

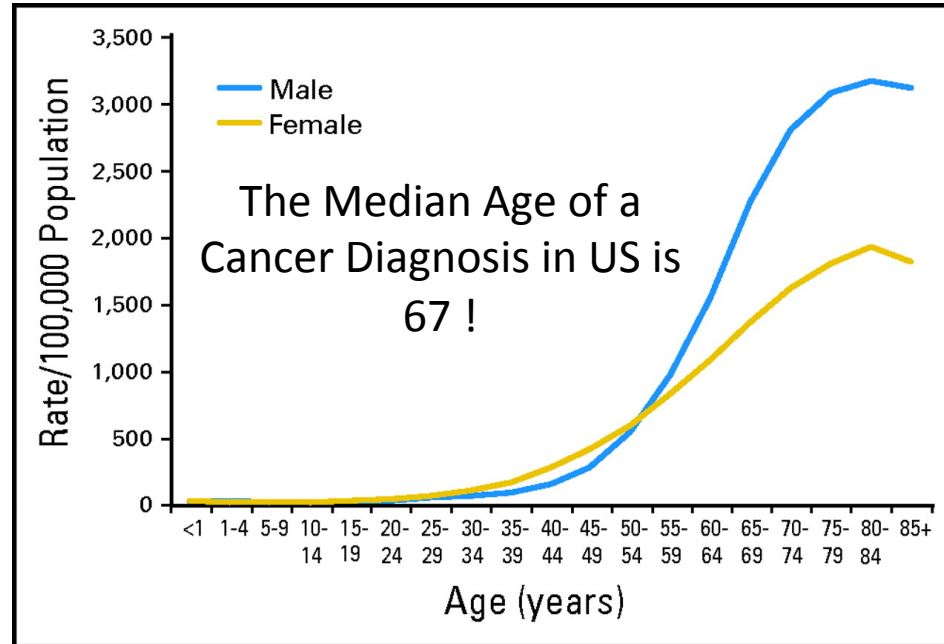
UNC Geriatric Oncology Research Symposium 12/2/2016

Skeletal Muscle and Frailty

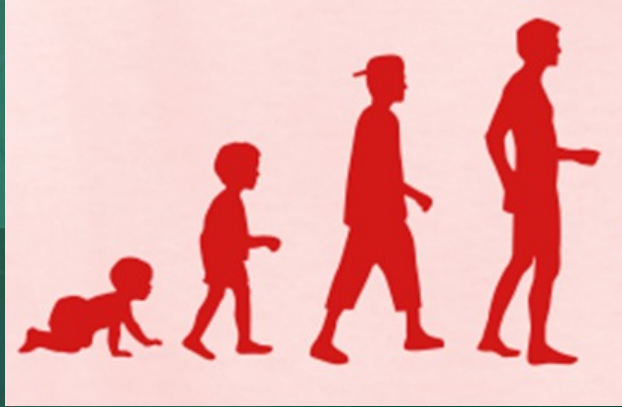
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UAB THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM
Knowledge that will change your world

Background



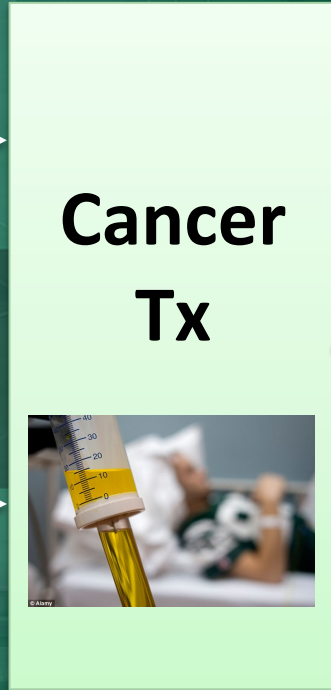
Aging is a heterogeneous process



Chronological age insufficient!

Outcomes in older adults with cancer highly variable

Cancer Diagnosis



Outcomes

Good

Intermediate

Poor

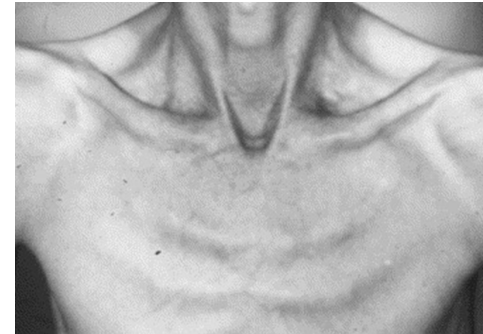
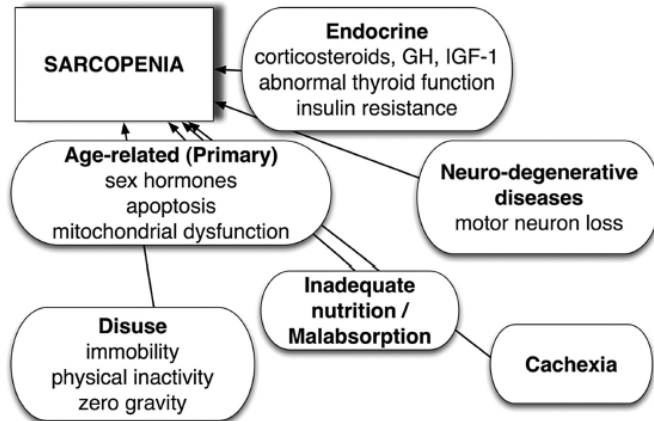
Assessing Older Adults with Cancer

- Remains a clinical challenge
- Chronological age and performance status alone insufficient
- Better ways to assess older adults are needed



Sarcopenia

- Age-related loss of skeletal muscle mass and strength
 - Greek 'sarx' or flesh + 'penia' or loss
- Highly prevalent in older adults and is a hallmark of disability
- Associated with adverse outcomes in oncology



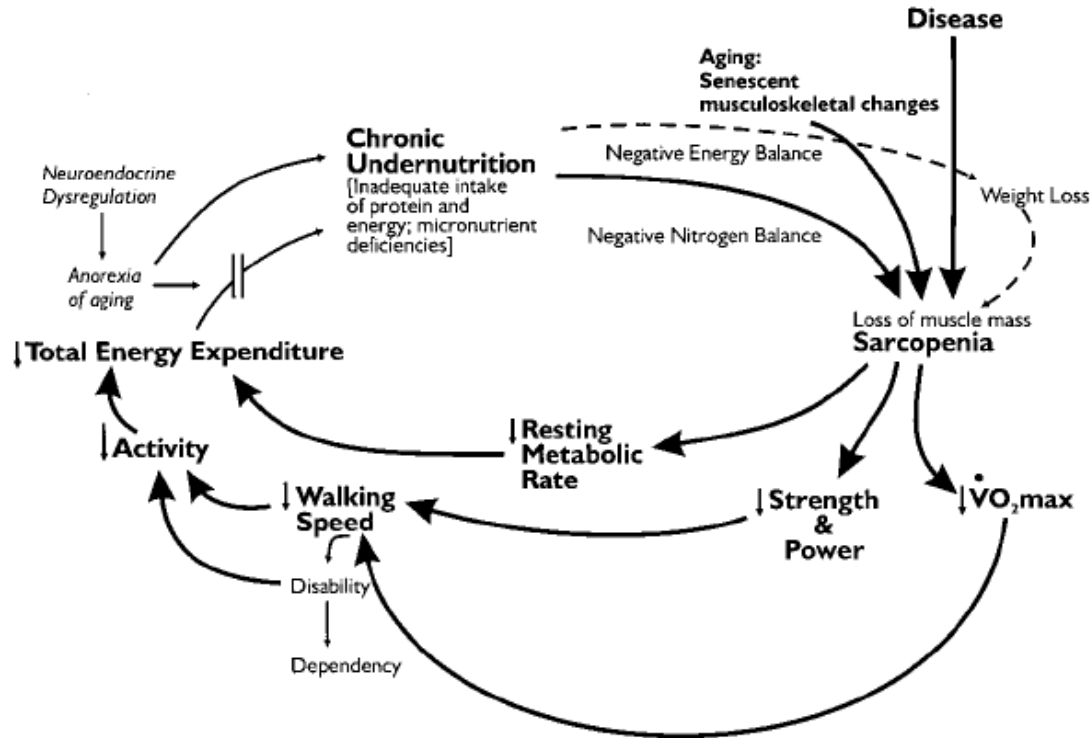
- Baumgartner *et al.* *Obes Res*, 2004.
- Cruz-Jentoft *et al.* *Age and Aging*, 2010.

Frailty

- Frailty is a geriatric syndrome that describes vulnerable older adults
- Frail adults with cancer have minimal homeostatic reserve capacity to recover from stressful events such as chemotherapy, radiation, or surgery and are at high risk for adverse health outcomes



Hypothesized core clinical presentations of frailty



Fried Phenotype

- Weight loss
- Weakness (grip strength)
- Exhaustion
- Slowness (gait speed)
- Low physical activity level

Fried et al. *J of Gerontology*. 2001

Frailty & Sarcopenia

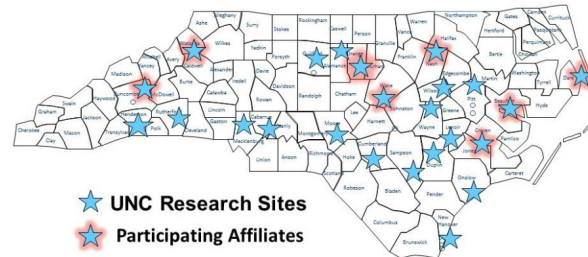
- Both are recognized geriatric syndromes that are prevalent in older adults and associated with adverse outcomes

Goal of our study

- To better understand their interrelationship in older adults with cancer

Methods

- **Participants:** Sample derived from the Carolina Senior Registry (CSR).
 - a registry of older adults with cancer started in 2009 with over 1000 patients from across NC that have completed geriatric assessment (GA)
- **Eligibility:** Any patients from UNC with CT imaging within 60 days +/- from baseline GA



Geriatric Assessment

- The CSR utilizes a well-validated GA tool designed specifically for use in older adults with cancer
- Developed by Hurria and colleagues, the GA contains reliable measures of geriatric domains
 - including instrumental activities of daily living (IADL), physical function, medications, comorbidities, nutritional status, mental health, social activity and support, and cognitive function

Hurria *et al*, Cancer 2005

Hurria *et al*, JCO 2011

Williams *et al*, JGO 2014

Carolina Frailty Index

- Developed based on the principles of deficit accumulation originally described by Rockwood and colleagues
- 36 variables from the GA met criteria as health deficits (each scored 0 to 1) and were included in the frailty index

Scoring. Each item is scored from 0-1

- Presence of deficit = 1.
- Absence of deficit = 0
- Individual scores are then added and divided by the total number of variables.

Categorization.

- Robust = 0-0.2, Pre-frail = 0.2-0.35, Frail = > 0.35

Frailty Index Variables Selected from the Geriatric Assessment

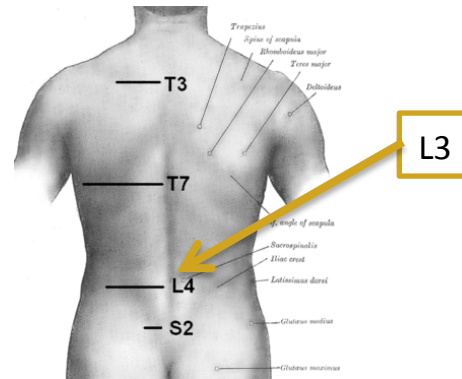
GA Domain	Variables
Independent Activities of Daily Living (IADLs)	Use of telephone, Avail transportation, Go shopping, Prepare meals, Do housework, Manage medications, Manage personal finances
Physical Function	Lifting groceries, Bending/Kneeling/Stooping, Bathing or Dressing, Ability to climb 1 flight of stairs, Ability to walk one block, Timed Up and Go
Medical Co-Morbidity	Hypertension, Heart Disease, Diabetes, Stomach or Intestinal disorders, Osteoporosis, Chronic Liver or Kidney disease, Stroke, Emphysema/Chronic Bronchitis, Glaucoma, Arthritis/Rheumatism, Other Cancers or Leukemia
Nutritional Status	Unintentional weight loss (>5% in past 6 months)
Sensory Function	Hearing, Vision
Mental Health	Felt calm or peaceful, Felt downhearted or blue, Physical or emotional health interfering with social activities
Cognition	Blessed Orientation-Memory-Concentration

Guerard *et al*, JCO 33, 2015 (abstr 9535)

Searle *et al*, BMC Geriatrics, 2008

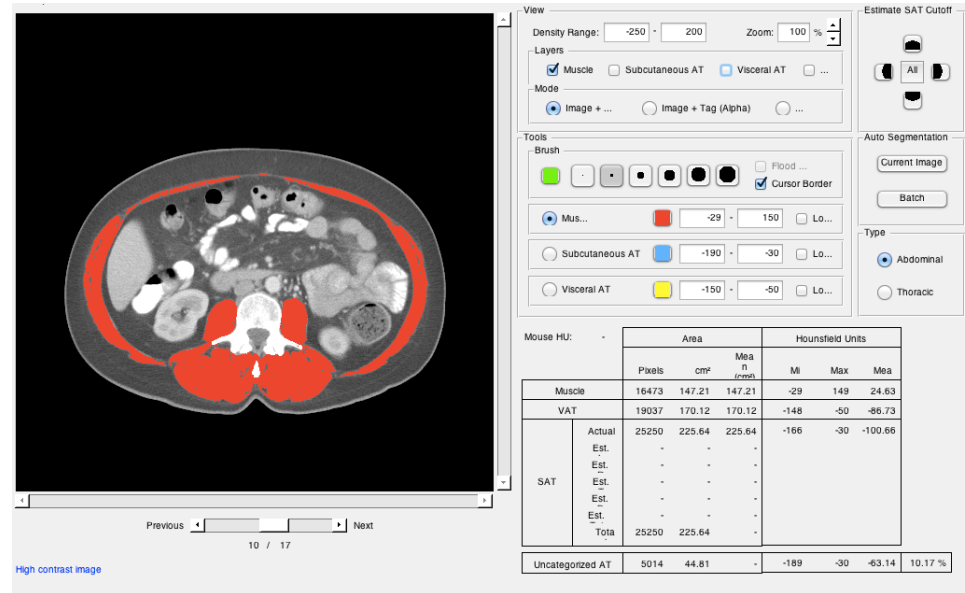
Body Composition Analysis

- Abdominal CT images were acquired from the UNC Picture Archiving and Communication office
- Using Impac radiological software (Mountain View, CA), transverse sections at the L3 vertebral level were identified and extracted for external analysis

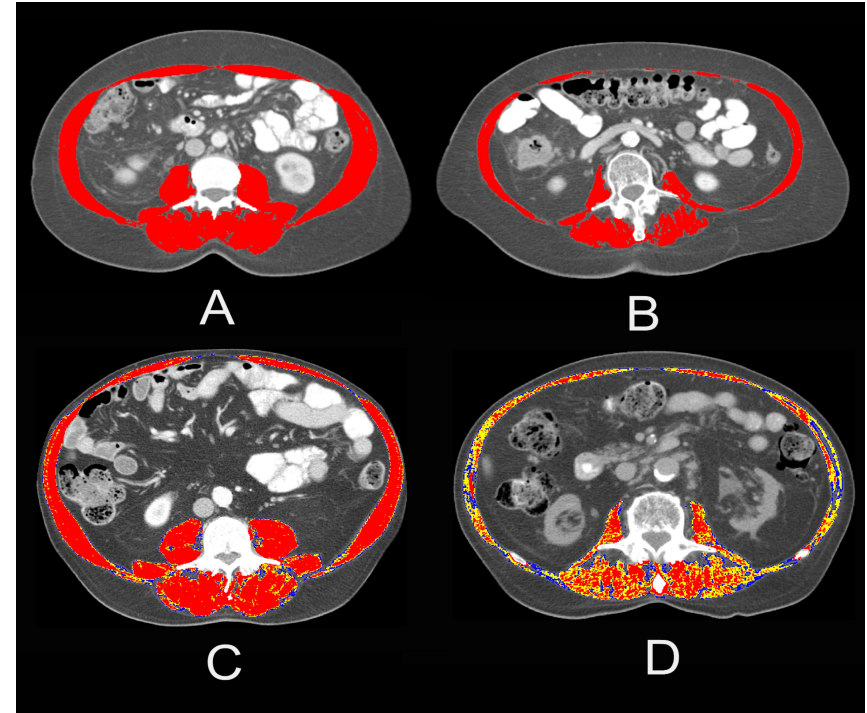


Automated image segmentation software was then used to analyze the L3 lumbar segments

- recognizes muscle tissue based on density thresholds between -29 and +150 Hounsfield Units (HU) of the cross-sectional skeletal muscle area



- Skeletal muscle area is then normalized for height (in meters) to calculate a **skeletal muscle index (SMI)** (cm^2/m^2)
- **Skeletal muscle density (SMD)** derived by averaging the HU of skeletal muscle of the cross-sectional image (indirect assessment of muscle fat content)



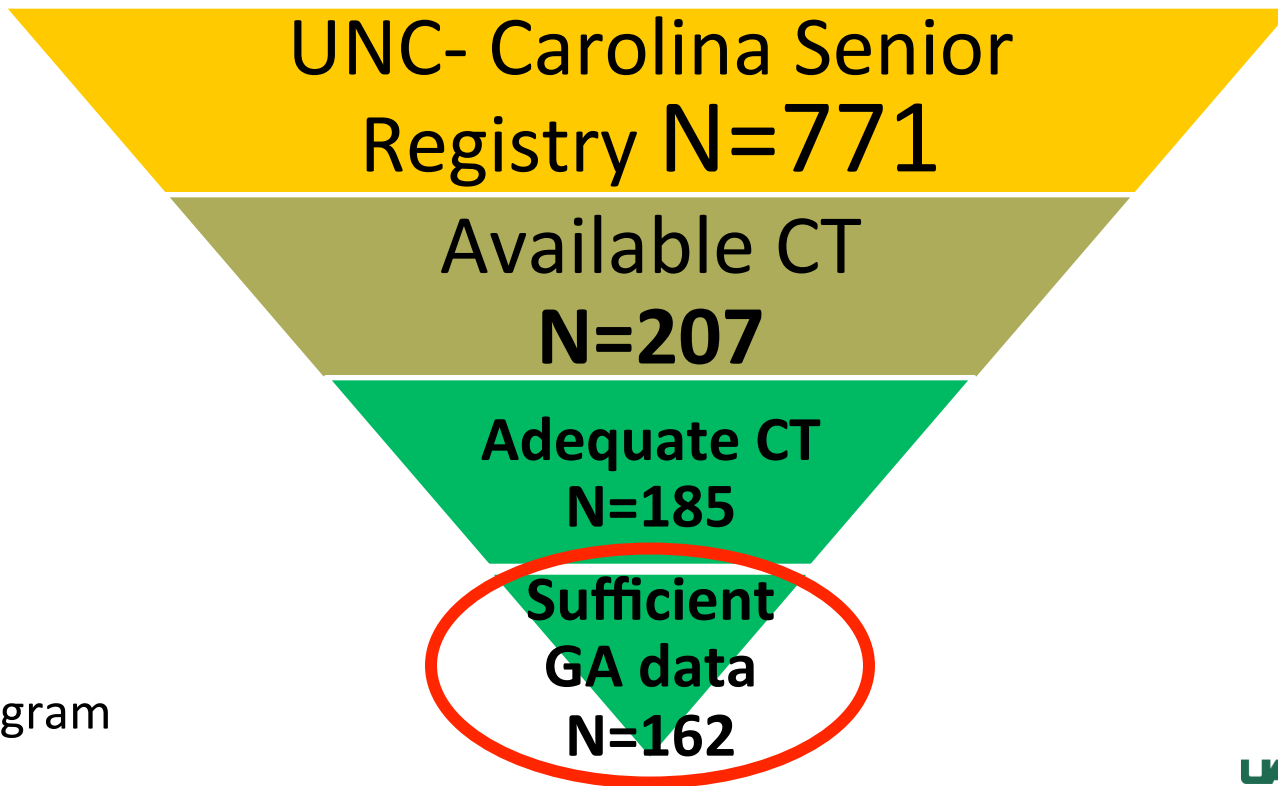
SMI and SMD integration

- **Skeletal Muscle Gauge (SMG)** is an integrated value of both SMI and SMD

$$\text{SMG} = \text{SMI} \times \text{SMD}$$

- First introduced by Weinberg *et al* and has shown better correlation with aging than either SMD or SMI alone
- The actual units for SMG are (cm² tissue area x average HU)/ (m² height) and for simplicity we chose to represent as arbitrary units (AU)

Results

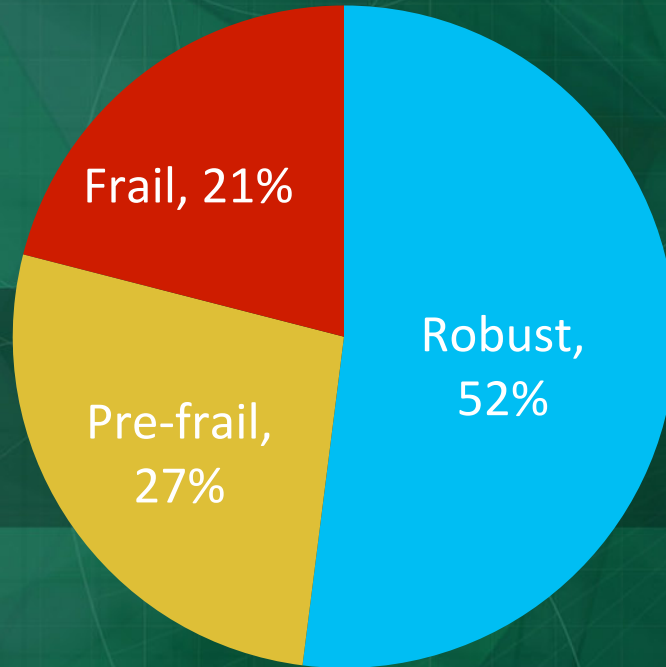


Consort Diagram

Age, mean (range)	73 (65-93)
Sex, n(%)	
Male	69 (43)
Females	93 (57)
Race, n(%)	
White	134 (83)
Black	26 (16)
Other	2 (1)
Cancer type, n(%)	
Breast cancer	46 (29)
Lung cancer	29 (18)
GI Malignancy	22 (14)
GU Malignancy	17 (11)
Heme Malignancy	16 (10)
Other	28 (18)

Treatment Phase, n(%)	
Before Treatment	49 (31)
During Treatment	78 (50)
After Treatment	30 (19)
Education, n(%)	
Some high school	24 (14)
High school degree	75 (47)
Associates/Bachelor's degree	35 (22)
Advanced degree	29 (18)

Carolina Frailty Index



Skeletal Muscle Measures

- SMI 41.8 cm²/m² (range 23-67)
- SMD 26.2 HU (range 3.9-47)
- SMG 1103 AU (range 90-2760)

Mean skeletal muscle measures for the various frailty categories

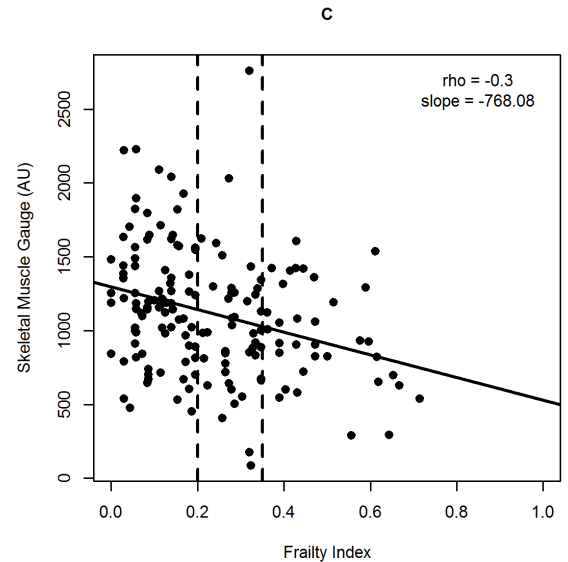
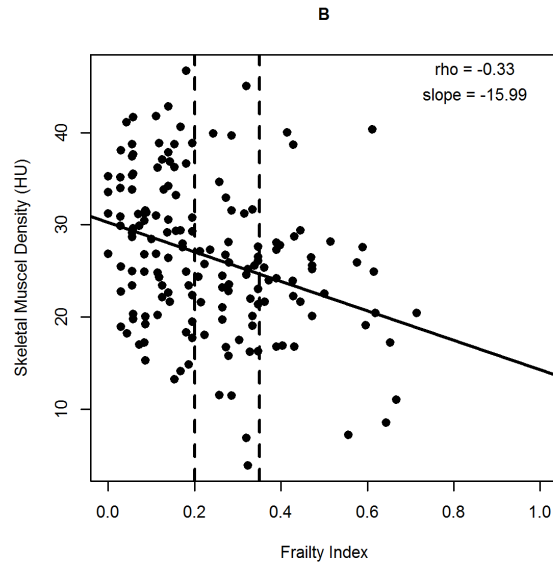
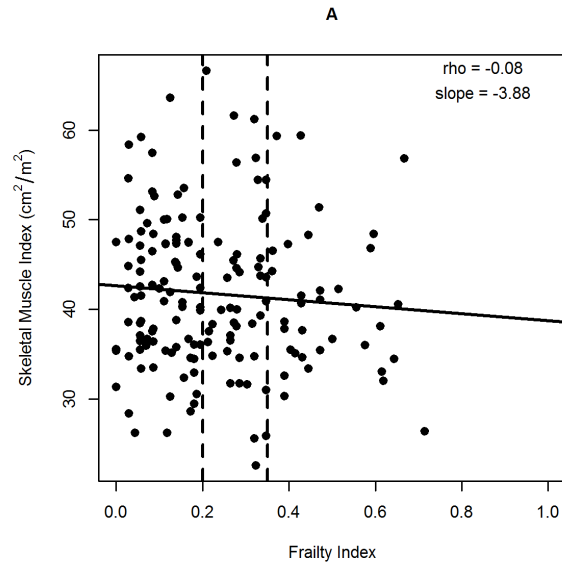
	Mean			Relative Risk [†] (CI) Frail vs Not Frail
	Robust	Pre-frail	Frail	
Skeletal Muscle Index (cm²/m²)	42.0	42.0	40.8	1.06 (0.94, 1.19)
Skeletal Muscle Density (HU)	29.1	23.8**	23.7**	0.83 (0.76, 0.91)
Skeletal Muscle Gauge (AU)	1224	1024*	965**	0.95 (0.90, 0.99)

* $p < 0.05$ ** $p < 0.01$ as compared to Robust

[†]Relative Risks for pre-frail and frail vs. robust are for 5 cm²/m² increase in skeletal muscle index, 5 HU increase in skeletal muscle density, and 100 AU increase in skeletal muscle gauge. Relative risks are adjusted for age and gender.

Abbreviations: HU, Hounsfield Units; AU, Arbitrary Units; CI, Confidence Intervals.

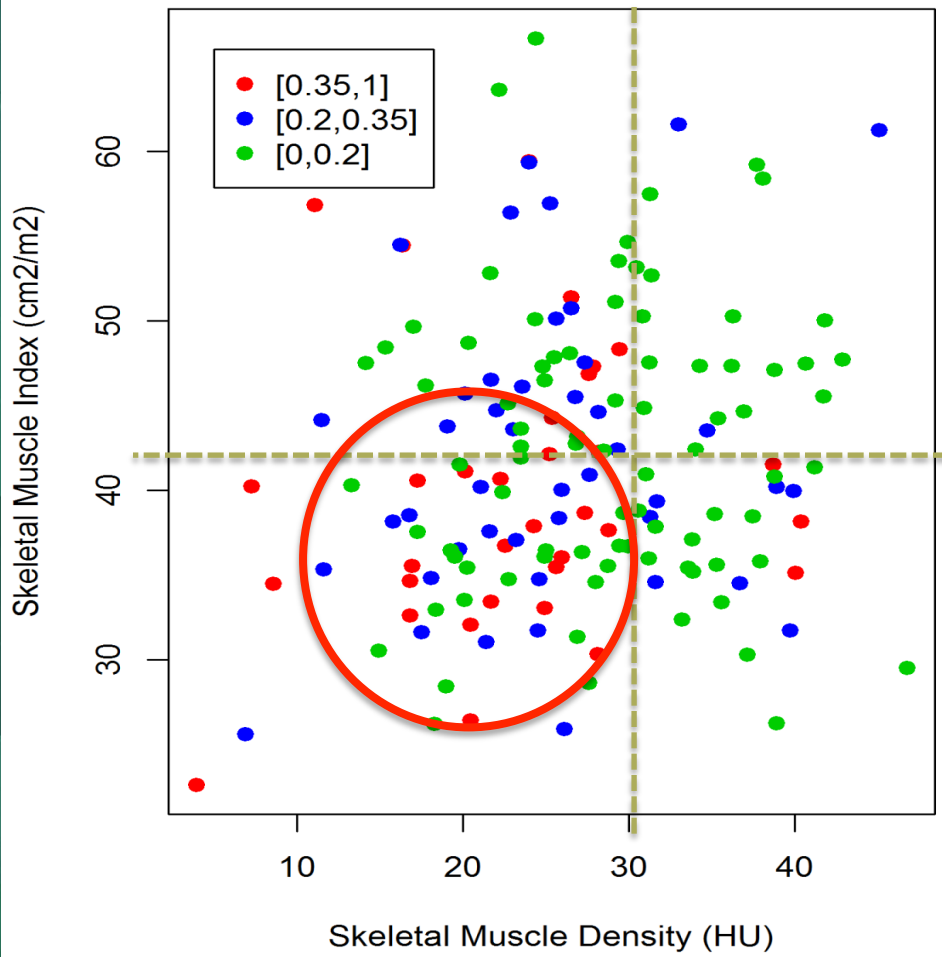
Frailty and Skeletal Muscle Measures



SMI

SMD

SMG





"You're fifty-seven years old. I'd like to get that down a bit."

Conclusions

- **Skeletal muscle index** as assessed from routine CT imaging was not associated with a GA-based frailty index
- **Skeletal muscle density**, which reflects muscle lipid content, was associated with frailty and may be helpful in identifying frail, at-risk older adults with cancer

- **Skeletal muscle gauge**, an integrated measurement of both muscle quality and quantity, may be a valuable tool that combines these two important measurements that warrants further evaluation

Other Studies

- Preliminary results from the ONCOSARCO project in Spain

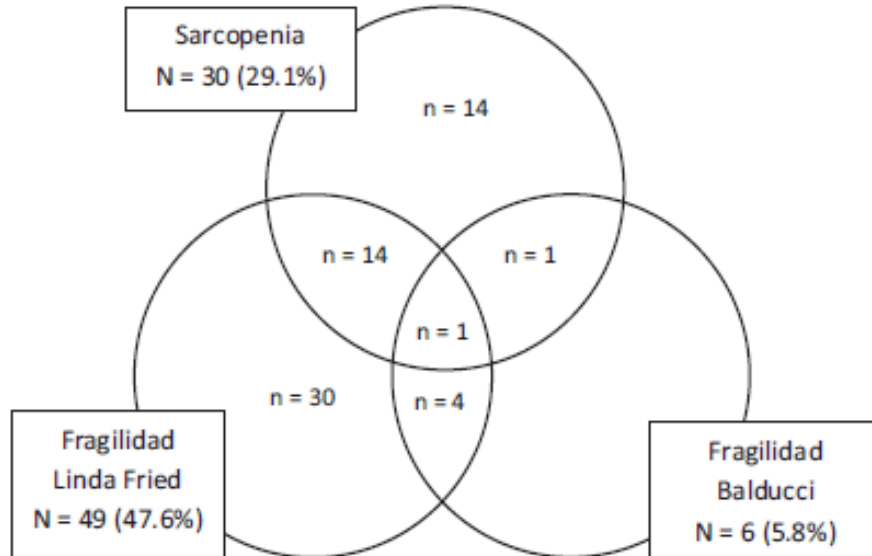


Fig. 1. Relationship between sarcopenia and frailty.

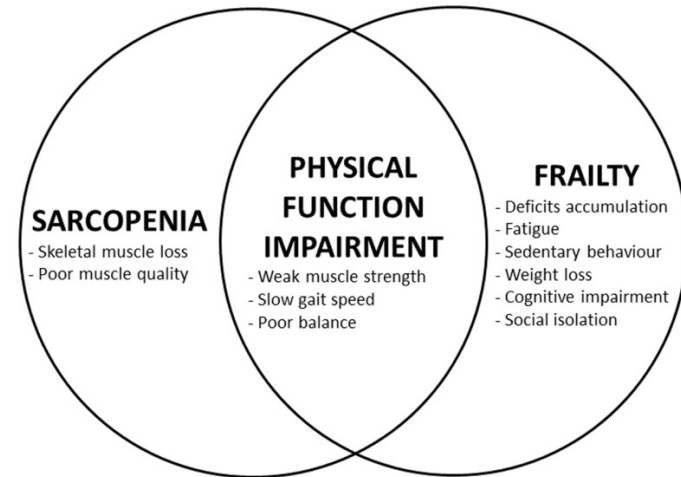
Conclusion

- There is no good interrelationship between sarcopenia and frailty

Molina-Garrido *et al.* JAMDA. 2016

Frailty & Sarcopenia: two sides of the same coin?

- Although sarcopenia may be a component of frailty, frailty is more multifaceted than sarcopenia alone
- Concept of frailty goes beyond physical factors and encompasses social and psychological dimensions as well
- Different therapeutic approaches
- While there is some overlap between sarcopenia and frailty, they are distinct syndromes



Cesari et al, Front Aging Neurosci. 2014.

Limitations

- Neither Frailty nor Sarcopenia have accepted consensus definitions
 - Regardless of definitions used, similar findings as our own have been found in other studies
- Single center, retrospective cross-sectional review
 - No causal relationship between frailty and skeletal muscle measures can be inferred

Acknowledgments



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Thank You!