

Menopausal status impacts the relationship between body mass index and tumor characteristics in invasive lobular carcinoma of the breast

Harriet Rothschild¹, Kent Goodman², Christopher Benz^{1&3}, Rita A Mukhtar²

¹UCSF School of Medicine ²UCSF Department of General Surgery ³Buck Institute for Research on Aging



Background

- ILC is the second most common type of breast cancer and is primarily ER positive.
- ILC is more strongly associated with risk factors that modulate sex steroid hormones, including obesity and use of hormone replacement therapy.
- BMI and metabolic syndrome may impact the molecular characteristics of ILC.
- **Metabolic syndrome (3 of 5):** Obesity, Hypertension, Hypercholesterolemia, Hypertriglyceridemia, or Diabetes mellitus.

We evaluated the relationship between BMI, metabolic syndrome, and tumor characteristics by menopausal status in a single institution cohort of women with newly diagnosed ILC between 1996-2020.

Results

Main Finding 1: Post-menopausal patients had different metabolic phenotypes and hormonal subtypes of ILC.

Overall post-menopausal patients had:

- BMI over 25 (53.4% versus 40.0%, $p = 0.017$)
- Higher rate of metabolic syndrome (21.7% versus 6.7%, $p < 0.001$)
- More ER+/PR- (81, (25.1%) versus 14, (9.7%), $p < 0.001$), especially with normal BMI
- Higher Oncotype RS (16.7 versus 13.8, $p = 0.006$)

Main Finding 2: Within the post-menopausal group, normal weight patient had more aggressive tumors.

- **Post-menopausal normal weight** patients had greater proportion of aggressive RS compared to **post-menopausal overweight/obese** patients (18.9% versus 4.8%, $p = 0.028$).

	Pre-menopausal		Post-menopausal		P value
	ER+/PR+	ER+/PR-	ER+/PR+	ER+/PR-	
Normal weight	79 (89.8)	9 (10.2)	107 (70.9)	44 (29.1)	0.001*
Overweight	33 (89.2)	4 (10.8)	74 (74.8)	25 (25.3)	0.067*
Obese	19 (95)	1 (5)	61 (83.6)	12 (16.4)	0.191

Table 1. Tumor receptor subtype stratified by menopausal status and BMI.

Conclusions

- These post-menopausal RS and ER+/PR- findings are unexpected since obesity is associated with worse outcomes for breast cancer.
- Raises the possibility that the hormonal pathogenesis/estrogenic drive behind ILC differs in pre- vs post-menopausal women consistent with their different PR positivity rates.
- Could be due to the more **local production of estrogen** from higher breast adiposity in post-menopausal women relative to the greater **systemic ovarian production of estrogen** in pre-menopausal women.

Methods

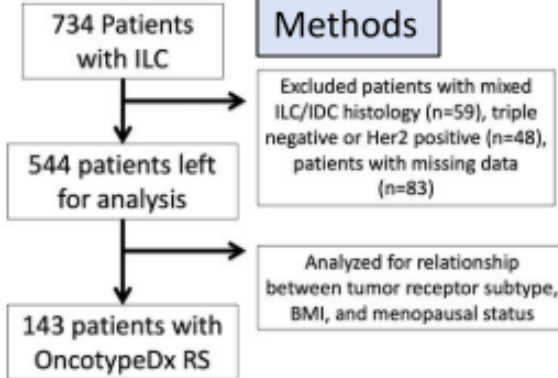


Figure 1. Consort diagram of case selection.

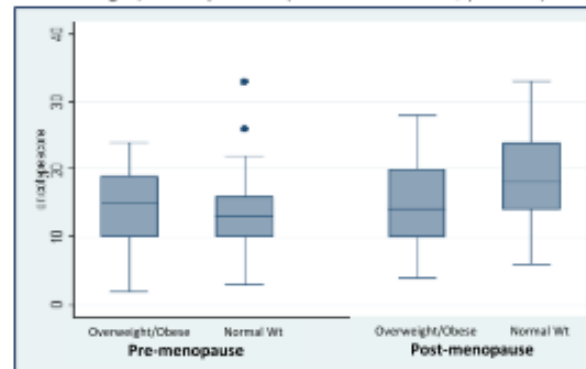


Figure 2. Oncotype score by menopausal status and BMI.

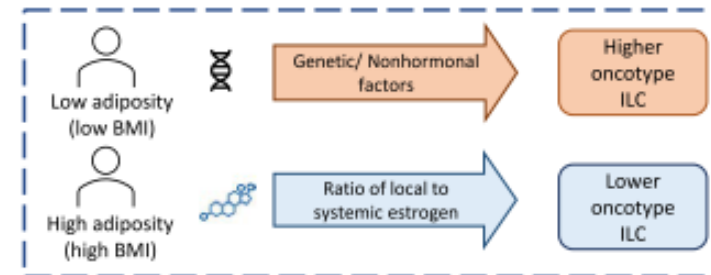


Figure 3. Simplified schematic of ILC development by BMI.