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

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Introduction

- Sarcopenia - progressive loss of muscle mass and function due to age; estimated 10% prevalence in people over 60.[1,2]
- Associated with impaired movement, decreased quality of life, and increased mortality.[1,2]
- Not clinically well-recognized - muscle estimation methods like dual-energy x-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) lack accuracy and consistency.[3]
- Deep learning 3D segmentation algorithms have been developed to accurately determine muscle mass from CT images, but applied to small sample size.[4]
- Goal: apply the algorithm to a large, diverse dataset and quantify population trends and identify risk factors associated with sarcopenia.

Materials and Methods

- Convolutional neural network was applied to CT scans in the Penn Medicine BioBank (Figure 1).
- Cohort Analysis: 6,747 patients
  - Abdominal muscles: psoas, quadratus lumborum, erector spinae, gluteus medius, rectus abdominis, and lateral abdominals
  - Visceral and subcutaneous fat volume
- Phenome-Wide Association Studies (PheWAS)
  - Identify phenotypes statistically associated with sarcopenia using Phecodes

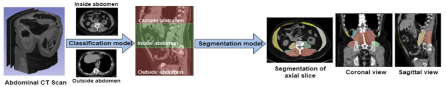


Figure 1: Overview of deep learning pathway for 3D segmentation. Adapted from Vu et al., 2024.

Results

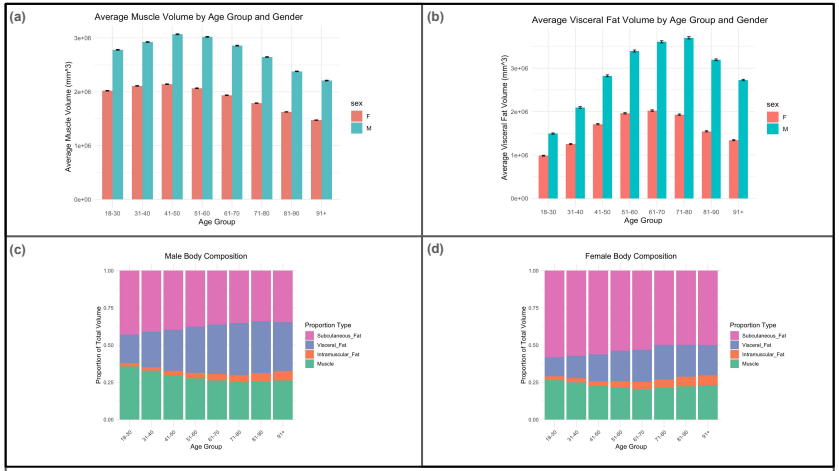
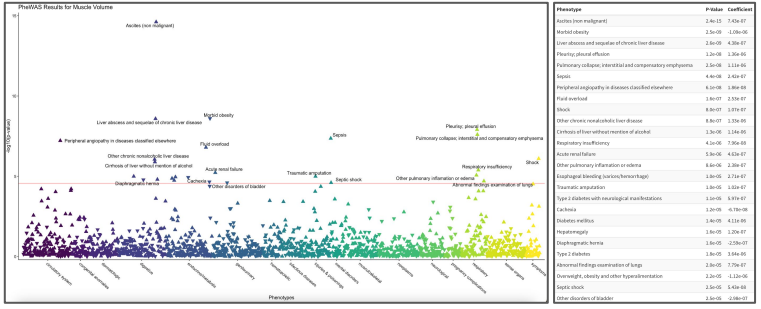


Figure 2: Total muscle and fat volume in relation to age and gender (N=6747). (a) Total muscle volume, (b) visceral fat volume, (c) male body composition, (d) female body composition. Error bars show +/- 1 SEM.



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	4.30e-07
Pleurisy; pleural effusion	1.2e-08	3.36e-06
Pulmonary collapse; interstitial and compensatory emphysema	2.5e-08	1.11e-06
Sepsis	4.4e-08	2.43e-07
Peripheral angiopathy in diseases classified elsewhere	6.1e-08	1.86e-06
Fluid overload	1.6e-07	2.55e-07
Shock	8.8e-07	1.37e-07
Other chronic nonalcoholic liver disease	8.8e-07	1.35e-06
Cirrhosis of liver without mention of alcohol	1.3e-06	1.14e-06
Respiratory insufficiency	4.1e-06	7.90e-08
Acute renal failure	5.9e-06	4.32e-07
Other pulmonary inflammation or edema	8.6e-06	2.30e-07
Esophageal bleeding (varices/hemorrhage)	1.8e-05	2.71e-07
Traumatic amputation	1.8e-05	1.02e-07
Type 2 diabetes with neurological manifestations	1.1e-05	5.97e-07
Cachexia	1.2e-05	-5.78e-08
Diabetes mellitus	1.4e-05	4.11e-06
Hepatomegaly	1.9e-05	1.20e-07
Diaphragmatic hernia	1.8e-05	-2.58e-07
Type 2 diabetes	1.8e-05	3.84e-06
Abnormal findings examination of lungs	2.0e-05	7.75e-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	-2.68e-07

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

Discussion

- The deep learning algorithm provided a quantitative understanding of body composition trends in a large population
- Total muscle volume increases until ages 41-50 before declining by 28% in males and 31.2% in females by age 91+
- Visceral fat doubled in females (age 18-30 to 61-70) and increased 2.5-fold in males (ages 18-30 to 71-80)
- PheWAS identified several phenotypes statistically associated with reduced muscle volume, particularly cachexia (wasting syndrome) and obesity
- Future research could involve running genome-wide association studies (GWAS) to study genetic variants associated with sarcopenia

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