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Meng-Yuan Tsai
Kaohsiung Veterans General Hospital
Zi-Han Yu
Kaohsiung Veterans General Hospital
Chen-Pin Chou
chouchenpin@gmail.com

Kaohsiung Veterans General Hospital https://orcid.org/0000-0003-3093-7999

Research Article

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Meng-Yuan Tsai[1,2,3], Zi-Han Yu[1], Chen-Pin Chou[1,2,3,4]

[1] Department of Radiology, Kaohsiung Veterans General Hospital, Kaohsiung 813414, Taiwan

[2] School of Medicine, National Yang Ming Chiao Tung University, Taipei 112304, Taiwan

[3] School of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan, ROC

[4] Department of Medical Laboratory Science and Biotechnology, Fooyin University, Kaohsiung 831, Taiwan

Corresponding Author:

Chen-Pin Chou, MD

Department of Radiology,

Kaohsiung Veterans General Hospital,

386 Ta-Chung 1st Rd., Kaohsiung 813, Taiwan, ROC

Tel: 886-7-3422121 ext 76254

Fax: 886-7-3507581

e-mail: chouchenpin@gmail.com

Author contributions

Conceptualization, Meng-Yuan Tsai and Chen-Pin Chou; methodology, Meng-Yuan Tsai and Chen-Pin Chou; formal analysis, Meng-Yuan Tsai; investigation, Meng-Yuan Tsai and Zi-Han Yu; resources, Chen-Pin Chou; data curation, Zi-Han Yu; validation, Chen-Pin Chou; writing—original draft preparation, Meng-Yuan Tsai; writing—review and editing, Meng-Yuan Tsai, Zi-Han Yu, and Chen-Pin Chou; visualization, Meng-Yuan Tsai; supervision, Chen-Pin Chou; project administration, Chen-Pin Chou; funding acquisition, Chen-Pin Chou. All authors read and approved the final manuscript.

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Abstract

Background: Digital breast tomosynthesis (DBT) improves lesion conspicuity compared with digital mammography (DM), but whether its use in diagnostic work-up is associated with survival remains uncertain. We evaluated whether diagnostic mammographic modality was associated with overall survival (OS) in women with symptomatic breast cancer undergoing concurrent whole-breast ultrasound.

Methods: This retrospective cohort included 794 consecutive women diagnosed with breast cancer during evaluation of breast symptoms at a single institution between 2011 and 2015. All underwent diagnostic DM or DBT with same-day bilateral whole-breast ultrasound before biopsy; modality was determined by scheduling and equipment availability. The primary endpoint was 5-year OS. Hazard ratios (HRs) were estimated with Cox regression adjusted for age, breast density, American Joint Committee on Cancer (AJCC) stage, and year of diagnosis. Sensitivity analyses included propensity score matching, restricted mean survival time (RMST), and a stage-stratified model.

Results: Among 794 women (DM, n = 591; DBT, n = 203), 139 died during a median follow-up of 6.7 years. Five-year OS was 87.1% with DM and 86.2% with DBT. DBT was not significantly associated with OS after adjustment (HR 0.80; 95% CI 0.52–1.23; P = 0.309) or after propensity score matching (HR 0.81; 95% CI 0.53–1.24; P = 0.335). The 5-year RMST difference was −0.29 months (95% CI −2.06 to 1.40). No significant modality interaction with breast density or stage was detected.

Conclusions: In women with symptomatic breast cancer evaluated with concurrent whole-breast ultrasound, DBT showed no significant OS advantage over DM. These findings do not support preferential use of DBT on survival grounds alone.

Keywords:
Breast Neoplasms; Mammography; Digital Breast Tomosynthesis; Ultrasonography, Mammary; Survival Analysis

Introduction

Breast cancer is the most common cancer diagnosis among women worldwide and remains the leading cause of cancer death in low- and middle-income countries, where organized screening programs are limited and most cancers are detected following patient-reported symptoms [1]. Even in high-income settings with established screening infrastructure, a substantial proportion of breast cancers are diagnosed during evaluation of clinical symptoms rather than through screening, and these cancers have worse prognosis than their screen-detected counterparts, even after adjustment for lead-time and length biases [2].

Diagnostic mammography is the recommended first-line imaging study for symptomatic patients, providing morphologic assessment of suspicious findings and guiding biopsy decisions [3]. Digital breast tomosynthesis (DBT) was developed to address tissue overlap inherent in conventional two-dimensional digital mammography (DM), which can obscure lesion visibility [4]. By acquiring multiple low-dose projections over a limited angular range and reconstructing thin-section images, DBT improves lesion conspicuity and margin delineation compared with standard planar imaging [5]. In diagnostic practice, DBT has been associated with changes in Breast Imaging Reporting and Data System (BI-RADS) final assessment [6], whereas reader studies in screening populations have demonstrated improved diagnostic performance when DBT is added to DM [7]. However, evidence from referred diagnostic populations suggests comparable overall performance between DM and DBT, with one retrospective cohort demonstrating similar diagnostic accuracy and cancer detection rates between modalities [8]. These findings suggest that the incremental diagnostic benefit of DBT over DM in diagnostic populations remains uncertain.

The incremental value of DBT in the diagnostic setting may further depend on concurrent imaging. Adjunctive breast ultrasound improves cancer detection when added to mammography in screening [9] and contributes independent information on local disease extent in the preoperative diagnostic setting [10]. Ultrasound is highly sensitive for noncalcified masses, whereas architectural distortion—which may be occult on both DM and ultrasound—may be better visualized with DBT [11, 12]. However, whether mammographic modality is associated with differences in survival when concurrent ultrasound is performed remains uncertain.

At our institution, DM and DBT have been used in parallel since 2011, providing a real-world setting for comparative evaluation [13]. Both DM and DBT are used in the diagnostic evaluation of symptomatic breast abnormalities [3]. In clinical practice, modality selection is often determined by institutional workflow and equipment availability rather than outcome-based evidence. More accurate depiction of tumor extent, multifocality, or contralateral disease could alter staging and treatment planning [14]. However, whether these diagnostic advantages translate into improved long-term survival remains uncertain, particularly when concurrent whole-breast ultrasound provides complementary diagnostic information. Therefore, we evaluated the association between diagnostic mammographic modality (DM versus DBT) and overall survival (OS) in women diagnosed with breast cancer following diagnostic evaluation of symptomatic breast abnormalities, excluding screening-detected cancers and cases recalled from screening, with concurrent whole-breast ultrasound performed in both groups.

Materials and Methods

Study Design and Population

This retrospective cohort study used institutional cancer registry and mammography data from Kaohsiung Veterans General Hospital and was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). The Institutional Review Board of Kaohsiung Veterans General Hospital approved the study (KSVGH22-CT11-01; September 22, 2022) and waived the requirement for informed consent because of the retrospective design. All data were de-identified before analysis. The study was retrospectively registered at ClinicalTrials.gov (NCT05600257) on October 31, 2022.

Between September 2011 and December 2015, 1,517 consecutive patients with breast cancer were identified from the institutional cancer registry. Of these, 178 patients were excluded: 64 because stage could not be determined from institutional records, 8 because stage could not be assigned after a complete pathologic response to neoadjuvant chemotherapy, 5 because they were male, 56 because they had bilateral disease, and 45 because mammographic images were unavailable, leaving 1,339 patients. Among these, 545 patients whose cancers were detected by mammography performed under Taiwan's nationwide biennial population-based screening program were further excluded. The final cohort comprised 794 women diagnosed with breast cancer following diagnostic mammography outside the national screening program, hereafter referred to as the diagnostic cohort (Fig. 1).

Survival Outcomes and Follow-up

The primary endpoint was overall survival (OS), defined as the interval from breast cancer diagnosis to death from any cause. Five-year OS was the principal fixed-time outcome. Vital status and follow-up information were obtained from the institutional cancer registry, with data updated through May 2022. Patients without a recorded death were censored at the date of their last documented hospital visit or clinical contact. OS was selected because cause-of-death data were unavailable [15].

Clinical and Imaging Variables

Study variables included age at diagnosis, breast density, cancer stage, mammographic modality, and vital status at last follow-up. Breast density was classified according to the fifth edition of BI-RADS as almost entirely fatty, scattered fibroglandular densities, heterogeneously dense, or extremely dense [16]. Cancer stage was the stage group recorded in the institutional cancer registry according to the seventh edition of the American Joint Committee on Cancer (AJCC) staging system (stage 0–IV) [17], based on pathologic findings when available and on clinical staging otherwise. The AJCC seventh edition was used because it reflected clinical practice during the study period (2011–2015). Restaging according to the AJCC eighth edition was not feasible because the biomarker data required for prognostic staging were unavailable.

Breast density was extracted from the original radiology reports and assessed by the interpreting radiologist on mediolateral oblique (MLO) and craniocaudal (CC) views from conventional DM images or synthesized two-dimensional (C-view) images. Mammographic modality was classified as digital mammography (DM) or digital breast tomosynthesis (DBT). The index mammographic examination was defined as the diagnostic DM or DBT examination associated with the breast cancer diagnostic episode. All index mammographic and ultrasound examinations were performed before biopsy in accordance with institutional standard operating procedures.

Modality Assignment

Both the DM system (Lorad Selenia, Hologic, Bedford, MA) and the DBT system (Selenia Dimensions, Hologic, Bedford, MA) were installed at our institution in September 2011; the first DBT examination included in the study cohort was performed in December 2011. Diagnostic breast imaging was performed during outpatient visits to facilitate same-day evaluation.

Mammographic modality was determined by the institutional scheduling workflow and equipment availability. An even-/odd-date convention was used as a scheduling guide when both modalities were available; however, modality assignment could be altered by equipment availability, with DM used when DBT was unavailable. The DBT unit was also unavailable for routine diagnostic examinations during two half-days each week because it was reserved for DBT-guided biopsy procedures. Because DBT use increased over the study period, year of diagnosis was included in all adjusted models and the propensity score model to account for potential temporal confounding.

Imaging Acquisition and Interpretation

Standard DM consisted of bilateral CC and MLO views, with additional spot-compression or magnification views obtained as clinically indicated. DBT was acquired using 15 low-dose projections over a 15° arc (typical technique, 29 kVp and 44 mAs; automatically adjusted by the automatic exposure control according to breast thickness and composition) and reconstructed into 1-mm-thick slices, with the number of slices varying according to breast thickness. In the DBT group, DBT was performed together with DM or synthesized two-dimensional mammography during the same breast compressions [18].

Regardless of mammographic modality, all patients underwent same-day bilateral whole-breast ultrasound as part of the diagnostic evaluation. Ultrasound examinations were performed by one of four registered ultrasound technologists using a Logiq 9 system (GE Healthcare, Milwaukee, WI) equipped with a 12-MHz linear-array transducer. Patients were examined in the supine position with the ipsilateral arm elevated. Both breasts and bilateral axillary regions were scanned in real time in longitudinal and transverse planes, and static images documenting the dimensions and imaging characteristics of each suspicious lesion were recorded for subsequent radiologist review.

The same ultrasound equipment and technologist–radiologist workflow were used in both mammographic groups. Mammographic and ultrasound examinations were interpreted by one of six fellowship-trained breast radiologists with 5–16 years of DM experience and more than 6 months of DBT interpretation experience at the beginning of the study.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) and categorical variables as frequencies and percentages; groups were compared with the Student t test and Pearson chi-square test. OS was estimated by the Kaplan–Meier method and compared with the log-rank test; 3- and 5-year OS with 95% confidence intervals (CIs) used Greenwood variance on the log(–log) scale, and median follow-up was estimated by the reverse Kaplan–Meier method. Because events were sparse within density strata, density was also dichotomized as dense (heterogeneously or extremely dense) versus non-dense. Interactions between modality and breast density or AJCC stage were tested by adding product terms to the multivariable model and comparing nested models with likelihood ratio tests.

Age at diagnosis, mammographic modality, breast density, AJCC stage, and year of diagnosis (categorical) were assessed by univariable Cox regression, with associations expressed as hazard ratios (HRs), and entered simultaneously into the multivariable model without variable selection. Because DBT and DM may differ in their ability to assess disease extent and stage, models with and without adjustment for AJCC stage were used to examine whether stage adjustment affected the association between mammographic modality and survival. The stage-adjusted

model was interpreted as the association after accounting for recorded stage, whereas the model without stage adjustment was interpreted as the association without controlling for stage.

The proportional hazards assumption was assessed with scaled Schoenfeld residuals using a logarithmic time transform. Because there was some evidence of non-proportional hazards for stage but not for modality, a stage-stratified Cox model was fitted as a sensitivity analysis. Five-year restricted mean survival time (RMST) was compared between groups (DBT minus DM) [19], with 95% CIs from 2000 bootstrap replicates [20]. Further sensitivity analyses comprised 1:1 propensity score matching on age at diagnosis, breast density, stage, and year of diagnosis (nearest-neighbor, caliper 0.2 SD of the logit [21]; balance defined as standardized mean difference ≤ 0.10) [22], with robust variance for matched hazard ratios and matching repeated with 20 random orderings to assess the stability of the results. An additional analysis was restricted to patients with stage I–IV disease.

All statistical tests were two-sided, with $P < 0.05$ considered significant. No sample size or equivalence margin was prespecified; precision was judged from 95% CIs, and nonsignificant results were not interpreted as equivalence. Analyses were performed with IBM SPSS Statistics version 30.0 (IBM, Armonk, NY) and R 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria) using the survival, *MatchIt*, and *survRM2* packages.

Results

Characteristics of the Diagnostic Cohort

Among 794 women (mean age, 54.5 ± 13.3 years; range, 23–89 years), 591 (74.4%) underwent DM and 203 (25.6%) underwent DBT (Table 1). The DBT group was older (57.4 ± 13.4 vs 53.5 ± 13.1 years; $P < 0.001$), and was diagnosed more recently, whereas breast density and AJCC stage distributions were similar ($P = 0.214$ and $P = 0.605$). Mean age decreased across density categories, from 66.9 ± 11.6 years (almost entirely fatty) to 46.0 ± 9.5 years (extremely dense; $P < 0.001$). During a median follow-up of 6.7 years (95% CI: 6.3, 6.9; maximum, 9.3 years), 139 women (17.5%) died: 107 (18.1%) in the DM group and 32 (15.8%) in the DBT group. Of the 655 patients without a recorded death, 84 (12.8%) had less than 5 years of follow-up (DM, 59/484 [12.2%]; DBT, 25/171 [14.6%]).

Overall Survival in the Diagnostic Cohort

Kaplan–Meier analysis showed progressively lower OS with advancing AJCC stage, with 5-year OS decreasing from 97.6% in stage 0 to 36.6% in stage IV disease (log-rank $P < 0.001$; Fig. 2). In contrast, OS did not differ significantly across BI-RADS breast density categories (log-rank $P = 0.440$; Fig. 3) or between DM and DBT (log-rank $P = 0.857$; Fig. 4). The 3- and 5-year OS estimates were 92.6% and 87.1% with DM and 91.5% and 86.2% with DBT, respectively (Table 1).

Subgroup Analyses by Mammographic Modality

Exploratory subgroup analyses detected no statistically significant difference in OS between DM and DBT across the nine stage- and density-defined subgroups (all log-rank $P \geq 0.074$; Table 2). The extremely dense subgroup included only 16 DBT patients with 4 deaths, resulting in an imprecise 5-year OS estimate (79.8%; 95% CI: 49.4%, 93.0%). No statistically significant interaction was detected between mammographic modality and AJCC stage (likelihood ratio $P = 0.301$). P values were not adjusted for multiplicity across the nine subgroup comparisons; therefore, these analyses should be considered exploratory and hypothesis-generating.

When density was dichotomized as dense versus non-dense, the distribution did not differ significantly between modalities ($P = 0.699$), and OS did not differ significantly between DM and DBT in either dense (5-year OS, 87.0% vs 84.2%; $P = 0.912$) or non-dense breasts (87.5% vs 94.8%; $P = 0.601$; log-rank tests over the entire follow-up). No interaction between mammographic modality and breast density was detected using either the four-category ($P = 0.110$) or dichotomous classification ($P = 0.386$).

Cox Regression Analysis

In univariable analysis, older age (HR per year, 1.03; 95% CI: 1.02, 1.05; $P < 0.001$) and advancing AJCC stage were associated with worse OS (stage II: HR, 3.07; 95% CI: 1.70, 5.54; stage III: HR, 6.70; 95% CI: 3.60, 12.45; stage IV: HR, 23.28; 95% CI: 12.34, 43.94; all $P < 0.001$; all versus stage I), whereas mammographic modality (DBT vs DM: HR, 0.96; 95% CI: 0.65, 1.43; $P = 0.857$), breast density (all $P \geq 0.309$), and year of diagnosis (likelihood ratio $P = 0.248$ across categories) were not associated with OS.

In the multivariable model (Table 3), DBT was not significantly associated with OS (HR, 0.80; 95% CI: 0.52, 1.23; $P = 0.309$). The shift from the unadjusted estimate (HR, 0.96) mainly reflected adjustment for age, as the DBT group was older (age-adjusted HR, 0.84; 95% CI: 0.56, 1.25). More advanced AJCC stage and older age were also associated with worse OS; adjusted HRs versus stage I ranged from 2.97 (95% CI: 1.64, 5.38) for stage II to 32.72 (95% CI: 17.02, 62.89) for stage IV (all $P < 0.001$). Breast density (likelihood ratio $P = 0.230$) and year of diagnosis (likelihood ratio $P = 0.305$) were not significantly associated with OS overall, although the HR for extremely dense

versus almost entirely fatty breasts changed from 0.89 (95% CI: 0.36, 2.18) in univariable analysis to 2.56 (95% CI: 0.99, 6.65; P = 0.053) after adjustment, a shift consistent with confounding by age, because women with extremely dense breasts were substantially younger. There was no evidence of non-proportional hazards for mammographic modality (P = 0.751); the global test indicated some departure from proportional hazards (P = 0.047), mainly for AJCC stage (P = 0.056). The modality estimate was similar in the stage-stratified model (HR, 0.79; 95% CI: 0.51, 1.22; P = 0.288) and in the model without AJCC stage (HR, 0.81; 95% CI: 0.53, 1.23; P = 0.322). The 5-year RMST was 56.73 months with DM and 56.44 months with DBT, a difference of −0.29 months (95% CI: −2.06, 1.40), indicating that any difference in mean survival over 5 years was unlikely to exceed about 2 months.

Sensitivity Analyses

Propensity score matching yielded 203 matched pairs, with all DBT patients successfully matched and all postmatching standardized mean differences ≤0.10 (Online Resource 1). In the matched cohort, 5-year OS was 85.2% with DM and 86.2% with DBT (log-rank P = 0.371), with a matched HR of 0.81 (95% CI: 0.53, 1.24; P = 0.335); estimates were similar across repeated matching orders.

Because stage 0 disease accounted for 16.0% of the cohort but only 5.8% of deaths (8 of 139), the analysis was repeated in the 667 women with invasive disease (stage I–IV; 131 deaths); the adjusted HR was 0.79 (95% CI: 0.50, 1.25; P = 0.311). Estimates from the covariate-adjusted, stage-unadjusted, stage-stratified, matched, and invasive-only analyses ranged from 0.79 to 0.81, with all 95% CIs including 1.0 (Online Resource 2), indicating broadly consistent modality estimates across alternative analyses.

Discussion

In this retrospective cohort of 794 women with symptomatic breast cancer, all of whom underwent mammography (DM or DBT) with concurrent whole-breast ultrasound, OS did not differ significantly between DBT and DM (adjusted HR, 0.80; 95% CI: 0.52, 1.23). The results were consistent across sensitivity analyses (HR range, 0.79–0.81) and showed no significant interaction with breast density or AJCC stage. The 5-year RMST difference was −0.29 months (95% CI: −2.06, 1.40), suggesting that any difference in mean survival was small. The 95% CI of the adjusted HR (0.52, 1.23) excluded a reduction in the hazard of death of more than 48% or an increase of more than 23% with DBT, although smaller differences in either direction could not be ruled out. These findings indicate that, in symptomatic women evaluated with concurrent whole-breast ultrasound, DBT provides no detectable survival advantage over DM.

The nonsignificant association between mammographic modality and OS should also be interpreted in the context of disease presentation. Once breast cancer has become clinically apparent, the opportunity for mammographic modality to influence stage at diagnosis may be smaller than in screening populations, although this mechanism could not be directly evaluated in our study. This interpretation is consistent with the poorer survival of symptomatic than screen-detected cancers even after adjustment for lead-time and length biases [2], suggesting that prognosis in this setting may be determined more by tumor characteristics and disease extent at presentation than by the imaging modality used for work-up.

Breast density was not significantly associated with OS overall after adjustment. However, the estimate for extremely dense versus almost entirely fatty breasts changed substantially after adjustment (HR, 0.89 to 2.56), suggesting potential confounding by age, which was associated with both breast density and survival. This pattern is consistent with previously described concerns regarding confounding in analyses of mammographic density and breast cancer survival [23]. Given the small number of events in some density categories and the wide confidence interval, these findings should be considered exploratory. Although DBT reduces the effect of overlapping breast tissue and may improve lesion conspicuity [14], whether such diagnostic advantages translate into improved survival remains uncertain. Synthesized 2D mammography may yield lower density classifications than conventional DM [24, 25], potentially contributing to the lower proportion of extremely dense breasts in the DBT group (7.9% vs 12.7%). No statistically significant interaction between mammographic modality and breast density was detected.

DBT and breast ultrasound provide complementary information in the diagnostic evaluation of breast cancer; in women with focal or palpable breast complaints, DBT detected few or no additional cancers when ultrasound was performed [26, 27]. In women who underwent same-day whole-breast ultrasound, we found no significant difference in OS between DBT and DM, which is compatible with the possibility that ultrasound captures much of the additional information provided by DBT.

In our cohort, 5-year OS declined markedly with advancing stage in both modality groups (DM, 97.8% to 34.4%; DBT, 96.8% to 44.4%). Stage 0 and stage I had similarly low crude all-cause mortality (8 of 127 [6.3%] and 14 of 231 [6.1%], respectively), with the low mortality in stage 0 consistent with the generally favorable prognosis of ductal carcinoma in situ [28]. There was no evidence of non-proportional hazards for mammographic modality but some evidence for AJCC stage; stage-specific HRs should therefore be interpreted as average effects over follow-up rather than constant effects over time.

DBT may require greater examination-related costs and resources than DM, although available evidence on its performance, costs, and cost-effectiveness derives primarily from screening settings [29–32]. Because economic outcomes were not evaluated in this study, the cost-effectiveness of DBT in patients undergoing diagnostic mammography with concurrent ultrasound remains unknown.

This study has several limitations. First, mammographic modality was determined by scheduling and equipment availability rather than randomization. Although multivariable adjustment and propensity score matching were performed, residual confounding remains possible. Second, data on tumor biology, comorbidities, treatment, and cause of death were unavailable, limiting adjustment for potential confounders and preventing analysis of breast cancer–specific survival. Third, follow-up relied on the institutional cancer registry, and 84 surviving patients (12.8%) had less than 5 years of follow-up, potentially resulting in missed deaths. Fourth, the limited number of deaths reduced the precision of survival estimates, particularly in subgroup analyses. With 139 deaths and 25.6% of patients in the DBT group, the study had 80% power (two-sided $\alpha = 0.05$) to detect a hazard ratio of approximately 0.58 or lower; smaller but potentially relevant survival differences therefore cannot be excluded. Fifth, because all patients had confirmed breast cancer and underwent concurrent whole-breast ultrasound, we could not compare the diagnostic performance of DBT and DM or determine their independent contributions to survival. Finally, this single-center study used equipment from one manufacturer, which may limit generalizability. Future multicenter prospective studies with standardized imaging protocols, comprehensive clinical and treatment data, complete survival follow-up, and larger sample sizes are needed to address these limitations and clarify the association between mammographic modality and long-term survival.

Conclusions

In women with symptomatic breast cancer undergoing mammography with concurrent whole-breast ultrasound, DBT showed no significant overall survival advantage over DM. These findings do not support preferential use of DBT based on survival outcomes alone.

Compliance with Ethical Standards

Funding: This work was supported by a research grant from Kaohsiung Veterans General Hospital (VGHKS110-121). The funder had no role in the study design, data collection, analysis, interpretation, or writing of the manuscript.

Conflict of interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (approval code KSVGH22-CT11-01; September 22, 2022).

Informed consent: For this type of study formal consent is not required. The Institutional Review Board waived the requirement for informed consent because of the retrospective design.

Data availability: Study data are not publicly available because of privacy restrictions. De-identified aggregate data and analysis code are available on reasonable request, subject to Institutional Review Board approval.

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Figure Legends

Fig. 1 Flow diagram of study population selection. DBT = digital breast tomosynthesis; DM = digital mammography

Fig. 2 Kaplan–Meier OS curves by AJCC stage. OS differed significantly across stages 0–IV (log-rank P < 0.001), declining progressively with advancing stage: 5-year OS was 97.6% in stage 0 and 36.6% in stage IV. Numbers at risk at each time point are shown below the x-axis

Fig. 3 Kaplan–Meier OS curves by BI-RADS breast density. Curves for almost entirely fatty, scattered fibroglandular, heterogeneously dense, and extremely dense breasts were largely overlapping, with no significant difference in OS across categories (log-rank P = 0.440). Numbers at risk at each time point are shown below the x-axis

Fig. 4 Kaplan–Meier OS curves by mammographic modality. Curves for digital mammography (DM, blue) and digital breast tomosynthesis (DBT, red). OS did not differ significantly between DM and DBT (log-rank P = 0.857). Five-year OS was 87.1% (95% CI: 84.1, 89.6) with DM and 86.2% (95% CI: 80.5, 90.3) with DBT. Numbers at risk at each time point are shown below the x-axis; maximum follow-up was 9.3 years with DM and 8.6 years with DBT, so estimates near the end of follow-up are imprecise because few patients remained at risk

Table 1. Baseline characteristics according to mammographic modality (N = 794).

Characteristics	Total	DM	DBT	*P*
	N = 794	n = 591	n = 203	
Age, years, mean ± SD	54.5 ± 13.3	53.5 ± 13.1	57.4 ± 13.4	<0.001
Breast density BI-RADS 5th edition				0.214
Almost entirely fatty	56 (7.1)	41 (6.9)	15 (7.4)	
Scattered fibroglandular	106 (13.4)	82 (13.9)	24 (11.8)	
Heterogeneously dense	541 (68.1)	393 (66.5)	148 (72.9)	
Extremely dense	91 (11.5)	75 (12.7)	16 (7.9)	
Stage AJCC 7th				0.605
0	127 (16.0)	95 (16.1)	32 (15.8)	
I	231 (29.1)	179 (30.3)	52 (25.6)	
II	288 (36.3)	206 (34.9)	82 (40.4)	
III	107 (13.5)	79 (13.4)	28 (13.8)	
IV	41 (5.2)	32 (5.4)	9 (4.4)	
Deaths	139 (17.5)	107 (18.1)	32 (15.8)	
Overall survival (OS), %				
3-year (95% CI)	92.3 (90.2, 94.0)	92.6 (90.1, 94.4)	91.5 (86.6, 94.6)	
5-year (95% CI)	86.9 (84.3, 89.1)	87.1 (84.1, 89.6)	86.2 (80.5, 90.3)	

Note.—Data are numbers (percentages) unless otherwise indicated. DM = digital mammography; DBT = digital breast tomosynthesis; AJCC = American Joint Committee on Cancer; BI-RADS = Breast Imaging Reporting and Data System; CI = confidence interval. P values were calculated with the Student t test or Pearson chi-square test. OS was estimated with the Kaplan–Meier method.

Table 2. Five-year overall survival according to mammographic modality within subgroups (N = 794).

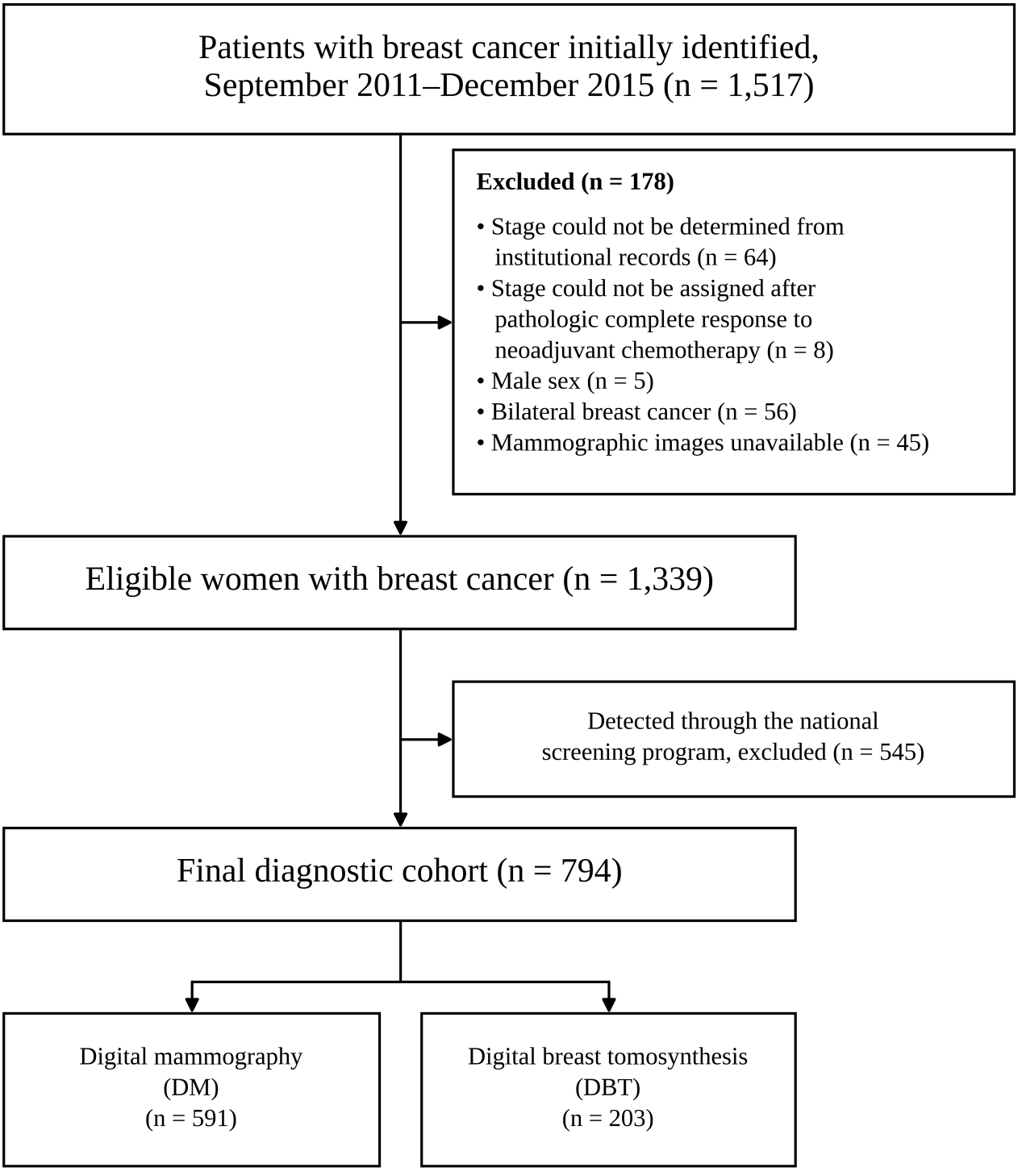
Characteristics	DM		DBT		*Log-rank P*
	deaths/n	5-year OS, % (95% CI)	deaths/n	5-year OS, % (95% CI)	
Breast density BI-RADS 5th edition					
Almost entirely fatty	6/41	92.3 (78.0, 97.5)	2/15	100.0 (CI not estimable)	0.954
Scattered fibroglandular	20/82	85.2 (75.4, 91.3)	3/24	91.5 (70.0, 97.8)	0.587
Heterogeneously dense	73/393	85.9 (82.0, 89.1)	23/148	84.6 (77.6, 89.6)	0.601
Extremely dense	8/75	93.0 (83.9, 97.0)	4/16	79.8 (49.4, 93.0)	0.074
Stage AJCC 7th					
0	5/95	97.8 (91.5, 99.4)	3/32	96.8 (79.2, 99.5)	0.297
I	13/179	97.0 (93.0, 98.7)	1/52	98.0 (86.9, 99.7)	0.246
II	38/206	86.4 (80.8, 90.5)	13/82	87.3 (77.6, 93.0)	0.877
III	25/79	75.9 (64.5, 84.1)	10/28	62.2 (41.0, 77.7)	0.421
IV	26/32	34.4 (18.8, 50.6)	5/9	44.4 (13.6, 71.9)	0.489

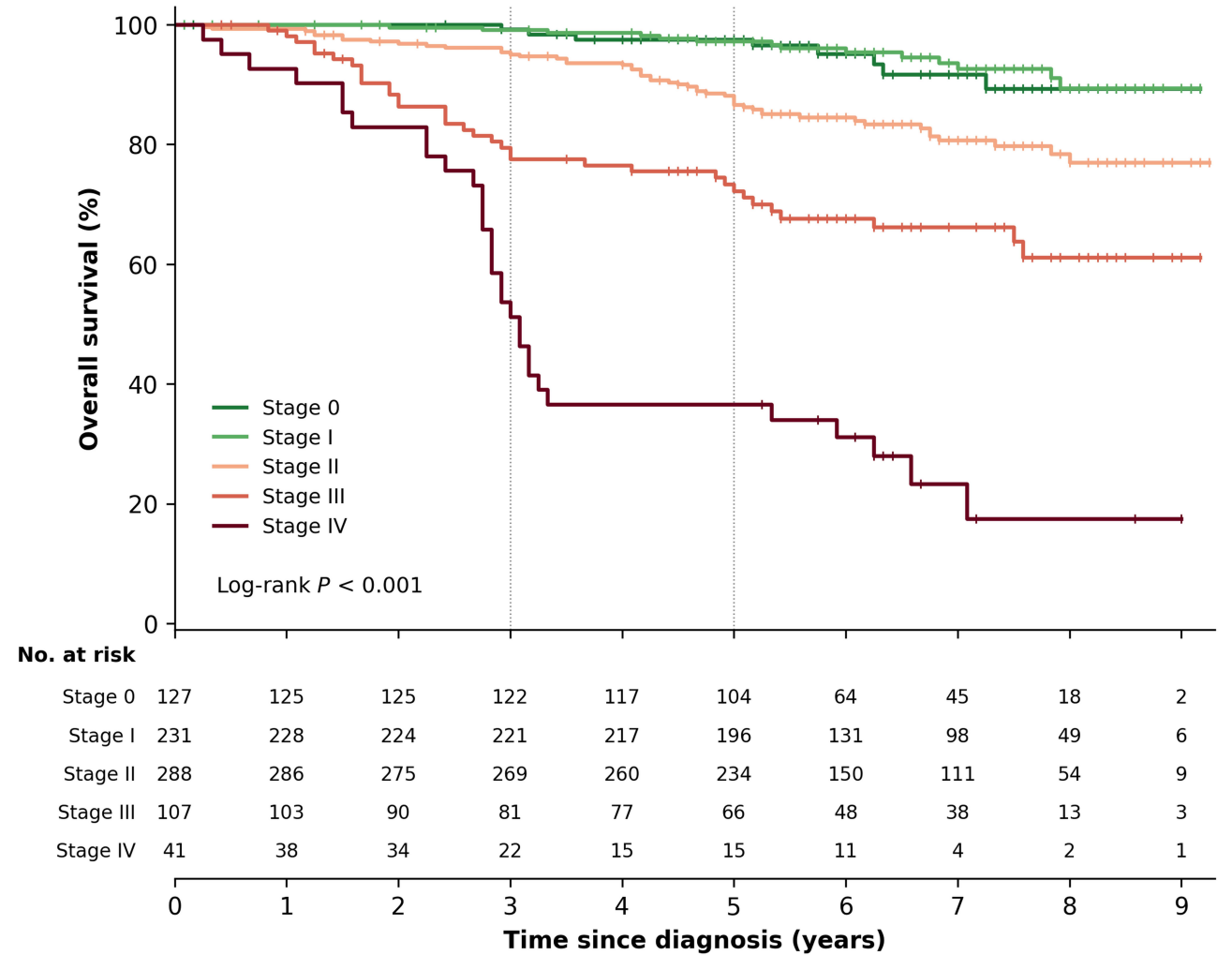
Note.—Five-year OS was estimated with the Kaplan–Meier method. DM = digital mammography; DBT = digital breast tomosynthesis; AJCC = American Joint Committee on Cancer; BI-RADS = Breast Imaging Reporting and Data System; CI = confidence interval. In the almost entirely fatty DBT subgroup, both deaths occurred after 5 years; therefore, the CI was not estimable. P values are from log-rank tests over the entire follow-up and were not adjusted for multiple comparisons.

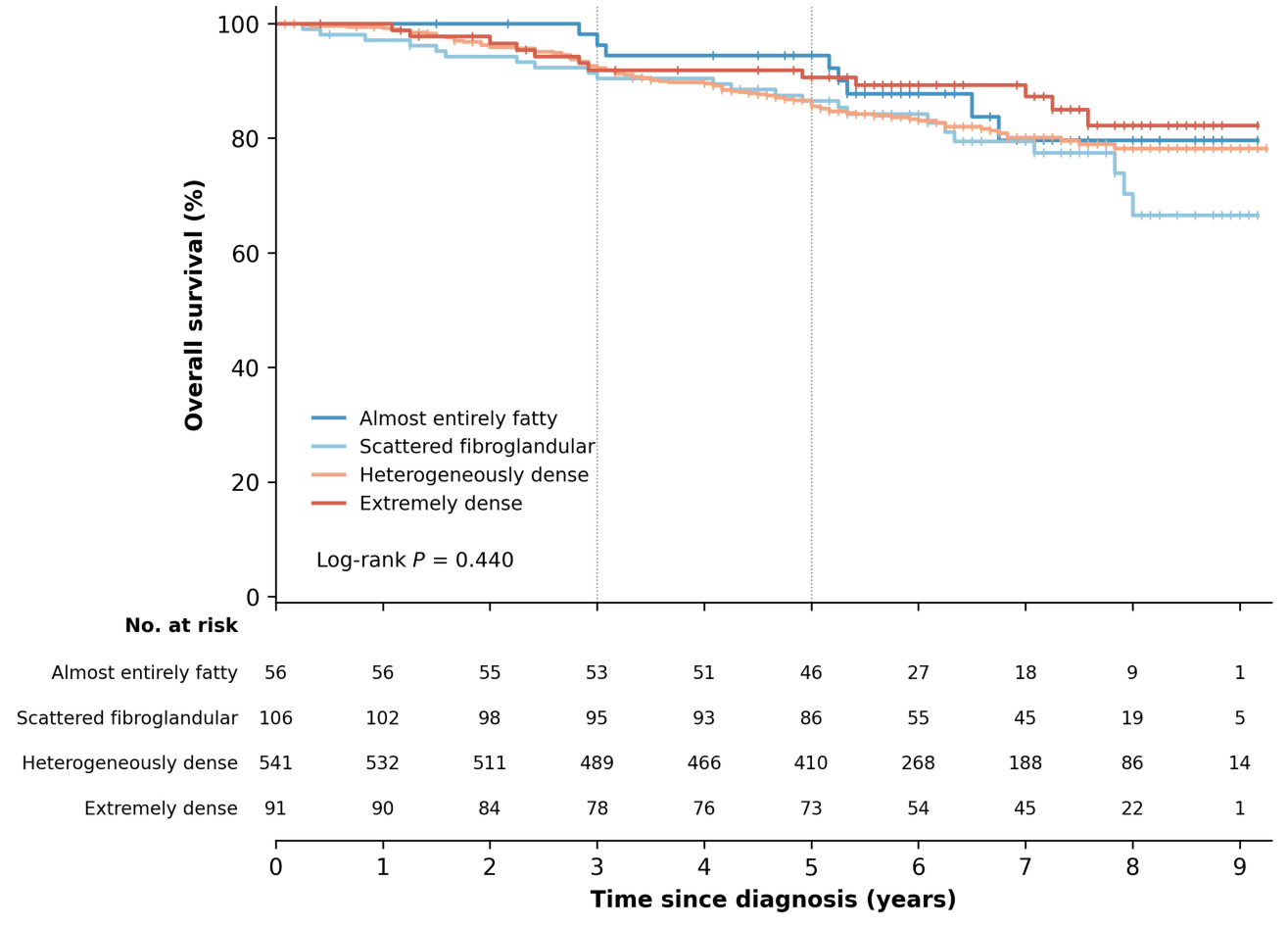
Table 3. Univariable and multivariable Cox regression analysis of OS in symptomatic patients (N = 794).

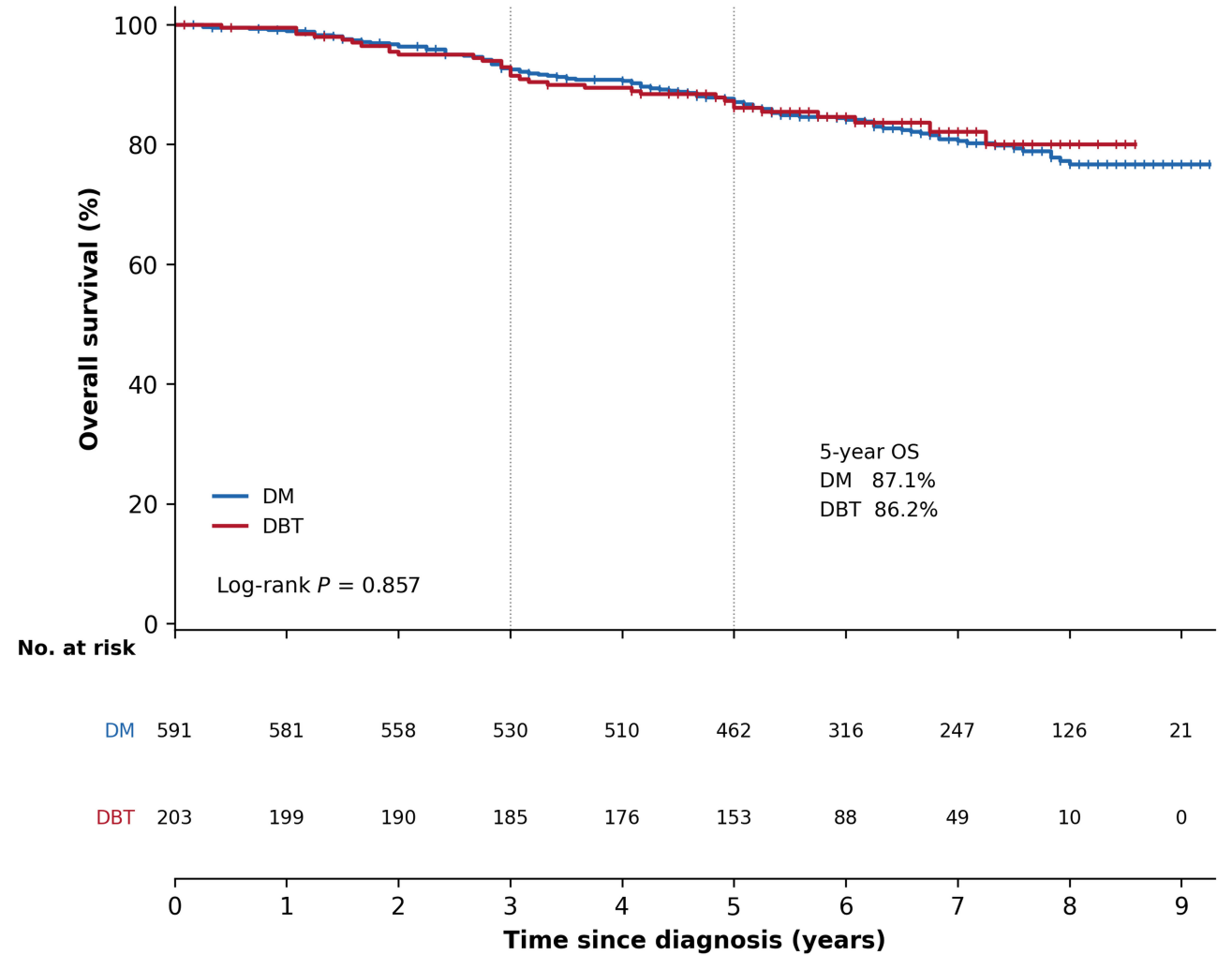
Characteristics	N	Univariable Analysis		Multivariable Analysis	
		HR (95% CI)	*P*	HR (95% CI)	*P*
Age, per year	794	1.03 (1.02, 1.05)	<0.001	1.05 (1.03, 1.06)	<0.001
Mammographic modality					
DM (reference)	591	1		1	
DBT	203	0.96 (0.65, 1.43)	0.857	0.80 (0.52, 1.23)	0.309
Breast density BI-RADS 5th edition					
Almost entirely fatty (reference)	56	1		1	
Scattered fibroglandular	106	1.52 (0.68, 3.39)	0.309	1.64 (0.73, 3.71)	0.230
Heterogeneously dense	541	1.27 (0.62, 2.61)	0.515	1.88 (0.89, 3.95)	0.098
Extremely dense	91	0.89 (0.36, 2.18)	0.800	2.56 (0.99, 6.65)	0.053
Stage AJCC 7th					
0	127	1.10 (0.46, 2.62)	0.833	1.13 (0.47, 2.70)	0.784
I (reference)	231	1		1	
II	288	3.07 (1.70, 5.54)	<0.001	2.97 (1.64, 5.38)	<0.001
III	107	6.70 (3.60, 12.45)	<0.001	6.85 (3.66, 12.80)	<0.001
IV	41	23.28 (12.34, 43.94)	<0.001	32.72 (17.02, 62.89)	<0.001

Note.—HR = hazard ratio; CI = confidence interval; DM = digital mammography; DBT = digital breast tomosynthesis; BI-RADS = Breast Imaging Reporting and Data System; AJCC = American Joint Committee on Cancer. The multivariable model was additionally adjusted for year of diagnosis (categorical; likelihood ratio P = 0.305). P values are Wald tests versus the reference category.


Patients with breast cancer initially identified, September 2011–December 2015 (n = 1,517)
Excluded (n = 178)
• Stage could not be determined from institutional records (n = 64)
• Stage could not be assigned after pathologic complete response to neoadjuvant chemotherapy (n = 8)
• Male sex (n = 5)
• Bilateral breast cancer (n = 56)
• Mammographic images unavailable (n = 45)
Eligible women with breast cancer (n = 1,339)
Detected through the national screening program, excluded (n = 545)
Final diagnostic cohort (n = 794)
Digital mammography (DM) (n = 591)
Digital breast tomosynthesis (DBT) (n = 203)


Overall survival (%)
100
80
60
40
20
0
Stage 0
Stage I
Stage II
Stage III
Stage IV
Log-rank P < 0.001
No. at risk
Stage 0 127 125 125 122 117 104 64 45 18 2
Stage I 231 228 224 221 217 196 131 98 49 6
Stage II 288 286 275 269 260 234 150 111 54 9
Stage III 107 103 90 81 77 66 48 38 13 3
Stage IV 41 38 34 22 15 15 11 4 2 1
0 1 2 3 4 5 6 7 8 9
Time since diagnosis (years)


Overall survival (%)
100
80
60
40
20
0
Almost entirely fatty
Scattered fibroglandular
Heterogeneously dense
Extremely dense
Log-rank P = 0.440
No. at risk
Almost entirely fatty 56 56 55 53 51 46 27 18 9 1
Scattered fibroglandular 106 102 98 95 93 86 55 45 19 5
Heterogeneously dense 541 532 511 489 466 410 268 188 86 14
Extremely dense 91 90 84 78 76 73 54 45 22 1
0 1 2 3 4 5 6 7 8 9
Time since diagnosis (years)


Overall survival (%)
100
80
60
40
20
0
DM
DBT
Log-rank P = 0.857
5-year OS
DM 87.1%
DBT 86.2%
No. at risk
DM 591 581 558 530 510 462 316 247 126 21
DBT 203 199 190 185 176 153 88 49 10 0
0 1 2 3 4 5 6 7 8 9
Time since diagnosis (years)

Supplementary Files

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