CT Attenuation and Cross-sectional-area Index of the Pectoralis Are Associated With Prognosis in Sarcoma Patients

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Abstract. Background/Aim: To identify prognostic imaging biomarkers from staging chest computed tomography (CT) in patients with sarcomas. Patients and Methods: CT scans for baseline staging, and surveillance 1-year CT scans in patients newly diagnosed with sarcoma were evaluated. Pectoralis muscle area (PMA), pectoralis muscle index (PMI) and pectoralis CT attenuation density (PMT) were measured. Cox proportional-hazard models were used to determine the association with progression-free survival (PFS) and overall survival (OS). Results: There were 147 patients (53.1% male) who were followed for a median 1,414 days (range=219-4851 days). Approximately 47.6% (70/147) of patients progressed and 29.9% (44/147) died. Multivariable Cox-proportional hazards models adjusting for gender, tumor grade and chemotherapy treatment showed that a higher baseline PMT and baseline PMI were associated with increased OS. Conclusion: Higher baseline PMI and PMT are associated with increased overall survival in patients with sarcoma.

Sarcomas are rare tumors of mesenchymal origin, and there are approximately 15,000 new cases of bone or soft tissue sarcoma diagnosed annually in the United States (1-3). Sarcomas have a propensity to primarily metastasize to the lungs (3-7). Patients with localized disease have a 5-year life expectancy of approximately 81%, however, patients with metastatic disease have a 5-year life expectancy that is closer to 16% (3-7). Sarcopenia is the loss of muscle mass, quality and strength (8). Patients with cancer often experience muscle loss, which is a key component of cancer cachexia (8). Recent reports have shown that measurements from computed tomography (CT) studies of the abdomen and pelvis can be utilized to evaluate muscle loss (9-15). The L3 skeletal muscle index (SMI) (areal lumbar muscle area at the third lumbar vertebra adjusted for height in meters squared) is commonly used as a proxy for sarcopenia (9-15). Low SMI at L3 has been associated with poor outcomes – decreased overall survival in patients with multiple cancers, including melanoma, breast, uterine, colon and esophageal cancer (9-15).

The accepted treatment for local control of sarcomas is radiation therapy and wide local surgical excision or amputation. Because over 70% of sarcomas occur in the legs/thigh (1-4), patients with sarcomas often undergo surgery/amputations of the extremities, in particular the lower extremity. These patients experience asymmetric muscle mass loss in the ipsilateral psoas – the predominant hip flexor after amputation/surgical reconstruction of the lower extremity (Figure 1). Because the SMI at L3 includes the psoas, the SMI at L3 is often an inappropriate marker for sarcopenia in most patients with sarcoma.

Patients with other cancers (including melanoma, breast, uterine, colon and esophageal cancer) undergo surveillance CT studies of the abdomen/pelvis as part of routine clinical care (11-15). However, patients with sarcomas usually undergo surveillance chest CT studies because the lung is the most common site of sarcoma metastasis (6, 7). The National Comprehensive Cancer Network (NCCN) guidelines recommend considering CT studies of the abdomen and pelvis only for surveillance chest CT studies because the lung is the most common site of sarcoma metastasis (6, 7). The National Comprehensive Cancer Network (NCCN) guidelines recommend considering CT studies of the abdomen/pelvis only for surveillance chest CT studies because the lung is the most common site of sarcoma metastasis (6, 7). Therefore, the SMI at L3 cannot be calculated for all sarcoma patients (11-15).

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Key Words: Sarcoma, CT attenuation, pectoralis, survival, prognosis, muscle index.
We hypothesized that imaging biomarkers that are predictive of prognosis in patients with sarcoma, could be obtained opportunistically from these surveillance chest CT studies. The aim of this paper was to assess if there exists a relationship between CT bone and muscle parameters, and progression-free survival (PFS) and overall survival (OS) in patients with sarcoma.

Patients and Methods

This retrospective study was Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant and the study protocol was reviewed and approved by the local institutional review board (IRB). The requirement for signed informed consent from each patient was waived by the IRB.

Patients. This study evaluated patients with newly diagnosed histologically confirmed bone or soft tissue sarcoma, who were treated at a single tertiary academic center between 01/01/2006 and 06/01/2018. Patients’ age, sex, height and weight at the time of diagnosis were extracted from the medical record. The maximum size of the primary tumor in centimeters at diagnosis, tumor grade, and sarcoma tumor subtype were recorded. Patients were excluded if they had sarcoma involving the T12 vertebral body, thoracic muscles at T12, or the pectoralis muscles.

Progression-free survival. The length of time in days from the date of histological diagnosis to the development of local recurrence or the development of pulmonary metastases was defined as the progression-free survival (PFS). The time to the development of pulmonary metastases in days was calculated as the time from the date of histological diagnosis (the date the diagnosis was confirmed histologically) until the time pulmonary nodules appeared on the first surveillance chest CT study. If the pulmonary nodules were indeterminate on that chest CT study, then the subsequent surveillance chest CT was reviewed. If the pulmonary nodules were growing in size or if they decreased in size after systemic chemotherapy on the subsequent surveillance chest CT and if the oncologist decided they were clinically consistent with metastases, then the date of the surveillance chest CT where the nodules were first identified was used to define the date of development of pulmonary nodules. If the pulmonary nodules were biopsied and histologically confirmed as metastases, then this date (the date the node was first identified on CT) was used as the date of development of pulmonary nodules. The time in days, from diagnosis to histologically confirmed local recurrence was calculated. The minimum time (time to the development of pulmonary metastases compared to the time to local recurrence) was used for the progression-free survival if both conditions occurred. If the patient was lost to follow-up, then the patient was considered censored at the last documented clinic visit/correspondence.

Overall survival. OS was calculated from the date the sarcoma diagnosis was first confirmed histologically until the date the patient was deceased. If the patient was lost to follow-up, then the
Table I. Demographic and clinical characteristics of study cohort.

| Variable                        | All (n=147) | Male (n=78) | Female (n=69) | p-Value |
|---------------------------------|-------------|-------------|---------------|---------|
| Age in years (SD)               | 47.5 (16.2) | 47.2 (17.3) | 47.7 (14.9)  | 0.853   |
| Height in m (SD)                | 1.72 (0.1)  | 1.75 (0.10) | 1.67 (0.09)  | <0.001  |
| Weight in kg (SD)               | 80.7 (22.7) | 84.1 (25.9) | 76.8 (20.8)  | 0.052   |
| Location                        |             |             | 0.007         |         |
| Abdomen/Pelvis                 | 28 (19.0%)  | 9 (11.5%)   | 19 (27.5%)   |         |
| Chest                           | 13 (8.8%)   | 11 (14.1%)  | 2 (2.9%)     |         |
| Head & Neck                     | 3 (2.0%)    | 3 (3.8%)    | 0 (0.0%)     |         |
| Lower extremity                 | 79 (55.8%)  | 40 (51.3%)  | 39 (56.5%)   |         |
| Retroperitoneal                 | 2 (1.4%)    | 2 (2.6%)    | 0 (0.0%)     |         |
| Upper extremity                 | 22 (15.0%)  | 13 (16.7%)  | 9 (13.0%)    |         |
| Maximum tumor size in cm (SD)   | 10.5 (6.3)  | 10.5 (6.1)  | 10.5 (6.5)   | 0.976   |
| Tumor grade, n (%)              |             |             | 0.918        |         |
| Low                             | 10 (6.8%)   | 6 (7.7%)    | 4 (6.0%)     |         |
| Intermediate                    | 10 (6.8%)   | 6 (7.7%)    | 4 (6.0%)     |         |
| High                            | 115 (78.2%) | 60 (76.9%)  | 55 (79.7%)   |         |
| Ungraded                        | 12 (8.2%)   | 6 (7.7%)    | 6 (8.7%)     |         |
| Chemotherapy, n (%)             | 105 (71.4%) | 58 (74.4%)  | 47 (68.1%)   | 0.468   |
| Radiation, n (%)                | 75 (51.0%)  | 39 (50.0%)  | 36 (52.2%)   | 0.869   |
| Surgery, n (%)                  | 124 (84.4%) | 65 (83.3%)  | 59 (85.5%)   | 0.821   |
| PMA in cm² (SD)                 | 41.68 (19.8) | 47.5 (20.6) | 34.8 (16.3) | <0.001  |
| PMI in cm²/m² (SD)              | 14.2 (6.7)  | 15.2 (6.5)  | 13.2 (6.9)   | 0.091   |
| PMT in HU (SD)                  | 40.3 (10.1) | 41.5 (7.9)  | 38.9 (12.1)  | 0.136   |
| TMA in cm² (SD)                 | 85.5 (27.2) | 95.9 (25.3) | 73.3 (24.2)  | <0.001  |
| TMI in cm²/m² (SD)              | 28.9 (9.0)  | 30.0 (7.8)  | 27.6 (10.1)  | 0.122   |
| TMT HU (SD)                     | 37.8 (9.0)  | 38.8 (8.5)  | 36.5 (9.4)   | 0.133   |
| T12 HU (SD)                     | 201.0 (53.6) | 202.8 (51.6) | 198.9 (51.5) | 0.662   |
| Delta PMA in cm² (SD)           | -4.32 (10.1) | -5.05 (10.2) | -3.46 (10.0) | 0.347   |
| Delta PMI in cm²/m² (SD)        | -1.49 (3.6)  | -1.72 (3.3) | -1.23 (4.0)  | 0.443   |
| Delta PMT in HU (SD)            | -1.3 (8.8)   | -2.29 (7.8) | -0.1 (9.9)   | 0.147   |
| Delta TMA in cm² (SD)           | -3.65 (11.7) | -4.94 (13.8) | -2.14 (8.3)  | 0.135   |
| Delta TMI in cm²/m² (SD)        | -1.26 (4.0)  | -1.70 (4.54) | -0.75 (3.2)  | 0.156   |
| Delta TMT in HU (SD)            | 2.4 (6.5)    | 3.14 (6.8)  | 1.57 (6.1)   | 0.148   |
| Delta T12 (HU)                  | -18.1(36.8)  | -19.2 (34.0) | -16.8 (40.0) | 0.700   |

Values presented are means (standard deviation) or numbers (percentages %). HU: Hounsfield Units; y: years; PMA: pectoralis muscle cross-sectional area at the time of diagnosis; PMI: pectoralis muscle index at the time of diagnosis; PMT: pectoralis muscle CT attenuation at the time of diagnosis; TMA: muscle cross-sectional area at T12 at the time of diagnosis; TMI: muscle index at T12 at the time of diagnosis; TMT: mean CT attenuation of the muscles at T12 at the time of diagnosis; Delta PMA: Pectoralis muscle cross-sectional area at 1-year, minus pectoralis muscle cross-sectional area at the time of diagnosis; Delta PMI: Pectoralis muscle index at 1-year, minus pectoralis muscle index at the time of diagnosis; Delta PMT: Pectoralis muscle CT attenuation at 1-year, minus pectoralis muscle CT attenuation at the time of diagnosis; Delta TMA: Muscle cross-sectional area at T12 at 1-year, minus muscle cross-sectional area at T12 at the time of diagnosis; Delta TMI: Muscle index at T12 at 1-year, minus muscle index at T12 at the time of diagnosis; Delta TMT: Mean CT attenuation of the muscles at T12 at 1-year minus mean CT attenuation of the muscles at T12 at diagnosis; Delta T12: T12 vertebral body CT attenuation in HU at 1-year minus the T12 vertebral body CT attenuation in HU at the time of diagnosis. p-Values in bold represent statistically significant values.

Patient was considered censored at the last documented clinic visit/correspondence.

Chest CT parameters. Unenhanced chest CTs were performed using a Siemens Somatom AS definition 128 slice CT scanner (Siemens Healthineers, Erlagen, Germany). The following parameters were used: 120 kVp, and slice thickness 1.25 mm. The tube current automatically varied depending on body part imaged and patient habitus to limit the radiation dose to the patient. Images were evaluated using the soft tissue kernel. Patients were imaged in the supine position with the arms placed above the head. Scanners were calibrated (tolerance<4.0 HU) per the American College of Radiology (ACR) guidelines using phantoms. All scans were obtained in the supine position.

Skeletal muscle measurements. The Digital Imaging and Communications in Medicine (DICOM) files from the CT studies were transferred into a database. CT images were processed using 3D Slicer software, and a previously published semi-automated image analysis method was used to calculate the muscle cross-
muscle and bone measurements remained predictors of PFS and OS in patients with sarcoma. Statistical analysis was performed using R statistical software v3.4 (Vienna, Austria). All statistical tests were two-sided. The Bonferroni correction was utilized to preserve the Type I error rate, and a p-value<0.005 was considered statistically significant.

Results

There were 147 patients retrospectively identified and followed for an average 1,708 days (range=219-4,851 days). Undifferentiated pleomorphic sarcoma (UPS)/Malignant fibrous histiocytoma (MFH) was the most common subtype (27/147=18.4%), followed by Ewing sarcoma (19/147=12.9%), leiomyosarcoma (18/147=12.2%), synovial sarcoma (15/147=10.2%) and myxofibrosarcoma (14/147=9.5%). Approximately 4.1% (6/147), 16.3% (24/147), 70/147 (47.6%), 29.9% (44/147) and 2.0% (3/147) of patients were American Joint Committee on Cancer (AJCC) stage I, II, III, IV and unknown, respectively. The mean (standard deviation) age of the patients was 47.5 (16.2) years. Approximately 53.1% (78/147) of the cohort were male. As expected, men were on average taller (p<0.001) than women. All baseline areal muscle measurements were on average larger in men than women. The average PMA (p<0.001) and TMA (p<0.001) were significantly larger in men than women (Table I). Approximately 47.6% (70/147) of patients progressed and 29.9% (44/147) died of their disease. Older age was negatively associated with lower PMT (r=−0.27, p=0.001), lower TMT (r=−0.51, p<0.001), and lower T12 HU (r=−0.60, p<0.001).

Among males, PMI was positively correlated with TMI (r=0.74, p<0.001). PMT and TMT were also correlated (r=0.83, p<0.001). Among males, T12HU was strongly correlated with PMT (r=0.25, p=0.027) and TMT (r=0.43, p<0.001) (Table II). Among females, PMI was also positively correlated with TMI (r=0.86, p<0.001). T12 HU was also strongly correlated with PMT (r=0.29, p=0.017) and TMT (r=0.50, p<0.001). We also found that PMT and TMT were positively correlated within females (r=0.75, p<0.001).

Table II. Correlations between bone and muscle CT measurements at the time of diagnosis.

|          | TMI     | TMT     | PMI     | PMT     | T12HU   |
|----------|---------|---------|---------|---------|---------|
| Females  |         |         |         |         |         |
| TMI      |         | -0.05 (0.604) | 0.74 (<0.001) | 0.15 (0.202) | 0.01 (0.903) |
| TMT      | 0.15 (0.256) |         | 0.67 (0.553) | 0.83 (<0.001) | 0.41 (<0.001) |
| PMI      | 0.86 (<0.001) | 0.25 (0.044) |         | 0.27 (0.023) | 0.23 (0.049) |
| PMT      | 0.09 (0.484) | 0.75 (<0.001) | 0.29 (0.023) |         | 0.25 (0.027) |
| T12HU    | 0.20 (0.116) | 0.50 (<0.001) | 0.30 (0.017) | 0.29 (0.017) |         |

Male correlations are in the upper triangle. Female correlations are in the lower triangle. Numbers in parenthesis represent p-values. PMI: Pectoralis muscle index at the time of diagnosis; PMT: pectoralis muscle CT attenuation at the time of diagnosis; TMI: muscle index at T12 at the time of diagnosis; TMT: mean CT attenuation of the muscles at T12 at the time of diagnosis; T12 HU: T12 vertebral body CT attenuation in HU at the time of diagnosis. p-Values in bold are statistically significant.
Univariate Cox proportional hazards analyses results for PFS and OS are shown in Table III. Kaplan–Meier curves evaluating sarcoma survival are shown for PMT (Figure 3A and B) and PMI (Figure 4A and B). Multivariable Cox-proportional hazards models adjusting for age, gender, tumor grade and chemotherapy treatment showed that higher baseline PMT (HR=0.97, 95%CI=0.95-0.99) and higher baseline PMI (HR=0.99, 95%CI=0.9987-0.9996) were associated with increased OS (Table IV).

Discussion

The results of this study show that sarcoma patients with higher baseline PMT and PMI had increased OS. This suggests that the amount of baseline cross sectional area and fatty infiltration of the pectoralis musculature were associated with increased OS independent of tumor grade and chemotherapy. The data also show that the CT attenuation of the T12 vertebral body was positively
correlated with PMI, TMT and PMT in both males and females.

Muscle loss is known to be an independent predictor of survival in patients with hepatocellular carcinoma after hepatectomy (12), stage III melanoma (15), pancreatic adenocarcinoma after resection (13, 14), lung adenocarcinoma (9-11), prostate cancer (29), ovarian cancer (30), breast cancer (22, 31), esophageal cancer (20, 21), and colorectal cancer (16). Therefore, other studies support our findings, and suggest that surveillance CT studies may have imaging biomarkers that can be used to predict patient prognosis, and show that muscle loss is associated with poor prognosis and decreased overall survival.
Variables—which gives our study more power to detect an association (32).

and bone density as continuous variables rather than binary
the prior study, only patients with soft tissue sarcoma were included in our study, whereas in
be used for sarcoma prognosis. Patients with both bone and
density and muscle mass are correlated.

This study has a few limitations. This study is based on
patients treated at a single tertiary care academic center.
The retrospective nature of the study makes it susceptible
to ascertainment biases due to referral patterns. Sarcomas
are a heterogeneous group of tumors of mesenchymal origin and the optimal treatment depends on the tumor
histology. Some tumor types such as osteosarcomas, Ewing sarcoma and myxoid round cell tumors, and metastatic
disease are treated with chemotherapy and corticosteroids.

Muscle loss is a key component of cancer cachexia, and
thought to be multifactorial. Environmental causes of muscle
loss may include decrease in physical activity and decrease
in nutritional intake (33). Patients with progressing sarcoma,
like other cancers, may be less active due to fatigue and pain
and may suffer from anorexia (33). Muscle loss may be
related to decreases in hormones that are important for
preservation of muscle mass such as testosterone, dehydro-
epiandrosterone sulfate (DHEAS), insulin-like growth factor
-1 and estrogen (33-38). It is unclear whether decreases in
these hormones contribute to muscle loss in patients with sarcoma. Future research is required to assess how all of these factors contribute to muscle loss in patients with sarcoma.

Another interesting finding was that PMI was strongly
correlated with the CT measure of bone mineral density in
both men and women. One possible explanation for this
finding is that individuals that are more active have larger
PMI and develop increased BMD, and suggests that bone
density and muscle mass are correlated.

This study has a few limitations. This study is based on
patients treated at a single tertiary care academic center.
The retrospective nature of the study makes it susceptible
to ascertainment biases due to referral patterns. Sarcomas
are a heterogeneous group of tumors of mesenchymal origin and the optimal treatment depends on the tumor
histology. Some tumor types such as osteosarcomas, Ewing sarcoma and myxoid round cell tumors, and metastatic
disease are treated with chemotherapy and corticosteroids.

Patients with these sarcoma subtypes and metastatic disease
may be more susceptible to increased muscle loss because
of their treatment, however our analysis adjusted for
chemotherapy treatment, which should have mitigated this
problem. In conclusion, increased baseline PMI and PMT
are associated with better OS after adjusting for patient age,
height, tumor grade and chemotherapy in patients with sarcoma.

Conflicts of Interest

The Authors’ declare no financial conflicts of interest in relation to
this study.

One prior study investigating muscle loss in patients with sarcoma found no association between muscle loss assessed by evaluating the height-adjusted psoas CSA at L3 and overall survival (16). However, there are key differences between our study and this prior study. We adjusted for gender, height, and grade rather than just height. We were not interested in estimating sarcopenia – instead we were interested in identifying a CT imaging biomarker that could be used for sarcoma prognosis. Patients with both bone and soft tissue sarcomas were included in our study, whereas in the prior study, only patients with soft tissue sarcoma were evaluated. In addition, we analyzed CT measures of muscle and bone density as continuous variables rather than binary variables – which gives our study more power to detect an association (32).

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tought to be multifactorial. Environmental causes of muscle
loss may include decrease in physical activity and decrease
in nutritional intake (33). Patients with progressing sarcoma,
like other cancers, may be less active due to fatigue and pain
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these hormones contribute to muscle loss in patients with sarcoma. Future research is required to assess how all of these factors contribute to muscle loss in patients with sarcoma.

### Table IV. Multivariable Cox-proportional hazards analyses predicting progression-free survival (PFS) and overall survival (OS) after adjusting for age, gender, grade and history of prior chemotherapy.

| Variable                        | PFS Hazard ratio | PFS 95%CI   | PFS p-Value | OS Hazard ratio | OS 95%CI   | OS p-Value |
|---------------------------------|------------------|-------------|-------------|-----------------|-------------|------------|
| PMI (cm²/m²)                    | 0.99             | (0.99, 0.99)| 0.004       | 0.99            | (0.99, 0.99)| <0.001     |
| PMT (HU)                        | 0.97             | (0.95, 0.99)| 0.019       | 0.97            | (0.95, 0.99)| 0.005      |
| TMI (cm²)                       | 0.99             | (0.99, 1.00)| 0.090       | 1.00            | (0.99, 1.00)| 0.179      |
| TMT (HU)                        | 0.95             | (0.92, 0.99)| 0.012       | 0.96            | (0.94, 0.99)| 0.016      |
| T12 HU (HU)                     | 0.99             | (0.98, 0.99)| 0.034       | 0.99            | (0.99, 1.00)| 0.570      |
| Delta PMI (cm²/m²)              | 1.00             | (0.99, 1.00)| 0.157       | 1.00            | (1.00, 1.01)| 0.014      |
| Delta PMT (HU)                  | 0.99             | (0.97, 1.01)| 0.523       | 0.99            | (0.97, 1.01)| 0.421      |
| Delta TMI (cm²/m²)              | 1.00             | (0.99, 1.00)| 0.984       | 1.00            | (0.99, 1.00)| 0.222      |
| Delta TMT (HU)                  | 0.99             | (0.95, 1.04)| 0.736       | 0.97            | (0.93, 1.01)| 0.165      |
| Delta T12 (HU)                  | 1.00             | (0.99, 1.01)| 0.056       | 1.00            | (0.99, 1.01)| 0.282      |

HU: Hounsfield Units; y: years; PMA: pectoralis muscle cross-sectional area at the time of diagnosis; PMI: pectoralis muscle index at the time of diagnosis; PMT: pectoralis muscle CT attenuation at the time of diagnosis; TMA: muscle cross-sectional area at T12 at the time of diagnosis; TMI: muscle index at T12 at the time of diagnosis; TMT: mean CT attenuation of the muscles at T12 at the time of diagnosis; T12 HU: T12 vertebral body CT attenuation in HU at the time of diagnosis; Delta PMA: Pectoralis muscle cross-sectional area at 1-year, minus pectoralis muscle cross-sectional area at the time of diagnosis; Delta PMI: Pectoralis muscle index at 1-year, minus pectoralis muscle index at the time of diagnosis; Delta PMT: Pectoralis muscle CT attenuation at 1-year, minus pectoralis muscle CT attenuation at the time of diagnosis; Delta TMA: Muscle cross-sectional area at T12 at 1-year, minus muscle cross-sectional area at T12 at the time of diagnosis; Delta TMI: Muscle index at T12 at 1-year, minus muscle index at T12 at the time of diagnosis; Delta TMT: Mean CT attenuation of the muscles at T12 at 1-year minus mean CT attenuation of the muscles at T12 at diagnosis; Delta T12: T12 vertebral body CT attenuation in HU at 1-year minus the T12 vertebral body CT attenuation in HU at the time of diagnosis. Bold p-values are statistically significant.
Authors’ Contributions

SJ: Data curation, manuscript editing, review and approval of final manuscript. RS: Conceptualization, writing – original draft, manuscript review and editing, formal statistical analysis, methodology, review and approval of final manuscript

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References

1 Siegel RL, Miller KD and Jemal A: Cancer statistics, 2019. CA Cancer J Clin 69(1): 7-34, 2019. PMID: 30620402. DOI: 10.3322/caac.21551

2 Bone and Joint Cancer - Cancer Stat Facts. SEER. Available at: https://seer.cancer.gov/statfacts/html/bones.html [Last accessed on October 1, 2019]

3 Soft Tissue Cancer - Cancer Stat Facts. SEER. Available at: https://seer.cancer.gov/statfacts/html/soft.html [Last accessed on March 27, 2019]

4 Cormier JN and Pollock RE: Soft tissue sarcomas. CA Cancer J Clin 54(2): 94-109, 2004. PMID: 15061599. DOI: 10.3322/canjclin.54.2.94

5 Skubitz KM and D’Adamo DR: Sarcoma. Mayo Clin Proc 82(11): 1409-1432, 2007. PMID: 17976362. DOI: 10.4065/82.11.1409

6 Chao C and Goldberg M: Surgical treatment of metastatic cancer. J Gastrointest Surg 16(8): 1478-1486, 2012. PMID: 22692586. DOI: 10.1007/s11605-012-1923-5

7 Amini N, Spolverato G, Gupta R, Margonis GA, Kim Y, Wagner D, Rezaee N, Weiss MJ, Wolfgang CL, Makary MM, Kamel IR and Pawlik TM: Impact of total psoas volume on short- and long-term outcomes in patients undergoing curative resection for pancreatic adenocarcinoma: A new tool to assess sarcopenia. J Gastrointest Surg 19(9): 1593-1602, 2015. PMID: 25925237. DOI: 10.1007/s11605-015-2835-y

8 Wilson RJ, Alamanda VK, Hartley KG, Mesko NW, Halpern JL, Schwartz HS and Holt GE: Sarcopenia does not affect survival or outcomes in soft-tissue sarcoma. Sarcoma 2015: 146481, 2015. PMID: 26696772. DOI: 10.1155/2015/146481

9 Nemec U, Heidinger B, Sokas C, Chu L and Eisenberg RL: Diagnosing sarcopenia on thoracic computed tomography: Quantitative assessment of skeletal muscle mass in patients undergoing transcatheter aortic valve replacement. Acad Radiol 24(9): 1154-1161, 2017. PMID: 28365235. DOI: 10.1016/j.acra.2017.02.008

10 Murray TE, Williams D and Lee MJ: Osteoporosis, obesity, and sarcopenia on abdominal CT: a review of epidemiology, diagnostic criteria, and management strategies for the reporting radiologist. Abdom Radiol (NY) 42(9): 2376-2386, 2017. PMID: 28386693. DOI: 10.1007/s00261-017-1124-5

11 Mourtzakis M, Prado CM, Liefers JR, Reiman T, McCargar LJ and Baracos VE: A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 33(5): 997-1006, 2008. PMID: 18923576. DOI: 10.1139/H08-087

12 Prado CM, Liefers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L and Baracos VE: Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: A population-based study. Lancet Oncol 9(7): 629-635, 2008. PMID: 18539529. DOI: 10.1016/S1470-2118(07)70153-0

13 Bosshier PR, Heneghan R, Markar SR, Baracos VE and Low DE: Assessment of body composition and sarcopenia in patients with esophageal cancer: a systematic review and meta-analysis. Dis Esophagus 31(1): 2018. PMID: 29846548. DOI: 10.1093/dote/doy047

14 Can BJ, Cespedes Feliciano EM, Prado CM, Alexeef S, Kroenke CH, Bradshaw P, Quesenberry CP, Weltzien EK, Castillo AL, Olobatuyi TA and Chen WY: Association of muscle and adiposity measured by computed tomography with survival in patients with nonmetastatic breast cancer. JAMA Oncol 4(6): 798-804, 2018. PMID: 29621380. DOI: 10.1001/jamaoncol.2018.0137

15 Can BJ, Meyerhardt JA, Kroenke CH, Alexeef S, Xiao J, Weltzien E, Feliciano EC, Castillo AL, Quesenberry CP, Kwan ML and Prado CM: Explaining the obesity paradox: The association between body composition and colorectal cancer survival (C-SCANS Study). Cancer Epidemiol Biomarkers Prev
26 Jacobs AJ, Michels R, Stein J and Levin AS: Improvement in overall survival from extremity soft tissue sarcoma over twenty years. Sarcoma 2015: 279601, 2015. PMID: 25821397. DOI: 10.1155/2015/279601
25 Rubbiéri G, Mossello E and Di Bari M: Techniques for the diagnosis of sarcopenia. Clin Cases Miner Bone Metab 11(3): 181-184, 2014. PMID: 25568650
26 Sebro R: Obesity, hepatic steatosis, and their impact on fat infiltration of the trunk musculature using unenhanced computed tomography. J Comput Assist Tomogr 41(2): 298-301, 2017. PMID: 28230568. DOI: 10.1097/RCT.0000000000000507
27 Romme EA, Murchison JT, Phang KF, Jansen FH, Rutten EP, Wouters EF, Smeenk FW, Van Beek EJ and Macnee W: Bone attenuation on routine chest CT correlates with bone mineral density on DXA in patients with COPD. J Bone Miner Res 27(11): 2338-2343, 2012. PMID: 22692725. DOI: 10.1002/jbmr.1678
28 Emohare O, Cagan A, Morgan R, Davis R, Asis M, Switzer J and Polly DW Jr: The use of computed tomography attenuation to evaluate osteoporosis following acute fractures of the thoracic and lumbar vertebra. Geriatr Orthop Surg Rehabil 3(2): 50-55, 2014. PMID: 25360331. DOI: 10.1016/j.bmr.1678
29 McDonald AM, Swain TA, Mathew DL, Cardan RA, Baker CB, Harris DM, Yang ES and Fiveash JB: CT measures of bone mineral density and muscle mass can be used to predict noncancer death in men with prostate cancer. Radiology 282(2): 475-483, 2017. PMID: 27598538. DOI: 10.1148/radiol.2016160626
30 Gadducci A and Cosio S: The prognostic relevance of computed tomography-assessed skeletal muscle index and skeletal muscle radiation attenuation in patients with gynecological cancer. Anticancer Res 41(1): 9-20, 2021. PMID: 33419795. DOI: 10.21873/anticancerres.14747
31 Villaseñor A, Ballard-Barbash R, Baumgartner K, Baumgartner R, Bernstein L, McKiernan A and Neuhausser ML: Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study. J Cancer Surviv 6(4): 398-406, 2012. PMID: 23034848. DOI: 10.1007/s11764-012-0234-x
32 Altman DG and Royston P: The cost of dichotomising continuous variables. BMJ 332(7549): 1080, 2006. PMID: 16675816. DOI: 10.1136/bmj.332.7549.1080
33 Walston JD: Sarcopenia in older adults. Curr Opin Rheumatol 24(6): 623-627, 2012. PMID: 22955023. DOI: 10.1097/BOR.0b013e328358d59b
34 McIntire KL and Hoffman AR: The endocrine system and sarcopenia: potential therapeutic benefits. Curr Aging Sci 4(3): 298-305, 2011. PMID: 21529322. DOI: 10.2174/1874609811104030298
35 Horstman AM, Dillon EL, Urban RJ and Sheffield-Moore M: The role of androgens and estrogens on healthy aging and longevity. J Gerontol A Biol Sci Med Sci 67(11): 1140-1152, 2012. PMID: 22451474. DOI: 10.1093/gerona/gls068
36 Jo E, Lee SR, Park BS and Kim JS: Potential mechanisms underlying the role of chronic inflammation in age-related muscle wasting. Aging Clin Exp Res 24(5): 412-422, 2012. PMID: 22717404. DOI: 10.3275/8464
37 McFarlane C, Plummer E, Thomas M, Hennebry A, Ashby M, Ling N, Smith H, Sharma M and Kambadur R: Myostatin induces cachexia by activating the ubiquitin proteolytic system through an NF-kappaB-independent, FoxO1-dependent mechanism. J Cell Physiol 209(2): 501-514, 2006. PMID: 16883577. DOI: 10.1002/jcp.20757
38 Baracos VE: Psoas as a sentinel muscle for sarcopenia: a flawed premise. J Cachexia Sarcopenia Muscle 8(4): 527-528, 2017. PMID: 28675689. DOI: 10.1002/jcsm.12221