QUALITY OF SKELETAL MUSCLE AND ADIPOSE TISSUE PREDICTS THE RISK OF TOXICITY TO CHEMOTHERAPY IN WOMEN WITH OVARIAN ADENOCARCINOMA

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BACKGROUND

Chemotherapy for ovarian cancer causes several toxic effects. To date, studies that associate body composition with toxicity to treatment, especially considering the effect of drug interactions in these patients, remain absent.

OBJECTIVE

The presente study aimed to evaluate the association of body composition with toxicity to first-line chemotherapy in women with ovarian adenocarcinoma.

METHOD

This retrospective cohort included 170 women with ovarian adenocarcinoma treated with carboplatin and paclitaxel between 2008-2017, in Rio de Janeiro - RJ. Pretreatment computed tomography (CT) scans were used to quantify the tissues muscular and adipose. The following parameters were evaluated: myopenia, by the skeletal muscle index (SMI) <38.9 cm^2/m^2; muscular quality, by mean muscle attenuation and high radiodensity skeletal muscle index (HRSMI), both <75th percentile (<p75); and adipose tissue, assessed by subcutaneous or intramuscular adipose tissue índex <p75. The study's outcomes were grade > 3 toxicity and therapeutic management by pharmacological toxicity (TMPT), defined as any dose reduction > 7 days, monotherapy and/or permanent discontinuation due to toxicity. Multiple logistic regression models were adjusted for age> 65 years, performance status (PS), Charlson Comorbidity Index, number of cycles, prescription of anticoagulants and antiemetics, moderate/severe drug interaction, monotherapy and dose reduction in the first cycle. We adopted a significance level of 5%.

RESULTS

Table 1.0 – Clinical and pathological features of women with ovarian adenocarcinoma (n=170).

Variables	n (%)
Age (years)	
< 65	124 (72.9)
≥ 65	46 (27.1)
Histological subtype (n=132)	
Serous	101 (76.5)
Endometrioid	12 (9.1)
Mucinous	8 (6.1)
Clear cells	5 (3.8)
Mixed	6 (4.5)
Tumor staging (n=152)	
Estage I	7 (4.6)
Estage II	10 (6.6)
Estage III	72 (47.4)
Estage IV	63 (41.4)
PS (n=169)	
0	41 (24.3)
1	69 (41.8)
2	40 (23.7)
3	19 (11.2)
CCI (sum)	
2	84 (49.4)
3	64 (37.6)
4	18 (10.6)
5	2 (1.2)
7	1 (0.6)
9	1 (0.6)
Treatment characteristcs	
Number of cycles	
< 6	43 (25.3)
≥ 6	127 (74.7)
First cycle dose reduction	31 (18.2)
First cycle monotherapy	31 (18.2)
Treatment-related complications	
Dose reduction	24 (14.1)
Carboplatin reduction	19 (11.2)
Paclitaxel reduction	6 (3.5)
Delay	28 (16.5)
Monotherapy	6 (3.5)
Interruption	24 (14.1)
Degree of toxicity	
≥ grade 2	139 (81.8)
≥ grade 3	74 (43.5)
TMPT	65 (38.2)

CCI – Charlson's comorbidity index; TMPT: Therapeutic management by pharmacological toxicity; PS – Performance status.

Table 2.0 – Body composition parameters of women with adenocarcinoma before chemotherapy treatment (n=170).

Variables	Results
SMI (cm^2/m^2)[a]	
< 38.9	62 (36.5)
≥ 38.9	108 (63.5)
HRSMI (cm^2/m^2)	
Percentile 25	17.9100
Percentile 50	21.7400
Percentile 75	27.4175
AMA (HU)	
Percentile 25	24.7698
Percentile 50	30.3990
Percentile 75	35.0105
IMATI (cm^2/m^2)	
Percentile 25	2.5425
Percentile 50	4.1050
Percentile 75	6.9125
SATI (cm^2/m^2)	
Percentile 25	39.9225
Percentile 50	61.9450
Percentile 75	91.5250

HU – Hounsfield unit; SMI – Skeletal muscle index; HRSMI – High radiodensity skeletal muscle index; IMATI – Intramuscular adipose tissue index; SATI – Subcutaneous adipose tissue index; AMA – Average muscle attenuation. a – results expressed in n (%).

Tabel 3.0 – Multivariate logistic regression models for toxicity ≥ grade 3.

Models[a]	Multivariate (n=170)		
	OR	CI (95%)	*p**
Model 1 – SMI			
Age ≥ 65 years	**0.405**	**0.169 – 0.966**	**0.042**
SMI <38.9 (cm^2/m^2)	1.546	0.734 – 3.255	0.251
SATI <p 75 (cm^2/m^2)	**3.202**	**1.223 – 8.385**	**0.018**
IMATI <p 75 (cm^2/m^2)	**3.037**	**1.193 – 7.733**	**0.020**
Model 2 – AMA			
Age ≥ 65 years	**0.364**	**0.151 – 0.882**	**0.025**
MAM <p 75 (HU)	2.339	1.000 – 5.471	0.050
SATI <p 75 (cm^2/m^2)	**3.648**	**1.397 – 9.525**	**0.008**
IMATI <p 75 (cm^2/m^2)	**4.060**	**1.531 – 10.764**	**0.005**
Model 3 – HRSMI			
Age ≥ 65 years	**0.351**	**0.144 – 0.856**	**0.021**
HRSMI <p 75 (cm^2/m^2)	**3.142**	**1.336 – 7.390**	**0.009**
SATI <p 75 (cm^2/m^2)	**3.468**	**1.310 – 9.181**	**0.012**
IMATI <p 75 (cm^2/m^2)	**4.034**	**1.533 – 10.616**	**0.005**

a – All models of multivariate analyzes were adjusted for: age ≥ 65 years, *PS* ≥ 2, CCI ≥ 3 points), number of chemotherapy cycles performed, first cycle dose reduction, first cycle monotherapy, moderate/severe drug interaction with the chemotherapy protocol and probable use of antiemetics.

Table 4.0 – Multivariate logistic regression models for therapeutic management by pharmacological toxicity.

Models[a]	Multivariate (n=170)		
	OR	CI (95%)	*p**
Model 1 - SMI			
SMI <38.9 (cm^2/m^2)	0.785	0.349 – 1.763	0.557
SATI <p 75 (cm^2/m^2)	1.100	0.418 – 2.892	0.847
ITAIM <p 75 (cm^2/m^2)	1.530	0.596 – 3.929	0.377
PS ≥ 2	**2.465**	**1.074 – 5.656**	**0.033**
First cycle monotherapy	**4.489**	**1.722 – 11.707**	**0.002**
Model 2 - AMA			
AMA <p 75 (HU)	2.060	0.804 – 5.279	0.132
SATI <p 75 (cm^2/m^2)	1.034	0.393 – 2.717	0.946
IMATI <p 75 (cm^2/m^2)	1.851	0.696 – 4.925	0.217
PS ≥ 2	**2.375**	**1.043 – 5.408**	**0.039**
First cycle monotherapy	**3.975**	**1.501 – 10.531**	**0.005**
Model 3 - HRSMI			
HRSMI <p 75 (cm^2/m^2)	2.324	0.919 – 5.880	0.075
SATI <p 75 (cm^2/m^2)	0.986	0.373 – 2.602	0.977
IMATI <p 75 (cm^2/m^2)	1.787	0.676 – 4.726	0.242
First cycle monotherapy	**4.312**	**1.632 – 11.395**	**0.003**

a – All models of multivariate analyzes were adjusted for: age ≥ 65 years, *PS* ≥ 2, CCI ≥ 3 points), first cycle dose reduction, first cycle monotherapy, moderate/severe drug interaction with the chemotherapy protocol and likely use of anticoagulants.

CONCLUSION

The pre-treatment body composition, including high radiodensity muscle and adipose tissue, was able to predict grade > 3 toxicity to chemotherapy in women with ovarian cancer and, therefore, should be considered in the antitumor treatment.

Projeto Gráfico: Área de Edição e Produção de Materiais Técnico-Científicos / INCA

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