

Survival rates of patients with breast cancer in countries in the Eastern Mediterranean Region: a systematic review and meta-analysis

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Abstract

Background: Breast cancer is the fourth leading cause of death and disability in the Eastern Mediterranean Region (EMR); although the incidence is lower than in the developed regions, there has been an increasing trend in recent decades.

Aims: Our aim was to calculate the pooled survival rate of patients with breast cancer in the EMR.

Methods: We searched electronic databases from 1946 to 19 January 2018, without language restrictions. We used a random effect model to estimate pooled 1-, 3-, 5- and 10-year survival rates for patients with breast cancer. Chi-squared and I^2 index were used to assess between-study heterogeneity. Subgroup analysis and meta-regression were used to investigate the potential source of heterogeneity.

Results: We found 80 articles eligible for inclusion in our review. The pooled 1-, 3-, 5- and 10-year survival rates in women with breast cancer in the EMR were 0.95, 0.80, 0.71, and 0.56, respectively. The I^2 index indicated considerable between-study heterogeneity (all $I^2 > 50\%$). The 5-year survival rate in the male subgroup was 0.63. The 5-year survival rate of women with breast cancer in age groups ≤ 39 , 40–64, and 65+ years were 0.74, 0.76 and 0.58, respectively. There was a statistically significant association between the Human Development Index ($\beta = 9$, $P = 0.01$) and decade of study ($\beta = 8.2$, $P = 0.04$) and 5-year survival rate.

Conclusions: The survival rate of women with breast cancer in those countries in the EMR which have better health care systems improved in the past decade; women aged 40–64 years had the best survival rate.

Keywords: review, breast cancer, survival rate, Eastern Mediterranean Region, meta-analysis

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Introduction

Breast cancer is among the 4 most common cancers in the world (1). It is the leading cause of death among women in developed countries and the second commonest cause of death in developing countries (2,3). In 2015, among women, an estimated 321 840 new cases of invasive breast cancer were projected (4). In the WHO Eastern Mediterranean Region (EMR), breast cancer is the fourth leading cause of death and disability (1,3,5) and the number one cancer in 16 of the 22 countries in the Region (6). The age-standardized incidence of breast cancer in this Region is 12–50 per 100 000 in women, with the lowest incidence in the Islamic Republic of Iran and Pakistan (3). Although the incidence in this Region is lower than in the developed regions, there has been an increasing trend in recent decades (10,11).

The EMR comprises 22 countries with varied ethnicity and cultures (7). The women in this Region generally have poor knowledge about screening methods for breast cancer (6). In Bahrain, Egypt, the Islamic Republic of Iran, Jordan, Kuwait, Lebanon, Oman, Saudi Arabia and Tunisia, breast cancer is usually diagnosed in women under age 50 years, i.e. younger than in other parts of the world (6).

An important factor that affects survival is the disease stage at diagnosis, ranging from $\geq 80\%$ in North America, Sweden and Japan to around 60% in middle-income countries and $< 40\%$ in low-income countries (7). In the EMR, patients with breast cancer are usually diagnosed for the first time at stages 2 and 3 (3,6). The difference in survival between developed and developing countries may be due to delays in diagnosis.

The aim of this study is to determine survival of patients with breast cancer by age, stage of disease and overall in the EMR by systematic review and meta-analysis.

Methods

Reporting guidelines

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was used to carry out and report this systematic review and meta-analysis (8).

Study selection

We used the following inclusion and exclusion criteria to select relevant articles in this meta-analysis. All

observational cohort studies that reported the survival rate of women with primary invasive breast cancer in different study populations in the EMR were included with no restriction for language, age, ethnicity or religion. We excluded articles that reported the survival rate after relapse. Letters to the editor, review articles and meeting abstracts were also excluded. Where we found several publications from the same study population, we choose the most recent one to include in our study. To select the relevant articles from the search results, 2 reviewers (KM and MK) independently screened the studies by title, abstract and full text; in the case of disagreement between the 2 reviewers, they entered into discussion and if required a 3rd investigator became involved to resolve the question.

Search strategy

A systematic search was carried out by 2 reviewers (KM and MK) independently in several electronic databases such as Medline/PubMed, Web of Science, Scopus, and Google Scholar covering material published from 1946 to 19 January 2018. The search strategy was made using the MeSH subject headings and free text words like (“breast neoplasms” [MeSH] or “breast cancer” or “breast carcinoma” or “breast tumour” or “breast malignant”) AND (“survival” or “survival analysis” or “survival rate” or “life table” or “Kaplan Meier” or “proportional hazard model” or “hazard ratio” or “Cox model” or “Cox regression”) AND (“cohort” or “prospective” or “retrospective” or “follow-up” or “longitude”). To identify additional relevant studies, we reviewed the reference lists of all included studies. To manage and screen eligible searched studies, we used EndNote X7 citation manager.

Quality assessment

To assess the quality of each eligible study and risk of bias we used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (9). We used several items from this checklist: define the source of participant selection, explain the eligibility criteria, explain about follow-up and how to address the missing data, clearly define how to measure the outcome and explain about the size of the study. The studies were classified into 3 groups based on this checklist. If the studies attained more than 80% of the total score, they were classified as high quality, 60–79% of total score as intermediate quality and 30–59% of total score as low quality. Two authors (KM and MK) independently investigated the quality of each study. The agreements between reviewers were assessed by weighted Kappa (86%).

Data extraction

For each eligible study, the variables were extracted on a prespecified sheet in Microsoft Excel 2010 as follows: first author name, year of publication, period of study, country of origin, source of data, study design, median follow-up time, sample size, mean age, gender frequency, type of survival, 1-, 3-, 5- and 10-year survival rates and 95% confidence interval (CI). Data extraction was performed independently by 2 reviewers (KM and MK).

Disagreement was resolved by discussion between the 2 reviewers and if required, a senior investigator solved the discrepancies.

Statistical analysis

We investigated statistical heterogeneity using the Q test at the 5% significance level ($P < 0.05$) and I^2 index. According to the significant between-study heterogeneity ($P < 0.05$), random effect models was used. Because some studies did not report the standard error and 95% confidence interval (CI), we also used binomial distribution to estimate the variance and 95% CII of all included studies.

To estimate the pooled survival rate we used metan and metaprop commands. The metaprop command was specific to binomial data and for proportions near boundaries (in this instance, 100% at 1-year survival or 0% at stage IV), which allows computation of exact binomial and score test-based CIs by allowing Freeman–Tukey double arcsine transformation to stabilize the variances (10).

To investigate the potential source of heterogeneity we used subgroup analyses based on sex, age and stage at diagnosis, ethnicity, Human Development Index (HDI) and decade of study. We also conducted subgroup analysis based on the level of development, income and health outcome, so all 22 countries were categorized into 3 subgroups. Group 1 includes countries that are developed in the past decade, Group 2 includes middle-income countries and Group 3 includes countries less developed than the others in the Region, e.g. Afghanistan (11,12).

Meta-regression was used based on decade of study, HDI, ethnicity, and sample size to find the source of heterogeneity. Publication bias was not assessed, because the probability of survival rate as a proportion is always a positive number and if we see asymmetry in a funnel plot, it is not due to publication bias.

We used EndNote X7 to manage the records and review the results of the systematic search and Microsoft Excel 2010 to prepare the data extraction sheet. We used Stata 11 to perform statistical analysis.

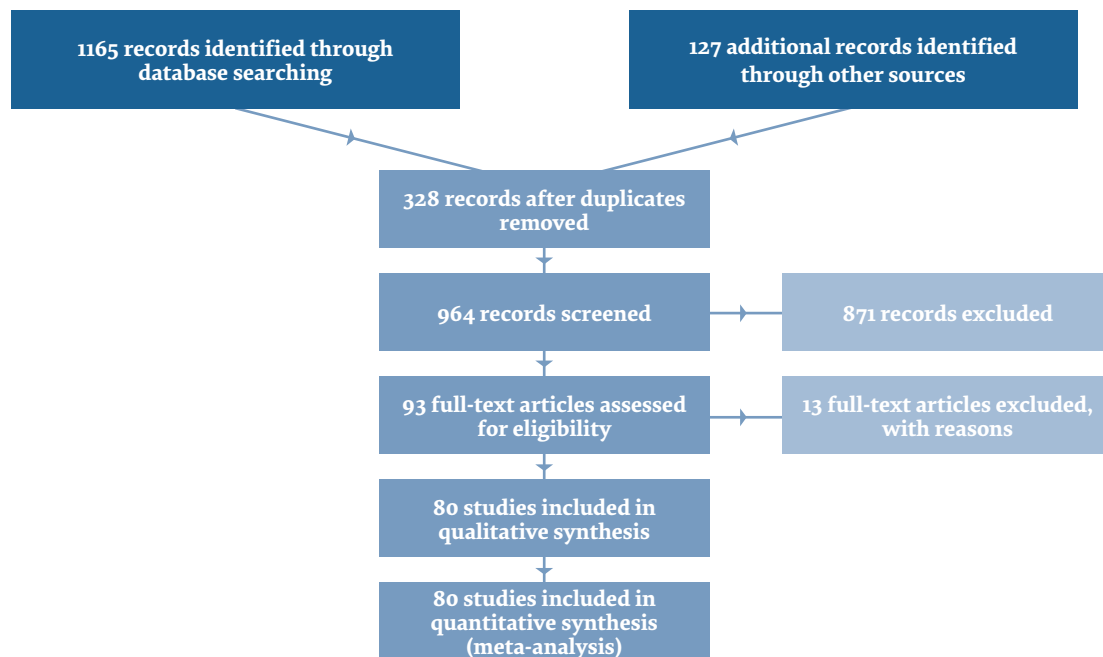
Results

Study characteristics

The initial search identified 1292 articles up to 19th January 2018. After removing duplicates and screening by title, abstract and full text, 80 eligible articles remained in our systematic review and meta-analysis. A flow diagram of selection process according to the PRISMA flowchart is shown in Figure 1.

The characteristics of these 80 studies are summarized in Table 1. These articles come from 12 countries in the EMR. Half of the studies were conducted in the Islamic Republic of Iran ($n = 40$); 12 articles were exclusively conducted on men and 68 on women. Also, 6 studies were exclusively conducted on women under 39 years. The total sample size from the 80 studies was 42 328, of whom 41 603 (98.2%) were female.

Figure 1 PRISMA flow diagram showing the different phases involved in the search process



Pooled survival rate

The pooled 1-, 3-, 5- and 10-year survival rate of women with breast cancer in the EMR were 0.95 (95% CI: 0.93–0.96), 0.80 (95% CI: 0.76–0.84), 0.71 (95% CI: 0.68–0.73) and 0.56 (95% CI: 0.48–0.63), respectively. We saw considerable heterogeneity in 1-year ($P < 0.001$, $I^2 = 92.83$), 3-year ($P < 0.001$, $I^2 = 96.38$), 5-year ($P < 0.001$, $I^2 = 92.24$) and 10-year ($P < 0.001$, $I^2 = 97.33$) survival rates among women with breast cancer.

Subgroup analysis

The results of the subgroup analyses are shown in Table 2. The pooled 5-year survival rate in women was 0.71 (95% CI: 0.68–0.73) and in men was 0.63 (95% CI: 0.59–0.67). In the age subgroups, the 5-year survival rates for women with breast cancer aged < 39, 40–64, and 65+ years were 0.74 (95% CI: 0.68–0.80), 0.76 (95% CI: 0.66–0.85) and 0.58 (95% CI: 0.46–0.69) respectively.

Meta-regression

To determine any potential source of bias, we covered the variables sample size, HDI, decade of study and ethnicity as independent variables and survival rate as a dependent variable in meta-regression. In the univariable model, there was a statistically significant association between HDI ($\beta = 9.0$, $P = 0.012$) and decade of study ($\beta = 8.2$, $P = 0.048$) and 5-year survival rate. The 5-year survival rate increased with the decade of study (Table 3).

Discussion

The aim of this study was to estimate the survival rate of women with breast cancer in the EMR. From the meta-analysis, the 1-, 3-, 5- and 10-year survival rates were 0.95 (95% CI: 0.93–0.96), 0.80 (95% CI: 0.76–0.84), 0.71 (95% CI: 0.68–0.73) and 0.56 (95% CI: 0.48–0.63) respectively.

The 1-year survival rate in a 2009 study from England (96%) and Australia (98.1%) is consistent with the results of our study (13). The 1- and 3-year survival rates were reported in a 2014 study from China as 76.0–83.1% and 51.5–74.1%, respectively (14). In a 2004 study conducted in India, the 1- and 3-year survival rates were 76% and 51.5% respectively (15). Our findings indicate that the 1-year survival rates in the EMR are similar to those in some developed countries and better than in some developing countries such as India.

In a 2015–2016 report from the American Cancer Society the 5- and 10-year relative survival rates were 89% and 83% respectively (16). In a study conducted in European countries in 2013, the 5-year relative survival rate was 69–84% (17). On the other hand, in a 2010 study conducted in developing countries, the 5-year relative survival rate varied from 52% in India to 82% in China (18). Comparing with our findings, the 5- and 10-year survival rates in the EMR were lower than in the high-income countries and similar to those in the developing countries.

An important factor that may account for the differences in survival rates among women with breast cancer in the EMR might be the (lack of) improvement of the health systems in some countries; a poorly developed health system can result in late diagnosis and improper treatment of patients with advanced cancer. Additionally, the lack of a population-based cancer registry in some countries may result in insufficient surveillance and a failure in monitoring any control programme. False beliefs and low levels of knowledge and awareness in some populations in the Region are other likely reasons for these differences (15,19). Survival data in the EMR depend on good registries. Some countries do have data, some have data but the quality is not known, and some

Table 1 Characteristics of studies on survival of breast cancer in the Eastern Mediterranean Region included in the meta-analysis

| First author (reference no.) | Year | Country | Time span | Sex | Mean (SD) age | Sample size | Median follow-up (months) | 1-year | 3-year | 5-year | 10-year |
|------------------------------|------|--------------|-----------|--------|---------------|-------------|---------------------------|--------|--------|--------|---------|
| Abdollahi A (45) | 2017 | Iran | 2004–2011 | Female | 54.8 (11.4) | 1329 | 4 | 0.96 | 0.78 | 0.66 | – |
| Al-Moundhri M (46) | 2004 | Oman | 1996–2002 | Female | 48.5 (10.8) | 150 | 35.6 | – | – | 0.67 | – |
| Abahssain H (24) | 2010 | Morocco | 2003–2007 | Female | 32 | 427 | 32.2 | – | 0.81 | – | – |
| Abdelkrim SB (47) | 2015 | Tunisia | 1993–2013 | Female | 23.7 | 25 | NR | – | 0.95 | 0.85 | 0.75 |
| Aghili M (48) | 2013 | Iran | 2007–2002 | Female | 9.6 (50.4) | 107 | 38.24 | – | – | 0.83 | – |
| Ahmed SB (49) | 2002 | Tunisia | 1998–1990 | Female | 50 | 729 | NR | – | – | 0.51 | – |
| Akbari ME (50) | 2011 | Iran | 2002–2010 | Female | 49.8 | 258 | 144 | – | – | 0.88 | 0.81 |
| Akbari ME (51) | 2008 | Iran | 1994–2007 | Female | 53.24 (12.41) | 435 | 50.5 | – | – | 0.81 | 0.77 |
| Akbari ME (52) | 2006 | Iran | 1996–1998 | Female | 48 (11.5) | 154 | 60 | – | – | 0.77 | – |
| Al-Idrissi HY (53) | 1992 | Saudi Arabia | 1981–1990 | Female | 40 | 130 | 46 | – | – | 0.76 | – |
| Alaoui SK (54) | 2016 | Morocco | 2007–1998 | Male | 61 | 140 | 91.1 | – | – | 0.68 | – |
| Amirifard N (41) | 2016 | Iran | 2016–2010 | Male | 49.2 (17.0) | 17 | 30 | – | – | 0.64 | – |
| Arkoob K (32) | 2010 | Jordan | 1979–1989 | Female | 50.2 (12.4) | 838 | 60 | 0.92 | 0.70 | 0.59 | – |
| Aziz Z (55) | 2008 | Pakistan | 2005–1996 | Female | 45 | 525 | 100 | – | – | 0.72 | 0.61 |
| Babai Gh (56) | 2005 | Iran | 1993–1991 | Female | NR | 176 | NR | 0.94 | 0.76 | 0.61 | – |
| Babai Gh (56) | 2005 | Iran | 1993–1991 | Male | NR | 10 | NR | 0.90 | 0.70 | 0.58 | – |
| Baghestani A (57) | 2015 | Iran | 1998–2013 | Female | 48.13 (10.7) | 366 | 120 | 0.93 | 0.75 | 0.52 | – |
| Baghestani A (57) | 2015 | Iran | 1992–2012 | Female | 48.37 (10.9) | 438 | 253 | 0.98 | – | – | – |
| Bakkach J (58) | 2017 | Morocco | 2015–2010 | Female | 36 | 82 | 27.4 | – | – | 0.89 | – |
| Ben Gobrane H (59) | 2007 | Tunisia | 2003–1994 | Female | 49.7 | 470 | 51.9 | – | – | 0.61 | – |
| Bhatti AB (60) | 2014 | Pakistan | 2009–1997 | Female | 43.2 | 443 | 49 | – | – | 0.83 | – |
| Bhatti AB (61) | 2015 | Pakistan | 2009–1997 | Female | 42 | 902 | 51 | – | – | – | 0.70 |
| Bouzd N (62) | 2013 | Tunisia | 2007–1995 | Female | 31.3 | 124 | 48.5 | – | – | 0.68 | – |
| Derkaoui T (63) | 2016 | Morocco | 2015–2010 | Female | 46 | 279 | NR | – | – | 0.71 | – |
| Dhiab TB (64) | 2005 | Tunisia | 1999–1979 | Male | 26 | 123 | 65 | – | – | 0.62 | – |

Table 1 Characteristics of studies on survival of breast cancer in the Eastern Mediterranean Region included in the meta-analysis (continued)

| First author (reference no.) | Year | Country | Time span | Sex | Mean (SD) age | Sample size | Median follow-up (months) | 1-year | 3-year | 5-year | 10-year |
|------------------------------|------|--------------|-----------|--------|---------------|-------------|---------------------------|--------|--------|--------|---------|
| El Amine Elhadj O (65) | 2017 | Tunisia | 2013–2004 | Female | 46.8 | 30 | 65 | – | 0.49 | 0.34 | – |
| El Mistiri M (66) | 2015 | Libya | 2003–2005 | Female | NR | 365 | NR | – | – | 0.56 | – |
| El-Baradie M (67) | 2012 | Egypt | 1999–2009 | Male | 58 | 123 | 38 | – | – | 0.62 | – |
| El-Beshbeshi W (68) | 2012 | Egypt | 2002–2009 | Male | 57.7 | 37 | 9 | – | – | 0.61 | – |
| El-Habbash MM (69) | 2009 | Libya | 2008–1990 | Male | 61 | 22 | NR | – | – | 0.57 | – |
| Elshafiey M (70) | 2011 | Egypt | 2000–2002 | Male | 59 | 32 | 58 | – | 0.78 | 0.65 | 0.57 |
| Fakhro AE (71) | 1999 | Bahrain | 1982–1994 | Female | 50.1 | 93 | NR | – | – | 0.64 | 0.36 |
| Fallahzadeh H (72) | 2014 | Iran | 2002–2007 | Female | 48.2 (11.7) | 200 | 60 | 0.95 | 0.82 | 0.7 | – |
| Faradmal J (73) | 2016 | Iran | 2000–2011 | Female | 47.02 (10.7) | 522 | 54–13 | 0.90 | 0.73 | 0.62 | – |
| Fardmal J (74) | 2014 | Iran | 2004–2011 | Female | 46.06 (10.82) | 542 | NR | 0.97 | 0.58 | 0.68 | 0.31 |
| Fayaz MS (75) | 2014 | Kuwait | 2009–1999 | Female | 11.7 (48.0) | 363 | 41.9 | – | 0.83 | 0.81 | – |
| Fazeli Z (76) | 2014 | Iran | 2007–2011 | Female | 50.28 (1.36) | 400 | NR | 0.98 | 0.92 | 0.87 | – |
| Haghighat Sh (77) | 2013 | Iran | 1997–2006 | Female | 46.3 (11.05) | 623 | 86.3 | – | – | 0.87 | – |
| Hajhosseini M (78) | 2015 | Iran | 1995–2013 | Female | 47.1 (10.7) | 529 | NR | – | – | 0.68 | – |
| Hamadeh RR (79) | 2014 | Bahrain | 2000–2010 | Female | 50.9 | 1005 | NR | 0.84 | – | 0.63 | 0.49 |
| Hamdan NA (80) | 2011 | Saudi Arabia | 1994–1996 | Female | NR | 298 | 57 | 0.95 | 0.80 | 0.61 | – |
| Heydari ST (81) | 2009 | Iran | 2001–2006 | Female | 46.5 (11.7) | 877 | NR | 0.97 | – | 0.67 | 0.45 |
| Hoseini M (82) | 2017 | Iran | 2015–2001 | Female | 47.1 | 140 | NR | – | – | 0.80 | 0.65 |
| Ibrahim EM (83) | 1998 | Saudi Arabia | 1985–1995 | Female | 42 (10.5) | 292 | 62 (8.9) | – | – | – | 0.55 |
| Iqbal J (84) | 2010 | Pakistan | 1997–2006 | Female | 45 | 200 | 90 | – | – | 0.52 | 0.31 |
| Jamy O (85) | 2015 | Pakistan | 1986–2009 | Male | 52 | 19 | NR | – | – | 0.61 | – |
| Kallel M (86) | 2015 | Tunisia | 2002–2008 | Female | 31.7 | 83 | 75 | – | – | 0.67 | – |
| Karimi A (87) | 2016 | Iran | 2006–2014 | Female | 46.1 (10.81) | 229 | 81 | 0.96 | – | 0.75 | – |
| Khanfir A (88) | 2006 | Tunisia | 2002–1995 | Female | 31.5 | 72 | NR | – | – | 0.57 | – |
| Kumar S (89) | 2016 | Pakistan | 2008–1999 | Female | 48 | 845 | 29 | – | – | 0.75 | – |

Table 1 Characteristics of studies on survival of breast cancer in the Eastern Mediterranean Region included in the meta-analysis (concluded)

| First author (reference no.) | Year | Country | Time span | Sex | Mean (SD) age | Sample size | Median follow-up (months) | 1-year | 3-year | 5-year | 10-year |
|------------------------------|------|--------------|-----------|--------|---------------|-------------|---------------------------|--------|--------|--------|---------|
| Kumar SH (90) | 2011 | Oman | 2003–2008 | Female | 47.1 (12.88) | 119 | 54 | – | – | 0.78 | – |
| Mechita NB (91) | 2016 | Morocco | 2008–2005 | Female | 51.1 (11.2) | 628 | NR | 0.97 | 0.89 | 0.81 | – |
| Moghadami Fard Z (92) | 2012 | Iran | 2005–2007 | Female | 51.3 (11.2) | 133 | 63 | – | – | 0.72 | – |
| El Mongy M (93) | 2010 | Egypt | 2003–1993 | Female | 9.74 (7.14) | 1009 | 68 | – | 0.96 | 0.91 | – |
| Mosavi-Naieni M (94) | 2009 | Iran | 1997–2005 | Female | 49.6 (11.2) | 242 | NR | 1 | 0.94 | 0.89 | – |
| Mousavi SM (95) | 2008 | Iran | 2001–1998 | Female | 12.5 (51.3) | 2358 | 60 | – | – | 0.50 | – |
| Movahedi M (96) | 2012 | Iran | 2001–2006 | Female | 49.84 (12.36) | 5975 | 88.2 | – | – | 0.72 | – |
| Movahedi M (96) | 2012 | Iran | 2001–2006 | Male | 49.84 (12.36) | 172 | 88.2 | – | – | 0.6 | – |
| Payandeh M (97) | 2015 | Iran | 2001–2014 | Female | 49.6 (12.6) | 950 | NR | – | 0.82 | 0.72 | 0.64 |
| Raeisi-Shahraki H (98) | 2015 | Iran | 1989–2008 | Male | 59.6 (12.8) | 50 | 140 | – | 0.92 | 0.77 | 0.26 |
| Rais G (99) | 2012 | Morocco | 2008–2007 | Female | 46 | 152 | 46 | – | – | 0.76 | – |
| Rajaeefard AR (100) | 2009 | Iran | 1994–2003 | Female | NR | 310 | 60 | 0.97 | 0.82 | 0.7 | 0.53 |
| Rampishesh Z (101) | 2014 | Iran | 2001–2013 | Female | 51.26 (13.87) | 300 | 65 | 0.95 | 0.78 | 0.68 | – |
| Ravichandran K (102) | 2005 | Saudi Arabia | 1994–1996 | Female | 48.3 (14.5) | 316 | 55.2 | 0.94 | 0.79 | 0.60 | – |
| Rezaianzadeh A (103) | 2009 | Iran | 2000–2005 | Female | 47 | 1148 | 34 | – | 0.76 | 0.58 | – |
| Salehi A (104) | 2011 | Iran | 1989–2008 | Male | 60.3 (12.7) | 56 | 60 | – | 0.83 | 0.66 | 0.45 |
| Sedehi M (105) | 2013 | Iran | 2002–2007 | Female | NR | 159 | NR | 0.83 | 0.67 | 0.51 | – |
| Shawky H (106) | 2013 | Egypt | 2000–2010 | Male | 52.8 | 29 | 53 | – | – | 0.71 | – |
| Soliman AA (107) | 2014 | Egypt | 2000–2007 | Male | 58 | 69 | NR | – | – | 0.46 | – |
| Vahdaninia M (108) | 2003 | Iran | 1997 | Female | 47.2 (13.5) | 128 | 60 | 0.93 | 0.75 | 0.62 | – |
| Vostakolaee FA (109) | 2012 | Iran | 1999–2001 | Female | 46 (12) | 1500 | 60 | – | – | 0.72 | – |
| Yaghmaei S (110) | 2008 | Iran | 1991–2002 | Female | 51.5 (14.0) | 50 | NR | 0.87 | 0.62 | 0.58 | 0.47 |
| Zanti K (111) | 2014 | Morocco | 2009–2004 | Female | 30.62 | 74 | NR | – | 0.88 | – | – |
| Zare N (112) | 2012 | Iran | 2005–2001 | Female | 47 | 1148 | 34 | – | – | 0.56 | – |
| Ziaei JE (113) | 2013 | Iran | 1997–2008 | Female | 48 | 271 | 120 | 0.96 | 0.86 | 0.81 | 0.76 |

SD = standard deviation.

Table 2 Subgroup analysis for 1-, 3-, 5- and 10-year survival rates of women with breast cancer in the Eastern Mediterranean Region (EMR), 1946–2018

| Category/ subgroup | Survival rate (95% confidence interval) | | | |
|---|---|------------------|------------------|------------------|
| | 1-year | 3-year | 5-year | 10-year |
| Sex | | | | |
| Female | 0.95 (0.93–0.96) | 0.80 (0.76–0.84) | 0.71 (0.68–0.73) | 0.56 (0.48–0.63) |
| Male | – | 0.84 (0.75–0.92) | 0.63 (0.59–0.67) | 0.41 (0.25–0.59) |
| Decade of study | | | | |
| 1990–1999 | 0.93 (0.92–0.94) | 0.76 (0.71–0.80) | 0.63 (0.58–0.68) | 0.50 (0.45–0.55) |
| 2000–2009 | 0.96 (0.93–0.98) | 0.84 (0.77–0.89) | 0.72 (0.68–0.75) | 0.58 (0.47–0.69) |
| 2010–2018 | 0.95 (0.91–0.97) | 0.77 (0.70–0.84) | 0.72 (0.67–0.76) | 0.56 (0.42–0.69) |
| Stage at diagnosis | | | | |
| I | – | – | 0.90 (0.81–0.97) | – |
| II | – | – | 0.77 (0.71–0.83) | – |
| III | – | – | 0.57 (0.49–0.64) | – |
| IV | – | – | 0.37 (0.19–0.57) | – |
| Age (years) | | | | |
| Under 39 | – | – | 0.74 (0.68–0.80) | – |
| 40–64 | – | – | 0.76 (0.66–0.85) | – |
| 65+ | – | – | 0.58 (0.46–0.69) | – |
| Ethnicity | | | | |
| Arab | 0.93 (0.88–0.97) | 0.83 (0.75–0.90) | 0.69 (0.62–0.75) | 0.51 (0.42–0.60) |
| Other | 0.95 (0.94–0.97) | 0.78 (0.74–0.82) | 0.71 (0.69–0.74) | 0.57 (0.47–0.66) |
| Human Development Index | | | | |
| Very high | 0.91 (0.83–0.97) | 0.81 (0.78–0.83) | 0.68 (0.60–0.75) | 0.48 (0.40–0.56) |
| High | 0.95 (0.94–0.97) | 0.78 (0.74–0.82) | 0.69 (0.66–0.72) | 0.59 (0.48–0.71) |
| Medium | 0.97 (0.95–0.98) | 0.89 (0.80–0.96) | 0.82 (0.73–0.90) | – |
| Low | – | – | 0.73 (0.64–0.80) | 0.54 (0.35–0.73) |
| EMR country grouping^a | | | | |
| Group 1 | 0.91 (0.83–0.97) | 0.80 (0.77–0.82) | 0.70 (0.64–0.75) | 0.48 (0.40–0.56) |
| Group 2 | 0.96 (0.94–0.97) | 0.78 (0.73–0.83) | 0.68 (0.66–0.71) | 0.54 (0.44–0.64) |
| Group 3 | – | – | 0.67 (0.57–0.77) | 0.58 (0.43–0.72) |

^aAll 22 countries in the Region are categorized into 3 groups based on level of development and income. Group 1: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and United Arab Emirates. Group 2: Egypt, Islamic Republic of Iran, Iraq, Jordan, Lebanon, Libya, Morocco, occupied Palestinian territory, Syrian Arab Republic and Tunisia. Group 3: Afghanistan, Djibouti, Pakistan, Somalia, Sudan and Yemen.

low-income countries have no published papers on survival. Consequently, our results actually represent the pooled survival rates of patients with breast cancer in those countries in the EMR which have better health care systems.

The results of the subgroup analysis indicated that women with breast cancer who were younger than 39 years may have the lowest survival rate. The highest survival rate was in those aged 40–64 years. In a study from Sweden in 2009 the 5-year survival rates in women aged 20–34, 35–39, 40–49 and 50–69 years were 74.7%, 83.8%, 88.3% and 87.8% respectively (20), which was consistent with the result of our study. Also, the results from a 2016 study in Canada (21) and a 2017 Iranian study (22) confirm our findings. Some research has reported that the age of onset of breast cancer in women of the EMR and also Asian women is lower than their European

and American counterpart (23). Breast cancer is a rare disease in young women, however the clinical and pathological outcomes are more aggressive than in older patients (20,21). Several studies have indicated that age is a significant predictor of survival in patients with breast cancer. A number of factors may affect the survival rates in women with breast cancer, e.g. late presentation and diagnosis at an advanced stage, more aggressive tumours in young women (20,24,25), and hormonal, immunological and biological differences between younger and older women (26,27). This hormonal difference in young women may result in more rapidly growing tumour and thus reduced survival rates (26,28). Also younger women with breast cancer may have more recurrence than other age groups (26).

One of the most important prognostic factors for survival of patients with breast cancer is stage at

Table 3 Meta-regression analysis for assessing the effect of suspected variables on the pooled 1-, 3-, 5- and 10-year's survival rate for women with breast cancer in the Eastern Mediterranean Region, 1946–2018

| Survival | Variable | Univariable model | | | Multivariable model | | |
|----------|-----------------|-------------------|------|---------|---------------------|------|---------|
| | | β | SE | P-value | β | SE | P-value |
| 1-year | Sample size | 2.7 | 2.4 | 0.281 | -0.7 | 2.3 | 0.761 |
| | HDI | 3.1 | 4.8 | 0.525 | 11.8 | 5.2 | 0.032 |
| | Decade of study | 3.1 | 3.0 | 0.763 | -5.9 | 3.2 | 0.091 |
| | Ethnicity | 4.4 | 2.2 | 0.068 | 9.7 | 3.1 | 0.007 |
| 3-year | Sample size | -1.9 | 4.6 | 0.612 | -1.3 | 4.3 | 0.752 |
| | HDI | 11.8 | 4.8 | 0.028 | 11.0 | 7.5 | 0.134 |
| | Decade of study | 4.0 | 5.0 | 0.482 | 1.5 | 6.0 | 0.823 |
| | Ethnicity | -4.2 | 4.1 | 0.329 | -0.6 | 5.9 | 0.914 |
| 5-year | Sample size | 3.6 | 3.1 | 0.234 | 3.0 | 2.9 | 0.325 |
| | HDI | 9.0 | 3.6 | 0.012 | 8.1 | 3.7 | 0.036 |
| | Decade of study | 8.2 | 3.9 | 0.048 | 5.4 | 4.1 | 0.179 |
| | Ethnicity | 2.9 | 3.0 | 0.397 | 2.2 | 9.9 | 0.425 |
| 10-year | Sample size | -2.7 | 9.2 | 0.752 | -0.6 | 11.0 | 0.981 |
| | HDI | -1.0 | 10.3 | 0.952 | -3.0 | 11.0 | 0.834 |
| | Decade of study | 10.5 | 12.1 | 0.443 | 11.0 | 20.0 | 0.516 |
| | Ethnicity | 5.5 | 9.6 | 0.526 | -0.3 | 37.7 | 0.327 |

SE = standard error.

HDI = Human Development Index.

diagnosis. The result of our study indicated that the 5-year survival rate of women with breast cancer in the EMR ranged from 90% for stage I to 37% for stage IV. In a 2016 report from the American Cancer Society the 5-year relative survival rate was between 99% at the local stage and 26% at the distant stage (16), similar to our findings. Also, a study from India in 2004 reported that the 5-year survival rate was from 69.7% at the local stage to 4% at the distant metastasised stage (15), which was much lower than our finding in the EMR. In developing region like the EMR, patients with breast cancer are usually diagnosed at an advanced stage due to the limited health care facilities, lack of awareness, and social barriers and cultural beliefs that can result in reduced survival (2).

Our findings indicated that the survival rate for women of all ages with breast cancer was better in the most recent decade. The 5-year survival rate in women in the EMR increased from 63% in 1990–1999 to 72% in 2010–2018. The result of studies conducted in Canada (29) and in England (13) confirm our findings. This progress may be due to the screening programmes and cancer prevention and control strategies in the countries of the Region (1,30).

The survival rate of women with breast cancer in the Arab populations was lower than in the non-Arab populations in this Region. In a 2016 meta-analysis conducted in the Islamic Republic of Iran, the pooled 1-, 3-, 5- and 10-year survival rates in women were 95%, 80%, 69% and 55% respectively (31) and in a study from Jordan in 2010 the 1-, 3- and 5-year survival rates were 91%, 70% and 59% respectively (32), confirming the result of our study. The results of some studies indicate that Arab

women with breast cancer may have a worse prognosis than other populations (33,34). The reasons for this may be the young age of women at presentation and also late diagnosis (34). Also some studies noted that the proportion of negative estrogen and progesterone receptors in Arab women with breast cancer was high, which can lead to poor survival (33,35,36).

In our meta-analysis we found that the 5-year survival rate in women was better than in men. Several studies indicate that sex is not an independent significant predictor for breast cancer survival (37–39) and the differences in survival may be due to the similarity between breast cancer in men and postmenopausal breast cancer in women (37,40). Some studies note that male breast cancer was diagnosed approximately 5–10 years later than in women (41,42). Also because of the general dearth of breast cancer screening programmes for males, they are usually diagnosed at a later stage than women (42,43). In some studies, the risk of local and regional recurrence in male breast cancer has been higher than women (42,44).

We found that the 5-year survival rate in the very high HDI subgroup was much lower than in the low HDI subgroup. In the medium and low HDI subgroups we have countries such as Afghanistan, Djibouti, Iraq, Palestine, Sudan, Somalia and Syrian Arab Republic but we did not have any relevant study about the survival rate for breast cancer in these countries, so the pooled survival rate in these subgroups are concluded from only a few countries, and therefore we should expect this bias.

One of the main limitations of this review is that, from the 22 countries in the EMR, we only have studies from

12 countries. So the estimate of the pooled survival rate in this Region can be representative of survival of only those countries which have a better health care system.

Conclusion

Although the search targeted all EMR countries, our results represented countries in the EMR with better health care systems, because the countries with no published papers on survival are mainly low income countries. The survival rate of women in the countries in the EMR

which have better health care systems is between the rates in the developed and developing regions. We found that, as in other parts of the world, survival rate have improved in recent decades. Although the survival rate will further improve owing to the implementation of screening and control programmes, we need more informative programmes to improve the awareness among females about the early sign and symptoms of this disease.

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Taux de survie des patients atteints de cancer du sein dans les pays de la Région de la Méditerranée orientale : analyse systématique et méta-analyse

Résumé

Contexte : Le cancer du sein est la quatrième cause de mortalité et d'incapacité dans la Région de la Méditerranée orientale ; bien que son incidence soit moindre que dans les régions développées, la tendance a été à la hausse au cours des dernières décennies.

Objectif : La présente étude avait pour objectif de calculer le taux de survie combiné des patients atteints de cancer du sein dans la Région de la Méditerranée orientale.

Méthodes : Nous avons effectué des recherches dans les bases de données électroniques de 1946 au 19 janvier 2018, sans restriction de langue. Un modèle à effet aléatoire a été utilisé pour estimer les taux de survie combinés à 1, 3, 5 et 10 ans pour les patients atteints de cancer du sein. Le test χ^2 et l'indice I^2 ont été utilisés pour évaluer l'hétérogénéité entre les études. Une analyse de sous-groupe et une méta-régression ont été utilisées pour étudier la source potentielle d'hétérogénéité.

Résultats : Nous avons trouvé 80 articles éligibles pour être inclus dans notre analyse. Les taux de survie combinés à 1, 3, 5 et 10 ans chez les femmes atteintes de cancer du sein dans la Région de la Méditerranée orientale étaient respectivement de 0,95 ; 0,80 ; 0,71 et 0,56. L'indice I^2 a mis en évidence une hétérogénéité considérable entre les études (toutes ayant rapporté un indice I^2 supérieur à 50 %). Le taux de survie à 5 ans dans le sous-groupe masculin était de 0,63. Le taux de survie à 5 ans chez les femmes atteintes de cancer du sein dans les tranches d'âge inférieur ou égal à 39, compris entre 40 et 64 ans et des plus de 65 ans étaient respectivement de 0,74 ; 0,76 et 0,58. Une corrélation statistiquement significative a été relevée entre l'indice de développement humain ($\beta = 9, p = 0,01$), la décennie de l'étude ($\beta = 8,2, p = 0,04$) et le taux de survie à 5 ans.

Conclusions : Le taux de survie des femmes atteintes de cancer du sein dans les pays de la Région de la Méditerranée orientale qui ont les meilleurs systèmes de santé s'est amélioré au cours de la dernière décennie. Les femmes dont l'âge était compris entre 40 et 64 ans avaient le meilleur taux de survie.

معدلات نجاة المرضى المصابين بسرطان الثدي في إقليم شرق المتوسط: استعراض منهجي وتحليل تلوي

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الخلاصة

الخلفية: سرطان الثدي هو رابع سبب رئيسي للوفاة والعجز في إقليم شرق المتوسط؛ وأصبح هناك اتجاه متزايد للإصابة بسرطان الثدي، على الرغم من أن معدل الإصابة به لا يزال أقل من المعدلات السائدة في الأقاليم المتقدمة.

الأهداف: تمثّل هدفنا في حساب معدل النجاة المجمعّة للمرضى المصابين بسرطان الثدي في إقليم شرق المتوسط.

طرق البحث: بحثنا في قواعد البيانات الإلكترونية في الفترة من عام 1946 إلى 19 يناير/كانون الثاني 2018، بدون أي قيود لغوية. وقد استخدمنا نموذجاً عشوائياً فعالاً لتقدير معدلات النجاة المجمعّة على مدار سنة واحدة، و3 سنوات، و5 سنوات و10 سنوات للمرضى المصابين بسرطان الثدي. واستخدم اختبار χ^2 ومؤشر I^2 لتقييم التباين بين الدراسات. كذلك استخدم تحليل المجموعات الفرعية والتحوّل التلوي لتحريّ المصدر المحتمل للتباين.

النتائج: وجدنا أن هناك 80 مقالاً صالحاً للإدراج ضمن المراجعة. وبلغت معدلات النجاة المجمعّة على مدار سنة واحدة، و3 سنوات، و5 سنوات و10 سنوات بين النساء المصابات بسرطان الثدي في إقليم شرق المتوسط 95، 80، 71، و56، على التوالي. وبين مؤشّر I^2 وجود

تباين لا يُستهان به بين الدراسات (كل مؤشرات $I^2 < 50\%$). وعلى مدار 5 سنوات، بلغ معدل النجاة في الفئة الفرعية من الرجال 63، 0، بينما بلغ في النساء المصابات بسرطان الثدي في الفئات العمرية 39 ≤، و64-40، وأكبر من 65 سنة 74، 0، و76، 0، و58، 0 على التوالي. وكان هناك ارتباط إحصائي قوي بين مؤشر التنمية ($\beta = 9$)، والقيمة الاحتمالية = 0، 01) والدراسة مدة 10 سنوات ($\beta = 8$)، والقيمة الاحتمالية = 0، 04، ومعدل النجاة على مدار 5 سنوات.

الاستنتاجات: تحسّن على مدار العَقْد الماضي معدل نجاة النساء المصابات بسرطان الثدي في بلدان إقليم شرق المتوسط التي لديها نُظُم رعاية صحية أفضل، وكانت أفضل معدلات النجاة بين النساء التي تتراوح أعمارهن بين 64-40 عاماً.

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