Breast Cancer in Women in Gaza: A Review of Clinical Characteristics and Short-Term Survival

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ABSTRACT

PURPOSE To understand how breast cancer is diagnosed in Gaza, and disease stage distribution, treatment, and survival.

MATERIALS AND METHODS A clinical record case series study of women diagnosed in 2017 and 2018 was conducted with follow-up until December 31, 2020. Breast cancer crude incidence rates and age-specific incidence rates were calculated. Clinical characteristics, including investigation, diagnosis, and treatment methods by year of diagnosis, were compared using the chi-square test. The 2-year cumulative risk of death from any cause was estimated using the Kaplan-Meier method, and univariate and multivariate Cox proportional hazard regressions estimated hazard ratios and their 95% CIs.

RESULTS Five hundred twenty-four new diagnoses (mean age, 53 years; range, 23-100) were recorded, giving a crude annual incidence rate of 27 per 100,000 population. Six percent (32/524) were diagnosed at stage I, 35% (185/524) at stage II, 33% (171/524) at stage III, and 19% (99/524) at stage IV. More than one half (52%, 271/524) underwent modified radical mastectomy. Seventy-seven percent (405/524) received chemotherapy, 70% (368/524) hormone therapy, and 39% (204/524) radiotherapy. Data on key prognostic factors were mostly available—stage (93%), estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2; 82%), tumor grade (77%), and tumor size (70%). The overall survival was 95.4% at 1 year and 86.6% at 2 years.

CONCLUSION Women with breast cancer in Gaza have a high short-term survival after diagnosis. However, one half were diagnosed with advanced disease, and their investigations were incomplete. Better reporting on family history, tumor grade, size, and ER, PR, and HER2 receptor status is needed for future studies.

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INTRODUCTION

In the occupied Palestinian territory (oPt), few routine data are available to estimate breast cancer incidence and mortality trends. However, available data for 2018 suggest a crude incidence rate of 33 per 100,000, which appears lower than in neighboring countries.[1] As Palestinian women's fertility declines (the fertility rate was 4.5 in 2018),[2,3] and the proportion of women age 60 years and older doubles by 2050, an increase of over 135% in patients with breast cancer is expected by 2040.[2] Breast cancer mortality is also expected to increase, and this rising cancer burden will increase the need for infrastructure for pathology, drug delivery, and training infrastructure. The only published study on survival after a diagnosis of breast cancer in Gaza reported an overall 5-year survival of 65% among 1,360 women diagnosed between 2005 and 2014.[4] Data on grade, disease stage, and treatment were not available for most cases and have not been examined. Nevertheless, there is a consensus that women are diagnosed at an advanced stage of their disease and have had poor access to treatment either because of reduced availability of chemotherapy at Gaza cancer care facilities, or the arduous journeys women take from Gaza to Jerusalem for every treatment course.

The Gaza Cancer Registry reported an estimated 2,800 new incident breast cancers from 2009 to 2018.[5] In 2017, 1,744 new cancers were detected in the oPt, with a crude incidence rate of 91 per 100,000 population. According to the Palestinian Ministry of Health (MoH),[5] the figures for 2021 were 1,952 and 92.6 per 100,000 population, respectively. Although these data reveal that the average incidence rate is

CONTEXT

Key Objective
To understand how breast cancer is diagnosed in Gaza, and disease stage distribution, treatment, and survival.

Knowledge Generated
Our findings reflect the remarkable adaptation of Palestinian women with breast cancer who have high short-term survival. Whether this translates into longer term survival is unknown.

Relevance
Methods of improving the reporting of diagnostic intervals through clearer referral guidelines are needed to assess what is causing the high percentage of advanced stages of breast cancer at diagnosis.

increasing, the Gaza Cancer Registry, unfortunately, does not publish figures by cancer type and single calendar year. Most information on breast cancer incidence comes from the mass media or health care providers. As a result, women in Gaza often receive mixed messages about breast cancer incidence and survival in their country. This important lack of data needs to be addressed to provide clear information about the quality of diagnostic care and treatment. This study therefore aimed to review the clinical characteristics of women with breast cancer in Gaza, including how the diagnosis of breast cancer was made, and how this is reflected in disease stage distribution, treatment received, and short-term survival.

MATERIALS AND METHODS

Case Identification

We reviewed clinical records of all women living in Gaza and diagnosed with breast cancer from January 1, 2017, to December 31, 2018, and followed up until December 31, 2020. Like many registries, the Gaza Cancer Registry does not start collecting data until well after a diagnosis. Therefore, information on 2017/2018 incident cases was not available as we began this study. Also, government hospitals providing cancer care in Gaza maintain paper or scanned cancer records. The main study data sources were the three government diagnostic facilities for cancer. Two research assistants read around 9,000 pathology reports identifying positive diagnoses or suspicious cases and following these up to identify further biopsies and positive results for inclusion. This was possible as histopathology reports were archived by the date of biopsy regardless of the biopsy location or whether the report result was positive, negative, or benign.

Information about possible omitted patients was also collected from (1) cancer records in hospitals providing treatment as well as referral reports for treatment outside Gaza and (2) death certificates from the national vital statistics database. A review with the Gaza Cancer Registry in 2019 allowed us to cross-check incident reports.

Quantitative Variables

Data on menopausal status, family history of breast or ovarian cancer, symptomatic or screening detection, time between the recognition of symptoms by the woman and consulting a health care provider, and location of surgery (if performed) were collected from women themselves. Information on marital status came from the Palestinian Ministry of Internal Affairs National Civil System.

Cancer hospitals collect information on each cancer stage on the basis of pathologic and clinical information provided by government or nongovernment facilities using the TNM classification.[25] Cancer stage in this study is categorized as I, II, III, IV, and unknown.

Clinical data collected from the medical records included the type of biopsy used to confirm the diagnosis, age at diagnosis (categorical), breast cancer morphology (ductal, lobular, other, and unspecified), cancer stage, tumor grade (1, 2, 3, or unknown), tumor size (in cm), lymph node status (pN0, pN1, pN2, or not removed and unknown), receptor subtype, and metastasis at diagnosis. Information on trastuzumab (yes or no), chemotherapy, hormone therapy, and radiotherapy was also collected. Information on chemotherapy was categorized as (1) not received; (2) neoadjuvant therapeutic; (3) adjuvant therapeutic; (4) therapeutic, then palliative; or (5) palliative.

Intention to give radiotherapy (yes or no) categorized whether there were plans for radiotherapy, on the basis of the oncologist's clinical notes. Received radiotherapy (yes or no) was based on whether a woman reported having received radiotherapy.

Methods of Analysis

Breast cancer crude incidence rates were calculated as patients per 100,000 women in the population in 2017 and 2018. Age-specific incidence rates (AIR) were calculated for 5-year interval age groups ranging from 0-4 years

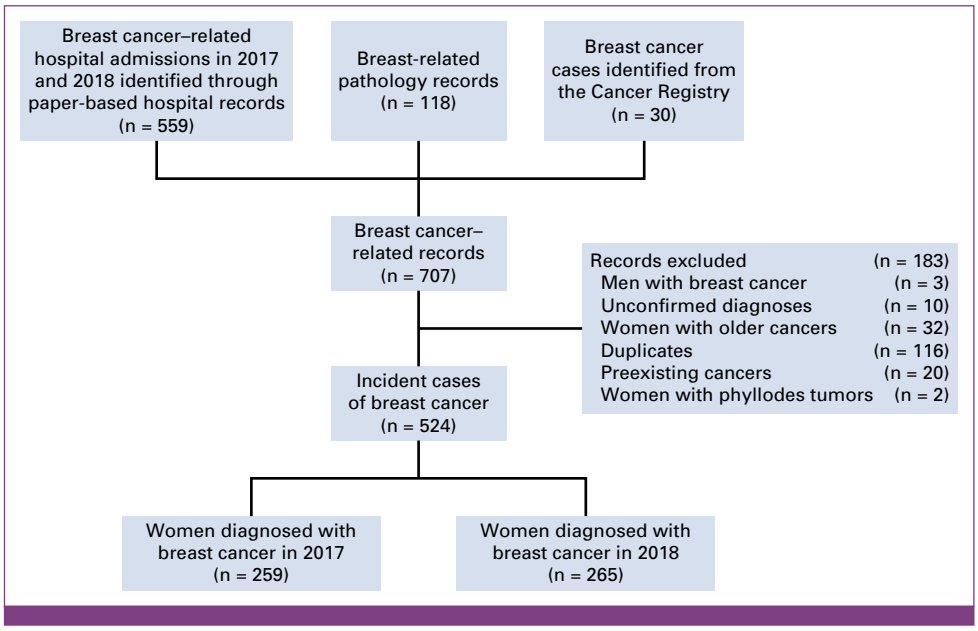

FIG 1. Study profile for women diagnosed with breast cancer in Gaza in 2017 and 2018.

through 75-79 years, and then for 80 years and older. The age-standardized incidence rate (ASIR) was a weighted average of the AIR for each age group, with the weightings being the proportions of people in the corresponding age groups of the world standard population. Quantitative variables were presented as frequencies and percentages. Clinical characteristics according to the year of diagnosis were compared using the chi-square test and Fisher's exact test. The tests were performed excluding the unknown information in quantitative variables. The differences between groups were considered statistically significant when the *P* value was ≤.05.

Age-standardized overall survival (OS) at 1 year and 2 years after diagnosis were calculated using the International Cancer Survival Weights, using a weighted average of survival estimates of the five age groups (15-44, 45-54, 55-64, 65-74, and 75-99 years).[6]

TABLE 1. Age-Specific and Age-Standardized Breast Cancer Incidence Rates (2017-2018) per 100,000 Palestinian Women Living in Gaza

Age Group, Years	No. of Patients	Person-Years at Risk	Age-Specific Incidence Rate	Segi World Standard	Expected No. of Patients in Standard World Population
0-4	0	284,356	0.00	12,000	0.00
5-9	0	274,684	0.00	10,000	0.00
10-14	0	237,930	0.00	9,000	0.00
15-19	0	191,504	0.00	9,000	0.00
20-24	4	189,570	2.11	8,000	0.17
25-29	15	176,030	8.52	8,000	0.68
30-34	32	133,472	23.98	6,000	1.44
35-39	44	102,522	42.92	6,000	2.58
40-44	53	85,114	62.27	6,000	3.74
45-49	61	65,770	92.75	6,000	5.56
50-54	80	56,098	142.61	5,000	7.13
55-59	68	44,490	152.84	4,000	6.11
60-64	59	30,950	190.63	4,000	7.63
65-69	46	23,212	198.17	3,000	5.95
70-74	31	15,476	200.31	2,000	4.01
75-79	17	11,606	146.48	1,000	1.46
≥80	14	5,804	241.21	1,000	2.41
Total	524	1,928,588	27.17	100,000	48.86

TABLE 2. Characteristics of 524 Women Diagnosed With Breast Cancer in Gaza Between 2017 and 2018

Category	Year of Diagnosis, No. (%)		
	2017 (n = 259)	2018 (n = 265)	Total (N = 524), No. (%)
Age group, years			
0-44	69 (27)	79 (30)	148 (29)
45-59	101 (39)	108 (41)	209 (40)
60-74	70 (27)	66 (25)	136 (26)
≥75	19 (7)	12 (4)	31 (5)
Marital status			
Married	184 (71)	181 (68)	365 (70)
Single	18 (7)	31 (12)	49 (9)
Widowed	49 (19)	40 (15)	89 (17)
Divorced	8 (3)	13 (5)	21 (4)
Menopause status			
Premenopausal	108 (42)	123 (46)	231 (44)
Postmenopausal	143 (55)	141 (53)	284 (54)
Unknown	8 (3)	1 (1)	9 (2)
Family history of breast or ovarian cancer			
No	114 (44)	157 (59)	271 (52)
Yes	66 (25)	70 (27)	136 (26)
Unknown	79 (31)	38 (14)	117 (22)
Disease discovery			
Self-discovered	241 (93)	251 (95)	492 (94)
Screen detected	4 (2)	4 (1)	8 (1)
Unknown	14 (5)	10 (4)	24 (5)
The time between recognition of symptoms and when a health care person was consulted			
Less than a month	126 (49)	134 (51)	260 (50)
Between 1 and 3 months	15 (6)	29 (11)	44 (8)
More than 3 months	16 (6)	38 (14)	54 (10)
Unknown	102 (39)	64 (24)	166 (32)

Survival time was measured from the date of diagnosis until the date on which women were last known to be alive or until December 31, 2020, whichever was first. Outcomes were censored at 36 months as all women were followed up until December 31, 2020, using clinical and mortality records. The 2-year cumulative probability of survival and the 2-year cumulative risk of death from any cause were estimated by using the Kaplan-Meier method. Univariate and multivariate Cox proportional hazard regressions were used to estimate hazard ratios (HRs) and their 95% CIs. Covariates in the survival analysis where data were sufficient for analysis were chosen as age, menopausal status, family history of breast or ovarian cancer, breast cancer morphology (ductal, lobular, other, and unspecified), TNM, stage, tumor grade, and estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) receptor status of the breast cancer. Given the known poor outcome associated with grade 3 tumors, data were regrouped by combining the first two grades and then retested against grade 3. TNM stages I and II were also combined in the Cox proportional hazards regression analyses. Mutual adjustment was included in the analysis to estimate the independent effects of age, TNM stage, tumor grade, and menopausal status. Missing observations on age, TNM stage, tumor grade, and menopausal status were then excluded to perform a complete-case analysis (385 patients) after mutual adjustment for the estimated independent effects of these variables.

Ethics

The study followed King's College Data Protection Regulations (DPRF-17/18-7596), and ethical clearance was obtained from the Palestinian Health Research Committee (PHRC/HC/354/18), the Palestinian MoH (223204), and the King's College Research Ethics Committee (HR-17/18-6982).

RESULTS

Incidence

There were 524 patients of breast cancer clinically diagnosed from January 1, 2017, to December 31, 2018. Of these, 259 women were diagnosed in 2017 and 265 in 2018 (Fig 1). About

TABLE 3. Clinicopathologic Characteristics

Category	Year of Diagnosis, No. (%)		Total (N = 524), No. (%)	*P* With Unknown Omitted
	2017 (n = 259)	2018 (n = 265)		
Type of biopsy				
FNAB only	71 (27)	51 (19)	122 (23)	.000
FNAB and TCB	69 (27)	66 (25)	135 (26)	
TCB only	57 (22)	106 (40)	163 (31)	
Excisional biopsy only	24 (9)	20 (8)	44 (8)	
Excisional biopsy and others	18 (7)	8 (3)	26 (5)	
Other or unknown	20 (8)	14 (5)	34 (7)	
Affected side				
Right	115 (44)	118 (45)	233 (44)	.246
Left	123 (48)	137 (51)	260 (50)	
Both	11 (4)	5 (2)	16 (3)	
Unknown	10 (4)	5 (2)	15 (3)	
Morphology				
Ductal	199 (77)	234 (88)	433 (82)	.054
Lobular	28 (11)	18 (7)	46 (9)	
Other or unknown	32 (12)	13 (5)	45 (9)	
Tumor size				
≤2 cm	35 (14)	42 (16)	77 (15)	.093
>2 cm ≤5 cm	130 (50)	125 (47)	255 (49)	
>5 cm	26 (10)	13 (5)	39 (7)	
Unknown	68 (26)	85 (32)	153 (29)	
Tumor grade				
1	9 (4)	8 (3)	17 (3)	.866
2	150 (58)	159 (60)	309 (59)	
3	37 (14)	43 (16)	80 (15)	
Unknown	63 (24)	55 (21)	118 (23)	
Stage at diagnosis				
I	13 (5)	19 (7)	32 (6)	.370
II	96 (37)	89 (34)	185 (35)	
III	88 (34)	83 (31)	171 (33)	
IV	43 (17)	56 (21)	99 (19)	
Unknown	19 (7)	18 (7)	37 (7)	
Lymph node status				
pN0 (not involved)	73 (28)	71 (27)	144 (27)	.827
pN1 (1-3)	61 (23)	53 (20)	114 (22)	
pN2 (4 or more)	55 (21)	56 (21)	111 (21)	
Not removed or unknown	70 (28)	85 (32)	155 (30)	
Involvement of skin				
No	157 (61)	157 (59)	314 (60)	.685
Yes	4 (1)	2 (1)	6 (1)	
Unknown	98 (38)	106 (40)	204 (39)	
ER				
Negative	35 (14)	22 (8)	57 (11)	.029
Positive	172 (66)	203 (77)	375 (71)	
Not performed or unknown	52 (20)	40 (15)	92 (18)	
PR				
Negative	34 (13)	23 (9)	57 (11)	.053
Positive	173 (67)	202 (73)	375 (71)	
Not performed or unknown	52 (20)	40 (15)	92 (18)	

(continued on following page)

TABLE 3. Clinicopathologic Characteristics (continued)

Category	Year of Diagnosis, No. (%)		Total (N = 524), No. (%)	*P* With Unknown Omitted
	2017 (n = 259)	2018 (n = 265)		
HER2 receptor (HER2)				
Negative	169 (65)	181 (67)	350 (66)	.802
Positive	36 (13)	42 (16)	78 (15)	
Not performed or unknown	54 (21)	42 (16)	96 (18)	
Tumor subtype on the basis of the hormone receptor and HER2 status				
HR+/HER2−	151 (58)	171 (65)	322 (62)	.113
HR+/HER2+	22 (8)	32 (12)	54 (10)	
HR−/HER2+	12 (5)	10 (4)	22 (4)	
Triple-negative	21 (8)	12 (5)	33 (6)	
Not performed or unknown	53 (21)	40 (14)	93 (18)	
Metastatic sites at diagnosis				
No metastasis	60 (23)	65 (25)	125 (24)	.502
Distant lymph nodes only	138 (53)	135 (51)	273 (52)	
Bone	17 (7)	17 (6)	34 (7)	
Liver	4 (2)	8 (3)	12 (2)	
Lung	13 (5)	8 (3)	21 (4)	
Brain	1 (0)	1 (0)	2 (0)	
Two or more sites	11 (4)	20 (8)	31 (6)	
Unknown	15 (6)	11 (4)	26 (5)	

Abbreviations: ER, estrogen receptor; FNAB, breast fine-needle aspiration; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor positive; HR−, hormone receptor negative; PR, progesterone receptor; TCB, Tru-Cut needle biopsy.

70% (369/524) received treatment at the Rantisi Hospital and 30% (155/524) at the European Gaza Hospital.

The crude annual incidence rate was 27 per 100,000 population, and the ASIR was 48.86 per 100,000. Table 1 shows the AIR and ASIR for women diagnosed with breast cancer in 2017 and 2018.

Descriptive Details

The mean age at diagnosis was 53 years (standard deviation [SD], 13.57; IQR, 43-63; range, 23-100 years), and half of the women (262/524) were between age 40 and 59 years. Table 2 shows the distributions of age, marital status, menopausal status, family history of breast or ovarian cancer, routes to diagnosis, and the time delay between recognition of symptoms and presentation to a health care provider. The unknown values in Table 2 include women who did not respond to the phone calls or had died before the date of the data collection.

Diagnosis Details

Before pathologic confirmation, the cancers were primarily assessed clinically using diagnostic mammography (37%, 193/524), ultrasound (22%, 116/524), and infrequently by computed tomography scan (3%, 14/524) or magnetic resonance imaging (1%, 4/524). Key prognostic factors were mostly available—stage (93%, 487/524), ER (82%, 432/524), PR (82%, 433/524), HER2 (82%, 428/524), and slightly less often for tumor grade (77%, 406/524) and tumor size (70%, 370/524). Women were most often diagnosed at stage II (35%, 185/524), followed by stage III (33%, 171/524), stage IV (19%, 99/524), and stage I (6%, 32/524). Table 3 lists the detailed clinicopathologic characteristics of women diagnosed by year of diagnosis.

Treatment Details

Table 4 shows that more than one half (52%, 271/524) underwent modified radical mastectomy, 22% (117/524) breast-conserving surgery (lumpectomy) alone, and 3% (17/524) reoperation and mastectomy (all within 60 days except for one patient). There was no statistically significant difference in the age and stage of women treated with lumpectomy and those treated with modified radical mastectomy. However, the percentage of women who underwent modified radical mastectomy was 55% (142/259) in 2017 and 49% (129/265) in 2018. Chemotherapy was administered to 77% (405/524) of the women. Radiotherapy was planned for 255 women (as recorded in their clinical notes or referral reports), but only 204 women had traveled outside Gaza to receive this treatment. All but one

TABLE 4. Treatment Details

Category	Year of Diagnosis, No. (%)		Total (N = 524), No. (%)	*P* With Unknown Omitted
	2017 (n = 259)	2018 (n = 265)		
Type of surgery				
Not performed	56 (22)	63 (24)	119 (23)	.481
Lumpectomy	52 (20)	65 (24)	117 (22)	
Mastectomy	142 (55)	129 (49)	271 (52)	
Both	9 (3)	8 (3)	17 (3)	
Surgery location				
Not performed	56 (22)	63 (24)	119 (23)	.524
Government	104 (40)	107 (40)	211 (40)	
Nongovernment	78 (30)	70 (26)	148 (28)	
Unknown location	21 (8)	25 (9)	46 (9)	
Chemotherapy				
Not received	62 (24)	57 (22)	119 (23)	.031
Neoadjuvant therapeutic	38 (15)	40 (15)	78 (15)	
Adjuvant therapeutic	124 (48)	122 (46)	246 (47)	
Therapeutic then palliative	16 (6)	7 (3)	23 (4)	
Palliative	19 (7)	39 (14)	58 (11)	
Chemotherapy regimen				
Not received	62 (24)	57 (22)	119 (23)	.108
Anthracycline, no taxane	41 (16)	61 (23)	102 (19)	
Anthracycline and taxane	136 (52)	132 (50)	268 (51)	
(1 or 2) and CGV	17 (7)	9 (3)	26 (5)	
Other	3 (1)	6 (2)	9 (2)	
Trastuzumab				
No	227 (88)	243 (92)	470 (90)	.127
Yes	32 (12)	22 (8)	54 (10)	
Planned to receive radiotherapy				
No	135 (52)	134 (51)	269 (51)	.721
Yes	124 (48)	131 (49)	255 (49)	
Received radiotherapy				
No	151 (58)	169 (64)	320 (61)	.199
Yes	108 (42)	96 (36)	204 (39)	
Hormone therapy				
No	65 (25)	91 (34)	156 (29)	.021
Yes	194 (75)	174 (66)	368 (71)	

Abbreviation: CGV, capecitabine and/or gemcitabine and/or vinorelbine.

had their radiotherapy covered through the Palestinian national insurance scheme in Augusta Victoria Hospital in East Jerusalem (96%, 196/204) or in Egypt (4%, 8/204). More than 70% (368/524) of women received hormone therapy (tamoxifen and/or letrozole; Table 4).

Survival Details

All death certificates reported breast cancer as the underlying cause of death. The Kaplan-Meier analysis showed that the 1-year OS was 95.4% and the 2-year OS was 86.6% (Fig 2). The 1-year age-standardized survival was 94.3% and the 2-year age-standardized survival was 84.2% (Table 5).

Figure 3 shows the Kaplan-Meier 2-year OS curve, comparing grade 1 and grade 2 (326 patients; 26 deaths), grade 3 (80 patients; 11 deaths), and unknown grade (118 patients; 33 deaths). Patients with missing data on tumor grade had a very high short-term mortality after diagnosis. The difference was statistically significant (log-rank test, $P < .001$). Poorer short-term survival was also noted among patients with unknown family history, unknown tumor subtype, and those with unknown lymph node status (log-rank test, $P < .001$). Stage at diagnosis was a strong predictor of survival. Most women with unknown stage of the disease were younger than 60 years (22/37) and had unknown tumor subtype, with around half (19/37) having unknown tumor grade.

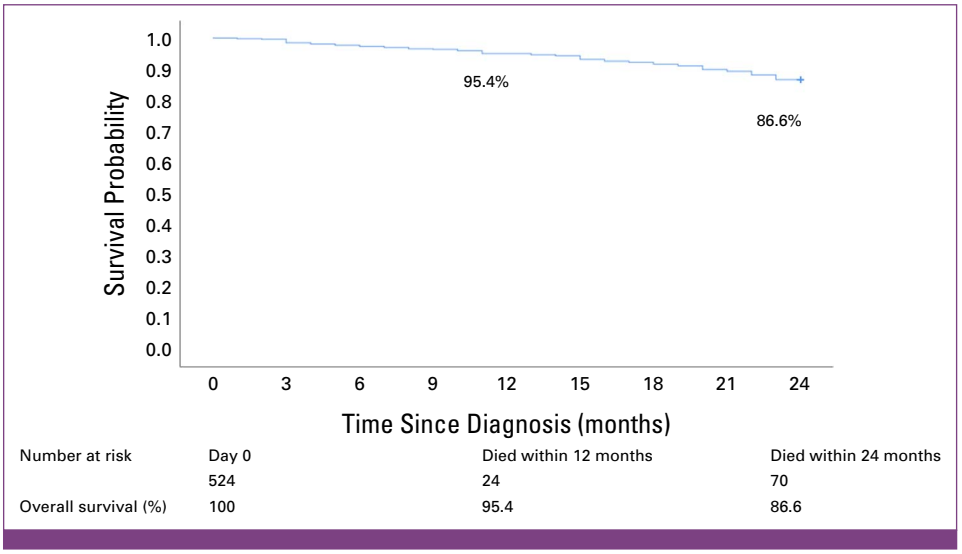

FIG 2. Kaplan-Meier curve of 1-year and 2-year overall survival for 524 women diagnosed between January 2017 and December 2018.

Table 6 shows the different Cox proportional hazards regression analyses. Univariate analysis shows that missing information on menopausal status, family history, morphology, cancer grade, and each receptor subtype was associated with a higher risk of mortality. Univariate analysis shows that only stage was a statistically strong predictor, with the highest risk of death being among those diagnosed with stage IV disease (HR, 16.58 [95% CI, 7.43 to 36.98]). The independent statistically significant effect of cancer stage remained strong after mutual adjustment of the independent effects of age, TNM stage, tumor grade, and menopause status and after complete-case analysis (Table 6).

DISCUSSION

This study found 524 women diagnosed with breast cancer in 2017 and 2018, giving a crude annual incidence rate of 27 per 100,000 population. Age was normally distributed with a mean age of 53 years (SD, 13.57; range, 23-100 years). Most women presented with self-discovered symptoms (94%, 492/524), and only 2% (8/524) had their cancers detected by breast screening. Women were most often diagnosed with stage II disease (35%, 185/524), followed by stage III (33%, 171/524), stage IV (19%, 99/524), and stage I (6%, 32/524). More than one half (52%, 271/524) had undergone modified radical mastectomy, 22% (117/524) had breast-conserving surgery (lumpectomy) alone, and 3% (17/524) underwent a second surgical intervention. Chemotherapy was administered to 77% (405/524) of women, and more than 70% (368/524) received hormone therapy. Radiotherapy was planned for 255 women, and 204 women traveled outside Gaza to receive this treatment. The 1-year OS was 95.4% and the 2-year OS was 86.6%. Cancer stage at diagnosis was a statistically significant predictor of mortality.

To our knowledge, this is the first study to provide detailed clinical and treatment information about women with breast cancer in Gaza. Although based on the best available data,

TABLE 5. Age-Standardized 1-Year and 2-Year OS (%) for Women (age 15-99 years) Diagnosed With Breast Cancer in 2017 and 2018 and Followed Up to 2020

Age-Group, Years	No. of Patients	%	One-Year Age-Specific Survival, %	Two-Year Age-Specific Survival, %	ICSS Weights
15-44	184	28	97.3	88.5	7
45-54	141	27	95.7	89.4	12
55-64	127	24	91.3	84.3	23
65-74	77	15	96.1	84.4	29
75-99	31	6	93.5	80.6	29
Total	524	100			100
OS			**95.4**	**86.6**	
Age-standardized OS			**94.3**	**84.2**	

NOTE. The bold highlights the result/estimates of overall survival and age-standarized overall survival in the two years.
Abbreviations: ICSS, International Cancer Survival Weights; OS, overall survival.

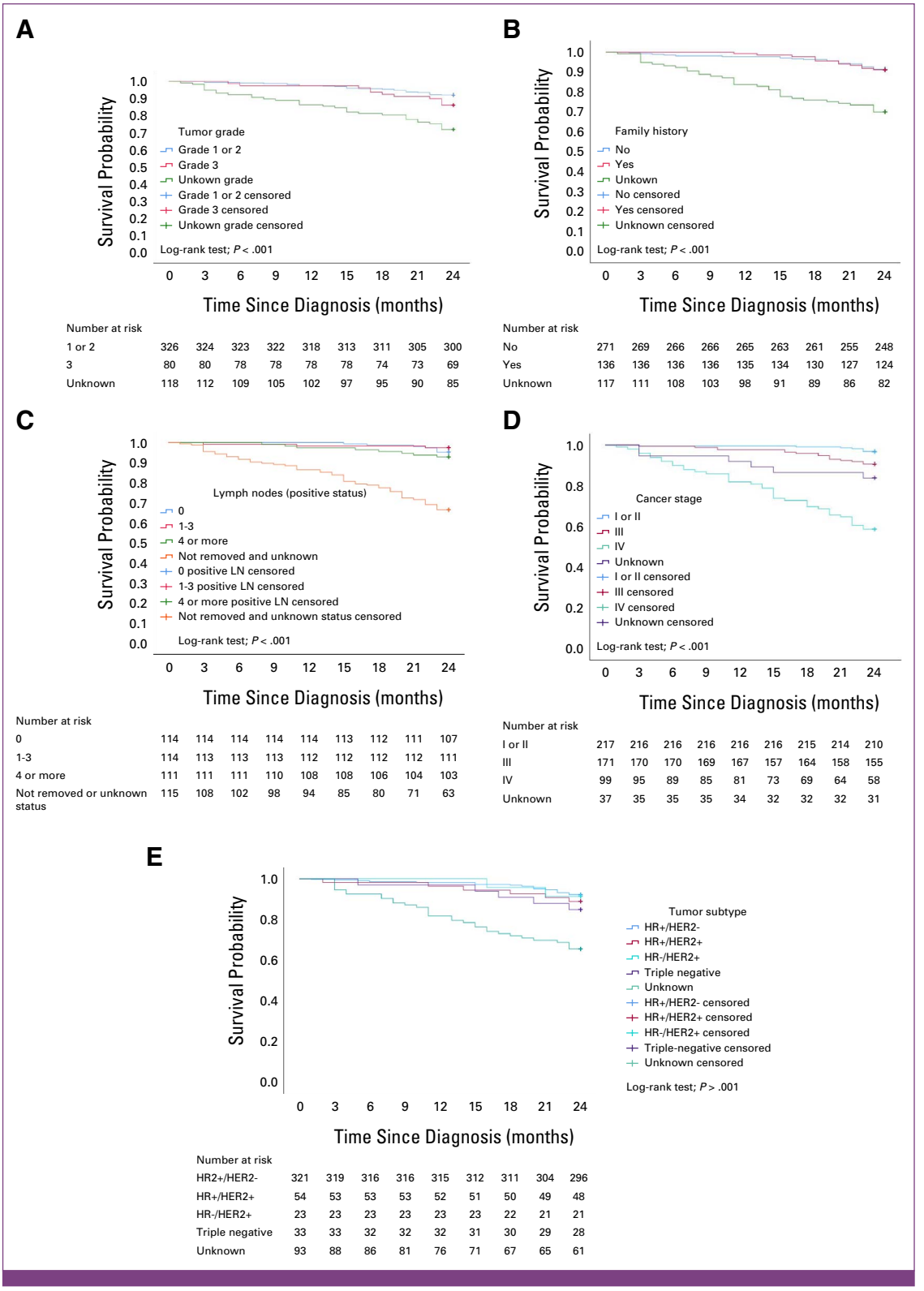

FIG 3. Kaplan-Meier curve of survival among patients with breast cancer, in relation to (A) tumor grade; (B) family history; (C) nodal status; (D) cancer stage; and (E) tumor subtype. HER2, human epidermal growth factor receptor 2; HR, hormone receptor; LN, lymph node.

TABLE 6. Distribution of Covariates in 2-Year Estimates of Cumulative Risk of Death of Women Diagnosed With Breast Cancer in 2017 and 2018 in Gaza

Characteristic	Count	%	Deaths Within 2 Years of Follow-Up	2-Year Cumulative Risk of Death (%)	Univariate HR (95% CI)	Mutually Adjusted (524 patients) HR (95% CI)	Mutually Adjusted Complete-Case Analysis (385 patients) HR (95% CI)
Age at diagnosis, years							
0-44	148	29	17	11.48	0.90 (0.49 to 1.66)	1.18 (0.52 to 2.68)	1.21 (0.44 to 3.28)
45-59 (reference)	209	40	26	12.40	1.00	1.00	1.00
60-74	136	26	21	15.44	1.25 (0.70 to 2.21)	1.11 (0.57 to 2.15)	1.58 (0.61 to 4.08)
≥75	31	5	6	19.35	1.58 (0.65 to 3.84)	1.07 (0.41 to 2.79)	1.19 (0.25 to 5.79)
Trend					$\chi^2(1) = 2.01$; $P = .16$	$\chi^2(1) = 0.10$; $P = .91$	$\chi^2(1) = 0.06$; $P = .81$
Menopause status							
Pre	231	46	23	9.96	0.66 (0.39 to 1.10)	3.24 (1.22 to 8.62)	1.39 (0.49 to 3.91)
Post (reference)	284	54	41	14.44	1.00	1.00	1.00
Unknown	9	2	6	66.67	7.62 (3.22 to 18.06)	0.72 (0.32 to 1.64)	
Heterogeneity (trend in complete-case analysis)					$\chi^2(2) = 40.88$; $P < .001$	$\chi^2(2) = 8.13$; $P = .17$	$\chi^2(1) = 0.39$; $P = .533$
TNM stage							
I and II (reference)	217	41	7	3.26	1.00	1.00	1.00
III	171	33	16	9.36	2.99 (1.23 to 7.27)	2.83 (1.16 to 6.69)	3.68 (1.33 to 10.22)
IV	99	19	41	41.41	16.58 (7.43 to 36.98)	12.39 (5.37 to 28.54)	14.70 (5.29 to 40.89)
Unknown	37	7	6	16.22	5.53 (1.86 to 16.47)	4.08 (1.32 to 12.63)	
Heterogeneity					$\chi^2(3) = 103.57$; $P < .001$	$\chi^2(3) = 47.03$; $P < .001$	$\chi^2(2) = 30.21$; $P < .001$
Tumor grade							
1 and 2 (reference)	326	62	26	7.98	1.00	1.00	1.00
3	80	15	11	13.75	1.75 (0.86 to 3.53)	1.82 (0.89 to 3.72)	2.06 (0.99 to 4.31)
Unknown	118	23	33	27.97	3.99 (2.39 to 6.67)	1.92 (1.11 to 3.34)	
Heterogeneity (trend in complete-case analysis)					$\chi^2(2) = 32.49$; $P < .001$	$\chi^2(2) = 6.17$; $P = .046$	$\chi^2(1) = 3.73$; $P = .053$

Characteristic	Count	%	Deaths Within 2 Years of Follow-Up	2-Year Cumulative Risk of Death (%)	Univariate HR (95% CI)
Family history					
No (reference)	271	52	23	8.49	1.00
Yes	136	26	12	8.82	1.03 (0.51 to 2.08)
Unknown	117	22	35	29.91	4.14 (2.45 to 7.01)
Heterogeneity					$\chi^2(2) = 40.85$; $P < .001$
Morphology					
Ductal (reference)	433	83	54	12.47	1.00
Lobular	46	9	5	10.87	0.85 (0.34 to 2.13)
Other	22	4	1	4.56	0.34 (0.05 to 2.48)
Unknown	23	4	10	43.48	4.49 (2.29 to 8.82)
Heterogeneity					$\chi^2(3) = 26.08$; $P < .001$
ER					
Positive (reference)	375	71	31	8.27	1.00
Negative	57	11	7	12.28	1.51 (0.67 to 3.43)
Not performed and unknown	92	18	32	34.78	5.12 (3.12 to 8.39)
Heterogeneity					$\chi^2(2) = 52.71$; $P < .001$
PR					
Positive (reference)	371	70	31	8.38	1.00
Negative	60	12	7	11.48	1.51 (0.67 to 3.43)
Not performed and unknown	93	18	32	34.41	5.12 (3.12 to 8.39)
Heterogeneity					$\chi^2(2) = 52.71$; $P < .001$

(continued on following page)

TABLE 6. Distribution of Covariates in 2-Year Estimates of Cumulative Risk of Death of Women Diagnosed With Breast Cancer in 2017 and 2018 in Gaza (continued)

Characteristic	Count	%	Deaths Within 2 Years of Follow-Up	2-Year Cumulative Risk of Death (%)	Univariate HR (95% CI)
HER2 receptor (HER2)					
Positive	78	15	8	10.26	1.21 (0.55 to 2.64)
Negative (reference)	350	66	30	8.57	1.00
Not performed and unknown	96	18	32	33.33	4.68 (2.84 to 7.71)
Heterogeneity					$\chi^2(2) = 47.39$; $P < .001$
Triple-negative					
No (reference)	400	76	33	8.25	1.00
Yes	33	6	5	15.63	1.96 (0.74 to 4.85)
Unknown	91	18	32	34.78	5.21 (3.19 to 8.47)
Heterogeneity					$\chi^2(2) = 54.54$; $P < .001$

NOTE. Mutual adjustment for the estimated effects of age, TNM stage, tumor grade, and menopause status.
Abbreviations: ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; PR, progesterone receptor.

this study has a short duration of follow-up, with survival analysis only of 1 year and 2 years. Although 1-year survival is a good predictor for long-term survival, it will be necessary to extend follow-up to 5 years, because the published survival estimates are worrying and lack clarity. The lack of population-based and cancer registry data on breast cancer has required manual abstraction of data from paper-based records, possibly introducing human error during the abstraction and recording of those data. However, this risk was minimized by checking and rechecking data during the follow-up period.

This study found that the crude annual breast cancer incidence rate in women in Gaza was 27 per 100,000 population. This confirms already available data suggesting that the crude incidence rate in the oPt is relatively low compared with other Middle Eastern countries, where it ranges from 30 per 100,000 women per annum in 2020 in Jordan to 58 per 100,00 in Lebanon.[7,8] Relatively low breast cancer incidence rates among Palestinian women reflect their reproductive patterns (early pregnancies, high fertility, and high breastfeeding rates), but these are changing. However, the current lower rates of breast cancer in the oPt and the Middle East compared with high-income countries could, as reported in other articles,[9] reflect incomplete reporting. The mean age of diagnosis in this study is comparable with those reported in the oPt and other Arab countries,[10-15] and is lower than in Western countries. Middle Eastern populations are generally skewed toward younger age distributions, so a lower mean age of breast cancer diagnosis in these countries does not mean that younger Arab women are more likely to have breast cancer.[16]

The percentage of modified radical mastectomy found was significantly lower than several other smaller scale studies have reported.[17,18] In the current study, the percentage of women who underwent modified radical mastectomy decreased from 55% in 2017 to 49% in 2018. These rates are also much lower than those reported in many other Arab countries—90% in Iraq,[19] 83% in Egypt,[20] 62% in Saudi Arabia, and 62% in Jordan.[9] The decline in the use of modified radical mastectomy in Gaza could relate to improved cancer care in recent years, especially after the development of a multidisciplinary evidence-based breast cancer team at Al-Shifa Hospital in Gaza coupled with the help of specialized visiting surgeons from the United Kingdom. However, rates of mastectomy in Gaza remain high, and this could be due to the lack of radiotherapy in Gaza.

Previously published survival figures among women in Gaza have been very low ranging from 40% to 60%,[10,21] but this study presents a more positive picture. The 1-year OS was 95.4% and the 2-year OS was 86.6%. Despite major challenges, Palestinian women with breast cancer have a high short-term survival after diagnosis. This should in turn encourage more collaboration and investment in breast cancer care in Gaza.

To promote and achieve a continued improvement in survival for women with breast cancer in Gaza, it is important to establish an ongoing audit of the extent to which current clinical practice reflects evidence-based guidelines. One possible explanation for the increase in survival could be an increased level of awareness of breast cancer and its symptoms among women in recent years, leading to their earlier presentation to the health services.[22] Also, in most cases, the onset of primary treatment was prompt, and most women received their treatments as planned. Having said that, the proportion of women diagnosed at advanced stages of breast cancer remains high. Over one half of the women were diagnosed with stage III or IV of the disease (52%, 270/524). This advanced stage at diagnosis could reflect (1) women delaying presentation for diagnosis; or (2) a delay within the health care system in scheduling diagnostic tests, or issues

related to misdiagnosis; or (3) both. Because of missing data, establishing which factor was the main cause is challenging.

Methods of improving the reporting of diagnostic intervals through clearer referral guidelines are needed to assess what is causing the high percentage of advanced stages of breast cancer at diagnosis. This requires health systems research into the various pathways that lead to a breast cancer diagnosis.[23,24] Establishing well-publicized early detection clinics at existing primary and secondary health care levels will allow (1) screening of asymptomatic women age 50-65 years and (2) diagnosis of women with any breast signs or symptom at early stages. This will both reduce the cost of treatment and increase women's survival and quality of life. Also, quality control of tests and training of health care providers must be considered to provide correct assessment and judgment of suspected patients, avoid misdiagnosis, and ensure proper follow-ups. Without robust recording of up-to-date data, an analysis of what is happening in the long run, and why it has been happening, will not be easy to achieve. The recent attacks on the local cancer hospitals, loss of paper cancer records, and the evacuation of some patients with cancer may make it extremely difficult to evaluate the care and the outcome of patients with cancer in Gaza.

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