



Muscle Mass as a Predictor of Treatment Outcomes

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Review

Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review



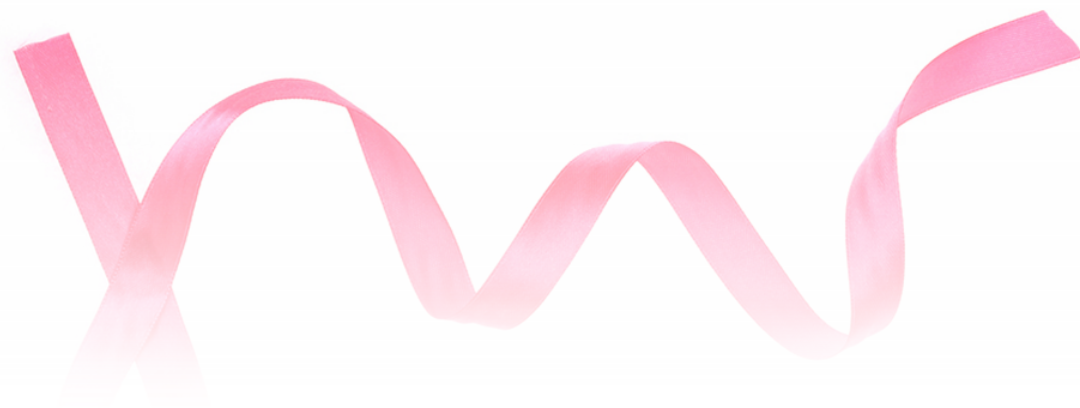
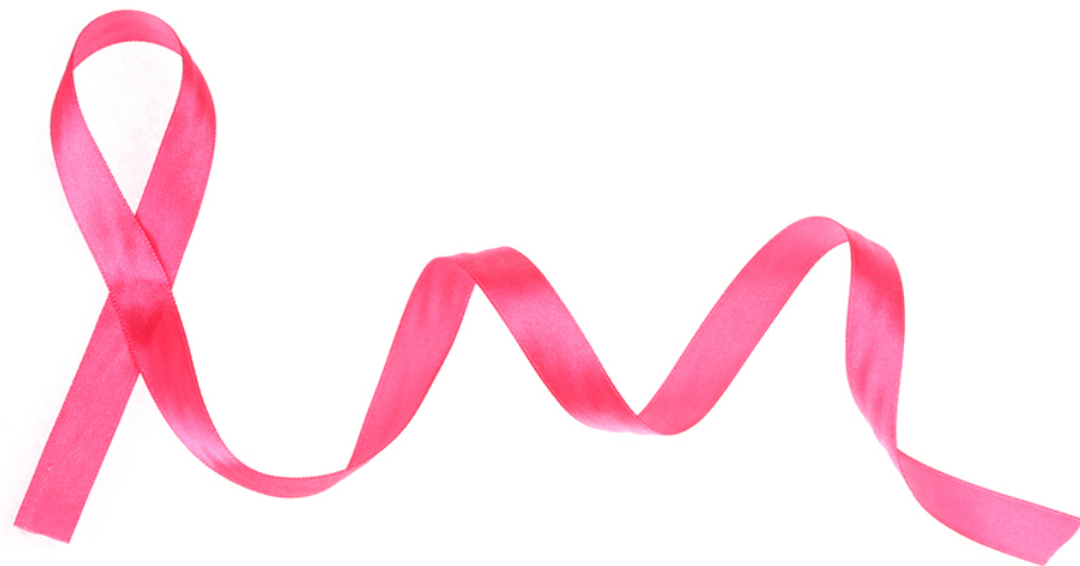
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Tomohiro F. Nishijima ^a

Prognostic Value of Sarcopenia in Adults with Solid Tumors: a Meta-Analysis and Systematic Review

	No. of Studies	No. of Patients	HR	95% CI	P-value
All cancer types	37		1.437	1.32-1.56	<0.001
<u>Type of tumor</u>					<0.001†
Hepatocellular carcinoma	11	2,347	2.160	1.54-3.03	<0.001
Pancreaticobiliary	6	904	1.293	0.98-1.70	0.066
Gastroesophageal	4	649	1.504	1.08-2.08	0.015
Urothelial Carcinoma	3	555	1.471	0.99-2.19	0.057
Renal cell carcinoma	3	572	1.748	1.29-2.37	<0.001
Colorectal cancer	3	493	2.247	1.63-3.09	<0.001
Other	7	2,259	1.457	1.11-1.91	0.006
<u>Disease stage</u>					<0.001†
Non-metastatic	16	2638	1.538	1.31-1.79	<0.001
Mixed	4	3197	2.045	1.27-3.28	0.003
Metastatic/advanced	17	1944	1.372	1.21-1.56	<0.001
<u>Type of analysis</u>					<0.001†
Multivariate	22		1.513	1.35-1.69	<0.001
Univariate	15		1.556	1.24-1.95	<0.001

Bottom Line

- Low skeletal muscle index affects overall survival
- HR= 1.44 (p<0.001)



Woman with
breast cancer



Man with flu



CLINICAL CALORIMETRY

TENTH PAPER

A FORMULA TO ESTIMATE THE APPROXIMATE SURFACE
AREA IF HEIGHT AND WEIGHT BE KNOWN*

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BSA

DuBois Formula:

$$BSA = 0.007184 \times W^{0.425} \times H^{0.725}$$

Mosteller Formula:

$$BSA (m^2) = \sqrt{\frac{Ht (Cm) \times Wt (kg)}{3600}}$$

Metastatic Breast Cancer & Sarcopenia

Metastatic breast cancer

- Xeloda in MBC (N=55)
- Shorter TTP
- Higher toxicity

Metastatic Breast Cancer & Sarcopenia

Inclusion criteria:

- Metastatic Breast Cancer (MBC) diagnosis
- First line taxane therapy
- CT scans within 45 days
- Toxicity data available

Toxicity

- Common Terminology Criteria for Adverse Events v4.0
 - Grade 1 Mild;
 - Grade 2 Moderate;
 - **Grade 3** Severe or medically significant but not immediately life-threatening;
 - **Grade 4** Life-threatening consequences;
 - **Grade 5** Death.
- Other relevant adverse events
 - Hospitalizations
 - Dose reductions
 - Dose delays
 - Treatment discontinuation

Results

Characteristics (N=40)	N (%) /median (IQR)
Age at metastatic diagnosis (years)	55 (47-63)
Age < 65 years	33 (83)
Disease free interval (years)	1.57 (0.05-5.66)
Days from scan to chemotherapy (range)	20 (2-36)
Subtype	
HR negative/HER2 negative	10 (25)
HER2 positive	15 (37.5)
HR positive/HER2 negative	15 (37.5)
Sites of metastasis at metastatic diagnosis	
Liver	12 (30)
Lung	5 (12)
Bone	25(62)

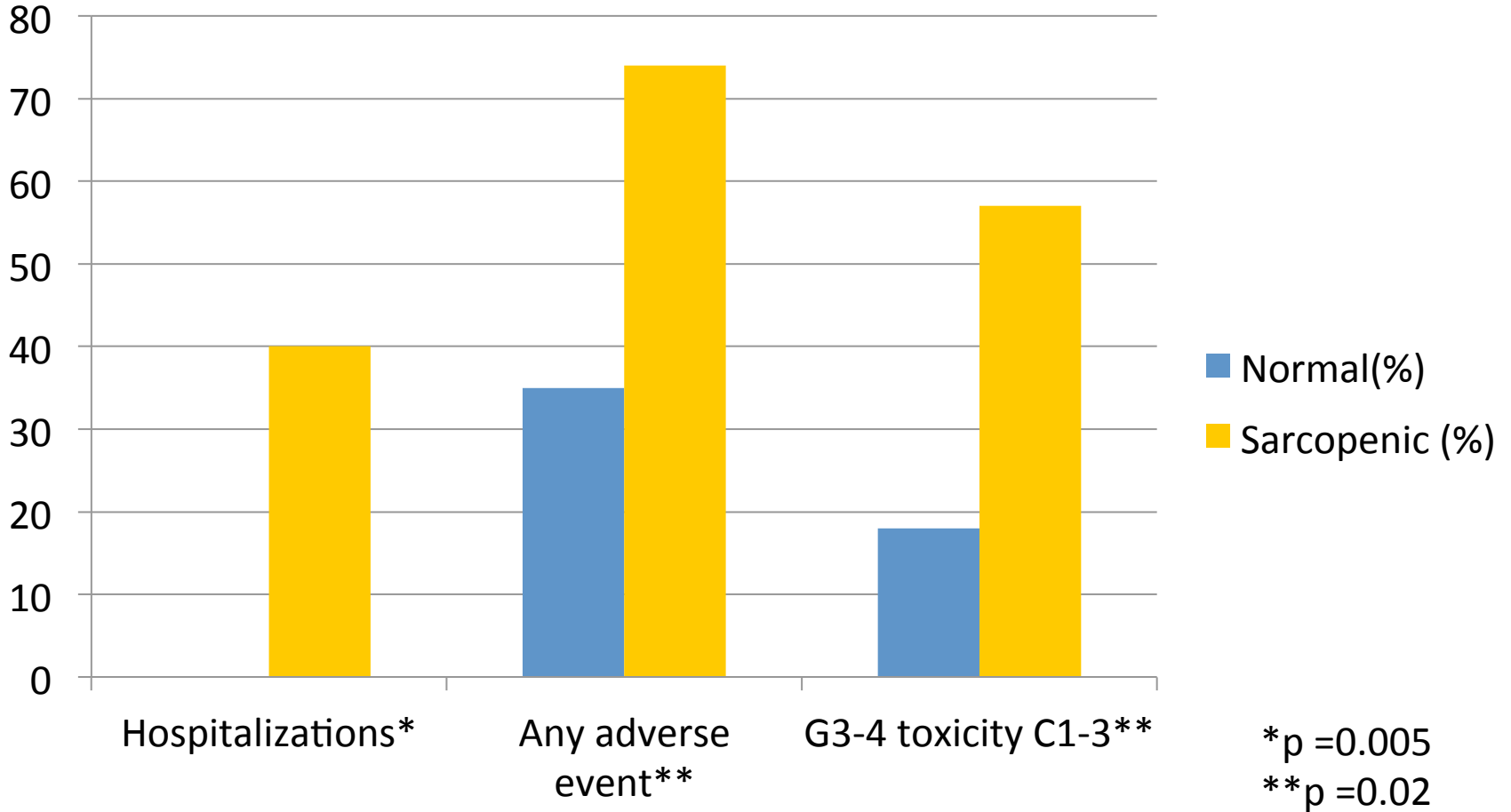
Treatment Characteristics

Biological therapy		N(%)
Trastuzumab		11 (27)
Pertuzumab/Trestuzumab		4 (10)
Bevacizumab		10 (25)
Chemotherapy		
Paclitaxel		31 (78)
Docetaxel		4 (10)
Abraxane		5 (12)

Body Composition Measures

Body composition measures	
Sarcopenia N (%)	23 (58)
Variable	Median (IQR)
SMI (cm ² /m ²)	40.46 (36.09-43.75)
SMD (HU)	29.20 (24.02-37.07)
SMG (AU)	1296 (943-1512)
BMI (kg/m ²)	28.44 (23.44-32.06)
BSA (m ²)	1.87 (1.66-2.00)
LBM* (kg)	38.04 (34.06-43.81)
Toxicity events	N(%)
Grade 3-4 Cycles1-3	16 (40)
Hospitalizations	9 (23)
Dose reductions	10 (25)
Dose delays	11 (28)
Any adverse event	23 (58)

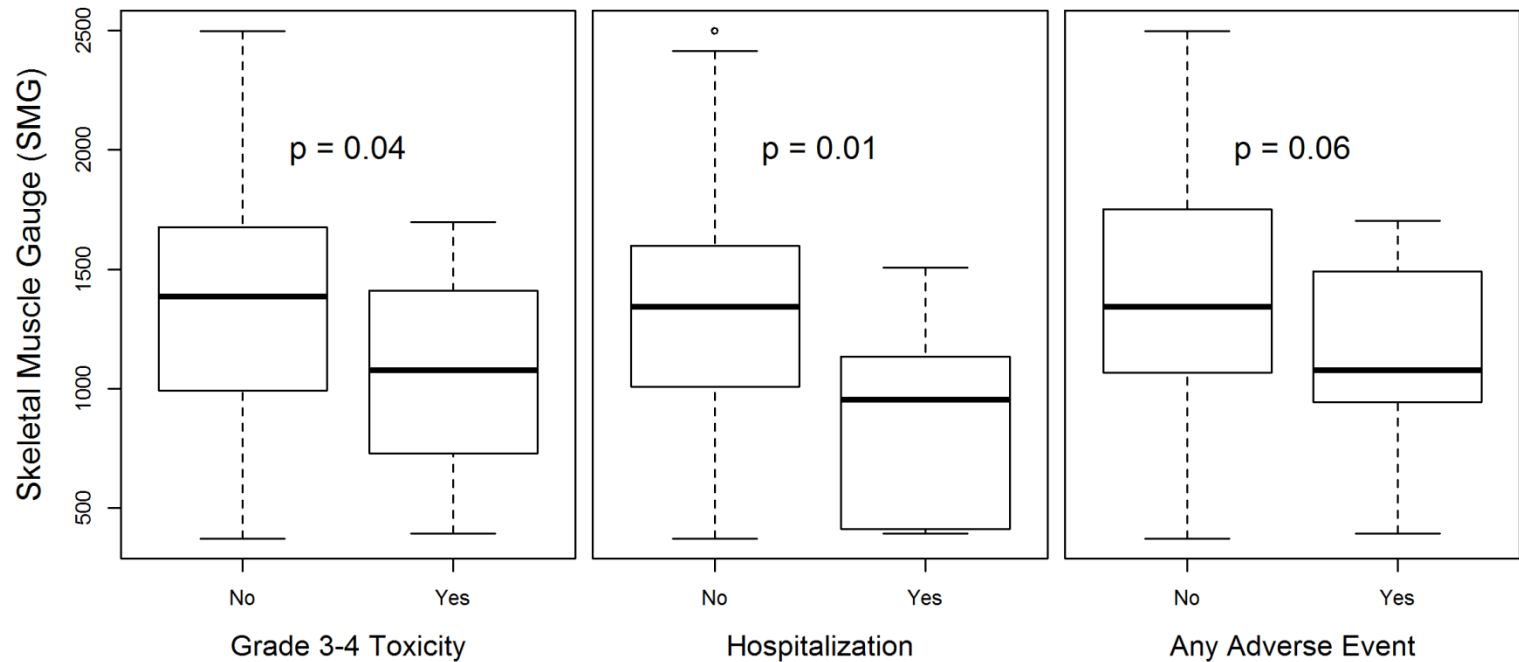
Sarcopenia and Outcomes in MBC



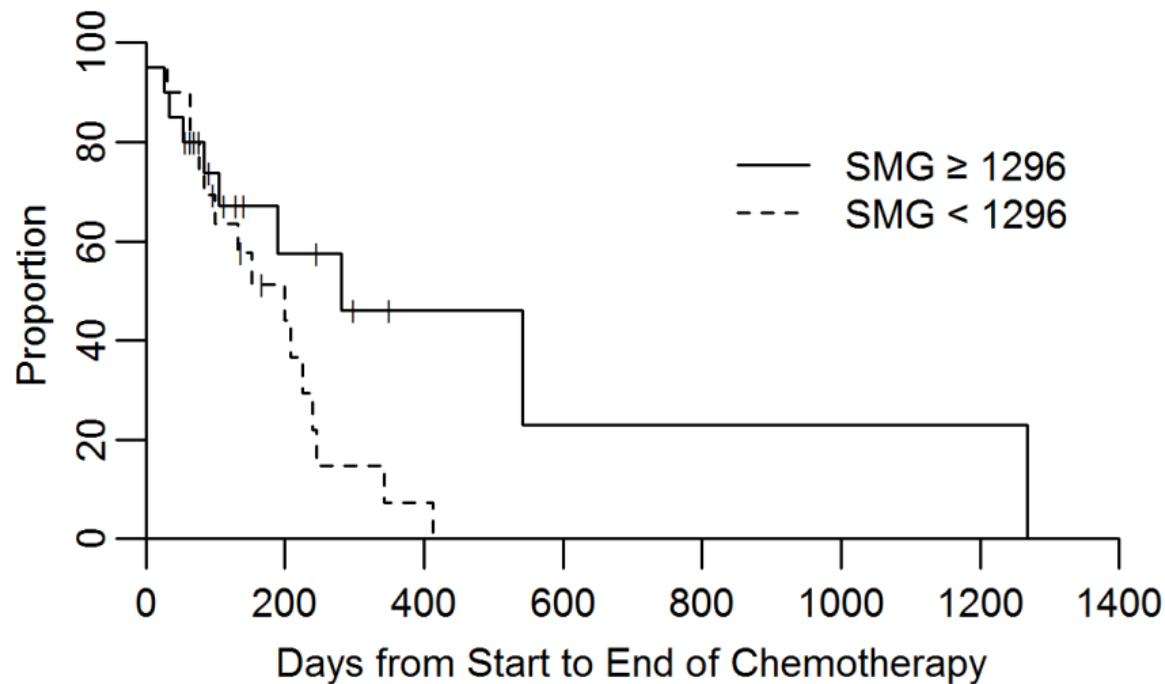
Outcomes

	Cycles 1-3 toxicity			Hospitalization			Any adverse event		
	No	Yes	<i>p</i> value	No	Yes	<i>p</i> value	No	Yes	<i>p</i> value
SMD (HU)	31.94	26.57	0.10	31.66	23.34	0.03	32.34	27.9	0.17
SMG (AU)	1385	1046	0.04	1362	862	0.01	1431	1115	0.06
BMI (kg/m ²)	27.65	31.06	0.15	28.55	30.61	0.47	27.58	30.04	0.29
BSA (m ²)	1.84	1.93	0.30	1.86	1.92	0.57	1.83	1.90	0.41
LBM* (Kg)	40.68	37.14	0.13	40.61	34.63	0.03	41.16	37.87	0.16

Skeletal Muscle Gauge and Outcomes in MBC

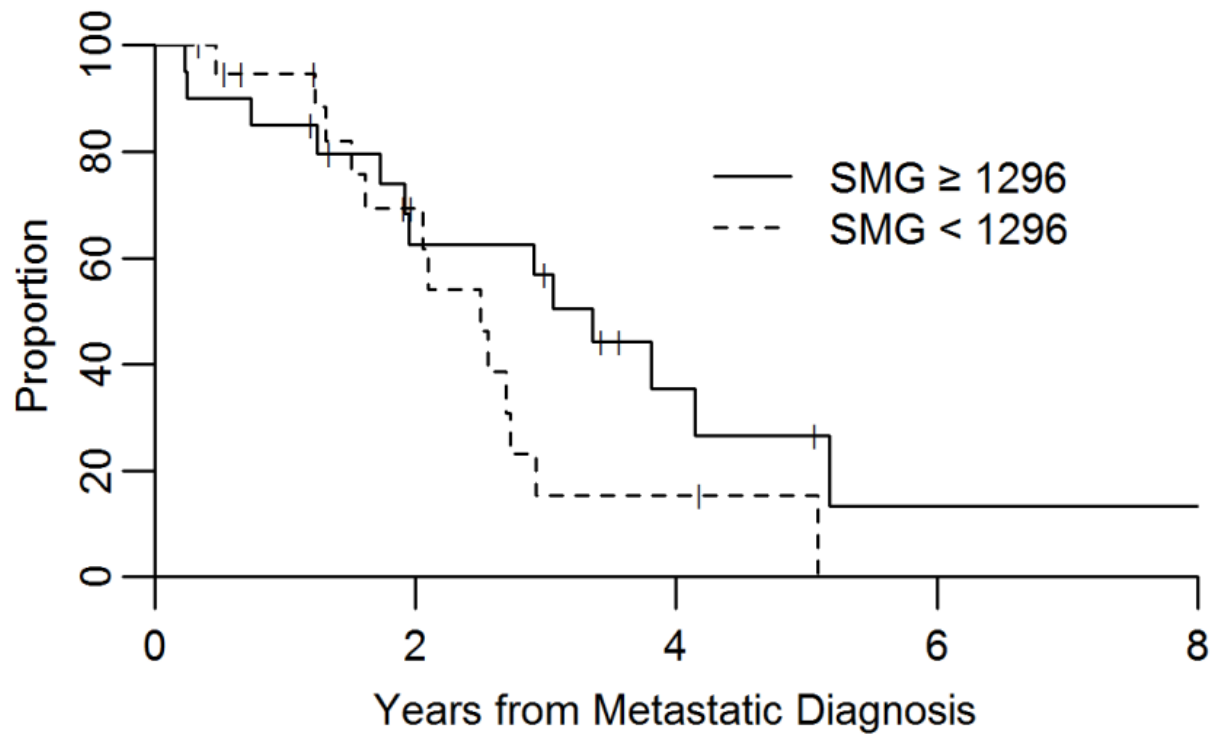


Time to Treatment Failure



Cut point of 1296 is the median value for this continuous variable; $p=0.03$

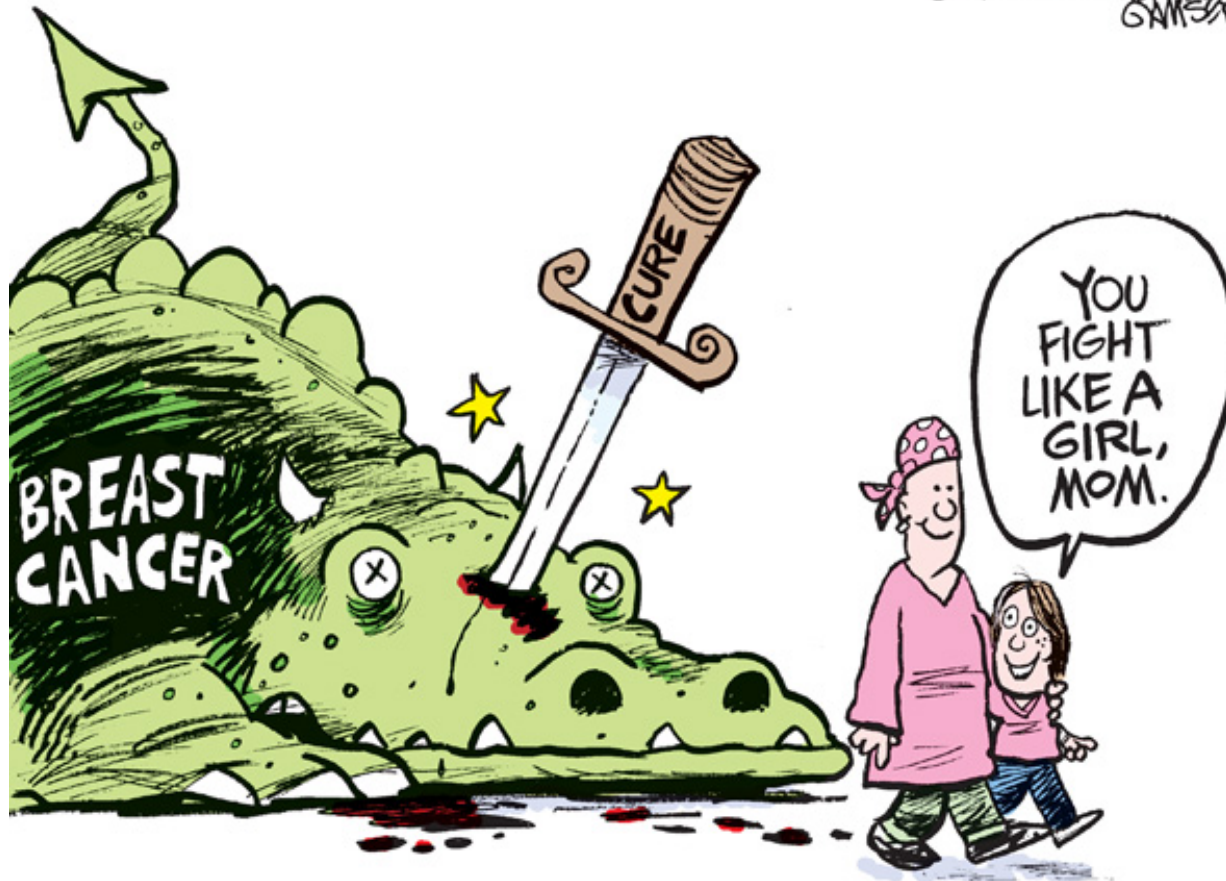
Overall Survival



$p=0.07$

Early Breast Cancer

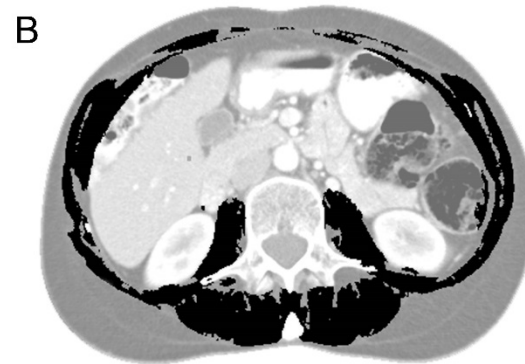
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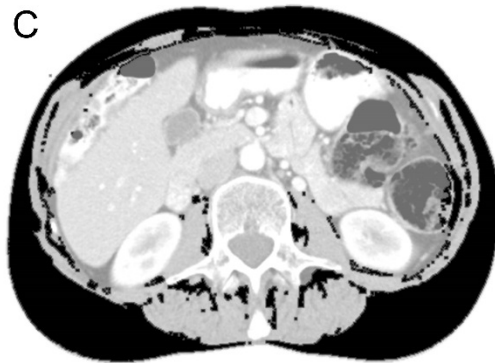
Body Composition in Early Breast Cancer



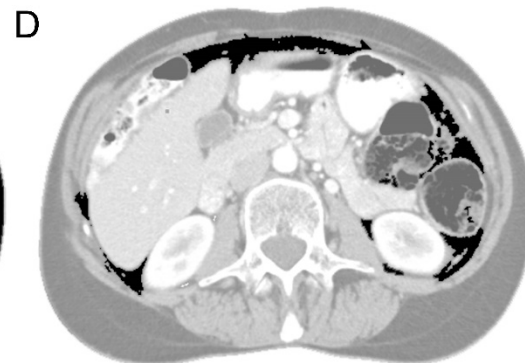
Original Image



Skeletal Muscle



Subcutaneous Adipose
Tissue (SAT)



Visceral Adipose
Tissue (VAT)

Early Breast Cancer Years 2008-2014

**Tumor registry
N=1080**

**Available CT
N=241**

**AC-taxane
N=151**

Patient's Characteristics

Patient's characteristics	
Age at diagnosis -years (range)	49.4(47.8-74.86)
Days from scan to chemotherapy - mean(SD)	22.55 (19.16)
Variable	N (%)
All	151 (100%)
Race – white	112(74.1%)
Stage I-II	65(43%)
Stage III	86(57%)
HR-/Her2-	37 (25%)
HR-/Her2+	13 (9%)
HR+ /Her2-	87 (58%)
HR+ /Her2+	14 (9%)
Adjuvant	64 (42%)

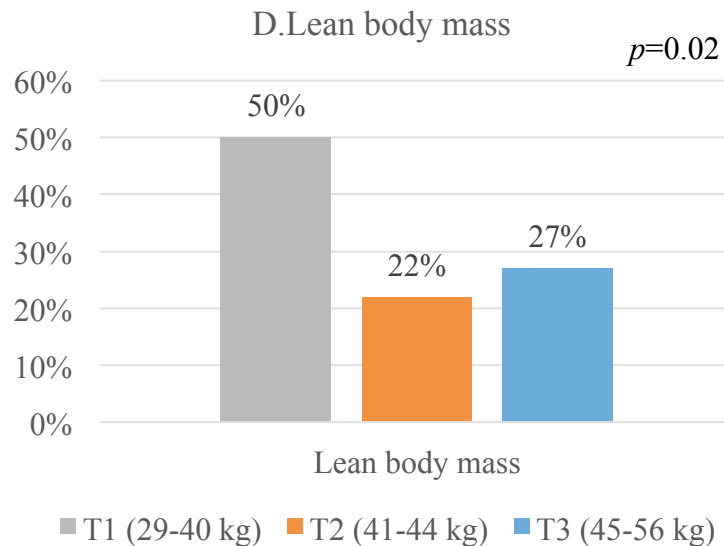
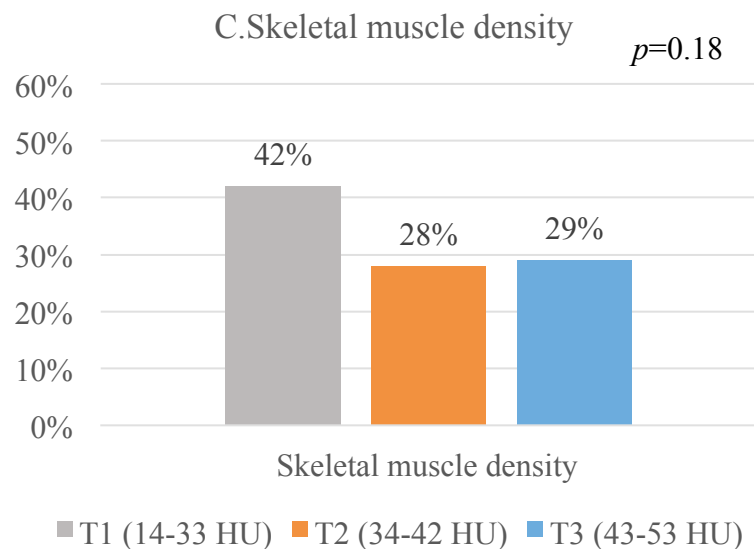
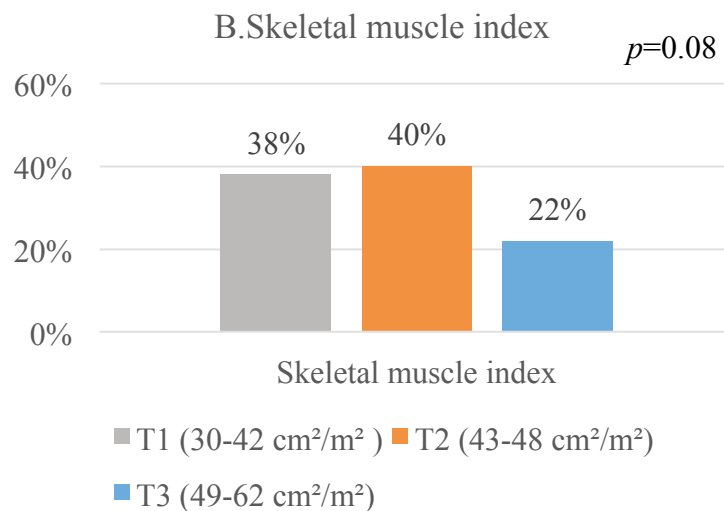
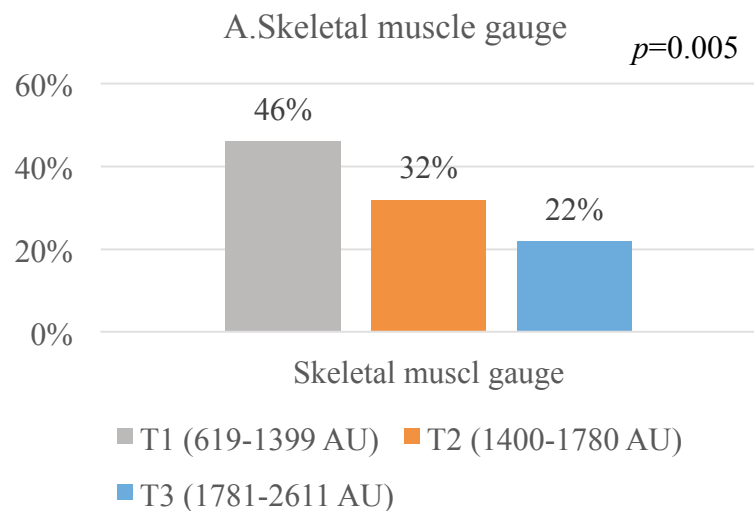
Body Composition Measurement

Body composition measurement	Mean (SD)
Mean BMI	28.78(6.5)
Mean BSA	1.86 (0.21)
Mean LBM	41.94 (5.42)
Mean SMI	44.72 (6.9)
Mean SMD	36.38 (8.9)
Mean SMG	1611 (423)
Days from scan to chemotherapy	22.55 (19.16)

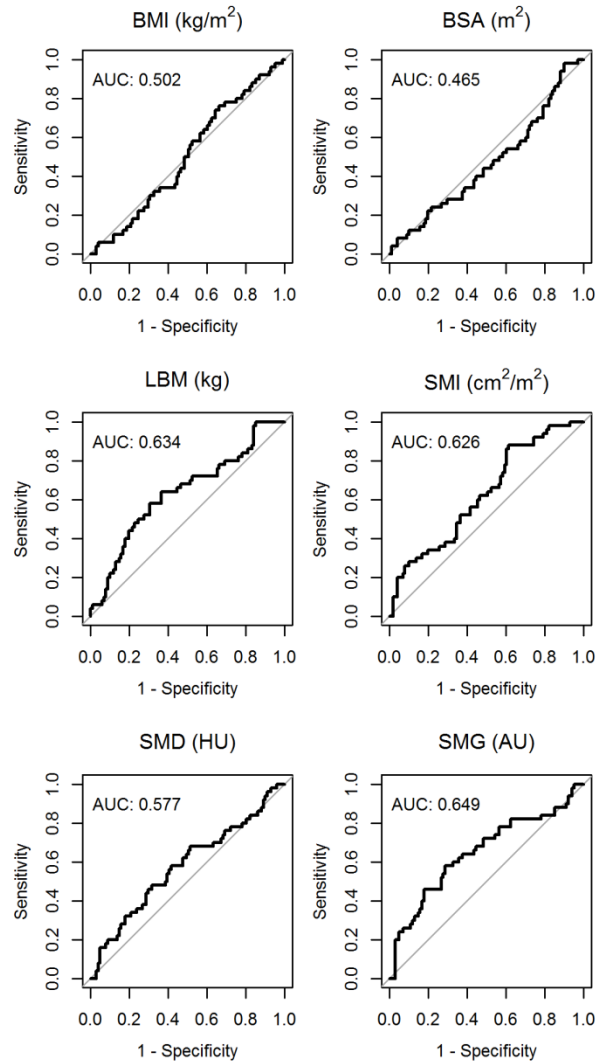
Outcomes

Outcome	N (%)
Grade 3-4 toxicity	51 (34%)
Grade 3-4 GI toxicity	7 (5%)
Grade 3-4 hematological toxicity	32 (21%)
Grade 3-4 neuropathy	11 (7%)
Hospitalization (N=145)	30 (21%)
Dose reduction	16 (11%)
Dose delays	35 (23%)

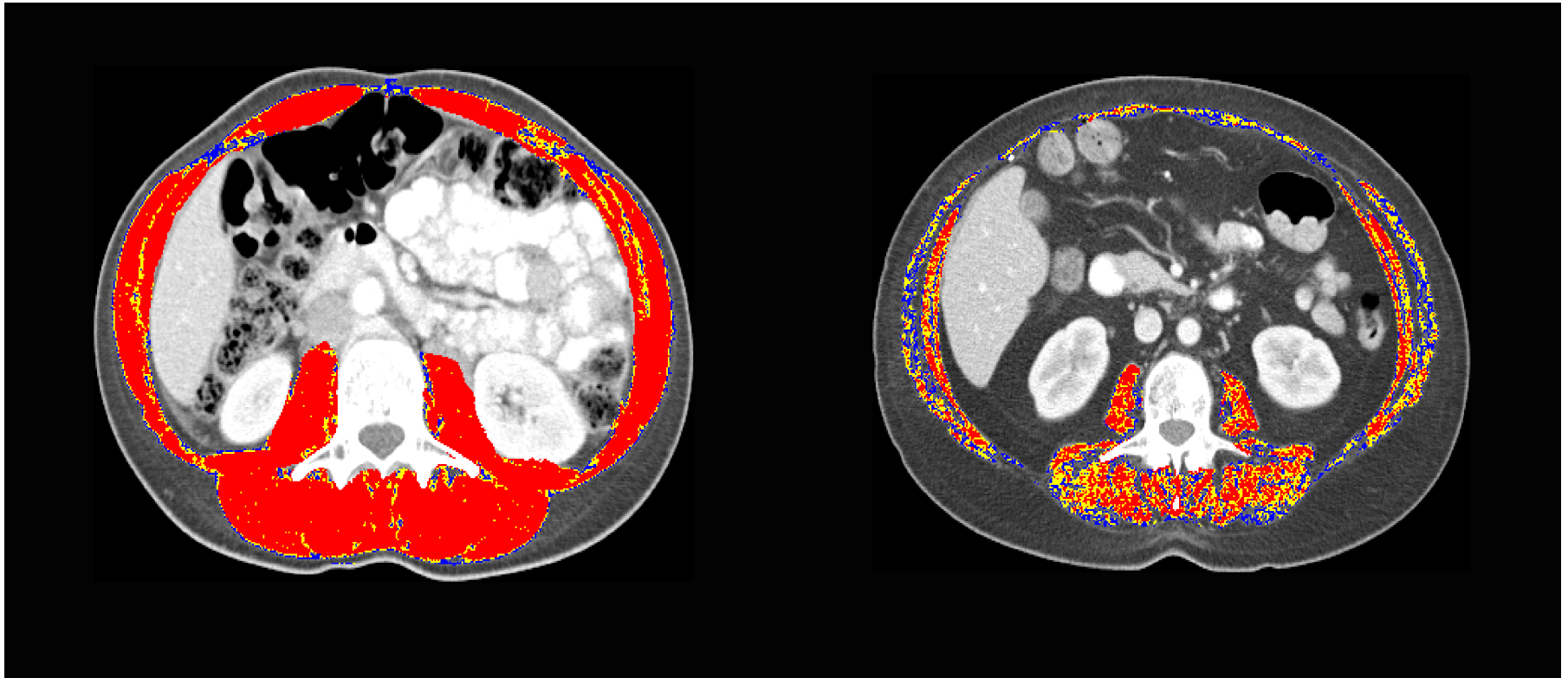
Risk of toxicity based on tertiles of body composition measures



ROCs for different body composition measures and any grade 3-4 toxicities



Both female-BSA 1.70



Normal skeletal muscle density

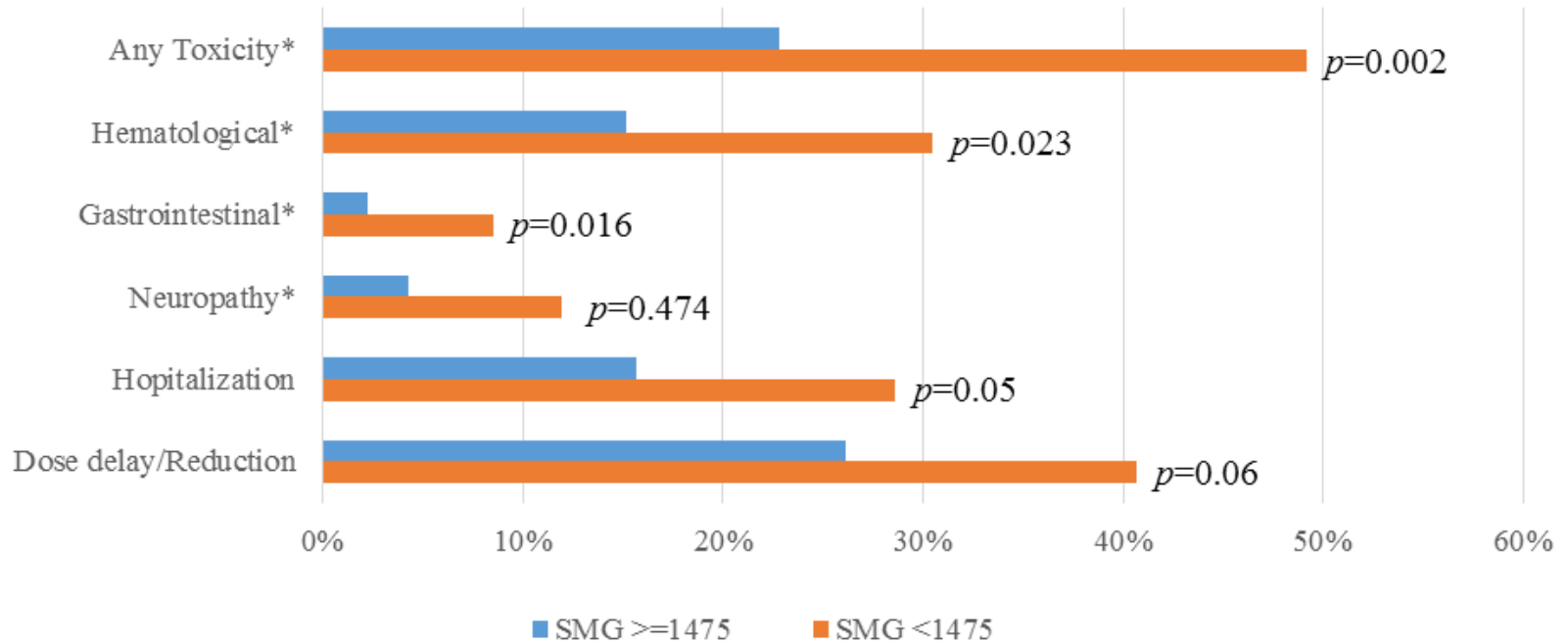
■ +30 to +150
HU

Abnormal (reduced) density in two ranges

■ -29 to 0 HU ■ +1 to +29 HU

Left-normal SMG (2535 AU), no toxicity; Right-low SMG (844 AU), had grade 3-4 toxicity

Risk of toxicity based on skeletal muscle gauge



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The next step?



EDITORIAL

Body-Surface Area as a Basis for Dosing of Anticancer Agents: Science, Myth, or Habit?

‘What should we do about the current situation? One might suggest that we should abandon BSA and switch to LBM based dosing. Unfortunately, there is no standard method for determining LBM, which is correlated with height, weight, and age.’

Conclusions

- Over the last decade body composition and its relationship to cancer outcomes has been a focus of cancer research
- Body composition is highly associated with **treatment outcomes** in early and advanced **breast cancer**
- More **prospective** work is needed to increase our understanding of the **impact of body composition** on **cancer outcomes** and **pharmacokinetics**
- **Interventions?**

Thank you!

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