6 ulusal CERRAHİ ONKOLOJİ KONGRESİ

24 - 27 Şubat 2022 | Gloria Golf Resort - ANTALYA

PROF. DR. SUAT KUTUN

SAĞLIK BİLİMLERİ ÜNİVERSİTESİ....
ANKARA ONKOLOJİ HASTANESİ.....
CERRAHİ ONKOLOJİ BD

GEBELİKTE MEME KANSERİ YÖNETİMİ

Pregnancy-associated breast cancer

-gebelik sırasında tanı
-postpartum ilk yıl
-laktasyonun herhangi bir aşaması

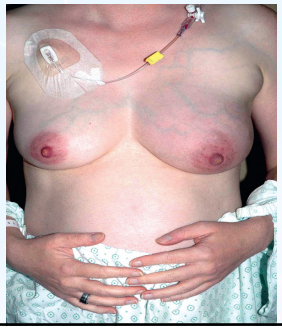
- Clinical Pharmacology During Pregnancy (Second Edition) 2022, Pages 203-219

  Sharon E Robertson, Jeanne M. Schilder

Gebelik ilişkili malignitelerde çok merkezli ve farklı ülke veri taramalarında

Meme ,serviks, lenfoma ve lösemi, melanom, tiroid ve kolorektal kanserler daha sık

- 100.000 doğumda 15-35 gebelik ilişkili meme ca
- 30 yaş altı %20
- 50 yaş üstü %5



- Gebelik sonlandırma
- Bireysel istek, fetal toksisite
- Anne kişisel prognoz
- Meme kanseri tedavisinin fertiliteye etkisi

The Breast
Volume 22, Issue 4, August 2013, Pages 515-519
Original article
Multidisciplinary approach to breast cancer diagnosed during pregnancy: Maternal and neonatal outcomes
OctaviCórdoba[a]ElisaLlurba[b]CristinaSaura[c]IsabelRubio[a]QueraltFerrer[d]JavierCortés[c]JordiKercavins[e]*

Clinical Breast Cancer
Volume 21, Issue 1, February 2021, Pages e120-e127

Review
Pregnancy-Associated Breast Cancer: A Multidisciplinary Approach
IdaParis[1]DanileDiGiorgio[2]LuisaCarbognin[1]GiacomoCorrado[1]GiorgiaGarganese[1,2]GianLucaFranceschini[1,2]AlejandroMartinSanchez[1]RosaPasqualinaDe Vincenzo[1,2]CristinaAccetta[1]DanielaAndreinaTerribile[1,2]StefanoMagno[1]AlbaDi Leone[2]SoniaBove[2]RiccardoMasetti[1,2]GiovanniScambia[1,2]*

European Journal of cancer ORIGINAL ARTICLE
Cancer during pregnancy: A qualitative study of healthcare experiences of Australian women
Lesley Stafford,Michelle Sinclair,Katrin Gerber,Leah Collins,Louise Newman,Christobel Saunders,Angela Ives,Kylie D. Mason,Michelle Peate,Jocelyn Lippey,Mark P. Umstad,Kerry Shanahan,Ruth Little
10 February 2021

Journal of Adolescent and Young Adult Oncology
Clinical Decision Making in the Management of Breast Cancer Diagnosed During Pregnancy: A Review and Case Series Analysis
Nadom Safi, Christobel Saunders, Antoinette Anazodo, Jan E. Dickinson, Frances Boyle, Angela Ives et al.

Prenatal vizitlerde normal meme takip tetkikleri yapılmalıdır.Meme usg semptomatik alanları değerlendirmek için rutin kullanılmalıdır. Meme cerrahisi tüm trimestrlerde güvenle uygulanabilir. Sistemik terapötik tedaviler 2. ve 3. trimestrde uygulanabilir.

Pregnancy After Breast Cancer: A Systematic Review and Meta-Analysis
Matteo Lambertini, MD, PhD[1,2]; Eva Blondeaux, MD[1,3]; Marco Bruzzone, MSc[4]; Marta Perachino, MD[1,2]; Richard A. Anderson, MD[5]; Evandro de Azambuja, MD, PhD[6]

6462 kayıtlı çalışmadan 39 çalışma dahil edilmiş.

8.093.401 kadın 112.480 meme kanserli hastadan 7505 gebelik ilişkili meme kanseri (relative risk, 0.40; 95% CI, 0.32 to 0.49).

Risk caesarean section (OR, 1.14; 95% CI, 1.04 to 1.25), düşük doğum ağırlığı (OR, 1.50; 95% CI, 1.31 to 1.73), preterm doğum (OR, 1.45; 95% CI, 1.11 to 1.88), ve erken yaş gebelik (OR, 1.16; 95% CI, 1.01 to 1.33) özellikle KT ye maruz kalanlarda genel populasyona göre anlamlı. Kongenital anomali ve reprodüktif komplikasyonlarda fark yok. Gebe olmayanlarda disease-free survival (HR, 0.66; 95% CI, 0.49 to 0.89) overall survival (HR, 0.56; 95% CI, 0.45 to 0.68). Tümör ve tedavi karakterleri, gebelik sonlanımı, ve gebe kalma zamanlaması arasında fark yok.

- Gestational breast cancer
- N Safi , Saunders C et al. **Plos One january 2021**
- 1994-2013 arası 122 gestasyonel meme ca
- >35 yaş risk artışı
- Preterm doğum ile tanı anında kanser evresi bağımsız
- Neonatal morbidite ile ilişki yok

Breast cancer in pregnancy: recommendations of an international consensus meeting.

Ali Amant F, Deckers S, Van Calsteren K, Loibl S, Halaska M, Brepoels L, Beijnen J, Cardoso F, Gentilini O, Lagae L, Mir O, Neven P, Ottevanger N, Pans S, Peccatori F, Rouzier R, Semi HJ, Struikmans H, Christiaens MR, Cameron D, Du Bois A SO

Eur J Cancer. 2010;46(18):3158.

-Meme kanseri tedavisi protokolleri
-tedavide fetusu koruma modifikasyonları
-elektif gebelik sonlandırma

Epidemiyoloji

Risk faktörleri

BRCA gen taşıyıcılarında BRCA2 gen mutasyonlularda gebelik ilişkili meme kanseri oranı daha düşük

Cullinane CA et al. Int J Cancer 2005 Effect of pregnancy as a risk factor for breast cancer in BRCA1/BRCA2 mutation carriers

BRCA gen taşıyıcılarında

Valachis et al Obstetric Gynecol Surv 2010 Safety of pregnancy after primary breast carcinoma in young woman: a meta analysis to overcome bias healty mother effect studies.

OK kullanımı düşük doz levonorgestrol istatistiksel olarak anlamı bulunmamış.

Alkol kullanımı ve aşırı kilo meme kanseri rekürrensi ile ilişkili.

Hormon reseptör durumu etkiler mi?

Her2 overexpression durumu

Primer tm

- Sweden çalışması Johansson ALV et al. Nationwide cohort study. Eur J Cancer
- 1970-2018 arası 42.000 kadın 975 meme ca
- HR1.72 (%95 CI 1.54-1.93) postpartum period, yaş ve evre ve subtipler arasında ist. anlamlı fark
- Amant F et al J Clin Oncol 2013
- 300 meme kanserli gebe hastada
- Yaş evre, subtip ve tedavi değ. Fark saptanmamış. Bu çalışmada 75 hasta standart KT kullanmış 2-3.trimestr Overall 5 yıllık survi de %72-%57 lik fark saptanmış.

- Committee on gynecologic Practise.ACOG Committee Opinion. İnduced abortion and breast cancer risk.Reaffirmed 2021.
- 15-44 yaş arası abortus oranı 1000 de 35
- İnduced abortion
- 2017 yılından itibaren abortus oranı gelişmiş ülkelerde düşmektedir
- Chinese females Cancer Causes Control 2014 Huang Y et al. Meme kanseri ile abortus arasında ilişki bildirirken ACOG Committee(2021) karşı görüş bildirmektedir.
- 83.000 abortus ve meme kanserli hastada yapılan meta analiz sonucu retrospektif seriler arasında bias bulunmaktadır. RR 0.93, %95 confidence interval, RR relative risk 1.11

Mamografi (200-400 milirad) abdominal shielding

USG

MRI(Gadolinium-enhanced meme MRI daha sensitif)laktasyon riskli

Gebelikte meme kanseri yönetimi

- Biopsi kitle ve lap
- Milk rejection sign erken tanıda şüpheli
- Meme kitlesi tanıda 2 aylık ort. Gecikmeye yol açar
- %80 benign biopsi
  - Laktasyon, duktus patolojisi, mastit, fiboadenom,kistik hast, lobüler hiperplazi, galaktosel, laktasyon adenoma, apse, lipoma, hamartoma, filoid tm, tbc, sarkom vb.

Patoloji

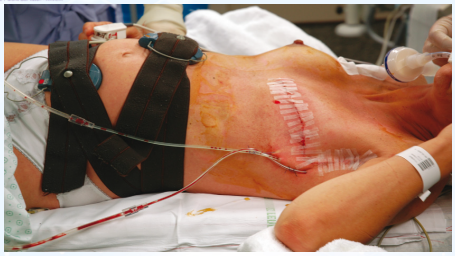
- Nongebelikte infiltratif duktal karsinom
- Gebelik ilişkili meme ca özellikle laktasyon döneminde ileri evre, inflamatuar meme ca aynı yaş grubuna göre daha sık
- Hormon reseptör negatifliği %25
- Her2 over expresyonunda fark yok

- Anderson BO Ann Surg Oncol 1996
- Middleton LP Cancer 2003
- Reed W Wirchows Arc 2003
- Stensheim H cohort study J Clin Oncol 2009
- Breast Cancer Association Consortium 2021
- Dutch Study 2021

Gebelikte meme kanseri yönetimi

- Sistemik evreleme
- Ac röntgen
- Kc,beyin MRI,USG
- Kemik (foley kateter radionükleid tarama 0.18-0.19 rad)
- MRI lomber alan
- Tanı ve evreleme tümör nod, tm boyutu ve metastaza göre evrelenir.
- AJCC,UICC

- Biopsi
- Lenf Nodu
- Sistemik evreleme
- CT
- Karaciğer ve beyin, kemik
- USG, MRI



Cerrahi

- İlk trimestr
- İkinci trimestr
- Üçüncü trimestr
- MKC
- Mastektomi
- Aksiller evreleme
- Neoadj.
- Onkoplasti

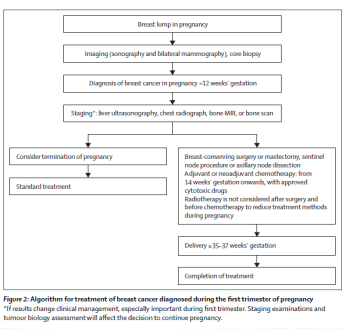


Figure 2: Algorithm for treatment of breast cancer diagnosed during the first trimester of pregnancy
*If results change clinical management, especially important during first trimester. Staging examinations and tumour biology assessment will affect the decision to continue pregnancy.

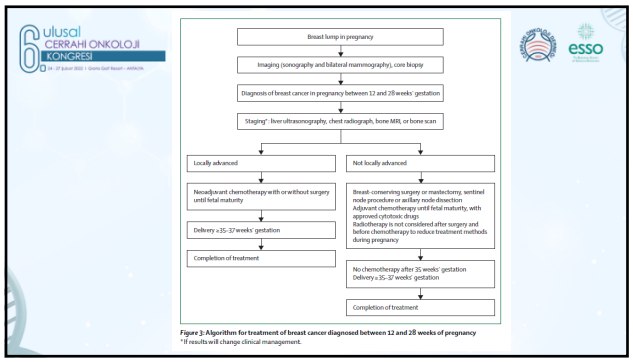


Figure 3: Algorithm for treatment of breast cancer diagnosed between 12 and 28 weeks of pregnancy
*If results will change clinical management.

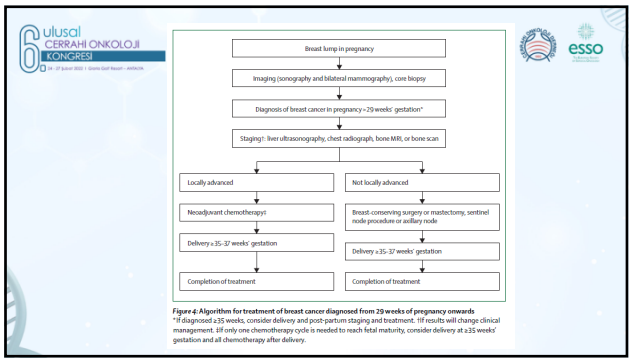


Figure 4: Algorithm for treatment of breast cancer diagnosed from 29 weeks of pregnancy onwards
*If diagnosed ≥35 weeks, consider delivery and post-partum staging and treatment. †If results will change clinical management. ‡If only one chemotherapy cycle is needed to reach fetal maturity, consider delivery at ≥35 weeks' gestation and all chemotherapy after delivery.

Radyoterapi

- RT nin gebelik sürecinde tedavide yeri yoktur.
- Doğum sonrası beklenmelidir.
- Kal HB. et.al. Lancet Oncol 2005
- Greskovich JE Jr et al. Semin Oncol 2000
- Centers for disease control and prevention. Radiation and Pregnancy 2019
- Gebelik kaybı, malformasyon, gelişim anomalisi, mutajenik ve karsinojenik. Yine de uygulanan eski çalışmalarda uygun fetal shielding ve diafragmatik koruma ile verilen hastalar. Tipik radyasyon dozu 46-60 Gray , external Beam Rt 50 Gray ilk trimetsr fetal dose 0.04-0.12 Gray
- Son trimestr 2 Gray

SLNB

- Aksiller evreleme meme kanseri tedavisinin en önemli komponenti. Halen sentinel lenf nodu işaretlemesi ile tartışılan konular vardır.
- NCCN 2022 SLNB Category IIA
- Çalışmalarda önerilen Radiolabeled sülfür colloid (kısıtlı data)
- SLNB?
  Potansiyel teratojenik etki
- Metilen mavisi ve isosulfan blue dye(lymphazurin) sistemik absorbsiyonundan dolayı kullanılmamalıdır.
- Gebelik lenfatik pathway değişir.
- Metilen mavisi küçük serilerde 1/25 doğumda bir yarık dudak izlenmiş

Breast Cancer Research and Treatment (2021) 186:699–704
https://doi.org/10.1007/s10549-021-06130-w

PRECLINICAL STUDY

Pregnancy-associated breast cancer: nationwide Dutch study confirms a discriminatory aggressive histopathologic profile

B. B. M. Suelmann[1] · C. van Dooijeweert[2] · E. van der Wall[1] · S. Linn[3] · P. J. van Diest[2]

Table 1 Characteristics of patients with pregnancy-associated breast cancer (PABC) (n = 741), age-matched 1:1 to non-PABC patients with invasive breast cancer (n = 741)

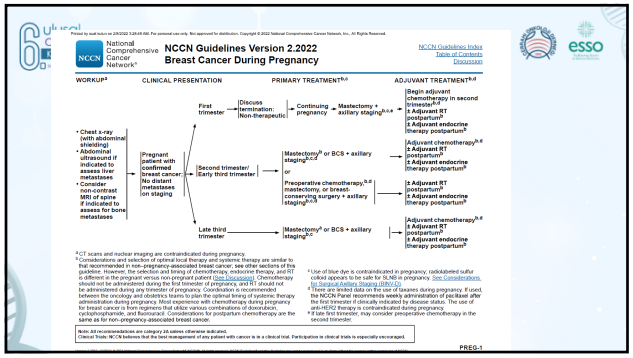
	PABC patients (n = 741)	Non-PABC patients (n = 741)	*p*-value
Age, median (range)	34.0 (19–45)[a]	34.0 (19–45)	1.000
Histological subtype, n (%)			
Ductal	707 (95.4%)	670 (90.4%)	0.000
Lobular	22 (3.0%)	31 (4.3%)	
Other	12 (1.6%)	40 (5.4%)	
Histological grade, n (%)			
Grade I	11 (1.5%)	92 (12.4%)	0.000
Grade II	124 (16.9%)	232 (31.3%)	
Grade III	595 (80.3%)	293 (39.5%)	
Unknown	11 (1.5%)	124 (16.7%)	
ER-receptor status, n (%)			
Positive	288 (38.9%)	505 (68.2%)	0.000
Negative	393 (53.0%)	200 (28.3%)	
Unknown	60 (8.1%)	26 (3.5%)	
PR-receptor status, n (%)			
Positive	251 (33.9%)	437 (59.0%)	0.000
Negative	415 (56.0%)	277 (37.4%)	
Unknown	75 (10.1%)	27 (3.6%)	
Her2-receptor status, n (%)			
Positive	149 (20.0%)	141 (10.0%)	0.000
Negative	483 (65.2%)	560 (75.6%)	
Unknown	109 (14.7%)	40 (5.4%)	
Gestational age			
First trimester	179 (24.2%)	N.a	
Second trimester	111 (15.0%)	N.a	
Third trimester	260 (35.1%)	N.a	
Postpartum: not lactating	94 (12.7%)	N.a	
Postpartum: lactating	83 (11.2%)	N.a	
Unknown gestational age	14 (1.9%)	N.a	

[a]Up to 6 months postpartum

Table 2 Surrogate intrinsic subtypes of patients with pregnancy-associated breast cancer (PABC) ($n=741$), age-matched 1:1 to non-PABC patients with invasive breast cancer ($n=741$)

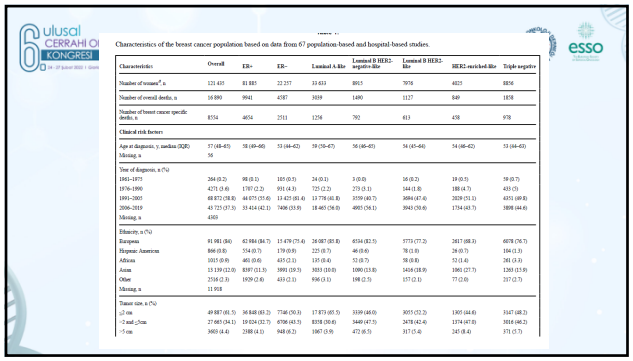
	PABC patients ($n=741$)	Non-PABC patients ($n=741$)	*p*-value
Surrogate intrinsic subtypes, *n* (%)			
Triple positive			
Triple positive (ER+, PR+, Her2+)	63 (8.5%)	89 (12.0%)	0.000
Triple positive unknown (ER, PR, or HER2 missing)	112 (15.1%)	44 (5.9%)	
Triple negative			
Triple negative (ER−, PR−, Her2−)	284 (38.3%)	163 (22.0%)	0.000
Triple negative unknown (ER, PR, or HER2 missing)	112 (15.1%)	44 (5.9%)	
Hormone-driven			
Hormone-driven (ER and/or PR+, Her2±)	281 (37.9%)	499 (67.3%)	0.000
Hormone-driven unknown (ER, PR, or HER2 missing)	112 (15.1%)	44 (5.9%)	
HER2-driven			
Her2-driven (ER±, PR±, Her2+)	149 (20.1%)	141 (19.0%)	0.000
HER2-driven unknown (ER, PR, or HER2 missing)	112 (15.1%)	44 (5.9%)	

- DUTCH Study
- 744 hasta
- Grade I: 1.5% vs. 12.4%, grade II: 16.9% vs. 31.3%, grade III: 80.3% vs. 39.5%, *p < 0.0001*
- (ER: 38.9% vs. 68.2% ve PR: 33.9%vs. 59.0%, *p < 0.0001*
- HER2 20.0% vs. 10.0%, *p < 0.0001*
- Triple-negative breast cancer 38.3% vs. 22.0%, *p < 0.0001*
- Daha kötü prognoz 37.9% vs. 67.3%, *p < 0.0001*
- *45 yaş altı hastalarda daha agresif*
- *BRCA1 ve BRCA2 tarama sonuçları geniş seri*



Cancer Epidemiol Biomarkers Prev: 2021 April ; 30(4): 623–642. doi:10.1158/1055-9965.EPI-20-0924.

Breast cancer risk factors and survival by tumor subtype: pooled analyses from the Breast Cancer Association Consortium



Characteristics of the breast cancer population based on data from 67 population-based and hospital-based studies.

Characteristics	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple-negative
Number of women[a], n	121 435	81 885	22 217	33 653	8915	7976	4025	8856
Number of overall deaths, n	16 890	9941	4387	3039	1490	1127	849	1858
Number of breast cancer specific deaths, n	8554	4654	2511	1258	792	613	458	978
Clinical risk factors								
Age at diagnosis, y, median (IQR)	57 (48–67)	58 (49–68)	53 (44–62)	59 (50–67)	56 (46–65)	54 (45–64)	54 (46–62)	53 (44–62)
Missing, n	56							
Year of diagnosis, n (%)								
1961–1975	264 (0.2)	98 (0.1)	105 (0.5)	24 (0.1)	3 (0.0)	16 (0.2)	19 (0.5)	59 (0.7)
1976–1990	4271 (3.4)	1707 (2.2)	931 (4.3)	725 (2.2)	273 (3.1)	144 (1.8)	188 (4.7)	433 (5)
1991–2005	68 872 (58.8)	44 075 (55.6)	13 425 (61.4)	13 778 (41.8)	3159 (40.7)	3694 (47.4)	2029 (51.1)	4351 (49.8)
2006–2019	43 725 (37.3)	33 414 (42.1)	7406 (33.9)	18 465 (56.0)	4905 (63.1)	3943 (50.6)	1754 (44.2)	3898 (44.6)
Missing, n	4303							
Ethnicity, n (%)								
European	91 981 (84)	62 984 (84.7)	15 476 (75.4)	26 087 (85.8)	6534 (82.5)	5773 (77.2)	2617 (68.3)	6078 (76.7)
Hispanic American	886 (0.8)	574 (0.7)	179 (0.9)	225 (0.7)	46 (0.6)	78 (1.0)	26 (0.7)	104 (1.3)
African	1015 (0.9)	401 (0.6)	435 (2.1)	135 (0.4)	53 (0.7)	58 (0.8)	52 (1.4)	241 (3.0)
Asian	13 139 (12.0)	8397 (11.3)	3891 (19.5)	3033 (10.0)	1090 (13.8)	1416 (18.9)	1061 (27.7)	1263 (15.9)
Other	2316 (2.1)	1929 (2.6)	433 (2.1)	936 (3.1)	198 (2.5)	157 (2.1)	77 (2.0)	217 (2.7)
Missing, n	11 928							
Tumor size, n (%)								
≤2 cm	49 887 (61.5)	36 848 (63.2)	7746 (50.3)	17 873 (65.5)	3339 (46.0)	3055 (52.2)	1305 (44.6)	3147 (48.2)
>2 and ≤5cm	27 665 (34.1)	19 024 (32.7)	6706 (43.5)	8358 (30.6)	3449 (47.5)	2478 (42.4)	1374 (47.0)	3016 (46.2)
>5 cm	3603 (4.4)	2388 (4.1)	948 (6.2)	1067 (3.9)	472 (6.5)	317 (5.4)	245 (8.4)	371 (5.7)

Tumor size, n (%)
≤2 cm 49 887 (61.5) 36 848 (63.2) 7746 (50.3) 17 873 (65.5) 3339 (46.0) 3055 (52.2) 1305 (44.6) 3147 (48.2)
>2 and ≤5cm 27 665 (34.1) 19 024 (32.7) 6706 (43.5) 8358 (30.6) 3449 (47.5) 2478 (42.4) 1374 (47.0) 3016 (46.2)
>5 cm 3603 (4.4) 2388 (4.1) 948 (6.2) 1067 (3.9) 472 (6.5) 317 (5.4) 245 (8.4) 371 (5.7)

Characteristics	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple negative
Missing, n	40 280							
Nodal status, n (%)								
Negative	59 569 (62.1)	43 212 (62.0)	11 156 (59.6)	20 203 (63.5)	4352 (51.4)	3930 (54.6)	1795 (50.5)	4874 (62.7)
Positive	36 395 (37.9)	26 476 (38.0)	7551 (40.4)	11 609 (36.5)	4112 (48.6)	3264 (45.4)	1759 (49.5)	2905 (37.3)
Missing, n	25 471							
Tumor stage, n (%)								
I	34 157 (44.5)	25 351 (45.9)	5147 (34.6)	12 222 (47.7)	1903 (29.4)	2209 (37.5)	839 (28.0)	2143 (34.6)
II	34 696 (45.2)	24 498 (44.3)	7663 (51.5)	11 154 (43.5)	3567 (55.2)	2838 (48.1)	1561 (52.1)	3314 (53.5)
III	7990 (10.4)	5411 (9.8)	2056 (13.8)	2243 (8.8)	997 (15.4)	850 (14.4)	597 (19.9)	742 (12)
Missing, n	44 592							
Grade, n (%)								
Grade 1	17 919 (19.2)	15 546 (22.6)	800 (4.5)	10 130 (30.1)	-	672 (9.3)	62 (1.8)	279 (3.7)
Grade 2	45 065 (48.3)	37 347 (54.3)	4614 (26.1)	23 503 (69.9)	-	3397 (47.0)	918 (26.4)	1709 (22.4)
Grade 3	30 231 (32.4)	15 852 (23.1)	12 253 (69.4)	-	8915 (100)	3151 (43.6)	2498 (71.8)	5651 (74)
Missing, n	28 220							
Surgery, n (%)								
No surgery	1160 (1.6)	437 (0.8)	152 (1.1)	108 (0.4)	26 (0.4)	37 (0.7)	22 (0.8)	35 (0.6)
Breast conserving surgery	29 530 (40.9)	22 923 (44.4)	4971 (36.8)	11 551 (47.5)	2371 (36.7)	2188 (40.3)	775 (28.9)	2168 (38.8)
Mastectomy	22 785 (31.6)	16 032 (31.1)	5237 (38.7)	6730 (27.7)	2156 (33.4)	2092 (38.5)	1378 (51.3)	1821 (32.6)
Type unknown	18 677 (25.9)	12 187 (23.6)	3155 (23.3)	5942 (24.4)	1907 (29.5)	1111 (20.5)	510 (19.0)	1561 (27.9)
Missing, n	49 283							
Radiation therapy, n (%)								
No	18 563 (27.6)	12 525 (26.3)	3684 (28.8)	5268 (25.7)	1250 (22.8)	1353 (26.1)	801 (30.8)	1217 (25.7)
Yes	48 616 (72.4)	35 037 (73.7)	9111 (71.2)	15 241 (74.3)	4243 (77.2)	3826 (73.9)	1797 (69.2)	3510 (74.3)
Missing, n	54 256							
Chemotherapy, n (%)								
No	27 667 (41.0)	21 895 (45.9)	2310 (16.5)	11 812 (53.0)	1632 (25.3)	1203 (21.9)	328 (11.3)	864 (15.2)

Characteristics	Overall	ER+	ER−	Luminal A-like	negative-like	like	HER2-enriched-like	Triple negative
Yes	39 815 (59.0)	25 796 (54.1)	11 729 (83.5)	10 465 (47.0)	4820 (74.7)	4294 (78.1)	2584 (88.7)	4816 (84.8)
Missing, n	53 953							
Endocrine therapy, n (%)								
No	19 688 (28.6)	7869 (15.6)	9232 (77.4)	3629 (15.5)	781 (13.1)	978 (17.2)	2209 (88.0)	3907 (84.5)
Yes	49 163 (71.4)	42 682 (84.4)	2689 (22.6)	19 859 (84.5)	5175 (86.9)	4702 (82.8)	302 (12.0)	717 (15.5)
Missing, n	52 584							
Trastuzumab, n (%)								
No	50 545 (95.1)	33 531 (95.4)	10 337 (91.6)	16 909 (99.7)	4849 (99.4)	2341 (60.9)	1306 (61.9)	5104 (99.6)
Yes	2598 (4.9)	1607 (4.6)	952 (8.4)	53 (0.3)	30 (0.6)	1505 (39.1)	805 (38.1)	18 (0.4)
Missing, n	68 292							
Reproductive and lifestyle risk factors								
Age at menarche, median (IQR)	13 (12–14)	13 (12–14)	13 (12–14)	13 (12–14)	13 (12–14)	13 (12–14)	13 (12–14)	13 (12–14)
Missing, n	35 355							
Parity, median (IQR)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)
Nulliparous, n (%)	12 932 (14.0)	8971 (14.2)	2066 (12.9)	3633 (14.1)	934 (15.0)	870 (15.0)	384 (13.5)	787 (12.8)
Parous, n (%)	79 415 (86.0)	54 292 (85.8)	13 955 (87.1)	22 162 (85.9)	5291 (85.0)	4928 (85.0)	2456 (86.5)	5376 (87.2)
Missing, n	29 088							
Age at first full term pregnancy[b], median (IQR)	25 (22–28)	25 (22–28)	24 (21–28)	24 (21–28)	25 (22–28)	25 (22–29)	25 (22–28)	24 (21–27)
Missing, n	50 965							
Breastfeeding, n (%)								
Never	24 906 (39.5)	16 660 (38.4)	4476 (39.9)	7039 (39.2)	1754 (41.9)	1716 (40.2)	831 (41.3)	1796 (42.5)
Ever	38 195 (60.5)	26 730 (61.6)	6734 (60.1)	10 912 (60.8)	2435 (58.1)	2555 (59.8)	1181 (58.7)	2433 (57.5)
Missing, n	58 334							
Duration in months[c], median (IQR)	7 (3–15)	7 (3–15)	7 (3–16)	7 (3–15)	7 (3–15)	7 (3–15)	8 (3–17)	6 (3–15)
Missing, n	68 870							

Characteristics	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple negative
Time since last full term birth[b,f], n (%)								
≥ 10 years	29 200 (64.2)	18 626 (63.3)	5795 (65.7)	7901 (65.5)	1822 (62.0)	1986 (63.0)	1096 (67.8)	2303 (67.3)
5 – 10 years	1926 (4.2)	1115 (3.8)	466 (5.3)	362 (3.0)	103 (3.5)	177 (5.6)	65 (4.0)	163 (4.8)
0 – 5 years	1179 (2.6)	601 (2.0)	393 (4.5)	161 (1.3)	70 (2.4)	101 (3.2)	51 (3.2)	130 (3.8)
Missing, n	75 975							
Oral contraceptives, n (%)								
Never use	29 677 (44.5)	20 263 (45.0)	5090 (43.4)	8398 (46.4)	1967 (45.1)	2018 (43.6)	1096 (48.6)	1923 (43.2)
Ever use	37 070 (55.5)	24 799 (55.0)	6629 (56.6)	9701 (53.6)	2395 (54.9)	2608 (56.4)	1159 (51.4)	2533 (56.8)
Missing, n	54 688							
Menopausal hormone therapy[f], n (%)								
Never use, postmenopausal	28 534 (37.1)	20 062 (38.3)	5088 (37.1)	9129 (41.4)	2315 (42.8)	2044 (39.0)	1108 (43.3)	2115 (39.0)
Former[e] use estrogen therapy	1394 (1.8)	1041 (2.0)	195 (1.4)	397 (1.8)	81 (1.5)	77 (1.5)	40 (1.6)	91 (1.7)
Former[e] use estrogen+progestin	1414 (1.8)	1035 (2.0)	246 (1.8)	490 (2.2)	91 (1.7)	94 (1.8)	49 (1.9)	124 (2.3)
Former[e] use (unknown type)	5972 (7.8)	4366 (8.3)	912 (6.7)	1960 (8.9)	481 (8.9)	291 (5.6)	164 (6.4)	405 (7.5)
Current[f] use estrogen therapy	2175 (2.8)	1456 (2.8)	272 (2.0)	562 (2.5)	103 (1.9)	129 (2.5)	48 (1.9)	119 (2.2)
Current[f] use estrogen+progestin	3755 (4.9)	2689 (5.1)	458 (3.3)	1251 (5.7)	181 (3.3)	287 (5.5)	79 (3.1)	205 (3.8)
Current[f] use (unknown type)	5854 (7.6)	4398 (8.4)	647 (4.7)	1896 (8.6)	300 (5.5)	247 (4.7)	102 (4.0)	236 (4.4)
Missing, n	44 547							
BMI[d], median (IQR)	25 (23–28)	25 (23–29)	25 (22–28)	25 (23–29)	26 (23–29)	25 (22–28)	25 (22–28)	25 (23–29)
18.5–25 kg/m², n (%)	43 302 (47.4)	29 382 (46.9)	7716 (47.9)	11 545 (44.2)	2813 (42.8)	2962 (49.4)	1428 (49.4)	2925 (45.8)
<18.5 kg/m², n (%)	1657 (1.8)	1103 (1.8)	355 (2.2)	405 (1.6)	117 (1.8)	143 (2.4)	72 (2.5)	132 (2.1)
25–30 kg/m², n (%)	29 960 (32.8)	20 776 (33.2)	5134 (31.9)	8939 (34.2)	2210 (33.6)	1857 (31.0)	933 (32.3)	2041 (32.0)
>=30 kg/m², n (%)	16 435 (18.0)	11 353 (18.1)	2891 (18.0)	5228 (20.0)	1430 (21.8)	1034 (17.2)	459 (15.9)	1284 (20.1)
Missing, n	30 081							
Adult height, median (IQR)	163 (158–168)	163 (159–168)	163 (158–168)	163 (159–168)	163 (158–168)	163 (158–168)	162 (157–167)	163 (158–168)

Characteristics	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple negative
Missing, n	33 481							
Smoking, n (%)								
Never	39 512 (59.0)	27 175 (59.3)	7352 (63.3)	11 767 (60.1)	2795 (62.4)	2961 (64.3)	1581 (68.7)	2856 (64.0)
Former[g]	17 407 (26.0)	12 082 (26.3)	2424 (20.9)	4954 (25.3)	1093 (24.4)	1069 (23.2)	387 (16.8)	903 (20.2)
Current[h]	10 073 (15.0)	6605 (14.4)	1840 (15.8)	2850 (14.6)	589 (13.2)	575 (12.5)	332 (14.4)	701 (15.7)
Missing, n	54 443							
Pack-years of smoking								
Former smokers[g], median (IQR)	0.8 (0.3–1.8)	0.8 (0.3–1.8)	0.7 (0.2–1.6)	0.9 (0.3–1.9)	0.8 (0.2–1.8)	0.7 (0.2–1.8)	0.6 (0.2–1.7)	0.7 (0.2–1.6)
Current smokers[h], median (IQR)	1.9 (0.9–3.1)	1.9 (1.0–3.1)	1.5 (0.7–2.6)	2.0 (0.9–3.2)	2.0 (1.0–3.1)	1.6 (0.7–2.5)	1.6 (0.8–2.7)	1.5 (0.6–2.6)
Missing, n	62 214							
Alcohol consumption[h], g/week, median (IQR)	14.7 (0.0–57.3)	16.0 (0.0–59.5)	10.8 (0.0–50.7)	12.0 (0.0–51.8)	12.0 (0.0–49.7)	15.0 (0.0–60.0)	6.0 (0.0–48.3)	6.0 (0.0–45.0)
Missing, n	100 522							
Cumulative alcohol consumption, g/day, median (IQR)	1.9 (0.0–7.9)	2.0 (0.0–8.2)	1.1 (0.0–6.1)	2.0 (0.0–8.4)	1.7 (0.0–7.0)	2.1 (0.0–7.8)	0.8 (0.0–5.6)	1.0 (0.0–5.7)
Missing, n	102 451							
Physical activity[h,i], median (IQR)	3 (1–8)	3 (1–9)	3 (1–8)	5 (1–11)	4 (2–11)	4 (1–9)	4 (1–9)	4 (1–10)
< 1.8 hours/week, n (%)	7103 (33.3)	4643 (31.6)	1043 (31.1)	1564 (27.1)	305 (24.6)	437 (28.2)	222 (29.1)	418 (31.0)
≥ 1.8 – < 5.5 hours/week, n (%)	7063 (33.1)	4679 (31.9)	1106 (33.0)	1545 (26.8)	424 (34.2)	491 (31.7)	231 (30.4)	382 (28.3)
≥ 5.5 hours/week, n (%)	7154 (33.6)	5363 (36.5)	1205 (35.9)	2656 (46.1)	510 (41.2)	619 (40.1)	308 (40.5)	549 (40.7)
Missing, n	100 115							

Percentages shown in the table might not sum up to 100% due to rounding.

[a]Numbers for subtypes do not add to total due to missing.

[b]For parous women only.

[c]For women who breastfed only.

Associations between individual risk factors and 10 years all-cause mortality by ER status and intrinsic-like subtype based on the imputed datasets.

Risk factor	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-positive-like	HER2-enriched-like	Triple negative
	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)
Age at menarche, per 1 year increase	2.3E-01 1.02 (1.00,1.04)	5.9E-01 1.01 (0.99,1.03)	8.0E-02 1.03 (1.00,1.06)	9.1E-01 1.00 (0.98,1.03)	6.9E-01 1.01 (0.98,1.04)	2.3E-01 1.03 (0.99,1.07)	2.4E-01 1.04 (0.99,1.09)	2.2E-01 1.03 (0.99,1.07)
Parity	1.4E-03	1.3E-04	1.5E-01	7.6E-04	1.4E-01	6.2E-01	9.1E-01	5.6E-02
0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1	0.87 (0.79,0.96)	0.87 (0.79,0.97)	0.85 (0.73,0.98)	0.86 (0.75,0.99)	0.88 (0.76,1.02)	0.91 (0.75,1.11)	0.87 (0.66,1.15)	0.80 (0.67,0.96)
2	0.86 (0.77,0.96)	0.83 (0.74,0.93)	0.92 (0.80,1.06)	0.81 (0.70,0.93)	0.86 (0.73,1.01)	0.87 (0.71,1.06)	1.00 (0.76,1.31)	0.84 (0.71,1.00)
3	0.90 (0.82,1.00)	0.88 (0.79,0.98)	0.92 (0.79,1.06)	0.86 (0.76,0.98)	0.90 (0.77,1.06)	0.92 (0.74,1.14)	0.97 (0.75,1.25)	0.86 (0.71,1.05)
4+	0.97 (0.88,1.06)	0.92 (0.83,1.02)	1.05 (0.90,1.23)	0.89 (0.78,1.02)	0.94 (0.79,1.12)	1.01 (0.80,1.29)	1.06 (0.80,1.41)	0.99 (0.80,1.24)
Age at first full term pregnancy[a], years	1.9E−14	2.5E−11	1.5E−02	4.3E−07	2.6E−02	4.3E−03	5.7E−01	3.9E−02
< 20	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
20 to < 25	0.88 (0.83,0.94)	0.86 (0.80,0.93)	0.93 (0.83,1.04)	0.84 (0.76,0.93)	0.92 (0.80,1.07)	0.83 (0.69,1.00)	0.94 (0.71,1.23)	0.91 (0.79,1.04)
25 to < 30	0.82 (0.76,0.87)	0.80 (0.73,0.86)	0.87 (0.77,0.99)	0.78 (0.70,0.87)	0.82 (0.71,0.95)	0.79 (0.65,0.97)	0.89 (0.67,1.17)	0.86 (0.73,1.01)
≥ 30	0.79 (0.73,0.86)	0.78 (0.71,0.87)	0.82 (0.71,0.96)	0.79 (0.68,0.91)	0.83 (0.70,1.00)	0.73 (0.58,0.91)	0.80 (0.58,1.10)	0.82 (0.69,0.98)
Time since last full term birth[a], years	9.5E−02	4.5E−04	7.5E−01	8.8E−03	7.6E−01	2.0E−01	8.1E−01	6.4E−01
≥ 10	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥ 5 – < 10	1.07 (0.96,1.19)	1.15 (1.01,1.33)	0.95 (0.81,1.12)	1.16 (0.98,1.38)	1.10 (0.83,1.45)	1.17 (0.92,1.50)	0.99 (0.73,1.34)	0.88 (0.70,1.10)
> 0 – < 5	1.21 (1.03,1.41)	1.36 (1.12,1.65)	1.02 (0.82,1.26)	1.55 (1.08,2.24)	1.11 (0.83,1.48)	1.28 (0.86,1.91)	1.07 (0.76,1.51)	0.93 (0.68,1.27)
Breastfeeding[a]								
Per 6 months increase	2.4E−01 1.02 (0.99,1.04)	5.4E−01 1.01 (0.99,1.04)	1.2E−01 1.03 (1.00,1.06)	4.7E−01 1.01 (0.99,1.04)	7.2E−01 1.01 (0.97,1.06)	4.1E−01 1.02 (0.99,1.06)	6.7E−01 1.01 (0.97,1.05)	1.1E−01 1.03 (1.00,1.06)
Ever vs never	7.5E−01 0.97 (0.85,1.10)	6.2E−01 0.95 (0.84,1.08)	9.1E−01 1.01 (0.84,1.23)	5.1E−01 0.93 (0.81,1.08)	9.1E−01 0.99 (0.83,1.17)	7.3E−01 0.94 (0.76,1.17)	9.5E−01 0.99 (0.75,1.31)	9.0E−01 1.02 (0.85,1.22)

Risk factor	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-positive-like	HER2-enriched-like	Triple negative
	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)
BMI, kg/m²								
All women	2.2E−02	5.9E−03	2.8E−01	5.9E−03	1.4E−01	1.6E−01	6.4E−01	3.2E−01
18.5 to < 25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
< 18.5	1.34 (0.96,1.87)	1.41 (1.03,1.95)	1.24 (0.82,1.87)	1.56 (1.12,2.18)	1.32 (0.80,2.18)	1.17 (0.71,1.94)	1.22 (0.69,2.14)	1.20 (0.78,1.83)
25 to < 30	1.05 (0.92,1.21)	1.06 (0.94,1.20)	1.03 (0.86,1.24)	1.03 (0.90,1.18)	1.07 (0.92,1.26)	1.13 (0.96,1.33)	0.98 (0.80,1.20)	1.04 (0.86,1.27)
≥ 30	1.23 (1.09,1.40)	1.24 (1.10,1.39)	1.20 (1.01,1.43)	1.24 (1.09,1.41)	1.22 (1.04,1.42)	1.23 (1.01,1.50)	1.19 (0.92,1.55)	1.21 (1.02,1.43)
Postmenopausal women	2.5E−07	3.4E−06	2.0E−02	1.2E−05	1.2E−01	2.4E−01	5.3E−01	1.2E−01
18.5 to < 25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
< 18.5	1.53 (1.30,1.80)	1.57 (1.30,1.89)	1.46 (1.09,1.95)	1.73 (1.41,2.12)	1.45 (0.89,2.38)	1.16 (0.67,2.00)	1.42 (0.80,2.50)	1.48 (1.03,2.13)
25 to < 30	1.05 (0.97,1.12)	1.06 (0.97,1.15)	1.02 (0.92,1.12)	1.02 (0.92,1.12)	1.09 (0.94,1.26)	1.16 (0.95,1.42)	0.95 (0.75,1.20)	1.02 (0.89,1.17)
≥ 30	1.20 (1.12,1.29)	1.22 (1.12,1.33)	1.15 (1.02,1.29)	1.21 (1.09,1.35)	1.20 (1.00,1.44)	1.20 (0.97,1.48)	1.19 (0.92,1.53)	1.14 (0.98,1.33)
Pre/perimenopausal women	5.4E−01	5.3E−01	6.9E−01	6.4E−01	6.2E−01	6.2E−01	9.1E−01	6.7E−01
18.5 to < 25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
< 18.5	1.08 (0.53,2.21)	1.14 (0.54,2.41)	1.03 (0.49,2.19)	1.17 (0.49,2.80)	1.17 (0.54,2.52)	1.17 (0.46,2.95)	1.02 (0.41,2.55)	0.90 (0.36,2.22)
25 to < 30	1.07 (0.76,1.49)	1.06 (0.77,1.48)	1.06 (0.72,1.57)	1.08 (0.70,1.66)	1.04 (0.76,1.41)	1.06 (0.76,1.49)	1.02 (0.71,1.47)	1.09 (0.68,1.74)
≥ 30	1.32 (0.94,1.85)	1.32 (0.96,1.82)	1.30 (0.88,1.94)	1.36 (0.87,2.12)	1.28 (0.96,1.72)	1.34 (0.94,1.92)	1.18 (0.75,1.88)	1.35 (0.90,2.04)
Adult height, per 5 cm increase	3.7E−01 0.97 (0.92,1.02)	4.6E−01 0.97 (0.91,1.03)	3.0E−01 0.97 (0.92,1.02)	4.1E−01 0.97 (0.91,1.03)	6.7E−01 0.98 (0.91,1.05)	6.4E−01 0.97 (0.90,1.05)	3.4E−01 0.95 (0.87,1.03)	4.4E−01 0.97 (0.92,1.03)
Oral contraceptive use	1.6E−04	7.8E−04	2.6E−02	8.9E−04	2.6E−01	1.5E−01	2.7E−01	5.9E−02
Ever vs never	0.88 (0.84,0.93)	0.89 (0.84,0.94)	0.88 (0.80,0.96)	0.87 (0.81,0.93)	0.91 (0.81,1.03)	0.89 (0.79,1.01)	0.90 (0.77,1.04)	0.88 (0.78,0.98)
Menopausal hormone therapy	0.0E+00	0.0E+00	3.0E−09	0.0E+00	6.2E−05	3.1E−04	3.9E−02	3.5E−03
Never use, postmenopausal	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former[b] use of ET	0.73 (0.64,0.84)	0.75 (0.65,0.88)	0.67 (0.48,0.93)	0.78 (0.64,0.94)	0.68 (0.49,0.94)	0.75 (0.50,1.13)	0.60 (0.27,1.31)	0.71 (0.46,1.10)
Former[b] use of EPT	0.81 (0.70,0.93)	0.80 (0.67,0.95)	0.89 (0.68,1.18)	0.75 (0.57,0.99)	0.86 (0.58,1.27)	0.77 (0.49,1.19)	0.97 (0.55,1.70)	0.93 (0.64,1.35)
Former[b] use (unknown type)	0.80 (0.75,0.85)	0.79 (0.74,0.85)	0.81 (0.71,0.94)	0.78 (0.70,0.86)	0.82 (0.68,1.01)	0.79 (0.63,0.99)	0.87 (0.66,1.15)	0.80 (0.68,0.94)

Risk factor	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-positive-like	HER2-enriched-like	Triple negative
	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)
Current[c] use of ET	0.70 (0.61,0.79)	0.68 (0.59,0.79)	0.75 (0.58,0.97)	0.73 (0.60,0.88)	0.64 (0.42,0.97)	0.64 (0.42,0.95)	0.53 (0.29,0.99)	0.83 (0.59,1.17)
Current[c] use of EPT	0.58 (0.52,0.65)	0.59 (0.52,0.67)	0.56 (0.45,0.70)	0.59 (0.50,0.70)	0.57 (0.40,0.82)	0.55 (0.40,0.76)	0.53 (0.34,0.84)	0.64 (0.48,0.85)
Current[c] use (unknown type)	0.75 (0.69,0.82)	0.72 (0.65,0.80)	0.87 (0.71,1.06)	0.72 (0.64,0.82)	0.70 (0.56,0.88)	0.72 (0.53,0.99)	0.81 (0.54,1.23)	0.96 (0.73,1.27)
Smoking	0.0E+00	0.0E+00	3.5E−03	0.0E+00	3.5E−03	3.0E−02	1.6E−01	4.8E−02
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former[d]	1.01 (0.97,1.05)	1.04 (0.98,1.09)	0.97 (0.88,1.06)	1.05 (0.98,1.13)	0.99 (0.89,1.12)	1.00 (0.88,1.14)	1.07 (0.86,1.33)	0.94 (0.83,1.05)
Current[e]	1.38 (1.30,1.45)	1.46 (1.37,1.56)	1.20 (1.10,1.32)	1.59 (1.48,1.71)	1.31 (1.14,1.50)	1.28 (1.09,1.50)	1.28 (1.04,1.59)	1.20 (1.04,1.37)
No. of pack-years of smoking, per 10 units increase	1.2E−03 1.11 (1.06,1.15)	1.2E−03 1.12 (1.07,1.17)	3.0E−03 1.08 (1.04,1.12)	5.0E−04 1.13 (1.08,1.18)	2.2E−02 1.10 (1.03,1.16)	1.9E−02 1.09 (1.03,1.15)	2.2E−02 1.10 (1.03,1.17)	2.2E−02 1.07 (1.03,1.12)
Alcohol consumption[e], per 10 g/week	8.8E−01 1.01 (0.99,1.01)	9.0E−01 1.00 (0.99,1.01)	8.8E−01 1.00 (0.99,1.01)	9.9E−01 1.00 (0.99,1.01)	8.4E−01 1.00 (0.99,1.01)	7.5E−01 1.00 (0.98,1.01)	9.1E−01 1.00 (0.99,1.02)	8.1E−01 1.00 (0.98,1.01)
Cumulative alcohol consumption, per 10 g/day	8.0E−01 1.01 (0.96,1.06)	7.8E−01 1.01 (0.96,1.06)	8.7E−01 1.01 (0.96,1.06)	7.5E−01 1.01 (0.96,1.07)	9.0E−01 1.01 (0.94,1.08)	9.1E−01 1.01 (0.95,1.06)	6.9E−01 1.02 (0.96,1.08)	9.1E−01 1.00 (0.94,1.07)
Physical activity[e,f], hours/week	8.3E−02	9.6E−02	8.2E−02	1.1E−01	2.1E−01	8.4E−03	6.1E−02	1.4E−01
< 1.8	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥ 1.8 – < 5.5	0.80 (0.38,1.68)	0.80 (0.38,1.70)	0.79 (0.38,1.65)	0.77 (0.33,1.80)	0.85 (0.40,1.81)	0.84 (0.55,1.28)	0.87 (0.52,1.46)	0.76 (0.29,1.97)
≥ 5.5	0.42 (0.21,0.85)	0.42 (0.20,0.88)	0.42 (0.20,0.85)	0.40 (0.18,0.89)	0.47 (0.21,1.06)	0.44 (0.27,0.71)	0.46 (0.25,0.87)	0.40 (0.18,0.90)

All the analyses were stratified by study and adjusted for lymph nodes status, tumor size, tumor grade and (neo)adjuvant systemic treatment. Age of the patients was used as time scale. Reported p-values (P) are from likelihood ratio tests comparing a model with and without a particular risk factor and are adjusted for multiple testing using the Benjamini-Hochberg method for false discovery rate (FDR) control on 136 tests. Heterogeneity test by subtype is shown in Table 3. Numbers of patients and events included in the corresponding complete-case analyses are shown in Supplementary Figures S1 (overall), S3 (ER+), S5 (ER−), S7 (Luminal A-like), S9 (Luminal B-HER2-negative-like), S11 (Luminal B-HER2-positive-like), S13 (HER2-enriched), and S15 (triple negative). Abbreviations: ET: estrogen therapy; EPT: combined estrogen and progestin therapy.

[a]Association estimated in parous women.

[b]More than 6 months before diagnosis.

[c]At diagnosis or within 6 months before diagnosis.

Breast Cancer Association Consortium BCAC

- Morra et al. (Hollanda) prognoz ve sağ kalım değ.
- 121435 invaziv stage I-II meme kanserli 67 çalışma
- 16890 ölüm(8554 meme kanserine bağlı)
- 10 yıllık period
- Cox regresyon ve Multivariate analiz
- Çoklu ve tek değişken parametreler
- Ölüm oranıyla heterojen risk faktörleri arasında kanıt yok p>0.30

Breast Cancer Association Consortium BCAC

- BMI>30 18.5-25kg/m2 HR 95%CI:1.19(1.06-1.34)
- Sigara kullanımı 1.37(1.27-1.47)
- Fiziksel aktivite 043(0.21-0.86)
- İlk gebelik yaşı>30 ve <20 0.79(0.72-0.86)
- İlk gebelik intervali 5-10 yıl 1.31(1.11-1.55)
- OK 0.91(0.87-0.96)
- HT 0.61(0.54-0.69)
- Zayıflık 1.11(1.02-1.21)

BCAC

- Tek değişkenli analizlerde daha önce doğum yapmışlarda daha iyi prognoz
- 35 yaş üstü daha iyi prognoz
- ER Luminal A tm ve Triple negatifler arasında fark yok HR 0.93(0.68-1.27)
- BMI 18.5kg/m2 den daha düşük olanlar riskli
- İlk doğum tarihi 5-10 yıl arasında daha kısa süreli olanlarda Luminal A grup Triple negatif olanlara göre daha iyi prognoz
- Çok değişkenli analizlerde
- Hormon tedavisi
- Östrojen,progestin kullanımı
- Sigara
- Fiziksel aktivite azlığı kötü prognoz

Associations between individual risk factors and 10-year breast cancer-specific mortality by ER status and intrinsic-like subtype based on the imputed datasets.

Risk factor	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple negative
	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)
Age at menarche, per 1 year increase	2.0E−01 1.02 (1.00,1.05)	6.1E−01 1.01 (0.99,1.04)	8.0E−02 1.04 (1.01,1.08)	6.7E−01 1.02 (0.98,1.05)	9.2E−01 1.00 (0.96,1.04)	4.8E−01 1.04 (0.99,1.09)	2.8E−01 1.06 (1.00,1.11)	4.8E−01 1.03 (0.99,1.08)
Parity	6.3E−01	3.3E−01	7.1E−01	7.8E−01	5.4E−01	1.0E+00	9.6E−01	8.7E−01
0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1	0.95 (0.87,1.04)	0.94 (0.85,1.05)	0.95 (0.80,1.12)	0.96 (0.82,1.13)	0.87 (0.73,1.04)	1.04 (0.78,1.39)	0.92 (0.68,1.23)	0.92 (0.73,1.16)
2	0.93 (0.86,1.02)	0.88 (0.80,0.97)	1.03 (0.88,1.21)	0.89 (0.76,1.03)	0.87 (0.74,1.03)	0.96 (0.75,1.22)	1.04 (0.77,1.40)	0.98 (0.80,1.20)
3	0.98 (0.89,1.07)	0.96 (0.86,1.06)	1.00 (0.83,1.19)	0.97 (0.83,1.14)	0.90 (0.75,1.08)	1.02 (0.78,1.34)	1.05 (0.78,1.41)	0.95 (0.75,1.19)
4+	1.06 (0.95,1.19)	0.98 (0.86,1.11)	1.21 (1.01,1.46)	1.01 (0.85,1.21)	0.96 (0.76,1.22)	1.01 (0.73,1.40)	1.17 (0.79,1.74)	1.17 (0.90,1.52)
Age at first full term pregnancy[a], years	5.0E−05	2.8E−03	5.2E−01	2.0E−01	2.6E−01	6.1E−01	7.2E−01	7.6E−01
< 20	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
20 – < 25	0.90 (0.82,0.98)	0.88 (0.78,0.98)	0.95 (0.82,1.08)	0.87 (0.75,1.01)	0.89 (0.73,1.08)	0.88 (0.67,1.15)	0.92 (0.67,1.26)	0.95 (0.80,1.13)
25 – < 30	0.86 (0.79,0.94)	0.85 (0.76,0.96)	0.91 (0.79,1.05)	0.87 (0.73,1.04)	0.81 (0.66,0.99)	0.86 (0.65,1.12)	0.85 (0.63,1.14)	0.91 (0.76,1.10)
≥ 30	0.83 (0.76,0.91)	0.82 (0.72,0.93)	0.87 (0.74,1.03)	0.83 (0.68,1.00)	0.82 (0.65,1.03)	0.81 (0.59,1.10)	0.81 (0.55,1.18)	0.88 (0.70,1.11)
Time since last full term birth[a], years	4.6E−02	2.2E−04	7.7E−01	5.5E−03	6.7E−01	4.1E−01	8.7E−01	6.5E−01
≥ 10	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥ 5 – < 10	1.10 (0.96,1.27)	1.24 (1.07,1.44)	0.92 (0.73,1.18)	1.25 (1.03,1.53)	1.16 (0.90,1.51)	1.23 (0.91,1.66)	1.05 (0.67,1.65)	0.82 (0.59,1.14)
> 0 – < 5	1.28 (1.11,1.49)	1.49 (1.22,1.81)	1.03 (0.83,1.29)	1.79 (1.27,2.51)	1.21 (0.85,1.70)	1.37 (0.95,1.99)	1.14 (0.75,1.74)	0.90 (0.65,1.24)
Breastfeeding[a]								
Per 6 months increase	4.6E−01 1.03 (0.99,1.06)	5.4E−01 1.02 (0.99,1.05)	4.1E−01 1.03 (1.00,1.07)	4.6E−01 1.03 (0.99,1.06)	7.2E−01 1.02 (0.97,1.07)	7.2E−01 1.02 (0.97,1.07)	6.8E−01 1.03 (0.96,1.11)	4.8E−01 1.03 (0.99,1.07)

Risk factor	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple negative
	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)
Ever vs Never	9.2E−01 1.02 (0.85,1.22)	9.7E−01 1.01 (0.84,1.20)	8.7E−01 1.05 (0.83,1.32)	9.7E−01 0.99 (0.80,1.23)	9.7E−01 0.99 (0.81,1.22)	8.7E−01 0.95 (0.71,1.26)	9.2E−01 1.04 (0.70,1.55)	7.2E−01 1.09 (0.89,1.34)
BMI, kg/m²								
All women	3.0E−01	2.6E−01	6.4E−01	4.8E−01	7.2E−01	4.6E−01	8.7E−01	7.8E−01
18.5 – < 25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
< 18.5	1.12 (0.78,1.60)	1.13 (0.76,1.66)	1.11 (0.73,1.68)	1.04 (0.66,1.65)	1.27 (0.74,2.17)	1.20 (0.65,2.23)	1.10 (0.52,2.31)	0.99 (0.56,1.73)
25 – < 30	1.07 (0.92,1.23)	1.09 (0.95,1.25)	1.03 (0.87,1.23)	1.07 (0.90,1.29)	1.06 (0.90,1.25)	1.16 (0.93,1.44)	0.96 (0.74,1.25)	1.05 (0.86,1.28)
≥ 30	1.19 (1.05,1.34)	1.19 (1.04,1.37)	1.16 (1.01,1.34)	1.21 (1.03,1.43)	1.12 (0.95,1.31)	1.27 (0.99,1.63)	1.19 (0.91,1.55)	1.15 (0.96,1.38)
Postmenopausal women	5.7E−02	1.2E−01	4.8E−01	5.4E−01	8.7E−01	4.8E−01	7.8E−01	7.8E−01
18.5 – < 25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
< 18.5	1.25 (0.98,1.59)	1.14 (0.84,1.56)	1.43 (0.99,2.06)	1.11 (0.66,1.84)	1.12 (0.46,2.68)	1.19 (0.52,2.71)	1.40 (0.64,3.07)	1.38 (0.79,2.39)
25 to < 30	1.08 (0.98,1.20)	1.12 (0.99,1.26)	1.02 (0.89,1.18)	1.08 (0.92,1.26)	1.10 (0.91,1.34)	1.25 (0.99,1.57)	0.93 (0.67,1.29)	1.05 (0.87,1.28)
≥ 30	1.15 (1.04,1.27)	1.17 (1.02,1.33)	1.12 (0.97,1.30)	1.18 (1.00,1.40)	1.08 (0.83,1.40)	1.22 (0.91,1.65)	1.21 (0.89,1.65)	1.08 (0.88,1.34)
Pre/perimenopausal women	6.3E−01	6.1E−01	7.8E−01	7.2E−01	7.4E−01	7.1E−01	9.7E−01	7.7E−01
18.5 – < 25	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
< 18.5	0.97 (0.52,1.83)	1.07 (0.55,2.10)	0.87 (0.42,1.81)	0.89 (0.39,2.01)	1.42 (0.74,2.71)	1.20 (0.45,3.22)	0.82 (0.28,2.42)	0.63 (0.20,2.02)
25 – < 30	1.04 (0.80,1.35)	1.04 (0.80,1.35)	1.05 (0.76,1.46)	1.07 (0.74,1.57)	1.00 (0.77,1.29)	1.04 (0.74,1.46)	1.00 (0.69,1.46)	1.06 (0.72,1.55)
≥ 30	1.27 (1.01,1.59)	1.28 (1.02,1.63)	1.23 (0.92,1.64)	1.32 (0.94,1.85)	1.19 (0.91,1.56)	1.39 (0.94,2.05)	1.14 (0.74,1.76)	1.27 (0.93,1.73)
Adult height, per 5 cm increase	9.6E−01 1.00 (0.95,1.05)	8.8E−01 0.99 (0.94,1.05)	9.0E−01 1.01 (0.95,1.07)	8.7E−01 0.99 (0.93,1.05)	1.0E+00 1.00 (0.94–1.06)	1.0E+00 1.00 (0.93,1.07)	8.7E−01 0.98 (0.90,1.08)	8.7E−01 1.02 (0.95,1.09)
Oral contraceptive use	3.3E−01	5.9E−01	3.3E−01	6.1E−01	8.7E−01	6.1E−01	7.2E−01	4.1E−01
Ever vs never	0.93 (0.86,1.00)	0.94 (0.87,1.03)	0.89 (0.79,1.00)	0.94 (0.83,1.05)	0.96 (0.80,1.16)	0.91 (0.77,1.07)	0.92 (0.76,1.12)	0.87 (0.75,1.02)
Menopausal hormone therapy	1.1E−10	4.3E−07	5.6E−03	1.9E−02	1.9E−01	5.2E−01	8.3E−01	4.6E−01
Never use, postmenopausal	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former[b] use of ET	0.82 (0.66,1.02)	0.79 (0.61,1.03)	0.95 (0.65,1.38)	0.73 (0.47,1.15)	0.80 (0.49,1.30)	1.10 (0.61,1.99)	0.91 (0.40,2.10)	0.92 (0.57,1.50)
Former[b] use of EPT	1.06 (0.87,1.30)	1.01 (0.79,1.30)	1.20 (0.85,1.69)	0.96 (0.67,1.38)	1.11 (0.64,1.93)	0.97 (0.55,1.71)	1.16 (0.57,2.38)	1.24 (0.79,1.97)

Risk factor	Overall	ER+	ER−	Luminal A-like	Luminal B HER2-negative-like	Luminal B HER2-like	HER2-enriched-like	Triple negative
	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)	P HR (95% CI)
Former[b] use (unknown type)	0.87 (0.79,0.96)	0.87 (0.78,0.96)	0.91 (0.76,1.08)	0.85 (0.72,1.01)	0.87 (0.66,1.14)	0.83 (0.59,1.16)	0.93 (0.66,1.31)	0.90 (0.73,1.12)
Current[c] use of ET	0.69 (0.55,0.86)	0.69 (0.54,0.88)	0.69 (0.48,1.00)	0.71 (0.50,1.01)	0.59 (0.33,1.07)	0.68 (0.42,1.12)	0.63 (0.27,1.50)	0.78 (0.49,1.26)
Current[c] use of EPT	0.60 (0.51,0.72)	0.61 (0.49,0.75)	0.59 (0.44,0.79)	0.63 (0.48,0.83)	0.59 (0.37,0.93)	0.58 (0.38,0.87)	0.60 (0.31,1.14)	0.63 (0.42,0.95)
Current[c] use (unknown type)	0.83 (0.73,0.94)	0.80 (0.69,0.93)	0.94 (0.74,1.20)	0.81 (0.66,0.98)	0.75 (0.53,1.06)	0.81 (0.51,1.30)	0.89 (0.53,1.50)	1.02 (0.73,1.42)
Smoking	5.7E−02	1.2E−01	6.3E−01	2.0E−01	6.5E−01	8.7E−01	8.7E−01	6.7E−01
Never	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Former[d]	0.93 (0.87,0.99)	0.94 (0.86,1.03)	0.91 (0.81,1.03)	0.93 (0.83,1.05)	0.91 (0.80,1.04)	0.94 (0.78,1.13)	1.04 (0.81,1.34)	0.89 (0.75,1.05)
Current[e]	1.11 (1.02,1.21)	1.14 (1.04,1.26)	1.04 (0.90,1.21)	1.19 (1.03,1.36)	1.09 (0.89,1.32)	1.06 (0.84,1.33)	1.12 (0.81,1.55)	1.07 (0.87,1.33)
No. of pack-years of smoking, per 10 units increase	6.7E−01 1.02 (0.98,1.07)	6.7E−01 1.02 (0.97,1.08)	7.8E−01 1.01 (0.97,1.06)	6.7E−01 1.03 (0.97,1.09)	8.4E−01 1.02 (0.94,1.10)	8.0E−01 1.02 (0.95,1.09)	6.1E−01 1.05 (0.97,1.13)	9.2E−01 1.01 (0.94,1.07)
Alcohol consumption[e], per 10 g/week	9.0E−01 1.00 (0.99,1.01)	9.6E−01 1.00 (0.99,1.01)	8.7E−01 1.00 (0.99,1.01)	9.8E−01 1.00 (0.99,1.01)	8.7E−01 1.00 (0.99,1.01)	8.5E−01 1.00 (0.98,1.01)	8.8E−01 1.00 (0.99,1.01)	8.7E−01 1.00 (0.98,1.01)
Cumulative alcohol consumption, per 10 g/day	7.8E−01 0.98 (0.91,1.05)	7.8E−01 0.97 (0.89,1.07)	8.7E−01 0.99 (0.93,1.05)	7.3E−01 0.96 (0.87,1.07)	9.2E−01 0.99 (0.89,1.10)	7.2E−01 0.96 (0.88,1.06)	9.7E−01 1.01 (0.90,1.12)	8.7E−01 0.99 (0.92,1.06)
Physical activity[e,f], hours/week	5.2E−01	5.4E−01	5.2E−01	6.0E−01	6.5E−01	2.8E−01	5.2E−01	5.9E−01
< 1.8	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
≥ 1.8 – < 5.5	0.76 (0.21,2.73)	0.77 (0.21,2.81)	0.75 (0.21,2.67)	0.78 (0.19,3.22)	0.79 (0.20,3.07)	0.72 (0.28,1.85)	0.82 (0.28,2.42)	0.72 (0.17,3.15)
≥ 5.5	0.39 (0.13,1.17)	0.40 (0.13,1.19)	0.38 (0.12,1.21)	0.39 (0.12,1.26)	0.44 (0.13,1.49)	0.38 (0.16,0.88)	0.42 (0.15,1.12)	0.38 (0.11,1.31)

All analyses were stratified by study and adjusted for lymph nodes status, tumor size, tumor grade and (neo)adjuvant systemic treatment. Age of the patients was used as time scale. Reported p-values (P) are from likelihood ratio tests comparing a model with and without a particular risk factor and are adjusted for multiple testing using the Benjamini-Hochberg method for false discovery rate (FDR) control on 136 tests. Heterogeneity test by subtype is shown in Table 3. Numbers of patients and events included in the corresponding complete-case analyses are shown in Supplementary Figures S2 (overall), S4 (ER+), S6 (ER−), S8 (Luminal A-like), S10 (Luminal B HER2-negative-like), S12 (Luminal B HER2-positive-like), S14 (HER2-enriched-like), and S16 (triple negative).

Abbreviations: *ET*: estrogen therapy; *EPT*: combined estrogen and progestin therapy.

[a]Association estimated in parous women.

[b]More than 6 months before diagnosis.

Risk factor	HR (95% CI)	P-value
Age at menarche	1.02 (1.00, 1.04)	6.8E−02
Parity		
0	Ref.	
1	1.02 (0.91, 1.15)	7.4E−01
2	0.99 (0.86, 1.15)	9.0E−01
3	1.01 (0.86, 1.18)	9.4E−01
4+	1.01 (0.86, 1.18)	9.2E−01
Age at first full term pregnancy, years		
< 20	Ref.	
20 to < 25	0.90 (0.84, 0.96)	1.9E−03
25 to < 30	0.84 (0.78, 0.90)	2.8E−06
≥ 30	0.79 (0.72, 0.86)	2.0E−07
Time since last full term birth, years		
≥ 10	Ref.	
≥ 5 – < 10	1.13 (1.01, 1.28)	3.2E−02
> 0 – < 5	1.31 (1.11, 1.55)	1.1E−03
Breastfeeding		
Ever vs never	0.94 (0.82, 1.06)	2.7E−01
Duration of breastfeeding, per 6 months	1.02 (1.00, 1.04)	6.9E−02
BMI, kg/m²		
18.5 to < 25	Ref.	
< 18.5	1.31 (0.96, 1.77)	5.6E−02
25 to < 30	1.04 (0.92, 1.18)	4.4E−01
≥ 30	1.19 (1.06, 1.34)	1.1E−03
Adult height, per 5 cm	0.98 (0.93, 1.03)	2.8E−01
Oral contraceptive use		
Ever vs never	0.91 (0.87, 0.96)	9.4E−05
Menopausal hormone therapy		
Never use, postmenopausal	Ref.	
Former[a] use of ET	0.75 (0.65, 0.86)	2.9E−05
Former[a] use of EPT	0.85 (0.73, 0.98)	3.0E−02
Former[a] use (unknown type)	0.81 (0.76, 0.86)	1.1E−11

Risk factor	HR (95% CI)	P-value
Current[b] use of ET	0.72 (0.64, 0.82)	8.3E−07
Current[b] use of EPT	0.61 (0.54, 0.69)	3.8E−15
Current[b] use (unknown type)	0.78 (0.72, 0.85)	4.9E−08
Smoking		
Never	Ref.	
Former[c]	1.03 (0.98, 1.07)	2.3E−01
Current[d]	1.37 (1.27, 1.47)	0.0E+00
Alcohol consumption[d], per 10 g/week	1.00 (0.99, 1.01)	6.6E−01
Cumulative alcohol consumption, per 10 g/day	1.00 (0.96, 1.05)	9.3E−01
Physical activity[d,e], hours/week		
< 1.8	Ref.	
≥ 1.8 – < 5.5	0.81 (0.39, 1.68)	5.2E−01
≥ 5.5	0.43 (0.21, 0.86)	6.3E−03

The Cox model was stratified by study and adjusted for lymph nodes status, tumor size, tumor grade, ER status, PR status, HER2 status and (neo)adjuvant systemic treatment. Age of the patients was used as time scale. All the risk factors were simultaneously included in the model. Corresponding complete-case analysis was based on 1264 cases and 158 deaths from all causes. A comparison between results from imputed data analysis and corresponding complete-case analysis are shown in Supplementary Figure S23.

[a]More than 6 months before diagnosis.

[b]At diagnosis or within 6 months before diagnosis.

[c]More than 1 year before diagnosis.

[d]At diagnosis or within a year before diagnosis.

[e]Categories based on the tertiles of the observed distribution of the variable. Abbreviations: *ET*: estrogen therapy; *EPT*: combined estrogen and progestin therapy.

Risk factor	HR (95% CI)	P-value
Age at menarche	1.03 (1.00, 1.05)	1.4E−02
Parity		
0	Ref.	
1	1.04 (0.90, 1.21)	5.5E−01
2	1.00 (0.83, 1.20)	1.0E+00
3	1.00 (0.81, 1.24)	1.0E+00
4+	1.01 (0.81, 1.25)	9.4E−01
Age at first full term pregnancy, years		
< 20	Ref.	
20 to < 25	0.90 (0.82, 0.99)	2.7E−02
25 to < 30	0.87 (0.79, 0.95)	2.8E−03
≥ 30	0.80 (0.72, 0.89)	4.4E−05
Time since last full term birth, years		
≥ 10	Ref.	
≥ 5 – < 10	1.16 (1.01, 1.34)	2.9E−02
> 0 – < 5	1.36 (1.15, 1.61)	2.4E−04
Breastfeeding		
Ever vs never	0.98 (0.81, 1.18)	8.2E−01
Duration of breastfeeding, per 6 months	1.02 (1.00, 1.05)	7.2E−02
BMI, kg/m²		
18.5 to < 25	Ref.	
< 18.5	1.10 (0.79, 1.53)	5.6E−01
25 to < 30	1.06 (0.93, 1.20)	3.6E−01
≥ 30	1.16 (1.04, 1.29)	4.7E−03
Adult height, per 5 cm	1.00 (0.95, 1.06)	8.7E−01
Oral contraceptive use		
Ever vs never	0.96 (0.89, 1.03)	2.5E−01
Menopausal hormone therapy		
Never use, postmenopausal	Ref.	
Former[a] use of ET	0.82 (0.66, 1.03)	8.2E−02
Former[a] use of EPT	1.11 (0.91, 1.35)	3.2E−01
Former[a] use (unknown type)	0.88 (0.80, 0.97)	1.0E−02

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Risk factor	HR (95% CI)	P-value
Current[b] use of ET	0.71 (0.57, 0.89)	2.6E−03
Current[b] use of EPT	0.64 (0.54, 0.76)	2.3E−07
Current[b] use (unknown type)	0.86 (0.76, 0.97)	1.3E−02
Smoking		
Never	Ref.	
Former[c]	0.94 (0.88, 1.01)	7.2E−02
Current[d]	1.11 (1.02, 1.21)	1.1E−02
Alcohol consumption[d], per 10 g/week	1.00 (0.99, 1.01)	8.4E−01
Cumulative alcohol consumption, per 10 g/day	0.98 (0.91, 1.06)	5.2E−01
Physical activity[d,e], hours/week		
< 1.8	Ref.	
≥ 1.8 – < 5.5	0.77 (0.22, 2.73)	6.4E−01
≥ 5.5	0.40 (0.13, 1.19)	5.7E−02

The Cox model is stratified by and adjusted for lymph nodes status, tumor size, tumor grade, ER status, PR status, HER2 status and (neo)adjuvant systemic treatment. Age of the patient was used as time scale. All risk factors were simultaneously included in the model. Corresponding complete-case analysis was based on 1264 cases and 114 deaths from breast cancer. A comparison between results from imputed data analysis and corresponding complete-case analysis are shown in Supplementary Figure S24.

[a]More than 6 months before diagnosis.

[b]At diagnosis or within 6 months before diagnosis.

[c]More than 1 year before diagnosis.

[d]At diagnosis or within a year before diagnosis.

[e]Categories based on the tertiles of the observed distribution of the variable. Abbreviations: *ET*: estrogen therapy; *EPT*: combined estrogen and progestin therapy.

- Vücut yüzey değişikliği ilaç farmakokinetiğini ve sitotoksik etkinliği değiştirir.
- Kan volümü artışı, hepatik klerens değ.,renal adaptasyon, oral ilaçta gastrik motilite değ,plazma alb azalması, östrojen seviyesi artışı, diğer plazma prot artışı, 3. alan amniotic sac, ilaç rezistansı gikoprotein direnci değişir.
- Sistemik Kt kullanımında dikkat edilmesi gerekir.
- Amant F et al. N Eng J. Med 2015
- Farklı olarak ilk trimestrde de kemoterapi uygulanabileceğini Antrasiklin bazlı 3 hf periodlar halinde
- Tedavi seçiminde Her2 negatifliği ve pozitifliği farklılık göstermektedir.

Kemoterapi

- Kt zamanlaması organogenesis 5-10 hf
- Kongenital anomaliler
- Kromozom abnormalitesi
- Ölü doğum
- Abortus
- Fetal malformasyon%15-20
- 2-3.trimestrde intrauterin gelişme geriliği
- Prematürite
- Düşük doğum ağırlığı
- Nonpregnantlarda kt gecikmesi 3-6 ay tolere edilebilir.Tm biolojik özellikleri değerlendirilmelidir.

kemoterapi

- Kt sonrası BK ve platelet düşüklüğü enf,kanama riski gözönünde bulundurulmalıdır.
- Myelosupresyon için kt pulmoner maturite için 34.hf öncesinde 3 hafta öncesi bırakılmalıdır.
- 2-3.trimestrde AC-FAC dose-related kardiomyopati
- Postnatal 2 yaşa kadar eko
- Taxanlar bias olmasına rağmen uygulanabilir.
- Trastuzumab,lapatinib oaral Cerb tirozin kinaz inh. Kontrendike.
- Oligohidramnioz, hipoplazi ve iskelet anomalisi
- HT tmx ve AI kanama kong. Malformasyon yapar kullanılmaz

Kemoterapi

- Kt sonrası alkilleyici ajanlar neonatal nötropeni yapabilir(Cyclophosphamide)
- Trastuzumab, lapatinib ve endokrin tedaviden kaçınılmalıdır.
- Murty RK et al. Outcomes of children exposed in utero to chemotherapy for breast cancer. Breast Cancer Res 2014 87 hasta AC ktsi %3 lük neonatal abnormalite.
- Kt sırasında antiemetikler promethazin, selektif 5-HT ant., difenhidramin, dexametazon
- Granülosit koloni stimülanları prospektif çalışma olmamasına rağmen uygulanabilir.

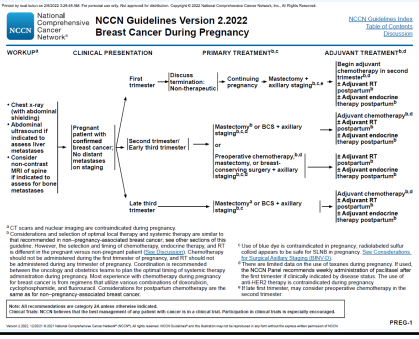
Panel: Checklist for care of pregnant patients with breast cancer

At diagnosis
- Confirm progressing pregnancy and define duration of pregnancy
- Exclude pre-existing fetal anomalies by ultrasonography before examinations or interventions

Obstetric follow-up during oncological treatment
- Consider intraoperative fetal monitoring from 24 to 26 weeks' gestation onwards, according to local policy
- Chemotherapy is possible during second or third trimester
  - Check for fetal wellbeing and general development
  - Check for preterm contractions
  - Check for intrauterine growth restriction
  - No chemotherapy after 35 weeks' gestation
- Radiotherapy is possible during first or second trimester
  - Check for fetal wellbeing and general development
  - Check for preterm contractions
  - Check for intrauterine growth restriction

Delivery
- Mode of delivery is determined by obstetric indications
- Timing of delivery
  - Preferably after 35–37 weeks' gestation
  - At least 3 weeks after last cycle of chemotherapy (delivered at 21 day intervals)
  - If preterm delivery is inevitable, fetal lung maturity is essential

Post-partum
- Examine placenta for metastatic disease
- Oncological treatment can be continued immediately after vaginal delivery, and a week after uncomplicated caesarean section
- Breastfeeding
  - If physiologically possible—eg, after radiotherapy
  - Contraindicated during and after chemotherapy



- Sabrınız için teşekkürler.

ulusal CERRAHİ ONKOLOJİ KONGRESİ

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ORIGINAL ARTICLE

Liaquat National Journal of Cancer Care 2020; 2(2): 39-44

Long-term Outcomes of Pregnancy-Associated Breast Cancer: A Single Institution Experience

Ikram A Burney[1,2*], Jawaher Al Sulaimi[1], Moza Al Kalbani[1], Vidayanathan Gowri[1], Farhan Zahid[1], Shiyam Kumar[1], Muhammad Furrukh[1], Syed G Rizvi[1] and Mansour Al Moundhri[1]

Gebelikle ilişkili meme kanserlerinde 2005-2012 arası opere meme kanserlerinde 59 ay uzun dönem takiplerinde %50 hastada Her-2/neu ekspresyonu ve 1/3 triple negatif hasta Kt yanıtı ve uzun dönem takibinde geniş serilere ihtiyaç var. 850/16

ulusal CERRAHİ ONKOLOJİ KONGRESİ

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- J Clin Imaging Sci. 2021 Sep 21;11:49.

Pregnancy Associated Breast Cancer

Frances Perez [1], Ashley Bragg [2], Gary Whitman [1]

Gebelik ilişkili meme kanserinde fizyolojik değişimlerin takibinin önemi , radyolojik değerlendirmelerin ve biopsi tekniklerinin özellikle emzirme döneminde farklılıkları vurgulanmaktadır.