Emerging Biomarkers of Cancer Cachexia and their Relationship to Sarcopenia

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Introduction and Aim

- Cancer cachexia can cause more than 20% of deaths in cancer with skeletal muscle loss, defined by **sarcopenia**, independently predicting mortality.
- The **ideal biomarker** for cachexia assessment, prognosis and blockade remains to be identified.
- **Emerging biomarkers** require baseline research of their relationships to cachexia and sarcopenia.
- The aim of the study was: i) to **establish differences** in biomarkers of cachexia and sarcopenia between patients with cancer cachexia and healthy matched controls, ii) to explore the **relationships and correlations** of these markers to sarcopenia.

Methods

- Prospective case-control study: including 40 patients with advanced cancer, mixed diagnoses and 40 gender, age-matched controls.
- Sarcopenia assessed using: skeletal muscle index (SMI) from bioelectrical impedance and handgrip strength (HGS) with hand dynamometry.
- Biomarkers assessed: albumin, haemoglobin (Hb), neutrophils, lymphocytes, platelets, C-reactive protein (CRP), tumor necrosis factor alpha (TNFα), Interleukin-6 (IL-6), Interleukin-8 (IL-8), C-X-C motif chemokine ligand 5 (CXCL5) and citrullinated histone H3 (H3Cit).
- Descriptive statistics & regression analyses for correlations were undertaken.

Long-term aim: to improve knowledge of the relationships between emerging biomarkers of cancer cachexia and sarcopenia so that future treatments may target cachexia and ultimately prognosis.

Results

- Forty three percent of cases were sarcopenic with a significantly lower SMI [6.67kg/m^2 (±1.34) vs. 7.67kg/m^2 (±1.08), p=<0.01] and HGS [24.42 (±9.53) kg versus 29.62 (±8.45) kg] compared to controls **(Figure 1).**

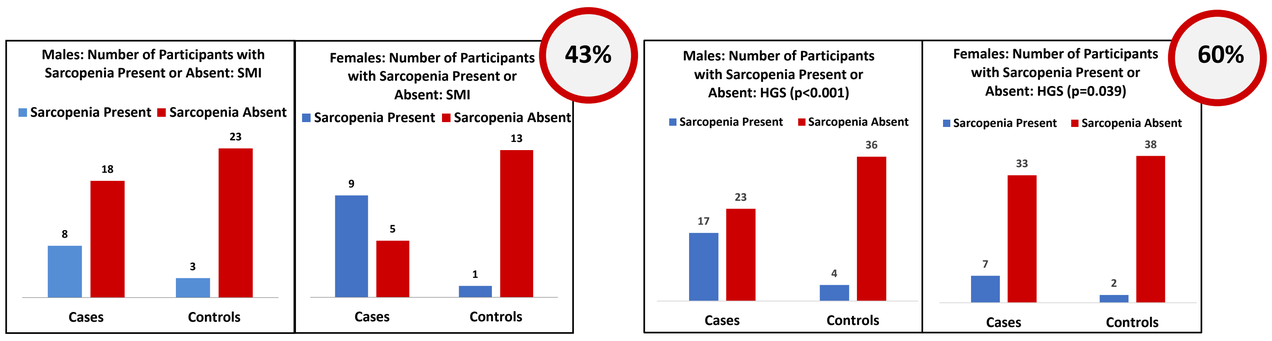

Figure 1: Presence of Sarcopenia According to Skeletal Muscle Index (SMI) and Handgrip Strength (HGS)

- For SMI, biomarkers that showed significance to the presence or absence of sarcopenia were albumin (p=0.03), Hb (p=0.008) and TNFα (p=0.036) **(Figure 2).**

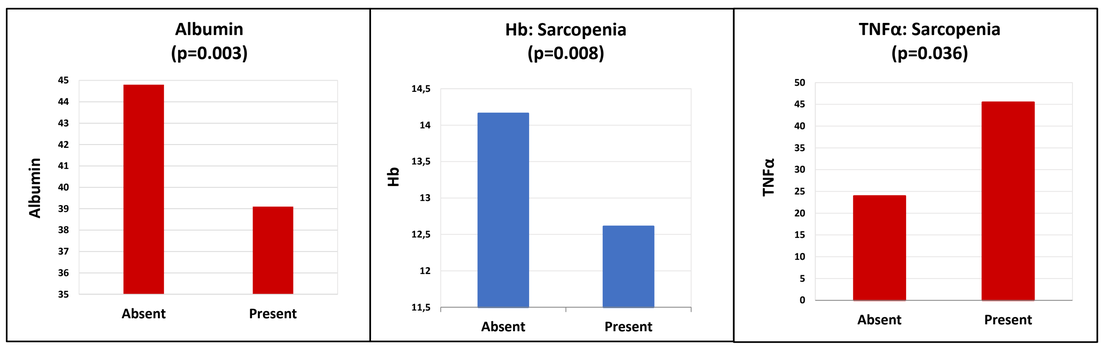

Figure 2: Biomarkers Showing Significance to the Presence of Sarcopenia

- Significant differences were found for albumin, lymphocytes, platelets, haemoglobin, platelet to lymphocyte ratio (PLR), systemic immune-inflammation index (SII), CRP, TNFα, all at p<0.01, neutrophil to lymphocyte ratio (NLR) (p=0.02), IL-6 (p<0.04) and IL-8 (p=0.02) between cases and controls **(Table 1).**

Table 1: Summary of Biomarker Analysis Results

Marker	Reference Ranges	Cases	Controls	P-value (Cases vs. Controls)	P-value (Cases vs. Reference Constant)
Albumin (g/L)	35-50	39.66 (±6.41)	46.99 (±2.21)	P < 0.01	
Haemoglobin (g/dL)	13.8-18.8	12.38 (±2.04)	15.13 (±0.92)	P < 0.01	
NLR	2.73	4.85 (±6.59)	2.31 (±1.10)	P = 0.02	P = 0.008
PLR	148.82	232.90 (±119.70)	119.18 (±34.63)	P < 0.01	P < 0.001
SII	791.96	1387.35 (±1866.47)	543.54 (±301.74)	P < 0.01	P = 0.051
CRP (mg/L)	2.775	31.65 (±56.54)	2.78 (±6.72)	P < 0.01	P = 0.002
TNFα (pg/mL)	20.745	43.52 (±52.77)	15.69 (±13.51)	P < 0.01	P = 0.009
IL-6 (pg/mL)	4.39	41.13 (±6.87)	35.64 (±69.07)	P = 0.04	P < 0.001
IL-8 (pg/mL)	9.175	33.08 (±59.90)	29.85 (±81.53)	P = 0.02	P = 0.023
CXCL5 (pg/mL)	42.28	91.37(±140.30)	61.74 (±59.01)	P = 0.22	P = 0.033
H3Cit (ng/mL)	1.295	2.38(±2.88)	2.38 (±6.72)	P = 0.99	P = 0.023

- No difference was found for CXCL5 (p=0.22) or H3Cit (p=0.99) between the groups.

- For HGS, correlations showed only albumin (p<0.01, r=0.45) and Hb, (r=0.44, p <0.001) to be significant **(Figure 3).** However, for HGS category correlations to continuous variables significances were found to PLR, TNFα, IL-6 and CRP.

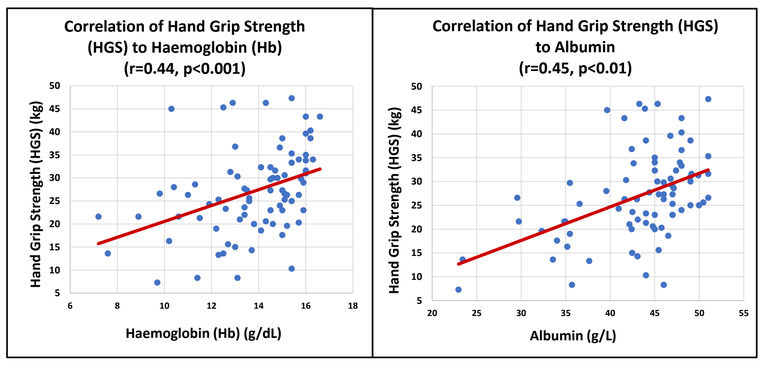

Figure 3: Correlations of Hand Grip Strength (HGS) to Haemoglobin (Hb) and Albumin

Conclusions

- **CRP, albumin and haemoglobin consistently showed baseline differences between cases and controls and in further correlations to sarcopenia.**
- **NLR, PLR, SII, TNFα, IL-6 and IL-8 showed inconsistent correlations of significance to baseline assessments.**
- **Emerging biomarkers CXCL5 and H3Cit were not found to be reliable biomarkers for cancer cachexia in defining correlations to sarcopenia and cachexia.**