

ORIGINAL RESEARCH ARTICLE

Risk factor analysis for human epidermal growth factor receptor 2-positive breast cancer patients with brain metastasis: A risk prediction model based on the Surveillance, Epidemiology, and End Results database

Supplementary Files

Table S1. Clinical characteristics of human epidermal growth factor receptor 2-positive breast cancer patients with brain metastases

Characteristics	Number of patients (n=576) (%)
Age at diagnosis (median=57 years)	
<57	279 (48.4)
>57	277 (48.1)
=57	20 (3.5)
Race, n (%)	
White	416 (72.2)
Black	83 (14.4)
Others	75 (12.8)
Unknown	3 (0.5)
Laterality, n (%)	
Right	273 (47.7)
Left	272 (47.2)
Others	31 (5.4)
Grade, n (%)	
Unknown	156 (27.1)
II	127 (22.0)
III/IV	277 (48.1)
I	16 (2.8)
T, n (%)	
TX	102 (17.7)
T2	123 (21.4)
T4	200 (34.7)
T1	57 (9.9)
T3	74 (12.8)
T0	20 (3.5)
N, n (%)	
N0	99 (17.1)
NX	64 (11.1)
N1	264 (45.8)
N3	87 (15.1)
N2	62 (10.8)

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Table S1. (Continued)

Characteristics	Number of patients (n=576) (%)
Pathology, n (%)	
Infiltrating duct carcinoma	433 (75.2)
Lobular carcinoma	23 (4.0)
Others	120 (20.8)
Bone metastasis, n (%)	
Yes	390 (67.7)
No	177 (30.7)
Unknown	9 (1.6)
Liver metastasis, n (%)	
Yes	256 (44.4)
No	305 (52.9)
Unknown	15 (2.6)
Lung metastasis, n (%)	
No	302 (52.4)
Yes	258 (44.8)
Others	16 (2.8)
Number of metastases excluding the brain, median (4.5)	
<4.5	574 (99.7)
>4.5	2 (0.3)
ER, n (%)	
Negative	270 (46.9)
Positive	306 (53.1)
PR, n (%)	
Negative	377 (65.5)
Positive	198 (34.4)
Unknown	1 (0.2)
Surgery, n (%)	
No	505 (87.7)
Yes	61 (10.6)
Unknown	7 (1.2)
Sequence of surgery and radiotherapy, n (%)	
No radiation and/or surgery	424 (73.6)
Radiation after surgery	133 (23.1)
Radiation prior surgery	13 (2.3)
Surgery both before and after radiation	2 (0.3)
Intraoperative radiation	1 (0.2)
Radiation both before and after surgery	3 (0.5)
Sequence of systemic treatment and surgery, n (%)	
No systemic therapy and/or surgical procedures	400 (69.4)
Systemic therapy after surgery	139 (24.1)
Systemic therapy both before and after surgery	18 (3.1)
Systemic therapy before surgery	14 (2.4)
Surgery both before and after systemic therapy	4 (0.7)

Abbreviations: ER: Estrogen receptor; N: Node stage; NX: Unknown node stage; PR: Progesterone receptor; T: Tumor stage; TX: Unknown tumor stage.

Table S2. Univariate and multivariate Cox regression analyses for factors associated with overall survival in patients

Characteristics	Number of patients (n=564)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% confidence interval)	p-value	Hazard ratio (95% confidence interval)	p-value
Subtype					
HER2+/HR+	316	Reference		Reference	
HER2+/HR-	248	1.301 (1.068–1.584)	0.009	0.437 (0.233–0.818)	0.010
Age	564	1.022 (1.013–1.031)	<0.001	1.025 (1.015–1.034)	< 0.001
Race					
Black	80	Reference		Reference	
White	410	0.754 (0.573–0.993)	0.045	0.755 (0.569–1.002)	0.052
Others	74	0.597 (0.403–0.883)	0.010	0.563 (0.377–0.841)	0.005
Laterality					
Right	269	Reference			
Left	264	0.963 (0.787–1.179)	0.717		
Others	31	0.964 (0.614–1.515)	0.874		
Grade					
I	16	Reference			
II	124	1.844 (0.853–3.986)	0.120		
III	271	2.018 (0.949–4.291)	0.068		
Unknown	153	2.006 (0.934–4.304)	0.074		
T					
T0	19	Reference		Reference	
T1	56	1.745 (0.810–3.757)	0.155	1.865 (0.840–4.143)	0.126
T2	121	2.108 (1.019–4.360)	0.044	2.252 (1.071–4.735)	0.032
T3	72	2.158 (1.017–4.579)	0.045	2.231 (1.025–4.856)	0.043
T4	197	2.625 (1.288–5.349)	0.008	2.657 (1.280–5.516)	0.009
TX	99	2.581 (1.242–5.363)	0.011	2.781 (1.311–5.899)	0.008
N					
N0	98	Reference		Reference	
N1	260	0.771 (0.590–1.008)	0.057	0.672 (0.506–0.893)	0.006
N2	59	0.623 (0.424–0.915)	0.016	0.578 (0.382–0.872)	0.009
N3	84	0.657 (0.464–0.930)	0.018	0.532 (0.371–0.762)	< 0.001
NX	63	0.847 (0.590–1.217)	0.370	0.551 (0.367–0.828)	0.004
Pathology					
Infiltrating duct carcinoma	424	Reference			
Lobular carcinoma	23	1.164 (0.703–1.926)	0.555		
Others	117	1.091 (0.866–1.375)	0.459		
Bone metastasis					
No	169	Reference			
Yes	386	1.001 (0.809–1.239)	0.993		
Unknown	9	1.356 (0.633–2.908)	0.434		
Liver metastasis					
No	297	Reference		Reference	
Yes	252	1.350 (1.106–1.648)	0.003	1.259 (0.960–1.650)	0.096
Unknown	15	1.452 (0.810–2.602)	0.211	1.527 (0.776–3.004)	0.220

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Table S2. (Continued)

Characteristics	Number of patients (n=564)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% confidence interval)	p-value	Hazard ratio (95% confidence interval)	p-value
Lung metastasis					
No	291	Reference		Reference	
Yes	257	1.460 (1.196–1.784)	< 0.001	1.626 (1.240–2.131)	<0.001
Others	16	1.397 (0.795–2.454)	0.245	1.076 (0.516–2.244)	0.845
Number of metastases excluding the brain	564	1.119 (1.040–1.203)	0.002	0.936 (0.794–1.102)	0.426
ER					
Negative	265	Reference		Reference	
Positive	299	0.718 (0.589–0.873)	<0.001	0.360 (0.205–0.633)	<0.001
PR					
Negative	371	Reference		Reference	
Positive	193	0.789 (0.640–0.973)	0.027	0.707 (0.527–0.950)	0.021
Surgery					
No	498	Reference		Reference	
Yes	60	0.526 (0.371–0.746)	<0.001	0.737 (0.456–1.190)	0.212
Unknown	6	0.565 (0.211–1.515)	0.257	0.535 (0.196–1.459)	0.221
Sequence of surgery and radiotherapy					
Radiation after surgery	130	Reference		Reference	
No radiation and/or surgery	421	1.779 (1.382–2.291)	<0.001	1.135 (0.721–1.786)	0.583
Radiation prior surgery	13	0.976 (0.449–2.120)	0.951	0.980 (0.389–2.470)	0.966
Sequence of systemic treatment and surgery					
Systemic therapy after surgery	137	Reference		Reference	
No systemic therapy and/or surgical procedures	396	1.859 (1.453–2.379)	<0.001	1.367 (0.886–2.110)	0.158
Systemic therapy before surgery	14	0.761 (0.332–1.746)	0.520	1.028 (0.385–2.741)	0.956
Systemic therapy both before and after surgery	17	0.973 (0.504–1.881)	0.935	1.492 (0.699–3.185)	0.301

Abbreviations: ER: Estrogen receptor; HER2+/HR+: Human epidermal growth factor receptor 2-positive and hormone receptor-positive; HER2+/HR-: Human epidermal growth factor receptor 2-positive and hormone receptor-negative; N: Node stage; NX: Unknown node stage; PR: Progesterone receptor; T: Tumor stage; TX: Unknown tumor stage.

Table S3. Univariate and multivariate Cox regression analyses for factors associated with breast cancer-specific survival in patients

Characteristics	Number of patients (n=564)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% confidence interval)	p-value	Hazard ratio (95% confidence interval)	p-value
Subtype					
HER2+/HR+	316	Reference		Reference	
HER2+/HR-	248	1.369 (1.110–1.689)	0.003	0.489 (0.249–0.958)	0.037
Age	564	1.023 (1.014–1.032)	<0.001	1.023 (1.013–1.033)	<0.001
Race					
Black	80	Reference		Reference	
White	410	0.775 (0.576–1.043)	0.092	0.797 (0.588–1.080)	0.143
Others	74	0.612 (0.402–0.932)	0.022	0.572 (0.372–0.878)	0.011
Laterality					
Right	269	Reference			
Left	264	0.963 (0.776–1.195)	0.731		
Others	31	1.045 (0.656–1.664)	0.853		
Grade					
I	16	Reference			
II	124	1.942 (0.846–4.460)	0.118		
III	271	2.075 (0.919–4.685)	0.079		
Unknown	153	2.035 (0.892–4.643)	0.091		
T					
T0	19	Reference		Reference	
T1	56	1.459 (0.668–3.185)	0.343	1.749 (0.783–3.909)	0.173
T2	121	1.914 (0.922–3.973)	0.081	2.077 (0.986–4.378)	0.055
T3	72	1.833 (0.855–3.928)	0.119	1.934 (0.881–4.246)	0.100
T4	197	2.313 (1.132–4.727)	0.021	2.313 (1.113–4.807)	0.025
TX	99	2.284 (1.093–4.770)	0.028	2.321 (1.093–4.932)	0.028
N					
N0	98	Reference			
N1	257	1.093 (0.808–1.478)	0.564		
N2	61	1.188 (0.804–1.757)	0.387		
N3	84	0.947 (0.650–1.379)	0.775		
NX	64	0.869 (0.566–1.335)	0.521		
Pathology					
Infiltrating duct carcinoma	424	Reference			
Lobular carcinoma	23	1.064 (0.609–1.859)	0.826		
Others	117	1.062 (0.828–1.360)	0.637		
Bone metastasis					
No	169	Reference			
Yes	386	0.957 (0.763–1.199)	0.700		
Unknown	9	1.517 (0.706–3.260)	0.286		

(Cont'd...)

Table S3. (Continued)

Characteristics	Number of patients (n=564)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% confidence interval)	p-value	Hazard ratio (95% confidence interval)	p-value
Liver metastasis					
No	297	Reference		Reference	
Yes	252	1.278 (1.032–1.582)	0.025	1.272 (0.948–1.705)	0.108
Unknown	15	1.479 (0.804–2.721)	0.209	1.474 (0.715–3.039)	0.293
Lung metastasis					
No	291	Reference		Reference	
Yes	257	1.492 (1.205–1.848)	<0.001	1.780 (1.323–2.396)	<0.001
Others	16	1.517 (0.844–2.729)	0.164	1.321 (0.620–2.813)	0.471
Number of metastases excluding the brain	564	1.107 (1.022–1.199)	0.012	0.868 (0.721–1.045)	0.134
ER					
Negative	265	Reference		Reference	
Positive	299	0.683 (0.554–0.843)	<0.001	0.361 (0.197–0.662)	<0.001
PR					
Negative	371	Reference		Reference	
Positive	193	0.744 (0.593–0.932)	0.010	0.716 (0.522–0.982)	0.038
Surgery					
No	498	Reference		Reference	
Yes	60	0.553 (0.384–0.797)	0.001	0.815 (0.493–1.348)	0.425
Unknown	6	0.643 (0.239–1.726)	0.380	0.655 (0.240–1.788)	0.409
Sequence of surgery and radiotherapy					
Radiation after surgery	130	Reference		Reference	
No radiation and/or surgery	421	1.831 (1.394–2.404)	<0.001	1.119 (0.695–1.800)	0.644
Radiation prior surgery	13	1.133 (0.519–2.475)	0.753	1.167 (0.452–3.013)	0.749
Sequence of systemic treatment and surgery					
Systemic therapy after surgery	137	Reference		Reference	
No systemic therapy and/or surgical procedures	396	1.895 (1.455–2.469)	<0.001	1.454 (0.927–2.279)	0.103
Systemic therapy before surgery	14	0.744 (0.300–1.844)	0.523	0.867 (0.299–2.517)	0.793
Systemic therapy both before and after surgery	17	1.011 (0.504–2.029)	0.975	1.342 (0.586–3.075)	0.487

Abbreviations: ER: Estrogen receptor; HER2+/HR+: Human epidermal growth factor receptor 2-positive and hormone receptor-positive; HER2+/HR-: Human epidermal growth factor receptor 2-positive and hormone receptor-negative; N: Node stage; NX: Unknown node stage; PR: Progesterone receptor; T: Tumor stage; TX: Unknown tumor stage.