Original Article

Anthropometric assessment of men with colorectal cancer after dietary supplement with *Agaricus sylvaticus* fungus

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Fortes RC, Lavor e Silva JR, Novaes MRCG. Anthropometric assessment of men with colorectal cancer after dietary supplement with *Agaricus sylvaticus* fungus. **J Coloproctol**, 2012;32(4): 365-371.

ABSTRACT: **Introduction**: Cancer is the second cause of death in Brazil, coming after cardiovascular disease. Medicinal fungi have been used in cancer patients due to their immunomodulatory effects. **Objective**: To evaluate the anthropometric status of men with colorectal cancer after supplementation with *Agaricus sylvaticus*. **Methods**: Randomized, double-blind, placebo-controlled clinical trial conducted in a public hospital in the Federal District. The sample consisted of 24 male patients with colorectal cancer, separated into *Agaricus sylvaticus* (30 mg/kg/day) and placebo groups. Weight, height, body mass index, arm circumference, triceps skinfold, arm muscle circumference and fat percentage were evaluated during treatment. The results were analyzed before treatment and after three and six months of supplementation with the Student's *t* test and F test, with 5% significance. **Results**: The *Agaricus sylvaticus* group showed significant increase in arm muscle circumference after six months of supplementation, but not in the placebo group. There were significant changes in both groups as to body mass index, arm circumference, percent body fat and triceps skinfold thickness during treatment. **Conclusion**: The dietary supplement with *Agaricus sylvaticus* is able to significantly improve muscle mass in male patients with colorectal cancer.

Keywords: anthropometry; colorectal neoplasms; neoplasms; *Agaricales*; *Agaricus sylvaticus*.

RESUMO: **Introdução**: O câncer é a segunda causa de óbitos no Brasil, subsequente às doenças cardiovasculares. Fungos medicinais têm sido utilizados em pacientes oncológicos devido a seus efeitos imunomoduladores. **Objetivo**: Avaliar o estado antropométrico de homens com câncer colorretal após suplementação com fungos *Agaricus sylvaticus*. **Métodos**: Ensaio clínico randomizado, duplo-cego, placebo-controlado realizado em um hospital público do Distrito Federal. Amostra de 24 pacientes com câncer colorretal, sexo masculino, separados em grupos *Agaricus sylvaticus* (30 mg/kg/dia) e placebo. Foram avaliados peso, estatura, índice de massa corporal, circunferência do braço, dobra cutânea tricipital, circunferência muscular do braço e percentual de gordura durante o tratamento. Os resultados foram analisados antes do tratamento, com três e seis meses de suplementação, por meio dos testes *t* de Student e F, com significância de 5%. **Resultados**: O grupo *Agaricus sylvaticus* apresentou aumento significativo da circunferência muscular do braço após seis meses de suplementação, fato não observado no grupo placebo. Não foram encontradas, em ambos os grupos, alterações significativas no índice de massa corporal, circunferência do braço, percentual de gordura corporal e dobra cutânea tricipital ao longo do tratamento. **Conclusão**: A suplementação dietética com *Agaricus sylvaticus* é capaz de melhorar significativamente a massa muscular de pacientes do sexo masculino com câncer colorretal.

Palavras-chave: antropometria; neoplasias colorretais; neoplasias; *Agaricales*; *Agaricus sylvaticus*.

INTRODUCTION

Cancer is the second cause of death in Brazil, after heart diseases. Its development is a result of the interaction of endogenous and environmental factors. The main factors related to oncogenesis are: heredity, physical inactivity, exposure to some kinds of viruses, bacteria and parasites, frequent contact with carcino-

Study carried out at the Coloproctology oupatient clinic of Hospital de Base from the Federal District – Brasília (DF), Brazil.
Financing source: none.
Conflict of interest: nothing to declare.

Submitted on: 08/01/2012
Approved on: 25/04/2012

genic substances, smoking, drinking, overweight or obesity, old age and improper diets[1].

Studies show that 25 to 50% of oncologic patients present with malnutrition at the time of diagnosis, and that 100% are malnourished at the time of death. Clinical manifestations, such as anorexia, weight loss, depletion of fat and muscle tissues, anemia, hypoalbuminemia, glucose intolerance, among others, are common among patients with cancer[2,3].

Combat therapies itself, as well as those that inhibit tumor growth, (chemotherapy, radiotherapy and surgery) exhibit different degrees of malnutrition due to complications and/or side effects such as nausea, vomit, diarrhea and anorexia, which makes the patients more prone to infections, causing a negative impact on their nutritional status[3].

Nutritional evaluation is relevant for patients with cancer, whose changes in nutritional status are mostly established during the course of the disease. Its main objectives are to define the degree of malnutrition, to identify patients who are at risk of developing complications resulting from nutritional deficit and to monitor nutritional support. Maintaining a proper nutritional status is an important goal to be reached[4].

Scientific evidence show that the *Agaricus sylvaticus* fungus (*A. sylvaticus*), which belongs to the order *Agaricales* and the family *Agaricaceae*, presents possible inhibiting effects on tumor growth, tumor regression and stimulation of both immune and hematopoietic systems, besides the beneficial effects on the improvement of quality of life and on the prognosis of oncologic patients[5].

The objective of this study was to analyze, by means of anthropometric measurements, the effects of supplement nutritional therapy with *A. sylvaticus* fungi on male oncologic patients assisted at a public hospital in Brasília (DF), Brazil.

MATERIALS AND METHODS

Study design

The study consists of a randomized, double-blind, placebo-controlled clinical trial. It was approved by the Human Research Ethics Committee of the State Health Secretariat of the federal district (CEP/SES/DF), protocol n. 051/04. The free informed consent form was obtained from the patients, who participated voluntarily. The work was conducted at the outpatient Coloproctology clinic of *Hospital de Base* of the federal district, from November 2004 to July 2006.

Sample

The sample consisted of patients with colorectal cancer separated into the groups placebo (Gp) and supplements with *A. sylvaticus* fungi (Gf), respecting the following inclusion criteria: male patients with confirmed diagnosis of colorectal cancer, at postoperative phase, from 3 months to 2 years after surgical intervention, older than 20 years of age. Exclusion criteria were: bedridden patients, with physical impairment, on alternative therapy, with other chronic noncommunicable diseases and with metastasis.

Extract of Agaricus sylvaticus

The *A. sylvaticus* fungus was first described in Switzerland and has a broad geographic distribution, occurring naturally in Brazil. Its identification has been confirmed by the Royal Botanic Gardens of London, and the document was provided by the Institute of Botanics at the State Environment Secretariat of Sao Paulo on November 10, 1995.

The fungus from the *Agaricaceae* family, whose popular name is sun mushroom, was obtained from a producer registered at the Brazilian Agricultural Research Corporation (EMBRAPA), from the Tapiraí region, in the state of São Paulo. The fungus extract was obtained by immersing the dehydrated material into hot water for 30 minutes, liquefied, sieved and dry with a dissector. The analysis of the composition of *A. sylvaticus* was performed by Japan Food Research Laboratories Center and showed the presence of carbohydrates (18.51 g/100 g), lipids (0.04 g/100 g), ergosterol (624 m/100 g), proteins (4.99 g/100 g), amino acids — arginine (1.14%), lysine (1.23%), histidine (0.51%), fenilalanin (0.92%), tyrosine (0.67%), leucine (1.43%), methionine (0.32%), valine (1.03%), alanine (1.28%), glycine (0.94%), proline (0.95%), glutamic acid (3.93%), serine (0.96%), threonine (0.96%), aspartic acid (1.81%), tryptophan (0.32%) and cysteine (0.25%) — and micronutrients in minute quantities.

The dry extract was transformed into pills, according to the pharmacotechnical procedure. The dose of fungus administered to the patients in the supplement group was equal to 30 mg/kg/day, fraction-

ated into two daily intakes (six pills a day, three in the morning and three in the afternoon, in between meals), considering the mean weight of the studied population during a period of six months. The group of patients who took the placebo received the same amount of pills, with the same excipient and energetic value, however, without the extract of *A. sylvaticus*, which was replaced by starch.

Clinical evolution

Patients were followed-up for six months. During the three first months, appointments took place every 15 days for clinical assessment. In the last three months, appointments were monthly.

Patients remained with their routine diet, even though they received general guidance on how to keep a healthy diet during treatment. After six months of follow-up, an individual diet was recommended for each patient, and they were referred to other professionals from the health field when necessary.

The anthropometric evaluation took place by means of body mass index (BMI), triceps skinfold (TSF), arm circumference (AC), arm muscle circumference (AMC) and fat percentage. The means of results were assessed in three distinct moments: before the beginning of supplementation, and after three and six months of treatment.

All patients were followed-up every week by the researchers for doubt clarification, analysis of the proper use of the mushroom and the confirmation of schedule, thus ensuring highest adhesion to treatment and control as to the continuity of the study.

Patients who gave up were those who did not attend the appointments during the whole six-month period. Those who died before the end of treatment were excluded from the sample.

Anthropometric evaluation

A special file was used for the anthropometric evaluation, which should be filled up in all appointments. Weight was measured with the patient barefoot, wearing light clothes, with no jewelry that could interfere with the measurement, standing in the center of the scale with the body weight equally distributed on both feet[6]. The scale was the digital Plenna® (Resolve), with bioimpedance (BIA), model MEA-02500, capacity for 150 kg and variation of 0.1 g, properly calibrated.

To measure the height, patients were in orthostatic position, barefoot, with the body extended to the maximum, straight head, looking ahead, in *Frankfört* position, with the back and the back part of the knees touching the wall, and the feet together[6]. The *Frankfört* anatomical position extends from the lower margin of the ocular orbit to the upper margin of the auditory meatus[7]. Height was measured once in centimeters (cm) with inelastic metric tape measuring 150 cm, fixed on a plane wall, without skirting, 50 cm from the ground. It was set in a square on the upper part of the head, thus obtaining a 0.1 cm precision measurement.

After obtaining data such as weight and height, BMI was measured by the division of the weight, in kilograms, by the square of the height, in meters. The value of BMI <18.5 kg/m^2 was used to characterize thinness; 18.5 kg/m^2 $<$BMI<25 kg/m^2, eutrophy; 25 kg/m^2$<$BMI<30 kg/m^2, overweight; and >30 kg/m^2, obesity, according to the classification suggested by the World Health Organization[8].

TSF was measured with the speed reading Cescorf® compass, with scale of up to 60 mm and a ±1 mm precision. Three consecutive measurements of TSF were taken, considering the arithmetic mean of the measured values. In order to measure AC, a metric tape with unextendable material with up to 150 cm, 1cm scale, was used. The value of AMC was obtained with the formula: AMC=AC–(0.314 x TSF)[8].

TSF, AM and AMC measurements were compared to the reference pattern by Frisancho[9], and the adjustment was calculated with the division of obtained values by the percentile 50, multiplied by 100. In order to classify the nutritional status, the following values were considered: >120% obesity; 110–120% overweight; 90–110% eutrophy; 80–90% mild malnutrition; 70–80% moderate malnutrition; e <70% severe malnutrition[10]. Fat percentage was obtained with the digital scale Plenna®.

Statistical analysis

The presented values were compared and analyzed by means of statistical tests such as Student's *t* and F, using the softwares Microsoft Excel 2007 and Statistical Package of the Social Sciences (SPSS<SPSS Inc, Chicago, EUA) for Windows, version 19.0. The probability of statistical significance was $p \leq 0.05$.

RESULTS

After a six-month follow-up at the outpatient Coloproctology clinic at *Hospital Base* in the federal district, 24 male patients with colorectal cancer, mean age of 61.5±13 years, stages I (n=08), II (n=04) and III (n=12), separated into the groups who took placebo (n=12) and *A. sylvaticus* (n=12), concluded the study.

Mean age of Gp was 58.63±14.41 years, and 56.87±15.16 years in the Gf (p=0.38).

When analyzing BMI, it was observed that Gp presented initial BMI of 23.52±4.45 kg/m^2; after 3 months, 23.80±3.96 kg/m^2 (p=0.15); and, in the sixth month, 24.80±3.80 kg/m^2 (p=0.11), however, these changes were not statistically significant (Figure 1).

The Gf presented initial BMI of 25.05±3.62 kg/m^2; after 3 months, 25.03±3.74 kg/m^2 (p=0.44); and in the sixth month, 25.23±3.58 kg/m^2 (p=0.18), results with no significant statistical difference (Figure 1).

Concerning AC, the Gp had initial mean of 29.30±4.32 cm; after 3 months, 30.00±2.62 cm (p=0.29), and after 6 months, 29.62±2.50 cm (p=0.40), however, these changes were not statistically significant (Figure 2).

Gf presented initial values for AC of 29.68±3.26 cm; after 3 months with supplements, 29.47±3.58 cm (p=0.27), and after 6 months, 29.66±3.44 cm (p=0.47), and these results do not differ statistically (Figure 2).

As to TSF, it was observed that Gp presented mean initial value of 14.40±6.69 mm; after 3 months, 14.40±5.89 mm (p=0.40), and, after 6 months, 14.30±5.82 mm (p=0.09), however, these changes were not statistically significant (Figure 3).

In Gif no significant changes were observed in TSF after 3 months (from 13.94±9.80 to 14.02±9.06 mm, p=0.33), and 6 months (from 13.94±9.80 to 13.44±8.69 mm, p=0.20) of supplements (Figure 3).

After calculating AMC, in Gp a non-significant decrease was observed after 3 months (from 24.65±2.67 to 24.59±1.72 cm, p=0.50), and 6 months (from 24.65±2.67 to 24.53±1.62 cm, p=0.40), (Figure 4).

Gf presented differences concerning AMC after 3 months (from 25.28±2.74 to 24.82±2.06 cm, p=0.28), however, with significant increase after 6 months of supplements (from 25.28±2.74 to 26.59±2.67 cm, p=0.04), (Figure 4).

As to the analyses of fat percentage, Gp initially presented mean value of 26.60±8.50% (p=0.50); after 3 months, of 26.60±5.45% (p=0.50), being constant until the sixth month, 26.60±8.50% (p=0.50), however, these changes were not statistically significant (Figure 5).

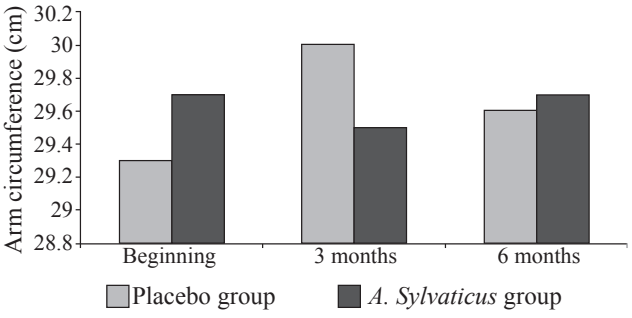

Figure 2. *Arm circumference (cm) of men with colorectal cancer from the placebo (n=12) and Agaricus sylvaticus (n=12) groups, assisted in a public hospital of the federal district during the whole follow-up period.*

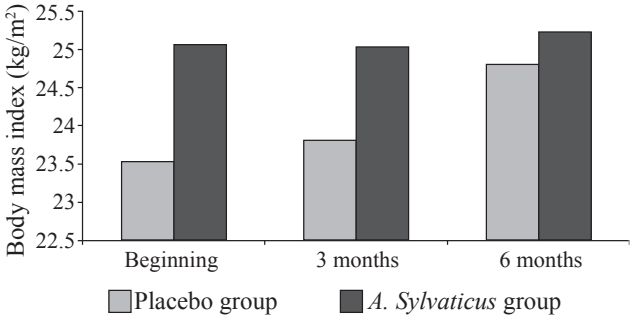

Figure 1. *Body mass index (kg/m^2) of men with colorectal cancer in groups placebo (n=12) and Agaricus sylvaticus (n=12) assisted at a public hospital in the federal district during the whole clinical follow-up.*

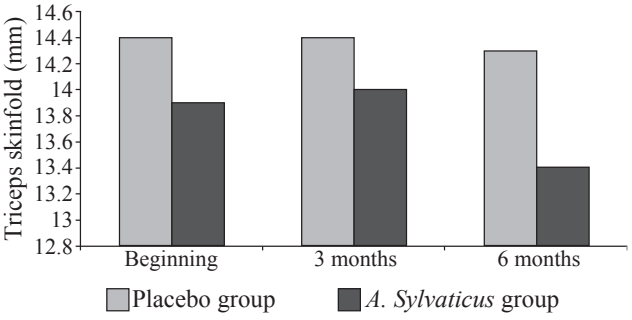

Figure 3. *Triceps skinfold (mm) of men with colorectal cancer of the placebo (n=12) and Agaricus sylvaticus (n=12) groups, assisted in a public hospital of the federal district during the whole follow-up period.*

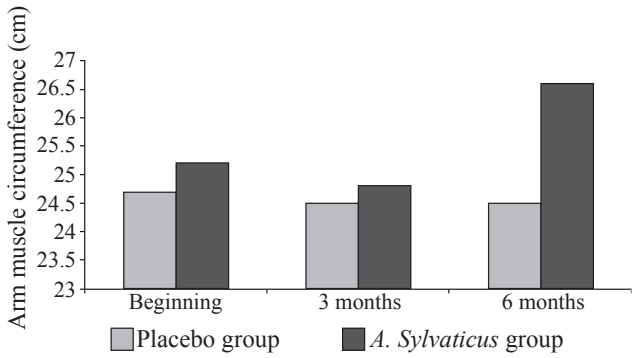

Figure 4. *Arm muscle circumference (cm) of men with colorectal cancer of the placebo (n=12) and Agaricus sylvaticus (n=12) groups, assisted in a public hospital of the federal district during the whole follow-up period.*

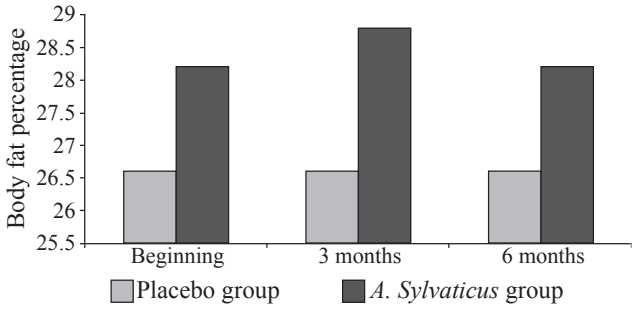

Figure 5. *Body fat percentage of men with colorectal cancer of the placebo (n=12) and Agaricus sylvaticus (n=12) groups, assisted in a public hospital of the federal district during the whole follow-up period.*

DISCUSSION

In this study, mean age of patients was 58 and 56 years old in both Gp and Gf, respectively. Studies show that colorectal cancer affects mostly the age group equal or superior to 50 years[1,11,12].

Both Gp and Gf presented initial BMI within the eutrophy range, with a tendency to overweight. Scientific research has shown a positive relation between overweight, obesity and risk of developing several types of cancer, and also mortality due to this disease[13].

Anthropometry is a technique developed to assess body composition in a more complete manner[14]. It is characterized by a simple and low cost method, which is non-invasive and highly reliable. The objective is to identify the quantity and the distribution of the main determiners of body composition[15]. Therefore, anthropometric data should be obtained to check for depletion, repletion and maintenance of studied compartments[14].

In patients with malignant neoplasms, it is observed that the depletion of the fat tissue is responsible for most of the weight loss. The loss of body nitrogen has also been reported in 50 to 70% of the malnourished oncologic patients, and the depletion of muscle tissue is considered as the main cause of the reduction of survival in these patients[1].

In this study, no statistically significant changes were observed in both groups in relation to the analyzed anthropometric parameters (BMI, AC, TSF, fat percentage), except concerning the thin mass (AMC), which increased significantly in Gf after six months of supplements, which was not observed in Gp. Scientific evidence points out that medicinal fungi have bioactive compounds that can avoid muscle protein catabolism, which is commonly present in these patients[1-3,5,11,16], which partly explain the observed results.

Catalano et al.[14] evaluated the nutritional status of patients with cancer by means of bioimpedance and anthropometric variables. They noticed that even though the anthropometric indexes presented normal values, bioimpedance revealed malnutrition with changes in the ratio of extracellular and intracellular mass.

The use of arm circumference and skin folds can be important to diagnose the nutritional status of a patient, especially when there is no body weight. AC represents the sum of bone, muscle and fat tissues; triceps skinfold refers to the estimate of layers and/or compromise of the fat tissue; and arm muscle circumference shows the quantity or degree of depletion of muscle layers[14].

Protein depletions are manifested especially by the atrophy of the skeletal muscle, atrophy of visceral organs, myopathy and hypoalbuminemia. The reduction of protein mass and the skeletal atrophy predispose patients with cancer to an increased risk of infections, difficulties to heal wounds, increased asthenia and decreased functional capacity[1-3].

There is also a positive association between excessive weight and risk of colorectal cancer among men when compared to women. This shows that abdominal distribution or central body fat, which is mostly a male characteristic, is the main component of the increased risk for heart disease, once it is connected to the peripheral resistance to insulin and hyperinsulin[13]. However, visceral fat was not assessed in this study.

Scientific evidence proves that medicinal fungi have anabolic effects, once they contain all the necessary amino acids, besides arginine and glutamine, which, in moments of metabolic stress, become conditionally essential, thus contributing with improvements in the nitrogen balance[1,16,17]. Other bioactive substances that are present in medicinal fungi also stand out, such as: glucans, proteoglucans, lectins, ergosterol and triterpenes, both able to modulate the different metabolic and immune actions in these patients[1,3,16-21].

The mechanisms of action of the bioactive compounds that are present in the fungi are not fully clear in literature yet, but scientific studies suggest that these substances can modulate the carcinogenesis in all stages of the disease, especially by stimulating the immune system[18,21,22].

In literature, no scientific articles were found that evaluated the nutritional or anthropometric status of people with malignant neoplasms after diet supplement with *A. sylvaticus* fungi and other medicinal fungi. However, scientific studies prove that medicinal fungi are able to cause beneficial changes in the metabolism of nutrients and in the hematopoietic, immune and gastrointestinal systems of patients with cancer, which reflects positively on their quality of life[1,3,5,11,16-23].

CONCLUSION

The results show that diet supplement with *A. sylvaticus* fungi is able to significantly improve the muscle mass of male patients with colorectal cancer. However, more clinical controlled and randomized trials are necessary to clarify the mechanisms of action of the bioactive principles that are present in the *A. sylvaticus* and the different clinical situations that could benefit from this supplement.

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