

## **Anatomical and Molecular Insights into Sarcopenia in Liver Cirrhosis: A CT-Based and Biomarker Case-Control Study**

Costel-George Gherghescu<sup>1,2</sup>, Radu Andrei Baz<sup>2,3</sup>, Constantin Dina<sup>3</sup>, Andrei Dumitru<sup>3,4</sup>, Georgeta Camelia Cozaru<sup>5</sup>, Mihaela Manea<sup>5</sup>, Ioana Popescu<sup>3,4</sup>, Ana-Maria Grigorescu<sup>3</sup>, Stere Popescu<sup>3,4</sup>, and Eugen Dumitru<sup>3,5,6,7</sup>

<sup>1</sup>PhD School of Medicine, Ovidius University, Constanta, Romania

<sup>2</sup>Clinical Laboratory of Radiology and Medical Imaging, Sf. Apostol Andrei Emergency County Hospital, Constanta, Romania

<sup>3</sup>Faculty of Medicine, Ovidius University, Constanta, Romania

<sup>4</sup>Department General Surgery, Sf. Apostol Andrei County Emergency Hospital, Constanta, Romania

<sup>5</sup>Department of Gastroenterology, Sf. Apostol Andrei Emergency County Hospital, Constanta, Romania

<sup>6</sup>Research Center for the Morphological and Genetic Study in Malignant Pathology, Ovidius University, Constanta, Romania

<sup>7</sup>Academy of Romanian Scientist, Bucharest, Romania

### **Abstract**

**Background:** Sarcopenia is a common complication and an important negative prognostic factor in patients with liver cirrhosis, being associated with reduced muscle mass and function, as well as increased mortality. Although computed tomography (CT) is considered the gold standard for assessing muscle mass, there is growing interest in identifying serum biomarkers that may facilitate the early diagnosis and monitoring of disease progression. The aim of this study was to evaluate the diagnostic value of osteonectin, the C-terminal agrin fragment (CAF), the N-terminal propeptide of type III procollagen (P3NP), and myostatin in patients with liver cirrhosis and sarcopenia, in correlation with CT-derived imaging parameters.

**Materials and Methods:** A prospective observational case–control study was conducted, including 60 participants: 30 patients with liver cirrhosis (with or without hepatocellular carcinoma) and sarcopenia, and 30 healthy control subjects. Sarcopenia was diagnosed according to the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) criteria, using the skeletal muscle index (SMI) and psoas muscle index (PMI) measured by computed tomography. Serum concentrations of osteonectin, CAF, P3NP, and myostatin were determined using enzyme-linked immunosorbent assay (ELISA). Statistical analyses included parametric and non-parametric tests, as well as Pearson correlation analysis.

**Results:** Patients with liver cirrhosis and sarcopenia exhibited significantly higher serum levels of osteonectin, CAF, P3NP, and myostatin compared with healthy controls ( $p < 0.001$  for all comparisons). The skeletal muscle index was significantly lower in cirrhotic patients, confirming the presence of muscle wasting. Correlation analysis demonstrated positive associations between osteonectin and CAF ( $r = 0.441$ ,  $p < 0.001$ ), osteonectin and P3NP ( $r = 0.313$ ,  $p = 0.016$ ), osteonectin and myostatin ( $r = 0.444$ ,  $p < 0.001$ ), as well as a strong correlation between CAF and myostatin ( $r = 0.882$ ,  $p < 0.001$ ). No significant associations were observed between biomarker levels and viral etiology or Child–Pugh class.

**Conclusions:** Simultaneous assessment of osteonectin, CAF, P3NP, and myostatin, combined with computed tomography-based imaging evaluation, may improve the diagnosis of sarcopenia associated with liver cirrhosis and facilitate the early identification of patients at increased risk of muscle deterioration. Larger multicenter prospective studies are warranted to validate the clinical utility of these biomarkers in routine medical practice.

**Key words:** sarcopenia, liver cirrhosis, biomarkers, osteonectin, myostatin, C-terminal agrin fragment, P3NP, muscle wasting, fibrosis, computed tomography