Analysis of CT imaging-derived phenotypes to determine risk factors associated with sarcopenia

Richard Zhuang[1], Walter Witschey[2], Hersh Sagreiya[2]

College of Arts & Sciences, University of Pennsylvania[1] Department of Radiology, Perelman School of Medicine[2]

Introduction

- Sarcopenia is characterized by progressive loss of muscle mass and function due to age [1].
- Estimated 10% prevalence rate in people over 60 years old [2].
- Associated with impaired movement, decreased quality of life, and increased morbidity and mortality [1, 2].
- Sarcopenia is not well-recognized in clinical practice and difficult to diagnose [3].
  - Dual-energy x-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) have been used to estimate muscle mass, but these methods are not always accurate or consistent.
- Vu et al. (2024) developed a deep learning 3D segmentation algorithm to accurately determine muscle mass of 6 abdominal muscle groups [4].
  - However, the algorithm was only applied to 295 patients.
- Goal: apply the algorithm to a larger dataset and identify trends and risk factors associated with muscle mass loss.

Materials and Methods

- A convolutional neural network was applied to abdominal CT scans in the Penn Medicine BioBank (Figure 1) to segment abdominal organ volume.

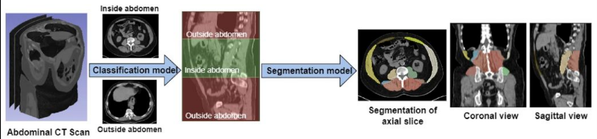


Figure 1: Overview of deep learning pathway for 3D segmentation. Adapted from [4].

- Cohort: 6,747 patients in the PMBB
- Data analysis
  - Abdominal muscle volume: left and right psoas, quadratus lumborum, erector spinae, gluteus medius, rectus abdominis, and lateral abdominals
  - Visceral and subcutaneous fat volume
  - Analyze relationships with age and sex
- Phenome-Wide Association Study (PheWAS)
  - Determine phenotypes that are statistically associated with muscle volume using Phecodes.

Results

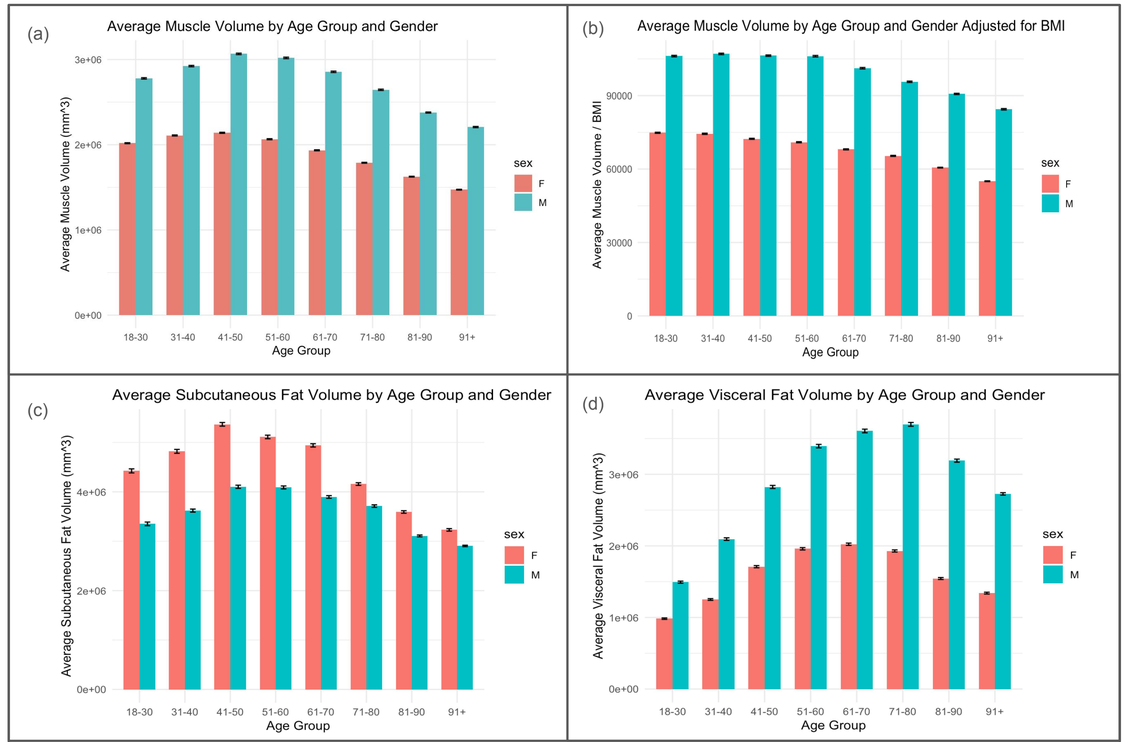
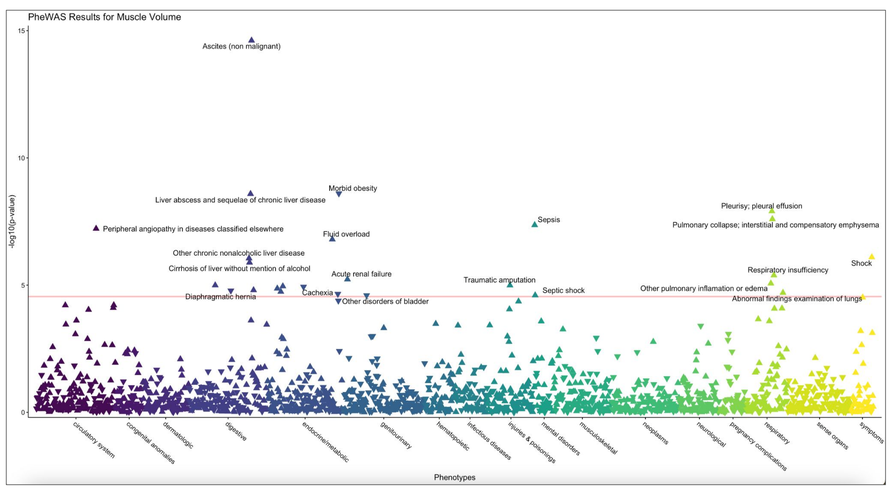


Figure 2: Summary of total muscle and fat volume in relation to age and gender (N=6747). (a) Total volume of 6 abdominal muscle groups, (b) total volume divided by BMI, (c) subcutaneous fat volume, (d) visceral fat volume. Error bars show +/- 1 SEM.



Phenotype	P-Value	Coefficient
Ascites (non malignant)	2.4e-15	7.43e-07
Morbid obesity	2.5e-09	-1.09e-06
Liver abscess and sequelae of chronic liver disease	2.6e-09	4.38e-07
Pleurisy; pleural effusion	1.2e-08	1.36e-06
Pulmonary collapse; interstitial and compensatory emphysema	2.5e-08	1.11e-06
Sepsis	4.4e-08	2.42e-07
Peripheral angiopathy in diseases classified elsewhere	6.1e-08	1.86e-08
Fluid overload	1.6e-07	2.53e-07
Shock	8.0e-07	1.07e-07
Other chronic nonalcoholic liver disease	8.8e-07	1.33e-06
Cirrhosis of liver without mention of alcohol	1.3e-06	1.14e-06
Respiratory insufficiency	4.1e-06	7.96e-08
Acute renal failure	5.9e-06	4.63e-07
Other pulmonary inflamation or edema	8.6e-06	2.38e-07
Esophageal bleeding (varices/hemorrhage)	1.0e-05	2.71e-07
Traumatic amputation	1.0e-05	1.02e-07
Type 2 diabetes with neurological manifestations	1.1e-05	5.97e-07
Cachexia	1.2e-05	-6.70e-08
Diabetes mellitus	1.4e-05	4.11e-06
Hepatomegaly	1.6e-05	1.20e-07
Diaphragmatic hernia	1.6e-05	-2.59e-07
Type 2 diabetes	1.8e-05	3.64e-06
Abnormal findings examination of lungs	2.0e-05	7.79e-07
Overweight, obesity and other hyperalimentation	2.2e-05	-1.12e-06
Septic shock	2.5e-05	5.43e-08
Other disorders of bladder	2.5e-05	-2.98e-07

Figure 3: Phenome-Wide Association Study (PheWAS) to analyze relationships between phenotypes and muscle volume. Statistical significance threshold was $p < 2.82E\text{-}05$ as determined by Bonferroni correction.

Discussion

- The deep learning algorithm provided a quantitative understanding of body composition and how it changes with age and gender.
- According to Fig. 2(a), muscle volume seems to increase until ages 41-50 before declining.
  - However, after adjusting for BMI, muscle volume remains stable and begins to consistently decrease starting at ages 51-60.
- Subcutaneous fat volume increases until 41-50 before declining with age, while visceral fat increases much more dramatically until ages 61-70 for females and 71-80 for males.
- In the PheWAS, several phenotypes are statistically associated with muscle volume. Cachexia (wasting syndrome) and obesity are negatively associated.
  - However, many phenotypes are positively associated—a finding that warrants further investigation, such as analyzing other factors related to body composition.
- Future research could involve running a Genome-Wide Association Study (GWAS) to study genetic variants associated with sarcopenia.

References

[1] Sayer, A. A., & Cruz-Jentoft, A. (2022). Sarcopenia definition, diagnosis and treatment: consensus is growing. Age and ageing, 51(10), afac220. https://doi.org/10.1093/ageing/afac220

[2] Pham, LA.T., Nguyen, B.T., Huynh, D.T. et al. Community-based prevalence and associated factors of sarcopenia in the Vietnamese elderly. Sci Rep 14, 17 (2024). https://doi.org/10.1038/s41598-023-50979-4

[3] Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A. A., Schneider, S. M., Sieber, C. C., Topinkova, E., Vandewoude, M., Visser, M., Zamboni, M., & Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2 (2019). Sarcopenia: revised European consensus on definition and diagnosis. Age and ageing, 48(1), 16–31. https://doi.org/10.1093/ageing/afy169

[4] Vu, P.T., Chahine, C., Chatterjee, N. et al. CT imaging-derived phenotypes for abdominal muscle and their association with age and sex in a medical biobank. Sci Rep 14, 14807 (2024). https://doi.org/10.1038/s41598-024-64603-6

Acknowledgements

Special thanks to Dr. Sagreiya and Dr. Witschey for their mentorship throughout the project. We also acknowledge the Penn Medicine BioBank (PMBB) for providing data. This work was funded by the Penn Undergraduate Research Mentoring Program.