REVIEW

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Systematic Review and Meta-Analysis of Treatment Effects on Survival in Patients with Inflammatory Breast Cancer

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Abstract

The objective of this study was to determine the survival rate and the effects of different treatments on patients with inflammatory breast cancer (IBC). The study employed a systematic approach that included a search strategy across four databases: Embase, Web of Sciences, PubMed, and Scopus. The results obtained were screened initially by titles and abstracts, followed by full-texts in EndNote 8 software. The next stage involved data extraction and qualitative evaluation, where the Metan command was used to estimate the pooled survival rate. A total of 28 studies with a sample size of 63,796 were finally analyzed. The overall 3- and 5-year survival rates (OS) for IBC patients were found to be 52% (95% CI; 46-58%, I2: 99.42%) and 61% (95% CI; 53-69%, I2: 93.63%), respectively. The 5-year OS rates in patients with non-metastatic and metastatic IBC were 59% (95% CI; 54-63%, I2: 98.31%) and 30% (95% CI; 26-35%, I2: 50.84%), respectively. The 5-year OS rate in non-metastatic patients who underwent BCS surgery was 60% (CI 95%; 26-94%, I2: 95.13%). The overall 5- and 3-year OS rates for patients with IBC were lower than those for all types of breast cancer, and the rates were even lower in patients with metastasis. Therefore, it is recommended that healthcare workers and women at risk should be vigilant of early symptoms of IBC to prevent metastasis by seeking medical attention on time.

Keywords: Inflammatory breast cancer- IBC- Treatment- Survival

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Introduction

Inflammatory breast cancer (IBC) is a clinically and pathologically aggressive form of breast cancer that presents with symptoms such as edema, rapid and extensive erythema, and a Peau d'orange appearance, often in the context of a palpable or non-palpable mass. These symptoms can develop quickly within a period of six months(Hance et al., 2005; Mamouch et al., 2018). Based on recorded reports from the United States (USA), 2% to 6% of all breast cancers diagnosed are of the IBC type, and approximately 7% of breast cancer-related deaths are attributed to IBC. These reports indicate that the 5-year survival rate for IBC patients ranges from 29% to 49%, depending on their disease stage and race (Chang et al., 1998; Hance et al., 2005; Anderson et al., 2006; Abraham et al., 2021). In France, Denmark, and the Netherlands, the 5-year survival rates for IBC patients ranged from 31% to 60%, 41%, and 69%, respectively (Monneur et al., 2017; Van Uden et al., 2017; Mele et al., 2019; Van Uden et al., 2019a; Van Uden et al., 2019b). These findings reveal major disagreement in findings because of the huge difference in reported survival rates across several trials. Numerous studies have examined various IBC treatments over the past few decades, and considerable advancements have been made in terms of improving survival rates. For instance, between 1978 and 1982, the mean survival rate for patients was 62.3 months, but between 2008 and 2012, it was 99.4 months(Abraham et al., 2021). In addition to surgery, radiotherapy, chemotherapy, hormone therapy, and immunotherapy are commonly employed in the treatment of inflammatory breast cancer (IBC). The current standard of care for IBC involves a multimodal approach, with neoadjuvant chemotherapy followed by radiotherapy, or surgery and radiotherapy, and hormone therapy added based on the patient's individual circumstances. It is generally advised against using surgery alone as the primary treatment for IBC due to the extensive nature of the disease, which may result in residual disease if the tumor is not completely excised. As a result, neoadjuvant chemotherapy, administered prior to surgery, is strongly recommended for IBC patients. Modified radical mastectomy (MRM) is the most frequently performed surgical procedure for IBC patients. Although Bonev et al. did not observe a significant change in median survival rates after breast-

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conserving surgery (BCS), they suggested considering this approach for patients who show a favorable response to neoadjuvant chemotherapy. Depending on the specific drugs used, neoadjuvant chemotherapy has the potential to increase the 5-year survival rate to approximately 50%. The most commonly utilized chemotherapy regimen for IBC involves a combination of anthracyclines, such as doxorubicin and epirubicin, and taxanes, such as paclitaxel and docetaxel. However, other drugs like methotrexate, 5-fluorouracil, and cyclophosphamide are also employed in certain cases. These chemotherapy agents work together to target and destroy cancer cells, inhibiting their ability to grow and spread. It's important to note that treatment approaches may vary depending on the individual patient, the stage of the disease, and other factors. The specific treatment plan for each IBC patient should be determined through careful evaluation and consultation with a multidisciplinary team of healthcare professionals who specialize in breast cancer treatment. With ongoing research and advancements in the field, the treatment landscape for IBC continues to evolve, offering new possibilities for improved outcomes and enhanced quality of life for individuals affected by this aggressive form of breast cancer(Bozzetti et al., 1981; Lamb et al., 1991; Ueno et al., 1997; Bertucci et al., 2004; Cristofanilli and Buchholz, 2010; Dawood et al., 2011; Bonev et al., 2014; Mamouch et al., 2018).

Bozzetti et al. found that radiotherapy after radical mastectomy did not significantly improve the survival rate in their study, whereas Muzaffar et al. reported that adjuvant radiotherapy increased the 5-year survival rate by 15% (Bozzetti et al., 1981; Muzaffar et al., 2018). Clinical trials are currently underway to evaluate the effectiveness of immunotherapy drugs, such as Ipilimumab and Pembrolizumab, in improving the treatment and survival outcomes of IBC (Koch et al., 2021). This study was conducted as a systematic review to determine the survival rates for IBC) at different stages and the impact of different treatments on these rates. This work was prompted by the high mortality rates associated with IBC, the conflicting data on survival and treatment outcomes, and the lack of systematic and thorough evaluations of overall survival in IBC patients. The researchers wanted to provide a more thorough picture of IBC survival and outcomes, so they decided to conduct a meta-analysis to collect and analyses the data that was already available. By shedding light on the prognosis of IBC patients at different stages and guiding the development of specialized treatment techniques, the results of this study have the potential to significantly advance the science of oncology. The results of this meta-analysis also have direct applications in clinical practice. Clinicians can make informed decisions about patient care and treatment plans based on the current clinical understanding of IBC survival and treatment outcomes. Based on these findings, guidelines can be developed to help standardize and optimize the treatment of IBC, ultimately improving patient survival and outcomes. The overall aim of this systematic review and meta-analysis is to fill knowledge gaps and provide insightful information that will benefit those diagnosed with IBC. Healthcare professionals can work towards more effective therapies, better patient outcomes and ultimately a better quality of life for people affected by IBC by improving our understanding of this aggressive form of breast cancer.

Materials and Methods

Search strategy and screening articles

To conduct this systematic review, all articles published between April 2012 and May 2021 were obtained from four databases, namely Embase, Web of Sciences, PubMed, and Scopus. A search strategy was developed using the primary keywords "Inflammatory breast cancer" and "Survival", and Mesh was used to identify synonyms of these keywords. The synonyms included "IBC", "Inflammatory Breast Neoplasm", "Inflammatory Breast Carcinomas", "Inflammatory Breast Cancers", "Survival", "Recurrence", "Recrudescence", "Relapse", and "Relapses". The articles retrieved from each database were organized in separate libraries in the Endnote 8 software and then combined into a single library. Duplicate articles were identified and removed using the default Endnote software and manual review. The remaining articles were screened based on their titles, abstracts, and full texts, according to the inclusion criteria. Two authors independently screened the articles, and any discrepancies were reviewed by a third author. The final selection of articles was made by evaluating their full texts.

Inclusion and exclusion criteria

This study aimed to determine the survival rate of IBC patients and the impact of different treatments on this disease. Only cohort studies were included, and all other study types were excluded. Studies without English full texts or those whose full texts were not available were also excluded. The selected studies focused on IBC survival or reported IBC survival separately with a defined frequency as part of the study. Only articles that reported 3- or 5-year overall survival (OS) were included in the analysis, and studies that did not report OS or reported it with different durations were excluded due to their lower frequency. Studies that used animal samples were also excluded from the meta-analysis.

Data extraction

After the screening phase, in which publications were selected on the basis of their titles, abstracts and full texts according to the inclusion criteria, data were extracted from the selected articles according to the research objective using a checklist. The following information was included in the checklist: name(s) of author(s), type of study, year of publication, total sample size, sample size of patients without metastatic disease and patients with metastatic disease, type of treatment, 5- and 3-year OS rates with different treatments, mean age at diagnosis, and duration of follow-up. Some trials did not report overall OS, but reported different OS rates at different frequencies. In these cases, the trial included all reported OS rates with a certain frequency. The direct mention of the metastatic status of each patient or the existence of a metastatic subgroup with a certain frequency and OS was

one of the inclusion criteria for studies on OS in metastatic disease. According to the AJCC guidelines, only patients with stage 4 cancer were included in trials that did not report the metastatic status of the patients (Edge, 2010).

Among the 28 studies reviewed, the analysis of the effects of surgery or radiotherapy on overall survival (OS) was conducted only on studies in which all patients had undergone surgery or radiotherapy or studies that had separately reported the 5- and 3-year OS of patients who had undergone surgery or radiotherapy. For the subtype analysis of surgery, the analysis was limited due to the small sample size and the inability to determine 5-year OS rates. The surgeries included Modified radical mastectomy (MRM), Total mastectomy (TM), Radical mastectomy (RM), and breast-conserving surgery (BCS). The effectiveness of BCS as part of the treatment was ambiguous, and therefore, its inclusion in the analysis was limited (Bonev et al., 2014), the patients were divided into BCS and non-BCS groups. In the section dealing with evaluation of the effect of Radiotherapy, all patients had received an adjuvant regimen, and the studies in which the patients had not received such a regimen or it was not clear that they had a history of receiving it were excluded due to the low frequency in the Radiotherapy analysis.

Qualitative evaluation of the studies

The quality of the studies included in this meta-analysis was assessed using the Newcastle Ottawa Scale (NOS) (Cook and Reed, 2015). Each study was evaluated based on the NOS, which awards a maximum of 9 points per study based on the following parameters: 4 points for participant selection, 2 points for comparability, and 3 points for outcome assessment.

Statistical analysis

The study checklist was used to extract patient frequencies and 5- or 3-year overall survival (OS) rates, if available, from all selected studies. The Metaprop and Metan commands were then used to calculate the overall survival rate and the effect of different treatments on it, based on the extracted information. Random Effect Model and Fixed Effect Model were used for general and subgroup analyses, respectively. The heterogeneity and variance of the studies selected for meta-analysis were checked using Cochran's Q and I2 tests. Data analysis was performed using STATA 17 software, with a confidence level of 95%.

Results

Qualitative results

Initially, a total of 571 articles were obtained from PubMed (207 studies) and Scopus, Embase, and Web of Sciences (364 studies). After removing duplicates and applying the exclusion criteria, 69 studies remained and were evaluated based on their full texts. Finally, 28 studies (Bates et al., 2012; Akay et al., 2014; Brown et al., 2014; Gogia et al., 2014; Fouad et al., 2015; Tsai et al., 2015; Warren et al., 2015; Wecsler et al., 2015; Biswas et al., 2016; Boudin et al., 2016; Brzezinska et al., 2016; Raghav et al., 2016; Denu et al., 2017; Monneur et al., 2017; Rosso et al., 2017; Van Uden et al., 2017; Muzaffar et al., 2018; Slaoui et al., 2018; Biswas et al., 2019; Loi et al., 2019; Stecklein et al., 2019; Van Uden et al., 2019a; Van Uden et al., 2019b; Wu et al., 2019; Fayanju et al., 2020; Li et al., 2020; Abraham et al., 2021; Grova et al., 2021) were included in the analysis (Table 1 and Figure 1).

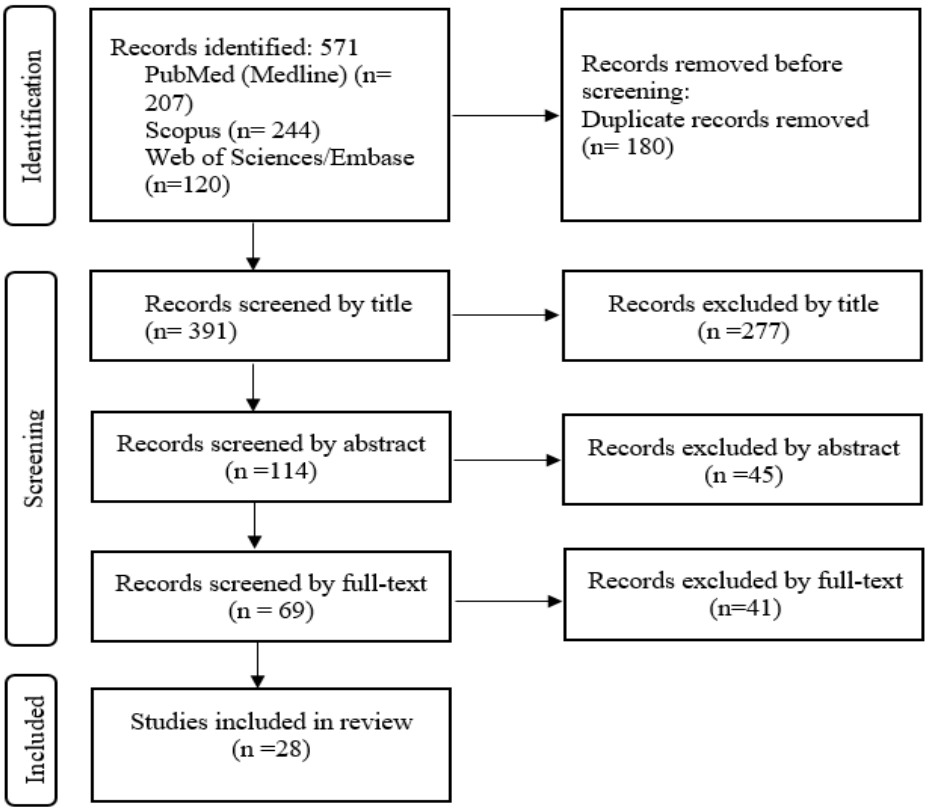

Figure 1. The Search Screening Results and Selected Studies

Table 1. Main Characteristics of All Studies Included in the Meta-Analysis

Author	Type of the study	Total No.	Metastatic No.	Treatment	3 Years OS	5 Years OS	Median age (Years)	Median follow up
Bates, T (2012)	Cohort	29	0	Chemotherapy + Radiotherapy + Hormone therapy (tamoxifen in ER +) + Surgery (in case of recurrence or residual lesion)	N/A	0.55	50.6	71
Brown, L. (2014)	Cohort	52	0	Chemotherapy (n=49) + Surgery + Radiotherapy + Chemotherapy (according to the physician opinion)	N/A	0.64	54	60
Gogia, A., et al. (2014)	Cohort	41	15	Chemotherapy (n=41) +Surgery (n=29) +Radiotherapy + Hormone therapy	0.4	N/A	45	30
Akay, C. L (2014)	Cohort	172	172	Chemotherapy + Surgery (n = 79) + Radiotherapy (n = 86) + Hormone therapy (n = 55)	N/A	0.29	52	33
Tsai, C. J (2015)	Cohort	260	0	Chemotherapy + Surgery + Radiotherapy + Hormone therapy (if the receptor is positive) + Chemotherapy	0.68	N/A	50	29
Warren, L. E(2015)	Cohort	227	54	Chemotherapy + Surgery + Radiotherapy	0.783, 0.443	0.596, 0.33	49-52	39.6
Fouad, T. M., et al. (2015)	Cohort	206	206	Chemotherapy(n=206), Surgery(n=81), Targeted therapy(n=46), Hormone therapy(n=9)	N/A	0.254	49.5	56.4
Wecsler, J. S., et al. (2015)	Cohort	761	0	Chemotherapy+ Surgery(n=761) + Radiotherapy(n=456)	N/A	0.52	57.1	N/A
Brzezinska, M. (2016)	Cohort	35	3	Chemotherapy (n = 20) + Hormone therapy (n = 14) + Surgery + Radiotherapy (1 patient had neither hormone therapy nor chemotherapy)	N/A	0.703	60.5	80
Biswas, T., et al. (2016)	Cohort	34	7	Chemotherapy(n=32) + Surgery(n=21) + Radiotherapy(n=24)	N/A	0.26	52	13
Boudin, L., et al. (2016).	Cohort	67	0	Chemotherapy(n=67) + Surgery(n=67) + Radiotherapy(n=67) + Hormone therapy+ Targeted therapy	N/A	0.74	47	80.04
Raghav, K., et al. (2016)	Cohort	659	165	Chemotherapy (490) + Surgery(n=642) + Radiotherapy(n=380) + Chemotherapy(n=242)	0.62 (0.67, 0.47)	N/A	49-53.5	29
Denu, R. A. (2017)	Cohort	170	63	Surgery, Chemotherapy, Radiotherapy	N/A	0.44	57.7	N/A
van Uden, D. J. P. (2017)	Cohort	3481	1276	Chemotherapy (n=1153) + Surgery (n=1619) + Chemotherapy (n=216) + Radiotherapy (n=1199) + Hormone therapy (n=1718) total trimodally= 928	N/A	0.302	61.6	N/A
Monneur, A (2017)	Cohort	144	0	Chemotherapy + Surgery + Radiotherapy (n = 136) + Hormone therapy (n = 77) + Neoadjuvant / adjuvant trastuzumab (n = 24)	N/A	0.69	50.5	57.07
Rosso, K. J., et al. (2017)	Cohort	114	0	Chemotherapy(n=114) + Surgery(n=114) + Radiotherapy(n=114)	N/A	0.694	52	43.2
Muzaffa,M. (2018)	Cohort	7304	0	Surgery (n=6895 total and n=409 partial) + Radiotherapy (n=4559)	N/A	0.49, 0.43, 0.55, 0.40	56	N/A
Slaoui, M., et al. (2018)	Cohort	219	66	Chemotherapy(n=209) + Surgery(n=125) + Chemotherapy(n=50) + Radiotherapy(n=104) + Targeted therapy(n=38) + Hormone therapy(n=62)	0.704, 0.419	N/A	36.7-57.3	13
van Uden, D. J. P. (2019)	Cohort	1061	0	Chemotherapy (n = 670) + Surgery (n = 799) + Radiotherapy (n = 679) + Hormone therapy (n = 559)	N/A	0.556	58.4-63.2	28.8
van Uden, D. J. P. (2019)	Cohort	744	744	Chemotherapy (n = 485) + Surgery (n = 149) + Radiotherapy (n = 145) + Hormone therapy (n = 344) Only 60 patients have received trimodally	N/A	0.336	57.5-62	16.1
Biswas, T., et al. (2019)	Cohort	8550	0	Chemotherapy(n=7754) + Hormone therapy + Surgery(n=8550) + Radiotherapy(n=6070) + Chemotherapy+ Hormone therapy Immune therapy	N/A	0.58	56	44.4
Loi, M., et al. (2019).	Cohort	95	0	Chemotherapy(n=95) + Surgery(n=91) + Chemotherapy(n=44) + Endocrine therapy(n=34) + Radiotherapy(n=84)	0.7	0.55	50.6	160.8
Stecklein, S. R., et al. (2019)	Cohort	103	0	Chemotherapy+ Targeted therapy+ Surgery(n=103) + Radiotherapy(n=103) + Chemotherapy(n=28) + Hormone therapy(n=51)	N/A	0.84, 0.559	52	43.2

Figure 2. Forest Plot Showing 5-Year Overall Survival of Entire Meta-Analysis

The 28 studies analyzed were cohort studies whose main populations or a certain part of their populations were IBC patients. According to Table 1, the total population of IBC patients was 63,796. The sample sizes of the patients whose 3- and 5-year survival rates had been mentioned were 2,315 and 61,802, respectively. The lowest mean age at the time of diagnosis was 45 years in Gogia et al.,'s (2014), 47 years in Boudin et al.'s (Boudin et al., 2016), and 49.5 years in Fouad et al.,'s (2015) studies respectively, and the highest mean age at diagnosis was 61.6 years in the study by Uden et al., (2017) . Among the studies that had mentioned the average follow-up, the highest and lowest follow-up rates were respectively related to the studies by Loi et al., (2019) with 160.8 months and Biswas et al., (2016) and Slaoui et al., (2018) with 13 months. In the present meta-analysis, the oldest study was that of Bates et al., (2012) and the newest one was the study by Abraham et al. ,(2021). The largest number of studies had been carried out in 2019 (n= 6). Among the studies presented in Table 1, the smallest and the largest sample sizes were related to the studies by Bates et al. (Bates et al., 2012) and Abraham et al. (Abraham et al., 2021) with the frequencies of 29 and 29,718 people, respectively.

Quantitative results

5-year survival rate

The sample size of the patients with IBC in the 28 studies (Bates et al., 2012; Akay et al., 2014; Brown et al., 2014; Gogia et al., 2014; Fouad et al., 2015; Tsai et

Table 1. Continued

Author	Type of the study	Total No.	Metastatic No.	Treatment	3 Years OS	5 Years OS	Median age (Years)	Median follow up
Wu, S. G., et al. (2019)	Cohort	626	229	Surgery(n=409), Radiotherapy(n=308), Chemotherapy(n=527)	0.527	N/A	N/A	28
Li, Z. W. (2020)	Cohort	188	45	94 patients received radiotherapy and 94 patients did not receive radiotherapy	0.582, 0.818	N/A	N/A	27
Fayanju, O. M., et al. (2020)	Cohort	3471	0	Chemotherapy(n=3471) + Surgery(n=3471) + Chemotherapy+ Radiotherapy(n=2828)	N/A	0.55, 0.64, 0.65	56	N/A
Grova, M. M., et al. (2021)	Cohort	5265	0	Chemotherapy(n=4726) + Surgery(n=4316) + Chemotherapy+ Radiotherapy(n=3620)	N/A	0.516	57	26.8
Abraham, H. G. (2021)	Cohort	29718	N/A	N/A	N/A	0.419	57.5-61.8	N/A

Table 2. Subgroup Analysis Based on Metastatic Statues, Receiving Radiotherapy, and Doing Type of Surgery

Outcomes	Number of Studies	Pooled Survival (% 95 CI)	Heterogeneity Assessment	Column1
			I Square	P value
5-year overall survival				
Metastatic Patients	4	30 % (26 – 35 %)	50.84%	0.11
Non-Metastatic Patients	21	59 % (54 – 63 %)	98.31%	0
No Determinant Condition (NA)	4	36 % (29 – 44 %)	98.22%	0
3-year overall survival				
Metastatic Patients	3	45 % (40 – 51 %)	0.01%	0.77
Non-Metastatic Patients	5	71 % (66 – 75 %)	58.00%	0.054
No Determinant Condition (NA)	4	59 % (42 – 76 %)	94.35%	0
5-year overall survival in non-metastatic patients (type of surgery)				
Patients who had BCS	2	60 % (26 – 94 %)	95.13%	0
Patients who had MRM	7	61 % (52 – 70 %)	94.76%	0
TM or RM and patients who had no determinant condition (NA)	12	58 % (53 – 63 %)	98.19%	0
5-year overall survival in non-metastatic patients (receiving radiotherapy)				
Yes	7	64 % (57 – 70 %)	91.20%	0
No/NA	14	56 % (51 – 62 %)	98.68%	0

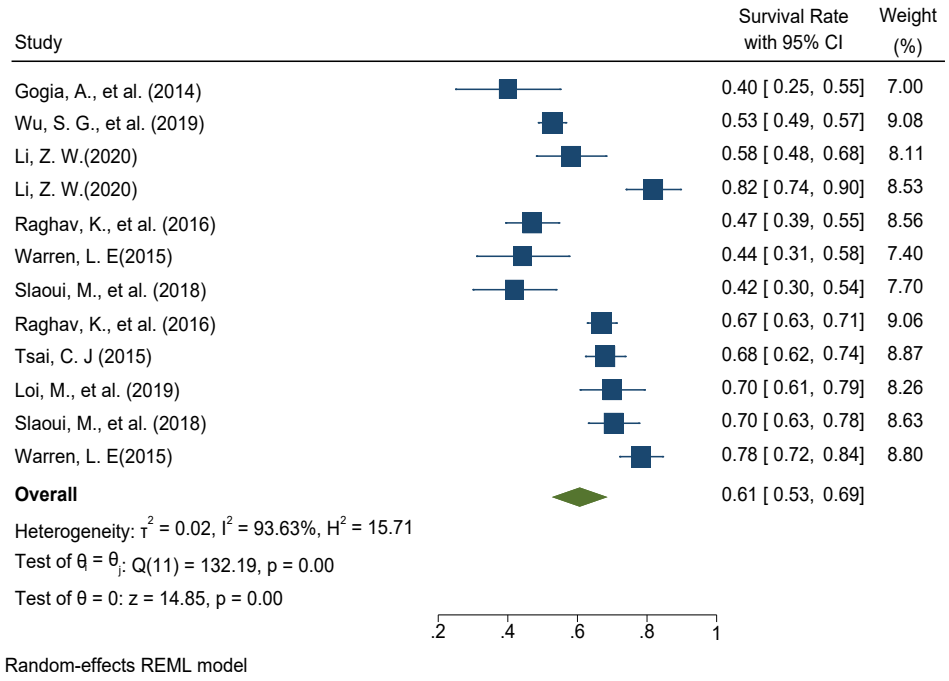

Figure 3. Forest Plot Showing 3-Year Overall Survival of Entire Meta-Analysis

al., 2015; Warren et al., 2015; Wecsler et al., 2015; Biswas et al., 2016; Boudin et al., 2016; Brzezinska et al., 2016; Raghav et al., 2016; Denu et al., 2017; Monneur et al., 2017; Rosso et al., 2017; Van Uden et al., 2017; Muzaffar et al., 2018; Slaoui et al., 2018; Biswas et al., 2019; Loi et al., 2019; Stecklein et al., 2019; Van Uden et al., 2019a; Van Uden et al., 2019b; Wu et al., 2019; Fayanju et al., 2020; Li et al., 2020; Abraham et al., 2021; Grova et al., 2021) was 63,796, of which 22 articles with a frequency of 61,802 patients had reported the 5-year OS of the IBC patients. The 5-year OS of the entire study was 52% (CI 95%; 46-58%, I2: 99.42%). The highest and lowest survival rates had been reported by Fouad et al., (2015) and Stecklein et al., (2019) with 25% (CI 95% 19-31%) and 84% (CI 95% 72-96%), respectively (Figure 1). In the present meta-analysis, the studies that had reported the 5-year OS underwent subgroup analysis based on having or not having metastasis, the type of surgery, and undergoing or not undergoing radiotherapy. Among the 22 articles that had mentioned the 5-year OS of the IBC patients, 34,528 had no metastases, 1,176 had metastases, and the metastases of 33,403 patients was unknown. The 5-year survival rates of the patients without metastasis, with metastasis, and with unknown metastasis were 59% (CI 95%; 54-63%, I2: 98.31%), 30% (CI 95%; 26-35%, I2: 50.84%), and 36% (CI 95%; 29-44%, I2: 98.22%), respectively (Figure 2).

The 5-year survival of the non-metastatic patients who

had undergone MRM, TM, or RM surgeries was 61% (CI 95%; 52-70%, I2: 94.76%). This rate was 60% (CI 95%; 94-26%, I2: 95.13%) in the patients who had undergone BCS, and 58% (CI 95%; 53-63 %, I2: 98.19%) in those whose surgery was unknown (Table 2).

The 5-year survival rate in non-metastatic patients who had undergone radiotherapy was 64% (CI 95%; 57-70%, I2: 91.02%). This rate was 56% (CI 95%; 51-62%, I2: 98.68%) in those whose receiving radiotherapy was unknown (Table 2).

3-year survival rate

Of 28 reviewed articles, 9 with a frequency of 2315 people had reported the 3-year survival rates of the IBC patients. The 3-year OS rate of the study was 61% (CI 95%; 53-69%, I2: 93.63%). The highest and lowest rates were respectively found in the studies by Gogia et al., (2014) and Li et al., (2020) with 40% (CI 95% 25-55%) and 82% (CI 95% 74-90%) (Figure 3).

In this meta-analysis, subgroup analysis was performed on studies that reported a 3-year OS based on the presence or absence of metastases. Among the 9 articles that reported the 3-year OS of IBC patients, 1,175 subjects did not have metastasis, 285 had metastasis, and the metastatic status of 855 patients was unknown. The 3-year survival rate for patients without metastasis was 71% (95% CI: 66-75%, I^2: 58.03%), while for those with metastasis, it was 45% (95% CI: 40-51%, I^2: 00.01%). The 3-year OS rate for patients with unknown metastatic status was 59% (95% CI: 42-76%, I^2: 94.35%) (Table 2).

Discussion

The aim of this meta-analysis was to investigate the OS of IBC patients and the effects of different treatments on it. After considering the inclusion criteria, the meta-analysis was conducted on 28 studies, which included a total of 63,796 female patients. The 3- and 5-year OS rates for the entire study were 61% and 52%, respectively, regardless of the presence or absence of metastasis. In a study by Denu et al., (2017), the 5-year survival rate for IBC patients was 44% regardless of metastatic status. However, according to Li et al., (2020) the rate varied from 58.2% to 81.8% depending on the type of treatment. Other studies have reported rates ranging from 30.2% to 70% (Brzezinska et al., 2016; Denu et al., 2017; Van Uden et al., 2017; Li et al., 2020). In a 2019 meta-analysis by Maajani et al., (2019) the 3- and 5-year OS rates for breast cancer patients, regardless of type and the presence or absence of metastasis, were 75% and 73%, respectively. The low OS rates of IBC compared to all breast cancers, especially in the long term, could be attributed to several factors. These include the high progression rate of IBC, its low prevalence, symptoms that can mimic mastitis, and misdiagnosis due to the lack of specific findings in mammography (Le-Petross et al., 2021). Given the high mortality rate associated with IBC, it is important to inform primary health workers and women at risk about the symptoms of IBC. According to this study, the 5-year OS rates for non-metastatic and metastatic patients were 59% and 30%, respectively. Various studies have reported 5-year OS rates for non-metastatic and metastatic patients, ranging from 40% to 84% and from 26% to 44%, respectively, depending on the type of treatment and other factors (Biswas et al., 2016; Denu et al., 2017; Muzaffar et al., 2018; Stecklein et al., 2019). There was high heterogeneity in the reports of most studies, possibly due to differences in treatment type, patient age at diagnosis, genetics, and environmental conditions. This heterogeneity reinforces the need for comprehensive studies to determine OS rates. In studies that reported 5-year OS rates for non-metastatic patients who underwent different surgeries as part of IBC treatment, the 5-year OS rate was 61% for patients who underwent mastectomy (MRM, TM, and RM surgeries), but only 60% for those who underwent breast-conserving surgery (BCS). However, since many patients underwent various surgeries during their treatment, it was not possible to compare the effects of surgery type on OS rates. Furthermore, only two studies with a sample size of 441 people reported 5-year OS rates for patients who underwent BCS, and some of these patients had no specific indication for undergoing BCS. Thus, if BCS is performed as part of IBC treatment, other factors such as response to chemotherapy, treatment eligibility, and disease stage should be considered to assess the risk of disease recurrence. In studies that reported the effect of radiotherapy on the OS rate of non-metastatic IBC patients, the 5-year OS rate was 64%, higher than the OS rate of all non-metastatic patients (58%). This suggests a positive effect of radiotherapy in increasing the survival of IBC patients. All studies that analyzed the effect of radiotherapy used adjuvant radiotherapy. The NCCN 2021 guideline also recommends adjuvant radiotherapy as part of IBC treatment due to the high possibility of lymph node involvement in adjacent areas. In studies by Brown et al. and Monneur et al., where almost all patients received neoadjuvant chemotherapy, the 5-year OS rates were 64% and 69%, respectively, which were higher than the 5-year OS rate for non-metastatic patients (58%) (Brown et al., 2014; Monneur et al., 2017). The NCCN 2021 guidelines recommend neoadjuvant chemotherapy as the standard treatment for IBC patients before surgery.

Limitations

One limitation of this meta-analysis was the insufficient number of studies reporting OS rates for IBC patients at different time periods. This led to a high degree of heterogeneity when combining studies, which resulted in the exclusion of studies reporting 1-, 2-, 10-, and in some cases, 3-year OS rates. Another limitation was the lack of sufficient studies to investigate the effect of different treatments on OS rates, making it impossible to compare the effects of performing specific treatments. Some studies only investigated epidemiological characteristics and did not address the effects of different treatments. Given the non-reporting of variables in the initial studies and the resulting high degree of heterogeneity, the results of this study should be interpreted with caution. Additionally, more studies are needed to make better decisions regarding survival rates and the effects of different treatments in IBC patients.

In conclusion, the 5- and 3-year OS rates for IBC patients were 52% and 61%, respectively, which were lower than those for all patients with breast cancer (73% and 75%, respectively). This highlights the need for primary health care workers and women at risk to be aware of the early symptoms of IBC to enable prompt referral and prevent disease progression, metastasis, and a reduction in OS. A combined treatment regimen including neoadjuvant chemotherapy, surgery, and adjuvant radiotherapy can be recommended for IBC patients, taking into account patient-specific limitations and conditions. However, more studies, especially clinical trials or cohort studies with large sample sizes, are required to make decisions on the type of surgery and to provide more conclusive evidence regarding the use of breast-conserving surgery.

Abbreviation

CI: Confidence Interval
OS: Overall Survival
IBC: Inflammatory Breast Cancer
MRM: Modified Radical Mastectomy
BCS: Breast Conserving Surgery
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Author Contribution Statement

Conceptualization, YM, PB; data curation, PB, YM, EN; Formal analysis, YM, EN; funding acquisition, not applicable; methodology, YM, GM; project administration, YM; visualization, YM, PB, GM; writing—original draft, PB, YM, EN, HM; writing—review and editing, YM, PB, HM. All authors have read and agreed to the published version of the manuscript.

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Ethics approval and consent to participate

This work was confirmed by the Deputy of Research of Kurdistan University of Medical Sciences, Sanandaj, Iran (IR.MUK.REC.1401.007).

Conflict of interest

Authors claim no competing interest and conflict of interest.

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