



Body Fat and Risk of Breast Cancer in Postmenopausal Women: What Is the Truth?

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Body fat has been connected with breast cancer risk in postmenopausal women with normal body mass index (BMI) [1]. A persistent association between higher trunk fat and increased risk of estrogen receptor (ER)-positive breast cancer has been found in women who remained in the normal BMI range during the follow-up period [1]. However, it is still unknown because excess adiposity is linked to increased risk in women with a normal BMI [1]. Moreover, the role of fat loss interventions and anti-estrogen therapy for breast cancer risk reduction in postmenopausal women with normal BMI and high body fat levels is not well-defined [1]. Obesity is related to an increased risk of breast cancer, including the ER-positive subtype in postmenopausal women [1]. Obesity has been shown to down-regulate the expression of microRNA-126 (miR-126) [2]. miR-126 has been proposed to act as a tumor suppressor in breast cancer growth and metastasis [3]. It has been reported that miR-126 expression is markedly down-regulated in human breast cancer tissues when compared with adjacent normal tissues [3]. Overexpression of miR-126 has been demonstrated to inhibit the invasion of breast cancer cell lines in vitro [3]. In healthy post-menopausal women, the serum levels of miR-126-3p have been detected to be much lower than that in healthy young women suggesting that 17 β -estradiol (E2) may regulate miR-126 -3p in physiological status [4]. miR-126 has emerged to be the direct target of estrogens in human endothelial cells [5]. E2 has been demonstrated to enhance miR-126-3p expression via up-regulation of Ets-1 [5]. Ets-1 represents the well-known transcription factor driving miR-126 expression [4]. Ets-1

transcription factor overexpression in breast cancers has been correlated with invasiveness and a poor prognosis by driving carcinoma cell invasion [5]. Ets-1 has been found to play a critical role in coordinating multiple invasive features of cancer cells [5]. Taken together, I suppose that estrogens seemingly play contradictory actions in breast cancer. On one hand, estrogens appears to reduce the chance of developing breast cancer by up-regulating miR-126 and, on the other hand, they seem to be directly involved in breast tumorigenesis by overexpression of Ets-1. Mechanistically, I hypothesize the existence of a negative-feedback loop between miR-126 expression and Ets-1-induced breast cancer. Further research examining the effect of estrogens, miR-126 and Ets-1 on breast cancer risk appears to be warranted among postmenopausal women. I suggest that fat loss interventions via physical activity and dietary management should represent a reasonable strategy for preventing breast cancer in postmenopausal women taking into account the impact of high body fat levels and the apparently contradictory actions of estrogens on cancer development.

Compliance with Ethical Standards

Conflict of Interest The author declares no potential conflicts of interest.

References

1. Iyengar NM, Arthur R, Manson JE, Chlebowski RT, Kroenke CH, Peterson L, Cheng TD, Feliciano EC, Lane D, Luo J, Nassir R, Pan K, Wassertheil-Smoller S, Kamensky V, Rohan TE, Dannenberg AJ (2018) Association of body fat and risk of breast cancer in postmenopausal women with normal body mass index: a secondary analysis of a randomized clinical trial and observational study. *JAMA Oncol* 5:155. <https://doi.org/10.1001/jamaoncol.2018.5327>
2. Gomes JL, Fernandes T, Soci UP, Silveira AC, Barretti DL, Negrão CE, Oliveira EM (2017) Obesity downregulates MicroRNA-126 inducing capillary rarefaction in skeletal muscle: effects of aerobic exercise training. *Oxidative Med Cell Longev* 2017:2415246

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3. Wang CZ, Yuan P, Li Y (2015 Jun 1) MiR-126 regulated breast cancer cell invasion by targeting ADAM9. *Int J Clin Exp Pathol* 8(6):6547–6553
4. Li P, Wei J, Li X, Cheng Y, Chen W, Cui Y, Simoncini T, Gu Z, Yang J, Fu X (2017) 17 β -estradiol enhances vascular endothelial Ets-1/miR-126-3p expression: the possible mechanism for attenuation of atherosclerosis. *J Clin Endocrinol Metab* 102(2):594–603
5. Furlan A, Vercamer C, Heliot L, Wernert N, Desbiens X, Poutier A (2019) Ets-1 drives breast cancer cell angiogenic potential and interactions between breast cancer and endothelial cells. *Int J Oncol* 54(1):29–40

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