Preliminary Comparisons between Cachexia in Patients with Esophageal and Pancreatic Cancers

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Introduction

- Cancer cachexia is a wasting syndrome characterized by weight loss, asthenia, and anemia. Cachexia a devasting condition affecting several cancers.
- Pancreatic ductal adenocarcinoma (PDAC) is among the deadliest of all common malignancies and the most studied.
- Weight loss is, however, a common symptom in several other gastrointestinal cancers, most notably esophagogastric adenocarcinoma (EGA).
- Systemic wasting is seen in 80% of patients with advanced disease.
- We hypothesize that anthropometric changes associated with cancer cachexia in PDAC and EGA are comparable, despite the diverse pathophysiology of both tumors.

Methods

- Clinical data was abstracted from the medical record in accordance with IRB protocols.
- Surrogate, blood-based markers of cachexia were compared, together with anthropometric measurements from routine computed tomography (CT) scans.
- All patients underwent surgery for potentially curative biopsy proven EGA or PDAC.
- Skeletal muscle index (SMI) was obtained at the L3, T4, T10-vertebra and thigh level using sliceOmatic™.
- Bone density is approximated by radiation attenuation of non-cortical bone in the lumbar vertebrae, known as lumbar vertebral radiodensity (LVR, Hounsfield Units).
- Levels of hemoglobin, albumin, and platelet count was also obtained between the patients with EGA and PDAC.

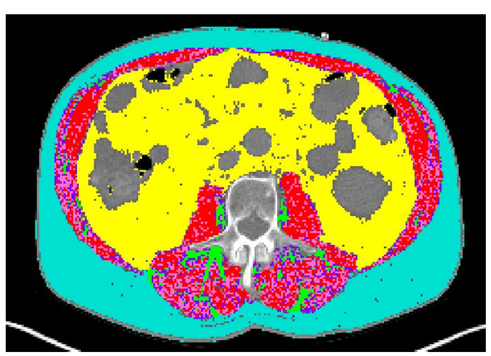


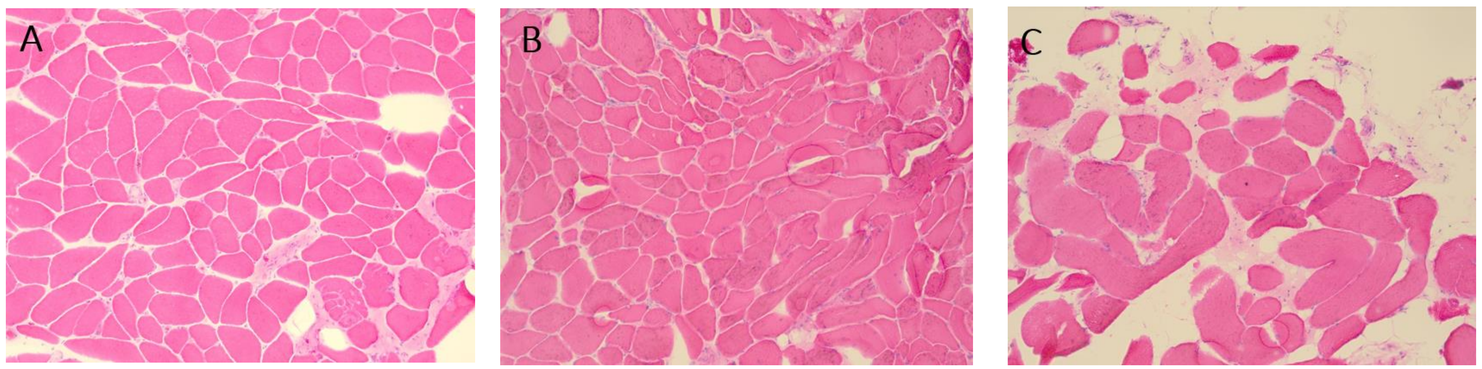
Figure 1 (left):
CT scan of a patient at the L3 level using sliceOmatic™ to obtain the skeletal muscle index for analysis. Mean radiation attenuation (MRA) and inter/intra-muscular adipose deposition may be determined following tissue segmentation.

Results

Table 1: Common Cachexia Measures in EGA and PDAC

	EGA	PDAC	p-value
L3 SMI (cm^2/m^2)	41.4	43.9	0.4
L3 MRA (HU)	32.5	32.2	0.9
LVR (HU)	115	142	0.02
Hemoglobin (g/dL)	12.3	12.5	0.3
Albumin (g/dL)	3.84	3.87	0.8
Platelet Count (x10^9/L)	273	260	0.5

Figure 2 (below):
Patient's hematoxylin-and-eosin-stained (H&E) cross-sectioned muscle fibers of rectus abdominis, diaphragm, and intercostal muscle, respectively. **(A) (B) (C)** No overt inflammatory pathology, characterized by prominent inflammatory cells surrounding non-necrotic muscle fibers, was revealed by the muscle fiber, **(A)**, as seen in PDAC patients. There is evidence of muscle fiber degeneration and regeneration, supported by occasional centralized nuclei scattered in between muscle fibers, present in **(B) & (C).**



- Both patient groups commonly demonstrated signs of cachexia, including body weight loss exceeding 5%, low SMI and low MRA.
- SMI was comparable between EGA (41.4 cm2/m2) and PDAC (43.9 cm2/m2, p = 0.4).
- MRA was similarly comparable: (32.5 HU v. 32.2 HU, p = 0.9).
- Curiously, we identified that patients with EGA have lower bone mineral density (115 HU) compared to those with PDAC (142, p = 0.0233)
- The representative muscle specimens came from a 64-year-old male that lost more than 20% of his body weight in the six months preceding diagnosis. This was reversed over the course neoadjuvant therapy and when a feeding jejunostomy tube was placed.

Conclusion

- EGA and PDAC are unique cancers that both cause severe wasting disorders.
- While non-invasive imaging techniques suggest equal degrees of muscle atrophy, it cannot be assumed that both tumors function in similar ways at the mechanistic level.
- A variety of factors may contribute to weight loss and muscle atrophy in EGA and PDAC.
- EGA is unique in that most patients present with obstruction and dysphagia.
- Supplementary enteral nutrition, such as feeding tubes, may mitigate cachexia and reverse weight loss before surgery.
- For these and the inherent differences in tumor biology, EGA cachexia deserves further attention clinically and in preclinical models.