Factors associated with mid-upper arm circumference and thigh circumference deterioration in critically ill children

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Purpose: Critically ill children can experience muscle mass depletion during Pediatric Intensive Care Unit (PICU) stay, and it is associated with worse clinical outcomes. Mid-upper arm circumference (MUAC) and thigh circumference (TC) are considered simple measures and easy-to-perform, and allow to evaluate the subcutaneous fat and muscle mass. Thus, to prevent the nutritional status deterioration and its complications, it is essential the early identification of the factors associated with nutritional depletion. We aimed to evaluate the association between anthropometric, inflammatory-nutritional, nutrition therapy (NT) and clinical parameters with MUAC and TC deterioration in critically ill children on mechanical ventilation (MV).

Methods: Prospective cohort study conducted in a PICU of a tertiary hospital in south of Brazil, between July 2013 and February 2016, with critically ill children on MV, aged between 1 month and 15 years. Nutritional status at PICU admission was evaluated by body mass index-for-age (BMI/A). MUAC and TC were performed at PICU admission and before PICU discharge, and delta (Δ) was calculated (Δ = PICU discharge *minus* PICU admission). Inflammatory-nutritional evaluation was composed of serum albumin, C-reactive protein (CRP) and CRP/albumin ratio. NT was evaluated by prior NT, early NT, route of administration, energy and protein adequacy, and cumulative energy and protein balance (calculated as the sum of daily energy and protein intake up to day 7 *minus* energy and protein goals). Pediatric Index of Mortality 2 (PIM2), diagnostic category, Complex Chronic Conditions and fluid overload were evaluated. MUAC and TC deterioration was defined as a reduction of at least 2% during PICU stay. Logistic regression adjusted for sex, age and PIM2 (Adjustment 1) and for sex, age and fluid overload (Adjustment 2) was applied. P-value <0.05 was considered significant.

Results: There were included 69 patients, 59% male with a median age of 15.6 (interquartile range 3.7; 92.8) months. The prevalence of undernutrition at PICU admission was 17.6% according BMI/A. MUAC deterioration was observed in 61% and TC deterioration in 67% of the patients. The patients presented a median ΔMUAC of -3.87% and a median ΔTC of -6.14%. Cumulative negative energy (OR 0.99; p=0.006) and protein (OR 0.85; p=0.032) balances were associated with MUAC deterioration in crude analysis (Table 1). In adjustment 1, higher CRP/albumin ratio (OR 5.00; p=0.047) and cumulative negative energy balance (OR 0.99; p=0.016) were associated with MUAC deterioration (Table 1). In adjustment 2, early NT (OR 0.27; p=0.040) and cumulative negative energy balance (OR 0.99; p=0.017) were associated with MUAC deterioration (Table 1). There were no association between anthropometric, inflammatory-nutritional, clinical or NT parameters with TC deterioration in the crude and adjusted analysis (Table 2).

Conclusion: Inflammatory-nutritional and NT parameters were associated with MUAC deterioration during PICU stay. The evaluation of MUAC and CRP/albumin ratio could be included in the nutritional status assessment of critically ill children, and the use of NT protocols to ensure the adequacy of NT should be incorporated in the PICU routine. Further

studies investigating the association of clinical and nutritional parameters with TC are necessary.

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Table 1 - Logistic Regression of factors associated with mid-upper arm circumference deterioration in critically ill children on mechanical ventilation in a Pediatric Intensive Care Unit, between July 2013 and February 2016.

Variables	Mid-upper Arm Circumference deterioration (n=39)					
	Crude		Adjustment 1[+]		Adjustment 2[++]	
	OR (95% CI)	p-value	OR (CI95%)	p-value	OR (CI95%)	p-value
Diagnostic (Surgical)	1.15 (0.30; 4.41)	0.840	1.14 (0.28; 4.65)	0.857	1.23 (0.29; 5.16)	0.778
CCC	1.08 (0.23; 4.97)	0.923	1.03 (0.21; 5.12)	0.968	1.05 (0.21; 5.40)	0.950
Albumin (g/dL)	1.04 (0.70; 1.54)	0.845	1.04 (0.70; 1.56)	0.833	1.07 (0.71; 1.61)	0.730
Hypoalbuminemia (< 3.0 g/dL)	1.73 (0.61; 4.86)	0.299	1.69 (0.57; 5.05)	0.344	1.59 (0.52; 4.82)	0.411
CRP (mg/dL)	1.00 (0.99; 1.01)	0.385	1.00 (0.99; 1.01)	0.334	1.00 (0.99; 1.01)	0.474
CRP/Albumin ratio (mg/dL:g/dL)						
1º tertile	1.00		1.00		1.00	
2º tertile	2.25 (0.60; 8.38)	0.227	3.14 (0.69; 14.31)	0.138	2.29 (0.56; 9.29)	0.245
3º tertile	2.81 (0.73; 10.77)	0.131	5.00 (1.02; 24.56)	**0.047**	2.50 (0.63; 9.90)	0.192
Nutritional status *						
Eutrophic	1.00		1.00		1.00	
Nutritional risk/ undernutrition(<-1)	0.73 (0.23; 2.28)	0.587	0.88 (0.26; 2.99)	0.844	0.84 (0.24; 2.87)	0.777
Overweight	0.78 (0.15; 3.99)	0.763	0.93 (0.17; 5.21)	0.934	0.76 (0.13; 4.29)	0.755
Prior NT	0.75 (0.27; 2.05)	0.570	0.81 (0.26; 2.51)	0.720	0.75 (0.24; 2.35)	0.627
Early NT (24 hours)	0.32 (0.10; 1.04)	0.058	0.34 (0.10; 1.14)	0.082	0.27 (0.08; 0.94)	**0.040**
Route of NT (parenteral)	1.69 (0.30; 9.47)	0.550	1.34 (0.21; 8.47)	0.757	1.55 (0.26; 9.19)	0.628
Energy adequacy (<66.7%)**	2.94 (0.84; 10.30)	0.092	2.38 (0.62; 9.17)	0.208	2.44 (0.66; 8.94)	0.180
Protein adequacy (<60%)**	3.09 (0.96; 9.92)	0.058	2.66 (0.80; 8.83)	0.109	2.72 (0.81; 9.10)	0.104
Cumulative energy balance (kcal/kg/day)**	0.99 (0.99; 1.00)	**0.006**	0.99 (0.99; 1.00)	**0.016**	0.99 (0.99; 1.00)	**0.017**
Cumulative protein balance (0.1g/kg)**	0.85 (0.74 ; 0.99)	**0.032**	0.87 (0.75; 1.01)	0.062	0.87 (0.75; 1.01)	0.064

OR: Odds Ratio; CI: Confidence Interval; CCC: Chronic Complex Condition; CRP: C-reactive protein; NT: Nutritional Therapy
[*] assessed at PICU admission, by body mass index-for-age; [**] average percentage of first 7 days
[+]Adjustment 1: sex, age and PIM 2; [++]Adjustment 2: sex, age and fluid overload

Table 2 - Logistic Regression of factors associated with thigh circumference deterioration in critically ill children on mechanical ventilation in a Pediatric Intensive Care Unit, between July 2013 and February 2016.

Variables	Thigh Circumference deterioration (n=41)					
	Crude		Adjustment 1[+]		Adjustment 2[++]	
	OR (95% CI)	p-value	OR (CI95%)	p-value	OR (CI95%)	p-value
Diagnostic (Surgical)	1.25 (0.22; 7.08)	0.801	0.85 (0.11; 6.56)	0.880	0.88 (0.10; 7.49)	0.905
CCC	0.97 (0.16; 5.82)	0.976	1.35 (0.17; 10.50)	0.773	1.20 (0.16; 9.06)	0.858
Albumin (g/dL)	1.18 (0.65; 2.15)	0.577	1.18 (0.65; 2.16)	0.584	1.16 (0.62; 2.16)	0.636

Hypoalbuminemia (< 3.0 g/dL)	1.11 (0.36; 3.46)	0.853	1.15 (0.31; 4.24)	0.835	1.22 (0.33; 4.52)	0.763
CRP (mg/dL)	1.00 (0.99; 1.01)	0.338	1.00 (0.99; 1.01)	0.971	1.00 (0.99; 1.01)	0.893
CRP/Albumin ratio (mg/dL:g/dL)						
1º tertile	1.00		1.00		1.00	
2º tertile	1.42 (0.34; 5.94)	0.633	1.65 (0.31; 8.93)	0.559	1.81 (0.35; 9.48)	0.479
3º tertile	1.17 (0.31; 4.46)	0.819	0.70 (0.14; 3.60)	0.672	1.00 (0.22; 4.55)	0.999
Nutritional status *						
Eutrophic	1.00		1.00		1.00	
Nutritional risk/ undernutrition (<-1)	0.43 (0.13; 1.43)	0.171	0.80 (0.20; 3.11)	0.742	0.81 (0.21; 3.19)	0.764
Overweight	1.15 (0.20; 6.70)	0.873	1.54 (0.22; 10.76)	0.666	1.58 (0.23; 10.60)	0.638
Prior NT	0.86 (0.29; 2.51)	0.781	1.75 (0.48; 6.36)	0.393	2.06 (0.55; 7.75)	0.284
Early NT (24 hours)	1.98 (0.65; 5.99)	0.228	2.28 (0.64; 8.12)	0.204	2.42 (0.67; 8.72)	0.178
Route of NT (parenteral)	2.64 (0.29; 24.24)	0.391	2.68 (0.13; 53.70)	0.519	1.91 (0.14; 25.57)	0.624
Energy adequacy (<66.7%)**	2.63 (0.65; 10.59)	0.173	1.78 (0.36; 8.17)	0.477	1.88 (0.36; 9.37)	0.443
Protein adequacy (<60%)**	1.73 (0.52; 5.72)	0.368	1.05 (0.27; 4.07)	0.948	1.11 (0.28; 4.43)	0.880
Cumulative energy balance (kcal/kg/day)**	1.00 (0.99; 1.00)	0.257	1.00 (0.99; 1.00)	0.862	1.00 (0.99; 1.00)	0.794
Cumulative protein balance (0.1g/kg)**	0.92 (0.80; 1.06)	0.238	0.96 (0.83; 1.12)	0.643	0.96 (0.82 ; 1.12)	0.600

OR: Odds Ratio; CI: Confidence Interval; CCC: Chronic Complex Condition; CRP: C-reactive protein; NT: Nutritional Therapy
* assessed at PICU admission, by body mass index-for-age; ** average percentage of first 7 days
+Adjustment 1: sex, age and PIM 2; ++Adjustment 2: sex, age and fluid overload

Supplementary Table 1 - Demographic, clinical and nutritional characterization of critically ill children on mechanical ventilation in a Pediatric Intensive Care Unit, between July 2013 and February 2016 (n=69).

Variables	N (%) / Median (IQR)
Sex (male)	41 (59.42)
Age (months)	15.57 [3.70; 92.79]
Diagnostic category	
Medical	58 (84.06)
Surgical	11 (15.94)
Chronic Complex Condition	8 (11.59)
PIM 2 (%)	6.20 [1.60; 24.50]
Nutritional status (n=68) *	
Undernutrition (< -2)	12 (17.65)
Nutritional risk (< -1)	7 (10.29)
Eutrophic	41 (60.29)
Overweight (> +2)	8 (11.76)
MUAC deterioration (%) (n=64)	-3.87 [-8.99; 0.00]
TC deterioration (%) (n=61)	-6.14 [-11.33; -0.65]
Prior Nutrition Therapy	35 (50.72)
Early Nutrition Therapy (24h)	45 (65.22)
Cumulative energy balance (kcal/kg/day)	-37.78 [-110.80; 34.53]
Cumulative protein balance (0.1g/kg/day)	-2.66 [-5.61; 0.18]
Clinical outcomes	
Nosocomial infection	29 (42.03)
Ventilator-associated pneumonia (n=29)	14 (48.28)
Duration of mechanical ventilation	11 [8; 22]
PICU LOS	14 [11; 21]
Hospital LOS	37 [21; 76]
Overall Mortality	14 (20.29)

IQR: Interquartile range; PIM 2: Pediatric Index of Mortality 2; MUAC: mid-upper arm circumference; TC: thigh circumference; PICU: Pediatric Intensive Care Unit; LOS: length of stay.
* assessed at PICU admission, by body mass index-for-age