. Baseline characteristics of the continuous variables of hospitalized geriatric patients (n=302).

Parameter	Class	Frequency	Percentage	Cumulative percentage	Dead (n)	Percentage
Patient characteristics						
Gender	Male	91	30.1	30.1	60	65.9
	Female	211	69.9	100.0	102	48.3
	Total	302	100.0		162	53.6
Status	Alive	140	46.4	46.4		
	Dead	162	53.6	100.0		
	Total	302	100.0			
Determinants						
Nutritional status	Malnourished	87	28.8	28.8	59	67.8
	Risk	127	42.1	70.9	69	54.3
	Normal	88	29.1	100.0	34	38.6
	Total	302	100.0		162	53.6
Muscle Mass	Low	164	54.3	80.8	93	56.7
	Normal	39	12.9	100.0	14	35.9
	Total	203	67.2		107	52.7
SPPB Scores	Low	168	55.6	60.9	105	62.5
	Intermediate	69	22.8	85.9	27	39.1
	High	39	12.9	100.0	15	38.5
	Total	276	91.4		147	53.3
Muscle Strength	Low	252	83.4	92.6	141	56.0
	Normal	20	6.6	100.0	4	20.0
	Total	272	90.1		145	53.3
Heart Failure	Not present	229	75.8	75.8	115	50.2
	Present	73	24.2	100.0	47	64.4
	Total	302	100.0		162	53.6
Orthopedic Surgery	Not Present	222	73.5	73.5	123	55.4
	Present	80	26.5	100.0	39	48.8
	Total	302	100.0		162	53.6

Table 2. Baseline characteristics of categorical variables of hospitalized geriatric patients (n=302).

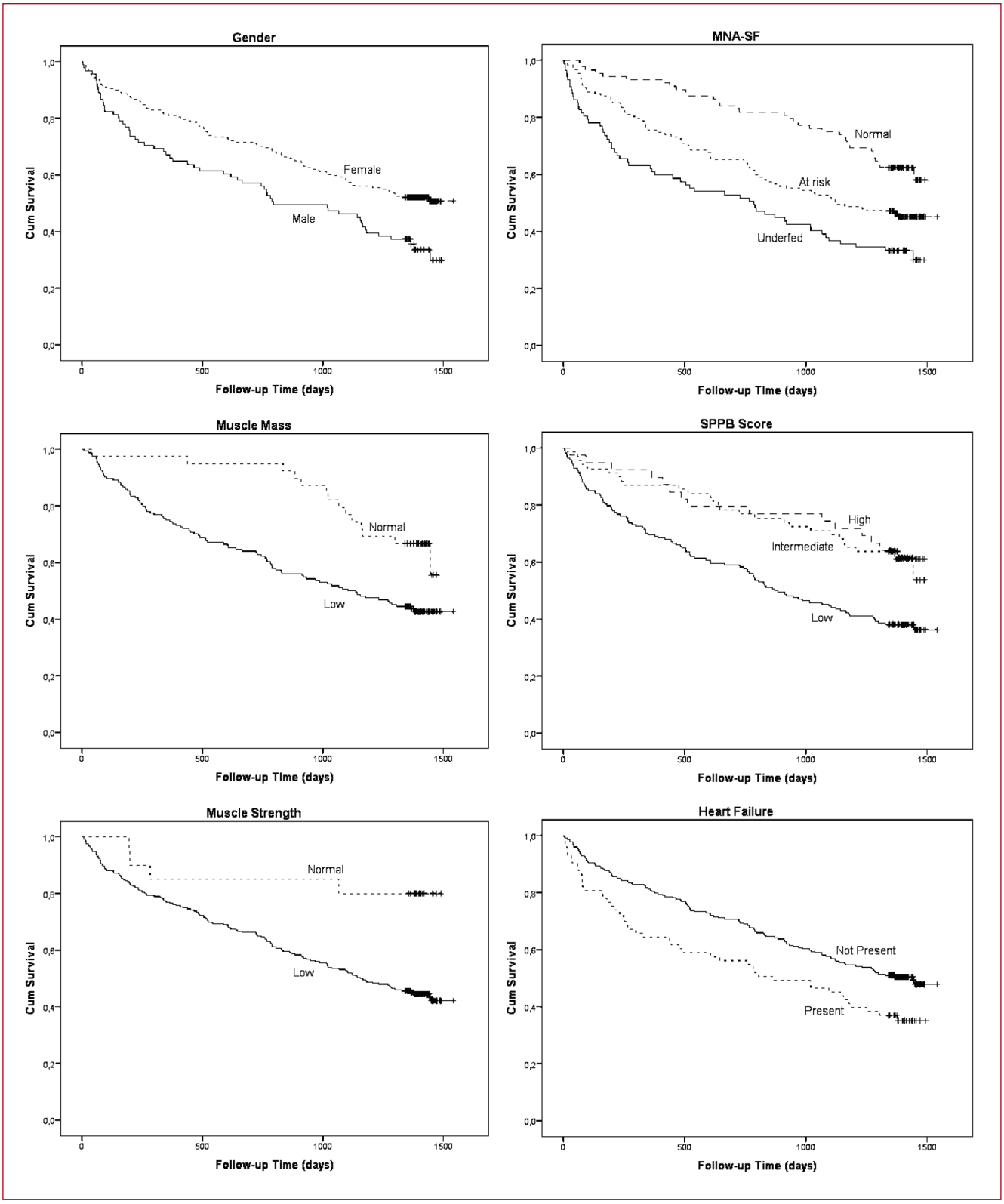

Figure 1. Survival curves of the significant class variables gender, nutritional status, muscle mass, muscle strength, physical performance and heart failure.

Results

Basic characteristics

The main basic characteristics are found in Table 1 and 2. One hundred percent follow-up was obtained. Mean follow-up time after admittance was 949.98±533.93 days. One hundred sixty-two (53.6%) patients died during the period of follow up.

Gender

Out of the 302 subjects, 211 (69.9%) were women. The mean follow-up time was 1007.82±513.79 days for women and 815.87±558.10 days for men. The difference between the follow-up time for women and men was significant (p=0.004). The mortality risk within 4 years for women compared to men is significantly lower (Figure 1), with a total of 39.1% (p=0.002; HR = 0.609; 95% CI 0.442-0.838).

Age

The overall mean age was 85.94±6.38 years (range 65-102 years), with a mean age of 84.92±6.32 years (range 68-102) and 86.39±6.37 years (range 65-102 years) for men and women, respectively. The difference in mean was not significant. A higher age was correlated with a lower muscle mass (p=0.010; PCC= -0.190) and a lower SPPB score (p=0.009; PCC= -0.191). Age was not significant in the determination of the mortality risk (p=0.176; HR= 0.982; 95% CI 0.957-1.008).

Nutritional status

The mean score on the MNA-SF was 9.23±3.08 (range 0-14), with a mean of 9.67±2.71 and 9.04±3.22 for men and women respectively. There were 87 patients (28.8%) classified in the 'Malnourished' group, 127 patients (42.1%) in the 'Risk of malnutrition' group and 88 (29.1%) in the 'Normal nutritional status' group. Higher MNA-SF scores were correlated with longer follow-up time (p <0.001; PCC = 0.389), bigger muscle mass (p<0.001; PCC=0.301), better SPPB-scores (p=0.004; PCC=0.211) and higher muscle strength (p=0.033; PCC=0.157). There was a negative correlation between MNA-SF score and mortality (p<0.001; PCC= -0.288). The mortality risk within 4 years for patients in the 'Risk of malnutrition' group and 'Malnourished' group was, respectively, almost two (p=0.004; HR=1.840; 95% CI 1.217-2.782) and three (p<0.001; HR=2.953; 95% CI 1.924-4.531) times higher compared to the 'Normal nutritional status' group (Figure 1).

Muscle mass

Radiologic data were collected from 203 patients (67.2%), with an overall mean of 0.52±0.21 kg (range 0.131-1.285 kg). Of these, 139 (68.5%) were women with a mean of 0.47±0.16 kg (range 0.13-0.85 kg) and 64 (31.5%) were men with a mean of 0.65±0.24 kg (range 0.15-1.29 kg). In thirty nine patients a CT-scan could not be done because of the presence of prosthesis material. There was a significant difference in muscle mass between women and men (p<0.001). 164 patients were classified in the 'Low Muscle Mass' group, 39 patients in the 'Normal Muscle Mass' group. There was a positive correlation with follow-up time (p<0.001; PCC=0.260), SPPB-scores (p<0.001; PCC=0.426) and muscle strength (p<0.001; PCC=0.549). A negative correlation was observed with gender (p<0.001; PCC= -0.402) and mortality (p=0.031; PCC= -0.160). Patients in the 'Low Muscle mass' group had a 55.7% higher mortality risk within 4 years compared to the 'Normal Muscle Mass' group (p=0.005; HR=0.443; 95% CI 0.251-0.780) (Figure 1).

Muscle strength

Overall mean handgrip strength was 13.09±8.36 kg (range 0-50.0 kg). The mean handgrip strength in women was 10.24±5.81 kg (range 0-26.5 kg) and in men 19.58±9.62 kg (range 0-50 kg). This measurement could not be performed for thirty patients because of various reasons (e.g. paralysis). There was a significant difference between women and men (p<0.001), with a negative correlation between gender and handgrip strength (p<0.001; PCC= -0.535). A positive correlation existed between handgrip strength and SPPB-scores (p<0.001; PCC=0.348). The patients were subdivided within 2 groups, of which 252 (83.4%) patients were classified in the 'Low Muscle Strength' group and 20 (6.6%) in the 'Normal Muscle Strength' group. Patients in the 'Low Muscle Strength' group had a 78.5% higher mortality risk compared to the 'Normal Muscle Strength' group (p=0.003; HR=0.215; CI 95% 0.079-0.587) (Figure 1).

Physical performance

Mean SPPB-score was 3.69±3.18 (range 0-12). Women and men had a mean of 3.64±3.11 (range 0-11) and 3.80±3.35 (range 0-12) respectively. A total of twenty six patients were unable to perform the necessary tests to determine the SPPB score for different reasons (e.g. paralysis). There was no significant difference between women and men. The SPPB-scores were subdivided into 3 groups, with 168 patients (55.6%) in the 'Low SPPB-scores' group, 69 patients (22.8%) in the 'Intermediate SPPB-scores' group and 39 patients (12.9%) in the 'High SPPB-scores' group. SPPB-scores were found to be negatively correlated with mortality (p=0.002; PCC= -0.224) and showed a positive correlation with follow-up time (p<0.001; PCC=0.269). The mortality risk within 4 years for patients in the 'Low SPPB-scores' group was 59.3% higher compared to the 'High SPPB-scores' group (p=0.001; HR=0.407; 95% CI 0.237-0.702) and 55.7% higher compared to the 'Intermediate SPPB-scores' group (p<0.001; HR=0.443; 95% CI 0.290-0.676) (Figure 1).

Parameter		B	SE	*p*-value	HR	95% CI for HR Low - high
Gender*	Women cf. men	-0.474	0.164	0.004	0.623	0.452 - 0.859
Age**	-	-0.018	0.013	0.176	0.982	0.957 - 1.008
Nutritional status***	Malnourished cf. normal	1.083	0.218	0.000	2.953	1.924 - 4.531
	Risk cf. normal	0.610	0.211	0.004	1.840	1.217 - 2.782
Muscle Mass***	Normal cf. low	-0.815	0.289	0.005	0.443	0.251 - 0.780
Muscle Strength***	Normal cf. low	-1.537	0.512	0.003	0.215	0.079 - 0.587
Physical perf.***	High cf. low	-0.898	0.277	0.001	0.407	0.237 - 0.702
	Intermediate cf. low	-0.814	0.215	0.000	0.443	0.290 - 0.676
Heart failure***	Present cf. not present	0.365	0.175	0.037	1.440	1.022 - 2.029
Orthopedic surg.***	Present cf. not present	-0.104	0.185	0.574	0.902	0.628 - 1.295

*B= variable coefficient; SE= Standard error, HR= Hazard ratio; CI= Confidence interval. *Adjusted for the confounding variable age. **Adjusted for the confounding variable gender. ***Adjusted for the confounding variables gender and age.*

Table 3. Hazard ratios of each individual determinant in geriatric patients.

Heart failure

In 73 patients (24.2%) heart failure was present, in which 45 (61.6%) were women and 28 (38.4%) men. There were no relevant correlations with other determinants. The mortality risk within 4 years was 44% higher in patients suffering from heart failure (p=0.037; HR=1.440; 95% CI 1.022-2.029) (Figure 1).

Orthopedic surgery

Among the subjects, there were 80 (26.5%) patients who had orthopedic surgery, of which 58 (72.5%) patients were women and 22 (27.5%) were men. No relevant correlations were found. A history of orthopedic surgery was not a significant factor in the determination of the mortality risk (p=0.574; HR=0.902; 95% CI 0.628-1.295).

Overall survival model

After forward model building and consideration of confounding factors, only the predictor variables gender, nutritional status and physical performance could be considered as statistically significant in determining the 4 years mortality risk.

Discussion

To our knowledge, this is the first study to examine the relationship between parameters of sarcopenia, nutrition and comorbidities, and the 4-year mortality risk in hospitalized geriatric patients.

In this study, the 4-year mortality was negatively correlated with nutritional status, muscle mass and physical performance, and positively correlated with heart failure. No significant correlation was found between mortality and the variables age and orthopedic surgery.

Table 3 summarizes the most important findings of this study concerning the dependency of the 4-year mortality risk on the different measured variables. Adjusted for age and gender, the variables gender, nutritional status, muscle mass, muscle strength, physical performance and heart failure have been shown to be significant. Comparing the magnitude of these risks between the different subclasses, the 'Malnourished' group of patients have an almost three times higher mortality risk compared to the 'Normal nutritional status'. The 'Low SPPB-scores' group have a fifty percent higher risk compared to the 'High SPPB-scores' group. These data of hospitalized geriatric patients confirm the results of other studies in different populations[4,10,13,15,21-23]. Figure 1 gives an overview of the Kaplan Meier curves of all these significant class variables.

The variables age and orthopedic surgery were, on the other hand, not significant. Although age was not significant, the mortality risk seems to reduce with increasing age. This seems contradictory, but the presence of sarcopenia on a younger age can indicate a worse health status. The findings about the variable orthopedic surgery can raise the question what the functional benefits are for sarcopenic patients to undergo such surgery when there is no significant better or worse mortality outcome. Aging has metabolic effects on both bone and muscle and can explain the relation and simultaneous existence of both osteoporosis and sarcopenia, which are independent predictors of fragility fractures as a result of the higher fall risk in these patients[3,24]. The prevention of those fragility fractures and their associated consequences is one of the several reasons why it would be

recommended to undergo surgery. For example, to prevent dysfunction and immobility and to achieve more comfort in patients with a hip fracture. This study didn't seek to determine the effect of each specific orthopedic procedure on the mortality risk. It could however be interesting to investigate this issue in the future. In this study there were also no data related to the quality of life. It may be interesting to include this information in further studies as well.

When considering all these variables in one model, only gender, nutritional status and physical performance remained significant. A possible explanation for the disappearing of several, initially significant variables, can be due to the presence of confounding correlations between these variables.

During this study there were some difficulties in obtaining the complete data from all the patients during their hospitalization. First of all, this was due to the lack of informed consent for muscle mass measurements with a CT-scan in sixty of the patients. Secondly, there were some difficulties in obtaining information about the history of heart failure or orthopedic surgery in the period of 2012 up to and including 2016 via medical records. When in doubt, these patients were considered to not have experienced heart failure or had orthopedic surgery in the past 4 years. Also our methodology for determining the different subgroups of the parameters was different from the criteria provided by the EWGSOP[7]. In the latter, the cut-off value for the parameter muscle mass was based on the measurements obtained from dual energy X-ray absorptiometry (DXA) or bio impedance analysis (BIA). However, we preferred to integrate the muscle volume measured by CT over a distance of 10 cm. This method is more specific for detecting sarcopenia because it measures the cross sectional area, while the other techniques measure a skeletal muscle index[3]. We defined the cut-off value for these groups based on the mean muscle mass within the different gender groups. Also the cut-off value for the parameter physical performance was based on only one subtest (Gait-speed) in the EWGSOP, whereas in our study the total SPPB-score was used. Another limitation to this study is the fact that the obtained conclusions are only applicable to hospitalized geriatric patients and not to the well-functioning community-dwelling elderly. The strengths of this study were the large sample of hospitalized patients, the easily obtained data due to routinely performed tests during hospitalization and the complete follow-up.

The results from this study can be used for defining the mortality risk in hospitalized geriatric patients and, therefore, can provide the opportunity to perform better follow-up and plan earlier interventions in these patients. It also allows generating risk tables in the future. These tables can contain the most important prognostic variables to determine the mortality risk. For this, however, more and larger comparative studies will be necessary in the future.

Conclusion

In conclusion, the determinants which have the greatest prognostic value in predicting the four year mortality risk were gender, nutritional status and physical performance. It is thus recommended to measure the nutritional status as well, beside the different components of sarcopenia of every geriatric patient admitted to the hospital. This screening tool is easy to apply in the clinical practice and can help the health care practitioners to predict the mortality outcome of the patient. Therefore, it should be taken into account in standard screening protocols.

Acknowledgements

No funds were received for this study. The authors would like to thank the departments of Occupational Therapy, Physical therapy and Dietetics of the Saint-Elisabeth hospital for their cooperation. Also many thanks to dr. Agus Surjadjaja of the Radiology Department for performing the muscle mass measurements.

Author Contributions

S.L., R.D., M.V. and S.P. conceived and designed the study; M.V. and S.P. collected the data; S.L. and R.D. analyzed the data; S.L. and R.D. wrote the paper; S.P. revised the manuscript.

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