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THE IMPACT OF PARITY AND AGE OF FIRST FULL TERM PREGNANCY ON THE PREVALENCE AND CHARACTERISTICS OF INVASIVE LOBULAR CARCINOMA

Karen Van Baelen[1,2], Ha-Linh Nguyen[1], François Richard[1], Maja Vangoitsenhoven[2], Giuseppe Floris[3,4], Hans Wildiers[5], Kevin Punie[5], Ann Smeets[6], Ines Nevelsteen[6], Frederic Amant[2,7], Sileny Han[2], Thaïs Baert[2], Patrick Neven[2,*], Christine Desmedt[1,*]

[1]Laboratory for Translational Breast Cancer Research, Department of Oncology, KU Leuven, Leuven, Belgium; [2]Department of Gynaecology and Obstetrics, University Hospitals Leuven, Leuven, Belgium; [3]Department of Pathology, University Hospitals Leuven, Leuven, Belgium; [4]Laboratory of Translational Cell & Tissue Research, Department of Imaging and Pathology, KU Leuven, Leuven, Belgium, [5]Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium; [6]Department of Surgical Oncology, UZ Leuven, Leuven, Belgium; [7]Gynecological Oncology, Department of Oncology, KU Leuven, Leuven, Belgium; (*) equal contribution

BACKGROUND and AIMS

- The risk for ER+/HER2- breast cancer (BC) is transiently augmented in the years after giving birth.[1]
- High parity and early 1st full term pregnancy (FTP) protect against the development of ER+/HER2- BC later in life.[1,2]
- >90% of invasive lobular carcinoma (ILC) (the second most common BC subtype) is ER+/HER2-.[3]
- Higher age of 1st FTP as well as nulliparity have been associated with increased risk of ILC.[4]
- The impact of reproductive factors on ILC characteristics is understudied.

Wie aimed at investigating whether parity and age at 1st FTP is associated with:

1. **the prevalence of ER+/HER2- pure ILC in an ER+/HER2- BC cohort**
2. **Standard clinical and pathological features of pure ILC**

PATIENTS and METHODS

Single center retrospective study in the University Hospitals of Leuven, Belgium with inclusion of patients that met following criteria:

- Diagnosed between January 2000 and November 2020
- Presence of non-metastatic ER+/HER2- BC

Outcome	Statistical models*
BC histology (pure ILC, i.e., not mixed) vs. all other BC histological types)	Multivariable models with following variables: - Parity (yes vs no and nulliparous, 1 child, 2 children, >2 children) - Age group at diagnosis (<30, 31-40, 41-50, 51-60, 61-70, >70) - Age 1st FTP (continuous and per age group: <21, 21-25, 26-30, >30) - Interval 1st FTP and diagnosis (continuous) - Year of birth - BMI Performed in overall group and per age group
Parity (yes vs no and ≥2 children vs. 1 child)	Multivariable models with following variables: - Age at diagnosis - BMI - Histological grade - Tumour size - Nodal involvement - PR-positivity Performed in overall group and per age group

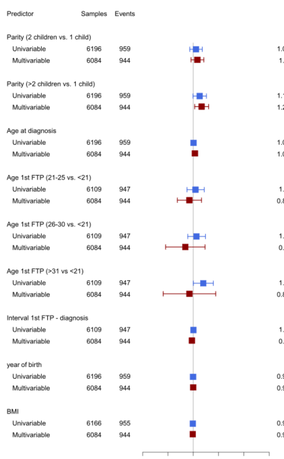
*Firth's logistical regression

All results will be illustrated by use of forest plots

RESULTS AIM 1: prevalence of pure ILC in an ER+/HER2- BC cohort

Parity of 2 and >2 children vs. 1 child in all age groups

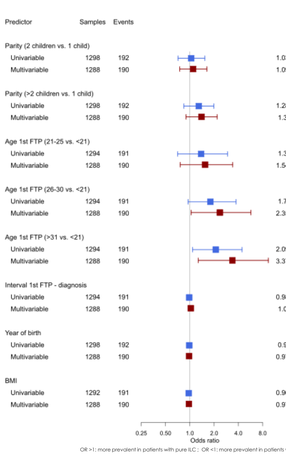
Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
Parity (2 children vs. 1 child)					
Univariable	6196	959	1.077 (0.908 − 1.279)	0.396	0.509
Multivariable	6084	944	1.119 (0.94 − 1.333)	0.207	0.373
Parity (>2 children vs. 1 child)					
Univariable	6196	959	1.191 (0.992 − 1.432)	0.061	0.138
Multivariable	6084	944	1.257 (1.039 − 1.521)	0.019	0.167
Age at diagnosis					
Univariable	6196	959	1.007 (1.002 − 1.013)	0.013	0.082
Multivariable	6084	944	1.045 (0.987 − 1.107)	0.127	0.373
Age 1st FTP (21-25 vs. <21)					
Univariable	6109	947	1.062 (0.842 − 1.35)	0.615	0.615
Multivariable	6084	944	0.898 (0.647 − 1.251)	0.524	0.674
Age 1st FTP (26-30 vs. <21)					
Univariable	6109	947	1.091 (0.86 − 1.395)	0.476	0.535
Multivariable	6084	944	0.805 (0.469 − 1.38)	0.429	0.644
Age 1st FTP (>31 vs <21)					
Univariable	6109	947	1.314 (1.002 − 1.73)	0.049	0.138
Multivariable	6084	944	0.899 (0.439 − 1.846)	0.772	0.772
Interval 1st FTP - diagnosis					
Univariable	6109	947	1.004 (0.999 − 1.01)	0.101	0.152
Multivariable	6084	944	0.963 (0.91 − 1.018)	0.182	0.373
year of birth					
Univariable	6196	959	0.994 (0.989 − 0.999)	0.018	0.082
Multivariable	6084	944	0.997 (0.985 − 1.009)	0.613	0.689
BMI					
Univariable	6166	955	0.988 (0.973 − 1.002)	0.095	0.152
Multivariable	6084	944	0.986 (0.971 − 1.001)	0.059	0.267



OR >1: more prevalent in patients with pure ILC ; OR <1: more prevalent in patients with other histological types

Parity of 2 and >2 children vs. 1 child in age group 41-50

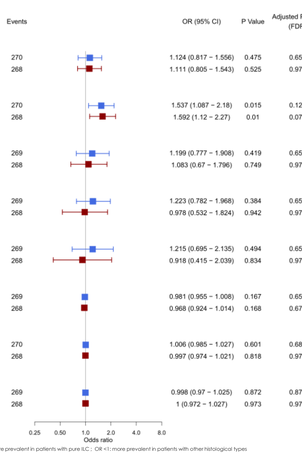
Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
Parity (2 children vs. 1 child)					
Univariable	1298	192	1.039 (0.713 − 1.533)	0.843	0.843
Multivariable	1288	190	1.097 (0.749 − 1.628)	0.638	0.638
Parity (>2 children vs. 1 child)					
Univariable	1298	192	1.289 (0.841 − 1.983)	0.244	0.326
Multivariable	1288	190	1.394 (0.895 − 2.18)	0.142	0.228
Age 1st FTP (21-25 vs. <21)					
Univariable	1294	191	1.38 (0.706 − 2.938)	0.359	0.41
Multivariable	1288	190	1.544 (0.759 − 3.395)	0.239	0.318
Age 1st FTP (26-30 vs. <21)					
Univariable	1294	191	1.798 (0.95 − 3.743)	0.073	0.194
Multivariable	1288	190	2.358 (1.039 − 5.705)	0.04	0.159
Age 1st FTP (>31 vs. <21)					
Univariable	1294	191	2.096 (1.082 − 4.435)	0.027	0.194
Multivariable	1288	190	3.372 (1.273 − 9.411)	0.014	0.112
Interval 1st FTP - diagnosis					
Univariable	1294	191	0.982 (0.952 − 1.012)	0.236	0.326
Multivariable	1288	190	1.027 (0.97 − 1.088)	0.363	0.415
Year of birth					
Univariable	1298	192	0.983 (0.96 − 1.006)	0.155	0.31
Multivariable	1288	190	0.978 (0.952 − 1.005)	0.107	0.228
BMI					
Univariable	1292	191	0.967 (0.931 − 1.003)	0.073	0.194
Multivariable	1288	190	0.973 (0.936 − 1.009)	0.14	0.228



OR >1: more prevalent in patients with pure ILC ; OR <1: more prevalent in patients with other histological types

Parity of 2 and >2 children vs. 1 child in all age group 51-60

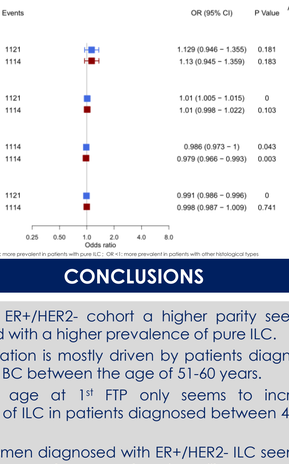
Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
Parity (2 children vs. 1 child)					
Univariable	1709	270	1.124 (0.817 − 1.556)	0.475	0.658
Multivariable	1687	268	1.111 (0.805 − 1.543)	0.525	0.973
Parity (>2 children vs. 1 child)					
Univariable	1709	270	1.537 (1.087 − 2.18)	0.015	0.121
Multivariable	1687	268	1.592 (1.12 − 2.27)	0.01	0.076
Age 1st FTP (21-25 vs. <21)					
Univariable	1693	269	1.199 (0.777 − 1.908)	0.419	0.658
Multivariable	1687	268	1.083 (0.67 − 1.796)	0.749	0.973
Age 1st FTP (26-30 vs. <21)					
Univariable	1693	269	1.223 (0.782 − 1.968)	0.384	0.658
Multivariable	1687	268	0.978 (0.532 − 1.824)	0.942	0.973
Age 1st FTP (>31 vs. <21)					
Univariable	1693	269	1.215 (0.695 − 2.135)	0.494	0.658
Multivariable	1687	268	0.918 (0.415 − 2.039)	0.834	0.973
Interval 1st FTP - diagnosis					
Univariable	1693	269	0.981 (0.955 − 1.008)	0.167	0.658
Multivariable	1687	268	0.968 (0.924 − 1.014)	0.168	0.672
Year of birth					
Univariable	1709	270	1.006 (0.985 − 1.027)	0.601	0.687
Multivariable	1687	268	0.997 (0.974 − 1.021)	0.818	0.973
BMI					
Univariable	1702	269	0.998 (0.97 − 1.025)	0.872	0.872
Multivariable	1687	268	1 (0.972 − 1.027)	0.973	0.973



OR >1: more prevalent in patients with pure ILC ; OR <1: more prevalent in patients with other histological types

Parous vs. nulliparous in all age groups

Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
Parity (yes vs. no)					
Univariable	7359	1121	1.129 (0.946 − 1.355)	0.181	0.181
Multivariable	7316	1114	1.13 (0.945 − 1.359)	0.183	0.244
Age at diagnosis					
Univariable	7360	1121	1.01 (1.005 − 1.015)	0	0
Multivariable	7316	1114	1.01 (0.998 − 1.022)	0.103	0.207
BMI					
Univariable	7317	1114	0.986 (0.973 − 1)	0.043	0.057
Multivariable	7316	1114	0.979 (0.966 − 0.993)	0.003	0.012
year of birth					
Univariable	7360	1121	0.991 (0.986 − 0.996)	0	0
Multivariable	7316	1114	0.998 (0.987 − 1.009)	0.741	0.741

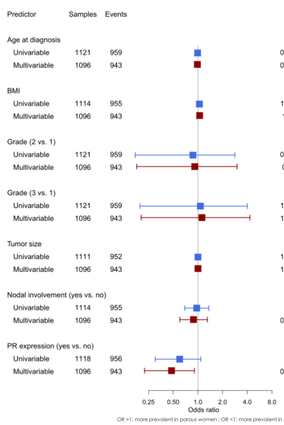


OR >1: more prevalent in patients with pure ILC ; OR <1: more prevalent in patients with other histological types

RESULTS AIM 2: standard clinical and pathological features of ER+/HER2- pure ILC

Parous vs. nulliparous in all age groups

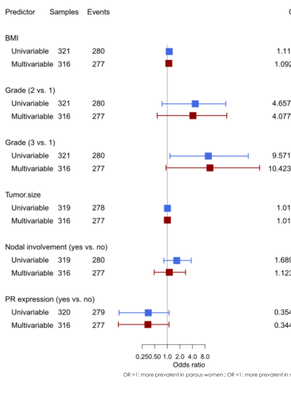
Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
Age at diagnosis					
Univariable	1121	959	0.993 (0.979 − 1.007)	0.315	0.736
Multivariable	1096	943	0.987 (0.973 − 1.002)	0.094	0.22
BMI					
Univariable	1114	955	1.046 (1.007 − 1.087)	0.019	0.131
Multivariable	1096	943	1.05 (1.009 − 1.093)	0.014	0.079
Grade (2 vs. 1)					
Univariable	1121	959	0.872 (0.172 − 2.829)	0.838	0.926
Multivariable	1096	943	0.915 (0.18 − 3.005)	0.896	0.896
Grade (3 vs. 1)					
Univariable	1121	959	1.072 (0.197 − 4.003)	0.926	0.926
Multivariable	1096	943	1.122 (0.203 − 4.307)	0.879	0.896
Tumor size					
Univariable	1111	952	1.002 (0.996 − 1.008)	0.53	0.926
Multivariable	1096	943	1.002 (0.996 − 1.009)	0.518	0.752
Nodal involvement (yes vs. no)					
Univariable	1114	955	0.967 (0.69 − 1.36)	0.847	0.926
Multivariable	1096	943	0.885 (0.602 − 1.308)	0.537	0.752
PR expression (yes vs. no)					
Univariable	1118	956	0.6 (0.303 − 1.084)	0.093	0.327
Multivariable	1096	943	0.477 (0.224 − 0.907)	0.022	0.079



OR >1: more prevalent in parous women ; OR <1: more prevalent in nulliparous women

Parous vs. nulliparous in all age group 61-70

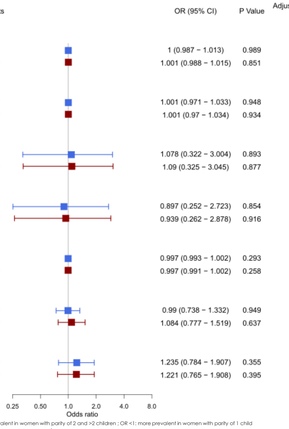
Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
BMI					
Univariable	321	280	1.115 (1.029 − 1.22)	0.007	0.04
Multivariable	316	277	1.092 (1.007 − 1.195)	0.032	0.151
Grade (2 vs. 1)					
Univariable	321	280	4.657 (0.754 − 24.758)	0.091	0.11
Multivariable	316	277	4.077 (0.576 − 26.276)	0.149	0.223
Grade (3 vs. 1)					
Univariable	321	280	9.571 (1.158 − 85.646)	0.037	0.11
Multivariable	316	277	10.423 (0.933 − 159.467)	0.057	0.151
Tumor.size					
Univariable	319	278	1.013 (0.999 − 1.03)	0.063	0.11
Multivariable	316	277	1.011 (0.995 − 1.03)	0.188	0.225
Nodal involvement (yes vs. no)					
Univariable	319	280	1.689 (0.825 − 3.711)	0.155	0.155
Multivariable	316	277	1.123 (0.488 − 2.725)	0.788	0.788
PR expression (yes vs. no)					
Univariable	320	279	0.354 (0.071 − 1.108)	0.078	0.11
Multivariable	316	277	0.344 (0.068 − 1.101)	0.075	0.151



OR >1: more prevalent in parous women ; OR <1: more prevalent in nulliparous women

Parity of ≥2 children vs. 1 child in all age groups

Predictor	Samples	Events	OR (95% CI)	P Value	Adjusted P Value (FDR)
Age at diagnosis					
Univariable	959	716	1 (0.987 − 1.013)	0.989	0.989
Multivariable	943	703	1.001 (0.988 − 1.015)	0.851	0.934
BMI					
Univariable	955	712	1.001 (0.971 − 1.033)	0.948	0.989
Multivariable	943	703	1.001 (0.97 − 1.034)	0.934	0.934
Grade (2 vs. 1)					
Univariable	959	716	1.078 (0.322 − 3.004)	0.893	0.989
Multivariable	943	703	1.09 (0.325 − 3.045)	0.877	0.934
Grade (3 vs. 1)					
Univariable	959	716	0.897 (0.252 − 2.723)	0.854	0.989
Multivariable	943	703	0.939 (0.262 − 2.878)	0.916	0.934
Tumor size					
Univariable	952	712	0.997 (0.993 − 1.002)	0.293	0.989
Multivariable	943	703	0.997 (0.991 − 1.002)	0.258	0.934
Nodal involvement (yes vs. no)					
Univariable	955	713	0.99 (0.738 − 1.332)	0.949	0.989
Multivariable	943	703	1.084 (0.777 − 1.519)	0.637	0.934
PR expression (yes vs. no)					
Univariable	956	713	1.235 (0.784 − 1.907)	0.355	0.989
Multivariable	943	703	1.221 (0.765 − 1.908)	0.395	0.934



OR >1: more prevalent in women with parity of 2 and >2 children ; OR <1: more prevalent in women with parity of 1 child

CONCLUSIONS

- Within an ER+/HER2- cohort a higher parity seems to be associated with a higher prevalence of pure ILC.
- This association is mostly driven by patients diagnosed with ER+/HER2- BC between the age of 51-60 years.
- Increased age at 1st FTP only seems to increase the incidence of ILC in patients diagnosed between 41-50 years of age.
- Parous women diagnosed with ER+/HER2- ILC seem to have less PR+ tumours in comparison to nulliparous women: this trend was seen mostly in the patients diagnosed at an older age.
- In parous women, the number of children does not seem to affect the clinicopathological features of ILC.

ABBREVIATIONS

- BC: breast cancer
- ER: estrogen receptor
- FTP: full term pregnancy
- HER2: human epidermal growth factor 2
- ILC: invasive lobular carcinoma
- PR: progesterone receptor

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