



Applied nutritional investigation

Association of dietary total antioxidant capacity with anthropometric indicators, C-reactive protein, and clinical outcomes in hospitalized oncologic patients



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ABSTRACT

Objective: Many studies have shown an inverse association between higher dietary total antioxidant capacity (DTAC) and chronic non-communicable diseases, including cancer. The aim of this study was to evaluate the association of the DTAC with anthropometric and biochemical indicators and clinical outcomes in hospitalized patients with cancer.

Methods: A cross-sectional study was carried out with 196 hospitalized patients diagnosed with cancer. The DTAC, determined by the ferric-reducing antioxidant power method, was calculated using a validated standard spreadsheet. Multivariate linear regression was used to assess the association, identifying anthropometric indicators that were associated with DTAC and the variables of interest. $P < 0.05$ was statistically significant.

Results: The individuals included in the last tertile of DTAC presented lower occurrences of death ($P = 0.032$), constipation ($P = 0.010$), dysphagia ($P = 0.010$), painful swallowing and chewing ($P = 0.019$), and dehydration ($P = 0.032$) than individuals in the first tertile. The C-reactive protein values were significantly lower ($P = 0.010$) and handgrip strength values were higher ($P = 0.037$) in individuals in the third tertile than in the other participants.

Conclusions: DTAC was associated with a better prognosis of hospitalized cancer patients, considering signs and symptoms of nutritional impact, as well as the inflammatory state of the patients. These factors may influence the length of hospital stay and mortality. The findings of this research provide important information for a preventive and nutritional management perspective in this population.

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Introduction

Food consumption and specific dietary components may directly influence the quality of life and prognosis of individuals with cancer [1,2]. Food intake of hospitalized patients with cancer is often compromised due to treatment side effects. These patients experience changes in taste perception and gastrointestinal (GI) symptoms, both of which lead to a worsening of nutritional status, complications, and aggravations during hospitalization [3,4].

Dietary total antioxidant capacity (DTAC) has been considered a useful tool to assess health benefits of the accumulated antioxidant capacity of foods, considering every food component with antioxidant properties in the diet [5,6]. Oxidative stress is a common pathogen among chronic non-communicable diseases [7] and many studies have shown an inverse association between higher DTAC and chronic non-communicable diseases, including cancer [8–12].

A diet rich in fruits and vegetables and low in fats can predict improved prognosis for individuals with cancer and may reduce the risk for recurrence, complications, and hospital length of stays (LOS) [13]. It can also help to recover the nutritional status of patients and improve treatment response [14–16]. On the other hand, diets poor in antioxidants are related to an increased formation of free radicals and reactive oxygen species that can impair

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cell function [17]. Therefore, there is a growing interest in the potential preventive effects of antioxidants in several types of cancers [18].

Much is known about the dietary effects on the incidence of cancer. However, the effect of food intake on individuals who are already undergoing cancer treatment in relation to prognosis has not been studied in depth. An adequate follow-up of patients with cancer is one of the main factors that contributes to a better prognosis [19]. In this sense, it is important to consider the protective factor of diets rich in antioxidants, which can delay certain cell damage and prevent the accumulation of reactive oxygen molecules that can promote genetic changes in cells [20–22].

Thus, the main objective of this study was to evaluate the association of the DTAC with anthropometric and biochemical indicators and clinical outcomes in hospitalized patients with cancer.

Methods

Sample and study design

A cross-sectional study was carried out with hospitalized individuals diagnosed with cancer and/or who received hematopoietic stem cell transplantation (HSCT). The sample consisted of men and women (≥ 20 y of age), who were admitted to a public or private hospital in the city of Belo Horizonte, between February and June 2018 and February and June 2019. Individuals who did not present a 24-h dietary recall or who had missing or incomplete anthropometric data and/or C-reactive protein (CRP) data in their medical records were not included in the study. The study protocol was approved by the Human Research Ethics Committee of the Federal University of Viçosa and by the Human Research Ethics Committee of the Federal University of Minas Gerais.

Food consumption assessment

A dietary record was primarily used to assess food consumption. The 24-h recall was applied in the cases of illiterate individuals, patients with no hospital companion, or those who were unable to complete the record due to cognitive alterations. On the dietary record, patients were instructed to write down the information related to quantity (household measurements) or percentage in relation to the total portion size of meals offered by the hospital or from outside the institution. The automated multipass method (MAMP) was applied on the day after the food record or after the 24-h recall [23].

A Microsoft Excel 2019 spreadsheet was created to quantify the macro- and micronutrients based on the portions offered by the hospital and the food from outside the hospital. The main sources of information on nutritional composition the Food Composition Table of the Brazilian Institute of Geography and Statistics [24], the Brazilian Food Composition Table [25], the U.S. Department of Agriculture Food Composition Table [26], and the nutritional information on food labels.

DTAC, determined by the ferric reducing antioxidant power (FRAP) method, was calculated using a validated standard spreadsheet [27]. To assign a DTAC value for foods unavailable in previous reports, the data for a similar food item (e.g., same botanic group) were used as a proxy. When DTAC values of cooked food were not available, DTAC levels of fresh food were used to calculate the estimate. The final DTAC score was calculated by adding the individual values of each food item from the dietary record, expressed in mmol/d [28].

Anthropometric, clinical, and biochemical assessment

The participants were weighed using a mechanical or digital platform scale with accuracy of 100 g. The weight was adjusted in cases of ascites and edema, disregarding the excess body water weight [29]. In individuals who had undergone limb amputation, the percentage of contribution of the missing limb segment to total body weight was subtracted [30]. The weight of bedridden individuals was estimated using predictive equations [31]. When it was not possible to measure or estimate the current weight, the usual/average weight of the individual was evaluated, and the percentage of weight loss was calculated and classified in relation to time according to Blackburn et al. [32]. Height measurements were informed by the patients or by their hospital companion.

Body mass index (BMI) was calculated as the body weight divided by the squared height (kg/m^2). Adults were classified according to the cutoff values proposed by the World Health Organization [33] and elderly individuals were classified according to Pan American Health Organization [34].

Arm circumference was measured at the midpoint between the acromion process of the scapula and the olecranon process and classified according to reference values proposed by Frisancho [35]. Calf perimeter was measured at the point of

maximal circumference considering cutoff points validated for the Brazilian population [36].

Handgrip strength (HGS) was measured using a digital hand dynamometer 90 kg capacity. Participants placed their forearm on a surface at elbow flexion angle of 90 degrees. The measurements were performed in triplicates with the dominant hand and the highest value was used [37,38]. The threshold for low HGS in adult men is <36.7 kg and for adult women is <20.8 kg [37,38]. For older participants, we used the cutoff points proposed by the consensus of the European Working Group on Sarcopenia in Older People (EWGSOP; 16 kg for women and 27 kg for men) [39].

Sociodemographic and lifestyle information of participants was obtained from their medical record. Information related to clinical outcomes, such as the hospital LOS; metastasis; clinical complications; discharge or death; CRP values; and the presence of GI symptoms with nutritional affect, such as diarrhea, constipation, nausea, vomiting, hypoxia, mucositis, xerostomia, and dysgeusia also were evaluated.

Statistical analysis

Categorical variables were presented absolute and relative frequency (%). Numerical variables were expressed as median and interquartile range (IQR). The Shapiro–Wilk test was used to test normality of data. DTAC values were categorized into tertiles. The variables of interest in the tertiles were compared by Pearson's χ^2 test or the analysis of variance corrected for heteroscedasticity (Brown–Forsythe F statistic) and the Games–Howell post hoc test.

Food consumption data were adjusted for daily caloric intake using the residual method [27]. Multivariate linear regression was used to assess the association, identifying anthropometric indicators that had association of DTAC with the variables of interest. The models were controlled for sex, age (y), and hospital LOS (d).

The calculation of the statistical power of the study was carried out. The software applications used to analyze the data were Microsoft Excel version 2016, SPSS version 25 (IBM, Armonk, NY, USA), and STATA version 14 (StataCorp, College Station, TX, USA), with statistical significance of $P < 0.05$.

Results

The study included 196 hospitalized patients with cancer (50% women) with an average age of 60 y (IQR, 22–92 y). Current smoking and alcohol ingestion was identified in 9.2% of the assessed individuals. The highest tertile of DTAC (>5.19 mmol/D) was found in single, non-smoking, and non-alcohol-consuming adults (Table 1).

Regarding clinical outcomes, the individuals included in the last tertile of DTAC also presented lower occurrences of death, constipation, dysphagia, painful swallowing and chewing, and dehydration than individuals in tertile 1 (Table 2). An interesting finding in this work was that CRP values were significantly lower and HGS values were higher in individuals in tertile 3, than in the other participants (Fig. 1).

Considering the food processing classification, fresh foods (57.3%) were the main contributors to DTAC, followed by ultraprocessed foods (25.9%). Among them, foods that contributed the most to DTAC were coffee and tea (59%), followed by fruits (13.4%; Fig. 2).

Finally, DTAC was positively associated with weight, BMI, arm and calf perimeters, and negatively associated with weight loss (in kg or %) and calf reduction during hospitalization, regardless of sex, age, and LOS (Table 3).

Discussion

To our knowledge, this was the first study to discuss the association of DTAC with anthropometric indicators and clinical outcomes in hospitalized patients with cancer.

DTAC was positively associated with HGS in the present study. Observational studies have shown positive associations between a higher antioxidant capacity of the diet and measurements related to low muscle function in adults and elderly people >60 years [40–43]. However, low levels of consumption of antioxidants are common among the general population [44–46], and this important factor should be evaluated, mainly in hospitalized individuals.

Table 1
Sociodemographic and clinical characteristics of individuals undergoing cancer treatment, according to DTAC tertiles

Variables	DTAC tertiles			P-value*
	T1 (n = 65)	T2 (n = 66)	T3 (n = 65)	
Age range (y)				
Adult (<60)	30 (32.6)	28 (30.4)	34 (37)	0.520
Elderly (≥60)	35 (33.7)	38 (36.5)	31 (29.8)	
Sex				
Men	31 (31.6)	35 (35.7)	32 (32.7)	0.820
Women	34 (34.7)	31 (31.6)	33 (33.7)	
Marital status				
Single	19 (37.3)	12 (23.5)	20 (39.2)	0.419
Married	32 (33)	32 (33)	33 (34)	
Widower	8 (30.8)	11 (42.3)	7 (26.9)	
Divorced	6 (27.3)	11 (50)	5 (22.7)	
Current smoker				
Yes	37 (31.6)	38 (32.5)	42 (35.9)	0.323
No	8 (44.4)	3 (16.7)	7 (38.9)	
Former smoker	20 (32.8)	25 (41)	16 (26.2)	
Alcohol consumption				
Yes	34 (36.2)	32 (34)	28 (29.8)	0.553
No	3 (16.7)	6 (33.3)	9 (50)	
Social drinker	11 (35.5)	8 (25.8)	12 (38.7)	
Former drinker	17 (32.1)	20 (37.7)	16 (30.2)	
Metastasis	20 (39.2)	19 (37.3)	12 (23.5)	0.228
Hospital LOS (d) [†]				
> 14 d	28 (30.1)	29 (31.2)	36 (38.7)	0.291
≤14 d	37 (35.9)	37 (35.9)	29 (28.2)	

DTAC, dietary total antioxidant capacity; LOS, length of stay.

T1: <2.45 mmol/d; T2: 2.45–5.19 mmol/d; T3: >5.19 mmol/d.

Qualitative variables presented in absolute and relative frequency (%).

*Pearson's χ^2 test.

[†]Hospitalization time categorized in relation to the sample median (≤14 d; > 14 d).

Results also suggest that a high consumption of antioxidants could be related to the prevention of sarcopenia and, in fact, there has been a growing interest in the assessment of the role of the redox balance in the etiology of sarcopenia [47,48]. With aging, the accumulation of reactive oxygen species (ROS) may cause oxidative damage. This process may lead to the loss of muscle strength and

Table 2
Clinical outcomes, signs and symptoms of individuals undergoing cancer treatment, according to DTAC tertiles

Variables	DTAC tertiles			P-value*
	T1 (n = 65)	T2 (n = 66)	T3 (n = 65)	
Outcomes				
Readmission within 30 d after hospital discharge	10 (34.5)	9 (31)	10 (34.5)	0.948
Transfer to the ICU during hospitalization	4 (33.3)	3 (25)	5 (41.7)	0.754
Death	16 (47.1)	13 (38.2)	5 (14.7)	0.032
Sepsis	10 (33.3)	14 (46.7)	6 (20)	0.163
Signs and symptoms				
Constipation	28 (49.1)	15 (26.3)	14 (24.6)	0.010
Diarrhea	10 (43.5)	10 (43.5)	3 (13)	0.093
Vomiting	10 (62.5)	2 (12.5)	4 (25)	0.027
Nausea	11 (42.3)	6 (23.1)	9 (34.6)	0.412
Dysgeusia or ageusia	30 (34.1)	33 (37.5)	25 (28.4)	0.402
Mucositis	4 (36.4)	3 (27.3)	4 (36.4)	0.899
Dysphagia	15 (65.2)	6 (21.6)	2 (8.7)	0.001
Painful swallowing and chewing	17 (51.5)	11 (33.3)	5 (15.2)	0.019
Dehydration	19 (47.5)	14 (35)	7 (17.5)	0.032
Xerostomia	42 (39.3)	34 (31.8)	31 (29)	0.127
Fistula	11 (50.0)	8 (36.4)	3 (13.6)	0.081
Fever	10 (35.7)	8 (28.6)	10 (35.7)	0.827

DTAC, dietary total antioxidant capacity; ICU, intensive care unit.

T1: <2.45 mmol/d; T2: 2.45–5.19 mmol/d; T3: >5.19 mmol/d.

Qualitative variables presented in absolute and relative frequency (%).

*Pearson's χ^2 test.

muscle mass due to the increased ROS levels and reduced enzyme antioxidant protection and mitochondrial function, which are associated with inadequate food intake of antioxidants [49–51].

In this sense, diets richer in fruits and vegetables have been associated with a greater muscle strength in the elderly population [52]. On the other hand, diets containing high amounts of saturated fat and less fruits and vegetables were associated with greater functional limitations after a 4-y follow-up period [53]. According to the recommendations of the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR), DTAC provides a more comprehensive overview of antioxidant intake than the analysis of individual nutrients [54]. In the present study, we evaluated the total daily diet, not a specific food group. This may be more effective than studies that have assessed single nutrients or specific food groups used to prevent the loss of muscle mass and strength in hospitalized individuals.

Nevertheless, patients with cancer experience micronutrient deficiencies due to their increased nutritional needs caused by a reduced intake [55] and GI changes that result from the cancer treatment, such as vomiting, nausea, mucositis, diarrhea, constipation, and dysgeusia [56]. In this context, the patients included in the highest tertile of DTAC had lower GI symptoms such as constipation, dysphagia, painful swallowing and chewing, and dehydration. Considering that dietary antioxidants are mainly present in fruits, vegetables, and other plant-derived foods, this result can be associated with the fact that patients tend to increase the consumption of such foods during hospitalization [57]. These results are relevant for clinical medical practice, as the mentioned symptoms have an important nutritional affect and may cause losses in muscle mass and increased mortality rates.

In this study, an inverse association was found between serum CRP and DTAC. This result had already been observed in a population of young adults [58]. Additionally, some studies have found an inverse association between dietary antioxidants, such as carotenoids, lycopene, and vitamins C and E with CRP marker in patients with cancer [59–64]. High levels of CRP have been positively associated with worse prognosis and diets with higher antioxidant capacity may be effective in the regulation and expression of this inflammatory marker [65].

We have found that the individuals in the highest tertile of DTAC had lower mortality rates than the patients in the first tertile. These results are in agreement with previous studies that found an association between DTAC and the reduction of all-cause mortality among adults in Spain [66], Sweden [67], and France [68], and in elderly adults in Australia [69]. A diet with high DTAC provides higher levels of antioxidant micronutrients and can affect the nutritional, antioxidant, and inflammatory status of patients. This was confirmed in the present study by the results of HGS, GI symptoms, and CRP. Nutritional and inflammatory status are important predictors of mortality in this population [70,71] and the monitoring of the DTAC could effectively control these factors.

The largest contributors of nutrients and dietary antioxidant components are fresh foods and their consumption is associated with antioxidant capacity [72]. Among the assessed foods, tea and coffee were the main contributors to DTAC. For the Brazilian population, coffee contributes to one of the highest daily consumption averages and is even higher than rice and beans [73]. Coffee is an important source of antioxidants, increasing life expectancy if consumed in the long term and delaying the progress of chronic diseases [74]. However, despite its benefits, it should be consumed with caution, as in Brazil, it is usually linked to a higher intake of added sugar [73].

The strengths of this study include the expansion of food composition databases, providing more complete data, which will help in the estimation of food intake in this specific population.

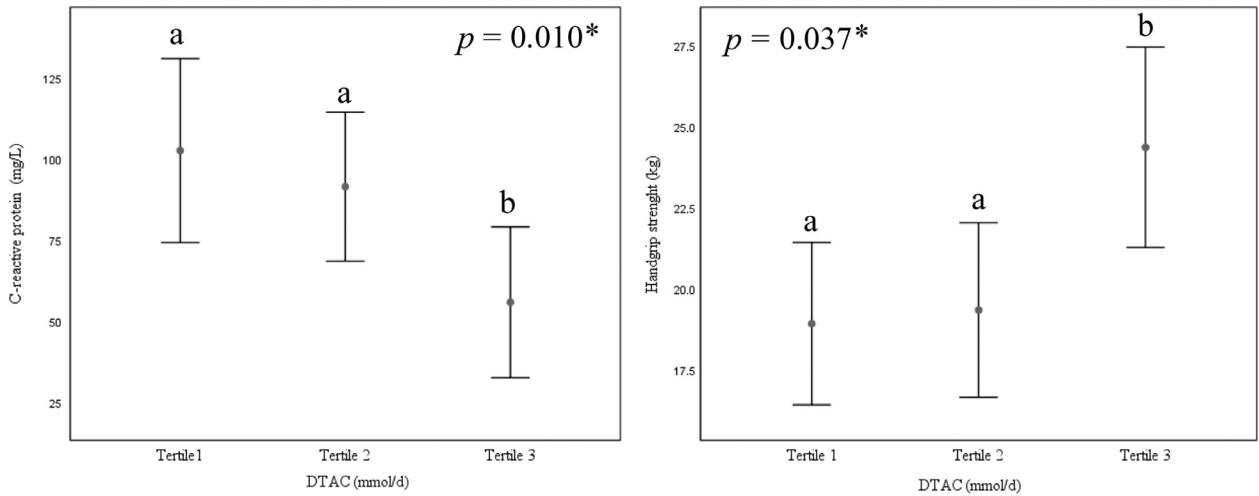


Fig. 1. C-reactive protein and handgrip strength according to tertiles of DTAC: tertile 1: <2.45 mmol/d (n = 65); tertile 2: 2.45–5.19 mmol/d (n = 66); tertile 3: >5.19 mmol/d (n = 65). Data expressed as mean and 95% CI.*Analysis of variance with correction by Brown–Forsythe and post hoc Games–Howell. Different letters (^{a,b}) indicate significant differences. DTAC, dietary total antioxidant capacity.

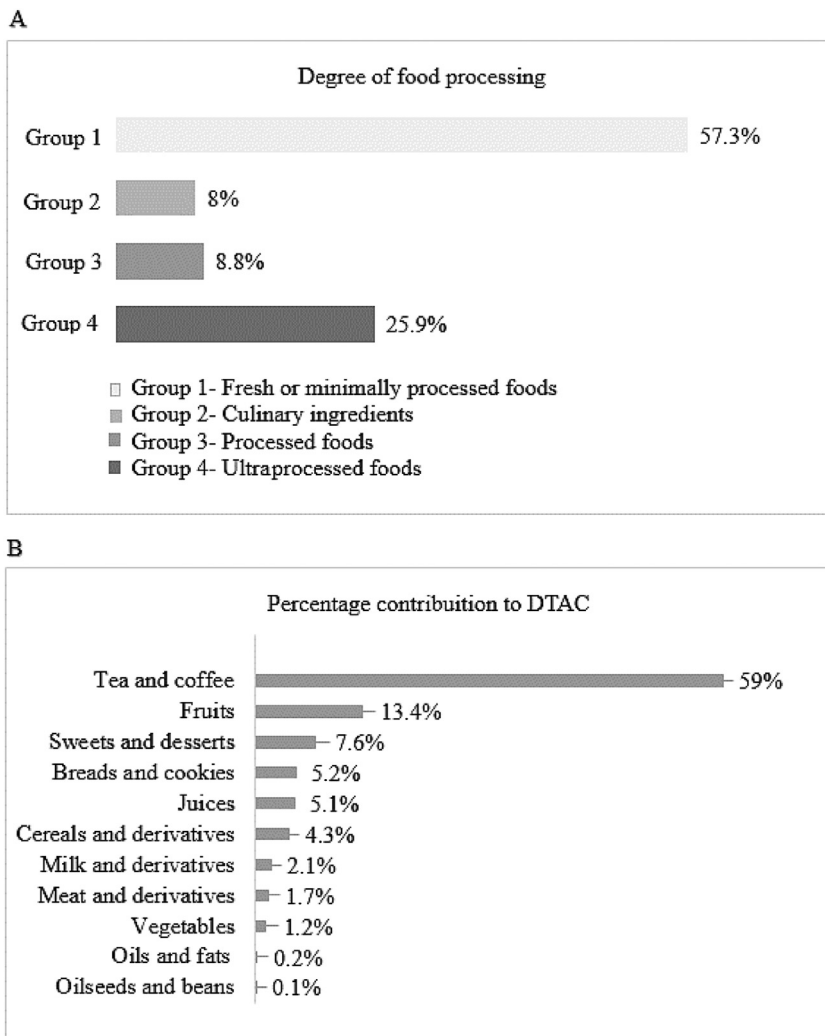


Fig. 2. Distribution of food according to the degree of processing (A) and the contribution to DTAC (B). DTAC, dietary total antioxidant capacity.

Table 3
Association of DTAC (independent variable) with anthropometric indicators

	Model 1*			Model 2 [†]		
	β and 95% CI	Adjusted r^2	P-value	β and 95% CI	Adjusted r^2	P-value
Weight (kg)	1.034 (0.365 to 1.704)	0.098	<0.001	0.989 (0.323 to 1.654)	0.112	< 0.001
BMI (kg/m ²)	0.300 (0.078 to 0.521)	0.040	0.012	0.284 (0.064 to 0.504)	0.057	0.004
Weight loss during hospitalization (kg)	-0.341 (-0.607 to -0.075)	0.032	0.029	-0.359 (-0.616 to -0.101)	0.095	<0.001
Weight loss during hospitalization (%)	-0.534 (-0.082 to -0.176)	0.042	<0.001	-0.576 (-0.924 to -0.227)	0.097	<0.001
Arm circumference (cm)	0.267 (0.062 to 0.471)	0.077	<0.001	0.256 (0.052 to 0.460)	0.085	<0.001
Calf perimeter (cm)	0.336 (0.147 to 0.526)	0.095	<0.001	0.331 (0.141 to 0.521)	0.094	<0.001
Calf perimeter reduction (cm)	0.001 (-0.128 to 0.129)	-0.003	0.448	-0.026 (-0.145 to 0.094)	0.145	<0.001

BMI, body mass index; DTAC, dietary total antioxidant capacity.

*Multivariate linear regression adjusted for sex and age.

[†]Multivariate linear regression adjusted for sex, age, and hospital length of hospital.

Additionally, the study investigated a practical application in the hospital environment, a field that has been little addressed in the literature. However, these findings are limited by the use of a cross-sectional design and it was not possible to infer causality. Furthermore, we did not consider clinical factors that may interfere with the nutritional status of patients, such as disease staging, the time of diagnosis, and the type of cancer treatment applied to the patient, which potentially increases variability of consumption data.

Conclusion

In the present study, DTAC was associated with a better prognosis of hospitalized patients with cancer, considering signs and symptoms of nutritional affect, and the inflammatory state of the patient. These factors may influence hospital LOS and mortality. The findings of this research provide important information for a preventive and nutritional management perspective in this population.

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