

# 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 The presente study aimed to evaluate the association of body composition with associate body composition with toxicity to treatment, especially considering the toxicity to first-line chemotherapy in women with ovarian adenocarcinoma. effect of drug interactions in these patients, remain absent.

## OBJECTIVE

## 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<sup>2</sup>/m<sup>2</sup>; 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 (ndex <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%.



Table 1.0 – Clinical and pathological features of women with ovarian adenocarcinoma (n=170). n (0/a)

Table 2.0 - Body composition parameters of

Tabel 3.0 – Multivariate logistic regression models for toxicity  $\geq$  grade 3. Multivariate (n=170) 16.1.1.1

Age (years)       women $< 65$ 124 (72.9)       women $\leq 65$ 46 (27.1)       chemotil         Histological subtype (n=132)       Vari         Serous       101 (76.5)       SMI (of         Mucinous       8 (6.1) $< 38$ .         Clear cells       5 (3.8) $\geq 38$ .         Mixed       6 (4.5) $\geq 38$ .         Tumor staging (n=152)       HRSM.         Estage I       7 (4.6)       Percee         Estage II       10 (6.6)       Percee         Estage IV       63 (41.4)       Percee         PS (n=169)       Percee       Percee         0       41 (24.3)       AMAA         1       69 (41.8)       AMAA         2       40 (23.7)       Percee         3       64 (37.6)       IMAAT         4       18 (10.6)       Percee         7       10.6)       Percee         9       1(0.6)       Percee         7       10.6)       Percee         7       10.6)       Percee         9       1(0.6)       Percee         9       1(0.6)       Percee         10.6) </th <th>variables</th> <th>ш (70)</th> <th></th>	variables	ш (70)	
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able 2.0 Doug	composition parameters of	
omen with	adenocarcinoma before	
nemotherapy treatm	nent (n=170).	
Variables	bles Results	
SMI (cm²/m²)a		
< 38.9	62 (36.5)	
≥ 38.9	108 (63.5)	
HRSMI (cm²/m²)		
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 (cm²/m²)		
Percentile 25	2.5425	
Percentile 50	4.1050	
Percentile 75	6.9125	
SATI (cm²/m²)		
Percentile 25	39.9225	
Percentile 50	61.9450	
Percentile 75	91.5250	
U – Hounsfield u	nit; SMI – Skeletal muscle	
dex; HRSMI – Hig	h radiodensity skeletal muscle	

Models <sup>a</sup>	OR	CI (95%)	D*
Model 1 – SMI			r
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 $$	3.202	1.223 - 8.385	0.018
IMATI 2/m <sup>2</sup> )	3.037	1.193 - 7.733	0.020
Model 2 – AMA			
Age $\geq$ 65 years	0.364	0.151 - 0.882	0.025
MAM <p (hu)<="" 75="" td=""><td>2.339</td><td>1.000 - 5.471</td><td>0.050</td></p>	2.339	1.000 - 5.471	0.050
SATI 2/m <sup>2</sup> )	3.648	1.397 - 9.525	0.008
IMATI 2/m <sup>2</sup> )	4.060	1.531 - 10.764	0.005
Model 3 – HRSMI			
Age $\geq$ 65 years	0.351	0.144 - 0.856	0.021
HRSMI 2/m <sup>2</sup> )	3.142	1.336 - 7.390	0.009
$C \wedge TI \sim 75 (am^2/m^2)$	2 460	1 410 0 101	0.012
$SA11$	3.408	1.310 - 9.181	0.012
IMATI  a – All models of multivariate analyzes we points), number of chemotherapy cycles p	5.408 4.034 re adjusted for: age 2 performed, first cycle	1.310 - 9.181 1.533 - 10.616 $2 65 \text{ years, } PS \ge 2,$ 2  dose reduction, find the second and the s	0.012 0.005 , CCI $\geq 3$ first cycle
IMATI  a – All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interactions use of antiemetics. Table 4.0 – Multivariate logistic regre	3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2,$ $2 \text{ dose reduction, filterapy protocol and}$ $1.533 - 10.616$	0.012 0.005 0.005 0.012 0.012 0.012 0.012 0.012 0.012 0.005 0
MATI <u>a</u> – All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interacts use of antiemetics. <b>Table 4.0 – Multivariate logistic regre</b> pharmacological toxicity.	5.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t	1.310 - 9.181 1.533 - 10.616 $2 65 years, PS \ge 2$ , 2 dose reduction, find the end of the e	0.012 0.005 0.012 0.012 0.012 0.012 0.012 0.012 0.012 0.012 0.012 0.005 0
MATI <u>a</u> – All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interaction use of antiemetics. Table 4.0 – Multivariate logistic regreses pharmacological toxicity. Models <sup>a</sup>	3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2, 6  dose reduction, for a set of the s$	0.012 $0.005$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$
Model 1 - SMI MATI  a - All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interaction use of antiemetics. Table 4.0 - Multivariate logistic regreses pharmacological toxicity. Models <sup>a</sup>	3.408 4.034 re adjusted for: age 2 performed, first cycle ion with the chemoth ession models for t NOR	1.310 - 9.181 1.533 - 10.616 2 65 years, $PS \ge 2$ , a dose reduction, find therapy protocol and herapeutic mana Multivariate (n=17) CI (95%)	0.012 $0.005$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.012$ $0.005$
Model 1 - SMI Model 1 - SMI Model 1 - SMI SMI <38.9 (cm <sup>2</sup> /m <sup>2</sup> ) MATI <pre> SMI &lt;38.9 (cm<sup>2</sup>/m<sup>2</sup>) </pre>	3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t <u>OR</u> 0.785	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2, 6  dose reduction, for a set of the s$	0.012 $0.005$ $0.005$ $0.005$ $0.005$ $0.005$ $0.005$
Model 1 - SMI Model 1 - SMI Model 1 - SMI SMI <pre>SMI <pre>SMI</pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>	3.408 4.034 re adjusted for: age 2 performed, first cycle ion with the chemoth ession models for t 0.785 1.100	1.310 - 9.181 1.533 - 10.616 2 65 years, $PS \ge 2$ , 3 dose reduction, finderapy protocol and herapeutic mana Multivariate (n=17) CI (95%) 0.349 - 1.763 0.418 - 2.892	0.012 0.005 0.005 0.005 0.012 0.012 0.012 0.0557 0.847
Model 1 - SMI SATI  a - All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interactive use of antiemetics. Table 4.0 - Multivariate logistic regreses pharmacological toxicity. Models <sup>a</sup> Model 1 - SMI SMI <38.9 (cm²/m²) SATI  ITAIM <p (cm²="" 75="" m²)<="" td=""><td>3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530</td><td>1.310 - 9.181 1.533 - 10.616 2 65 years, <math>PS \ge 2</math>, 3 dose reduction, finderapy protocol and herapeutic mana Multivariate (n=17) CI (95%) 0.349 - 1.763 0.418 - 2.892 0.596 - 3.929</td><td>0.012 0.005 0.005 0.005 0.012 0.012 0.005 0.005 0.000 <math>p^*</math> 0.557 0.847 0.377 0.377</td></p>	3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530	1.310 - 9.181 1.533 - 10.616 2 65 years, $PS \ge 2$ , 3 dose reduction, finderapy protocol and herapeutic mana Multivariate (n=17) CI (95%) 0.349 - 1.763 0.418 - 2.892 0.596 - 3.929	0.012 0.005 0.005 0.005 0.012 0.012 0.005 0.005 0.000 $p^*$ 0.557 0.847 0.377 0.377
SATI 2/m <sup>2</sup> ) <u>IMATI 2/m<sup>2</sup>)</u> <u>a</u> – All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interactive use of antiemetics. <b>Table 4.0 – Multivariate logistic regression</b> <u>Models<sup>a</sup></u> <u>Model 1 - SMI</u> SMI <38.9 (cm <sup>2</sup> /m <sup>2</sup> ) SATI 2/m <sup>2</sup> ) ITAIM 2/m <sup>2</sup> ) $PS \ge 2$ First avale monotherapy	3.408 4.034 re adjusted for: age 2 performed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530 2.465 4.490	1.310 - 9.181 1.533 - 10.616 2 65 years, $PS \ge 2$ , 3 dose reduction, f derapy protocol and herapeutic mana Multivariate (n=17) CI (95%) 0.349 - 1.763 0.418 - 2.892 0.596 - 3.929 1.074 - 5.656 1.722 - 11.707	0.012 0.005 0.005 0.005 0.012 0.005 0.0000 0.0000
SATI <pre>SATI <pre>Satistic <pre>SATI <pre>Satistic <pre>Satisti</pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>	3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530 2.465 4.489	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2, 2  dose reduction, for a reduction, for a reduction, for a reduction and the rapeutic mana for a reduction in the rapeutic mana reduct$	0.012 0.005 0.005 0.02 0.005 0.005 0.557 0.847 0.377 0.033 0.002
SATI <pre>SATI <pre>SATI</pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>	3.408 4.034 re adjusted for: age 2 berformed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530 2.465 4.489	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2, 6  dose reduction, for a service of the service o$	0.012 0.005 0.005 0.005 0.0000 0.557 0.847 0.377 0.033 0.002
SATI <pre>SATI <pre>Sati</pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>	3.408 4.034 re adjusted for: age a performed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530 2.465 4.489 2.060 1.024	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2, 6  dose reduction, for a reduction, for a reduction, for a reduction and for a reduction of the rapeutic mana for a reductic mana for $	0.012 0.005 0.005 0.005 0.012 0.005 0.0000 0.0000 0.0000 0.0000 0.0000
SATI 2/m <sup>2</sup> ) <u>IMATI 2/m<sup>2</sup>)</u> <u>a</u> – All models of multivariate analyzes we points), number of chemotherapy cycles p monotherapy, moderate/severe drug interactiv use of antiemetics. <b>Table 4.0 – Multivariate logistic regression</b> pharmacological toxicity. <u>Models<sup>a</sup></u> <u>Model 1 - SMI</u> SMI <38.9 (cm <sup>2</sup> /m <sup>2</sup> ) SATI 2/m <sup>2</sup> ) ITAIM 2/m <sup>2</sup> ) <i>PS</i> $\geq$ 2 First cycle monotherapy <u>Model 2 - AMA</u> AMA  SATI 2/m <sup>2</sup> ) IMATI 2/m <sup>2</sup> )	3.408 4.034 re adjusted for: age a berformed, first cycle ion with the chemoth ession models for t 0.785 1.100 1.530 2.465 4.489 2.060 1.034 1.951	$1.310 - 9.181$ $1.533 - 10.616$ $2 65 \text{ years, } PS \ge 2, 6  dose reduction, for a series of the series of the$	0.012 0.005 0.005 0.005 0.012 0.0012 0.0012 0.0012 0.557 0.847 0.377 0.033 0.002 0.132 0.946 0.217

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

ATI – Intramuscular adipose tissue index; Subcutaneous adipose tissue index; AMA muscle attenuation. a – results expressed in

Model 3 - HRSMI			
HRSMI $$	2.324	0.919 - 5.880	0.075
SATI 2/m <sup>2</sup> )	0.986	0.373 - 2.602	0.977
IMATI 2/m <sup>2</sup> )	1.787	0.676 - 4.726	0.242
First cycle monotherapy	4.312	1.632 - 11.395	0.003
		66 D.C	A 67.67

3.975 1.501 - 10.531

0.005

a – All models of multivariate analyzes were adjusted for: age  $\geq$  65 years,  $PS \geq 2$ , CCI  $\geq$  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



First cycle monotherapy