Cancer and Body Composition: An Association of Global Relevance

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Abstract

Context: Worldwide, cancer is the second leading cause of death, with a rapidly increasing global incidence: it is present in high and in lower-middle income countries (LMICs). Overweight and obesity are also a major global health concern, and while they were once considered conditions specific to the ‘Western’ world, this geographic patterning has begun to shift.

Evidence Acquisition: Given the large body of evidence regarding associations between lower socioeconomic status and greater cancer incidence and mortality, we undertook a narrative review focusing on global cancer burden and risk, and the association between cancer and body composition, particularly in LMICs. Using the MeSH terms ‘cancer’ and ‘body composition’, and keywords ‘overweight’ or ‘obesity’, and the phrase ‘lower-and middle-income countries’, we identified relevant articles for inclusion in this narrative review.

Results: The key diagnostic mechanism underpinning these associations may be the varied prevalence and distribution of the risk factors most commonly associated to cancer incidence, including smoking, alcohol and diet. Approximately one-third of cancer-related deaths in high income countries (HICs) are due to dietary and behavioural risk factors, which includes overweight and obesity and physical inactivity, and these same risk factors are prevalent in LMICs, which is where the current, yet minimal, priorities for cancer prevention are aimed at reducing.

Conclusions: These data have specific relevance to LMICs in context of increasing levels of obesity, fewer healthcare resources in many LMICs, and lower financial investment into the prevention and management of cancer. Recognising and understanding the process by which cancer risk is linked to body composition parameters and obesity-related lifestyle factors will inform future intervention and prevention efforts. The focus needs to be directed towards implementing and practising such programs across all sectors of the globe, especially within low socioeconomic subpopulations.

Keywords: Lower- and Middle-Income Countries, Cancer, Body Composition, Overweight, Obesity

1. Context

The International Agency for Research on Cancer, part of the World Health Organization (WHO), has established that overweight and obesity are known risk factors for many types of cancers (1-9); the incidence of these cancers is also exponentially increasing and becoming a major global health issue (5, 10). Overweight and obesity prevalence has grown to be a pandemic situation globally (11-13), with over 1.9 billion adults worldwide being overweight or obese (14). Overweight and obesity were once considered conditions of the ‘Western’ world, but many lower-middle income countries (LMICs) are no exception to this, with markedly increased prevalence now observed in the incidence and prevalence of obesity (15-18). Indeed, recent data from the WHO Study on ageing indicated that more than 70% of participants from Russian Federation and South Africa were in classes 1 and 2 of obese body mass index (BMI) categories (19). Lower-middle income countries (LMICs) can no longer be absent from discussions regarding obesity prevalence.

The millennium development goals, which sought to reduce extreme poverty and improve health, were replaced by the sustainable development goals in 2015 (20), which broadened to include non-communicable diseases, such as cancer, and indicators that consider the interaction of environmental, societal and economic factors on health (21). The United Nations defines LMICs as encompassing all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia (22). Globally, LMICs account for 57% of cancer cases, despite their larger share of the population (22). Indeed, chronic conditions are becoming the dominant health concern in

LMICs above and beyond communicable diseases such as malaria and human immunodeficiency virus (HIV) (23).

To date, financial investment of LMICs in addressing cancer prevalence has not to date been commensurate with need (23). For instance, populations of LMICs experience the greatest number of cancer-related deaths and disability (22-24), however only 5% of all cancer-directed global health resources are invested in these countries, making it an equity issue (23).

Here we present a review of cancer and body composition in both LMICs and non-LMICs; this is of global importance due to the ever-increasing incidence of both cancer and overweight and obesity seen worldwide, and the lack of knowledge and prevention efforts within LMICs, even though a greater level of burden and rates of death due to cancers are experienced.

2. Evidence Acquisition

Using the MeSH terms ‘cancer’ AND ‘body composition’, with keywords of ‘overweight’ OR ‘obesity’, and the phrase ‘lower-and middle-income countries’, we identified articles that investigated the association between cancer and body composition, particularly in LMICs, and included them in this narrative review.

3. Results

3.1. Burden of Cancer

The increasing incidence of cancer incidence affects people of all demographics and across the entire world (25, 26). With cancer survival rates at an all-time high (27), the rapid increase in incidence far exceeds the advancement of current survival chances (1). Cancer is the second leading causes of death worldwide (24) and the WHO estimated that there were approximately 14.9 million new cases of cancer in 2013, along with 8.2 million cancer-related deaths (24, 26). Cancer is prevalent in high income countries (HICs) and in LMICs, and affects those of all socioeconomic backgrounds (3, 5, 28), with 56% of incident cancers, 62% of deaths, and 70% of disability-adjusted life years (DALYs) occurring in LMICs (22-24). The notable increase in cancer incidence is accentuated by 2015 data showing 18.6 million newly diagnosed cases of cancer (~25% increase in incidence since 2013), and the predicted rise to 22 million (75% increase) within the next two decades (26).

The morbidity associated with cancer has a profound effect in the population, where in 2013 there is an estimation total of 196.3 million DALYs lost due to cancer globally (24), making it a foremost significant health burden in the global population (29). DALYs are a combined measurement of premature death, in terms of the years of life lost, and non-fatal health outcomes, in terms of ‘healthy’ life lost, due to disease, disability or injury (29). The more accumulated DALYs that are associated with a particular disease, the greater the burden of that disease (29).

Given that death rates attributable to cancer are increasing in LMICs, understanding the processes by which obesity is suggested as being one of the key risk factors for cancer will inform where and how best to intervene in efforts to reduce the worldwide burden of cancer. In addition, a greater understanding will increase public awareness, identify appropriate targets and pathways for prevention, and will enhance global efforts to reduce cancer-related mortality. Indeed, data from HICs suggest that as many as 54% of gallbladder cancers and 44% of esophageal adenocarcinomas are attributed to overweight or obesity (30), thus indicating the extent of cancer burden that could be decreased by reducing the prevalence of obesity.

3.2. Social Gradient of Cancer

The social determinants of health are defined by the WHO as the conditions in which a person is born, lives, grows, works and ages (31). These determinants encompass the distribution of economic and social conditions that influence individual and group differences in health status (31, 32). The ‘social gradient of health’ is a concept that refers to poorer health outcomes being more likely observed in socially disadvantaged population groups (33). Indeed, evidence from LMICs suggests that SES across the life-course influences cancer-related risk factors (34). Furthermore, data suggests that SES influences cancer incidence and mortality; however, this varies by cancer type. For example, lung cancer incidence is higher for those of lower SES, whereas breast cancer incidence is higher amongst women of higher SES (34). The diagnosis of breast cancer may likely occur prior to symptoms, thus the difference in associations, particularly in LMICs where access to diagnostic testing is limited, may be related to diagnosis itself varied prevalence (34).

Approximately 30% of cancer-related deaths in HICs are due to leading dietary and behavioural risks, including overweight and obesity, and physical inactivity (26, 35, 36). However, priorities for cancer prevention appear to primarily aim at reducing tobacco and alcohol consumption, rather than reducing risk factors for obesity or obesity per se (23). Given the marked increase in obesity in LMICs, populations are thus already predisposed to developing a preventable cancer. Cancer care is prioritized according to a cost-effective hierarchy, and the prevention of preventable cancers is foremost of the cancer-elimination
It is imperative to recognise the link between modifiable risk factors and cancer, to inform the development of effective intervention strategies aimed at reducing the number of preventable cancer cases that are associated with increased adiposity (5).

3.3. Cancer and Body Composition

Reports from extant literature identify greater BMI as a risk factor for some cancers (1-7). However, BMI is limited as an indicator of the relative amounts of fat and lean tissue in the body because it is simply a measure of body weight-for-height (25, 37), and so it remains unclear about the contribution of fat and lean tissue components of body composition that affect cancer risk. Nonetheless, the ascertainment of BMI is quick, easy and cost-effective, thus increasing the practicality of measuring this modifiable risk factor for cancer in healthcare settings in LMICs.

Similarly, accessible measures in LMICs are anthropometric factors such as waist circumference and waist/hip ratio are more direct measures of centrally-accumulated body fat that are strongly associated with cancer risk (38). Much less readily available in LMICs are imaging techniques such as dual-energy X-ray absorptiometry (DXA), which enable to the quantification of centrally-accumulated body fat (38). DXA measures enable the clinical quantification of lean and fat mass, and the distribution of lean tissue of the individual, which may also potentiate the risk for cancer development (13, 39). However, DXA is not recommended for clinical assessment of body composition to determine risk factors for cancer, thus LMICs are not disproportionately disadvantaged in this area.

While the Global Burden of Disease Study 2016 (21, 40, 41) describes cancer prevalence and incidence in LMICs and HICs, to the best of our knowledge, there are no data specifically from LMICs regarding associations between cancer and body composition, including fat and lean mass. This paucity of data highlights the need for further investigation into LMICs to elucidate modifiable risk factors for cancer, which will subsequently inform prevention, policy and public health action.

3.4. Cancer and Body Fat

Globally, approximately 1.46 billion people in 2008 were overweight (≈ 33% of the total global population), with 500 million of these considered obese (42-44). By 2013 the number of overweight individuals had increased to more than 2 billion, 671 million of which were obese (43). The rising incidence of overweight and obesity has profound clinical implications on cancer (6, 37): importantly, the modifiable nature of obesity means that adipose-associated cancer is preventable (14). Furthermore, overweight and obesity can also be predictors of tumour pathogenicity and aggressiveness in cancers that are obesity-attributable (45), and obesity has been identified as an etiologic factor in various cancers (46), and associated with many others (1-7).

In a study by Renehan et al. excess BMI-attributable cancer burden was estimated using pooled data from 30 European countries in order to inform future predictions, and it was found that approximately 70,000 new cancer cases were attributable to excess BMI in 2002 in these countries (25). A prospective Australian study of 24,479 women aged 40-69 years, with 13,974 postmenopausal women assessed for the role of body composition in the risk of invasive breast cancer (38). It was found that at ~ 15 years post-menopause, the association of body size and cancer risk increased greatly. Furthermore, tumours that were estrogen receptor positive or of high grade showed a stronger obesity-breast cancer relationship (38). Whilst that study focused only on breast cancer, the use of clinically-ascertained measures of anthropometry was essential to the strength of that study. For instance, it is imperative that both the amount and distribution of body fat is measured accurately, as regional accumulation of fats can have varying physiological effects which may play a role in the etiology or type of the developing cancer. High levels of estrogen promote tumorigenic effects both directly and indirectly (5). Given that obese women have more fat tissue, the production of estrogen is greater, which subsequently leads to more rapid growth and increased aggressiveness of breast tumours (3). However, associations may also depend on menopausal status (6). Overweight and obese postmenopausal women, and their higher circulating levels of estrogen, increase the susceptibility to developing estrogen- or hormone-receptive breast cancer (3, 47). Furthermore, premenopausal women who are overweight or obese are at a predisposition of developing triple-negative breast cancer (5). Regardless of tumour type, overweight and obese breast cancer patients also have a significantly worse prognosis than their non-obese peers (5). For instance, Osman and Hennessy (3) reported that obese premenopausal women with breast cancer were more likely to experience metastases development compared to non-obese women.

3.5. Cancer and Lean Tissue

Lean body mass constitutes metabolically active fat-free mass and comprises muscles, skin, connective tissue, and the lean components of adipose tissue, including water and protein (48). Given that lean tissue is imperative for immune function, protein synthesis, and mobility, there is
a clear imperative to maintain muscle, in order to avoid extensive physiological impairments (39).

Decreased lean mass is an outcome of cancer cachexia, which is characterized by involuntary and progressive weight loss, increased muscle protein catabolism, adipose tissue wasting, and metabolic alterations (39). While adipose tissue loss accounts for the greater portion of weight loss, the decline in the lean tissue is what causes physical and clinical deterioration (39). In other non-malignant diseases it has been noted that skeletal muscle depletion has been associated with increased clinical and physical implications, as well as increased mortality (39, 49). Whereas cachexia is a known outcome of cancer (39), the concept of lean tissue mass as being either a risk or protective factor for cancer development is still essentially novel thus requiring further investigation.

Like visceral fat, muscle tissue also produces metabolically active myokines, such as interleukins and leukaemia inhibitory factor (50), which may have anti-proliferative effects on tumours (51). While a role for lean tissue in the risk for cancer has been little investigated, there is biological plausibility for such an association. For instance, Zhang et al. suggested that physical inactivity, or a low level of cardiorespiratory fitness, increased the risk of cancer-related deaths (28). While an increasingly sedentary lifestyle has been found to be a major contributor to obesity (52), it also contributes to loss of lean tissue (53). By contrast, regular physical activity, and the resultant increase in lean tissue, may contribute to cancer prevention by modifying the production of myokine interleukin-6, a muscle-derived anti-inflammatory cytokine, and heat-shock proteins, as well as by inhibiting the release of pro-inflammatory mediators from visceral fat (53), which are known to promote the development of malignancies (3, 54, 55). The current physical activity guidelines, as specified by the WHO, is for at least 150 minutes of moderate-intensity aerobic exercise throughout the week, or at least 75 minutes of vigorous-intensity aerobic activity throughout the week, or a combination of both for those aged 18 years and older (56, 57). Moderate and regular physical activity has been shown by Theriau et al. to reduce the incidence of breast cancer in women by 20% - 30% when compared to women who are physically inactive, and likely to have decreased lean tissue (52).

4. Conclusions

Cancer is becoming one of the most significant health burdens across the globe (23). Being the second leading cause of death worldwide (24), it is imperative that modifiable risk factors for cancer onset and progression be identified and addressed in high, as well as LMICs (8, 26). Overall, weight and obesity are well-established as being a modifiable risk factor for a potentially preventative group of cancers in HICs (9); an association which is also becoming increasingly prevalent amongst the developing world. While the incidence of preventable cancers is increasing globally, the number of deaths from these cancers is taking the greatest effect within LMICs, yet there is still only a minority of the world’s total global cancer prevention resources being directed into these countries (23).

The preclusion of preventable cancers is the first and foremost pathway to take when trying to reduce the global incidence and burden of cancer (23), and we need to focus on delineating the current worldwide cancer prevention efforts, such as the Sustainable Development Goals, into LMICs and put them into practice where they are accessible to all sociodemographic groups. By utilising the modifiable aspect of body composition and by recognising that specific interventions differentially target fat and lean tissue, there are evident clinical and public health implications for any relationships found between body fat, lean tissue, and cancer.

4.1. Implication of Manuscript

Compared to HICs, LMICs currently have very few resources and policies in place to stem the progression of preventable cancer incidence. By identifying the modifiability of body composition, we can inform future health policy and prevention strategies in populations of LMICs.

Footnotes

Authors’ Contribution: Darci Green, Julie Anne Pasco, Lana Jane Williams and Sharon Lee Brennan-Olsen conceptualised the aim for this review article, and all authors edited and reviewed the aim. Darci Green and Julie Anne Pasco drafted the manuscript, and all authors edited and contributed to the writing of this paper. All authors, Darci Green, Julie Anne Pasco Lana Jane Williams and Sharon Lee Brennan-Olsen, read and approved the final version and guarantee the review.

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