Prevalence of malnutrition in COVID-19 inpatients: the Nutricov study

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Abstract

Background: Recent ESPEN guidelines highlighted the interest of prevention, diagnosis and treatment of malnutrition in the management of coronavirus disease 19 (COVID-19) patients. The aim of our study was to evaluate the prevalence of malnutrition in patients hospitalized for COVID-19.

Methods: Prospective observational cohort study on COVID-19 inpatients admitted to a tertiary hospital. Malnutrition was diagnosed according to the Global Leadership Initiative on Malnutrition two-step approach. Patients were divided in two groups according to the diagnosis of malnutrition. Covariate selection for the multivariate analysis was based on *P* value <0.2 in univariate analysis, with a logistic regression model and a backward elimination procedure. A partitioning of the population was represented using a Classification and Regression Tree analysis.

Results: 80 patients were prospectively enrolled in the study. Thirty patients (37.5%) had criteria for malnutrition. The need for ICU admission (n=46, 57.5%) was similar in the two groups. Three patients who died (3.75%) were malnourished. Multivariate analysis exhibited that low BMI (OR=0.83, 95% CI [0.73-0.96], p=0.0083), dyslipidemia (OR=29.45, 95% CI [3.12-277.73], p=0.0031), oral intakes reduction <50% (OR=3.169, 95% CI [1.04-9.64], p=0.0422) and GFR (CKD-EPI) at admission (OR=0.979, 95% CI [0.96-0.998], p=0.0297) were associated with the occurrence of malnutrition in COVID-19 inpatients.

Conclusions: We demonstrate the existence of a high prevalence of malnutrition (37.5%) in a general cohort of COVID-19 inpatients according to GLIM criteria. Considering this high prevalence, nutritional support in COVID-19 care seems an essential element.

Trial registration: Ethical Committee N° 2020-A01237-32)(RC31/20/0165 NUTRI-COV

Background

Coronavirus disease 2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) appeared in China in December 2019 and is spreading worldwide [1, 2]. It can evolve to pneumonia requiring hospitalization up to severe Acute Respiratory Distress Syndrome (ARDS) managed in Intensive Care Unit (ICU) [3]. Infectious respiratory diseases lead to malnutrition, which can worsen the prognostic [4, 5]. In COVID-19 population, studies have reported that about half of the patients describe olfactory and gustatory dysfunction [6–8]. These disorders may contribute to a reduction in nutritional intakes. Li and *al*. showed a high prevalence of malnutrition (52.7%) on a cohort of 182 elderly patients with COVID-19 [9]. Recent ESPEN (European Society of Parenteral and Enteral Nutrition) guidelines highlighted the interest of prevention, diagnosis and treatment of malnutrition in the management of COVID-19 patients [10]. However, to date there are no data about the prevalence of malnutrition in patients hospitalized for COVID-19.

The aim of our study was to evaluate the prevalence of malnutrition in patients hospitalized for COVID-19.

Methods

This was a prospective observational cohort study (NUTRI-COV) conducted in Toulouse tertiary hospital from March to April 2020.Approval for this study (Ethical Committee N° 2020-A01237-32)(RC31/20/0165 NUTRI-COV) was provided by the 'Comité de Protection des Personnes OUEST I', France on March 2020. All patients were included in this observational study after verification of informed consent.

Patients

Eligibility criteria were as follows: (1) age > 18 years, (2) SARS-CoV-2 pneumonia (confirmed by RT-PCR, (3) hospitalization in wards or ICU, (4) without end-of-life decisions, (5) affiliated to social security. Patients were excluded if they were pregnant or if they refused to participate.

Procedures

At admission, patients were examined by medical practitioner who collected the following data: weight, body mass index (BMI) calculation, recent weight loss, daily oral intake self-reported during the week prior to hospitalization, self-reported factors influencing oral intake reduction, NRS-2002 (Nutrition Risk Screening 2002).

During the hospitalization, daily oral intake was recorded by specialist dietitian.

Demographic characteristics, comorbidities, treatments and biologic data were collected from the patient medical record including C reactive protein (CRP), albuminemia, protidemia, serum creatinine, glomerular filtration rate (GFR) (CKD-EPI formula), lymphocyte count, D-dimers at admission.

Malnutrition was diagnosed according to the Global Leadership Initiative on Malnutrition (GLIM) two-step approach defined by the association of one phenotypic criterion (especially non-volitional weight loss, low BMI) and one etiologic criterion (reduced food intake or assimilation, disease burden/inflammatory condition) [11].

To estimate muscle mass, the pectoralis muscle area was analyzed according to Morley et *al*. [12]. Based on chest CT scans which were routinely performed as part of COVID-19 management, pectoralis muscle area was measured by a trained radiologist. For comparability, pectoralis muscle area was indexed to body surface area (pectoralis muscle index) (expressed in cm^2/m^2) [13].

End-points

The primary end-point of the study was the prevalence of malnutrition defined by the number of malnourished patients on the total number of studied patients.

The secondary end-points were: the prevalence of severe malnutrition (BMI < 17 kg/m^2 and/or > 10% non-volitional weight loss in one month and/or albuminemia < 30 g/L and/or NRS-2002 ≥ 5), pectoralis

muscle index on chest CT scan and the association between malnutrition and outcome (need for ICU admission, hospital and ICU length of stay, mechanical ventilation duration, in-hospital mortality).

Statistical analysis

First, variables distribution was verified with Shapiro Wilk test. Patients were divided in two groups according to the diagnosis of malnutrition. Then, data are presented as median and interquartile ranges or mean and standard deviation. Qualitative data are expressed as numbers and percentages.

To compare the different parameters, parametric and non-parametric tests were used as appropriate (t test or Mann and Whitney for quantitative variables and *chi2* or Fisher's exact test for qualitative variables).

Covariate selection for the multivariate analysis was based on P value < 0.2 in univariate analysis, with a logistic regression model and a backward elimination procedure. For the validation of the selected model, we used the Hosmer and Lemeshow (goodness of fit test), the percentage of prediction of the model and its area under the curve. To highlight coavariates associated with malnutrition, a partitioning of the population was represented using a Classification and Regression Tree (CART) analysis. The advantage of this multivariate analysis approach is to describe the means of distribution of the population in homogeneous groups according to the existence of malnutrition and the covariates selected from the multidimensional analysis.

Statistical analyses were conducted using SPSS® for Window version 24 (IBM Corporation, Chicago, IL). A p-value ≤ 0.05 was considered statistically significant.

Results

Characteristics of the population

From March to April 2020, 80 patients were prospectively enrolled in the study. The baseline characteristics of the patients are shown in Table 1. Seventeen patients (21.2%) were over 70 years old. The median time from the onset of COVID-19 symptoms to hospitalization was 7 [5.5–11] days. Patients reported dysgeusia (27.8%), anorexia (27.8%), asthenia (21.5%) and anosmia (20.3%). Thirty-seven (46.2%) declared a reduction in oral intake of more than 50%.

Table 1
Baseline characteristics of the population.

	General characteristics of the population at admission n = 80	
	Median [25-75P]	Min-Max
Demographic characteristics		
Age (years)	59.5 [49.5–68.5]	19–87
Sex ratio (M/F)	60 (75%) / 20 (25%)	-
SAPS II	36 [29–44]	8–76
In-hospital mortality	3 (3.75%)	-
Basis weight (kg)	87.5 [76–100]	61–135
Weight at admission (kg)	83 [72-95.5]	58–130
Absolute weight loss (kg)	-3.8 [-6- -2]	0- -9.3
BMI (kg/m^2)	28.3 [25–31]	20.4–46.8
>50% oral intakes reduction*	37 (46.2%)	-
NRS-2002	4 [3–5]	2–7
Medical history		
Active smoking	9 (11.3%)	-
Diabetes	24 (30%)	-
Dyslipidemia	8 (10%)	-
Hypertension	34 (42.5%)	-
Organ transplantation	10 (12.5%)	-
Onco-hematologic disease	10 (12.5%)	-
Paraclinic parameters		
Albuminemia (g/L) (n = 65)	24 [18–27]	12–39
Prealbuminemia (g/L) (n = 56)	0.12 [0.085–0.22]	0.03–0.76
CRP (mg/mL) (n = 75))	88 [43.8-133.4]	2.5–403
Serum creatinine (µmol/L)	83.5 [66.5–122]	36–680

	General characteristics of the population at admission n = 80	
GFR (ml/min/1.73 m^2)	82 [53–100]	5-118
Kaliemia (mmol/L)	3.5 [3.3–3.7]	2.5–4.5
Phosphataemia (mmol/L) (n = 66)	0.77 [0.61–0.94]	0.29–1.35
Magnesemia (mmol/L) (n = 51)	0.8 [0.5–1.31]	0.5–1.31

Values were expressed as medians [25th-75th percentiles] or number (%). *7days before admission. SAPSII: Simplified Acute Physiology Score; BMI: Body Mass Index; NRS-2002: Nutrition Risk Screening; CRP: C - reactive protein; GFR: Glomerular Filtration Rate.

Primary outcome

Thirty patients (37.5%) had criteria for malnutrition of which 21/30 (70%) met criteria for severe malnutrition. The comparison between patients with malnutrition or not is presented in Table 2. They were comparable except for the glomerular filtration rate (CKD-EPI) at arrival, more impaired in the malnutrition group (71.5 [41–91] versus 85.5 [64–101] ml/min/1.73 m^2).

Secondary outcomes

Twenty-one (26%) patients met criteria for severe malnutrition. NRS-2002 was more elevated in malnourished patients (5 [4–5]) in comparison with patients without malnutrition (4 [3–5]) (p = 0.026). Serum albumin concentration was 25 [17-29.3] g/L in the group without malnutrition versus 20.5 [18-25.5] g/L in the malnutrition group (p = 0.162). Hypoalbuminemia (< 30 g/L) was similar between the two groups (75.6% (n = 31) versus 91.7% (n = 22), p = 0.11) respectively in the group without malnutrition in comparison with malnutrition group. Pectoralis muscle index was not different between the groups without malnutrition versus the malnutrition group (respectively 7.40 [5.81–9.3] versus 7.448 [4.88–9.64] cm^2/m^2, p = 0.644).

The need for ICU admission (n = 46, 57.5%) was similar in the two groups, respectively 56% (n = 28) in the no malnutrition group versus 60% (n = 18) in the malnutrition group (p = 0.72). There was not statistical difference between mechanical ventilation duration, ICU and hospital lengths of stay between the two groups.

Table 2
Comparison between patients with malnutrition or not.

	No malnutrition **n = 50**	**Malnutrition** **n = 30**	***P* value**
Demographic characteristics			
Age (years)	57 [49–65]	63.5 [53–69]	0.116
Sex ratio (M/F)	32 (72%)/14(28%)	24 (80%)/6 (20%)	0.427
SAPS II	37 [29-47.5]	34 [26–43]	0.499
In-hospital mortality	0 (0%)	3 (10%)	**0.049**
Basis weight (kg)	89.5 [79–102]	86.9 [73–99]	0.253
Weight at admission (kg)	87.3 [76–100]	80.9 [67–92]	**0.029**
Absolute weight loss (kg)	-3 [-3 - -1.5]	-6 [-7 - -6]	**< 0.0001**
BMI (kg/m^2)	28.4 [25.8–32.8]	26.4 [22.8–30.6]	**0.033**
>50% oral intakes reduction*	19 (38%)	18 (60%)	0.058
NRS-2002	4 [3–5]	5 [4–5]	**0.026**
Medical history			
Active smoking	6 (12%)	3 (10%)	0.999
Diabetes	12 (24%)	12 (40%)	0.108
Dyslipidemia	2 (4%)	6 (20%)	**0.0185**
Hypertension	20 (40%)	14 (46.7%)	0.477
Organ transplantation	5 (10%)	5 (16.7%)	0.485
Onco-hematologic disease	4(8%)	6 (20%)	0.16
COVID-19 characteristics			
Delay between onset of symptoms and hospitalization (days)	7.5 [6–11]	7 [5–11]	0.671
Dysgeusia	11 (22%)	11 (36.7%)	0.130

Values were expressed as medians [25th-75th percentiles] or number (%). *7 days before the admission. SAPS II: Simplified Acute Physiology Score II; BMI: Body Mass Index; NRS-2002: Nutrition Risk Screening. COVID: CoronaVirus Disease; CRP: C reactive Protein; GFR: Glomerular Filtration Rate. Results are expressed as median and [25–75] percentiles or numbers and percentages. P < 0.05 is significant.

	No malnutrition n = 50	Malnutrition n = 30	*P* value
Anosmia	9 (18%)	7 (23.3%)	0.516
Anorexia	13 (26%)	9 (30%)	0.633
Asthenia	13 (26%)	4 (13.3%)	0.206
Paraclinic parameters			
Albuminemia (g/L)	25 [17-29.3]	25 20.5[18-25.5]	0.162
Prealbuminemia (g/L)	0.11 [0.07–0.24]	0.13 [0.09–0.19]	0.689
CRP (mg/mL)	87 [39.5–128]	96 [5-154.8]	0.414
Serum creatinine (µmol/L)	80.5 [63–107]	101.5 [69–153]	0.060
GFR (ml/min/1.73 m^2)	85.5 [64–101]	71.5 [41–91]	**0.020**
Pectoralis muscle area (cm^2)	22.35 [16.4–27.6]	22.2 [16-28.6]	0.768
Pectoralis muscle index (cm^2/m^2)	7.401 [5.81–9.3]	7.448 [4.88–9.64]	0.644

Values were expressed as medians [25th-75th percentiles] or number (%). *7 days before the admission. SAPS II: Simplified Acute Physiology Score II; BMI: Body Mass Index; NRS-2002: Nutrition Risk Screening. COVID: CoronaVirus Disease; CRP: C reactive Protein; GFR: Glomerular Filtration Rate. Results are expressed as median and [25–75] percentiles or numbers and percentages. P < 0.05 is significant.

Among the 80 patients included in the study, 30 (37.5%) presented malnutrition. Three patients who died (3.75%) were malnourished. Multivariate analysis exhibited that low BMI (OR = 0.83, 95% CI [0.73–0.96], p = 0.0083), dyslipidemia (OR = 29.45, 95% CI [3.12-277.73], p = 0.0031), oral intakes reduction < 50% (OR = 3.169, 95% CI [1.04–9.64], p = 0.0422) and GFR (CKD-EPI) at admission (OR = 0.979, 95% CI [0.96–0.998], p = 0.0297) were associated with the occurrence of malnutrition in COVID-19 inpatients (Table 3).

Table 3
Multivariate analysis

Significant Covariates	Odds ratio	95% CI	*P value*
BMI (kg/m^2)	0.8363	0.73 to 0.96	0.0083*
Dyslipidemia	29.4532	3.12 to 277.73	0.0031*
Oral food intakes 7 days before admission < 50%	3.1687	1.04 to 9.64	0.0422*
GFR (CKD-EPI) (ml/min/1.73 m^2)	0.9785	0.96 to 0.998	0.0297*
BMI : Body Mass Index, GFR: Glomerular Filtration Rate, CI Confidence Interval			
Hosmer & Lemeshow test 0.7; Model prediction percentage 77%, AUC 0.82 [0,72 to 0,898]			

Results of Classification and Regression Trees (CART) are shown in Fig. 1. CART has been used extensively as an alternative to the classical linear and additive prediction models.

Results are presented in the form of a tree with a hierarchical sequential structure that can be easily understood. The segmentation (multivariate analysis) shows the most important variables in homogeneous groups according to malnutrition. The percentage of estimation of this CART analysis was 80%. For example, patients with BMI ≤ 22.5 kg/m² presented a malnutrition status in 87.5% of the cases. In contrast, patients with BMI > 22.5 kg/m² and with dyslipidemia were malnourished in 75% of the cases. In case of absence of dyslipidemia and if GFR is ≤ 39 ml/min/1.73m², 60% of the patients were malnourished.

Discussion

To our knowledge, this study is the first reporting the prevalence of malnutrition in patients hospitalized for SARS-CoV-2 pneumonia. It showed a high prevalence (37.5%) of malnutrition in hospitalized patients with 26% of severe malnutrition. Median albuminemia was very low (24 [18–27] g/L) and pectoralis muscle area index was not associated with recent malnutrition. There were no association between recent malnutrition and the need for ICU admission. However, there were more deaths in the malnutrition group. The included population was comparable to recent publications of COVID-19 cohorts in terms of age, sex ratio [14] and comorbidities (BMI, diabetes mellitus, hypertension) [15]. The population of the study was overweight (median BMI 28.5 [25–31] kg/m²) consistent with numerous previous studies [16, 17].

A recent Chinese publication found a high prevalence (52.7%) of malnutrition in 182 elderly patients with COVID-19 [9] diagnosed with the Mini Nutritional Assessment (MNA) [18]. The mean age of the population was 68.5 years old. Interestingly, in this younger cohort (59.5 [49.5–68.5] years old), we described more than one third of malnourished patients (37.5%). The diagnosis of malnutrition was based on international GLIM criteria [19], not specific to an elderly population and easy to use. All

hospitalized patients got the etiological criterion (pneumonia), the phenotypic criterion being based solely on a recent weight loss of 5% in our overweight population.

Concerning the weight loss and the importance of fasting, almost forty-six percent (n = 37) of the patients reported decreased food intakes with multiple reasons. They mentioned anorexia (27.5%), asthenia (21.25%), dysgeusia (27.5) and anosmia (20%). Surprisingly, no statistical association was made between the self-reported importance of starvation and the existence of malnutrition. In a recent publication, Bouëtté and al. found an association between oral intakes < 7/10 and the existence of malnutrition according to GLIM criteria in a population of general medicine practice patients [20]. One first explanation of our results could be a lack of power for this criterion. Another explanation could be related to the inflammatory nature of COVID-19 malnutrition. In 97 patients, Hedlund and al. found an association between hypoalbuminemia, inflammation and outcome in patients hospitalized for community-acquired pneumonia [21]. The authors argue that hypoabuminemia is explained by the inflammatory status more than their nutritional status [21].

It should be noted that the nutritional assessment was conducted at admission, with a median onset of COVID-19 symptom of 7 days. Thus, we highlighted an acute malnutrition. The concept of acute malnutrition is described and might need a specific management [22].

Concerning metabolic disorders, hyperlipidemia affects immune functions and could promote COVID-19 susceptibility [23]. Hypercholesterolemia is associated with cholesterol accumulation in immune cells, which participate to inflammatory responses and may affect the response to infections [24]. Our multivariate analysis found an association between malnutrition and dyslipidemia in this context of inflammatory disease. To our knowledge, there is no data that can specifically explain this association.

Pectoralis muscle index has been suggested as a prognostic marker in relation to muscularity in an oncology population [25]. In our population, there was no difference in this index between malnourished and non-malnourished patients. This could be explained by the recent development of this malnutrition. There was no statistical association between the pectoralis muscle index and patients' outcomes.

The three patients who died (3.75%) were malnourished. One of them died after withdrawal of life-sustaining measures. The others, with extracorporeal life support (ECLS), died from severe intracranial hemorrhage. Our study was not designed to analyze this association. Association between nutritional status and outcome is well known [26, 27]. In contrast, there was no association between malnutrition and the need for ICU admission or hospital length of stay in our study.

Strengths and weaknesses

NUTRICOV strengths are the prospective design of the study, which allowed for an exhaustive collection and the use of international tools (GLIM definition and NRS-2002). Therefore, this is the first study analyzing malnutrition in a general population of COVID-19 inpatients. The limits are the declarative nature of some collected data (basis weight, oral intakes prior to hospitalization). We used GLIM criteria

to define malnutrition. GLIM definition may lead to higher prevalence because of requiring fewer criteria in comparison with ESPEN definition. In a recent publication, Clark and *al*. exhibited a small agreement between GLIM and ESPEN definition for malnutrition [28].

Conclusion

SARS-CoV-2 is responsible for severe forms of pneumonia requiring hospitalization. ESPEN recently suggest the existence of a nutritional risk and recommend to routinely check for malnutrition in COVID-19 patients to improve global patient care. We demonstrate the existence of a high prevalence of malnutrition (37.5%) in a general cohort of COVID-19 inpatients according to GLIM criteria. Considering this high prevalence, nutritional support in COVID-19 care seems an essential element.

Abbreviations

ARDS
Acute Respiratory Distress Syndrome
BMI
Body Mass Index
CART
Classification and regression tree
Covid-19
Coronavirus Disease
CRP
C Reactive Protein
CT scan
Computed Tomography
ESPEN
European Society of Parenteral and Enteral Nutrition
GLIM
Global Leadership Initiative on Malnutrition
GFR
Glomerular Filtration Rate
ICU
Intensive Care Unit
NRS-2002
Nutrition Risk Screening 2002
RT-PCR
Reverse Transcriptase Polymerase Chain Reaction
SAPS II
Simplified Acute Physiology Score

SARS-CoV-2
severe Acute Respiratory Syndrome – Coronavirus 2

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Conceptualization (JMC, AR, VM, PL); Data curation (AR, PL, OM, BM, OL); Formal analysis (AR, FV-B, JMC, VM); Funding acquisition (N/A); Investigation (AR, PL); Methodology (JMC, VM, AR, PL, LB); Supervision (JMC, VM, OF); Roles/Writing - original draft (AR, FV-B); Writing – review (VM; JMC) & editing (VM, JMC, AR,FV-B).

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29. BMI. Body Mass Index, GFR: Glomerular Filtration Rate.

Figures

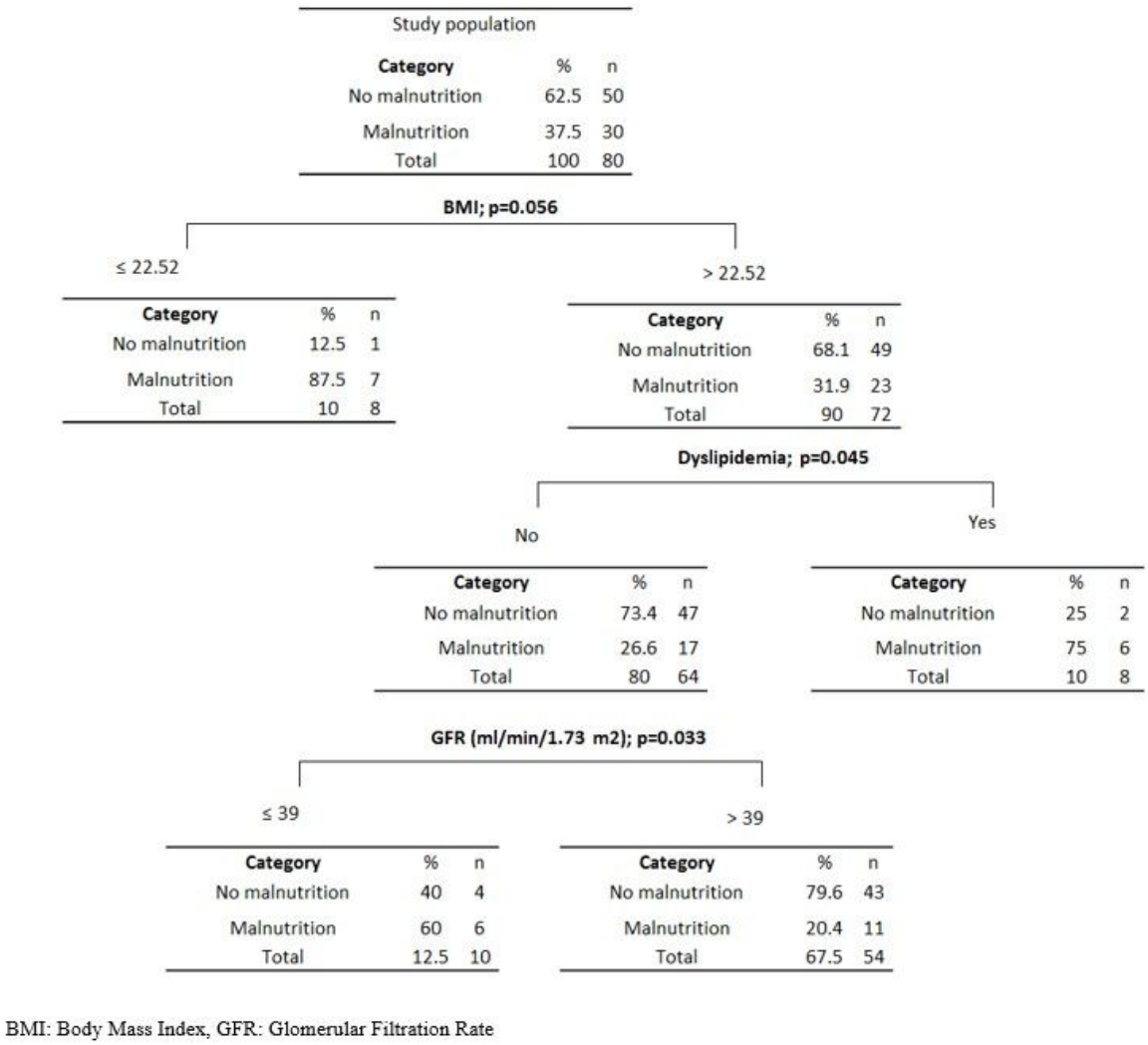

Figure 1

Classification and regression tree (CART) according to BMI, Dyslipidemia and GFR.

Supplementary Files

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