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META ANALYSIS

Meta-Analysis of Acute Sarcopenia among Hospitalized Elderly Patients

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Abstract

Objective: To determine the prevalence of acute sarcopenia in elderly hospitalised patients.

Search strategy: The electronic bibliographic databases used are MEDLINE via PUBMED and The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register). The search strategy included a combination of appropriate MeSH and other free-text terms including the following key words: "sarcopenia", "acute care", "hospitalisation", and "elderly". There was no language restriction for the searches. Abstracts and subsequently selected full studies reporting the prevalence of sarcopenia in elderly adults admitted to inpatient hospitals were reviewed as long as the diagnosis of sarcopenia included at least the assessment of muscle mass.

Selection criteria: Observational studies involving elderly Patient > 65 y/o, admitted in an acute care hospital with no sarcopenia. Diagnosis of sarcopenia upon discharged based on EWGSOP or AWGS definition.

Data collection and analysis: All published reports of all eligible studies were evaluated by two independent reviewers. Data were extracted data and pooled analysis was done on the different variables collected.

Main results: The present study identified six observational studies involving 2106 participants with 418 hospitalized elderly noted to have sarcopenia, showing a prevalence of 19.8%. The age of elderly patients with sarcopenia was significantly higher than those without sarcopenia by 2.91 years (95% CI, 2.18 to 3.65) while the BMI was significantly lower. No significant difference was noted in the proportion of male elderly with or without sarcopenia. A higher proportion of smokers were noted among those with sarcopenia. The risk of smokers for sarcopenia was 1.26x higher than non-smokers (RR = 1.26; 95% CI: 1.07-1.48). No significant difference was observed in the length of stay, but a higher risk for mortality (RR = 2.69; 95% CI: 1.96-3.69) and readmission (RR = 1.48; 95% CI: 1.27-1.72) was noted among hospitalized elderly patients with sarcopenia.

Conclusion: The results of this review showed that the prevalence of acute sarcopenia among elderly hospitalized patients was 19.8%. The age of elderly patients with sarcopenia was significantly higher than those without sarcopenia while the BMI was lower. The proportion of smokers was also higher among elderly patients with sarcopenia. Moreover, the results of this meta-analysis showed that the length of stay.was not significantly different between elderly patients with or without sarcopenia. However, mortality and readmission rate were significantly higher among elderly patients.

Keywords

Acute Sarcopenia, Elderly, Hospitalization

Introduction

Sarcopenia is a common disease associated with the ageing process wherein there is a degenerative loss of skeletal muscle mass, quality, strength and function that leads to physical disability, poor quality of life, functional decline, higher rate of fall, higher rate of hospitalizations, increase health care expenditures and death [1-4]. It was also found to be a consistent predictor of chronic disease progression, all-cause mortality, poorer functional outcomes, and higher postoperative complications [5].

The causes of sarcopenia in elderly population appear to be multifactorial and these are: Environmental causes, inflammation, disease triggers, hormonal changes, decrease nutrition and sedentary lifestyle [6]. Acute sarcopenia refers to acute loss of muscle mass and function associated with hospitalization and studies concerning the incidence of sarcopenia among older people admitted during hospital stay are few [7]. In older patients, besides the negative effect of the acute event, hospitalization itself might represent



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an additional stressor. After 3 days of hospitalization, elderly inpatients lost approximately the same amount of lean leg muscle mass as healthy older subjects experienced in 10 days of inactivity-approximately three-fold greater loss of lean leg muscle mass than a younger cohort confined to bed for 28 days [8,9].

Worldwide, the prevalence of sarcopenia is 10% and Asian people appear to have a higher prevalence of sarcopenia thanin any other regions. Its prevalence varies from 9.6-22.1% in men and 7.7-21.8% in women [10-12]. Majority of the studies regarding sarcopenia are in Europe and America. Current available studies in Asia have been published from eastern Asia, namely Japan, China, Taiwan, Korea and Thailand. The causes of sarcopenia in elderly population appears to be multifactorial, hence the objective of this study was to conduct a meta-analysis of reported prevalence of acute sarcopenia in elderly admitted patients.

Objective

General objective

The objective of this study was to conduct a metaanalysis of reported prevalence of acute sarcopenia in elderly hospitalised patients.

Specific objectives

- 1. To determine the prevalence of acute sarcopenia on elderly patients when admitted.
- 2. To identify risk factors for the development of sarcopenia at the time of admission and during hospitalization.
- 3. To determine the presence of acute sarcopenia among elderly patients with in-hospital outcomes i.e. length of hospital stay, length of bed rest, transfer to intensive units, hospital acquired pneumonia, mortality.

Methods

The meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.

Type of study & time period & target population:

Type of study: Retrospective

- Target Population-Geriatric patients > 65-yearold admitted in an acute care hospital.
- Time Period Studies published between January 1988 (chosen because the term "sarcopenia" was coined by Rosenberg in 1989) [13] and December 2019.

Inclusion criteria and Exclusion criteria for subject selection Inclusion criteria for the studies:

a) Elderly Patient \geq 65 y/o

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- b) Admitted in an acute care hospital with no sarcopenia
- c) Diagnosis of sarcopenia upon discharged based on EWGSOP or AWGS definition

Exclusion criteria:

a) Bedridden patients upon admission

Operational definitions:

 Sarcopenia- as defined by the Asian Working Group for Sarcopenia (AWGS), muscle mass measurements of 7.0 kg/m2 for men and 5.7 kg/ m2 for women by using bioimpedance analysis, handgrip strength (< 26 kg for men and < 18 kg for women), and usual gait speed (< 0.8 m/s).

Description of study procedure

The electronic bibliographic databases used are MEDLINE via PUBMED and The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register). The search strategy included a combination of appropriate MeSH and other free-text terms including the following key words: "sarcopenia", "acute care", "hospitalisation", and "elderly". There was no language restriction for the searches provided the abstracts are available in English. Abstracts and subsequently selected full studies reporting the prevalence of sarcopenia in elderly adults admitted to inpatient hospitals were reviewed irrespective of design, as long as the diagnosis of sarcopenia included at least the assessment of muscle mass.

Data were extracted independently by the reviewer according to a standardized data extraction form. The following data were extracted: Study population, participant demographics and baseline characteristics, reported prevalence of sarcopenia, method of sarcopenia diagnosis, and study methodology.

Data analysis

Overall effect for each meta-analysis was derived by using both random effects model. Whenever needed, a fixed effects model was utilized. For the outcomes mortality and readmission, since this is a binary measure, the pooled statistics were reported as the odds ratio (OR) between the experimental and control groups with 95% confidence intervals (CI). Other outcomes stated in the objective are transfer to intensive units and hospital acquired pneumonia, however, these were not reported in all the studies included in this meta-analysis. For binary outcomes, the number of subjects with an event and the total number of subjects in the group were extracted from the individual study. For numerical data, length of stay and length of bed rest, the mean and SD was used to calculate the mean difference (MD). Pooled estimates of the weighted mean differences and 95% CI were calculated using either a random effects



model if heterogeneity was found among studies, otherwise, a fixed-effects model was utilized. Statistical heterogeneity between studies was evaluated using Cochran's Q test and I-squared [14]. P values ≤ 0.05 was considered statistically significant. All meta-analyses were performed both with a fixed-effect and a random-effects model. Review Manager 5.2 (RevMan 5.2) was utilized in the analysis.

Results

The literature search and review retrieved a total of 398 citations (Figure 1). After screening of publications, 354 remaining papers were screened for eligibility. Of these, 324 were further excluded. The text of the remaining 30 citations was analyzed further in detail and only 6 met the inclusion criteria and were included in the meta-analysis [4,14-18].

Study characteristics

The present study identified six studies determining the prevalence of acute sarcopenia among hospitalized elderly. Table 1, Table 2 and Table 3 summarizes the characteristics of the included observational studies. Six studies [4,14-18] involving 2106 participants (418 with sarcopenia and 1665 without sarcopenia) met the inclusion criteria.

All six studies were observational studies. One study had subjects from a previous RCT, 1 is multicenter observational study and the others were all prospective observational studies. All participants were elderly. Although one study included elderly aged \ge 60 years, however, the minimum age was > 65-years-old.

A total of 418 participants were noted to have sarcopenia, showing a prevalence of 19.8%. In one study [15], 23 had uncertain diagnosis. The diagnosis of sarcopenia was based on the algorithm proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) or the AWGS. Muscle mass was quantified with the bioelectrical impedance analysis (BIA) and estimated using the equation developed by Janssen & Colleagues in four studies, while one study assessed muscle mass by measuring mid-arm muscle circumference (MAMC). Another study assessed muscle mass by measuring Appendicular Skeletal Muscle Mass (ASM) using validated equation in Chinese population. Muscle strength was assessed using handgrip dynamometer while physical performance was assessed using gait speed (4m).

Outcomes analyzed included length of stay, length of bed rest, transfer to intensive units, hospital acquired pneumonia, and mortality. However, none of the studies reported transfer to intensive units and hospital acquired pneumonia. Readmission was also collected and included in the outcome of the study.

Quality assessment

The methodology of each included trial was evaluated using the New Castle-Ottawa Scale (NOS). Of

1 Cent. etal. Isbyl (15) Constructions (15) Elder/y adults (15) Cent. etal. (15) Constructions (15) Constructions (16) Constructions (16) <th>No.</th> <th>Author, year, country</th> <th>Design/ Duration</th> <th>Participants</th> <th>Type</th> <th>c</th> <th>Criteria for Sarcopenia</th> <th>Tool Used to Assess Muscle Mass</th> <th>Tool Used to Assess Muscle Strength</th> <th>Tool Used to Assess Physical Performance</th> <th>Sarcopenia</th>	No.	Author, year, country	Design/ Duration	Participants	Type	c	Criteria for Sarcopenia	Tool Used to Assess Muscle Mass	Tool Used to Assess Muscle Strength	Tool Used to Assess Physical Performance	Sarcopenia
2 Garbala & Observational with suble medical view low low presents with suble medical view low low low low low low low low low lo		Cerri, et al. Italy [15]	Prospective Observational Study/3 months	Elderly adults ≥ 65 years hospitalized with malnutrition or at risk of malnutrition	Geriatrics	103	EWGSOP	Measured using BIA and estimated using the equation developed by Janssen & Colleagues	Hand Grip Dynamometer	Gait speed (4m)	With = 22 (21.4%) W/o = 58 (56.3%) Uncertain = 23 (22.3%)
3 Martone, et labyl 4 Observational patients 2.65 years internal work sarropenia at work sarropenia at mark baseline work sarropenia at mark baseline	5	Gariballa & Alessa, UK [14]	Observational Study, patients who took part in a previous RCT.	Subjects ≥ 65 years with stable medical condition	Geriatrics	432	EWGSOP	Was measured by mid-arm muscle circumference (MAMC)	Hand Grip Dynamometer		With = 44 (10.2%) W/o = 388 (89.8%)
4 Rossi, et al. Observational Caucasians ≥ 65 Gariatrics 119 EWGSOP Measured using the equation developed by using the equation developed by Min = 31 (26%) 1 Ruly [16] Cohort Study cognitively stable Paradestimated using the equation developed by Min = 31 (26%) Min = 31 (26%) 5 Vetrano. et al. Muticenter Patients ≥ 65 years F Janssen & Colleagues Min = 31 (26%) 5 Vetrano. et al. Muticenter Patients ≥ 65 years Geriatrics 770 EWGSOP Measured using BlA Hand Grip Min = 214 (28%) 6 Yang, et al. Muticenter Patients ≥ 65 years Geriatrics 770 EWGSOP Measured using BlA Hand Grip Min = 214 (28%) 6 Yang, et al. Muticenter Patients ≥ 65 years Geriatrics 770 EWGSOP Measured using BlA Hand Grip Min = 214 (28%) 6 Yang, et al. Prospective Subjects ≥ 60 years, et al. 770 EWGSOP Appendicular Skeltal Hand Grip Min = 29 (72%) 6 Yang, et al. Prospective Subjects ≥ 60 years, et al. Subject ≥ 60 years,	σ	Martone, et al. Italy [4]	Observational Study	Patients ≥ 65 years w/o sarcopenia at baseline In 12 acute care wards in Italy	Internal Med & Geriatrics	394	EWGSOP	Measured using BIA and estimated using the equation developed by Janssen & Colleagues	Dynamometer	Gait speed (4m)	With = 58 (14.7%) W/o = 336 (85.3%)
5Vetrano, et al, Italy [17]Multicenter ObservationalPatients ≥ 65 years770EWGSOPMeasured using BIAHand Grip DynamometerMith = 214 (28%)al, Italy [17]Observational StudyObservationalWith = 214 (28%)With = 214 (28%)With = 214 (28%)6Yang, et al. China [18]Prospective StudySubjects ≥ 60 years, of West China Hosp.Geriatrics288AWGSAppendicular Skeletal Muscle Mass (ASM)Mith = 49 (17.0%)6Yang, et al. China [18]Prospective StudySubjects ≥ 60 years, of West China Hosp.Geriatrics288AWGSAppendicular Skeletal Muscle Mass (ASM)Mith = 49 (17.0%)6Yang, et al. China [18]Prospective StudySubjects ≥ 60 years, of West China Hosp.Geriatrics288AWGSAppendicular Skeletal Muscle Mass (ASM)With = 49 (17.0%)6Yang, et al. StudyProspective of West China Hosp.Subjects ≥ 60 years, GeriatricsMith = 49 (17.0%)With = 239 (83.0%)	4	Rossi, et al. Italy [16]	Observational Cohort Study	Caucasians ≥ 65 cognitively stable	Geriatrics	119	EWGSOP	Measured using BIA and estimated using the equation developed by Janssen & Colleagues	Hand Grip Dynamometer	Gait speed (4m)	With = 31 (26%) (low muscle mass) W/o = 88 (74%) (normal muscle mass)
6 Yang, et al. Prospective Subjects ≥ 60 years, Geriatrics 288 AWGS Appendicular Skeletal Hand Grip Gait speed (4m) With = 49 (17.0%) China [18] Study of West China Hosp. of West China Hosp. In Chinese pop'n i	ប	Vetrano, et al, Italy [17]	Multicenter Observational Study	Patients ≥ 65 years	Geriatrics	770	EWGSOP	Measured using BIA	Hand Grip Dynamometer	Gait speed (4m)	With = 214 (28%) W/o = 556 (72%)
	Q	Yang, et al. China [18]	Prospective Observational Study	Subjects ≥ 60 years, in acute care ward of West China Hosp.	Geriatrics	288	AWGS	Appendicular Skeletal Muscle Mass (ASM) using validated equation in Chinese pop'n	Hand Grip Dynamometer	Gait speed (4m)	With = 49 (17.0%) W/o = 239 (83.0%)

Table 1: Characteristics of the Studies Included.

				1 91	JIE Z. FACIOI	s of variables Co	Jilipaleu					
No.	Author, year, country	z	Sarcopenia	Age (yrs)	F/M	BMI	NGH	Diabetes	SMI	ADL	Smoker	Alcohol
						(kg/m2)			(kg/m²)	Score		
-	Cerri, et al. Italy [15]	103	With = 22	87.4 ± 4.8	12/10	21.1 ± 4.2		7	7.7 ± 0.8*			
			W/o = 58	83.1 ± 7.9	36/22	23.9 ± 5.1		15	$10.3 \pm 1.2^{*}$			
			Uncertain = 23	84.2 ± 5.9	13/10	21.5 ± 4.5		4	7.8±0.7*			
2	Gariballa & Alessa,	432	With = 44	79.0 ± 7.0	29/15						1	5
	UK [14]		W/o = 388	77.0 ± 6.0	176/212						70	51
3	Martone, etal.	394	With $= 58$	82.0 ± 7.2	29/29	25.0 ± 3.8	38	12	8.4 ± 1.5	2.1 ± 2.3		
-	Italy [4]		W/o = 336	79.2 ± 6.2	182/154	27.6 ± 4.9	256	114	9.0 ± 1.8	1.2 ± 1.7		
4	Rossi, et al.	119	With $= 31$	82.9 ± 6.5	18/13	22.5±3.5			6.8 ± 1.0	5.7 ± 0.6		
	Italy [16]		W/o = 88	79.5 ± 6.9	28/60	27.6 ± 4.7			9.0 ± 1.3	5.8±0.7		
5	Vetrano, et al.	770	With $= 214$	82.8±6.9	101/113		154	55		2.6 ± 2.4	103	52
	Italy [17]		W/o = 556	80.0 ± 7.1	327/229		429	179		2.1 ± 2.4	219	172
9	Yang, et al. China [18]	288	With = 49	83.7 ± 5.9	11/38	19.0 ± 2.5	23	6	6.7 ± 1.0		7	4
			W/o = 239	80.5 ± 6.6	52/187	23.3 ± 3.3	151	77	7.8 ± 1.0		21	29
SMI-Sk	eletal Mass Index; *among ma	les; AE	DL-Activities of Dai	ily Living								
Table	3: Outcomes.											
No.	Author, year, country	2	Sarcope	enia	Leng	th of Stay (days)) Fe	ength of Bed re	st	Mortality	Rea	dmission
~	Cerri, et al. Italy [15]	103	With $= 2$	2	9 (6-1	4.3)				7 (31.8%)	ł	
			W/o = 58	8	10 (8-	14)	1			3 (5.2%)	1	
			Uncertai	in = 23	11 (8-	.15.3)				1 (4.3%)	ł	
5	Gariballa & Alessa, UK [1-	4] 432	With = 4	4	13.4 ±	Ł 8.8				12 (27%)	24 (55%)
			W/o = 3	88	9.4 ±	7.0				38 (10%)	125	(32%)
3	Martone, et al. Italy [4]	394	With $= 5$	8	12.1 ±	± 10.3	5.	1 ± 6.7		1	ł	
			W/o = 3;	36	9.9 ±	7.6	ĉ	2 ± 5.3		1	1	
4	Rossi, et al. Italy [16]	119	With = 3	31	1		1			ł	1	
			W/o = 8{	8	ł					ł	ł	
5	Vetrano, et al.	770	With $= 2$	214	-		1			10 (6%)	ł	
	Italy [17]		W/o = 5{	56	1					12 (2%)	1	

.

9

40 (81.6%) 143 (59.8%)

20 (40.8%) 38 (15.9%)

| |

| |

With = 49 W/o = 239

288

Yang, et al. China [18]

Italy [17]

No.	Author, year, country	Selection	Comparability	Outcome/Exposure	Total Score
		(4 stars)	(2 stars)	(3 stars)	(9 stars)
1	Cerri, et al. Italy [15]	3	2	2	7
2	Gariballa & Alessa, UK [14]	3	2	3	8
3	Martone, et al. Italy [4]	4	2	2	8
4	Rossi, et al. Italy [16]	3	2	2	7
5	Vetrano, et al, Italy [17]	3	1	3	7
6	Yang, et al. China [18]	3	2	3	8





Figure 2: Comparison of age between patients with or without sarcopenia (fixed effects model).

	With Sarco	penia	Without Sarco	openia		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% C
Cerri, et al 2015	10	22	22	58	9.6%	1.20 [0.68, 2.11]	_1
Gariballa & Alessa 2013	15	44	212	388	13.4%	0.62 [0.41, 0.95]	
Martone, et al 2017	29	58	154	336	18.3%	1.09 [0.82, 1.45]	
Rossi, et al 2014	13	31	60	88	12.9%	0.62 [0	
Vetrano,et al 2014	113	214	229	556	23.0%		
Yang, et al 2016	38	49	187	239			
Total (95% CI)		418					
Total events	218						
Heterogeneity: Tau ² = 0.0							
Test for overa							

Figure 3: Comparison of the distribution of male elderly patients with or without sarcopenia (random effects model).

the 6 citations included, three studies scored 7/9 [15-17] on the NOS, and 3 scored 8/9 [4,14,18], indicating good quality (Table 4).

Synthesis of results (pooled analysis)

Comparison of age of elderly patients with or without sarcopenia: All six studies [4,14-18] compared age of elderly hospitalized patients with or without sarcopenia and the analysis of pooled data demonstrated that there was a significant difference noted using the fixed effects model (Z = 7.78; p < 000001) (Figure 2). The age of elderly patients with sarcopenia was significantly higher than those without sarcopenia by 2.91 years (95% CI, 2.18 to 3.65). A fixed effects model was used because there was no significant (p = 0.87) heterogeneity noted in the studies included and the $I_2 = 0\%$. **Comparison of the proportion of male elderly patients with or without sarcopenia:** Again all six studies [4,14-18] compared data on the sex distribution of elderly hospitalized patients with or without sarcopenia and the analysis of pooled data demonstrated that there was no significant difference noted in the proportion of males elderly with or without sarcopenia using the random effects model (Z = 0.33; p = 0.74) (Figure 3). There was a significant (p = 0.003) heterogeneity noted in the studies included and the I_2 = 73%, hence, a random effects model was preferred in the analysis over the fixed effects model.

Comparison of BMI of elderly patients with or without sarcopenia: Four studies [4,15,16,18] compared BMI of elderly hospitalized patients with

	With Sa	arcope	enia	Without	Sarcop	enia		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 9
Cerri, et al 2015	21.1	4.2	22	23.9	5.1	58	16.2%	-2.80 [-4.99, -0.61]	
Martone, et al 2017	25	3.8	58	27.6	4.9	336	28.6%	-2.60 [-3.71, -1.49]	
Rossi, et al 2014	22.5	3.5	31	27.6	4.7	88	22.6%	-5.10	
Yang, et al 2016	19	2.5	49	23.3	3.3	239	3		
Total (95% CI)			160						
Heterogeneity: Tau ² =	0.89; Chi								
Testfor overall e									

Figure 4: Comparison of BMI between patients with or without sarcopenia (random effects model).

	With Sarco	penia	Without Sarc	openia		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 9
Martone, et al <mark>20</mark> 17	38	58	256	336	20.6%	0.86 [0.71, 1.05]	
Vetrano, et al 2014	154	214	429	556	65.3%	0.93 [0.85, 1.03]	
Yang, et al 2016	23	49	151	239	14.1%	0.7	
Total (95% CI)		321					
Total events	215						
Heterogeneity: Chi ² = :	2.31, df						
Test for overall e							

Figure 5: Comparison of HPN between patients with or without sarcopenia (fixed effects model).

	With Sarcor	oenia	Without Sarco	openia	Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95%	
Cerri, et al 2015	2	22	15	58 4.9%	0.35 [0.09, 1.41]		
Martone, et al 2017	12	58	114	336 20.0%	0.61 [0.36, 1.03]		
Vetrano, et al 2014	55	214	179	556 59.4%	0.80 [0.62		
Yang, et al 2016	9	49	77	239 15.6%			
Total (95% CI)		343					
Total events	78						
Heterogeneity: Chi ² = 2	2.61, d						
Test for overall							

Figure 6: Comparison of diabetes between patients with or without sarcopenia (fixed effects model).

or without sarcopenia and the analysis of pooled data demonstrated that there was a significant difference noted using the fixed effects model (Z = 7.78; p < 000001) (Figure 4). The BMI of elderly patients with sarcopenia was significantly lower than those without sarcopenia by 3.75 (95% CI, -4.90 to -2.60). A random effects model was used because there was a significant (p = 0.03) heterogeneity noted in the studies included and the $I_2 = 68\%$.

Comparison of HPN between elderly patients with or without sarcopenia: Three studies [4,17,18] compared data on the proportion hypertension among elderly hospitalized patients with or without sarcopenia, and the analysis of pooled data demonstrated that there was a significant difference noted in the proportion of hypertension among elderly with or without sarcopenia (Z = 2.66; p = 0.008) (Figure 5). The study showed that a lower proportion of patients with hypertension was noted among those with sarcopenia than those without sarcopenia which does not indicate that its a risk factor as shown by the RR that is < 1 (RR=0.89; 95% CI: 0.82-0.97). A fixed effects model was used because there was no significant (p = 0.32) heterogeneity noted in the studies included although the I₂ = 13%.

Comparison of diabetes between elderly patients with or without sarcopenia: Four studies [4,15,17,18] compared data on the proportion diabetes among elderly hospitalized patients with or without sarcopenia, and the analysis of pooled data demonstrated that there was a significant difference noted in the proportion of hypertension among elderly with or without sarcopenia (Z = 3.22; p = 0.001) (Figure 6). The study showed that a lower proportion of patients with diabetes was noted among those with sarcopenia than those without sarcopenia (RR = 0.70; 95% CI: 0.57-0.87). A fixed effects model was used because there was no significant (p = 0.46) heterogeneity noted in the studies included and the $I_2 = 0\%$.

Comparison of Skeletal Mass Index (SMI) of elderly patients with or without sarcopenia: Four studies [4,15,17,18] compared SMI of elderly hospitalized patients with or without sarcopenia and the analysis of pooled data demonstrated that there was a significant difference noted using the random effects model (Z = 3.67; p = 0.0002) (Figure 7). The SMI of elderly patients with sarcopenia was significantly lower than those without sarcopenia by 1.62 (95% CI, -2.48 to -0.75). A random effects model was used because there was a significant (p < 0.00001) heterogeneity noted in the studies included and the $I_2 = 95\%$.

Comparison of Activities Of Daily Living (adl) of elderly patients with or without sarcopenia: Three studies [4,16,17] compared ALD of elderly hospitalized patients with or without sarcopenia and the analysis of pooled data demonstrated that there was no significant difference noted using the random effects model (Z = 1.32; p = 0.19) (Figure 8). A random effects model was used because there was a significant (p-0.002) heterogeneity noted in the studies included and the I₂ = 84%.

Comparison of smoking between elderly patients with or without sarcopenia: Three studies [14,17,18] compared data on the proportion smokers among elderly hospitalized patients with or without sarcopenia, and the analysis of pooled data demonstrated that there was a significant difference noted in the proportion of



Figure 7: Comparison of skeletal mass index (smi) between patients with or without sarcopenia (random effects model).

	Expe	rimen	tal	Without	Sarcop	enia		Mean Difference		Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl		IV,	Random, 959	% CI	
Martone, et al 2017	2.1	2.3	58	1.2	1.7	336	27.6%	0.90 [0.28, 1.52]				·	_
Rossi, et al 2014	5.7	0.6	31	5.8	0.7	88	37.8%	-0.10 [-0.36, 0.16]					
Vetrano, et al 2014	2.6	2.4	214	2.1	2.4	556	<mark>34.7%</mark>	0.50 [0.12, 0.88]					
Total (95% CI)			303			980	100.0%	0.38 [-0.19, 0.95]					
Heterogeneity: Tau ² =	0.21; Ch	i² = 12	.50, df=	= 2 (P = 0.0	002); l² :	= 84%			-	1		1	
Test for overall effect:	Z = 1.32	(P = 0	.19)						Favo	ours [w/ Sarco	penia] Favou	irs [w/o Sard	openia

Figure 8: Comparison of activities of daily living (adl) between patients with or without sarcopenia (random effects model).

	With Sarcop	enia	Without Sarco	penia		Risk Ratio			Risk Ratio) () () () () () () () () () (
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	1	M-H	I, Fixed, 95	5% CI	
Gariballa & Alessa 2013	11	44	70	388	10.0%	1.39 [0.80, 2.41]			-		
Vetrano, et al 2014	103	214	219	556	85.0%	1.22 [1.03, 1.45]			-		
Yang, et al 2016	7	49	21	239	5.0%	1.63 [0.73, 3.61]					
Total (95% CI)		307		1183	100.0%	1.26 [1.07, 1.48]				•	
Total events	121		310						312		
Heterogeneity: Chi² = 0.62	df = 2 (P = 0.	73); l² =	0%				0.2	0.5	1	2	5

Figure 9: Comparison of smoking between patients with or without sarcopenia (fixed effects model).



Figure 10: Comparison of alcohol drinking between patients with or without sarcopenia (fixed effects model).



Figure 11: Comparison of length of stay (in days) between patients with or without sarcopenia (random effects model).

smokers among elderly with or without sarcopenia (Z = 2.77; p = 0.006) (Figure 9). The study showed that a higher proportion of smokers were noted among those with sarcopenia than those without sarcopenia. The risk of smokers for sarcopenia was 1.26x higher than non-smokers (RR = 1.26; 95%CI: 1.07-1.48). A fixed effects model was used because there was no significant (p = 0.73) heterogeneity noted in the studies included and the $I_3 = 0\%$.

Comparison of alcohol drinking between elderly patients with or without sarcopenia: Three studies [14,17,18] gave data on the comparison of alcohol drinking among elderly hospitalized patients with or without sarcopenia, and the analysis of pooled data demonstrated that there was a significant difference noted in the proportion of alcohol drinkers among elderly with or without sarcopenia (Z =1.93; p = 0.05) (Figure 10). The study showed that a lower proportion of alcohol drinkers were noted among those with sarcopenia than those without sarcopenia (RR = 0.78; 95% CI: 0.61-1.00). A fixed effects model was used because there was no significant (p = 0.93) heterogeneity noted in the studies included and the $I_2 = 0\%$.

Comparison of outcomes

Comparison of Length of Stay (in days) between elderly patients with or without sarcopenia: All six studies [4,14-18] compared length of stay between elderly hospitalized patients with or without sarcopenia and the analysis of pooled data demonstrated that there was no significant difference noted using the random effects model (Z = 1.20; p = 0.23) (Figure 11). A random effects model was used because there was a significant (p = 0.04) heterogeneity noted in the studies included and the I_2 = 69%.

Comparison of mortality between elderly patients with or without sarcopenia: Four studies [14,15,17,18] compared data on mortality among elderly hospitalized patients with or without sarcopenia, and the analysis of pooled data demonstrated that there was a significant difference noted (Z = 6.13; p < 0.00001) (Figure 12). The study showed that risk for mortality among elderly patients with sarcopenia was almost 3x higher than those without sarcopenia (RR = 2.69; 95%CI: 1.96-3.69). A fixed effects model was used because there was no significant (p = 0.56) heterogeneity noted in the studies included and the l₂ = 0%.

Comparison of readmission between elderly patients with or without sarcopenia: Two studies [14,18] compared data on readmission among elderly hospitalized patients with or without sarcopenia, and the analysis of pooled data demonstrated that here was a significant difference noted (Z = 4.94; p < 0.00001) (Figure 13). The study showed that risk for readmission among elderly patients with sarcopenia was 1.48x higher than those without sarcopenia (RR = 1.48; 95%CI: 1.27-1.72). A fixed effects model was used because there was no significant (p = 0.20) heterogeneity noted in the studies included although the I_2 = 38%.

Discussion

A total of 398 relevant published literatures were

	With Sarcor	enia	Without Sarce	openia		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	1	M-I	I, Fixed, 95%	6 CI	
Cerri, et al 2015	7	22	3	58	5.6%	6.15 [1.74, 21.69]			1. Starter 1. Starter1		
Gar <mark>iballa &</mark> Alessa 2013	12	44	38	388	26.3%	2.78 [1.58, 4.92]			-	<u></u>	
Vetrano, et al 2014	10	214	12	556	22.7%	2.17 [0.95, 4.94]					
Yang, et al 2016	20	49	38	230	45.4%	2.47 [1.58, 3.86]			-		
Total (95% CI)		329		1232	100.0%	2.69 [1.96, 3.69]			•		
Total events	49		91								
Heterogeneity: Chi ² = 2.0	8, <u>df</u> = 3 (P = 0.	56); l² =	0%						<u> </u>		
Test for overall effect: Z =	6.13 (P < 0.00	001)					0.01 Favou	0.1 Irs [w/Sarcor	1 Denia <u>l Favou</u>	10 <u>رچ (</u> w/o Sarc	openia]

Figure 12: Comparison of mortality between patients with or without sarcopenia (fixed effects model).

	With Sarcop	enia	Without Sarco	penia		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	1	M-	H, Fixed, 95%	CI	
Gariballa & Alessa 2013	24	44	125	388	34.4%	1.69 [1.25, 2.30]			-		
Yang, et al 2016	40	49	143	239	65.6%	1.36 [1.15, 1.61]					
Total (95% CI)		93		627	100.0%	1.48 [1.27, 1.72]			۲		
Total events	64		268								
Heterogeneity: Chi ² = 1.6	2, df=1 (P=0.	20); l ² =	38%					-	-	1	
Test for overall effect: Z =	4.94 (P < 0.00	001)					0.01 Favou	0.1 Jrs [w/ Sarco	1 penia] Favour	10 s [w/o Sarce	100 openia]

Figure 13: Comparison of readmission between patients with or without sarcopenia (fixed effects model).

searched in *PubMed*, *MEDLINE*, and *Cochrane*. Six observational studies were included in the metaanalysis after screening [4,14-18]. The 6 included studies were of good quality based from the NOS score. Of the 2106 hospitalized elderly patients, 418 (19.8%) had sarcopenia. The results of this meta-analysis showed that the age of elderly patients with sarcopenia was significantly higher than those without sarcopenia.

In some of the analysis, heterogeneity was noted among the included studies. However, in majority of the analysis, heterogeneity was not observed. This is due to the uniform criteria for the identification of sarcopenia among the elderly patients and the meta-analysis only included a specific group of patients that is elderly with acute sarcopenia. In some studies, the heterogeneity is usually due to the inconsistency in the study design, especially in terms of the selection of participants, interventional strategy, and criteria for identifying outcomes.

Our systematic review has a series of strengths. We conducted the review according to the recommendations stated in The Cochrane Handbook for Systematic Review of Interventions. We set predefined participants, outcomes, and comparisons in order, to avoid biases in the review process. As to the author's belief, we performed an extensive literature search to identify relevant studies based on our predefined inclusion criteria.

However, any meta-analysis is only as good as the

constituent studies. All studies included in our analysis may have had methodological limitations. Several operational definitions of sarcopenia are currently proposed in the scientific literature. Although the definition proposed by the EWGSOP is one of the most widely used in current epidemiological studies, it still needs to obtain scientific validation and be recognized as able to predict the health and clinical outcomes of sarcopenia. The present systematic review provides key elements favorable to this validation. Indeed, the majority of studies identified by this systematic review showed an association between sarcopenia, as defined by the EWGSOP, and health-related clinical outcomes such as mortality and readmission.

Although the included studies were not significantly heterogeneous, given the small number of studies, statistical conclusions on determinants of heterogeneity might be flawed. Further, we cannot fully exclude publication bias. Although a statistical test for the detection of publication bias can be performed, however, because there are < 10 studies, we are aware that these tests have very low power in the meta-analysis of only a few studies. To limit the risk of publication bias, we did not impose restrictions by language on the publication.

Conclusion

In summary, this meta-analysis showed that the prevalence of acute sarcopenia among elderly hospitalized patients was 19.8%. The age of elderly patients with sarcopenia was significantly higher than those without sarcopenia while the BMI was lower. The proportion of smokers was also higher among elderly patients with sarcopenia. Moreover, the results of this meta-analysis showed that the length of stay was not significantly different between elderly patients with or without sarcopenia. However, mortality and readmission rates were significantly higher among elderly patients with acute sarcopenia.

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