



# HHS Public Access

Author manuscript

*Cancer Epidemiol Biomarkers Prev.* Author manuscript; available in PMC 2018 February 28.

Published in final edited form as:

*Cancer Epidemiol Biomarkers Prev.* 2017 January ; 26(1): 13–16. doi:10.1158/1055-9965.EPI-16-0439.

## The obesity paradox in cancer – moving beyond BMI

Shlomit Strulov Shachar, MD<sup>1,2</sup> and Grant R. Williams, MD<sup>1</sup>

<sup>1</sup>UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA

<sup>2</sup>Division of Oncology, Rambam Health Care Campus, Haifa, Israel

### Abstract

Body mass index (BMI) and simple counts of weight are easy and available tools in the clinic and in research. Recent studies have shown that cancer patients with low-normal BMI (or those with weight loss) have worse outcomes than obese patients. These results suggest that obesity has a protective effect and has been termed the ‘obesity paradox’. In this commentary, we discuss hypothetical explanations and take a step beyond BMI or simple weights alone to present other useful and more specific body composition metrics such as muscle tissue mass, visceral, and subcutaneous fat mass. Body composition is highly variable between individuals with significant differences seen between various races and ages. Therefore, it is critical to consider that patients with the exact same BMI can have significantly different body compositions and different outcomes. We encourage further studies to examine body composition beyond BMI and to use other body composition metrics to develop individualized treatments and intervention strategies.

The usage of Body Mass Index (BMI) to characterize the different body/obesity types has been common place for decades, yet limitations persist in its use. BMI is a calculated value (body weight (Kg) divided by square height (m<sup>2</sup>)) and exists as an easy and simple tool in the clinic and in research to differentiate and categorize patients as underweight (BMI<18.5), normal weight (18.5–24.99), overweight (25–29.99), and obese (>30). In a large scale British study (1) (over 5 million individuals), BMI was significantly associated with 17 of 22 cancers, among them liver, colon, and postmenopausal breast cancers. Although obesity in the general population is associated with an increased risk of death(2), there are conflicting reports about the relationship between obesity and mortality among individuals with cancer and several other chronic diseases.(3–5) This phenomenon, known as the “obesity paradox”, suggests a potential protective effect in overweight and mildly obese patients. Mortality curves for BMI for any population are usually U-shaped (with increased mortality at both ends), but the debate primarily lies as to where the nadir for mortality exists.(6) Two studies in this issue evaluate the association of weight changes in a large cohort of patients with two common early stage cancers: breast and colorectal. Cespedes *et al* concluded that weight loss and gain are equally common after breast cancer, and weight loss is a consistent marker of mortality risk.(7) Meyerhardt *et al* demonstrated that weight loss after a colorectal cancer diagnosis was associated with worse cancer-

\*Corresponding author: Shlomit Strulov Shachar, 170 Manning Drive, Campus Box 7305 Chapel Hill NC 27599, USA. shlomits@email.unc.edu, Phone; +1-919-966-2891, Fax numbers;+1-919-627-3221.

**Conflict of interest:** none

specific and overall mortality.(8) The third study by Greenlee *et al* is a pooled analysis of 22 clinical trials from SWOG (n=11,724) and showed that BMI  $\geq 25\text{kg/m}^2$  was associated with better overall survival among men (HR=0.82;  $P=.003$ ), unlike in women (HR=1.04;  $P=.86$ ). (9) Both methodological and physiological explanations exist for explaining this phenomenon and these results, but what is the clinician supposed to recommend patients today? Should we enter the clinic tomorrow and tell our patients to gain weight? Or stop encouraging them to keep within the “normal” range of BMI?

Many hypothetical explanations exist that help explain the obesity paradox. One of them is the collider stratification bias (a form of selection bias) that may in part explain the phenomenon,(10, 11), but this unlikely fully accounts for the observed findings. (12) The increased nutritional reserves provided by excess fat stores and higher lean body mass in obese patients(13) may provide an added advantage during periods of acute illness.(14) Additionally, it is plausible that lower BMI categories disproportionately include sicker patients, and in turn, are at higher risk of mortality. The loss of weight could also be associated with smoking and related to other comorbidities which can be another confounder. (15) Weight loss amongst even the general older adult population is associated with frailty and an increased mortality risk.(16, 17) Weight loss at a cancer diagnosis is often a marker of more aggressive cancer and/or advanced disease. Even in earlier stage patients, lower weights may be a marker of subclinical tumor activity. Changes in weight can be seen over 6 months prior to a cancer diagnosis and appreciable subclinical impacts on lipid metabolism can start as early as two years before a diagnosis is made.(18) Of note, the impact of cancer on body metabolism and cachexia varies greatly by tumor type and stage, and clearly cancer can have a significant impact on weight and the distinction between intentional and non-intentional weight loss is a major issue.(19)

Although BMI and simple weight measurements are the easiest and most available clinical measures and have helped gain an enormous amount of knowledge regarding the relationship of obesity and cancer prevention as well as cardiovascular diseases (20), one major flaw and limitation of both are their inability to differentiate fat and muscle mass. Body composition and BMI differ considerably between different ethnic groups (see table 1). While African Americans have higher BMI on average, they also have higher lean body mass (LBM) and subcutaneous fat with lower visceral fat, while Caucasians generally have higher visceral fat and lower subcutaneous and LBM. Of note, south Asians have almost ‘normal’ average BMI, but have a lower LBM and higher visceral fat than African Americans.(21) Age is another factor associated with alterations in body composition and with age there is a decrease in muscle mass and strength, known as sarcopenia.(22–24) The assumption that adults have an optimal weight range (corrected for height) is probably sound, but assuming that this is the same for all individuals regardless of ethnicity, age, and health status is challenging. Furthermore nutritional status is also an important component, and BMI/weight is not always an adequate indicator of nutrition status. (25)

In oncology, body composition has been shown to have a substantial impact on outcomes. (26, 27) Many studies demonstrate an association between different indices and prognosis in different tumors. Table 2 highlights the multitude of body measures used in the literature, their measurement calculations, and some example findings in oncology. In a recent meta-

analysis, sarcopenia (low muscle mass) derived from CT imaging was significantly associated with inferior survival across tumor types and disease stages.(27) Assuming the impact of weight is the same regardless of the degree of adiposity or skeletal muscle ignores a growing body of evidence within oncology and elsewhere. Patients with lower muscle mass have higher rates of surgical complications,(28) which may delay the preferable timing of adjuvant treatment initiation, a known factor for inferior outcomes.(29) In addition, sarcopenic patients have higher rates of treatment toxicity (26, 30, 31) that, in turn, can cause dose delays and reductions, resulting in lower dose intensity and worse outcomes.(32, 33) Also, recent evidence in a large cohort of patients with early stage colorectal cancer demonstrated that decreased muscle mass and attenuation was significantly associated with markers of systemic inflammation, but neither have correlation with BMI. This highlights the significant interaction of body composition and the inflammation process that can impact metabolism, weight loss, and body resistance to tumor growth.(34) Although body composition analysis is much more accurate in quantifying muscle mass and adiposity, it is not yet a standard component of clinical care in oncology or elsewhere.

In cancer, as well as other diseases, physical activity should be discussed alongside body composition as physical activity has an important influence on the prevention of cancer (35) and survival after diagnosis. (36) Physical activity can also increase muscle mass and augment metabolic and hormonal axes (37), as well as be used as an important intervention tool.

The evolving field of personalized medicine in oncology is playing an increasing role in cancer prevention, diagnosis, prognosis, and therapeutics.(38) In the last decade there has been great progress in understanding tumor characteristics including proliferation rate, mutation load and type, and when utilized to guide cancer therapy there is potential for improved survival.(39, 40) The impact of host factors remains underappreciated and poorly understood. Personalized medicine should go beyond only tumor genetics and pharmacogenomics, but should also include a patient's body composition, physical function, and comorbidities. These factors can also greatly impact treatment decisions and drug dosing with an overall impact on outcomes. In the same way that treatments in oncology are rarely one size fits all, the "right" weight for a given individual is likely dependent on a multitude of factors and should also be individualized.

The studies in this issue highlight the importance of body measures in cancer and add to the growing literature in this emerging field. So what should clinicians be telling their patients regarding weight loss or weight gain after a cancer diagnosis? The answer is complex and not yet clear with many unresolved questions remaining. Is weight loss a sign for tumor activity, and if it is, can we even reverse that process? Will future randomized control trials with the goal of achieving the "right" BMI improve survival? Will it be the right BMI or the right body composition? Is it the amount of LBM or the ratio between the LBM to fat (adiposity/muscularity ratio)? Is it the size/quantity of muscle or as recent evidence has shown, the quality of muscle (radiodensity) that impacts survival.(41, 42) To date we have more questions than answers, and we need to gear up with focused studies about the impact of body composition on different outcomes and step forward with intervention and prevention strategies.

## Acknowledgments

**Funding Sources:** This work was supported, in part, by the UNC Oncology Clinical Translational Research Training Program (G.R. Williams, NCI 5K12CA120780-07). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

## References

1. Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet*. 2014; 384:755–65. [PubMed: 25129328]
2. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *Jama*. 2013; 309:71–82. [PubMed: 23280227]
3. Tobias DK, Pan A, Jackson CL, O'Reilly EJ, Ding EL, Willett WC, et al. Body-mass index and mortality among adults with incident type 2 diabetes. *The New England journal of medicine*. 2014; 370:233–44. [PubMed: 24428469]
4. Andersen KK, Olsen TS. The obesity paradox in stroke: Lower mortality and lower risk of readmission for recurrent stroke in obese stroke patients. *International journal of stroke : official journal of the International Stroke Society*. 2013
5. Curtis JP, Selter JG, Wang Y, Rathore SS, Jovin IS, Jadbabaie F, et al. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med*. 2005; 165:55–61. [PubMed: 15642875]
6. Dixon JB, Egger GJ. A narrow view of optimal weight for health generates the obesity paradox. *The American journal of clinical nutrition*. 2014; 99:969–70. [PubMed: 24670944]
7. Cespedes, Elizabeth MCHK., Bradshaw, Patrick T., Chen, Wendy Y., Prado, Carla M., Weltzien, Erin K., Castillo, Adrienne L., Caan, Bette J. Post-diagnosis Weight Change and Survival Following a Diagnosis of Early Stage Breast Cancer *Cancer Epidemiology Biomarkers & Prevention*. 2016
8. Meyerhardt, Jeffrey ACHK., Prado, Carla M., Kwan, Marilyn, Castillo, Adrienne, Weltzien, Erin, Cespedes, Elizabeth M., Xiao, Jingjie, Caan, Bette J. Association of Weight Change after Colorectal Cancer Diagnosis and Outcomes in the Kaiser Permanente Northern California Population. *Cancer Epidemiology Biomarkers & Prevention*. 2016
9. Heather Greenlee JMU, LeBlanc Michael, Ramsey Scott, Hershman Dawn L. Association between body mass index (BMI) and cancer survival in a pooled analysis of 22 clinical trials. *Cancer Epidemiology Biomarkers & Prevention*. 2016
10. Colantonio LD, Burrone MS. Factors involved in the paradox of reverse epidemiology. *Clinical nutrition (Edinburgh, Scotland)*. 2014; 33:729.
11. Banack HR, Kaufman JS. From bad to worse: collider stratification amplifies confounding bias in the “obesity paradox”. *European journal of epidemiology*. 2015; 30:1111–4. [PubMed: 26187718]
12. Sperrin M, Candlish J, Badrick E, Renehan A, Buchan I. Collider Bias Is Only a Partial Explanation for the Obesity Paradox. *Epidemiology (Cambridge, Mass)*. 2016; 27:525–30.
13. Broughman JR, Williams GR, Deal AM, Yu H, Nyrop KA, Alston SM, et al. Prevalence of sarcopenia in older patients with colorectal cancer. *Journal of geriatric oncology*. 2015; 6:442–5. [PubMed: 26365898]
14. Gioulbasanis I, Baracos VE, Giannousi Z, Xyrafas A, Martin L, Georgoulas V, et al. Baseline nutritional evaluation in metastatic lung cancer patients: Mini Nutritional Assessment versus weight loss history. *Annals of oncology : official journal of the European Society for Medical Oncology / ESMO*. 2011; 22:835–41.
15. Klesges RC, Meyers AW, Klesges LM, La Vasque ME. Smoking, body weight, and their effects on smoking behavior: a comprehensive review of the literature. *Psychological bulletin*. 1989; 106:204–30. [PubMed: 2678202]
16. Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP. Weight change in old age and its association with mortality. *J Am Geriatr Soc*. 2001; 49:1309–18. [PubMed: 11890489]

17. Wallace JI, Schwartz RS. Involuntary weight loss in elderly outpatients: recognition, etiologies, and treatment. *Clinics in geriatric medicine*. 1997; 13:717–35. [PubMed: 9354751]
18. Kritchevsky SB, Wilcosky TC, Morris DL, Truong KN, Tyroler HA. Changes in plasma lipid and lipoprotein cholesterol and weight prior to the diagnosis of cancer. *Cancer research*. 1991; 51:3198–203. [PubMed: 2039996]
19. Petruzzelli M, Wagner EF. Mechanisms of metabolic dysfunction in cancer-associated cachexia. *Genes & development*. 2016; 30:489–501. [PubMed: 26944676]
20. Twig G, Yaniv G, Levine H, Leiba A, Goldberger N, Derazne E, et al. Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood. *The New England journal of medicine*. 2016; 374:2430–40. [PubMed: 27074389]
21. Shah AD, Kandula NR, Lin F, Allison MA, Carr J, Herrington D, et al. Less favorable body composition and adipokines in South Asians compared with other US ethnic groups: results from the MASALA and MESA studies. *International journal of obesity (2005)*. 2016; 40:639–45. [PubMed: 26499444]
22. Cruz-Jentoft AJ, Landi F, Schneider SM, Zuniga C, Arai H, Boirie Y, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age and ageing*. 2014; 43:748–59. [PubMed: 25241753]
23. Cruz-Jentoft AJ, Landi F, Topinkova E, Michel JP. Understanding sarcopenia as a geriatric syndrome. *Current opinion in clinical nutrition and metabolic care*. 2010; 13:1–7. [PubMed: 19915458]
24. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age and ageing*. 2010; 39:412–23. [PubMed: 20392703]
25. Habicht JP. Some characteristics of indicators of nutritional status for use in screening and surveillance. *The American journal of clinical nutrition*. 1980; 33:531–5. [PubMed: 7355836]
26. Kazemi-Bajestani SM, Mazurak VC, Baracos V. Computed tomography-defined muscle and fat wasting are associated with cancer clinical outcomes. *Seminars in cell & developmental biology*. 2015
27. Shachar SS, Williams GR, Muss HB, Nishijima TF. Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review. *European journal of cancer (Oxford, England : 1990)*. 2016; 57:58–67.
28. Zhuang CL, Huang DD, Pang WY, Zhou CJ, Wang SL, Lou N, et al. Sarcopenia is an Independent Predictor of Severe Postoperative Complications and Long-Term Survival After Radical Gastrectomy for Gastric Cancer: Analysis from a Large-Scale Cohort. *Medicine*. 2016; 95:e3164. [PubMed: 27043677]
29. de Gagliato DM, Gonzalez-Angulo AM, Lei X, Theriault RL, Giordano SH, Valero V, et al. Clinical impact of delaying initiation of adjuvant chemotherapy in patients with breast cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2014; 32:735–44. [PubMed: 24470007]
30. Prado CM, Lima IS, Baracos VE, Bies RR, McCargar LJ, Reiman T, et al. An exploratory study of body composition as a determinant of epirubicin pharmacokinetics and toxicity. *Cancer chemotherapy and pharmacology*. 2011; 67:93–101. [PubMed: 20204364]
31. Prado CM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 2009; 15:2920–6. [PubMed: 19351764]
32. Joseph N, Clark RM, Dizon DS, Lee MS, Goodman A, Boruta D Jr, et al. Delay in chemotherapy administration impacts survival in elderly patients with epithelial ovarian cancer. *Gynecologic oncology*. 2015; 137:401–5. [PubMed: 25839911]
33. Wood WC, Budman DR, Korzun AH, Cooper MR, Younger J, Hart RD, et al. Dose and dose intensity of adjuvant chemotherapy for stage II, node-positive breast carcinoma. *The New England journal of medicine*. 1994; 330:1253–9. [PubMed: 8080512]



34. Malietzis G, Johns N, Al-Hassi HO, Knight SC, Kennedy RH, Fearon KC, et al. Low Muscularity and Myosteatosis Is Related to the Host Systemic Inflammatory Response in Patients Undergoing Surgery for Colorectal Cancer. *Annals of surgery*. 2016; 263:320–5. [PubMed: 25643288]
35. Moore SC, Lee IM, Weiderpass E, Campbell PT, Sampson JN, Kitahara CM, et al. Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. *JAMA internal medicine*. 2016; 176:816–25. [PubMed: 27183032]
36. Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. *Jama*. 2005; 293:2479–86. [PubMed: 15914748]
37. Engel F, Hartel S, Wagner MO, Strahler J, Bos K, Sperlich B. Hormonal, metabolic, and cardiorespiratory responses of young and adult athletes to a single session of high-intensity cycle exercise. *Pediatric exercise science*. 2014; 26:485–94. [PubMed: 25050695]
38. Jackson SE, Chester JD. Personalised cancer medicine. *International journal of cancer*. 2015; 137:262–6. [PubMed: 24789362]
39. Baselga J, Cortes J, Kim SB, Im SA, Hegg R, Im YH, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *The New England journal of medicine*. 2012; 366:109–19. [PubMed: 22149875]
40. Shaw AT, Kim DW, Nakagawa K, Seto T, Crino L, Ahn MJ, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. *The New England journal of medicine*. 2013; 368:2385–94. [PubMed: 23724913]
41. Sjøblom B, Grønberg BH, Wentzel-Larsen T, Baracos VE, Hjørnstad MJ, Aass N, et al. Skeletal muscle radiodensity is prognostic for survival in patients with advanced non-small cell lung cancer. *Clinical Nutrition (Edinburgh, Scotland)*. 2016
42. Blauwhoff-Buskermolen S, Versteeg KS, de van der Schueren MA, den Braver NR, Berkhof J, Langius JA, et al. Loss of Muscle Mass During Chemotherapy Is Predictive for Poor Survival of Patients With Metastatic Colorectal Cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2016; 34:1339–44. [PubMed: 26903572]
43. Niraula S, Ocana A, Ennis M, Goodwin PJ. Body size and breast cancer prognosis in relation to hormone receptor and menopausal status: a meta-analysis. *Breast cancer research and treatment*. 2012; 134:769–81. [PubMed: 22562122]
44. Abrahamson PE, Gammon MD, Lund MJ, Flagg EW, Porter PL, Stevens J, et al. General and abdominal obesity and survival among young women with breast cancer. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2006; 15(10):1871–7.
45. Playdon MC, Bracken MB, Sanft TB, Ligibel JA, Harrigan M, Irwin ML. Weight Gain After Breast Cancer Diagnosis and All-Cause Mortality: Systematic Review and Meta-Analysis. *Journal of the National Cancer Institute*. 2015:107.
46. Villasenor A, Ballard-Barbash R, Baumgartner K, Baumgartner R, Bernstein L, McTiernan A, et al. Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study. *J Cancer Surviv*. 2012; 6:398–406. [PubMed: 23054848]
47. Antoun S, Bayar A, Ileana E, Laplanche A, Fizazi K, di Palma M, et al. High subcutaneous adipose tissue predicts the prognosis in metastatic castration-resistant prostate cancer patients in post chemotherapy setting. *European journal of cancer (Oxford, England : 1990)*. 2015; 51:2570–7.
48. Ballian N, Lubner MG, Munoz A, Harms BA, Heise CP, Foley EF, et al. Visceral obesity is associated with outcomes of total mesorectal excision for rectal adenocarcinoma. *Journal of surgical oncology*. 2012; 105:365–70. [PubMed: 21751219]
49. Balentine CJ, Enriquez J, Fisher W, Hodges S, Bansal V, Sansgiry S, et al. Intra-abdominal fat predicts survival in pancreatic cancer. *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2010; 14:1832–7. [PubMed: 20725799]
50. Ladoire S, Bonnetain F, Gauthier M, Zanetta S, Petit JM, Guiu S, et al. Visceral fat area as a new independent predictive factor of survival in patients with metastatic renal cell carcinoma treated with antiangiogenic agents. *The oncologist*. 2011; 16:71–81.
51. Tartari RF, Ulbrich-Kulczynski JM, Filho AF. Measurement of mid-arm muscle circumference and prognosis in stage IV non-small cell lung cancer patients. *Oncology letters*. 2013; 5:1063–7. [PubMed: 23426523]

**Table 1**

Differences in body composition between various ethnic groups

|                           | Body mass index* (kg/m <sup>2</sup> )<br>Mean | Lean mass area (cm <sup>2</sup> )<br>Mean (95% CI) | Visceral fat (cm <sup>2</sup> )<br>Mean (95% CI) | Subcutaneous fat (cm <sup>2</sup> )<br>Mean (95% CI) |
|---------------------------|---|--|--|--|
| White<br>N=785            | 27.8  | 98 (95–100)  | 159 (153–165)                                    | 253 (243–264)  |
| African American<br>N=407 | 30.2  | 104 (101–108)                                      | 128 (120–136)                                    | 298 (283–313)  |
| Latino<br>N=501           | 29.4  | 99 (95–102)  | 164 (157–172)                                    | 264 (250–278)  |
| South Asian<br>N=903      | 25.8  | 93(91–69)  | 134 (129–140)                                    | 237 (227–246)  |
| Chinese American<br>N=251 | 24  | 89 (85–94)   | 114 (104–125)                                    | 177 (160–195)  |

\* BMI recorded from the all MASALA/MESA studies.

Reprinted by permission from Macmillan Publishers Ltd: International Journal of Obesity (21), copyright 2016

Table 2

Selected body measures and their association with cancer outcomes

| Body measure                        | Method of calculation/measure                          | Examples for prognostic evidence  |
|-------------------------------------|--|---|
| Weight at diagnosis                 | Weight scale (kg)                                      | Breast cancer-worse overall survival (OS) (HR = 1.31 (95% CI 1.17–1.46)) for heavier vs lighter(43)   |
| BMI at diagnosis                    | Weight scale/meter weight(kg)/height (m <sup>2</sup> ) | Contradicting evidence:<br>- Better survival for higher BMI in men-SWOG trials (HR=0.82;p=0.003)(9)<br>- Worse survival in early breast cancer with higher BMI (HR=1.48,95% CI 1.09–2.01)(44)   |
| Weight changes after diagnosis      | Weight scale(kg)                                       | Contradicting evidence in early breast cancer<br>- Meta-analysis weight gain 10.0% associated with all-cause mortality (HR = 1.23, 95% CI 1.09–1.39)(45);<br>Breast cancer-large cohort-weight loss 10% was associated with worse survival, all-cause mortality 2.63 (2.12, 3.26)(7)<br>Colorectal cancer-specific mortality (HR)3.20; 95% [CI]. 2.33–4.39; p < 0.0001(8) |
| Sarcopenia (low muscle mass)        | DEXA/CT scan/MRI                                       | Recent meta-analysis in different types and stages (HR=1.44, 95% CI = 1.32–1.56, p < 0.001)(27)<br>HEAL-early breast cancer survivors-higher overall mortality in sarcopenic patients (HR = 2.86, 95 % CI, 1.67–4.89)(46)   |
| Muscle radiodensity-(mean (HU))     | CT scan/MRI  | Several studies low radiodensity associated with short survival (41, 42)  |
| Subcutaneous adipose tissue (SAT)   | CT scan/MRI  | Advanced prostate cancer-in multivariate analysis, SAT index was statistically significant predictors of OS (p = 0.036)(47)   |
| Visceral adipose tissue (VAT)       | CT scan/MRI  | Mainly reported VAT/SAT ratio-increasing ratio result in better overall survival (48)<br>Higher VAT associated with worse survival (49, 50)   |
| Mid-arm muscle circumference (MAMC) | Measuring tape (cm)                                    | Better OS with normal MAMC (HR=0.21, 95% CI, 0.09–0.5)(51)  |

Abbreviations: BMI-body mass index; HR-hazard ratio; CI-confidence interval; DEXA-Dual-energy X-ray absorptiometry; CT-computed tomography; MRI - magnetic resonance imaging; HU-Hounsfield unit; SWOG-Southwest Oncology Group