Nutritional Predictors of Mortality after Discharge in Older Patients with type 2 Diabetes

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Nutritional predictors of mortality after discharge in older patients with type 2 diabetes

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Background: Older patient with type 2 diabetes (T2D) and malnutrition have a greater chance of negative events during hospitalization and a higher risk of mortality. The aim of this study was to investigate nutritional markers as mortality predictors following discharge hospitalized older patients with T2D.

Methods: This is a prospective cohort study with follow-up of four years. All patients were subjected to Mini Assessment Nutrition, Subjective Global Assessment, calf circumference, arm circumference and adductor pollicis muscle thickness, obtained all within 48 h of admission. Mortality data were verified by medical registry and analyzed using Cox-proportional hazard models and survival curves.

Results: 311 patients were included; the mean age was 71.35 years. There were 113 (36.3 %) deaths in the follow-up period. Nutritional status evaluated according to BMI identified 54.5% (n = 168) were overweight, for other hand the MAN identified 45.7% of patients were at risk of malnutrition and 37.7% malnutrition and the SGA identify 61.7% (n = 192) presented normal nutrition in admission. Malnutrition patients (OR=2.02), with low calf circumference (OR=1.43) or with APMT less than 5th percentile (2.33) were associated with post-discharge mortality.

Conclusion: Malnutrition, reduced calf circumference and reduced APMT were nutritional predictors of mortality after hospital discharge in older patients with diabetes

Keywords: type 2 diabetes; calf circumference; mortality; adductor pollicis muscle thickness malnutrition.

Introduction

Older people with type 2 diabetes (T2D) are more susceptible to adverse events and complications during a hospital stay, which can cause a to increased length of stay, malnutrition, functional decline, unscheduled surgeries and higher rates mortality.¹⁻³ The prevalence of malnutrition in older patients with T2D at admission can be vary between 18,5% a 22.7%.⁴⁻⁶

In fact, the body composition of patients with diabetes has particularities, such as: high body fat, lower strength and muscle mass⁷⁻⁹ and greater risk for sarcopenia⁴. Thus, the nutritional assessment of these patients needs to be carried out with caution and using tools that make it possible to detect body changes, functional changes as well as changes in nutritional status.

In the hospital routine, different tools are used to identify nutritional risk and assessment nutritional status such Subjective Global Assessment (SGA)¹⁰ and Mini Assessment Nutrition (MAN)¹¹, but most tool no quantify into account the muscle mass or functional capacity. For this purpose, for many years some anthropometric variables have been used such as: mid-arm circumference (MAC)¹²., calf circumference (CC)¹³ and adductor pollicis muscle thickness (AMPT)¹⁴ in different populations, but particularly in the older patients.

The tool SGA, it has been validated for different populations and clinical situations, it is considered a fast application tool with good prediction for nutritional status, length of stay and mortality¹⁵ Previous studies show good prediction in post-operative outcomes.¹⁶ The MNA was specifically structured to evaluate the older patient¹¹, however, it requires a longer time for application. Was evaluated as a predictor of mortality in older patients, not exclusively with T2D in Italy¹⁷. Others anthropometric measurements such as WC and MAC are sensitive in assessing muscle quantity, as well as APMT. Studies in Chinese¹⁸ and Taiwanese¹⁹ populations have identified WC^{18,19} and MAC^{18,20} such predictor of mortality.

Faced with this, this study aims to assess whether SGA, MNA, CC, MAC and APMT can predict mortality after discharge from this population.

Methods

A sample of patients of both sexes, hospitalized in a clinical ward of a university hospital in Southern Brazil was evaluated from July 2015 to December 2016 as part of the cohort study entitled: Clinical and nutritional predictors of mortality and readmission in older patients with and without type 2 diabetes was performed according to the recommendations established by the Declaration of Helsinki and approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre (# 150068).

Were included patients with type 2 diabetes (T2D) older than 60 years, with up to 48 hours of hospital admission, who agreed to participate in the study and signed the consent form. Were excluded patients with any mental decline or advanced motor sequelae; those who were treated at the Intensive Care Unit, and those who were in hospital for less than two days. The medical record was consulted for general information.

The body composition, and biochemical parameters (albumin) were evaluated in admission. Were performed the body circumferences: Calf circumference (CC), mid-arm circumference (MAC) and waist circumference (WC) using a metric tape. The height and the weight were measured for calculation body mass index (BMI).

The patients' nutritional status was evaluated in the admission through the Mini Nutritional Assessment (MNA) and by Subjective global assessment (SGA). The patients were classified according to the cut points by MNA: normal nutrition 24 to 30 points, risk of malnutrition with 17 to 23.5 points and malnutrition <17 points ¹¹ and by SGA those who obtained SGA-A were considered with normal nutrition, ASG-B moderate malnutrition and ASG-C with severe malnutrition. ¹⁰

To evaluate the independence level, the Instrumental Activities of Daily Living test (IADL) ¹⁷ was performed. The IADL is a scale that assesses eight tasks providing information about functional skills necessary to live independently in the community.

The APMT was performed according to proposed technique per Lameu et al²¹: The average of 3 measurements of the dominant hand was considered as the average adductor muscle thickness. The APMT was considered as < or equal 18 mm for men and < or equal 16 mm for women as indicator of muscle depletion and malnutrition. These

values refer to the 5th percentile, proposed in a previous study that described cutoffs, stratified by sex, for healthy adults and older people.²² Therefore, we have used APMT lower 5th percentile (APMT<p5) as a group of risk.

Survival data were consulted via telephone contact with all participants. The calls were made 30 days after hospital discharge and every 3 months until completing 12, 24 and 48 months. All death events were confirmed using the local death record database. The period from the first investigation to the date of death was recorded for participants who died during followup, the same was performed for all the other participants. The severity of comorbid diseases was recorded and scored according to Charlson comorbidity index (CCI) and was calculated according to the scoring system established by Charlson et al.²³.

Statistical Analysis

All variables had normality assessed by Kolmogorov-Smirnov test, the results were described as average and standard deviation or median and interquartile range (IQR). Categorical variables were reported as frequencies. T test for independent variables for parametric variables or Mann Whitney for non-parametric variables were performed, chi-square test for categorical variables.

Kaplan Meier curves were performed to assess the impact of malnutrition or anthropometric variables on mortality. The differences between the curves were evaluated by the log-rank test. The mortality time was counted in months, considering the date of the first admission until the date of death. Univariate and multivariate Cox proportional-hazard models were applied to calculate the hazard ratio (HR) and 95% confidence interval (CI). Significant covariates identified in the univariate Cox models ($P < 0.20$) were included in the multivariate Cox model. The variables that were included in the multivariate analysis were: age, sex, level of independence, MNA, CC, MAC and Charlson index >2 scores.

We used the Receiver Operating Characteristic (ROC) to determine whether the anthropometric variables and MAN correlated with mortality. The sample calculation was based on previous study³⁹ we would need 518 patients, 259 with T2D and 259 without T2D. We increased the sample to 610 patients, predicting a possible loss of follow-up of around 15%. This study showed that patients with T2D had

a 3-fold higher mortality than those without T2D. The estimated power was 90% with a alpha error of 5%, $p < 0.05$. All statistical analyses were performed in the SPSS program version 18 (SPSS Inc. Chicago, IL, USA)

Results

The characteristics overall at baseline were described in **Table 1**. There were 113 (36.3%) deaths in the follow-up period. Were included 311 patients with average age 73.7 ± 6.34 , 51% were females, 72% Caucasian and 84.9% sedentary. Neoplasia and hypertension were present in 69 (25.9%) and 232 (75.3%) respectively. The median length of stay was 14 (9-24) days. Nutritional status evaluated according to BMI identified 54.5% ($n = 168$) were overweight, for other hand the MAN identified 45.7% of patients were at risk of malnutrition and 37.7% malnutrition and the SGA identify 61.7% ($n = 192$) presented normal nutrition in admission.

Among those who died, the prevalence of malnutrition by MNA and ASG in admission was 24.3% ($n=28$) and 7.2% ($n=10$), respectively. Furthermore, presented lower CC (32.84 ± 3.14 vs. 35.89 ± 3.75 ; $p=0.019$) and lower APMT (9.08 ± 3.52 vs. 12.01 ± 4.38 ; $p=0.001$) when compared with patients alive

Univariate analysis showed independent association between malnutrition (MAN and SGA), calf circumference (<33 cm for woman; <34 cm for man), adductor pollicis muscle thickness ($<P5$), CCI and mortality after hospital discharge. In this sample, there was no association between mortality and BMI, MAC, abdominal circumference, arterial hypertension and IADL (**Graph 1**).

Multivariate analyzes post discharge mortality were described in **Table 2**. In model 1, with adjustments, malnutrition patients, with APMT less than the 5th percentile and WC (less than 33 cm for women, 34 cm for men) had a higher risk of post-discharge mortality. In model 2, both maintained an association with mortality after discharge.

In a combined model, we evaluated MNA and APMT and both remained associated with mortality after adjustment, as well as the coexistence of both (APMT + malnutrition).

However, when evaluating APMT and CC in the same model, only APMT <5 th percentile increased the risk of mortality.

The subjective global assessment and albumin were not significant in this sample of patients.

Survival curves the MNA and APMT are presented in **Fig. 1A and 1B**. The survival curves were statistically different by the log-rank test ($p=0.030$ and $p=0.002$), indicating that patients with diabetes plus malnutrition or APMT $<P5$ had a higher risk of mortality when compared to older patients with normal nutrition and with APMT $>P5$. The prediction power calculated by the area below the ROC curve was statistically significant for MAN (0.591) and APMT (0.671), as shown in **Graph 2**.

Discussion

This study investigated the relationship between anthropometric variables, MNA, SGA and mortality after 4 years hospital discharge within in older patients with T2D. We found that older malnutrition patients with reduced calf circumference (<33 cm for women and <34 cm for men) or with adductor pollicis muscle thickness below the 5th percentile had a higher risk of mortality after hospital discharge. In addition, patients with malnutrition plus APMT <5 had a 40% risk of mortality after discharge.

These results demonstrate to the importance of assessing older patients with T2D in the hospital environment more broadly. Hospital malnutrition is still a prevalent theme, and despite the numerous negative outcomes, it is still often neglected²⁴. In this sample 168 (54.5%) were overweight and had elevated waist circumference ($103.2 \text{ cm} \pm 13.2$ for men and 100.7 ± 14.8 for women), however, 136 (44%) had low WC, 275 (88.4%) APMT below the 5th percentile and 142 (45.7%) with nutritional risk.

This was the first study to evaluate the relationship between APMT and mortality in older patients with T2D. It is known that patients with T2D have lower muscle mass when compared to patients without DM²⁵ but most studies assess the relationship between overweight and obesity with negative outcomes without assessing muscle mass. In our data, patients with T2D were overweight, evaluated by the BMI, and also APMT $<p5$ (median 11mm), but there was no relation between overweight and mortality. On the other hand, when evaluated by MNA, they presented 17.9% of malnutrition, being associated with post-discharge mortality

The APMT has been evaluated in different clinical situations²⁶⁻²⁹ and in the healthy population.²² Regarding the APMT association and mortality, previous studies²⁷⁻³⁰ associated the lower APMT with mortality under different scenarios. Caparossi et. al²⁹

in his study with surgical patients showed that among patients who died, APMT values were significantly lower (11.4 ± 4.1 in the right hand and 11.2 ± 3.9 in the left $p = 0.03$). Likewise, Bragnolo et al.²⁷ showed that postoperative mortality was 25% higher in patients with APMT below the cut-off point considered for dominant hand in the older patients $<12.2\text{mm}$ (women) and $<14.4\text{mm}$ for men and Ghorabi et.al³⁰ in patients from intensive care unit, 11.12 ± 2 mm in the patients who died and 16.7 ± 2.2 mm in those who survived ($P = .05$).

In our sample, 43.7% of patients had, at the time of admission, the calf circumference below the cohort point. In last years, there was an increase in publications with calf circumference to in different populations for different outcomes, mainly because it is a good marker of muscle mass in older patients³¹, has an association with sarcopenia³², is a predictor of readmission³³ and mortality.³⁴ Because it is an easy-to-measure and low-cost measure, it can be part of the routine assessment of hospitalized patients.

The MNA it is a tool that better detects malnutrition or the risk of malnutrition in hospitalized older people than BMI.¹¹ Other studies evaluated the relationship between MNA and mortality in different clinical situations. Joaquin C et. al³⁵ in a study of cohort, malnutrition was an independent predictor of 2-year all-cause death in 151 outpatients with heart failure (OR:4.56 CI95% 1.55-13.4). Similarly, Van Wilssen J et al.³⁶ showed the association between the preoperative MNA score and mortality after surgery for hip fractures in 226 older patients, with mortality in hospital and 1-year mortality of 27% and 46% in malnutrition patients, respectively.

The dependence level also showed an evident association with mortality after 4 years of hospital discharge. The more dependent older patients (with less points in the IADL) had a higher mortality rate when compared to the independent patients; the association between IADL and mortality already described for other authors.^{37,37}

As shortcomings, the APMT measurement was performed only once, 48 hours after admission, and it was not possible to assess whether the patients further reduced the thickness during hospitalization. As strength of our study, we highlight the prospective design, as well as the significant number of patients evaluated for a significant time after hospital discharge. It is becoming increasingly important to include the assessment of muscle mass and functionality in the older individual as a complementary way to nutritional assessment.

Conclusions

In fact, the nutritional status during the hospitalization is important and can be a risk factor for other problems, often not related to the main reason for hospitalization. Thus, body changes in the older patient with type 2 diabetes can mask muscle and functional loss. Despite technological advances in body assessment methods, anthropometrics assessments, such as the circumference of the calf and the thickness of the adductor pollicis muscle, are still a safe, low-cost and validated method that can be used in combination with other tools to identify body changes in older patients.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Beretta MV and Rodrigues TC were responsible for the study concept design, data analysis, interpretation of findings and drafted the manuscript. Feldman JV and Silva CN contributed to data acquisition. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate: This project follows the recommendations established by the Declaration of Helsinki and was approved by the Ethics Committee of Hospital de Clínicas de Porto Alegre under number: 15008.

Consent for publication: Not applicable in this section.

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Table 1. Baseline clinical and nutrition characteristics of older patients with T2D

	All patients (n=311)	Alive (n=198)	Dead (n=113)	P*
Age (years)	73.7 ± 6.34	74.85 ± 6.60	73.10 ± 6.11	0.019
Gender (Women)	159 (51)	89 (45)	70 (62)	0.005
Caucasian	224 (72)	143 (72.2)	81 (71.7)	0.432
Elementary School	201 (64.6)	129 (65)	72 (63.7)	0.369
Smokers n (%)	45 (14.5)	34 (17.2)	11 (9.7)	0.128
Alcoholics n (%)	43 (13.8)	32 (16.2)	11 (9.7)	0.222
Sedentary n (%)	264 (84.9)	169 (8.4)	95 (84.1)	0.744
Malignant neoplasm n (%)	69 (25.9)	30 (18.1)	39 (39)	0.001
SAH n (%)	232 (75.3)	151 (76.6)	81 (73)	0.49
More than 5 drougs n(%)	114 (36.7)	80 (40.4)	34 (30)	0.087
IADL (dependent) n(%)	246 (79)	158 (79.8)	88 (77.9)	0.772
LOS (days)	14 (9-24)	14 (9-23)	15 (9-27)	0.268¥
IMC (kg/m2)	27.91 ± 5.71	27.88 ± 5.08	27.98 ± 5.61	0.87
Normal nutrition	111 (34.7)	70 (35.4)	38 (35.4)	0.74
malnutrition	32 (10.4)	22 (11.1)	10 (9.1)	
overweight	168 (54.5)	106 (53.5)	62 (56.4)	
ASG (score)		18.07 ± 2.41	19.19 ± 2.57	0.18
Normal nutrition	192 (61.7)	130 (65.5)	63 (56.8)	0.039
moderate malnutrition	104 (33.4)	64 (32.5)	40 (36)	
malnutrition	15 (3.9)	4 (2.0)	10 (7.2)	
MNA (score)		25.05 ± 4.73	23.55 ± 4.61	0.007
Normal nutrition	111 (35.7)	82 (41.1)	30 (27)	0.004
risk of malnutrition	142 (45.7)	88 (44.7)	54 (48.6)	
malnutrition	58 (37.7)	28 (14.2)	29 (24.3)	
AC (men)	103.2 ± 13.21	102.13 ± 13.16	103.65 ± 13.27	0.561
AC (woman)	100.7 ± 14.8	100.03 ± 14.91	101.28 ± 15.34	0.628
Arm circumference (cm)	30.31 ± 3.97	30.47 ± 3.76	30.04 ± 4.33	0.36
Calf circumference (cm)	33.51 ± 3.77	35.89 ± 3.75	32.84 ± 3.14	0.019
< 33cm woman; <34cm men)		78 (39.4)	58 (52.3)	0.020
AMPT (mm)	10.60 ± 4.21	12.01 ± 4.38	9.08 ± 3.52	0.001
APMT <P5	275 (88.4)	169 (85.4)	106 (93.8)	0.027
Albumin (g/dl)	3.70 ± 0.67	3.75 ± 0.64	3.59 ± 0.70	0.04
Causes of hospitalization				
Cardiovascular	80 (25)			
Neoplasias	50 (16)			
Infectious diseases	98 (18.8)			
Surgery	34 (11)			
COPD	18 (6.0)			
Death n (%)	113 (36.3)			

*Student's t-test or Pearson chi-square test when appropriate. ¥ Mann-Whitney test. SAH: Systolic arterial hypertension IADL: Instrumental Activity of Daily Living; LOS: length of stay; BMI: body mass index; SGA: subjective global assessment; MNA: mini nutrition assessment; CC: calf circumference; AC: abdominal circumference; APMT: adductor pollicis muscle tickness; COPD: Chronic obstructive pulmonary disease

Graphic 1. Unadjusted analysis between nutritional markers and mortality

OR: odds ratio; CI 95%: confidence interval 95%; MNA: mini nutrition assessment; APMT: adductor pollicis muscle thickness; SGA: subjective Global assessment; BMI: body mass index; SAH: systolic arterial hypertension, IADL: instrumental Activity of Daily Living

Table 2. Adjusted analysis of the relationship between nutritional markers and mortality

	MNA (risk)	MNA (malnutrition)	APMT (< p5)	APMT (<p5) + malnutrition	CC (<33cm; <34 cm)	SGA malnutrition	Albumin (g/dl)
	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)
Model 1	1.45 (0.92-2.27)	2.02 (1.19-3.43)	2.37 (1.10-5.11)		1.48 (1.15-2.89)	2.04 (0.96-4.31)	0.79 (0.59-1.07)
Model 2	1.42 (0.91-2.23)	1.92 (1.13-3.24)	2.33 (1.08-5.03)	1.40 (1.04-1.30)	1.03 (1.00-1.06)		
Combined model (MNA and APMT)	1.41 (0.90-2.20)	1.78 (1.05-3.03)	2.91 (1.18-7.17)				
Combined model (CC and APMT)			2.83 (1.14-7.02)		1.30 (0.88-1.90)		

Model 1: adjusted for age and gender; Model 2: Adjusted for age, gender, CCI; Combined model: analyzes adjusted for the same variables as model 1 and model 2, but performed with the combination: MNA and APMT or CC and APMT.

OR: odds ratio; CI 95%: confidence interval; MNA: mini nutrition assessment; CCI: Charlson comorbidity index : APMT: adductor pollicis muscle tickness; CC: calf circumference

Figure 1A. Relationship between adductor pollicis muscle thickness and mortality

		APMT<p5		APMT>P5	
		Chi-Square	Sig.	Chi-Square	Sig.
Log Rank (Mantel- Cox)	APMT<p5			4.72	0.030
	APMT>P5	4.72	0.030		

Figure 1B. Relationship between mini assessment nutrition and mortality

		Normal nutrition		risk of malnutrition		malnutrition	
		Chi-Square	Sig.	Chi-Square	Sig.	Chi-Square	Sig.
Log Rank (Mantel- Cox)	Normal nutrition			3.73	0.053	9.22	0.002
	risk of malnutrition	3.73	0.053			2.46	0.116
	malnutrition	9.22	0.002	2.49	0.11		

Graph 2. ROC curve of MNA and APMT

Area Under the Curve

Test Result Variable(s)	Area	Asymptotic Sig. ^b	Confidence Interval	
			Lower Bound	Upper Bound
APMT	0.671	0.000	0.608	0.733
MNA	0.591	0.008	0.525	0.657

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Figures

OR: odds ratio; CI 95%: confidence interval 95%; MNA: mini nutrition assessment; APMT: adductor pollicis muscle thickness; SGA: subjective Global assessment; BMI: body mass index; SAH: systolic arterial hypertension, IADL: instrumental Activity of Daily Living

Figure 1

Unadjusted analysis between nutritional markers and mortality

Figure 2

Relationship between adductor pollicis muscle thickness and mortality

		Normal nutrition		risk of malnutrition		malnutrition	
		Chi-Square	Sig.	Chi-Square	Sig.	Chi-Square	Sig.
Log Rank (Mantel- Cox)	Normal nutrition			3.73	0.053	9.22	0.002
	risk of malnutrition	3.73	0.053			2.46	0.116
	malnutrition	9.22	0.002	2.49	0.11		

Figure 3

Relationship between mini assessment nutrition and mortality

Area Under the Curve				
Test Result Variable(s)	Area	Asymptotic Sig. ^b	Confidence Interval Lower Bound	Confidence Interval Upper Bound
APMT	0.671	0.000	0.608	0.733
MNA	0.591	0.008	0.525	0.657

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Figure 4

Graph 2. ROC curve of MNA and APMT