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EPIDEMIOLOGY

Time-to-surgery and overall survival after breast cancer diagnosis in a universal health system

Yvonne L. Eaglehouse[1,2,3] · Matthew W. Georg[1,3] · Craig D. Shriver[1,2,4] · Kangmin Zhu[1,3,5,6]

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Abstract

Purpose It is unclear whether time between breast cancer diagnosis and surgery is associated with survival and whether this relationship is affected by access to care. We evaluated the association between time-to-surgery and overall survival among women in the universal-access U.S. Military Health System (MHS).

Methods Women aged 18–79 who received surgical treatment for stages I–III breast cancer between 1998 and 2010 were identified in linked cancer registry and administrative databases with follow-up through 2015. Multivariable Cox regression models were used to estimate risk of all-cause death associated with time-to-surgery intervals.

Results The study included 9669 women with 93.1% survival during the study period. The hazards ratios (95% confidence intervals) of all-cause death associated with time-to-surgery were 1.15 (0.93, 1.42) for 0 days, 1.00 (reference) for 1–21 days, 0.97 (0.78, 1.21) for 22–35 days, and 1.30 (1.04, 1.61) for $\geq$ 36 days. The higher risk of mortality associated with time-to-surgery $\geq$ 36 days tended to be consistent when analyzed by surgery type, age at diagnosis, and tumor stage.

Conclusions In the MHS, longer time-to-surgery for breast cancer was associated with poorer overall survival, suggesting the importance of timeliness in receiving surgical treatment for breast cancer in relation to overall survival.

Keywords Lumpectomy · Mastectomy · Breast surgery · Overall survival · Clinical outcomes

Abbreviations

CCR	Central Cancer Registry
CI	Confidence interval
CPT	Current Procedural Terminology
ER	Estrogen receptor
FORDS	Facility Oncology Registry Data Standards
HCPCS	Healthcare Common Procedure Coding System
HR	Hazards ratio
ICD	International Classification of Diseases
MDR	Military Health System Data Repository
MHS	Military Health System
PR	Progesterone receptor
SEER	Surveillance, Epidemiology, and End Results Program
TTS	Time-to-surgery

✉ Kangmin Zhu
kzhu@murthacancercenter.org

1 Murtha Cancer Center Research Program, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

2 Department of Surgery, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

3 Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, MD, USA

4 Walter Reed National Military Medical Center, Bethesda, MD, USA

5 Department of Preventive Medicine and Biostatistics; F. Edward Hébert School of Medicine, Uniformed Services University, Bethesda, MD, USA

6 Murtha Cancer Center Research Program, Uniformed Services University of the Health Sciences, 6720A Rockledge Drive, Suite 310, Bethesda, MD 20817, USA

Introduction

Time-to-surgery (TTS) has been proposed as a quality care indicator for treatment of local and regional breast cancer [1, 2]. Surgery delays may be associated with poorer response to treatment, delays in adjuvant therapy, more rapid disease progression, or other adverse health events [3, 4]. While it is generally accepted that efforts be made to minimize the interval from breast cancer diagnosis to treatment to reduce these risks, there are currently no standard guidelines for

TTS [1]. Moreover, there is mixed evidence as to whether TTS is associated with long-term clinical outcomes including survival [5].

Two recent studies in the U.S. have demonstrated an increased risk for mortality with increasing TTS after breast cancer diagnosis [6, 7]. The first study reported significant 9% and 10% higher risks of overall mortality for each incremental 30-day interval between diagnosis and surgery in two national databases [6]. The authors also reported a 26% higher risk of breast cancer-specific mortality for each 60-day increase in TTS in the database with information on cause of death. The second study found an 82% higher risk of mortality for patients with TTS > 6 weeks compared to < 2 weeks in a single state-wide cancer registry [7]. Nonetheless, several studies in the U.S. have shown no association between TTS and clinical outcomes [4, 5, 8].

Breast cancer treatment planning depends on multiple factors which may affect both TTS and clinical outcomes. It is important to acknowledge that adequate time for necessary pathology, imaging assessments, and treatment planning may inherently increase TTS for patients. Other factors that may influence TTS and outcomes include patient and family health history (including breast cancer), treatment concerns [9], tumor features [10, 11], surgery type [8, 12–14], the patient's age and menopausal status [15–18], and comorbid conditions [18–20]. As a result, TTS may be reflective of different reasons for expedition or delay and may have differential effects on mortality.

In addition, access to care and insurance status contribute largely to differences in cancer care delivery [21]. These may influence treatment receipt and timing [7, 22, 23] and survival outcomes [23–27]. Individuals with private insurance tend to be more likely to receive recommended treatments and may have shorter TTS than those with public or no insurance [7, 21, 22]. Patients with access to care and those with private insurance also tend to have better overall survival compared to their respective counterparts [21]. In the general U.S. population, accessibility to care and insurance coverage vary by socio-demographic factors including age, race, education level, and income [28, 29]. These characteristics have been associated with differences in TTS [7, 12] and in overall survival [22, 30, 31]. Therefore, it is hard to assess the effects of TTS on survival independent of access to care in the general population.

The U.S. Military Health System (MHS) provides universal access to health care, including primary care and specialty services, through over 50 military hospitals, 350 ambulatory military clinics, and a supporting network of over 400,000 participating civilian providers [32]. Patients in the MHS have no or relatively low out-of-pocket costs and therefore less financial barriers to care as compared to patients in the general US population [32]. Thus, the MHS is an unparalleled resource for assessing the relationship between TTS for cancer treatment and survival with reduced effects of access to care on results. This study aimed to examine the relationship between TTS and overall survival for women diagnosed and treated for non-metastatic breast cancer in the MHS.

Materials and methods

Data sources

The Department of Defense Central Cancer Registry (CCR) [33] and the MHS Data Repository (MDR) [34] linked databases were used for this study. The CCR contains information on demographics, cancer diagnosis, and cancer treatment for patients diagnosed or treated at military treatment facilities beginning in 1998 [33]. The CCR follows all patients for vital status following the Commission on Cancer's Facility Oncology Registry Data Standards (FORDS) [35], using multiple sources including, but not limited to: contact with patient or patient's family, contact with managing physician(s), and verification via death certificates. The MDR contains medical claims data for inpatient, outpatient, and ancillary services [34]. The CCR and MDR data linkage was approved by the Walter Reed National Military Medical Center and the Defense Health Agency Institutional Review Boards.

Study population

Patients with a pathologic diagnosis of primary breast cancer [International Classification of Diseases for Oncology Third Revision (ICD-O-3) topography codes C500–506 and C508–509] were identified from the CCR data. Eligible patients were women aged 18–79 who were diagnosed with stage I–III tumors between January 1, 1998 and December 31, 2010 and who had documented surgical treatment in either CCR or MDR (Fig. 1). Women over age 79 at diagnosis were excluded because treatment recommendations are less clear in older women [36]. Patients with multiple primary cancer diagnoses were excluded to minimize potential effects of other cancers on results.

Study variables

Cancer diagnosis and treatment

The CCR contains diagnosis date, pathologic and clinical stage, tumor grade (well-, moderately-, poorly-, or non-differentiated), and estrogen (ER) and progesterone receptor (PR) status. Tumor stage was consolidated using American Joint Committee on Cancer criteria to stage I, II, or III [37, 38]. Breast cancer treatments were identified from the linked

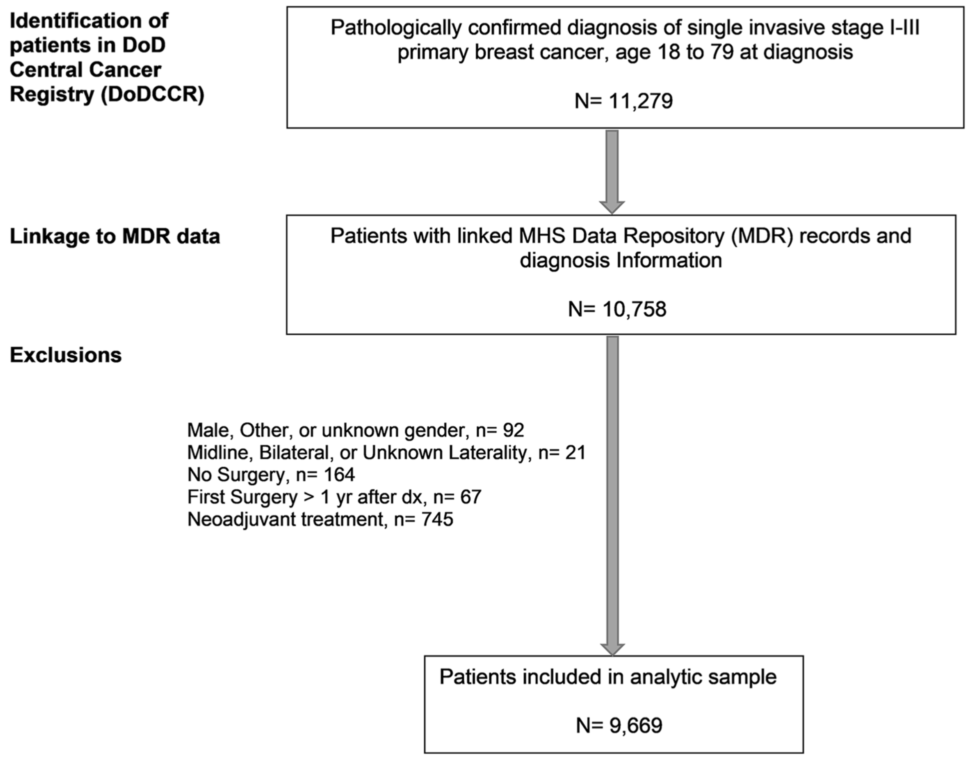

Fig. 1 Selection of patients diagnosed with invasive primary breast cancer and treated with surgery in the Department of Defense Central Cancer Registry (CCR) and Military Health System Data Repository (MDR) linked data, 1998–2010

databases. In CCR, site-specific FORDS surgery codes were used to identify mastectomy (codes 30, 40–76) and lumpectomy (codes 20–24). The first date for chemotherapy, radiation, or hormone treatment was also extracted for each patient. In MDR, ICD-9 diagnosis and procedure, Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) codes were utilized to identify the first surgery, with an algorithm to exclude those for diagnostic purposes, and other cancer treatment [39]. The first surgery and other treatment dates used for analyses were determined from deliberated consolidation procedures. Patients with neoadjuvant radiation or chemotherapy were excluded from the analyses (Fig. 1) due to co-indication of longer TTS for these patients and diagnosis with more advanced or aggressive tumors which may be related to higher mortality risk. Hormone therapy was confined to those with hormone receptor-positive tumors (ER+ or PR+). Surveillance mammograms were identified in the MDR records in the 3 years following diagnosis.

Time-to-surgery

The TTS was calculated as the number of days between cancer diagnosis and first surgery. TTS was categorized as 0 days, 1–21 days (≤ 3 weeks), 22–35 days (> 3–5 weeks), and 36 days or more (> 5 weeks) based on practical intervals needed for specialist referral and planning to provide recommended treatments [14, 36, 40]. Patients with same-day diagnostic confirmation and surgery (TTS 0 days) were categorized as a separate treatment group because patients with more advanced or aggressive tumor features that prompt immediate treatment may also have potentially worse outcomes than those with minimal surgical wait-times [5], resulting in confounding by indication [5, 41]. Patients with TTS > 365 days were excluded (Fig. 1) because this exceeds the time interval recommended for primary breast cancer treatment [36] and the surgery may be related to progression or recurrence of disease.

Patient variables

Demographic variables included age at diagnosis, race (White, Black, Asian, or other), ethnicity (Hispanic, Latina, or Spanish origin), marital status (married, single, or separated, divorced, or widowed), active-duty status, military branch (Army, Navy, Marines, Air Force, or other), and TRICARE service region (North, South, West, or Overseas). Other variables included benefit type in the 3 months before and up to 3 months after diagnosis (TRICARE Prime, Standard, or Extra) [42] and care source (military or civilian) in the 3 months before diagnosis and up to the first surgery date. Comorbid conditions were identified in MDR records using ICD-9-CM codes for medical conditions included in the Charlson Comorbidity Index [43], with the exception of cancer since breast cancer was the condition of interest and other cancers were excluded from the study.

Study outcome

The primary outcome was overall survival, determined from vital status in CCR data. Survival time was calculated as time between cancer diagnosis and date of death for those who died, date of last contact, or data end date of December 31, 2015, whichever occurred first.

Statistical analyses

Distributions of patient demographic, tumor, and treatment characteristics by TTS intervals were examined using χ^2 or Fisher exact tests. We evaluated the association between TTS and overall survival in Cox Proportional Hazards regression models. The TTS interval of 1–21 days was used as the reference level for TTS in this analysis to minimize potential confounding by indication for same-day surgery (TTS 0 days) described above. Individual hazards ratios (HR) and 95% CIs for all-cause death were modeled for each TTS interval in univariable and in multivariable models adjusted for demographic, tumor, and treatment characteristics. Planned subgroup analyses included Cox models by surgery type (mastectomy or lumpectomy), age at diagnosis (18–49, 50–64, or ≥ 65 years), and tumor stage (I, II, or III). To assess potential effects of including TTS in the follow-up time, we repeated analyses using the first surgery date as the index date. Analyses were conducted in SAS 9.4 (SAS Institute Inc., Cary, NC) using two-sided statistical tests with significance at the alpha = 0.05 level.

Results

Patients ($n = 9669$) had a mean age of 54.5 (SD 11.8) years at diagnosis and an average follow-up of 9.0 (SD 4.4) years. The median TTS was 21 (interquartile 7, 35) days. The distributions of demographic, pathologic, and clinical features by TTS intervals are presented in Table 1. Patients with a shorter TTS were more likely to be aged 18–49, an active-duty service member, live in the South or overseas at diagnosis, use purchased care, and be diagnosed prior to 2003. Women with same-day surgery were more likely to receive lumpectomy than women in the other TTS groups. Women with stage I or grade I tumors were less likely to have TTS 1–21 days while those with stage II or grade III were more likely to be in this group. Women in the middle two TTS groups (1–21 and 22–35 days) were more likely to be non-Hispanic White, have Prime benefit type, and have ER-/PR- tumors compared to the other TTS groups. Women with TTS ≥ 36 days tended to have stage I tumors, were less likely to have post-operative chemotherapy or radiation, and were more likely to have at least 1 comorbid condition.

There were 667 deaths during the study period. In survival analyses, there was a significantly lower risk for all-cause death for women with TTS 22–35 days compared to 1–21 days in the univariable model (Table 2). This association was attenuated and non-significant in the multivariable model. There was a significant 30% higher risk for mortality for women with TTS ≥ 36 days (95% CI 1.04, 1.61) compared to women with TTS of 1–21 days in the multivariable analysis (Table 2). The higher risk for all-cause mortality associated with a TTS ≥ 36 days tended to be consistent when analyzed by surgery type, age at diagnosis, and tumor stage in multivariable models (Table 3); however, only statistically significant among women receiving lumpectomy, age 65–79, and with stage I cancer. Associations between TTS of 22–35 days compared to 1–21 days varied within strata and results did not reach statistical significance. Women with TTS 0 days had a significantly higher risk for all-cause mortality among those diagnosed at age 18–49 (HR 1.61, 95% CI 1.13, 2.31) and those with stage I cancer (HR 1.60, 95% CI 1.07, 2.38) compared to women in the same strata with TTS 1-21 days (Table 3). Results were similar when the surgery date was used as the index date in analyses (data not shown).

Discussion

In the MHS, we found a higher risk of all-cause death associated with breast cancer TTS ≥ 36 days compared to modest surgery delays. This finding is important considering MHS beneficiaries have universal access to care and less financial barriers (i.e., out-of-pocket expenses) to health care than individuals in the general US population [32]. Thus, the effects of access to care on cancer treatment and survival observed in the general population [21–27] are minimized in the MHS and we can better investigate the effects of TTS on outcomes relatively independent of access to care. Time-to-treatment involves the care pathway from diagnosis, referral, making appointment(s), to treatment. This process may occur more quickly in the MHS than in other settings due to the policies and rules for the network of military facilities and participating civilian providers connecting patients to needed services [32]. This may be reflected in the shorter time-to-surgery in our study than that in other populations [4, 8]. Even so, our study provides evidence that patients with longer TTS after a breast cancer diagnosis may experience poorer overall survival compared to patients who have surgery within approximately 1 month of diagnosis, consistent with other studies [6, 7]. Research on potential reasons for patient- or health system-level delays between diagnosis and breast cancer surgery in the MHS and its effects on

Table 1 Demographic, pathologic, and clinical characteristics by surgery type for women diagnosed with breast cancer in the U.S. Military Health System, 1998–2010

Characteristic	Time to surgery				*p* value
	0 days	1–21 days	22–35 days	≥36 days	
	No. (%)	No. (%)	No. (%)	No. (%)	
Total	2083 (100)	2754 (100)	2571 (100)	2261 (100)	
Age at diagnosis					< 0.001
18–39	281 (13.5)	392 (14.2)	213 (8.3)	200 (8.8)	
40–49	573 (27.5)	706 (25.6)	615 (23.9)	491 (21.7)	
50–59	550 (26.4)	753 (27.3)	726 (28.2)	612 (27.1)	
60–69	479 (23.0)	629 (22.8)	709 (27.6)	632 (27.9)	
70–79	200 (9.6)	274 (9.9)	308 (12.0)	326 (14.4)	
Race and ethnicity					< 0.001
Non-Hispanic White	1377 (66.1)	1891 (68.7)	1689 (65.7)	1422 (62.9)	
Non-Hispanic Black	337 (16.2)	365 (13.2)	381 (14.8)	384 (17.0)	
Non-Hispanic Asian	205 (9.8)	249 (9.0)	271 (10.5)	247 (10.9)	
Non-Hispanic other	44 (2.1)	89 (3.2)	61 (2.4)	70 (3.1)	
Hispanic	120 (5.8)	160 (5.8)	169 (6.6)	138 (6.1)	
Marital status					< 0.001
Married	1713 (82.2)	2278 (82.7)	2098 (81.6)	1770 (78.3)	
Single	54 (2.6)	77 (2.8)	65 (2.5)	57 (2.5)	
Divorced/widowed/separated	265 (12.7)	325 (11.8)	359 (14.0)	388 (17.2)	
Unknown	51 (2.4)	74 (2.7)	49 (1.9)	46 (2.0)	
Military service/sponsor branch					< 0.001
Army	681 (32.7)	911 (33.1)	865 (33.6)	734 (32.5)	
Navy	463 (22.2)	460 (16.7)	456 (17.7)	417 (18.4)	
Marine Corps	101 (4.8)	105 (3.8)	103 (4.0)	73 (3.2)	
Air Force	558 (26.8)	862 (31.3)	778 (30.3)	676 (29.9)	
Other	185 (8.9)	221 (8.0)	153 (5.9)	147 (6.5)	
Unknown	95 (4.6)	195 (7.1)	216 (8.4)	214 (9.5)	
Active duty at diagnosis					0.024
Yes	168 (8.1)	220 (8.0)	168 (6.5)	142 (6.3)	
No	1915 (91.9)	2534 (92.0)	2403 (93.5)	2119 (93.7)	
TRICARE region					< 0.001
North	690 (33.1)	789 (28.6)	745 (29.0)	733 (32.4)	
South	739 (35.5)	958 (34.8)	857 (33.3)	702 (31.0)	
West	507 (24.3)	871 (31.6)	905 (35.2)	769 (34.0)	
Overseas	147 (7.1)	136 (4.9)	64 (2.5)	57 (2.5)	
Benefit type					< 0.001
Prime	1239 (59.5)	1749 (63.5)	1578 (61.4)	1316 (58.2)	
Non-prime (standard or extra)	358 (17.2)	384 (13.9)	308 (12.0)	302 (13.4)	
Other Health Insurance (in addition to MHS coverage)	486 (23.3)	621 (22.5)	685 (26.6)	643 (28.4)	
Medical care source					< 0.001
Direct (Military)	1278 (61.3)	1704 (61.9)	1671 (65.0)	1323 (58.5)	
Purchased (Private)	360 (17.3)	306 (11.1)	166 (6.5)	153 (6.8)	
Both (Military and Private)	445 (21.4)	744 (27.0)	734 (28.5)	785 (34.7)	
Diagnosis year					< 0.001
1998–2002	1146 (55.0)	1356 (49.2)	880 (34.2)	776 (34.3)	
2003–2006	608 (29.2)	795 (28.9)	793 (30.8)	645 (28.5)	
2007–2010	329 (15.8)	603 (21.9)	898 (34.9)	840 (37.2)	
Tumor stage (AJCC)					< 0.001
I	1108 (53.2)	1261 (45.8)	1381 (53.7)	1283 (56.7)	

Table 1 (continued)

Characteristic	Time to surgery				*p* value
	0 days	1–21 days	22–35 days	≥36 days	
	No. (%)	No. (%)	No. (%)	No. (%)	
II	781 (37.5)	1206 (43.8)	960 (37.3)	788 (34.8)	
III	194 (9.3)	287 (10.4)	230 (8.9)	190 (8.4)	
Tumor grade (AJCC)					< 0.001
Well differentiated (G1)	503 (24.1)	468 (17.0)	591 (23.0)	567 (25.1)	
Moderately differentiated (G2)	716 (34.4)	1035 (37.6)	947 (36.8)	893 (39.5)	
Poorly differentiated (G3)	617 (29.6)	951 (34.5)	762 (29.6)	552 (24.4)	
Non-differentiated (G4)	15 (0.7)	35 (1.3)	21 (0.8)	17 (0.7)	
Undetermined (GX)	232 (11.1)	265 (9.6)	250 (9.7)	232 (10.3)	
Hormone receptor status					< 0.001
ER+/PR+	1144 (54.9)	1483 (53.8)	1548 (60.2)	1380 (61.0)	
ER+/PR−	172 (8.3)	254 (9.2)	248 (9.6)	262 (11.6)	
ER−/PR+	64 (3.1)	56 (2.0)	41 (1.6)	34 (1.5)	
ER−/PR−	363 (17.4)	597 (21.7)	492 (19.1)	358 (15.8)	
Unknown	340 (16.3)	364 (13.2)	242 (9.4)	227 (10.0)	
Hormone therapy[a]					0.001
Yes	741 (53.7)	1075 (60.0)	1061 (57.8)	917 (54.7)	
No	639 (46.3)	718 (40.0)	776 (42.2)	759 (45.3)	
Surgery type					< 0.001
Lumpectomy	1673 (80.3)	1657 (60.2)	1552 (60.4)	1260 (55.7)	
Mastectomy	410 (19.7)	1097 (39.8)	1019 (39.6)	1001 (44.3)	
Adjuvant chemotherapy					< 0.001
Yes	1459 (70.0)	2053 (74.5)	1756 (68.3)	1440 (63.4)	
No	624 (30.0)	701 (25.5)	815 (31.7)	821 (36.3)	
Adjuvant radiotherapy					< 0.001
Yes	1392 (66.8)	1922 (69.8)	1781 (69.3)	1467 (64.9)	
No	691 (33.2)	832 (30.2)	790 (30.7)	794 (35.1)	
Surveillance mammogram					< 0.001
Yes	1201 (57.7)	1604 (58.2)	1625 (63.2)	1377 (60.9)	
No	882 (42.3)	1150 (41.8)	946 (36.8)	884 (39.1)	
Comorbid conditions					< 0.001
None	1664 (79.9)	2170 (78.8)	1846 (71.8)	1594 (70.5)	
1	286 (13.7)	397 (14.4)	496 (19.3)	412 (18.2)	
2 or more	133 (6.4)	187 (6.8)	229 (8.9)	255 (11.3)	

AJCC American Joint Committee on Cancer

[a]Hormone therapy for women with hormone receptor-positive tumors (ER+ or PR+)

survival and other clinical outcomes is warranted to better understand the observed associations.

Our current findings are consistent with two recent population-based studies [6, 7]. Bleicher et al. [6] evaluated TTS in intervals of 30 days among women aged ≥ 66 years in the Surveillance, Epidemiology, and End Results Program (SEER)-Medicare data and separately among women aged ≥ 18 years in the National Cancer Database who were diagnosed with stages I–III breast cancer. The HRs for all-cause mortality were 1.09 (95% CI 1.06–1.13) and 1.10 (95% CI 1.07–1.13) for each 30-day TTS interval increase in the respective studies. Smith et al. [7] evaluated time-to-treatment in 2-week intervals among women aged 15–39 years with stage I–IV breast cancer in the California Cancer Registry database. Among patients receiving surgery as the primary treatment, the HR for all-cause mortality was 1.82 (95% CI 1.21, 2.74) for TTS > 6 weeks compared to < 2 weeks. The higher risk of mortality associated with longer TTS in our study among women with universal health care access and insurance coverage provides further evidence of the effects of treatment delays on overall mortality risk with minimized effects of access to care on the

Table 2 Time-to-surgery and associated hazards ratios (HR) and 95% confidence intervals (CI) for all-cause death among women diagnosed with breast cancer in the U.S. Military Health System, 1998–2010

Time to surgery (days)	*N*	Person-years	Deaths (*n*)	Univariable model HR (95% CI)	Multivariable model[a] HR (95% CI)
0	2083	19,899	173	1.16 (0.95, 1.43)	1.15 (0.93, 1.42)
1–21	2754	25,712	196	1.00 (reference)	1.00 (reference)
22–35	2571	22,355	145	0.80 (0.65, 0.99)*	0.97 (0.78, 1.21)
≥ 36	2261	18,897	153	0.98 (0.79, 1.21)	1.30 (1.04, 1.61)*
p^b				0.011	0.042

[a]Model includes age at diagnosis, race-ethnicity, marital status, military service branch, active-duty status, year of diagnosis, tumor stage, tumor grade, hormone receptor status, surveillance mammography, surgery type (breast conserving or mastectomy), adjuvant chemotherapy (y/n), adjuvant radiation treatment (y/n), hormone treatment (y/n), benefit type, care source, TRICARE region, and comorbid conditions

[b]*p*-value for global effect of time-to-surgery in model

*$p < 0.05$

results. The potential effects of longer TTS on mortality may be related to poorer treatment response, adjuvant therapy delays, and other adverse effects previously described in the literature [3, 4].

We also found a significant elevated risk of all-cause death for TTS 0 days compared to TTS of 1–21 days among women age 18–49 at diagnosis and among women with stage I tumors. The higher risk of mortality for TTS 0 days may support the idea of a non-linear association between TTS and overall survival [5]. It is possible that TTS 0 days in our data represents local excision at time of biopsy, which may be less invasive or remove lower tissue volumes compared to other procedures. This may be related to residual disease after surgery or undetected lymph node involvement at time of diagnosis [44, 45] which may increase risk of breast cancer recurrence and mortality. However, without relevant data on residual disease and breast cancer-specific death we were unable to assess this possibility. Further research is needed to determine potential effects of same-day surgery on clinical outcomes.

Breast cancer TTS has been documented to be increasing over time [8, 12, 46] and was also shown in our data. The more recent use of preoperative genetic testing, planning for oncoplastic surgery, or planning for intraoperative radiation may result in increasing TTS [47]. The use of neoadjuvant chemotherapy to shrink operable tumors will also increase TTS and is an important clinical consideration, although we excluded these patients in our analysis. Also, with the development and use of immunotherapy and targeted therapy in breast cancer [48, 49], TTS may increase to allow treatment planning and care coordination. The factors related to increasing TTS and their effects on long-term clinical outcomes will be important for future research. Further, the role of TTS as a quality care indicator may need to be evaluated within the context of receiving these other treatments.

To our knowledge, this is the first study to examine TTS and overall survival in a U.S. representative population of women with universal access to care. However, our study had limitations. First, while breast cancer-specific mortality is a better outcome for assessing the effects of TTS, we used overall survival as the primary outcome because information on cause of death was not complete in the CCR data. Second, information on HER2 status was not complete as testing and reporting in cancer registries was not standard during the years of our data. Thus, we cannot rule out its potential effects on treatment and survival outcomes [50, 51]. Third, administrative data are subject to errors. However, the errors might not be prevalent enough to have substantially influenced our results. Last, smaller sample sizes and event counts in subgroup analyses prevented us from investigating potential joint effects of surgery type, age, and tumor stage on the results.

Conclusions

We found evidence that longer TTS is associated with poorer overall survival in a universal healthcare system, supporting the role of TTS as a quality care indicator in breast cancer. We also found risk associated with TTS may vary by surgery type, age, and tumor stage. Future research that includes short-term and breast cancer-specific outcomes are needed to increase our understanding of the association between TTS and clinical outcomes.

Table 3 Time-to-surgery and associated hazards ratios (HR) and 95% confidence intervals (CI) for all-cause death by surgery type, age at diagnosis, and tumor stage for women with breast cancer in the U.S. Military Health System, 1998–2010

Surgery type

Time to surgery (days)	Lumpectomy				Mastectomy			
	N	Person-years	Deaths (*n*)	Adjusted[a] HR (95% CI)	N	Person-years	Deaths (n)	Adjusted[a] HR (95% CI)
0	1673	15,857	114	1.07 (0.81, 1.42)	410	4042	59	1.23 (0.87, 1.72)
1–21	1657	15,460	95	1.00 (reference)	1097	10,251	101	1.00 (reference)
22–35	1552	13,497	58	0.90 (0.64, 1.25)	1019	8857	87	1.05 (0.79, 1.41)
≥ 36	1260	10,739	73	1.40 (1.02, 1.92)*	1001	8157	80	1.16 (0.86, 1.58)
p[d]				0.072				0.604

Age at diagnosis

Time to surgery (days)	18–49				50–64				65–79			
	N	Person-years	Deaths (*n*)	Adjusted[b] HR (95% CI)	*N*	Person-years	Deaths (*n*)	Adjusted[b] HR (95% CI)	N	Person-years	Deaths (*n*)	Adjusted HR[b] (95% CI)
0	854	8053	70	1.61 (1.13, 2.31)*	860	8491	57	0.91 (0.64, 1.30)	369	3353	46	1.19 (0.77, 1.83)
1–21	1098	10,171	60	1.00 (reference)	1185	11,239	85	1.00 (reference)	471	4301	51	1.00 (reference)
22–35	828	7163	44	1.23 (0.83, 1.83)	1185	10,456	64	0.99 (0.71, 1.38)	558	4734	37	0.78 (0.51, 1.21)
≥ 36	691	5792	36	1.41 (0.92, 2.16)	1.023	8714	55	1.17 (0.82, 1.66)	547	4390	62	1.50 (1.02, 2.21)*
p[d]				0.065				0.670				0.018

Tumor stage

Time to surgery (days)	I				II				III			
	N	Person-years	Deaths (*n*)	Adjusted[c] HR (95% CI)	*N*	Person-years	Deaths (*n*)	Adjusted[c] HR (95% CI)	*N*	Person-years	Deaths (*n*)	Adjusted[c] HR (95% CI)
0	1108	10,886	67	1.60 (1.07, 2.38)*	781	7427	70	1.05 (0.77, 1.44)	194	1584	36	1.02 (0.62, 1.67)
1–21	1261	12,301	43	1.00 (reference)	1206	11,014	112	1.00 (reference)	287	2290	41	1.00 (reference)
22–35	1381	12,128	39	1.14 (0.73, 1.77)	960	8382	70	0.92 (0.68, 1.25)	230	1646	36	1.21 (0.75, 1.95)
≥ 36	1283	10,948	58	1.67 (1.11, 2.52)*	788	6385	64	1.24 (0.90, 1.71)	190	1211	31	1.24 (0.75, 2.04)
p[d]				0.028				0.394				0.771

[a]Model adjusted for age at diagnosis, race-ethnicity, marital status, military service branch, active-duty status, year of diagnosis, tumor stage, tumor grade, hormone receptor status, surveillance mammography, adjuvant chemotherapy (y/n), adjuvant radiation treatment (y/n), hormone treatment (y/n), benefit type, care source, TRICARE region, and comorbid conditions

[b]Model adjusted for race-ethnicity, marital status, military service branch, active-duty status (except model age 65–79), year of diagnosis, tumor stage, tumor grade, hormone receptor status, surveillance mammography, surgery type, adjuvant chemotherapy (y/n), adjuvant radiation treatment (y/n), hormone treatment (y/n), benefit type (except model age 65–79), care source, TRICARE region, and comorbid conditions

[c]Model adjusted for age at diagnosis, race-ethnicity, marital status, military service branch, active-duty status, year of diagnosis, tumor grade, hormone receptor status, surveillance mammography, surgery type, adjuvant chemotherapy (y/n), adjuvant radiation treatment (y/n), hormone treatment (y/n), benefit type, care source, TRICARE region, and comorbid conditions

[d]*p*-value for global effect of time-to-surgery in model

*$p < 0.05$

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Data availability The data that support the findings of this study are not publicly available due to the sensitive nature of the data and presence of protected health information (PHI). The Department of Defense Central Cancer Registry (CCR) data may be requested from the Joint Pathology Center; and the Military Health System Data Repository (MDR) data may be requested from the Defense Health Agency. Restrictions apply to the access and use of these data.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The data linkage project was reviewed and approved by the institutional review boards of the Walter Reed National Military Medical Center and the Defense Health Agency for compliance with ethical standards. All study activities were conducted in accordance with the ethical standards of the institutional review boards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. It was determined by the institutional review boards that formal consent was not required for this type of study.

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