The Breast 68 (2023) 133–141

Contents lists available at ScienceDirect

The Breast

journal homepage: www.journals.elsevier.com/the-breast

Decision regret in breast cancer patients after adjuvant radiotherapy

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ARTICLE INFO

Keywords:
Breast cancer
Radiotherapy
Decision regret
Physical health
Mental health
Quality of life

ABSTRACT

Purpose: Breast cancer patients often engage in shared decision-making to select an individualized treatment regimen from multiple options. However, dissatisfaction with treatment outcomes can lead to decision regret. We evaluated decision regret and physical and psychological well-being among breast cancer patients who underwent adjuvant radiotherapy and explored their associations with patient, tumor, treatment, and symptom characteristics.

Methods: This cross-sectional study involved retrospectively obtaining clinical data and data collected through interviews carried out as part of regular long-term medical aftercare. Decision regret regarding the radiotherapy was assessed using the Ottawa Decision Regret Scale, physical and psychological well-being were assessed using the PROMIS Global Health-10 questionnaire, and patients were asked about their treatment outcomes and symptoms. The questionnaire was administered 14 months to 4 years after completion of radiotherapy.

Results: Of the 172 included breast cancer patients, only 13.9% expressed high decision regret, with most patients expressing little or no decision regret. More decision regret was associated with volumetric modulated arc therapy, chest wall irradiation, use of docetaxel as a chemotherapy agent, lymphangiosis carcinomatosa, new heart disease after radiotherapy, and lower psychological well-being.

Conclusion: Although most patients reported little or no decision regret, we identified several patient, treatment, and symptom characteristics associated with more decision regret. Our findings suggest that psychological well-being influences patients' satisfaction with therapy decisions, implying that practitioners should pay special attention to maintaining psychological well-being during shared decision-making and ensuring that psychological assessment and treatment is provided after cancer therapy to deal with long-term effects of radiotherapy.

1. Introduction

Breast cancer affects at present a large proportion of the global population [1]. In Germany, every 8th woman develops breast cancer over the course of her life, with breast cancer comprising almost 30% of all cancer diagnoses among women. Approximately 69,000 German women are diagnosed with breast cancer each year, and 18,591 women died of the disease in 2018. Men, who can also develop breast cancer, comprise ~1% of the patient population [2]. Patients with breast cancer have heterogeneous tumor subtypes and disease courses, which has led to highly individualized therapy regimens that ideally are developed through shared decision-making and patients' freedom of choice.

According to national treatment guidelines, a patient's wishes for receiving therapy for cancer should be assessed through several interviews with a healthcare provider [3]. In particular, patients should be informed about the long-term consequences of adjuvant therapy as well

Abbreviations: DRS, Decision Regret Scale; BMI, body mass index; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; PROMIS, Patient-Reported Outcomes Measurement Information System; Ki67, proliferation marker; V, invasion of the venous system; L, invasion of lymphatic drainage; R, recurrence; IGRT, image-guided radiation therapy; IMRT, intensity-modulated radiation therapy; VMAT, volumetric modulated arc therapy.

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https://doi.org/10.1016/j.breast.2023.01.014
Received 22 November 2022; Received in revised form 26 January 2023; Accepted 28 January 2023
Available online 1 February 2023

as strategies for preventing or dealing with side effects, the need for medical follow-up, the possibility of rehabilitation, availability of psycho-oncological support, and patients' personal responsibilities during recovery. Among various available adjuvant therapies, post-operative radiotherapy provides local tumor control, reduces mortality, and has relatively low risks, although the individual benefit-risk ratio decreases with age [4–6]. Radiotherapy can be given via hypofractionation or conventional fractionation, with hypofractionation primarily used for cancer cases not involving the lymphatic drainage pathway [7,8]. Furthermore, intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) should preferentially be used due to their lower risk of side effects [9–11].

One possible result of the availability of alternative treatment options for different types of tumors is patient regret over therapy decisions. That is, when patients are partially responsible for choosing their therapeutic approach from a multitude of options, they may feel burdened by and anxiety over this medical decision-making, resulting in decisional conflict and less satisfaction with their healthcare decisions [12]. Decision regret is defined as feeling that one would not repeat an action under similar circumstances or feeling an undue sense of personal responsibility for a decision [13,14]. Decision regret can co-occur with lower psychological or cognitive states, such as depression, sadness, and guilt [15,16]. For example, Zeelenberg defines regret as "the negative, cognitively-based emotion that we experience when realizing or imagining that our present situation would have been better if we acted differently." [17].

When preparing for radiotherapy at our institution, patients are offered shared decision making (SDM) for establishing an equal and cooperative physician-patient relationship. SDM is a process in which both a physician and a patient share information about a disease, discuss its actual and potential effects on the patient, review the medically appropriate treatment options, and then ultimately reach a consensus together regarding the most appropriate treatment approach for that specific patient [18,19]. Depending on patient comorbidities, type of malignancy, and on tumour stage, various radiotherapy approaches are available. These include different irradiation types (i.e. external beam radiation therapy, brachytherapy, proton therapy), fractionation schemes (i.e. stereotactic radiotherapy, hyper-, hypo- or norm fractionation) and combinations with systemic therapy options (neoadjuvant, concomitant, adjuvant). All treatment alternatives with their correlated advantages and disadvantages, as well as therapy associated inherent benefits and risks uncover numerous opportunities for SDM.

However, not all patients achieve their desired therapeutic outcomes, which can lead to decision regret. To better understand decision regret among breast cancer patients, we administered a questionnaire through a telephone interview to collect self-reported information on patients' mid-to long-term decision regret, physical and psychological well-being, and symptoms experienced after adjuvant radiotherapy. We evaluated experienced decision regarding the radiotherapy regret using the Ottawa Decision Regret Scale (DRS), physical and psychological well-being using the Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health-10 questionnaire, and therapy outcomes and symptom burden using additional questions [20].

2. Methods

2.1. Study design

This cross-sectional study involved retrospectively obtaining clinical data and data collected through interviews performed as part of regular long-term medical follow-up. Clinical data between 2018 and 2020 was obtained from the clinical information system of our University Medical Center, and the questionnaire commenced April 7, 2022. The questionnaire was administered 14 months to 4 years (median = 2.8 years) after patients completed adjuvant radiotherapy.

All study collaborators were subject to general confidentiality, and all data were kept confidential according to current national regulations and laws. To protect data during telephone interviews, we confirmed the identity of patients at the beginning of the interview by requesting personal data (e.g., name, date and place of birth). Patients were informed in advance of their rights, especially their right to information, deletion, and revocation, as well as the scope, purpose, and voluntary nature of the study. Participation by the patients was based on verbal consent. Questionnaire data were pseudonymized, anonymized, and protected from access by unauthorized persons by technical barriers (e.g., password protection). Study quality in terms of reliability, objectivity, and validity was ensured by following best practices in data collection, analysis, and reporting.

2.2. Study population

Patients who underwent adjuvant radiotherapy for breast cancer at the Department of Radiation Therapy and Radiation Oncology, University Medical Center between May 2017 and April 2021 were considered for inclusion in the study. This population was selected because patients underwent long-term follow-up care, and complete clinical data were also available. Patients were included in this study only if they voluntarily provided verbal informed consent before completing the questionnaire, were able to conduct the telephone interviews by themselves, were not under time pressure, were of legal age, spoke and understood German, and had no cognitive or neurological impairments. Patients with tumors of all histological subtypes were included. Patients were excluded if they had second time implant replacement after initial mastectomy with implant replacement (n = 2), developed cancer after breast augmentation (n = 1), or had squamous cell carcinoma (n = 1).

Clinical data regarding gender, age, number of days of hospital stay for the operation, date of diagnosis, ICD-10 diagnosis code, and TNM classification, early toxicity according to the discharge report using CTCAE and RTOG Score, and previous diseases were obtained from the clinical information system. Regarding tumor classification, we obtained information on the degree of differentiation (G1-G3), tumor receptor status, clinical and histological subtypes. Lobular carcinoma in situ and lobular intraepithelial neoplasia normally do not require the use of radiotherapy and only those with radiotherapy and this diagnosis were included here. In addition, local and distant recurrence and metastasis were recorded, but the individual manifestations of the variables were pooled for improved statistical analysis purposes. Regarding surgical options, we obtained information on operation types, operation date, whether the operation involved the lymphatic drainage pathway (sentinel node biopsy or axillary dissection), and the total number and number of positive lymph nodes obtained. Regarding systemic therapy, we obtained information on the timing of chemotherapy (none, neoadjuvant, adjuvant, or neoadjuvant plus adjuvant), first and last dates of chemotherapy, duration of chemotherapy, degree of regression based on Sinn et al. [21] chemotherapeutic agent(s), use of antihormone therapy and, and use of antibody therapy and antibodies. Regarding radiotherapy, we obtained information on the timing of irradiation, date of treatment plan, first and last dates of radiotherapy, total or partial breast irradiation, chest wall irradiation, and regional lymph node irradiation, total radiation dose, fraction dose, cumulative dose, and fraction dose of radiation boost targeted at the tumor bed.

2.3. Questionnaire development and implementation

We developed a questionnaire to collect self-reported information on mid-to long-term decision regret, physical and psychological well-being, and therapy outcomes and symptoms experienced by breast cancer patients after adjuvant radiotherapy (see Table 7 Supplemental Materials) [22]. The questionnaire was based on guidelines and recommendations and was designed to meet the highest scientific standards and minimize potential bias [23–25]. After reviewing the literature, we chose to

administer a questionnaire via telephone interview, as communication over the telephone creates an equal distance between the patient and interviewer, which was deemed most appropriate for answering our research questions [26].

During the interview, patients were first requested for their general demographic information, height and weight, and occurrence of new heart disease or second cancer after adjuvant radiotherapy. Patients were then asked about late symptoms experienced after radiotherapy. Pain, skin problems, such as itchy, dry or scaly skin, unusual discoloration or skin rash, and arm mobility were assessed using items from the EORTC-QLQ BR23 [27], and existing lymphedema of the arm was assessed using questions adopted from the EORTC-QLQ BR23 and CTCAE-PRO [28]. Shortness of breath and the occurrence of rib fractures, were also assessed. Next, physical and psychological well-being were assessed using the PROMIS Global Health-10 questionnaire, which consists of 10 items and serves to compare the respondent's quality of life with that of the general population. Responses were used to calculate Global Physical Health and Global Mental Health scores, which were converted to percentages [29]. Finally, experienced decision regret regarding radiation therapy was measured using the Ottawa DRS, a five-item scale with demonstrated internal consistency, reliability, and validity [30,31]. As there is no German version of the questionnaire, we translated the questionnaire using forward-backward translation. DRS scores range from 0 to 100 with 0 representing no regret and 100 representing the highest degree of regret. Patients were made aware of the fact that the questionnaire section containing the Decision Regret Score referred to radiotherapy only. Overall questionnaire validity was achieved by strict definitions of item goals, expert consensus on the construction and organization of content, and the use of pre-existing questionnaires and item pools as guidance (for an overview see Table 6. Supplemental Materials).

The questionnaire was administered by two trained final year medical students under the supervision of a senior physician during telephone interviews with patients as a part of their long-term follow-up care. The interview was conducted using an interview guide that included a standardized introduction and conclusion. There were no time constraints on questionnaire completion. Although questionnaire items were designed to be clearly worded, interviewers were provided with standardized responses to common patient questions.

2.4. Statistical analysis

As neither DRS score (Kolmogorov-Smirnov and Shapiro-Wilk tests, $p < 0.001$, df = 172) nor Global Physical Health or Global Mental Health scores (Kolmogorov-Smirnov and Shapiro-Wilk tests, $p < 0.005$, df = 172) were normally distributed, we conducted Mann-Whitney U tests for dichotomous variables and Kruskal-Wallis tests for variables with more than two categories. During the test procedure, groups were compared in the statistical test. This group classification was based on the particular answer options and configurations of the variables. Correlations between variables were also computed using Spearman rho correlation coefficients. Due to the large number of tests, Bonferroni correction was applied to minimize alpha inflation. Whether treatment characteristics and symptom burden were predictive of DRS score was tested using multiple linear regression. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 28.0.1.1; IBM Corp., Armonk, NY).

3. Results

Of 315 potentially eligible breast cancer patients, 45 did not receive adjuvant radiotherapy, 15 died after receiving radiotherapy, 60 could not be contacted, and 19 declined to participate. In total, 172 patients fully completed the interview (Fig. 1).

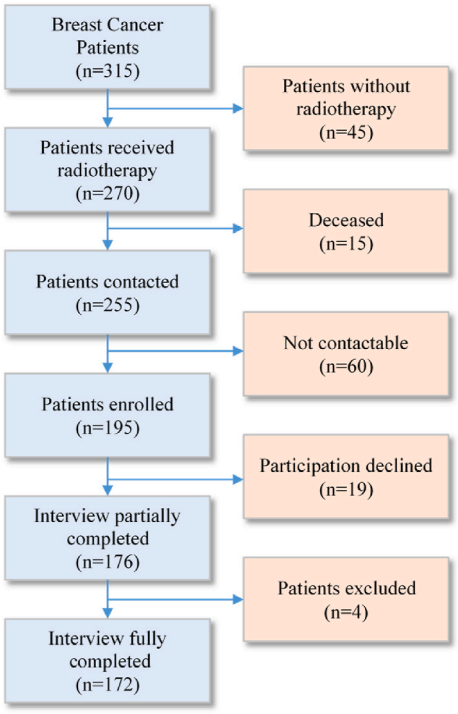

Fig. 1. Flow diagram depicting the patient inclusion process.

3.1. Patient, tumor, treatment, and symptom characteristics

The median age of the patients was 63 years (standard deviation (SD), 0.9; range, 31–89) at the time of the interview and were mostly

Table 1
Patient characteristics.

Patient and tumor characteristics	% (n = 172)
Sex	
Female	99.4%
Male	0.6%
Age	
Mean	62 years
Range	31.48–89.49 years
Mean height	1.66 m
Mean weight	72 kg
Mean BMI	25,36 kg/m^2
Side of affected breast	
Left	51.7%
Right	41.3%
Bilateral	7.0%
Location in %	
C50.1 Malignant neoplasm: Central portion of breast	4.1
C50.2 upper inner quadrant	11.6
C50.3 lower inner quadrant	4.7
C50.4 upper outer quadrant	34.3
C50.5 lower outer quadrant	7.0
C50.8 more than one area	8.7
C50.9 unspecified	27.9
D05.1 Intraductal carcinoma in situ of breast	1.2
D05.9 Carcinoma in situ of breast, unspecified	0.6
Histological classification in %	
Carcinoma NST	66.7
Invasive lobular carcinoma	14.5
Others	18.8
Tumor grade in %	
Low grade	15.1
Intermediate	35.5
High	31.4
Inflammatory carcinoma	2.9
Metastasis (M1)	2.9
Recurrences	9.9

women (99.4%). Patients received radiotherapy for an average of 28 days (SD, 12.4) (see Table 1). Patients' median DRS score was 10 with a range of 55 (minimum 0, maximum 55). When divided into three grades of decision regret based on a previous study [30], 27.9% of patients did not express decision regret (DRS score of 0), 58.2% expressed mild decision regret (DRS score of 1–25), and 13.9% expressed high decision regret (DRS score >25). The Median of the Global Physical Health and Global Mental Health scores were 70% (range 75%, minimum 25%, maximum 100%) and 65% (range 70%, minimum 25%, maximum 95%). Additional treatment and symptom characteristics are shown in Table 6 included in the supplementary material.

3.2. Associations between patient, tumor, symptom, and treatment characteristics and DRS score

Docetaxel administration during chemotherapy, Global Mental Health score, VMAT use, occurrence of new heart disease after radiotherapy, and the presence of inflammatory carcinoma were associated with a higher DRS score (Table 2). Global mental health score's negative spearmen's rho reflects that global mental health decreases and DRS increases. All other variables listed in the method section, displaying no statistical significance ($p > 0.05$) were not discussed further.

3.3. Associations between patient, tumor, treatment, and symptom characteristics and Global Physical Health score

A lower Global Physical Health score was significantly associated with greater body weight, a higher body-mass index (BMI), a lower Global Mental Health score, early toxicity after radiotherapy, new heart disease after radiotherapy, receiving chemotherapy during the neo-adjuvant plus adjuvant or adjuvant period, more arm or shoulder pain, more pain around the affected breast, greater limitations in arm

Table 2
Associations between patient, tumor, treatment, and symptom characteristics and DRS score.

Characteristic	*N*		Spearman's rho	*p*-value	
Age	172		0.91	0.233	
Height	168		−0.92	0.237	
Weight	167		−0.006	0.942	
BMI	168		−0.23	0.767	
Diagnosis code	172		−0.43	0.573	
HER2 status in Percentage	157		0.18	0.824	
Ki67 status in Percentage	149		−0.72	0.385	
ER status in Percentage	157		−0.45	0.572	
PR status in Percentage	157		−0.007	0.929	
Docetaxel	**95**		**0.556**	**0.048**	
Total cumulative dose	95		0.105	0.312	
Global Physical Health score	172		−0.148	0.053	
Global Mental Health score	**172**		**−0.173**	**0.023**	
Early toxicity transcribed in numbers	172		0.006	0.936	
Pre-existing conditions transcribed in numbers	172		−0.127	0.098	
Characteristic	***n***	**Middle rank**	**Wilcoxon W**	**Mann-Whitney U**	***p*-value Mann-Whitney U**
Triple-negative breast cancer	21	85.69	1799.5	1568.5	0.903
Invasion of the venous system	3	92.83	278.5	272.5	0.479
Invasion of lymphatic drainage	26	77.92	2026	1675	0.751
Recurrence	16	78.13	1250	1114	0.633
Metastasis	5	124.13	14381.5	185.5	0.120
IMRT	147	85.79	12611.5	1733.5	0.646
VMAT	**50**	**96.49**	**8870.5**	**2200.5**	**0.015**
Chest wall irradiation	9	102.11	13,959	593	0.327
Irradiation after mastectomy	25	56.88	1365	1065	0.787
Partial breast irradiation	10	67.95	679.5	624.5	0.385
Co-irradiation for lymphatic drainage	43	92.71	3986.5	3040.5	0.297
Antihormonal therapy	126	86.30	10,874	2873	0.930
Antibody therapy	32	84.20	2694.5	2166.5	0.769
Heart disease	**17**	**110.71**	**1882**	**1729**	**0.032**
Rib fracture	9	109	981	936	0.157
Inflammatory carcinoma	**5**	**133**	**665**	**650**	**0.031**
Characteristic	***n***	**Kruskal-Wallis H**	**Df**	***p*-value Kruskal-Wallis test**	***p*-value after Bonferroni correction**
Age over 60 years	172	42.560	5	0.763	–
Tumor grade	172	3.329	5	0.649	–
Histological subtype	159	13.527	11	0.260	–
Operation type	170	4.392	4	0.356	–
Operation involving lymphatic drainage	165	1.469	2	0.480	–
Positive lymph nodes	123	2.714	6	0.844	–
Timing of radiation therapy	170	1.927	2	0.383	–
Total dose	170	10.472	11	0.489	–
Fraction dose	170	6.306	11	0.852	–
Fraction	171	4.517	11	0.952	–
Total cumulative dose	95	8.623	11	0.657	–
Timing of chemotherapy	172	0.876	3	0.831	–
Arm or shoulder pain	172	0.208	4	0.995	–
Pain around the affected breast	172	4.489	4	0.303	–
Skin problems around the affected breast	172	22.497	11	0.021	0.251
Arm or hand swelling	172	11.106	4	0.025	0.180
Limited arm mobility	172	7.942	4	0.094	–
Shortness of breath	172	4.171	4	0.383	–
Global Physical Health score	172	9.919	15	0.825	–
Global Mental Health score	172	24.710	14	0.038	0.532

Note: Bold indicates statistical significance. $p \leq 0.05$ was considered to be significant.

Table 3
Associations between patient, tumor, treatment, and symptom characteristics and Global Physical Health score.

Characteristic	*n*	Spearman's rho	*p*-value
Age	172	0.045	0.559
Height	168	−0.220	0.777
Weight	**167**	**−0.169**	**0.029**
BMI	**168**	**−0.157**	**0.043**
Diagnosis code	172	−0.121	0.95
HER2 status in Percentage	157	−0.009	0.907
Ki67 status in Percentage	149	−0.080	0.330
ER status in Percentage	157	−0.009	0.915
PR status in Percentage	157	0.272	0.060
Docetaxel	22	0.125	0.566
Total cumulative dose	95	0.142	0.168
Global Mental Health score	**172**	**0.564**	**<0.001**
Early toxicity transcribed in numbers	**172**	**0.139**	**0.014**
Pre-existing conditions transcribed in numbers	172	−0.070	0.360

Characteristics	***N***	**Middle rank**	**Wilcoxon W**	**Mann-Whitney U**	***p*-value Mann-Whitney U**
Triple-negative breast cancer	21	90	1890	1659	0.578
Invasion of the venous system	3	102.83	308.5	302.5	0.268
Invasion of lymphatic drainage	26	74.96	1949	1598	0.944
Recurrence	16	77.59	1241.5	1105.5	0.603
Metastasis	5	74.5	298.0	288.0	0.624
IMRT	146	86.11	12658.5	1780.5	0.803
VMAT	50	86.49	9370.5	2700.5	0.534
Chest wall irradiation	9	179.32	46005.5	1752.5	0.298
Irradiation after mastectomy	43	87.72	3772	2826	0.791
Partial breast irradiation	10	75.55	755.5	700.5	0.751
Co-irradiation for lymphatic drainage	79	80.96	6007	2926	0.584
Anti-hormonal therapy	**126**	**81.56**	**10,277**	**2276**	**0.031**
Antibody therapy	32	83.55	2673.5	2145.5	0,709
Heart disease	**17**	**60.85**	**1034.5**	**881.5**	**0.025**
Rib fracture	9	77.50	697.5	652	0.576
Inflammatory carcinoma	5	108.3	541.5	526.5	0.318

Characteristic	***N***	**Kruskal-Wallis H**	**df**	***p*-value Kruskal-Wallis test**	***p*-value after Bonferroni correction**
Age over 60 years	172	58.732	50	0.86	–
Tumor grade	172	4.970	5	0.420	–
Histological subtype	157	2.128	11	0.831	–
Operation type	149	48.281	4	0.156	–
Operation involving lymphatic drainage	159	22.780	2	0.545	–
Positive lymph nodes	157	15.721	6	0.252	–
Timing of radiation therapy	157	34.961	2	0.282	–
Total dose	170	6.637	11	0.679	–
Fraction dose	165	1.213	11	0.173	–
Fraction	123	7.809	11	0.424	–
Total cumulative dose	95	20.099	11	0.127	–
Timing of chemotherapy	**172**	**10.486**	**3**	**0.015**	**0.045**
Arm or shoulder pain	**172**	**17.163**	**4**	**0.002**	**0.008**
Pain around the affected breast	**172**	**19.012**	**4**	**<0.001**	**<0.001**
Skin problems around the affected breast	172	7.124	4	0.129	–
Arm or hand swelling	172	9.652	4	0.047	0.339
Limited arm mobility	**172**	**24.317**	**4**	**<0.001**	**<0.001**
Shortness of breath	**172**	**15.092**	**4**	**0.005**	**0.021**
Global Mental Health score	**172**	**64.077**	**14**	**<0.001**	**0.014**

Note: Bold indicates statistical significance. $p \leq 0.05$ was considered to be significant.

mobility, and more shortness of breath (Table 3).

3.4. Associations between patient, tumor, treatment, and symptom characteristics and global mental health score

A lower Global Mental Health score was associated with greater body weight, a higher BMI, ICD-10 code for Malignant neoplasm of central portion and lower inner quadrant of the breast, lower cumulative dose of radiotherapy, a lower Global Physical Health score, early toxicity after radiotherapy, use of hormone therapy, the occurrence of new heart disease after radiotherapy, a cumulative radiotherapy dose >50 Gy, more arm or shoulder pain, more pain around the affected breast, and greater limitations in arm mobility (Table 4).

3.5. Factors predicting decision regret

To determine whether symptom burden or treatment characteristics as independent variables predicted DRS score, we performed standard multiple linear regression assessing interaction regression, as simple regression can only provide coherent and conclusive results for a limited number of independent variables [32]. First, we performed multiple regression analyses on the variables group-wise. These statistical tests did not show any significance and are not discussed in more detail for reasons of clarity. In another process we only included variables that were significantly associated with DRS score in the statistical analysis into the regression models. The variables were included using a standard procedure in which all independent variables were included. The model including symptom burden variables was statistically significant ($F = 3.068$, $p = 0.011$), with an R of 0.291 and adjusted R^2 of 0.057, indicating a low association between symptom burden variables and DRS score (Table 5). The Global Mental Health score was significantly associated with DRS score. The model including treatment variables was also statistically significant ($F = 4.007$, $p = 0.010$), with an R of 0.347 and adjusted R^2 of 0.120, indicating a low association between

Table 4
Associations between patient, tumor, treatment, and symptom characteristics and Global Mental Health Score.

Characteristic	*n*	Spearman's rho		*p*-value	
Age	172	0.032		0.679	
Height	168	−0.011		0.886	
Weight	**167**	**−0.174**		**0.024**	
BMI	**168**	**−0.192**		**0.013**	
Malignant neoplasm of lower-inner quadrant of breast	**17**	**−0171**		**0.028**	
Malignant neoplasm of central portion of breast	**12**	**−0.177**		**0.020**	
HER2 status	157	−0.019		0.816	
Ki67	149	−0.046		0.580	
ER status	95	0.060		0.457	
PR status	95	−0.083		0.301	
Docetaxel	22	0.128		0.570	
Total cumulative dose	**95**	**0.236**		**0.021**	
Global Physical Health score	**172**	**0.564**		**<0.001**	
Early toxicity transcribed in numbers	**172**	**0.139**		**0.015**	
Pre-existing conditions transcribed in numbers	172	−0.09		0.235	
Characteristic	***n***	**Middle rank**	**Wilcoxon W**	**Mann-Whitney U**	***p*-value Mann Whitney U**
Triple-negative breast cancer	21	82.60	1734.5	1503.5	0.847
Invasion of the venous system	3	102.83	308.5	302.5	0.268
Invasion of lymphatic drainage	26	74.96	1949	1598	0.944
Recurrence	16	77.59	1241.5	1105.5	0.603
Metastasis	5	51.75	207	197	0.155
IGRT	104	69.5	7228.5	1768.5	0.620
IMRT	146	86.11	12658.5	1780.5	0.803
VMAT	50	86.49	9370.5	2700.5	0.534
Chest wall irradiation	9	89.99	809	764	0.833
Irradiation after mastectomy	24	48.83	1172	872	0.111
Partial breast irradiation	10	93.25	11787.5	612.5	0.343
Co-irradiation for lymphatic drainage	43	87.72	3772	2826	0.791
Anti-hormonal therapy	126	84.96	2703.5	10407.5	0.498
Antibody therapy	32	85.34	2731	2203	0.883
Heart disease	**17**	**54.76**	**931**	**778**	**0.005**
Rib fracture	9	80.33	723	678	0.701
Inflammatory carcinoma	5	110.7	14324.5	296.5	0.267
Cumulative dose over 50 Gy	**11**	**33.60**	**280.5**	**214.5**	**0.002**
Characteristic	***n***	**Kruskal-Wallis H**	**Df**	***p*-value Kruskal-Wallis test**	***p*-value after Bonferroni correction**
Age over 60 years	172	58.732	50	0.186	–
Tumor grade	172	4.970	5	0.420	–
Histological subtype	159	11.093	14	0.679	–
Operation type	170	6.637	4	0.156	–
Operation involving lymphatic drainage	165	1.213	2	0.545	–
Positive lymph nodes	123	7.809	6	0.252	–
Timing of radiation therapy	170	2.535	2	0.282	–
Total dose	170	8.277	14	0.874	–
Fraction dose	170	9.088	14	0.825	–
Fraction	171	9.499	14	0.798	–
Timing of radiation therapy	170	2.535	2	0.282	–
Total cumulative dose	95	16.969	13	0.201	–
Timing of chemotherapy	172	1.293	3	0.731	–
Arm or shoulder pain	**172**	**12.509**	**4**	**0.014**	**0.010**
Pain around the affected breast	**172**	**16.188**	**4**	**0.003**	**0.012**
Skin problems around the affected breast	172	2.065	4	0.039	0.251
Arm or hand swelling	172	11.887	4	0.018	0.346
Limited arm mobility	**172**	**13.779**	**4**	**0.008**	**0.013**
Shortness of breath	172	9.787	4	0.044	0.225
Global Physical Health score	**172**	**64.077**	**15**	**<0.001**	**0.015**

Note: Bold indicates statistical significance. $p \leq 0.05$ was considered to be significant.

Table 5
Linear regression models including symptom burden and treatment variables for predicting DRS score.

	Nonstandardized regression coefficient	Standard error	Standardized beta coefficient	*p*-value	Tolerance
Symptom burden variables					
Constant DRS score when all variables are at zero)	22.97	4.89	–	<0.001	4.70
Inflammatory carcinoma	10.83	6.03	0.13	0.074	1.80
Heart disease	5.81	3.46	0.13	0.095	1.68
Arm or hand swelling	−1.54	1.02	−0.12	0.131	−1.52
Skin problems around the affected breast	1.27	1.03	0.09	0.218	1.23
Global Mental Health score	**−0.16**	**0.07**	**−0.17**	**0.032**	**−2.17**
Treatment variables					
Constant DRS score when all variables are at zero)	7.165	0.631	–	<0.001	11.353
Total cumulative dose	0.013	0.058	0.22	0.825	0.222
Chest wall irradiation	**7.937**	**2.667**	**0.301**	**0.004**	**2.976**
VMAT	0.730	0.586	0.127	0.216	1.245

Note: Bold indicates statistical significance. $p \leq 0.05$ was considered to be significant.

treatment variables and DRS score. Other than the Global Mental Health score, chest wall irradiation also had a significant association with DRS score, with a higher significance level as it had a P value of 0.004. Neither tolerance nor variance inflation factor values indicate multicollinear processes, although the independent variables included in the model share common benchmarks.

4. Discussion

Limited number of studies have been conducted to present with the objective of evaluating decision regret among cancer patients after irradiation of various tumor locations [33,34]. In the present study, we examined associations between patient, tumor, treatment, and symptom characteristics and self-reported decision regret, physical well-being, and psychological well-being among breast cancer patients who received adjuvant radiotherapy. We found that 27.9% of patients did not express decision regret and 58.2% expressed mild decision regret. Thus, most patients experienced a low degree of regret over their therapy decisions, consistent with previous findings [35].

Regarding type of irradiation, our findings surprisingly suggest that VMAT was associated with higher decision regret, although 70% of the patients in our analysis received irradiation in IMRT technique. While both the inverse planning modalities lead to improved coverage, better conformity index (CI), and better homogeneity index (HI) and decreases high dose volumes in OARs, an increment in low-volume irradiation of heart, lungs, and body was reported in previous studies that focused on VMAT. Further, in comparison to IMRT, VMAT has been observed to perform better with regard to coverage and decreasing lung irradiation with comparable heart irradiation in patients, especially of left-sided breast cancer after modified radical mastectomy [36,37]. There might be confusing factors regarding the significance of a correlation between VMAT and higher decision regret. Such factors could include toxicity rates or increased target volumes. There might be other factors related to baseline features, such as disease prognosis or concomitant treatments. This finding is subject of bias, due to its retrospective nature and prospective assessments are required to elucidate this result. Patients who received docetaxel as a chemotherapeutic agent stated more decision regret. This finding was not unexpected, as patients receiving docetaxel often experience short- and long-term adverse effects [3]. However, significant associations between type of surgery and decision regret was not observed, and this had also been noted by similar previous studies [37]. In addition, the use of anti-hormone therapy was associated with lower physical well-being.

A higher cumulative dose of radiotherapy was associated with a higher Global Mental Health score. This could indicate that the higher the cumulative dose, the better patients' psychological well-being. One interpretation of the relationship between cumulative radiotherapy dose and psychological well-being could derive from the perception of a better protection against recurrences.

Thus, further investigation of this relationship with a larger number of participants could be more informative. We found no associations between radiotherapy technique and physical well-being, in contrast to previous findings, which do indicate radiotherapy especially volume dose relations to be a factor influencing physical wellbeing [38]. Furthermore, we found no associations between radiotherapy technique and psychological well-being, consistent with previous findings [39].

A higher Global Mental Health score was associated with a lower DRS score, indicating that patients with better psychological well-being had lower decision regret. Furthermore, Global Mental Health score was the only variable that significantly predicted DRS score in a multiple linear regression model including symptom burden variables. Thus, it is important to follow up patients' psychological well-being and provide long-term mental health assessment and treatment after breast cancer therapy [40]. Although it is not yet clear which psychological factors increase decisional conflict and subsequent regret, previous research points toward patients' knowledge of therapy as an influential factor. Degner and Sloan showed in their analysis that women who experienced lower satisfaction with preparatory information were more likely to experience moderate to strong regret, compared to those experiencing no regret. In the light of these findings, is important that women are provided with adequate information concerning all aspects and consequences of breast reconstruction, and that sufficient measures are taken to ensure that women have processed and understood the available information [41].

Long-term symptoms following radiotherapy, including shortness of breath, arm or shoulder pain, pain around the affected breast, and limited arm mobility, were associated with lower physical well-being, which was in turn associated with poor psychological well-being. Thus, breast cancer patients must be prepared for these known outcomes of radiotherapy, which can restrict daily function, and should receive psychological assessment and treatment over the long term [42–44]. Such functional physical limitations can lead to less participation in social life, which has a negative psychological impact and is a frequently considered a secondary consequence of breast cancer [45]. This interrelatedness of physical health, mental health, and social relationships is consistent with the biopsychosocial health model, which posits that the interaction of body, soul, and social environment is important for the processing of illness [46]. Furthermore, in agreement with our findings, several previous studies show that quality of life is related to decision regret [47,48]. Although breast cancer survivors may return to a high quality of life, fatigue is the main predictor of low quality of life [49].

Some of the results of our study could be logically inferred. For example, the occurrence of new heart disease after radiotherapy was associated with lower physical well-being and more decision regret, which is understandable because heart disease, especially in old age, has a large impact on quality of life and can be directly related to irradiation [50]. Patients who had inflammatory carcinoma also showed more decision regret, which could be related to the pain associated with this condition. Also, patients with arm or hand swelling reported more decision regret, although patients with the highest amount of arm swelling ($n = 6$) testified low decision regret, which could be due to these patients receiving more attention for this common post-radiotherapy symptom and the availability of effective treatments, such as lymphatic drainage. Furthermore, a higher BMI was associated with lower physical well-being. Although the causative nature of this relationship cannot be determined with our study design, it is possible that the patients' altered psychological well-being might have resulted in changes in feeding and dietary habits leading to increment in the BMI index, which, in turn, might have led to worse physical well-being [51]. Our study has some limitations that should be addressed. The limited number of 172 patients displaying heterogeneous histological subtypes and disease courses, make a considerable impact on detecting significant associations. Due to the nature of a cross-sectional study, delay between radiotherapy and participation in an interview might lead to recall bias. Some patients may have had difficulties with communication and attention, which may have influenced their responses in the interview. In addition, patients may have tended to give more positive responses, and patients in better health may have been more likely to answer the phone or have the will to participate in the interview, thus introducing agreement bias and self-selection bias, respectively. Additional qualitative answers could offer a dynamic approach to the study, as it would give the researcher and interviewers an opportunity to aptly follow-up on the answers offered by the interviewees in real time, thereby generating valuable discussions around the subject, an aspect that is hardly possible with structured surveys and questionnaire. Patient-reported outcome measures (PROMs) as Breast-Q in combination with photo evaluation documenting subjective breast appearance could be valuable instruments for prospective decision regret analysis evaluations. In conclusion, this study is one of the first to evaluate decision regret and physical and psychological well-being in breast cancer patients who underwent adjuvant radiotherapy and to explore their associations with patient,

tumor, treatment, and symptom characteristics. We found most breast cancer patients reveal little or no decision regret. However, more decision regret was associated with VMAT and the use of docetaxel or anti-hormonal therapy. Our findings also suggest that psychological well-being influences patients' satisfaction with therapy decisions, implying that practitioners should pay special attention to maintaining psychological well-being during shared decision-making and ensuring that psychological assessment and treatment is provided after therapy to deal with long-term consequences. Healthcare providers should also identify patients' priorities in everyday life and plan multimodal therapy accordingly, with adequate education and follow-up with regard to radiotherapy-related side effects. Future investigations of psychological aspects of decision regret, its social context, and the impact of combined therapies will help contextualize these results and further enhance our understanding of the origin of and interactions between decision regret and its causes.

Statements and declarations

Funding

This research received no external funding.

Competing interests

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Author contributions

MK formulated the research goals and aims, designed the study, and was responsible for research planning and execution, including providing mentorship external to the core team. AS and CH performed data collection. MK and CH analysed the data. MK and CH wrote the main manuscript text. All authors reviewed the manuscript for critical content. All authors approved the final version of the manuscript and attest to the validity and legitimacy of the data as well as its interpretation.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participant

All procedures performed in studies involving human participants, including participants provision of an informed consent prior to enrolment in the study, were in accordance with the ethical standards of the institutional Ethics committee approval number 024/21 dated 22nd January 2021 and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2023.01.014.

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