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Systematic review and meta-analysis of hypofractionated and conventional fractionated radiotherapy on survival in breast cancer patients

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Abstract

Introduction: Breast cancer is the most common malignancy among women around the world, and considering the low α/β ratio, it appears that the efficiency of hypofractionated radiotherapy (HFRT) is equal to conventional fractionated radiotherapy (CFRT). Accordingly, the goal of this meta-analysis was to estimate the survival rate of patients with breast cancer after hypofractionated radiotherapy and CFRT treatments.

Materials and Methods: Databases Web of Science, Cochrane, Scopus, PubMed, Embase, and Google Scholar search engine were used for articles published until August 20, 2025. Data was analyzed using STATA 14. Tests with *P* values<0.05 were considered statistically significant.

Results: The overall survival rate of breast cancer patients after CFRT and their disease-free survival (DFS) rate were 89% and 86%, respectively. The overall survival rate of breast cancer patients after hypofractionated radiotherapy and ultra - hypofractionated radiotherapy was 83% and 85%, respectively. Furthermore, the overall survival rate of breast cancer patients after hypofractionated radiotherapy in Asia was 79%, Europe 83%, America 86%, Africa 90%, in follow-ups under 5 years was 89%, in follow-ups equal to 5 years or longer was 81%, in women aged 40 to 49 was 82%, women aged 50 to 59 was 85%, women aged 60 to 69 was 86%, women aged 70 to 79 was 82%, and women aged 80 to 89 was 59%. The DFS rate of breast cancer patients after hypofractionated radiotherapy and U- hypofractionated radiotherapy was 87% and 95%, respectively. Additionally, the DFS rate of breast cancer patients after hypofractionated radiotherapy in women aged 40 to 49 was 82%, women aged 50 to 59 was 86%, women aged 60 to 69 was 97%, women aged 70 to 79 was 88%, in Asia 77%, Europe 95%, America 93%, Africa 95%, in follow-ups under five years was 94%, and in follow-ups equal to or longer than five years was 84%.

Conclusion: There was a slight difference in overall survival between the two methods of hypofractionated radiotherapy and CFRT, whereas their DFS rate after hypofractionated radiotherapy and U- hypofractionated radiotherapy was higher than that of CFRT. Furthermore, the overall survival rate following hypofractionated radiotherapy in Africa and follow-ups under five years was equal to or higher than that of CFRT treatment. Considering the reduced number of treatment sessions and costs in the hypofractionated radiotherapy method and the minor difference in the overall survival rates of hypofractionated radiotherapy and CFRT methods, it appears that hypofractionated radiotherapy is a more effective treatment method.

Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD420251135054) and Research Registry (UIN: reviewregistry2040) websites.

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Introduction

Breast cancer is the most common malignancy among women around the world, as it constitutes about 25% of the total cancer cases of women (1). The annual rate of breast cancer is 2.3 million cases, which will reach 3 million by 2040 (2). Radiotherapy is a standard post-surgery treatment conducted with the aim of improving overall survival rates and reducing local recurrence rates (3).

The conventional fractionated radiotherapy (CFRT) method, which recommended a dose of 50 Gy/50.4 Gy in 25 to 28 sessions of 1.8-2 Gy per day, was the most popular standard dose of radiotherapy for years (4). Due to the longer course of CFRT treatment, the financial burden on patients increases while their quality of life and self-confidence decrease (5). On one hand, numerous studies demonstrated that increasing the dose in each

Key point

In this systematic review and meta-analysis in breast cancer patients, we found a slight difference in overall survival between the two methods of hypofractionated radiotherapy (HFRT) and conventional fractionated radiotherapy (CFRT). We also found that, disease-free survival rates after hypofractionated radiotherapy and ultra-HFRT were higher than CFRT.

fraction and reducing the number of fractions, known as hypofractionation, leads to a similar or better effect on the local-regional recurrence rate, overall survival, and aesthetic consequences among patients (6-8). On the other hand, breast cancer had a low α/β ratio in the 2.0-4.0 Gy range, indicating that the effectiveness of hypofractionated radiation therapy (HFRT) was equal to CFRT (9).

During the last two decades, two distinct types of hypofractionation regarding breast cancer have been brought to attention: moderate hypofractionation, in which the doses are more than 2 Gy, yet they remain less than 3 Gy per fraction, and ultra-hypofractionation, which includes the administration of doses greater than 5 Gy per fraction (10). A moderate hypofractionation usually provides 40 to 42.5 Gy during an approximate three-week period (11,12). Ultra-HFRT(i.e., five fractions of 5.2 or 5.7 Gy) was introduced in 2020, during the onset of the COVID-19 pandemic (13). Hypofractionated radiation therapy can reduce the cost of cancer treatment, provide patients with a more convenient therapy, and enable healthcare providers to treat a greater number of patients (11).

According to the study by Gharib et al (14), the overall survival rate of patients in the CFRT method was higher than that of HFRT. However, based on another study by Pinitpatcharalert et al (15), the overall survival of patients in the CFRT method was lower than that of HFRT. Since various studies presented different results, the current systematic review and meta-analysis aimed to estimate the overall survival of breast cancer patients after HFRT and CFRT methods, to reach a general result.

Materials and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was conducted to design the present study (16), and its protocol was registered at the PROSPERO (International Prospective Register of Systematic Reviews) and Research Registry websites.

Search strategy

The databases Web of Science, Cochrane, Scopus, PubMed, Embase, and Google Scholar Search Engine were used to search for articles published by August 20, 2025, without any language or publication time restrictions. The Medical Subject Headings (MeSH) and their equivalents were used during the searching process. Boolean Operators (AND, OR) were conducted to combine the keywords. In the end, the process included a manual search. The search strategy in the Embase database was as follows: ('breast neoplasms':ab,ti OR 'breast tumor':ab,ti OR 'breast cancer':ab,ti) AND ('overall survival':ab,ti OR 'disease-free survival':ab,ti) AND ('radiation dose hypofractionation':ab,ti OR 'radiotherapy minibeam':ab,ti OR 'conventional fractionated radiotherapy':ab,ti).

PECO components

- Population: Articles designed with the aim of investigating the effect of hypofractionated and CFRT on the survival of patients with breast cancer.
- Exposure: HFRT.
- Comparison: Women who had undergone CFRT.
- Outcomes: Overall survival and disease-free survival (DFS).

Inclusion criteria

Articles designed to examine the effect of hypofractionated and CFRT on the survival of breast cancer patients, and reported the data as percentages.

Exclusion criteria

Reviews, meta-analyses, studies that did not determine the radiotherapy dose, systematic reviews, abstracts without accessible full text, studies with low qualitative score, duplicate studies, and those that did not provide our required data were excluded.

Quality assessment

Two authors independently examined the clinical trials using the Cochrane Collaboration's Checklist for Assessing Risk of Bias in Randomized Trials (17). The checklist included seven questions, each assessing one of the critical biases of clinical trials. Each question had three options to answer; high bias risk, low bias risk, and unclear.

The quality of observational studies was assessed using the Newcastle-Ottawa Scale. This tool assigns a maximum of one star to each question, except for the comparative question. Therefore, a score of zero indicated the lowest quality, and a score of ten showed the highest quality. Then, studies with scores lower than five were considered low-quality (18).

Data extraction

Two researchers extracted data, including age, number of samples, overall survival, type of HFRT, country of origin, follow-up, continent, year, DFS, number of sessions, radiotherapy dose, and the author's name. Then, the third researcher addressed the discrepancies.

Statistical analysis

The variance of each study was calculated using the binomial distribution formula. The I^2 index was used to examine the heterogeneity between studies. Subgroup analysis was conducted to investigate the causes of

heterogeneity. A randomized effects model was used to combine the studies. Data analysis was conducted using STATA 14 software. Tests with *P* values lower than 0.05 were considered statistically significant.

Results

Overall, 1023 articles were found during the search stage. Then, 465 duplicate studies were identified and removed. The abstracts were reviewed, and 12 studies without accessible full texts were removed. Out of the 546 remaining articles, 258 lacked the required data for analysis and were excluded. Among the 288 articles that entered the next step, 251 studies were removed due to other exclusion criteria, and 37 articles remained (Figure 1).

Overall, 37 observational and clinical trials were reviewed, among which 33 articles examined the effect of HFRT on the survival rate of breast cancer patients, while the other four assessed the effect of ultra-HFRT (Table 1).

The overall survival rate of patients with breast cancer after HFRT was 83% (95% CI: 80%, 86%) and after ultra-HFRT was 85% (95% CI: 79%, 92%). Furthermore, the overall survival rate of breast cancer patients after HFRT in Asia was 79% (95% CI: 71%, 88%), Europe 83% (95% CI: 78%, 88%), America 86% (95% CI: 80%, 92%), Africa 90% (95% CI: 83%, 97%), follow-ups under five years 89% (95% CI: 84%, 93%), and follow-up equal to or longer than five years 81% (95% CI: 78%, 85%). Meanwhile, the overall survival rate of patients with breast cancer after HFRT in women aged 40 to 49 was 82% (95% CI: 70%, 94%), 50 to 59 was 85% (95% CI: 80%, 90%), 60 to 69 was 86% (95% CI: 81%, 92%), 70 to 79 was 82% (95% CI: 70%, 94%), and 80 to 89 was 59% (95% CI: 18%, 99%) (Figures 2 to 5).

The DFS rate of patients with breast cancer after HFRT and ultra-HFRT was 87% (95% CI: 83%, 91%) and 95% (95% CI: 91%, 100%), respectively. The DFS rate of patients with breast cancer after HFRT in women aged 40 to 49 was 82% (95% CI: 72%, 92%), 50 to 59 was 86% (95% CI: 76%, 96%), 60 to 69 was 97% (95% CI: 97%, 98%), 70 to 79 was 88% (95% CI: 81%, 95%), in Asia was 77% (95% CI: 68%, 86%), Europe 95% (95% CI: 93%, 97%), America 93% (95% CI: 87%, 100%), Africa 95% (95% CI: 90%, 100%), in follow-ups under five years was 94% (95% CI: 92%, 96%),

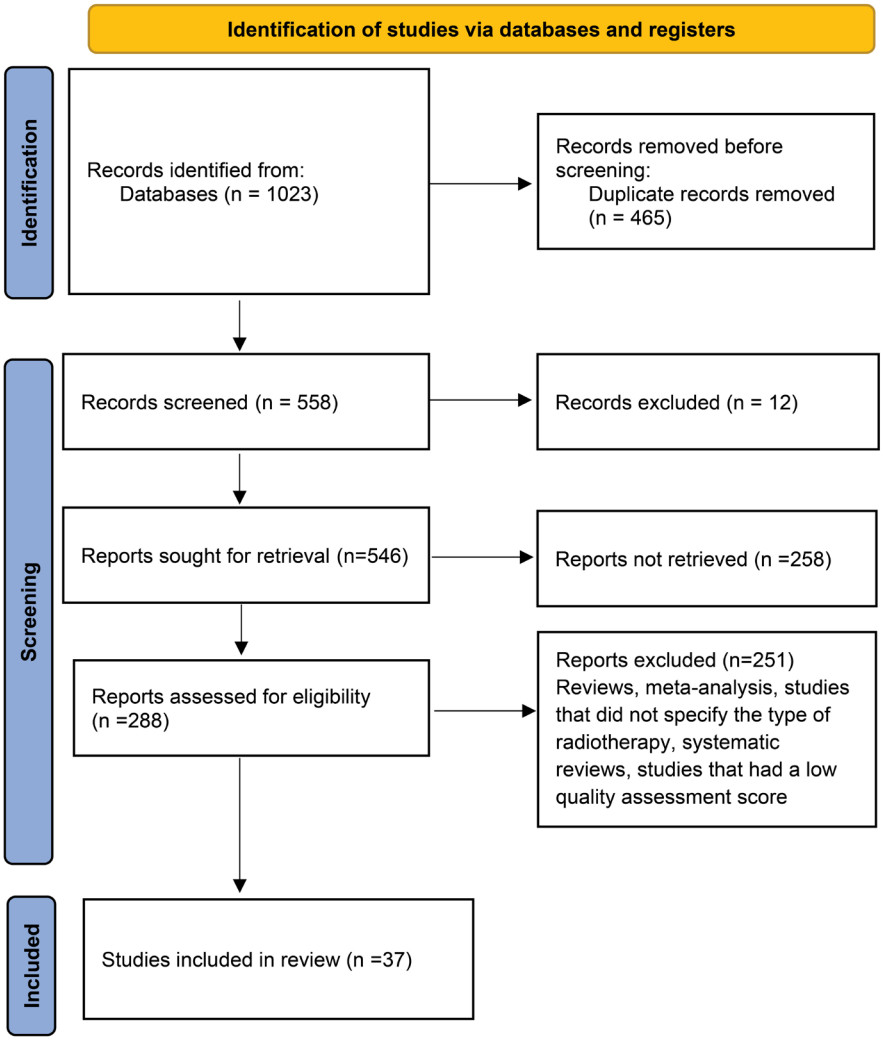

Figure 1. The PRISMA flow chart of study selection.

Table 1. Summarized information of the studies

Author, year	Continent	Country	Time of study	Sample size in HFRT group	Mean age in HFRT group	Sample size in CFRT group	Mean age in CFRT group	Follow-up (year)	HFRT dose	Fractions
Gharib F, 2025 (14)	Africa	Egypt	from January 2019 to December 2023	70	51	61	51	3	42.5 Gy	16
Zhang X, 2025 (19)	Asia	China	From Sep 2018 to July 2022	66	39	67	38	3	42.56 Gy	16
Fang M, 2025 (20)	America	Brazil	between January 2019 and February 2021	96	73.5	NR	NR	3	5.7 Gy	5
Lee J, 2024 (21)	Asia	Korea	from January 2017 to October 2022	27	52	NR	NR	2	66.8 Gy	5
Ratosa I, 2024 (22)	Europe	Slovenia	from July 2020 to September 2023	276	52	NR	NR	1	26 Gy	5
				NR	NR	NR	NR	2		
				NR	NR	NR	NR	3		
Calvo Tudela A, 2024 (23)	Europe	Spain	Between July 2020 and December 2021	160	64	NR	NR	2	26 Gy	5
Goldberg M, 2023 (24)	America	Canada	Between April 1993 and September 1996	38	NR	NR	NR	10	42.5 Gy	16
				1196	NR	NR	NR			
Chuang WK, 2022 (25)	Asia	Taiwan	Between 2012 and 2016	510	56	359	56	5	40-42.5 Gy	15-16
Chen F, 2022 (26)	Asia	China	between 2015 and 2019	903	47	107	42	4	40.05 Gy	15
Lee A, 2022 (27)	Asia	Korea	from September 2016 to December 2020	100	NR	180	NR	3	42.56 Gy	16
de Siqueira GS, 2022 (28)	America	Brazil	between 2010 to 2019	670	57	NR	NR	5	40Gy or 42.4Gy	15 or 16
				NR	NR	NR	NR	3		
De Matteis S, 2022 (29)	Europe	Italy	between October 2016 and March 2020	122	58	NR	NR	1	42.4 Gy	16
				NR	NR	NR	NR	2		
				NR	NR	NR	NR	3		
Yadav BS, 2022 (30)	Asia	India	Between January 1990 to December 2010	359	≤ 35	NR	NR	10	35–40 Gy	15
				1885	> 35	NR	NR	10		
Fodor A, 2021 (31)	Europe	Italy	From February 2009 to May 2017	1325	NR	NR	NR	5	40 Gy	15
Yadav BS, 2021 (32)	Asia	India	Between June 2013 and October 2014	50	51	NR	NR	5	34 Gy	10
Najas GF, 2021 (33)	America	Brazil	From March 2009 to December 2016	393	63.9	NR	NR	5	267 cGy and 265 cGy	15 or 16
				NR	NR	NR	NR	10		
Saksornchai K, 2021 (34)	Asia	Thailand	Between October 2009 and June 2010	37	49.8	36	50	10	43.2 Gy	16

Table 1. Continued

Author, year	Continent	Country	Time of study	Sample size in HFRT group	Mean age in HFRT group	Sample size in CFRT group	Mean age in CFRT group	Follow-up (year)	HFRT dose	Fractions
Offersen BV, 2020 (6)	Europe	Denmark, Germany and Norway	from 2009-2014	917	59	937	59	9	40-Gy	15
Tovanabutra C, 2020 (35)	Asia	Thailand	between January 2012 and December 2014	334	50.6	128	50.6	5	39.7-47.8 Gy	15-19
Sindhu M, 2020 (36)	Asia	India	Between 2013 and 2015	81	54	NR	NR	5	40 Gy	15
				NR	NR	NR	NR	3		
Tramacere F, 2022 (37)	Europe	Italy	Between 2010 and 2018	57	60	NR	NR	7	40.05 Gy or 42.56 Gy	15 or 16
Choudhary S, 2020 (38)	Asia	India	Between 2012 and 2016	34	45	NR	NR	4	39 Gy	13
				35	45	NR	NR	4	40 Gy	15
Aliyu UM, 2020 (39)	Africa	Nigeria	from January 2015 to February 2019	83	66.08	NR	NR	2	45 Gy	18
Milano MT, 2019 (40)	America	USA	2001-2011	12	43.9	NR	NR	5	50 Gy	10
				NR	NR	NR	NR	10		
				36	60	NR	NR	5		
				NR	NR	NR	NR	10		
Reboucas LM, 2019 (41)	America	Brazil	From October 2013 to October 2016	44	70.5	NR	NR	2	30 Gy	10
Sanz J, 2018 (42)	Europe	Spain	Between 1992 and 2016	486	79	NR	NR	5	30–37.5 Gy	6
Akl FM, 2018 (43)	Africa	Egypt	between January, 2015 till January, 2017	50	47	50	50	2	40 Gy	15
De Felice F, 2017 (44)	Europe	Italy	Between May 2012 and September 2015	120	58	NR	NR	2	42.5 Gy	16
Zhao S, 2017 (45)	Asia	China	Between January 2006 and December 2007	53	42.17	54	45.33	10	42.56 Gy	16
Cante D, 2017 (46)	Europe	Italy	Between 2005 and 2007	178	>50	NR	NR	10	45 Gy	20
Arcadipane F, 2016 (47)	Europe	Italy	Between 2005 and 2015	493	64	NR	NR	5	40.05 Gy or 46 Gy	15 or 20
Janssen S, 2016 (48)	Europe	Switzerland	NR	140	69	NR	NR	3	41.6 Gy	13
Min C, 2014 (49)	America	USA	Between 2000 and 2012	84	81	NR	NR	5	23 Gy	4
Janssen S, 2014 (50)	Europe	Switzerland	Between2009 and 2012	98	69	NR	NR	2	41.6 Gy	13
Pinitpatcharalert A, 2011 (15)	Asia	Thailand	From 2004 to 2006,	148	50	67	48	5	42.4-47.7 Gy	16-18
Courdi A, 2006 (51)	Europe	France	Between 1987 and 1999	115	82.7	NR	NR	5	32.5 Gy	5
Ortholan C, 2005 (52)	Europe	France	Between 1987 and 1999	150	78	NR	NR	5	32.5 Gy	5
				NR	NR	NR	NR	10		

HFRT: Hypofractionated radiotherapy; CFRT: Conventional fractionated radiotherapy; NR: Not reported.

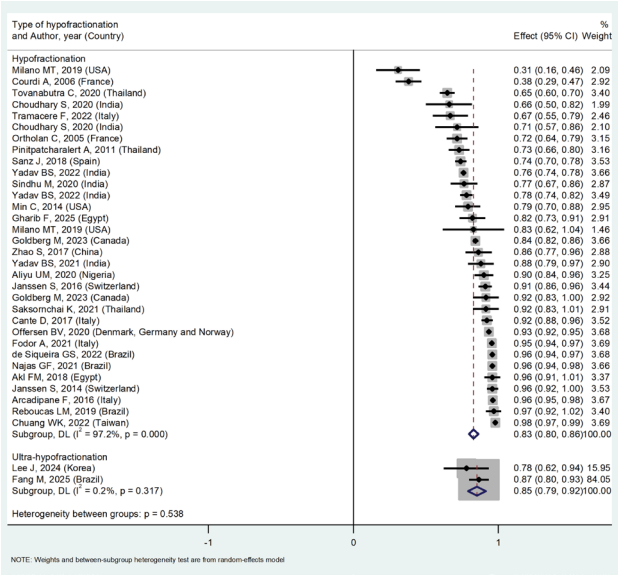

Figure 2. Forest plot showing overall survival rates for breast cancer patients after HFRT.

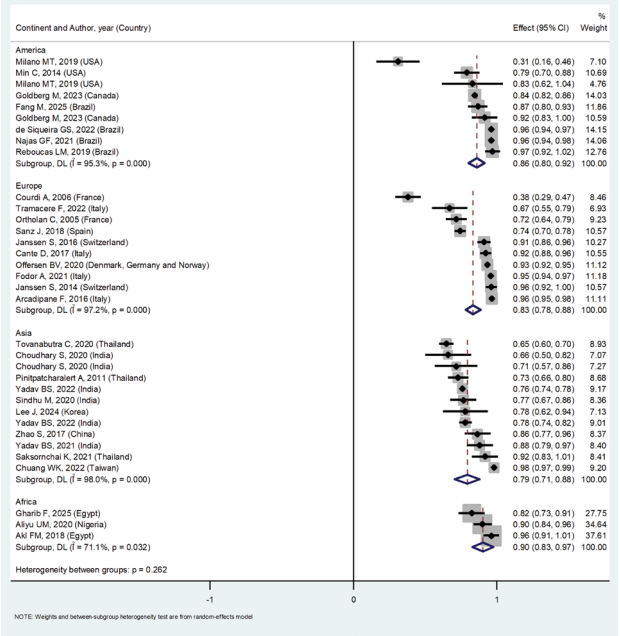

Figure 3. Forest plot showing overall survival rates for breast cancer patients after HFRT by continent.

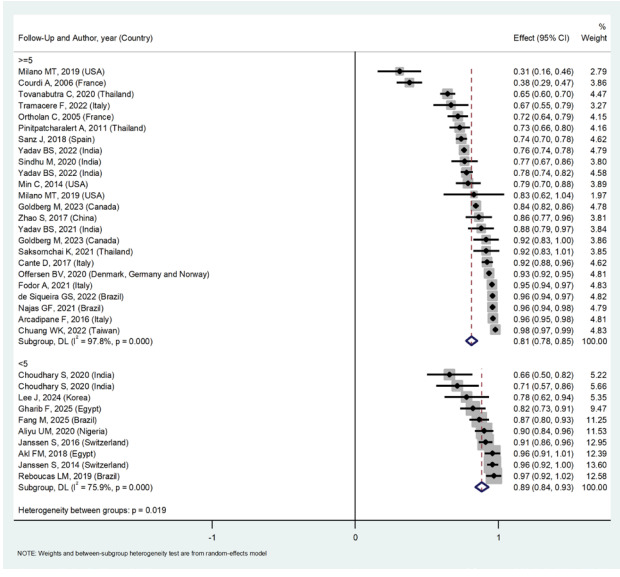

Figure 4. Forest plot showing overall survival rates for breast cancer patients after HFRT by follow-up.

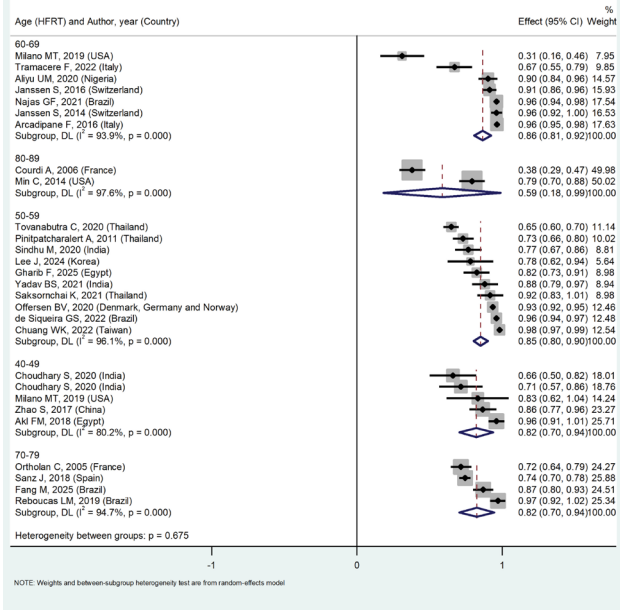

Figure 5. Forest plot showing overall survival rates for breast cancer patients after HFRT by mean age.

and in follow-ups equal to or longer than five years was 84% (95% CI: 79%, 90%) (Figures 6 and 9).

The overall survival rate of breast cancer patients after CFRT was 89% (95% CI: 85%, 94%), and their DFS rate was 86% (95% CI: 78%, 94%) (Figures 10 and 11).

Discussion

There was a slight difference in overall survival between the two methods, HFRT and CFRT. Additionally, in subgroups, the overall survival rate of breast cancer patients after HFRT in the continent of Africa and follow-ups under five years was equal to or higher than that of the CFRT method. However, the number of studies that examined the effect of CFRT was lower than those that assessed the effect of HFRT, which may be the reason for the discrepancy between the HFRT and CFRT regarding the overall survival rate. On the other hand, their DFS rates after HFRT and ultra-HFRT were higher than CFRT. Particularly, the DFS rate of patients with breast cancer after HFRT in women aged over 50 years, in follow-up periods lower than five years, and in the continents Europe, America, and Africa was higher than that of the CFRT method. The fact that HFRT has been more effective in Africa may be due to the location of the continent in terms

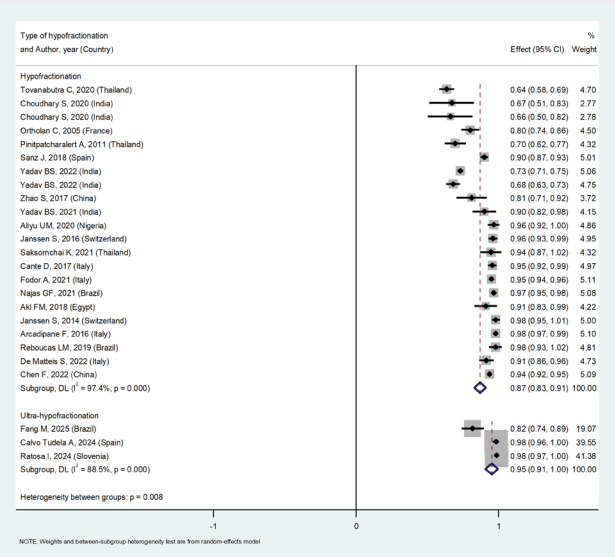

Figure 6. Forest plot showing disease-free survival rates for breast cancer patients after HFRT.

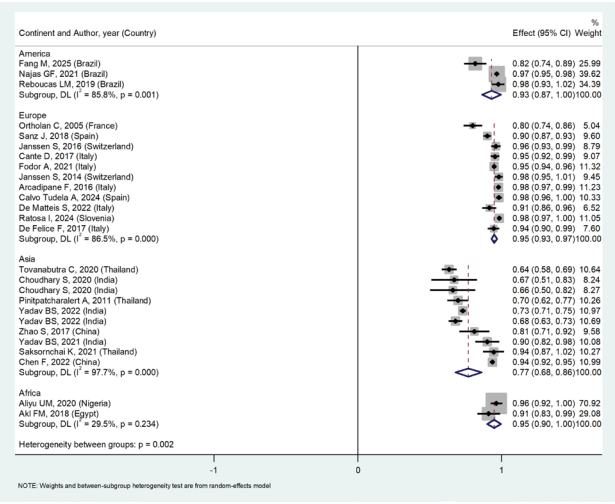

Figure 7. Forest plot showing disease-free survival rates for breast cancer patients after HFRT by continent.

of road access and facilities. Due to the lack of facilities and economic poverty, Africans use HFRT more often because it requires fewer treatment sessions. It is also possible that Africans respond better to HFRT. The study by Gharib et al demonstrated that the three-year overall survival rate for CFRT and HFRT were 88.9% and 82.3%, respectively (14). According to the study by Chuang et al, the five-year overall survival rates of HFRT and CFRT groups were 98.1% and 98.9%, respectively (25). In a study by Zhang et al, the three-year DFS in the CFRT and HFRT were 95% and 100%, respectively (19). According to the study by Lee et al, the three-year DFS in the HFRT and CFRT groups were 100% and 98.4%, respectively (43). These studies were consistent with ours and demonstrated that HFRT is more effective than CFRT in terms of DFS; however, CFRT is more effective than HFRT regarding patients' overall survival.

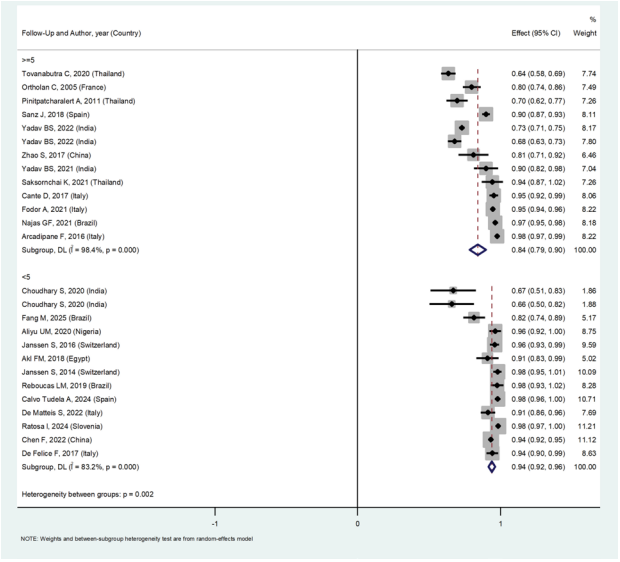

Figure 8. Forest plot showing disease-free survival rates for breast cancer patients after HFRT by follow-up.

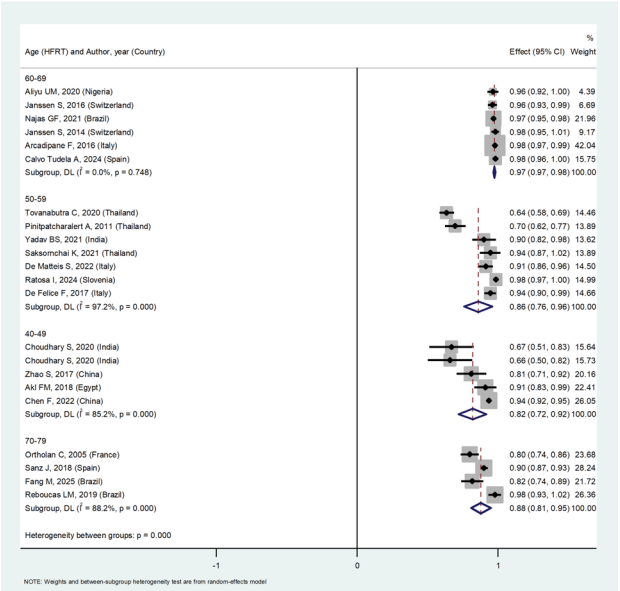

Figure 9. Forest plot showing disease-free survival rates for breast cancer patients after HFRT by mean age.

Based on the results of a meta-analysis by Roy et al on patients with neck and head cancer, there was no significant difference between the overall survival (odd ratio [OR]: 0.83, 95% CI: 0.16, 4.40) and DFS (OR: 0.87, 95% CI: 0.20, 3.83) of the HFRT and CFRT groups (53). In a meta-analysis by Zhang et al on patients with non-small cell lung cancer, the findings revealed that HFRT did not improve the patient's OR compared with CFRT after two-year (OR: 1.29; 95% CI: 0.98, 1.71) and three-year (OR: 0.55; 95% CI: 0.34, 0.87) follow-ups (54). The difference in the overall survival and DFS rates of patients in the HFRT and CFRT groups was not significant. However, the type of cancer in their investigation and our studies was different.

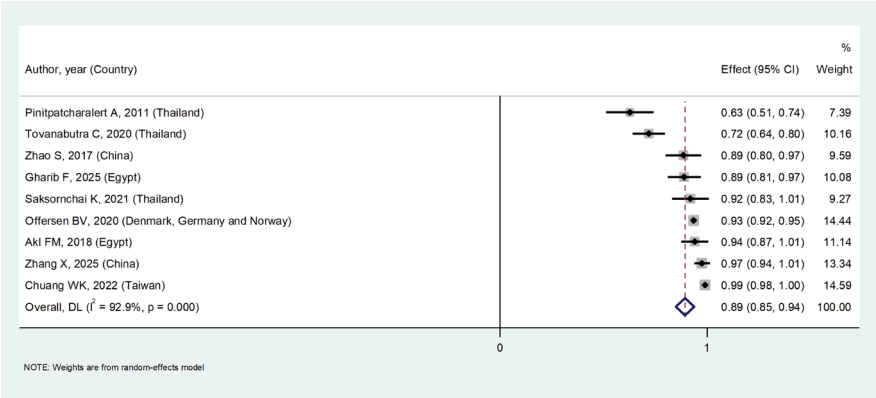

Figure 10. Forest plot showing overall survival rates for breast cancer patients after CFRT.

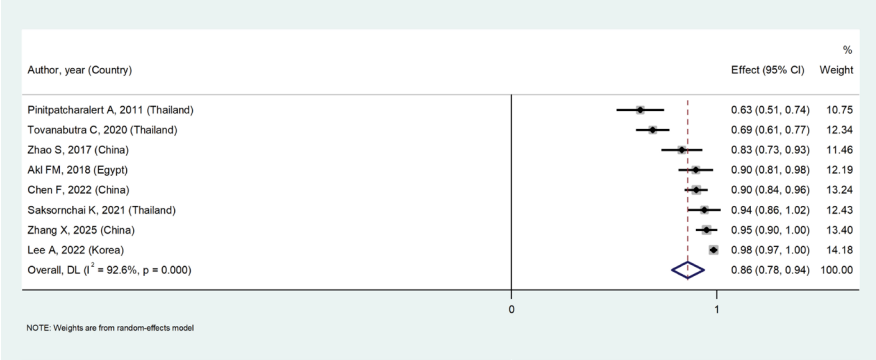

Figure 11. Forest plot showing DFS rates for breast cancer patients after CFRT.

According to the results of the meta-analysis by Royce et al on patients with localized prostate cancer, compared with the CFRT group, HFRT improved the DFS (HR: 0.86; 95% CI: 0.75, 0.99), but not the overall survival (HR: 0.84; 95% CI: 0.66, 1.07) rate (55). This study was consistent with our results; however, it was different than ours regarding the patients' sex and cancer type.

The results of a recent meta-analysis by Marta et al on eight studies indicated that there was no significant difference between the DFS (HR: 0.97, 95% CI: 0.79, 1.20) and overall survival (HR: 0.95, 95% CI: 0.83, 1.09) of patients with breast cancer in the HFRT and CFRT groups (56). Additionally, another meta-analysis by Zhou et al demonstrated that the difference between the overall survival (RR: 1.40, 95% CI: 0.56, 3.53) and DFS (RR: 1.98, 95% CI: 0.42, 9.28) rates of patients with breast cancer in the HFRT and CFRT groups was not significant (57). In a meta-analysis by Liu et al on patients with breast cancer who underwent mastectomy, there was no significant difference between the overall survival (OR: 1.08, 95% CI: 0.87, 1.33) and DFS (OR: 1.13, 95% CI: 0.91, 1.40) of the HFRT and CFRT groups (58). According to the results of a meta-analysis by Lu et al, the difference in the efficiency of HFRT and CFRT regarding the DFS (OR: 1.20, 95% CI: 1.01, 1.42) and overall survival (OR: 1.08, 95% CI: 0.93, 1.26) in patients with breast cancer was insignificant (59). In another meta-analysis by Gu et al, there was no significant difference in overall survival (HR: 1.00, 95% CI: 0.97, 1.03) between the HFRT and CFRT groups of breast cancer patients after surgery (60). In the mentioned studies, the DFS and overall survival rates of patients with breast cancer in the HFRT and CFRT groups indicated no statistically significant difference. However, it must be noted that these studies reported their results using a correlational design and based on odds ratio, hazard ratio, and risk ratio indices. However, the present meta-analysis presented the data in the form of percentages. Nonetheless, they confirm that the HFRT can be on par with the CFRT level.

Conclusion

The DFS rate of breast cancer patients in HFRT and ultra-HFRT methods was higher than that of CFRT. There was a slight difference in overall survival between the two methods, HFRT and CFRT. Considering the reduction of treatment costs for the individual and society, in addition to the number of treatment sessions in the HFRT method, and given the negligible difference in overall survival rates between the HFRT and CFRT methods, it appears that the HFRT method is the more practical method on both overall survival and DFS grounds.

Limitations of the study

Subgroup analysis based on dose was not possible. The

findings of this examination depend on the quality of the primary studies, which may be different in methodology, age, associated diseases, and follow-up duration. The studies were not evenly distributed among the continents, which limits the generalizability of our results.

Authors' contribution

Conceptualization: Mohammad Esmaeil Akbari.
Data curation: Azadeh Haghiri, Jayran Zebardast.
Formal analysis: Jayran Zebardast, Majid Shakiba.
Funding acquisition: Mohammad Esmaeil Akbari.
Investigation: Mohammad Esmaeil Akbari, Azadeh Haghiri, Jayran Zebardast.
Methodology: Mohammad Esmaeil Akbari, Jayran Zebardast.
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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD420251135054) and Research Registry website with (Unique Identifying Number (UIN) reviewregistry2040) websites. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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