Body composition by computed tomography scan as a predictor of chemotherapy toxicity in patients with renal cell carcinoma

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Background

- Identification of biomarkers associated with cancer outcome or treatment related toxicity is a challenge.
- Several recent studies demonstrate an association between severe skeletal muscle depletions (sarcopenia) and excess chemotherapy toxicity (Baracos et al 2010, Prado et al 2008)
- CT = considered a gold standard method used to assess body composition
- Renal cell carcinoma (RCC) patients have a strikingly heterogeneous weight and BMI-potential source of variation in drug concentration and metabolism
- Sex specific cut offs for sarcopenia =55.4 cm^2/m^2 males and 38.9 cm^2/m^2 females (Prado et al 2008)

Prado et al. Lancet Oncol. 2008;9:629-635.

Baracos et al. Am J Clin Nutr 2010;91(suppl):1133S–7S

Aims

- Describe skeletal muscle tissue and adipose tissue in a cohort of patients with renal cell carcinoma
- Study the effect of sarcopenia (at the start of chemotherapy) on chemotherapy toxicity
- Determine what percentage of patients are sarcopenic and establish if low muscle mass is a key predictor of chemotherapy toxicity and efficacy

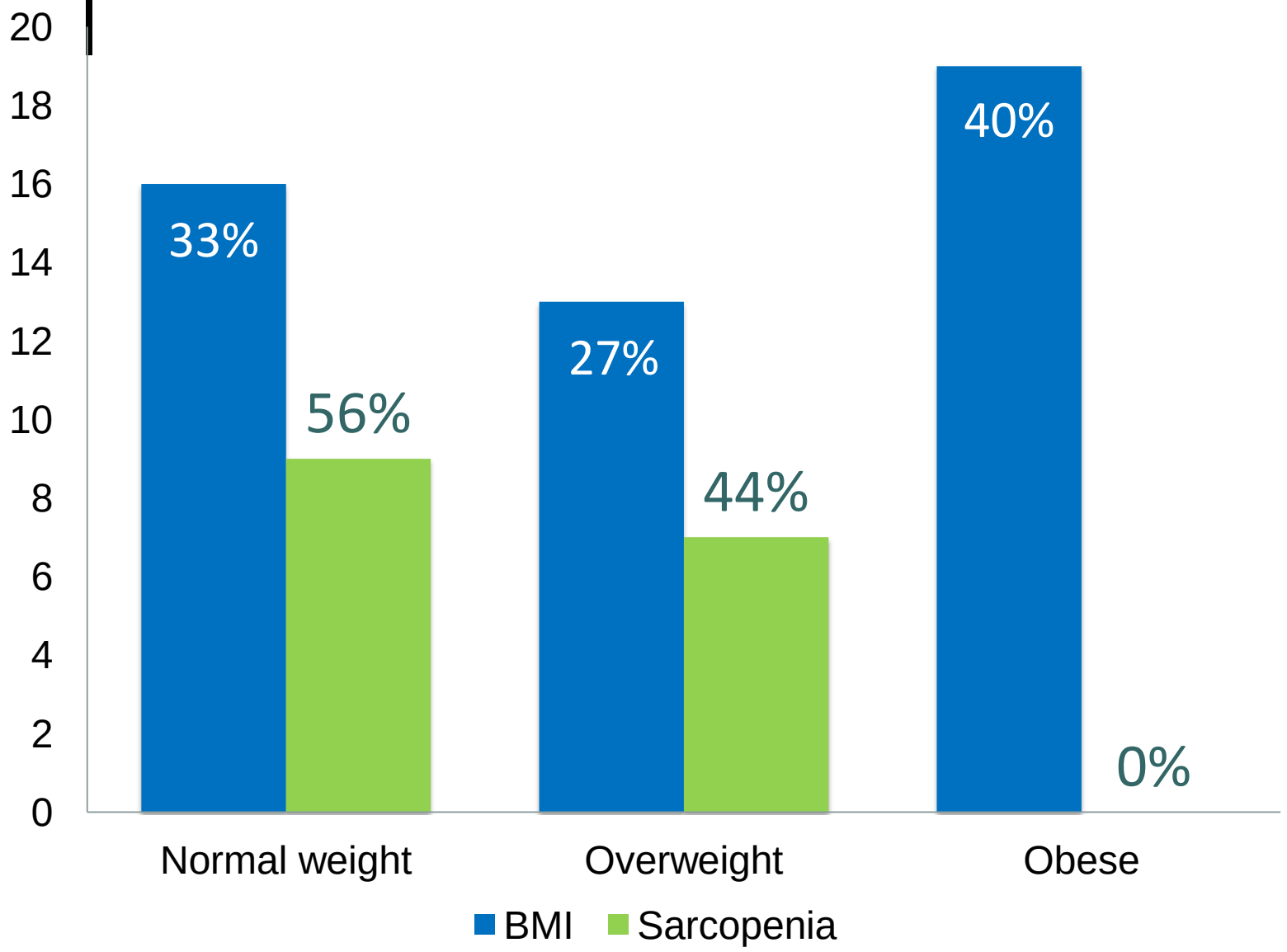
Methods

- Retrospective analysis of prospectively collected data
- **Inclusion criteria**: Adult (male and female) patients > 18 years with metastatic clear cell renal cell carcinoma between 2007-2012, ECOG 0-1 and treated with Sunitinib (50mg)
- Participating hospitals: Mercy University Hospital, St Vincent's University Hospital Dublin, Cork University Hospital
- Two consecutive CT images- taken within ±30 days before or after the initiation of cycle 1
- Lumbar vertebral landmark(L3) was selected
- Fat free mass was calculated using pre determined regression equations by Mourtzakis et al 2008

Demographics

	Total (n=55)
Males :	43
Females:	12
Mean age (SD)	64 (10.6)
Hospital	
Dublin, *n* (%)	21 (38.1)
Cork, *n* (%)	34 (61.8)
BMI (kg/m^2)	
Average (range)	28.6 (19.9-41.4)
Sarcopenia, *n* (%)	18 (33)
Dose limiting toxicity (DLT), *n* (%)	40 (73)

Sarcopenia and BMI



Results

A

Male

BMI 27

Non sarcopenic (63.5cm²/m²)

DLT > 6 months

B

Male

BMI 27

Sarcopenic (52.7cm²/m²)

DLT < 6 months

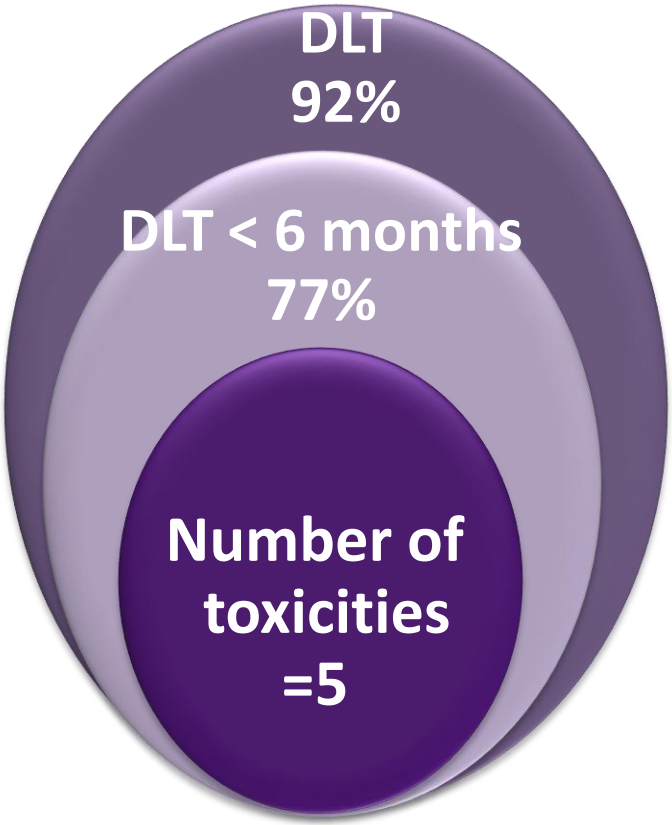
Toxicities
in < 6 months vs. > 6 months

	DLT in < 6months *n*=29	DLT in > 6months *n*=26	P value
Skeletal Muscle L3 area (cm^2)	151.5	173.7	0.019
Skeletal muscle L3 index (cm^2/m^2)	51.8	59.4	0.012
Total Fat Free Mass (FFM) (kg)	51.4	57.7	0.03
Adipose tissue index (cm^2/m^2)	132	127.9	NS
Dose Sunitinib mg/FFM	1.01	0.89	0.02
Number of Toxicities	4.4	2.3	0.002

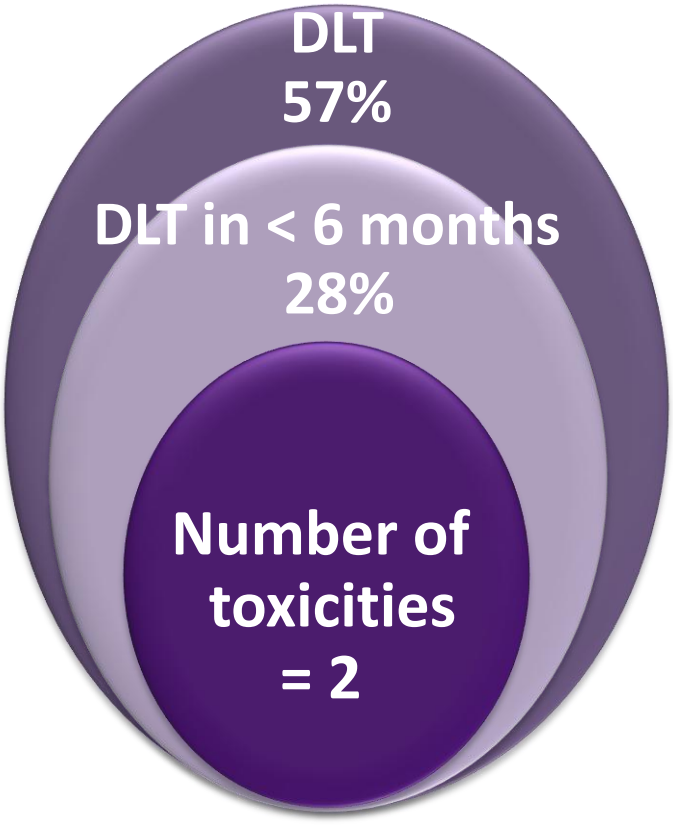
Skeletal Muscle Mass (SMM) and Toxicity

SMM below the 25th centile vs. above the 75th centile

< 25th centile
(<44.8cm²/m²)
***n*= 13**



>75th centile
(>63.2cm²/m²)
***n*= 14**



Conclusion

- Sarcopenia is prevalent in patients with RCC
- Its an occult condition in patients with normal/high BMI
- Importance of muscle mass independent of weight or BMI
- Significant predictor of DLT
- Potential use of baseline body composition to predict toxicity