Validation of the Modified Preoperative Endocrine Prognostic Index (mPEPI) in a single institution cohort of patients with invasive lobular carcinoma

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The mPEPI Score

The Preoperative Endocrine Prognostic Index (PEPI) score is a validated tool that estimates recurrence risk following neoadjuvant endocrine therapy (NET). Prior studies have demonstrated that patients with PEPI=0 have significantly lower recurrence risk compared to those with PEPI>0.[1]

Background

- Invasive lobular carcinoma (ILC) is the second most common subtype of breast cancer, accounting for up to 15% of cases
- ER-signaling biology in ILC is distinct from that of invasive ductal carcinoma, which may contribute to its differential response to systemic therapies
- NET is increasingly used in early-stage ER+/HER2- breast cancer to downstage tumors
- Neither the PEPI nor the modified PEPI (mPEPI) score have been studied specifically in ILC, which lacks validated markers of treatment response
- In this study, we evaluated the ability of the mPEPI score to predict recurrence risk in patients with ILC

Methods

- We retrospectively analyzed a prospectively maintained institutional ILC database
- Patients with ER+/HER2- ILC who received NET, underwent surgery, and had available Ki-67 data were identified
- For each patient, an mPEPI score was calculated as 0-3, with 1 point given for each of the following:
  - Pathologic tumor size >5 cm
  - Positive pathologic nodal status
  - Post-treatment Ki-67 >2.7%
- mPEPI scores were compared individually and as composite groups:
  - 0 versus 1+
  - 0-1 versus 2-3
- Kaplan-Meier method and log-rank test were used to compare recurrence-free survival (RFS), local recurrence-free survival (LRFS), distant recurrence-free survival (DRFS), and overall survival (OS) across mPEPI scores. Follow-up was administratively censored at 100 months.

In ILC patients treated with neoadjuvant endocrine therapy, higher mPEPI scores were associated with worse recurrence outcomes, specifically in postmenopausal patients.

Figure 1. Distribution of mPEPI scores (n=124)

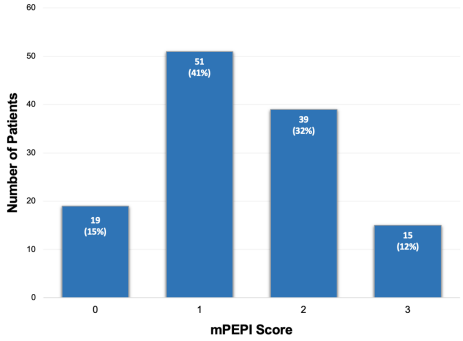
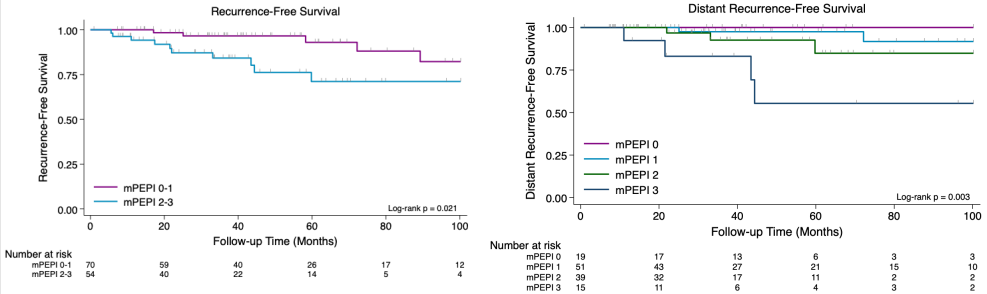


Table 1. Clinicopathologic and treatment characteristics

	Overall (n=124)	mPEPI 0-1 (n=70)	mPEPI 2-3 (n=54)	p-value
Median age, years (range)	59.4 (29-89)	63.5 (34-86)	52.6 (29-89)	0.001
Menopausal status, n (%)				0.045
Premenopausal	43 (34.7%)	19 (27.1%)	24 (44.4%)	
Postmenopausal	81 (65.3%)	51 (72.9%)	30 (55.6%)	
Mean pathologic tumor size, cm (SD)	4.5 (3.2)	3.0 (2.2)	6.5 (3.2)	<0.001
Pathologic N stage, n (%)				<0.001
0	78 (62.9%)	64 (91.4%)	14 (25.9%)	
1	31 (25.0%)	4 (5.7%)	27 (50.0%)	
2	12 (9.7%)	2 (2.9%)	10 (18.5%)	
3	3 (2.4%)	0 (0%)	3 (5.6%)	
Overall pathologic stage, n (%)				<0.001
1	23 (18.5%)	23 (32.9%)	0 (0%)	
2	72 (58.1%)	45 (64.3%)	27 (50.0%)	
3	28 (22.6%)	2 (2.9%)	26 (48.2%)	
4	1 (0.8%)	0 (0%)	1 (1.9%)	
Tumor grade, n (%)				0.421
1	37 (29.8%)	22 (31.4%)	15 (22.8%)	
2	83 (66.9%)	47 (67.1%)	36 (66.7%)	
3	4 (3.2%)	1 (1.4%)	3 (5.6%)	
Mean Ki-67, % (SD)	5.7 (6.2)	3.9 (3.6)	7.9 (7.9)	<0.001
Neoadjuvant endocrine therapy, n (%)				0.008
Aromatase Inhibitor	88 (72.1%)	58 (82.9%)	30 (57.7%)	
CDK4/6 Inhibitor + Endocrine Therapy	7 (5.7%)	1 (1.4%)	6 (11.5%)	
SERD[a]	6 (4.9%)	2 (2.9%)	4 (7.7%)	
Tamoxifen	21 (17.2%)	9 (12.9%)	12 (23.1%)	

[a]Selective estrogen receptor degrader

Figure 2. Kaplan-Meier estimates of recurrence-free survival and distant recurrence-free survival of the overall cohort (pre- and postmenopausal patients) by mPEPI score



Results

- Compared to low mPEPI scores (0-1), high scores (2-3) were associated with significantly worse RFS, LRFS, and DRFS in the overall cohort and postmenopausal cohort (all p<0.05), but not in premenopausal patients
- When comparing individual mPEPI scores (0/1/2/3), higher mPEPI scores were associated with worse DRFS in the overall cohort and postmenopausal cohort
- No significant differences in OS were observed across mPEPI scores

Conclusions

- In this single institution study of patients with ILC, higher mPEPI scores were associated with significantly worse recurrence outcomes compared with lower scores. When stratified by menopausal status, mPEPI scores remained prognostic only in the postmenopausal subgroup
- These findings validate the mPEPI score as a prognostic indicator after NET in postmenopausal patients with ILC. Further work is needed to identify early endpoints of therapy, specifically for premenopausal patients with ILC

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References

[1] Ellis MJ, et al. Outcome prediction for estrogen receptor-positive breast cancer based on postneoadjuvant endocrine therapy tumor characteristics. J Natl Cancer Inst. 2008.