



# Measurement of Lean Body Mass Using CT Scans

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## Body Mass Index (BMI) and Weight Loss: Conventional Elements of How Cachexia and Nutritional Status Have Been Defined in Cancer Patients

**O**ur understanding of cancer cachexia in the past has focused on losses of body weight. Since ancient times, the relationship between loss of body weight over time and poor cancer outcomes has been known. Even though measures such as loss of lean body mass may be better predictors of patient outcomes, weight loss remains firmly entrenched as a criterion for identification of malnutrition and cachexia. Body weight loss, for instance, still is used as a major criterion of inclusion and also as a principal endpoint in randomized clinical trials for various forms of cachexia treatment, including nutritional support. In a review of 55 clinical trials looking at the effect of appetite stimulants on cancer cachexia, Yavuzsen et al<sup>1</sup> reported that 91% of studies examined used overall body weight change as an outcome.

Progressive loss of weight is conventionally viewed as culminating in a cachectic (ie, emaciated) state. Current demographics of cancer patients, however, are progressively affected by increasing rates of obesity, as well as by an increasing prevalence of cancer in obese people. As a result, patients with advanced disease are reported to have a high prevalence of obesity in spite of ongoing weight losses.<sup>2</sup>

Despite considerable weight loss in some of these patients, the classic image of cachexia (ie, emaciation) is becoming less common. We conducted population-based profiling of BMI and weight loss history in a cohort (n=2695) of patients with gastrointestinal cancer. Patients were newly referred to medical oncology clinics in a regional cancer center. A computerized database of all cancer cases in the province (Alberta Cancer Registry) was used to capture disease site and morphology, along with biological, clinical, and demographic information. Analysis of BMI reveals an

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average BMI clinical, and demographic information. Analysis of BMI reveals an average BMI  $>26 \text{ kg/m}^2$  and a preponderance of overweight and obese patients, with only 5% presenting with a BMI  $<18.5 \text{ kg/m}^2$ . A history of weight loss was common, with an average loss of  $8.6 \pm 8.9\%$ . The population quartiles of 6 month weight loss were -19.3%, -10.6%, -4.5%, and +2.4%. In the following Table, the data are stratified by time to death.

**Table. BMI Distribution (%) and 6-Month Weight Loss at Different Times From Death in Patients With Advanced Solid Tumors (n=2695)**

	Days to Death				
	<90 (n=509)	90 to 180 (n=312)	181 to 360 (n=346)	361 to 540 (n=396)	>540 (n=1132)
BMI <20.0 (%)	23	22	15	12	8
BMI 20.0 to 24.9 (%)	39	44	37	38	38
BMI 25.0 to 29.9 (%)	28	25	36	35	36
BMI $\geq 30.0$ (%)	10	9	12	15	18
BMI (Mean $\pm$ SD)	23.9 $\pm$ 5.3	23.7 $\pm$ 4.6	24.9 $\pm$ 5.0	25.5 $\pm$ 5.4	26.0 $\pm$ 5.0
6 month weight loss (%, Mean $\pm$ SD)	11.7 $\pm$ 9.0	9.3 $\pm$ 8.8	7.8 $\pm$ 8.8	7.0 $\pm$ 7.5	5.5 $\pm$ 7.9

Despite a mean weight loss of about 12%, the mean BMI of patients within 90 days of death was high at  $23.9 \text{ kg/m}^2$ . Owing to high body weights, many patients remained obese or overweight in spite of considerable weight loss. These data appear to reflect the generally heavier body weights in Westernized countries.

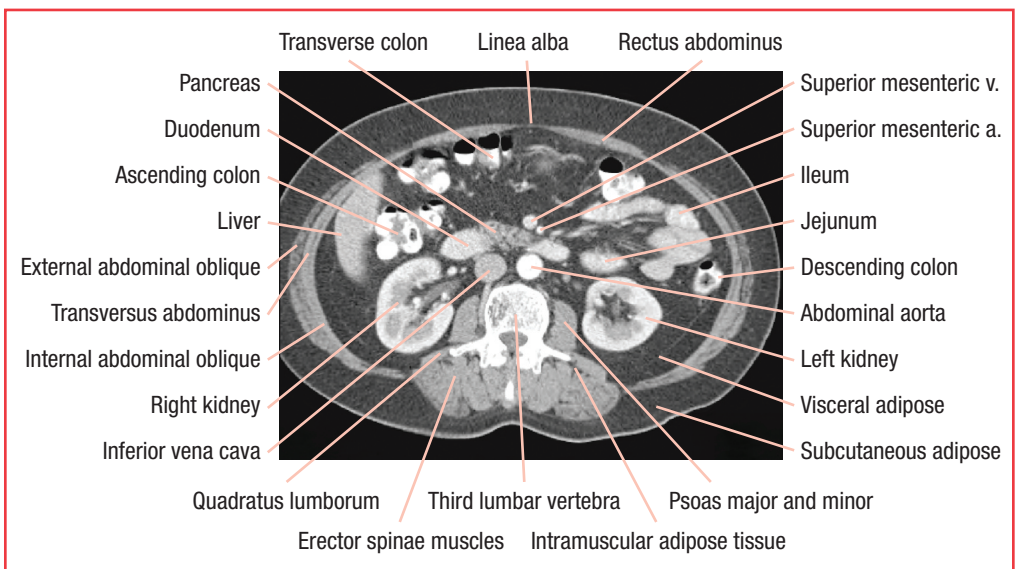
## A Reconceptualization of Cancer Cachexia

Skeletal muscle wasting can hide within the bulk of body weight and body weight change, and recognition of sarcopenia (age-related muscle wasting) as a clinically important phenomenon is emerging. The term *sarcopenia* denotes a reduced quantity of skeletal muscle (ie,  $>2$  standard deviations below that typical of healthy adults).<sup>3</sup> Sarcopenia is associated with loss of physical function, disability,<sup>2-4</sup> risk of fractures and of falls,<sup>3</sup> increased length of hospital stay,<sup>5</sup> nosocomial infections,<sup>6</sup> and decreased survival<sup>7</sup> in nonmalignant diseases. Sarcopenia is not restricted to people who are thin or wasted.<sup>2,8</sup> The aging process is often paralleled by decreases in muscle and increases in fat mass, which may culminate in *sarcopenic obesity*.<sup>9,10</sup> Recent studies<sup>11,12</sup> point to an increasing prevalence of sarcopenic obesity in elderly people in North American and Europe.

Experts are starting to acknowledge the independent behavior of muscle and adipose tissues on wasting syndromes. A recently convened consensus conference on the definition of cachexia<sup>13</sup> notably made a distinction between the behavior of skeletal muscle and adipose tissue: “Cachexia, is a complex metabolic syndrome associated with underlying illness and *characterized by loss of muscle with or without loss of fat mass*. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children....” This perspective acknowledges the possibility of a persistent muscle loss in the absence of any change in fat mass.

## The Use of Diagnostic Images To Assess Body Composition Changes and Sarcopenia in Cancer Patients

A highly differentiated understanding of human body composition has evolved in tandem with image-based technologies such as computed tomography (CT) and magnetic resonance imaging (MRI). These methods enjoy a high degree of specificity for the separate discrimination of many organs and tissues (Fig 1).



**Fig 1. Structures present in a computerized tomography image at the 3rd lumbar vertebra.**

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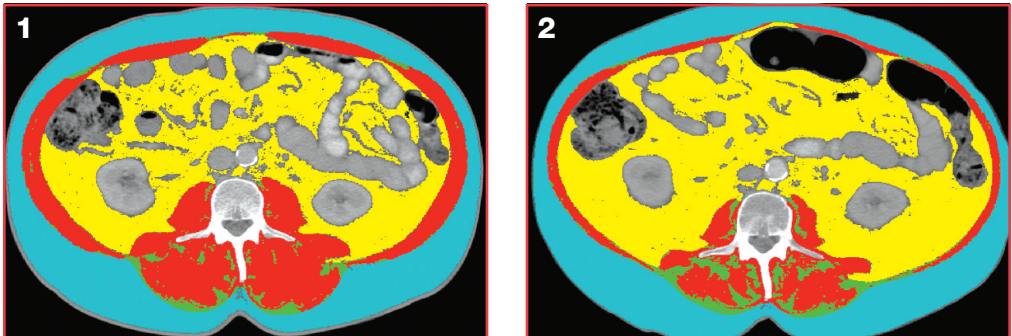
CT is considered a gold standard method used to assess body composition<sup>14</sup>; however, its use in noncancer populations is limited.

Cancer patients undergo frequent routine scans for diagnosis and to monitor disease progression. Although these patients are routinely evaluated by high-resolution diagnostic imaging, the information content of these images is barely exploited, in part owing to lack of deployment of relevant methods and concepts in a cancer care setting. We have proposed the opportunistic use of these high-quality images, which are readily available in the medical records of these patients, to provide accurate and practical studies of body composition across the cancer trajectory.<sup>15</sup> These images are a considerable resource and are now in many institutions stored and accessible in a digitized format. For example, our large cohort of patients with solid tumors of the lung and gastrointestinal tract typically undergo imaging four times a year during active treatment. An extensive reliance on diagnostic imaging gives specialists in cancer care an unprecedented ability to evaluate their patients' body composition, including repeated measures over time.

The premise of CT scans for body composition research has been described in detail elsewhere.<sup>14,15</sup> It is important to note that these methods are accessible. Image analysis software is commercially available, and the quantification can be done by any qualified person with appropriate knowledge of human anatomy, the nature of the images, and the capacities of the software.

Diagnostic images taken in cancer care do not usually encompass the whole body; this requires that patients be evaluated at a standardized location. Specific skeletal landmarks in the lumbar region appear in a majority of work in non-malignant disease as well as in cancer.<sup>2,15</sup> As illustrated in Fig 1, this region contains visceral, subcutaneous, and intermuscular adipose tissue, *psoas* and paraspinal muscles (*erector spinae* and *quadratus lumborum*), as well as *transversus abdominus*, external and internal oblique abdominals, and *rectus abdominus*. Since the cross-sectional areas of tissues in single images in the lumbar area are strong correlates of whole-body adipose tissue, muscle, and lean tissue mass,<sup>15-17</sup> we make use of the 3rd lumbar vertebra (L3) in our characterization of cancer patients. Individuals may be compared directly on this basis; however, these quantities may be translated to approximate whole-body tissue masses using regression equations from earlier work.<sup>15-17</sup> Specific tissues are identified based on their anatomical features (Fig 1) and then demarcated and quantified (Fig 2) based on pre-established thresholds of Hounsfield units (units of radiation attenuation) using commercially available imaging analysis software.

Cross-sectional areas (cm<sup>2</sup>) are computed automatically by the program once the desired tissues are demarcated. Demarcated images (Fig 2) illustrate body composition changes in a lung cancer patient over time; this person lost skeletal muscle during progressive disease.



**Fig 2. Skeletal muscle loss in a patient with lung cancer.** Segmented CT images for a male lung cancer patient at two separate timepoints. Number 1 was taken 390 days before death, and 2 was taken 58 days before death. Segmented tissues of interest: ■ is skeletal muscle, ■ is visceral adipose tissue, ■ is subcutaneous adipose tissue, and ■ is intramuscular adipose tissue. During this 332-day period, skeletal muscle area decreased from 173 cm<sup>2</sup> to 86.7 cm<sup>2</sup>.

## Conclusions

Current demographics of weight and body composition suggest a need to reconceptualize cancer cachexia. Substantial depletion of skeletal muscle is a widespread abnormality of body composition in patients with advanced solid tumors, which is present in people at any BMI and strongly related to outcome. Valid and convenient approaches for determining muscularity are required to evaluate this feature in cancer patients, and the secondary analysis of CT images is an accessible means of making this evaluation.

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