Original Article

Nutritional status and body composition are already affected before oncology treatment in ovarian cancer

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Poor nutritional status is a common problem among ovarian cancer patients. In order to detect changes in nutritional status and body composition this study investigates anthropometrical and biochemical parameters among these patients. This study included women with ovarian cancer and woman without cancer. Body composition was assessed by bioelectrical impedance analysis (BIA), anthropometrically, and with DXA scan, and total serum protein, albumin, transferrin, hemoglobin, hematocrit levels and total lymphocyte count was also measured. Data from DXA scan and body composition as assessed by BIA was collected from thirty-one women. Student *t*-test was used to compare differences in means between groups. This study included 120 women, 57 with ovarian cancer and 63 with benign tumors. Both groups of women were overweight. Body fat by skin-fold thickness, arm circumference, serum albumin, total lymphocytes count, as well as transferrin levels were significantly lower in the ovarian cancer group ($p<0.05$). Ovarian cancer women had lower fat reserves by skin-fold thickness and lower serum proteins even though they were overweight. However, further studies need to use a body composition assessment on all subjects to confirm these results.

Key Words: ovarian Cancer, nutritional status, body composition, nutritional assessment, bioelectrical impedance analysis

INTRODUCTION

Ovarian cancer is one of the most lethal cancers in women. It represents the sixth leading form of cancer in women and the third most common gynecological malignancy with 140,200 cases and 225,500 deaths worldwide. It is the second most common gynecological cancer in Australia, and in Mexico it is one of the leading types of gynecological cancer and the second leading cause of cancer death in women, with 3.4/100,000 deaths.[1-3] Diagnosis is performed in advanced stages in more than 50% of the patients, a fact responsible for very high mortality rates, and a 5-year survival rate of 44%.[4] This is an asymptomatic disease with non-specific signs and symptoms, but recent studies have reported pelvic/abdominal pain, increased abdominal size/bloating, difficulty eating/feeling full and changes in nutritional status such as unexplained weight gain/loss.[5-7]

Malnutrition is a clinical status that includes the imbalance in energy and other nutrients that affects tissue and body composition. It is common among cancer patients and has been associated with an increased risk of complications, decreased response to antineoplastic treatment, a low survival rate, poor quality of life and higher health care costs.[8,9] However, changes in body composition in patients with ovarian cancer with an early diagnosis are still controversial. While some studies on ovarian cancer patients and overweight controls report no differences in body weight between ovarian cancer and benign tumor patients,[10] other reports show that patients with ovarian cancer that has been detected early are 19 times more likely to develop malnutrition than those with benign tumors.[11] Patients with ovarian cancer are likely to have a higher BMI, most of them are overweight or even obese. Six months post diagnosis ovarian cancer patients have shown more weight loss and a significant decrease in their BMI and serum albumin levels.[11] This situation has been worsened by the side effects of antineoplastic treatment, because it has been shown that weight loss post-treatment accounts for up to 14.5% of the initial bodyweight.[12] It is important to assess nutritional status at early stages of ovarian cancer in order to detect nutritional risk and be able to start nutritional interventions in time to improve nutritional status and outcome, as well as quality of life.

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There are several techniques that have been used either alone or in combination to assess nutritional status. The most commonly used tools are, anthropometrical measurements (eg, weight loss, BMI, triceps skinfold thickness and arm circumference) and biochemical data (eg, serum albumin, prealbumin, total protein transferrin, hemoglobin and serum vitamins status).[10,13] Anthropometrical measurements like weight and BMI are often used to detect malnutrition, however studies suggest that weight changes and BMI fail to detect malnutrition because it does not detect real changes in body composition.[13] There are measurements aimed to detect changes in body composition like percentage of body fat or lean mass such as bioelectrical impedance analysis (BIA) and dual energy X-ray absorptiometry (DXA).[14,15] The most commonly used biochemical indicators for detecting malnutrition are albumin, prealbumin and transferrin.[16-18] They are used to evaluate visceral protein storage, either to diagnose anemia (a common problem among oncology patients) or as a marker for malnutrition. Low levels correlate with nutritional depletions and an inadequate nutritional status.[19-22]

The aim of the study was to find the possible differences in nutritional status and body composition in ovarian cancer women before starting cancer treatment.

MATERIALS AND METHODS

The Research and Ethics Committee of the Hospital General de México approved this cross-sectional, observational study. One hundred and twenty women with suspected diagnosis of ovarian tumor were evaluated. After the oncology specialists diagnosed the type of tumor, the population was divided into groups: those who had a benign tumor and those with ovarian cancer. Both groups included women between the ages 18 and 70 years. Most of the women with malignant tumors were detected in stages II or III, therefore surgery and later chemotherapy was part of the treatment proposed; none of the patients were in stage I or IV.

Anthropometrical measurements were taken after signing the informed consent form and before ovarian surgery and pathological diagnosis. Body composition was assessed by anthropometry (weight, height, arm circumference and 4 skinfold thickness measurements: bicipital, tricipital, subscapular and suprailiac skinfold), BIA and DXA. In order to measure weight and height, the patients were asked to take off shoes and clothes so they only wore a hospital gown. Lean body mass was determined by arm circumference. Skinfold thickness was measured with a Lange Skinfold caliper using the Lohman technique.[23] Durnin-Womersley equation was used to estimate body density and Siri equation to estimate body fat percentage,[24] BIA by Tanita® TBF 300 and DXA scan were used to determine the percentage of fat mass.[25] The Tanita and DXA scan was only performed on 31 patients (20 ovarian cancer women and 11 women with benign tumor). Due to the high cost of the procedure DXA was not applied to all of the patients involved. In order to eliminate bias all the anthropometrical measurements were taken by one standardized dietitian according to the Habicht method.[26] The purpose of this method is to be certain that the person or dietitian performing the measurement has consistency and specificity, which means that it is a reliable measurement. The procedure is based on repeating the same measurement on 10 different subjects to obtain consistency and accuracy when performing the anthropometrical measurements.

Biochemical indicators were taken to assess total serum protein, serum albumin, serum transferrin, hemoglobin levels, hematocrit and total lymphocyte count. The laboratory techniques used for the biomarkers above were as follows: total serum protein was determined by Biuret method that consists of staining the serum with a violet product while the protein preserves the color, in order to perform the measurement with spectrophotometry at 550 nm. Albumin was determined by Tagle BCP albumin procedure that is based on capabilities of the linkage-dyeing serum albumin with bromcresol purple at 300nm and is directly proportional to the concentration of the albumin present. Hemoglobin, hematocrit and lymphocyte counts were determined by a cell blood count sample centrifuged at 3000-3500 rpm during 3-5 minutes to obtain blood products.

Qualitative variables were presented in means, standard deviation (SD) and 95% confidence interval (CI) in tables. Student t-test was used to compare differences between groups. A p-value <0.05 was used for statistical significance of data.

RESULTS

This study included one hundred and twenty women, 47.5% (n=57) of them had ovarian cancer and 52.5% (n=63) had benign tumors. Table 1 shows the differences

Table 1. Differences of anthropometrical variables between groups.

Variables	Women with ovarian cancer (Mean ± SD)	Women with benign ovarian tumors (Mean ± SD)	95% CI	*p-value*
Age (years)	45.5±10.5	41.6±11.9	-8.21 - 0.175	0.06
Body mass index (kg/m2)	26.2±4.93	27.6±4.49	-0.25 - 0.17	0.94
Weight (kg)	60.4±11.9	63.5±11.8	-1.20 - 7.35	0.157
Height (m)	152±7.07	152±7.93	-3.18 - 2.29	0.747
Arm circumference (cm)	26.5±4.20	29.2±3.73	1.25 - 4.14	0.000*
Arm muscle area (cm2)	54.4±16.8	64.8±15.6	4.44 - 16.21	0.001*
Body fat from skinfolds (%)e	38.8±5.96	41.8±5.28	1.03 - 5.27	0.004*
Body fat from DXA (%)	28.5±8.65	32.7±8.19	-2.40 - 10.84	0.202
Lean body mass (%)	15.8±3.26	16.9±3.45	-0.67 - 2.90	0.218
Total body water (%)	33.6±9.38	39.1±6.82	-0.48 - 11.50	0.070
Body fat from Tanita (%)	31.1±3.48	31.0.±3.54	-2.90 - 2.68	0.936

Sample: Ovarian cancer, n= 57; Benign tumor, n=63. SD= Standad deviation. CI= Confidence interval.
*Values with statistical differences (p<0.05)

Table 2. Differences of biomedical variables between groups.

Biochemical parameters	Women with ovarian cancer (Mean ± SD)	Women with benign ovarian tumors (Mean ± SD)	Normal parameters †	*p-value*
Albumin (g/dL)	3.56±0.79	4.05±0.54	3.5 - 4.8	0.001*
Transferrin (mg/L)	20.0±6.1	55.2±5.2	25.0 - 30.0	0.000*
Hemoglobin (g/dL)	12.7±1.85	13.2±2.03	12 - 16	0.187
Hematocrit (%)	38.0±5.07	38.8±5.63	36.1 - 44.3	0.392
Lymphocytes (u/L)	1508±886	2008±824	1000 - 3000	0.002*

Ovarian cancer, n= 57; Benign tumor, n=63. SD= Standard deviation.
*Values with statistical differences ($p<0.05$)
†Normal range of biochemical parameters used at the Hospital General de Mexico.

in anthropometrical measurements. Average age in this population was 43.5 ± 11.6, years. The ovarian cancer group and the benign tumor group had an average weight of 60.4±11.9 kg and 63.5±11.8 kg, respectively. The whole population was within the limit of low height average for Mexican women, the ovarian cancer group measured in average 152±7.07 cm and the benign tumors group 152±7.93 cm. Weight and height were not statistical different between group. Regarding the measurements of Skin-fold thickness at four sites and arm circumference, the cancer group ($p<0.05$) was statically lower values. The data showed in Table 1 also demonstrates that body fat and protein reserves appeared to be lower when measured by a subjective estimation like the Siri equation, exactly like the arm muscle area ($p<0.05$), however when fat mass was measured by DXA scan or with a Tanita scale (BIA), there were no statistical differences between the groups.

On the other hand, Table 2 shows that biochemical parameters like albumin, transferrin, hemoglobin, lymphocytes levels were significantly lower in the cancer group ($p<0.05$). Hemoglobin and hematocrit were not statistically different but levels were lower in the ovarian cancer group, as well as the rest of the biochemical parameters compared with the benign tumors group.

DISCUSSION

Malnutrition is a problem in cancer patients; among those with gynecological cancer, patients with ovarian cancer are more likely to experience rapid changes in their nutritional status and body composition. Studies showed that ovarian cancer patients are more likely to have a BMI classified as overweight, low serum protein levels and malnutrition.[11.13] According to the criteria for the Mexican population, our results showed that both groups had normal height (normal height >150 cm) and a weight above the recommended even in other countries. When we calculate BMI the classification obtained was overweight in both the ovarian cancer group and the benign tumors group (26.2±4.93 vs 27.6±4.49 kg/m^2, respectively). Laky *et al* (2006) obtained similar results in a study with patients having either ovarian cancer or benign tumors reporting an average in BMI of 28.8±4.3 versus 30.5±9.8 kg/m^2, respectively. They also measured malnutrition with the Patient-Generated Subjective Global Assessment (PG-SGA), a score for nutritional assessment in cancer patients that includes weight changes, dietary intake, symptoms and functional capacity.[28] They mentioned that if only BMI or weight loss were used as an indicator of malnutrition, many ovarian cancer patients would not have been detected as malnourished in their study.[11] BMI is a measurement commonly used for early detection of hospital malnutrition but this parameter fails to detect the early changes in body composition. This makes it a non-reliable parameter for this purpose.[11,13,30]

On the other hand, as expected, the skinfold measurements of the triceps, biceps, subscapular and iliac crest were significantly lower in patients with ovarian cancer. When these values were used in estimation formulas of fat mass percentage and arm muscle area, the results were statistically significant, and therefore fat mass percentage and arm muscle area turned out to be lower in patients with ovarian cancer compared with the benign cancer patients. However, these results were not confirmed when we determined the percentage of fat mass by DXA and BIA. Percentages of fat mass obtained were similar between groups. One of the limitations of our study was that BIA and DXA (one of the most accurate methods), were only used in 31 patients (10 ovarian cancer patients and 21 patients with benign tumors) due to its high cost.[31,32]

Regarding biochemical data, literature shows a decrease in albumin and transferrin levels in ovarian cancer patients, which are related to malnutrition.[10,11,13] One of our past studies in 2008 showed that women with recent diagnosis of ovarian cancer had a decrease in albumin and transferrin levels. However, our current study shows that a decrease is not only seen in albumin and transferrin; but also lymphocytes levels that were statistically lower in the cancer group. Changes in protein status, low levels of protein and blood cell start from early stages of ovarian cancer and are not attributable to antineoplastic treatment, which had not even started in our population.[16]

The results obtained in this study, suggest that when fat mass was measured by skin-fold thickness it was lower in ovarian cancer group in stages II and III. However we can't assure it, because BIA and DXA did not confirm these results. However, depletion indicators in this study were statistically different between groups, which can suggest that protein reserves are being depleted in the body. This was confirmed with the results of arm circumference and arm muscular area. In further studies, it is necessary to encourage the use of accurate methods such as DXA or BIA in all subject studied, in order to confirm the early changes observed in body compartments and biochemical parameters. It is also necessary to use a larger amount of parameters to detect deficiencies and malnutrition in patients in order to avoid underestimating the nutritional status, due to women frequently being over-

weight. To detect this on time will allow both nutrition and oncology professionals to establish an early nutritional or medical intervention that could help improve nutritional status, cancer therapy outcome and quality of life in this type of patients.

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AUTHOR DISCLOSURES

There are no conflicts of interest with any individual nor institution and we declare that we have full control of all data related to the manuscript.

REFERENCES

1. Globocan: Country Fast stats: World. 2008 [cited 2012/3/26]; Available from: http://globocan.iarc.fr/fact sheets/populations/factsheet.asp?uno=900
2. Globocan: Country Fast stats: México. 2008 [cited 2012/3/26]; Available from: http://globocan.iarc.fr/fact sheets/populations/factsheet.asp?uno=484
3. Cancer Australia. Report to de nation-Ovarian cancer 2012. [cited 2012/6/15]; Available from: http://www.canceraustralia.gov.au/sites/default/files/publications/report_to_the_nation_-_ovarian_cancer_2012_506d31b18d56f.pdf
4. Gallardo-Rincon D, Cantu-de-león D, Alanís-López P, Álvarez-Ávila MA, Bañuelos-Flores J, Herbert-Nuñez GS et al. Third national consensus of ovarían cáncer, Research Group in Ovarian Cancer and Gynecological Tumors from Mexico. Rev Invest Clin. 2011;63:665-702.
5. Bankhead CR, Kehoe ST, Austoker J. Symptoms associated with diagnosis of ovarian cancer: a systematic review. BJOG. 2005;112:857-65. doi: 10.1111/j.1471-0528.2005.00 572.x
6. Goft BA, Mandel LS, Drescher CW, Urban N, Gough S, Schurman KM et al. Development of an ovarian cancer symptom index: Possibilities for earlier detection. Cancer. 2007;109:221-7. doi: 10.1002/cncr.22371
7. Vine MF, Calingaert B, Berchuck A, Schildkraut JM. Characterization of prediagnostic symptoms among primary epithelial ovarian cancer cases and controls (Abstract). Gyn Oncol. 2003;90:75-82. doi: 10.1016/S0090-8258(03)00175-6
8. Shike M. Nutrition therapy for the cancer patients. Hematol Oncol Clin North Am. 1996;10:221-34. doi: 10.1016/S0889-8588(05)70336-1
9. Gil KM, Frasure HE, Hopkins MP, Jenison EL, Von VE. Body weight and composition changes in ovarian cancer patients during adjuvant chemotherapy. Gyn Oncol. 2006;103: 247-52. doi: 10.1016/j.ygyno.2006.03.005
10. Fuchs-Tarlovsky V, Álvarez C, Hernández-Steller H, Gutierrez G, Oliva JC. Differences in nutritional parameters in patients with ovarian tumors. RNC. 2008;26:69-74.
11. Laky B, Janda M, Bauer B, Vavra C, Cleghorn G, Obermair A. Malnutrition among gynaecological cancer patients. Eur J Clin Nutr. 2007;61:642-6. doi: 10.1038/sj.ejcn.1602540
12. Balogun N, Forbes A, Widschwendter M, Lanceley A. Changes in nutritional status of women diagnosed and treated for ovarian cancer (abstract). American institute for cancer research annual research meeting on food, nutrition, physical activity and cancer. 2011.[cited 2012/4/12]; Available from: http://discovery.ucl.ac.uk/1326965/
13. Laky B, Janda M, Cleghorn G, Obermain A. Comparison of different nutritional assessments and body-composition measurements in detecting malnutrition among gynecologic cancer patients. Am J Clin Nutr. 2008;87:1678-85.
14. Demura S, Sato S, Kitabayashi T. Percentage of total body fat as estimated by three automatic bioelectrical impedance analyzers. J Physiol Anthropol Appl Hum Sci. 2004;23:93-9. doi: 10.2114/jpa.23.93
15. Pichard C, Kyle UG, Slosman DO. Fat-free mass in chronic illness: comparison of bioelectrical impedance and dual-energy X-ray absorptiometry in 480 chronically ill and healthy subjects. Nutrition. 1999;15:676-688. doi: 10.1016/S0899-9007(99)00122-7
16. Fuchs-Tarlovsky V, Casillas Rivera MA, Alvarez K, Lopez-Alvarenga JC, Ceballos-Reyes GC. Antioxidant supplementation has a positive effect on oxidative stress and hematological toxicity during oncology treatment in cervical cancer patients. Supportive Care Cancer. 2013;21:1359-63. doi: 10.1007/s00520-012-1674-6
17. Ahmed N, Oliva KT, Barker G, Hoffmann P, Reeve S, Smith IA et al. Proteomic tracking of serum protein isoforms as screening biomarkers of ovarian cancer. Proteomics. 2005;5:4625-32. doi: 10.1002/pmic.200401321
18. Ronco DA, Manahan KJ, Geisler JP. Ovarian cancer risk assessment: a tool for preoperative assessment. Eur J Obstet Gynecol Reprod Biol. 2011;158:325-9. doi: 10.1016/j.ejogrb.2011.05.018
19. Carlson TH. Laboratory data in nutrition assessment. In: Mahan LK, Escott-Stump S. editors. Krause´s food, nutrition and diet therapy. 11ª ed. EUA: Saunders, Elsevier; 2004. pp.440.
20. Boles JM, Garre MA, Youinou PY. Simple assessment of the nutritional status in the critically ill patient. Resusitation. 1984;11:233-41. doi: 10.1016/0300-9572(84)90020-0
21. Seltzer MH, Bastidas MA, Cooper MD, Engler P, Slocum B, Fletcher SH. Instant nutritional assessment (Abstract). JPEN.1979;3:157-9. doi: 10.1177/014860717900300315 7
22. Van SJ, Cocquyt V. Impact of haemoglobin levels on the outcome of cancers treated with chemotherapy (Abstract). Crit Rev Oncol Hematol. 2003;47:1-11. doi: 10.1016/S1040-8428(03)00093-3
23. Lohman TG, Roche AF, Martonell R. Antropometric standardization reference manual. Campaing. IL; Human Kinetics; 1988. pp. 55-70.
24. Durnin JV, Womersley J. Body fat assessed from body total density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr. 1974;32:77-97. doi: 10.1079/BJN19740060
25. Siri WE. Body composition of fluid spaceand density. In: Brozerk J & Handschel A, editors. Technique for measuring body composition. Washington DC: National Academy of Science; 1961: pp. 223-44.
26. Habicht J P, Yarbrough C, Martonell R. Anthropometric fiel methods. In: D.B. Jelliffe y E.E.P. Jelliffe, editors. Nutrition and growth. New York; Plenum press: 1979. pp. 365-87.
27. Tchernof A, Poehlman ET. Effect of menopause transition on body fatness and body fat distribution. Obes Res. 1988; 6:246-54. doi: 10.1002/j.1550-8528.1998.tb00344.x
28. Ottery FD. Definition of standardized nutritional assessment and interventional pathways in oncology. Nutrition. 1996;12: S15-9. doi: 10.1016/0899-9007(95)00067-4
29. Toth MJ, Tchernof A, Sites CK, Poehlman ET. Effect of menopausal status on body composition and abdominal fat distribution. In J Obes Relat Metab Disord. 2000;24:226-31. doi: 10.1038/sj.ijo.0801118
30. Parkin DM, Boyd L. Cancers attributable to overweight and obesity in the UK in 2010. Br J Cancer. 2011;105:S34-7. doi: 10.1038/bjc.2011.481
31. Pavelka JC, Brown RS, Karlan BY, Cass I, Leuchter RS. Effect of obesity on survival in epithelial ovarian cancer. Cancer. 2006;107:1520-4. doi: 10.1002/cncr.22194

32. Neovius M, Hemmingssun E, Freyschuss B, Uddén J. Bioelectrical impedance underestimates total and truncal fatness in abdominally obese women. Obesity. 2006;14:1731-8. doi: 10.1038/oby.2006.199.

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卵巢癌患者接受腫瘤治療前的營養狀態及體組成變化

卵巢癌患者營養狀態不佳是常見的問題。本研究以體位及生化參數，評估患者營養狀態及體組成的變化。研究對象為 120 位女性，其中 57 位患有卵巢癌，63 位為良性卵巢瘤，本研究依此將其分為兩組比較。體組成的測量，包括體脂肪(生物電阻抗法)、體位測量、雙能量骨密度檢測。血液生化值，則包含總血清蛋白、白蛋白、運鐵蛋白、血紅素、血球容積比，以及總淋巴球計數。僅 31 位女性具有雙能量骨密度檢測及體脂肪資料。獨立 t 檢定用於比較兩組的平均值差異。兩組別婦女皆過重。卵巢癌患者的皮下脂肪厚度、臂圍、血清白蛋白、總淋巴球計數，以及運鐵蛋白濃度皆顯著較低(p<0.05)。卵巢癌女性雖過重，但其皮下脂肪儲量以及血清蛋白偏低。然而，此結果仍需要所有參與者的體組成評估做進一步的確認。

關鍵字：卵巢癌、營養狀態、體組成、營養評估、生物電阻抗分析