Defining postpartum breast cancer based on 21-gene Recurrence Score® result

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Introduction & Background

- Postpartum breast cancer (PPBC), thought to arise during breast involution following childbirth and lactation, is associated with worse outcomes in young women with breast cancer (YWBC).[1,2]
- Definitions of PPBC vary, ranging breast cancer (BC) diagnosed from 0-5 years postpartum (pp) to up to 10 years pp.[3]
- Recent studies show PPBC has distinct transcriptomic profiles and elevated pseudo-21-gene assay compared to nulliparous BC.[4]
- We aimed to refine the temporal definition of PPBC by assessing whether Recurrence Score® (RS) result elevation is concentrated within postpartum interval.

Methods

- Single institution retrospective cohort study of patients (pts) aged ≤45 years with hormone receptor (HR)-positive, HER2-negative BC who underwent RS testing between 2011 and 2024.
- Pts were classified as nulliparous, ≤ 5 years pp, >5-10 years pp, or >10 years pp based on last childbirth prior to BC diagnosis.
- Pts diagnosed during pregnancy or with incomplete reproductive data were excluded.
- Models were adjusted for age of diagnosis and lymph node stage

Results

- We included 385 pts diagnosed with HR+/HER2- BC between 7/1/2015 to 10/9/2024 who met inclusion criteria. **Table 1.**
- RS result was significantly higher by 13.1 points in the ≤1 year pp group (p<0.001) compared to nulliparous pts, with a trend toward a 4.5 point increase up to 3 years pp (p=0.10). **Figure 1**

Table 1: Characteristics of the patient cohort

	Nulliparous (n = 153)	0-5 Years Postpartum (n = 85)	5-10 Years Postpartum (n = 85)	10+ Years Postpartum (n = 62)	p-value	Total (n = 385)
Age at Diagnosis	39.2 [26.6, 45.9]	40.3 [29.9, 45.9]	42.4 [32.7, 45.8]	43.1 [36.1, 45.8]	<0.001***	40.7 [26.6, 45.9]
Age at First Childbirth	NA	34.3 [17.0, 42.9]	30.9 [14.7, 40.1]	25.1 [15.4, 34.3]	<0.001***	30.6 [14.7, 42.9]
pT Stage					0.390	
0	2 (1.3%)	0 (0%)	0 (0%)	1 (1.6%)		3 (0.8%)
1	83 (54.2%)	56 (65.9%)	58 (68.2%)	33 (53.2%)		230 (59.7%)
2	64 (41.8%)	26 (30.6%)	24 (28.2%)	26 (41.9%)		140 (36.4%)
3	4 (2.6%)	3 (3.5%)	3 (3.5%)	2 (3.2%)		12 (3.1%)
pN Stage					0.075	
0	123 (80.4%)	62 (72.9%)	68 (80.0%)	47 (75.8%)		300 (77.9%)
1	27 (17.6%)	19 (22.4%)	15 (17.6%)	10 (16.1%)		71 (18.4%)
2 or 3	0 (0%)	4 (4.7%)	0 (0%)	2 (3.2%)		6 (1.6%)
Missing	3 (2.0%)	0 (0%)	2 (2.4%)	3 (4.8%)		8 (2.1%)
Ki67 category					0.010**	
0 - 19%	82 (53.6%)	38 (44.7%)	58 (68.2%)	36 (58.1%)		214 (55.6%)
≥20%	70 (45.8%)	47 (55.3%)	25 (29.4%)	25 (40.3%)		167 (43.4%)
Missing	1 (0.7%)	0 (0%)	2 (2.4%)	1 (1.6%)		4 (1.0%)

Continuous variables summarized by mean [minimum, maximum]. Categorical variables summarized by count (percent).
*Increasing number of * represent statistical significance at alpha = 0.05, 0.01, 0.001;*
p-values from ANOVA if variable is continuous, chi-squared test if variable is categorical

Figure 2: Systemic treatments by cohort

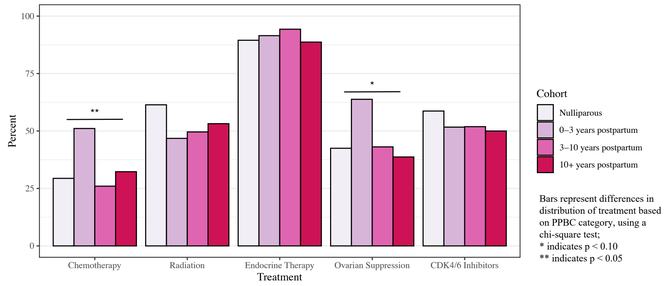


Figure 1: RS result by year postpartum

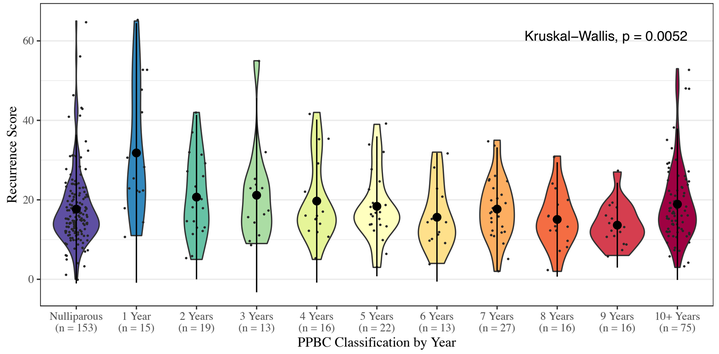


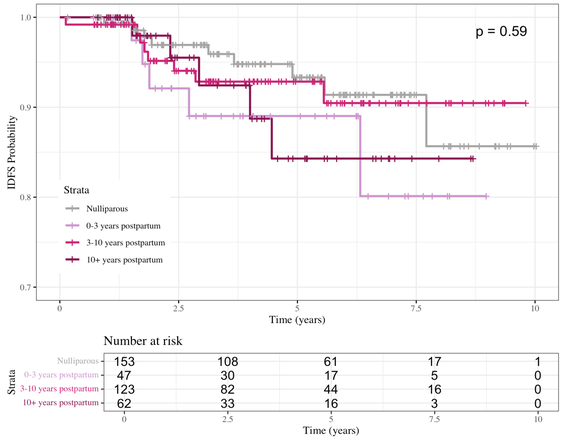
Table 2: Comparison of effect of different definitions of postpartum cohort on RS result

	Continuous Recurrence Score *[0.0, 65.0]*		Categorical Recurrence Score *(0-15, 16-25, >25)*	
PPBC Definition	**Beta (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
PPBC, 0-5 years pp				
0-5 years pp	4.38 (1.84, 6.92)	<0.001***	2.23 (1.33, 3.74)	0.002**
5-10 years pp	0.66 (-1.97, 3.30)	0.62	1.14 (0.66, 1.97)	0.63
10+ years pp	2.70 (-0.30, 5.71)	0.078	2.04 (1.11, 3.75)	0.022*
PPBC, 0-3 years pp				
0-3 years pp	6.44 (3.37, 9.52)	<0.001***	2.83 (01.51, 5.34)	0.001**
3-10 years pp	0.95 (-1.39, 3.29)	0.42	1.28 (0.79, 2.07)	0.32
10+ years pp	2.61 (-0.38, 5.59)	0.087	2.02 (1.10, 3.72)	0.023*

All models adjusted for pN grade (0, 1, 2-3) and age at diagnosis; Reference group is nulliparous;
*Increasing number of * represent statistical significance at alpha = 0.05, 0.01, and 0.001;*
PPBC = postpartum breast cancer; pp = postpartum; OR = odds ratio; CI = confidence interval

- BC diagnosed within 3 years pp showed a mean RS increase of 6.44 (p<0.001) and 2.83-fold higher odds of being in a higher RS category (p=0.001) compared to nulliparous pts.
- Extending the window of PPBC diagnosis up to 5 years pp attenuated the effect (mean RS +4.38, p<0.001; OR=2.23, p=0.002). **Table 2.**
- Patients in the PPBC ≤3 years cohort had significantly higher odds of presenting with a higher pathologic grade compared with nulliparous patients (OR, 2.35; *p* = .009). No significant differences in odds of higher pathologic grade were observed in the PPBC 3–10 years or >10 years cohorts.

Figure 3: Invasive disease-free survival by cohort



- After a median follow-up of 49 months, there was a trend towards lower probability of IDFS in the 0-3 year pp cohort compared with nulliparous pts (HR=1.95, p=0.23). **Figure 3.**

Conclusions and Discussion

- Year-by-year pp analysis shows RS result is highest in the first-year pp, with clinically meaningful increases up to 3 years.
- The period of greatest RS result appears concentrated within 0-3 years pp, supporting a narrower definition of PPBC.
- This refinement may improve understanding of PPBC in YWBC and guide treatment escalation and risk stratification.

References

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