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Original article

Prevalence and outcome of malnutrition in pediatric patients with chronic diseases: Focus on the settings of care

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SUMMARY

Background: Information on disease-related malnutrition and related outcomes in pediatric patients with chronic diseases in different settings of care is not available.

Methods: Consecutive eligible patients attending the out-patient clinic ($n = 177$) or admitted to the day-hospital clinic ($n = 163$) or to hospital ($n = 201$) were screened for the presence of malnutrition (BMI and/or height/length for age z-scores < -2). We recorded data on emergency care admissions to hospital that occurred during the 3 years before screening and related total days of stay, as well as data on emergency care admissions to hospital occurring within 6 months after screening.

Results: Prevalence of malnutrition was 2-fold higher ($P < 0.001$) in in-patients (56.7% [95% CI, 49.6–63.7]) than in patients assessed at the out-patient (33.3% [95% CI, 26.4–40.8]) and day-hospital (28.3% [95% CI, 21.5–35.8]) clinics. Estimates were heterogeneous across diagnostic groups with higher rates in patients with neurologic (61%) and cardiac (56%) diseases. Stunting was more frequent among in-patients, who also had more evident nutritional derangements. Multivariate logistic regression (covariates: age, gender, healthcare setting and disease group), showed that malnutrition (OR = 1.86 [95% CI, 1.21–2.88]; $P = 0.005$) was significantly associated with prolonged hospitalization ($\geq$15 days) in the 3 years before screening. In-patients were also more likely to have been hospitalized $\geq$15 days (using out-patients as reference category, OR = 2.24 [95% CI, 1.39–3.63], $P = 0.001$), but we did not find any modifying effect (interaction) of the setting of care on the association between malnutrition and prolonged hospitalization.

Discussion: The rates of malnutrition in children with chronic diseases are very high and increase hospital care needs, especially when they are admitted to hospital. Nutritional care in this patient population is recommended.

1. Introduction

Disease-related malnutrition (DRM) is likely the most frequent comorbidity in all healthcare settings [1,2]. This is true for adult patients, but it is even more so for children. Although the interest in this condition in this segment of the population has grown considerably over the last ten years, prevalence data are still limited and heterogeneous, and have been mainly collected in an acute hospital care setting [3–6].

Studies have shown that estimates of nutritional derangements are high especially in children with underlying diseases and clinical conditions [4,7]. Patients with chronic diseases are not only more prone to acute complications and, therefore, to admission to hospital, but are also likely to undergo active follow-up and to be referred to out-patient and day-hospital clinics. However, information on the prevalence of malnutrition in these healthcare settings is limited and generally refers to only one disease [8–13].

The importance of DRM lies in its association with adverse clinical outcomes, including developmental delay, impaired social achievements and intellectual deficits, as well as prolonged length of hospital stay (LOS) and increased care costs [2,3,14]. Therefore, early identification of nutritional depletion followed by tailored interventions should be mandatory.

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We designed the present study to collect data on the prevalence of malnutrition in different pediatric healthcare settings and diagnostic groups. The association between malnutrition and hospitalization-related outcomes (admission to the emergency unit, hospital admissions and LOS) was also investigated.

2. Methods

2.1. Study design

We designed a single-center, prospective, observational study along with a cross-sectional and a retrospective analysis of outcomes of interest. First, consecutive eligible patients attending the out-patient clinic or admitted to the day-hospital clinic or admitted to the medical and surgical wards of the Pediatric Hospital “Bambino Gesù” (Rome, Italy) over a 10-month period (from July 1st 2015 to June 30th 2016) were screened. Then, data on the number of emergency care admissions to hospital occurring during the 3 years before and the 6 months after the screening visit were retrieved. We decided to proceed with a 3-year retrospective data analysis, as we considered it a more reliable time-frame to account for the reduced resilience of patients suffering from chronic conditions.

2.2. Subjects and assessments

Patients were included in the present study if they were aged <18 years, suffered from a chronic acquired or congenital disease – as defined by Mokkink et al. [15] – and parents (or caregivers/legal representatives) provided written informed consent. Preterm infants (<37 weeks gestational age) during the first 12 months of life and infants <1-month of age, as well as patients with an acute disease or admitted to intensive care units were excluded.

In addition to general clinical and demographic information (age, gender, diagnosis and ongoing follow-up by the local nutritional team) the following study variables were collected:

- anthropometric parameters: body weight (to the nearest 0.1 kg) and height/length (to the nearest 0.5 cm). Accordingly, body mass index (BMI) was calculated and BMI for age z-scores and height/length for age (HFA) z-scores were derived using reference data provided by Cole et al. [16] and WHO reference curves [17], respectively. History of recent unintentional weight loss (WL) during the previous month was also investigated with discussion with the patients and/or parents/caregivers. Presence was recorded independently of its amount.
- daily energy intake and requirements; particularly, mean intakes during the last week were evaluated by a dietician through dietary recall associated with the use of a food atlas, while requirements were estimated using Italian age and gender-specific recommended equations [18], with the exception of neurologic patients, in whom requirements were calculated taking into account mobility, functional capacity and disease severity [19].
- phase angle (PhA); it was evaluated in standard conditions using bioelectrical impedance vectorial analysis (NutriLAB®, Akern/RJL) and the associated software (Bodygram Plus®, Akern srl) [20].
- nutrition-related symptoms/conditions (vomiting, diarrhea, constipation and dysphagia) potentially affecting nutritional intake and balance.
- nutritional therapy (none, diet, oral nutritional supplements, enteral and parenteral nutrition).
- biochemistry; venous blood samples were drawn after an overnight fast, for the assessment of serum total protein, albumin, hemoglobin and C-reactive protein (CRP).

2.3. Study endpoints

The primary endpoint was the prevalence of DRM in the whole study population and in the various healthcare settings. In this context of patients with chronic diseases, it was defined as either BMI z-score < -2 or HFA z-score < -2 (stunting) [4,17]. The prevalence of severe underweight (BMI z-score $<$ -3) and stunting (HFA z-score $<$ -3) was estimated, as well as the prevalence of malnutrition in different diagnostic groups (according to organ/system involved mainly: neurological, cardiac, hepatic, gastro-intestinal, genito-urinary and respiratory) were also estimated. Finally, information on the following outcome measures was retrospectively and prospectively retrieved by linking to the administrative records database of the Italian Healthcare System: emergency care admissions to hospital - and the related total days of hospital stay – that occurred in the 3 years preceding the baseline visit (retrospectively); the number of hospitalizations that occurred during the 6 months following the baseline visit (prospectively).

2.4. Statistical analysis

Sample size was estimated on the primary end point. Accordingly, we computed it using literature data (for the hospital setting) [4,7] or defining a frequency of DRM a priori (for the out-patient and day-hospital setting). Expecting a prevalence of DRM of 15% in the hospital setting and of 10% in the out-patient and day-hospital clinics, with a margin of error of 5%, we calculated that we had to enroll at least 200 in-patients and 140 patients in both the out-patient and day-hospital clinics.

First, descriptive statistics in the overall population and main diagnostic groups were provided as counts and percentages (categorical variables) and as mean and standard deviation (continuous variables with normal distribution) or median and inter-quartile range (IQR; continuous variables with non-normal distribution). Prevalence estimates were provided along with their binomial exact 95% confidence interval. Then, the features of the population in the various healthcare settings and nutritional status categories were compared using one-way ANOVA (normal distribution) or Kruskal–Wallis test (non normal distribution) and the Fisher's exact test. A general linear regression model was built to investigate which independent variables (age, gender, DRM, new-case referral, setting of care and recent WL) were associated with energy intake. Finally, study outcome variables were addressed. First, between-group differences in continuous or dichotomus variables were made using Kruskal–Wallis test and the Fisher's exact test, respectively. Then, logistic regression analysis adjusted for potential non collinear confounders (age, gender, healthcare setting, new referral and disease group - checked with the Pearson's statistic) was conducted to investigate the independent association between study outcomes and malnutrition. Outcomes were coded as follows: 3-year previous admission to emergency unit, yes or no and $\geq$3 [upper quartile of the distribution]; 3-year previous admission to hospital, yes or no; 3-year previous hospitalization (LOS) $\geq$15 days [upper quartile of the distribution]; hospitalization in the 6 months following the baseline visit, yes or no.

All statistical analyses were performed using MedCalc Statistical Software version 17.2 (MedCalc Software bvba, Ostend, Belgium), establishing the level of significance at a two-tailed p-value of <0.05.

2.5. Ethics

The study was performed in accordance with good clinical practices and in compliance with local regulatory requirements. The Pediatric Hospital “Bambino Gesù” is authorized to perform research and clinical studies by the Ministry of Health. Therefore, informed consent is acquired on a routine basis at admission for all patients, enabling the systematic inclusion in all non-intervention studies.

3. Results

A total of 541 consecutive subjects (males, 50.6%; new cases, 59.7%) were assessed: hospital, n = 201; day-hospital clinic, n = 163; out-patient clinic, n = 177. The features of the whole study sample and the patient populations belonging to the three healthcare settings are reported in Table 1, while the distribution of each diagnostic group in the overall population and in each healthcare setting is presented in Supplementary Fig. 1. In the whole study population, the most frequent diagnostic groups were patients with neurological (25.5%), gastro-intestinal (28.1%) and genitourinary diseases (26.6%). Diagnostic groups were almost homogeneous across settings, with exception of neurological and gastro-intestinal which were more frequent in the hospital and out-patient setting, respectively.

Overall prevalence of malnutrition in the study population was 40.5% [95% CI, 36.3–44.8] (severe, 21.6% [95% CI, 18.3–25.3]). Particularly, the prevalence of low BMI (z-score < −2) and stunting (HFA z-score < −2) was 19.4% [95% CI, 16.2–23.0] and 30.3% [95% CI, 26.5–34.4], respectively. Estimates were 2-fold higher (χ^2 test, $P < 0.001$) in in-patients (56.7% [95% CI, 49.6–63.7]) than in patients assessed at the out-patient (33.3% [95% CI, 26.4–40.8]) and day-hospital (28.3% [95% CI, 21.5–35.8]) clinics (Fig. 1). A similar picture (χ^2 test, $P < 0.001$) was observed for severe malnutrition (hospital, 33.8% [95% CI, 27.3–40.8]; day-hospital clinic, 12.3% [95% CI, 7.7–18.3]; out-patient clinic, 16.4% [95% CI, 11.3–22.7]). Finally, prevalence of malnutrition was significantly different across the different diagnostic groups (χ^2 test, $P < 0.001$), with higher rates in patients with neurologic, cardiac and respiratory diseases (Fig. 2).

Stunting was more frequently observed among in-patients (Table 2), who were younger and had more evident nutritional derangements and higher rates of vomiting/nausea, constipation and dysphagia.

Mean energy intakes appeared to be almost adequate in terms of covering estimated requirements independently of the setting of care, although they were lower in patients who were not in active follow-up by the local nutritional team (new cases; Supplementary Table 1, $P < 0.001$). Lower intakes were also associated with WL (Supplementary Table 2), which was not a predominant feature due to its low prevalence (in the overall study population, 13.5%) and lack of association with both malnutrition and the setting of care (Tables 1 and 3). Descriptive data on the frequency and type of ongoing (old cases) and prescribed (new cases) nutritional interventions – from dietary counseling to any-type (integrative or total) of artificial nutrition – are summarized in Supplementary Table 3.

Malnutrition was more frequent in patients already being followed by the Clinical Nutrition team and was associated with younger age, lower Pha and nutrition-related symptoms/conditions (vomiting, constipation and dysphagia; Table 3).

Then, we investigated the association among malnutrition, setting and relevant outcomes. Overall, during the 3 years before the baseline visit, about half (51.6%) and one fifth (20.7%) of the patients had at least one and 3 or more admissions (median [IQR], 1 [0–2]; range, 0–30) to an emergency unit, respectively. In the same period, 44% experienced at least one hospitalization (range, 0–16) with a median duration of total stay of 22 days (IQR, 7–63 days; range, 1–408 days). In addition, about 15% of the patients were hospitalized in the 6 months following the inclusion in the present study. In univariate analysis, a significant association was found between the setting of care and the number of days of hospitalization (≥15 days) in the previous 3 years, as well as between the setting of care and hospitalization in the 6 months following the initial visit (Table 1). Malnutrition and its degrees were significantly associated only with prolonged hospitalization ($P < 0.001$; Tables 3 and 4). In

Table 1
Characteristics of the population by healthcare setting.

		Overall (n = 541)	Hospital (n = 201)	Day-hospital (n = 163)	Outpatient (n = 177)	P-value[a]
New referral, n (%)		323 (59.7)	118 (58.7)	106 (65.0)	99 (55.9)	0.22
Male gender, n (%)		274 (50.6)	102 (50.7)	85 (52.1)	87 (49.2)	0.86
Age (years), mean (SD)		7.5 (5.4)	5.4 (5.1)*	8.7 (5.0)	8.7 (5.4)	<0.001
BMI (kg/m^2), mean (SD)		16.8 (3.9)	16.3 (4.2)	17.1 (3.8)	16.9 (3.6)	0.11
BMI z-score, mean (SD)		−0.55 (2.01)	−0.71 (2.39)	−0.36 (1.75)	−0.53 (1.74)	0.26
HFA z-score, mean (SD)		−1.23 (1.91)	−1.72 (2.17)*	−0.89 (1.57)	−0.99 (1.79)	<0.001
Recent weight loss, n (%)		73 (13.5)	31 (15.4)	18 (11.0)	24 (13.6)	0.48
Energy intake (%), mean (SD)[b]		109 (35)	104 (35)‡	114 (34)	111 (34)	0.024
Phase angle (°), mean (SD)		4.6 (1.7)	3.5 (1.6)*	4.9 (1.8)	4.6 (1.6)	<0.001
Total protein (g/dL), mean (SD)		6.9 (0.9)	6.5 (1.0)*	7.0 (0.7)	7.1 (0.9)	<0.001
Albumin (g/dL), mean (SD)		4.2 (0.6)	4.1 (0.7)*	4.4 (0.5)	4.3 (0.6)	<0.001
Hemoglobin (g/dL), mean (SD)		12.3 (1.7)	11.9 (1.7)*	12.8 (1.5)	12.5 (1.6)	<0.001
C-reactive protein (mg/dL), mean (SD)		0.42 (0.72)	0.47 (0.61)	0.47 (0.84)	0.33 (0.72)	0.11
Symptoms/conditions, n (%)						
Vomiting		37 (6.8)	18 (9.0)	3 (1.8)	16 (9.0)	0.010
Diarrhea		81 (15.0)	20 (10.0)	22 (13.5)	39 (22.0)	0.004
Constipation		143 (26.4)	69 (34.3)	30 (18.4)	44 (24.9)	0.002
Dysphagia		132 (24.4)	69 (34.3)	27 (16.6)	36 (20.3)	<0.001
3-year retrospective outcomes						
Admission(s) to emergency unit	n (%)	279 (51.6)	105 (52.2)	79 (48.5)	94 (53.1)	0.66
	≥3[c], n (%)	112 (20.7)	43 (21.4)	32 (19.6)	37 (20.9)	0.92
Hospitalizations (≥1), n (%)		238 (44.0)	101 (50.2)	69 (42.3)	68 (38.4)	0.061
Total length of stay ≥15 days[c], n (%)		137 (25.3)	70 (34.8)	33 (20.2)	34 (19.2)	<0.001
6-month hospitalization(s), n (%)		79 (14.6)	42 (20.9)	15 (9.2)	22 (12.4)	0.004

Abbreviations: SD, standard deviation; IQR, interquartile range; BMI, Body Mass Index; HFA, height/length for age.
[a] For comparison using ANOVA or Kruskal–Wallis test (post-hoc comparison test: * significantly different from the other groups; ‡ significantly different from the "day-hospital" group) or Fisher's exact test as appropriate.
[b] Reported as percentage of estimated requirements during the last week.
[c] Upper quartile of the distribution.

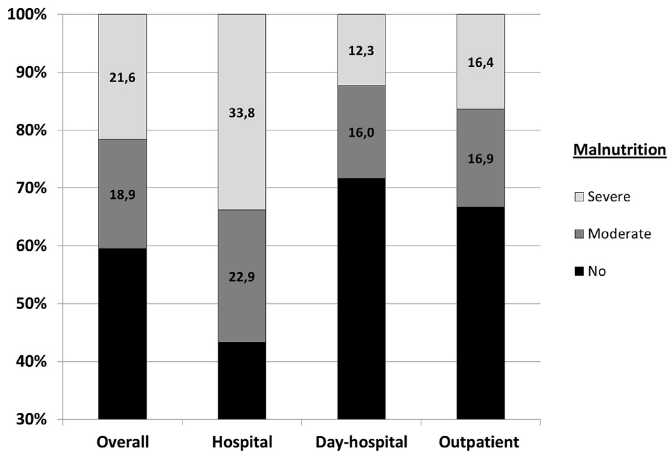

Fig. 1. Prevalence of nutritional status conditions by healthcare setting.

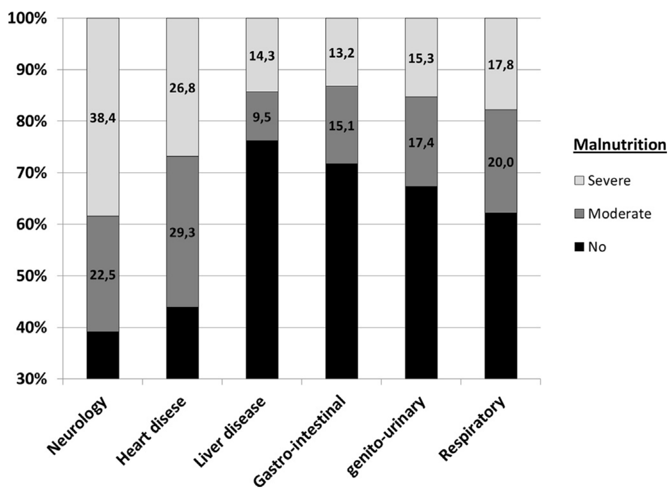

Fig. 2. Prevalence of nutritional status conditions by diagnostic group.

multivariate analysis, this last association was found to be independent of age, gender, healthcare setting, and disease group: for moderate-severe malnutrition, OR = 1.86 [95% CI, 1.21–2.88] ($P = 0.005$; Table 4); over degrees of malnutrition (from no/mild malnutrition to moderate malnutrition to severe malnutrition), OR = 1.57 [95% CI, 1.22–2.02] ($P < 0.001$). Furthermore, in-patients were more likely to have been hospitalized more than two weeks (using out-patients as reference category, OR = 2.24 [95% CI, 1.39–3.63], $P = 0.001$; for trend over increasing setting-related intensity of care, OR = 1.54 [95% CI, 1.21–1.96], $P < 0.001$). No modifying effect (test for interaction) of the setting of care on the association between malnutrition and prolonged hospitalization was observed. Age was also inversely associated with all the outcomes considered.

4. Discussion

To the best of our knowledge, this is the first study providing a specific focus on DRM and related outcomes in pediatric patients suffering from different chronic diseases and evaluated in different healthcare settings. We found that the overall prevalence of malnutrition was about 40%, rates being twice as high in in-patients (~57%) as in patients assessed at the out-patient (~33%) and day-hospital (~28%) clinics. Prevalence was markedly heterogeneous among diagnostic groups, with higher rates in patients with neurologic, cardiac and respiratory diseases. In addition, malnutrition was associated with prolonged hospitalization in the previous three years.

Estimates of malnutrition in hospitalized patients with chronic diseases were considerably higher than those reported in previous studies including unselected patients [3–6]. No reliable comparison with the literature could be made for patients attending the day-hospital and out-patient clinics. We found that estimates in these last two settings were higher than those reported in the literature for in-patients [3–6]. In the largest multi-center and multi-country study conducted in the hospital setting [4], using similar diagnostic criteria, Hecht et al. found a prevalence of 18% in patients suffering from chronic diseases. On the other hand, a recent study conducted by Murphy et al. [8] has highlighted that rates may be as high as 30% when patients treated for clinical conditions (e.g. cancer or Crohn's disease or cystic fibrosis) are considered. In the national study conducted in the Netherlands the rates of malnutrition were higher in academic hospitals than in general hospitals, and children with a chronic disease were more likely to be admitted to an academic hospital [21,22]. This is also consistent with a recent Italian survey reporting higher prevalence in pediatric hospitals than in pediatric wards of general hospitals [23]. The Pediatric Hospital "Bambino Gesù" in Rome is a highly specialized pediatric academic hospital and a national referral center for the management of several inherited and acquired diseases. Therefore, it is reasonable to argue for unintentional inclusion bias associated with the type of institution where we performed the study. Indeed, the difference in estimates found across the different healthcare settings is not surprising and is consistent with previous data collected in other age groups [1]. In-patients are likely to require more intense care – which is also suggested by the increased need for hospital care in the previous 3 years – and had more evident nutritional derangements (lower phase angle and energy intakes, worse biochemical parameters and higher rates of stunting).

Our study raised the issue again of how malnutrition should be diagnosed. In our study, we used the new WHO child-growth charts [17]. Currently, the use of country-specific and disease-specific growth references has been proposed to overcome this limitation [7,24,25]. In our study, the use of specific references – as applicable – in neurologic patients would have resulted in a reduction in the prevalence of malnutrition from 61% to 30%, an estimate that is consistent with Wang et al. [12] in children with cerebral palsy. However, reference curves for several medical conditions date back decades ago [7] and do not take into account growth trends across

Table 2
Prevalence of malnutrition criteria by setting of care.

	Hospital (n = 201)	Day-hospital (n = 163)	Outpatient (n = 177)
HFA z-score < −2 [%]	28.4	14.1	19.2
BMI z-score < −2 [%]	12.4	10.4	7.3
Both criteria [%]	15.9	3.7	6.8

Abbreviations: HFA, Height For Age; BMI, Body Mass Index.

Table 3
Characteristics of the population by nutritional status.

		Degree of malnutrition			
		Severe (n = 117)	Moderate (n = 102)	No malnutrition (n = 322)	P-value[a]
New referral, n (%)		57 (48.7)	56 (54.9)	210 (65.2)	0.004
Male gender, n (%)		60 (51.3)	62 (60.8)	152 (47.2)	0.057
Age (years), mean (SD)		6.7 (5.7)	6.3 (4.9)	8.1 (5.3)*	0.002
BMI (kg/m^2), mean (SD)		14.9 (3.6)	15.1 (2.6)	18.0 (3.8)*	<0.001
BMI z-score, mean (SD)		−1.89 (2.65)*	−1.24 (1.76)*	0.16 (1.41)*	<0.001
HFA z-score, mean (SD)		−3.32 (2.25)*	−1.95 (1.15)*	−0.24 (1.09)*	<0.001
Recent weight loss, n (%)		21 (17.9)	16 (15.7)	36 (11.2)	0.14
Energy intake (%), mean (SD)[b]		116 (36)‡	113 (34)	106 (34)	0.009
Phase angle (°), mean (SD)		3.9 (2.4)	3.9 (1.4)‡	4.8 (1.5)	0.004
Total protein (g/dL), mean (SD) 6.9 (0.8)		6.8 (0.9)	6.9 (1.0)	0.29	
Albumin (g/dL), mean (SD)		4.3 (0.5)	4.2 (0.7)	4.3 (0.6)	0.51
Hemoglobin (g/dL), mean (SD)		12.0 (1.7)	12.4 (1.9)	12.4 (1.6)	0.16
C-reactive protein (mg/dL), mean (SD)		0.52 (0.86)	0.46 (0.87)	0.38 (0.61)	0.18
Symptoms/conditions, n (%)					
Vomiting		16 (13.7)	11 (10.8)	10 (3.1)	<0.001
Diarrhea		18 (15.4)	20 (19.6)	43 (13.4)	0.30
Constipation		49 (41.9)	28 (27.5)	66 (20.5)	<0.001
Dysphagia		58 (49.6)	32 (31.4)	42 (13.0)	<0.001
3-year retrospective outcomes					
Admission(s) to emergency unit	n (%)	65 (55.6)	50 (49.0)	163 (50.6)	0.44
	≥3[c], n (%)	26 (22.2)	28 (27.5)	58 (18.0)	0.18
Hospitalizations (≥1), n (%)		57 (48.7)	48 (47.1)	133 (41.3)	0.13
Total length of stay ≥15 days[c], n (%)		47 (40.2)	30 (29.4)	60 (18.6)	<0.001
6-month hospitalization(s), n (%)		24 (20.5)	15 (14.7)	40 (12.4)	0.11

Abbreviations: SD, standard deviation; IQR, interquartile range; BMI, Body Mass Index; HFA, height/length for age.
[a] For comparison using ANOVA or Kruskal–Wallis test (post-hoc comparison test: * significantly different from the other groups; ‡ significantly different from "no malnutrition") or Fisher's exact test as appropriate.
[b] Reported as percentage of estimated requirements during the last week.
[c] Upper quartile of the distribution.

Table 4
Association between moderate-severe malnutrition (BMI z-score <−2 and/or HFA z-score <−2 [4,14,15]) and outcome (multivariable logistic regression analysis including relevant covariates [p-value <0.10 at univariable analysis]).

	Unadjusted model (OR [95% CI])	P-value	Fully-adjusted model (OR [95% CI])	P-value
3-year retrospective outcomes				
Admission(s) to emergency unit	1.08 [0.77–1.52]	0.67	0.92 [0.63–1.35][a]	0.67
≥3[c]	1.49 [0.98–2.26]	0.062	1.31 [0.84–2.05][a]	0.24
Hospitalizations (≥1)	1.31 [0.93–1.85]	0.13	1.09 [074–1.59][a]	0.67
Total length of stay ≥15 days[c]	2.37 [1.60–3.51]	<0.001	1.86 [1.21–2.88][a]	0.005
6-month hospitalization(s)	0.92 [0.63–2.47]	0.083	1.26 [0.75–2.12][b]	0.39

Abbreviations: OR, odds ratio; 95%CI, 95% confidence interval.
[a] Model including: age, gender, healthcare setting, and disease group.
[b] Model including: age, gender, healthcare setting, new referral, and disease group.
[c] Upper quartile of the distribution.

more recent generations. A recent reappraisal has been considered for patients with cerebral palsy [26]. However, a major issue is the impact of malnutrition on health-related outcomes and reference curves should be reasonably updated and revised in respect to this issue. This validation approach has been scantly considered and only curves proposed for patients with cerebral palsy have undergone this evaluation [26].

We also believe that the features of malnourished patients are closely linked to the issue of definition of malnutrition. We observed that WL was infrequent and unrelated to malnutrition. Moreover, energy intakes were apparently adequate to cover estimated requirements - even in new cases - and higher in malnourished patients of which about 50% were already prescribed a nutritional intervention. These observations potentially raise the issue of whether methods for assessing energy requirements should be reconsidered – and additionally adjusted for a "malnutrition factor" (e.g. setting them on ideal body weight and height for age) – and highlight the importance of how nutrition-related symptoms/conditions are addressed by nutritional therapy. Malnutrition was significantly associated with nutrition-related symptoms/conditions, particularly dysphagia, vomiting/nausea, and constipation, which suggest that inadequate intake is a more important determinant of nutritional derangements in patients with chronic diseases. Furthermore, they support the value of the recent reappraisal and redefinition of the criteria for documenting pediatric malnutrition [27]. Accordingly, for patients suffering from chronic diseases and malnutrition, it is reasonable to consider a "dynamic" diagnostic approach based on the use of two or more data points, which could be more accurate, as it provides information on the ongoing inter-relationship between nutritional status and the underlying disease, as well as the efficacy of nutritional interventions.

Our study confirmed that malnutrition is associated with prolonged hospitalization [3,22], which could be considered a valuable indicator of the need for more intense care and higher resource use. Although the retrospective collection of most outcome data is an important limitation that does not enable us to support a true cause-effect relationship, we could argue that chronic malnutrition is a slow process, which develops over time. Being responsible for reduced resilience, it requires more intense care – as suggested by the association with increased hospital stay – due to complications. These, in turn, could be responsible for further deterioration of nutritional status. However, taking into account the only outcome evaluated prospectively, contrary to what has been reported for adult patients [28], malnutrition was not found to be a risk factor for hospitalization in the 6 months following the baseline visit. A possible explanation could be that the general functional conditions of patients suffering from chronic diseases are already poor and require higher levels of care, making the negative effect of reduced resilience associated with malnutrition more difficult to detect. For the same reason, we decided to focus only on emergency care admissions as relevant outcome measure. Although it could be considered a limitation, we believed that it would have more reliably accounted for the care needs of malnourished patients. Nonetheless, the confounding effect of a more appropriate nutritional care could not be excluded. Finally, we recognize that the time-frames chosen for retrospective and prospective data analysis may be questionable. However, there are no studies in pediatrics suggesting which could be the most appropriate. In view of the aforementioned considerations on malnutrition, as a slow process developing over time in chronic diseases, we decided to focus on 6-month prospective and 3-year retrospective data as we believed that it would have more reliably accounted for resource use in patients in whom care needs are already high.

In conclusion, the rates of malnutrition in children with chronic diseases are very high and increase hospital care needs, especially when they are admitted to hospital. Systematic inclusion of nutritional management (assessment and treatment) in the clinical work-up of patients with chronic diseases is recommended. Further studies are warranted to refine the most appropriate diagnostic criteria for malnutrition and to evaluate the impact of nutritional support in this patient population.

Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.07.008.

References

[1] Cereda E, Pedrolli C, Klersy C, Bonardi C, Quarleri L, Cappello S, et al. Nutritional status in older persons according to healthcare setting: a systematic review and meta-analysis of prevalence data using MNA(®). Clin Nutr 2016 Dec;35(6):1282–90.

[2] Hartman C, Shamir R, Hecht C, Koletzko B. Malnutrition screening tools for hospitalized children. Curr Opin Clin Nutr Metab Care 2012 May;15(3):303–9.

[3] Daskalou E, Galli-Tsinopoulou A, Karagiozoglou-Lampoudi T, Augoustides-Savvopoulou P. Malnutrition in hospitalized pediatric patients: assessment, prevalence, and association to adverse outcomes. J Am Coll Nutr 2016 May-Jun;35(4):372–80.

[4] Hecht C, Weber M, Grote V, Daskalou E, Dell'Era L, Flynn D, et al. Disease associated malnutrition correlates with length of hospital stay in children. Clin Nutr 2015 Feb;34(1):53–9.

[5] Joosten KF, Hulst JM. Prevalence of malnutrition in pediatric hospital patients. Curr Opin Pediatr 2008 Oct;20(5):590–6.

[6] Moeeni V, Walls T, Day AS. Nutritional status and nutrition risk screening in hospitalized children in New Zealand. Acta Paediatr 2013 Sep;102(9):e419–23.

[7] Joosten KF, Hulst JM. Malnutrition in pediatric hospital patients: current issues. Nutrition 2011 Feb;27(2):133–7.

[8] Murphy AJ, Hill RJ, Buntain H, White M, Brookes D, Davies PSW. Nutritional status of children with clinical conditions. Clin Nutr 2017 Jun;36(3):788–92.

[9] Murphy AJ, Buntain HM, Wainwright CE, Davies PS. The nutritional status of children with cystic fibrosis. Br J Nutr 2006 Feb;95(2):321–4.

[10] Murphy AJ, White M, Davies PS. The validity of simple methods to detect poor nutritional status in paediatric oncology patients. Br J Nutr 2009 May;101(9):1388–92.

[11] Valentini L, Schaper L, Buning C, Hengstermann S, Koernicke T, Tillinger W, et al. Malnutrition and impaired muscle strength in patients with Crohn's disease and ulcerative colitis in remission. Nutrition 2008 Jul-Aug;24(7–8):694–702.

[12] Wang F, Cai Q, Shi W, Jiang H, Li N, Ma D, et al. A cross-sectional survey of growth and nutritional status in children with cerebral palsy in west China. Pediatr Neurol 2016 May;58:90–7.

[13] Blasquez A, Clouzeau H, Fayon M, Mouton JB, Thambo JB, Enaud R, et al. Evaluation of nutritional status and support in children with congenital heart disease. Eur J Clin Nutr 2016 Apr;70(4):528–31.

[14] Freijer K, van Puffelen E, Joosten KF, Hulst JM, Koopmanschap MA. The costs of disease related malnutrition in hospitalized children. Clin Nutr ESPEN 2018 Feb;23:228–33.

[15] Mokkink LB, van der Lee JH, Grootenhuis MA, Offringa M, Heymans HS. Dutch National Consensus Committee Chronic Diseases and Health Conditions in Childhood. Defining chronic diseases and health conditions in childhood (0-18 years of age): national consensus in The Netherlands. Eur J Pediatr 2008 Dec;167(12):1441–7.

[16] Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. BMJ 2007 Jul 28;335(7612):194.

[17] WHO Multicentre Growth Reference Study Group. WHO child growth standards based on length/height, weight and age. Acta Paediatr 2006;450:1–101.

[18] Società Italiana di Nutrizione Umana, SINU. Livelli di Assunzione di Riferimento di Nutrienti ed energia per la popolazione italiana, IV revisione. Milano: SICS Editore; 2014.

[19] Hogan SE. Energy requirements of children with cerebral palsy. Can J Diet Pract Res 2004;65(3):124–30. Fall.

[20] Caccialanza R, Cereda E, Klersy C, Bonardi C, Cappello S, Quarleri L, et al. Phase angle and handgrip strength are sensitive early markers of energy intake in hypophagic, non-surgical patients at nutritional risk, with contraindications to enteral nutrition. Nutrients 2015;7:1828–40.

[21] Joosten KF, Zwart H, Hop WC, Hulst JM. National malnutrition screening days in hospitalised children in The Netherlands. Arch Dis Child 2010 Feb;95(2):141–5.

[22] Hulst JM, Zwart H, Hop WC, Joosten KF. Dutch national survey to test the STRONGkids nutritional risk screening tool in hospitalized children. Clin Nutr 2010 Feb;29(1):106–11.

[23] Lezo A, Diamanti A, Capriati T, Gandullia P, Fiore P, Lacitignola L, et al., on behalf of the SIGENP Nutrition Day Group. Italian pediatric nutrition survey. Clin Nutr ESPEN 2017;21:72–8.

[24] Milani S, Buckler JM, Kelnar CJ, Benso L, Gilli G, Nicoletti I, et al. The use of local reference growth charts for clinical use or a universal standard: a balanced appraisal. J Endocrinol Invest 2012 Feb;35(2):224–6.

[25] Zemel BS, Riley EM, Stallings VA. Evaluation of methodology for nutritional assessment in children: anthropometry, body composition, and energy expenditure. Annu Rev Nutr 1997;17:211–35.

[26] Brooks J, Day S, Shavelle R, Strauss D. Low weight, morbidity, and mortality in children with cerebral palsy: new clinical growth charts. Pediatrics 2011 Aug;128(2):e299–307.

[27] Becker P, Carney LN, Corkins MR, Monczka J, Smith E, Smith SE, et al. Academy of nutrition and dietetics; American society for parenteral and enteral nutrition. Consensus statement of the academy of nutrition and dietetics/American society for parenteral and enteral nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). Nutr Clin Pract 2015 Feb;30(1):147–61.

[28] Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. Clin Nutr 2008 Feb;27(1):5–15.