Weight Gain in Young Women Alters Risk for Some Breast Cancer Subtypes

March 17, 2014

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Anthropometric traits, such as body weight and height, have been shown to impact breast cancer risk. Body mass index (BMI) is negatively associated, and height is positively associated, with breast cancer risk in premenopausal women. Less studied is the impact of changes in BMI over time, however, or of the impact of anthropometric traits on molecular subtypes of breast cancer, which have distinct biologies and unique etiologies. Given that some of the more aggressive breast cancer subtypes are associated with age, evaluating the effect of these anthropomorphic traits on risk of breast cancer subtypes in young women may be useful. In a recent study published in *Cancer*, Drs. Masaaki Kawai and Christopher Li in the Public Health Sciences Division report that changes in BMI since age 18 do impact breast cancer risk for some molecular subtypes of breast cancer, but not others. Additionally, the authors also found that these associations may depend on whether or not a woman has ever had a live birth (parity status).

To evaluate these questions, the authors analyzed data from a Seattle-based cohort study investigating breast cancer risk in women aged 20-44 (Li *et al.*, 2012). Breast cancer cases were grouped into three categories, based on the molecular subtype of the breast cancer: ER-positive (estrogen receptor positive), ER-negative/HER2-positive (estrogen receptor negative, human epidermal growth factor receptor 2 positive), and triple-negative (estrogen receptor negative, human epidermal growth factor receptor 2 negative, and progesterone receptor negative). The authors then evaluated the association between various anthropometric traits and each of these molecular subtypes.

Overall, the authors found no association between height, BMI at age 18, or recent BMI for any of the molecular subtypes. However, the authors did find an association when evaluating changes in BMI since age 18. Weight gain since age 18 was associated with a 7% increased risk of triple-negative breast cancer per 1 unit increase in BMI (odds ratio 1.07, 95% confidence interval 1.02-1.11). Furthermore, when compared to a BMI change less than 5 units, a BMI change of 10 or more was associated with a two-fold increased risk of triple-negative breast cancer (odds ratio 2.0, 95% confidence interval 1.2-3.3). According to Dr. Masaaki Kawai, the post-doctoral fellow who led the

study, "these results suggest that weight gain may be associated with risk of an aggressive type of breast cancer."

Since prior studies have identified differences in the risk associated with various reproductive and lifestyle characteristics across molecular subtypes of breast cancer, the authors further evaluated the potential impact of these additional factors. Of these, parity (whether or not a woman had ever had a live birth) was found to significantly modify the association between BMI change and the risk of ER-positive breast cancer (see figure). BMI change since age 18 was associated with a decreased risk of ER-positive breast cancer in nulliparous women (those who never had a live birth), but no association was observed in parous women (those who had at least one live birth). The opposite was observed for triple-negative breast cancer, where a positive association was observed in parous women, but not among nulliparous women.

While these results are interesting, said Kawai, "the underlying biological mechanisms are largely unknown." Obesity exerts a range of biologic effects, including on hormone and insulin-like growth factor-I levels, and the inverse association between BMI and premenopausal breast cancer risk overall is primarily hormonally driven. It is possible that the subtype-specific inverse association observed in this study may reflect that changes in breast tissue induced by pregnancy outweigh the effects of BMI on breast cancer risk. As such, "these results require confirmation by other studies," said Kawai. In the meantime, these results point to the potential insights that may be gained from investigating cancers according to their molecular subtypes.

Other PHS investigators contributing to this project were Drs. Kathleen Malone and Mei-Tzu Tang.

Kawai M, Malone KE, Tang MT, Li CI. 2014. Height, body mass index (BMI), BMI change, and the risk of estrogen receptor-positive, HER2-positive, and triple-negative breast cancer among women ages 20 to 44 years. *Cancer*. 2014 Feb 5. Doi: 10.1002/cncr.28601. [Epub ahead of print]

See also:

Li CI, Beaber EF, Tang MT, Porter PL, Daling JR, Malone KE. 2012. Effect of depo-medroxyprogesterone acetate on breast cancer risk among women 20 to 44 years of age. *Cancer Res*. 72(8):2028-35.

			Molecular subtype			
			ER-positive		Triple-negative	
Parity status (ever/never had a live birth)	Parous	BMI gain from age 18	OR	95% CI	OR	95% CI
		Per 1 unit	1.00	0.97-1.02	1.06	1.02-1.10
		< 5	1.0	ref.	1.0	ref.
		5 to 10	0.9	(0.7-1.2)	1.2	0.8-1.9
		≥10	1.0	0.7-1.4	2.1	1.3-3.4
		p-trend	0.70		0.008	
	Nulliparous	BMI gain from age 18	OR	95% CI	OR	95% CI
		Per 1 unit	0.93	0.89-0.97	0.97	0.91-1.04
		<5	1.0	ref.	1.0	ref.
		5 to 10	0.5	0.3-0.9	1.3	0.6-2.6
		≥10	0.3	0.2-0.6	0.5	0.2-1.5
		p-trend	<0.001		0.40	

Image provided by Dr. Jonathan Kocarnik

Association between change in BMI since age 18 and molecular subtype of breast cancer, by parity status. Among parous women, BMI gain was associated with increased risk of triple-negative breast cancer. Among nulliparous women, BMI gain was associated with decreased risk of estrogen receptor-positive breast cancer.