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Impact of Oncotype DX Recurrence Score on Treatment Selection and Survival in Early-Stage Hormone Receptor-Positive Breast Cancer

Azheen Ali Qadir[1,2*], Hazha Abdullah Mohammed Ameen[1,2]

[1]Department of Clinical Sciences, College of Medicine, University of Sulaimani, Sulaymaniyah, Kurdistan Region, Iraq.
[2]Hiwa Hospital, Sulaimani, Kurdistan, Iraq.
*Correspondence to: Azheen Ali Qadir (E-mail: azheen.ali91@gmail.com)
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Abstract

Objective: Breast cancer incidence has nearly doubled in recent years, making it the most diagnosed cancer among women. This study investigates the role of the Oncotype DX assay in treatment decision-making and its impact on survival outcomes for patients with early-stage, hormone receptor-positive, node-negative breast cancer.

Methods: This retrospective cohort study (2015–2025) at Hiwa Oncology Hospital analysed female patients with early-stage (T1/T2), HR+/HER2–, node-negative (N0) breast cancer who underwent Oncotype DX testing. Inclusion required available recurrence scores (RS) (categorised as low [RS 0–10], intermediate [RS 11–25], or high [RS ≥26]) and adjuvant chemotherapy eligibility. Data included demographics, tumour characteristics (grade, subtype, Ki-67, etc.), conventional clinical risk classification, treatment details (surgery, systemic therapy), and outcomes (overall survival, recurrence). Statistical analysis employed descriptive statistics, chi-square tests, and Kaplan-Meier survival curves with log-rank tests using SPSS v27.

Results: Among 294 HR+/HER2– breast cancer patients, Oncotype DX classified 60.5% as intermediate-risk, 21.5% high-risk, and 18.0% low-risk. Discordance with clinical risk classification was observed ($P = 0.091$): 52.8% of Low Oncotype DX-risk patients were High clinical risk versus 31.7% of High-DX-risk patients classified Low clinically. High-risk patients exhibited higher ductal histology (98.4%; $P = 0.010$), grade III tumours (41.3%; $P < 0.001$), LVI (27.0%; $P = 0.031$), Luminal B (93.7%; $P < 0.001$), and Ki-67 >14% (93.7%; $P < 0.001$). Chemotherapy use varied dramatically (low-risk: 1.9% vs. high-risk: 95.2%; $P < 0.001$). Five-year survival was 100% (low/intermediate) vs. 96.8% (high-risk; Log Rank $P = 0.025$).

Conclusion: It appears that utilising Oncotype DX risk categorisation serves as a more appropriate criterion for treatment decision-making compared to conventional risk classification, owing to its superior prognostic prediction for patients. Oncotype DX-guided therapy may reduce unnecessary adjuvant chemotherapy administration.

Keywords: Adjuvant chemotherapy, early-stage breast cancer, oncotype DX, survival outcome, treatment selection

Introduction

Early-stage breast cancer typically refers to malignancies classified within the initial phases of breast cancer staging according to standard oncology criteria, encompassing stage 0 to II.[1] Historically, treatment decisions for early-stage breast cancer relied primarily on clinicopathologic factors such as tumour size, grade, and nodal status. However, this approach often led to overtreatment and undertreatment due to limited insight into individual tumour biology, creating uncertainty about optimal therapy and exposing patients to unnecessary toxicity.[2,3] Over time, with the aim of treatment de-escalation and preventing unnecessary complications, histological and clinical parameters gradually gave way to molecular and genetic markers.[4] This shift led to the development and clinical integration of gene expression signatures over the past two decades. These commercially available prognostic assays classify patients into risk groups based on tumour gene expression profiles.[5,6]

The Oncotype DX test is a gene assay that analyses the expression of 21 genes and generates a recurrence score (RS) from 0 to 100. This score classifies patients into risk categories: low risk (RS < 11), intermediate risk (RS 11–25), and high risk (RS ≥ 26).[7] The use of the Oncotype DX test in the clinic has transformed the approach to selecting treatment methods by providing quantitative, evidence-based results. This tool allows oncologists to make decisions about patients' treatment plans with greater confidence. In cases where the cancer recurrence score (RS) is low, endocrine therapy alone can be safely used, preventing the physical, psychological, and economic complications of chemotherapy. Conversely, those with high scores are identified as candidates who derive significant benefit from chemotherapy. The intermediate-risk category, initially the most challenging to manage, has been clarified through landmark clinical trials.[8] The TAILORx study, which is the largest adjuvant breast cancer trial, showed that women with RS 0–25 achieve excellent 10-year survival (>90%) with endocrine therapy alone, confirming that nearly 70% of patients can safely undergo chemotherapy.[9] Similarly, the RxPONDER trial extended these findings to node-positive patients, showing that postmenopausal women with 1–3 positive nodes and RS ≤ 25 do not benefit from chemotherapy.[10]

The primary objective of this study is to investigate the role of the Oncotype DX assay in treatment decision-making for patients with early-stage breast cancer, with the secondary objective being to assess its subsequent influence on survival outcomes. Consequently, this study will specifically address the following research questions: (A) How does the Oncotype DX Recurrence Score influence treatment selection in patients with early-stage breast cancer? (B) What is the association between Recurrence Score-guided treatment decisions and subsequent survival outcomes?

Materials and Methods

This retrospective cohort study was conducted on patients diagnosed with breast cancer between 2015 and 2025 at Hiwa

Oncology and Haematology Hospital, a cancer treatment centre in Sulaymaniyah. Before initiating data collection, necessary administrative approvals were obtained from the College of Medicine, Scientific Committee, Medical Ethics Committee, and Sulaymaniyah Health Directorate.

Inclusion criteria comprised female patients with hormone receptor-positive (ER+/PR+) breast cancer, HER2-negative status, and no lymph node involvement (N0) who received treatment. Eligible patients were required to have early-stage disease (T1/T2), available Oncotype DX recurrence score results, and eligibility for adjuvant chemotherapy. Exclusion criteria included HER2-positive or triple-negative breast cancer patients, unavailability of Oncotype DX results or insufficient follow-up data, and recipients of neoadjuvant chemotherapy.

Data were systematically collected from hospital records and registries. Demographic information included age, educational level, occupation, comorbidity status, body mass index (BMI), menopausal status, age at first birth, age at menarche, age at menopause, and parity status.

Recorded tumour characteristics encompassed histopathological subtype (ductal, lobular, mixed ductal/lobular, or special pure type), tumour focality (unifocal, multifocal, or multicentric), tumour grade (I, II, or III based on the Nottingham system),[11] lymphovascular invasion (LVI), perineural invasion, T stage (T1 or T2 per TNM classification),[12] N stage (N0 or N1mic), luminal subtype (Luminal A or Luminal B), Ki-67 proliferation index (stratified as ≤14% or >14%,[13] hormonal receptor status (ER/PR positive in all cases), and HER2 status (positive, negative, or low).[14]

Treatment details included breast surgery type, axillary procedure, and adjuvant systemic therapy. Systemic therapy comprised chemotherapy and hormonal therapy. Clinical risk stratification followed MINDACT trial protocols: 1) All node-positive patients were deemed high-risk except those with grade 1 tumours ≤2 cm; 2) Node-negative patients required tumour diameters >10 mm (grade 3), >20 mm (grade 2), or >30 mm (grade 1) for high-risk designation.[15] The RS was calculated on a 0–100 scale, with patients stratified into low-risk (RS 0–10), intermediate-risk (RS 11–25), and high-risk (RS ≥26) groups. Outcome data recorded cancer recurrence information and date/cause of death. The primary study endpoint was overall survival (OS), defined as the time from diagnosis/treatment initiation to death from any cause.

Using SPSS version 27, data were first summarised with descriptive statistics (mean/median for continuous variables and percentages for categorical variables). Chi-square tests then determined differences between risk groups across examined variables. Kaplan-Meier survival curves compared survival rates among groups, and Log Rank tests identified associations between survival outcomes and risk categories.

Results

In the present study, a total of 294 women with breast cancer (mean age 52.30 ± 10.22 years) were included in the final analysis. Risk classification based on the Oncotype DX score revealed that the majority of patients (60.5%) were in the intermediate-risk group (RS 11–24). 21.5% and 18% of patients were classified into high-risk and low-risk groups, respectively (Figure 1).

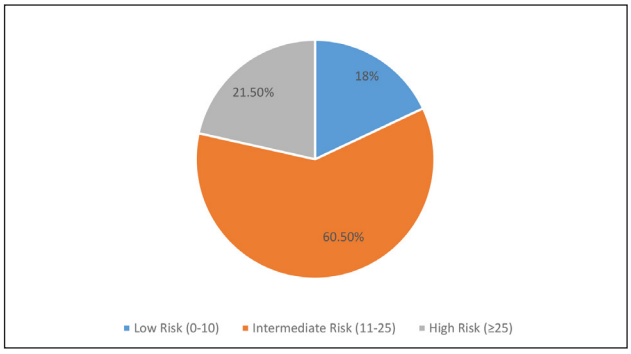

Fig. 1 **Risk classification based on Oncotype DX score in the studied patients.**

Comparing demographic and baseline characteristics across different risk classes (low, intermediate, high), the only factor associated with Oncotype DX risk classification was comorbid conditions. The low-risk group showed a significantly higher prevalence (45.3%) compared to intermediate (27.5%) and high-risk (25.4%) groups ($P = 0.030$). No statistically significant differences were observed among risk groups for other characteristics (Table 1).

Among clinicopathological characteristics, several were associated with Oncotype DX risk groups. Chi-square analysis revealed a significantly higher proportion of ductal carcinoma in the high-risk group (98.4%) compared to the low (71.7%) and intermediate (82.6%) groups. Similarly, lobular carcinoma was significantly less frequent in the high-risk group (1.6%) ($P = 0.010$). Tumour grade differed significantly, with the high-risk group having more grade III tumours (41.3%) versus the low-risk (5.8%) and intermediate (10.9%) groups ($P < 0.001$). LVI prevalence was significantly higher in the high-risk group (27.0%) compared to the low-risk (17.0%) and intermediate (10.1%) groups ($P = 0.031$). Luminal subtypes showed a significant association, with Luminal B correlating with high risk and Luminal A with low risk ($P < 0.001$). The prevalence of Ki-67 proliferation index >14% was significantly higher in the high-risk group (93.7%) compared to the low-risk (17.0%) and even intermediate-risk (60.7%) groups ($P < 0.001$). No statistically significant differences were observed for tumour focality, perineural invasion, T stage, or N stage ($P > 0.05$) (Table 2).

As presented in Table 3, chemotherapy administration differed significantly ($P < 0.001$) among the Oncotype DX risk groups. While the low-risk group overwhelmingly avoided chemotherapy (98.1%), the high-risk group largely received it (95.2%). Combined hormonal therapy was prescribed significantly less frequently in low-risk patients (11.3%) compared to high-risk (23.8%) and intermediate (29.2%) groups ($P = 0.029$). However, when considering only premenopausal patients ($n = 129$), this difference was not significant ($P = 0.148$). Breast surgery type and axillary procedure showed no significant association with Oncotype DX risk groups ($P > 0.05$). The results demonstrate significant discordance between Oncotype DX and conventional clinical risk stratification ($P = 0.091$). A substantial proportion (52.8%) of patients classified as Low genomic risk by Oncotype DX were concurrently categorised as High clinical risk, potentially leading to overtreatment. Conversely, discordance was also observed in the High genomic risk group, where 31.7% were classified as

Table 1. **Distribution of demographic and baseline characteristics by Oncotype DX risk group**

	Oncotype DX risk group			Total	*P*-value
	Low (*N* = 53)	Intermediate (*N* = 178)	High (*N* = 63)		
Age Group					
<50 years	18 (34.0%)	80 (44.9%)	22 (34.9%)	120 (40.8%)	0.203
≥50 years	35 (66.0%)	98 (55.1%)	41 (65.1%)	174 (65.1%)	
Educational Level					
Illiterate	12 (22.6%)	42 (23.6%)	13 (20.6%)	67 (22.8%)	0.984
Non-University	27 (50.9%)	93 (52.2%)	33 (52.4%)	153 (52.0%)	
University	14 (26.4%)	43 (24.2%)	17 (27.0%)	74 (25.2%)	
Comorbidities					
No	29 (54.7%)	129 (72.5%)	47 (74.6%)	205 (69.7%)	**0.030**
Yes	24 (45.3%)	49 (27.5%)	16 (25.4%)	89 (30.3%)	
Occupation					
Housewife	33 (62.3%)	128 (71.9%)	46 (73.0%)	207 (70.4%)	0.352
Employed	20 (37.7%)	50 (28.1%)	17 (27.0%)	87 (29.6%)	
BMI Group					
Normal (≤25)	9 (17.6%)	30 (16.9%)	15 (24.2%)	54 (18.6%)	0.443
Abnormal (>25)	42 (82.4%)	147 (83.1%)	47 (75.8%)	236 (81.4%)	
Menstrual Status					
Premenopausal	21 (39.6%)	81 (45.5%)	27 (42.9%)	129 (43.9%)	
Postmenopausal	32 (60.4%)	97 (54.5%)	36 (57.1%)	165 (56.1%)	0.738
Total	53 (100%)	178 (100%)	63 (100%)	294 (100%)	
Age at First Birth					
≤30	44 (97.8%)	141 (92.2%)	48 (87.3%)	233 (92.1%)	0.153
>30	1 (2.2%)	12 (7.8%)	7 (12.7%)	20 (7.9%)	
Age at Menarche					
≤12 years	13 (24.5%)	50 (28.2%)	13 (20.6%)	76 (25.9%)	0.480
>12 years	40 (75.5%)	127 (71.8%)	50 (79.4%)	217 (74.1%)	
Age at Menopause					
<50 years	15 (48.4%)	50 (54.3%)	24 (63.2%)	89 (55.3%)	0.453
≥50 years	16 (51.6%)	42 (45.7%)	14 (36.8%)	72 (44.7%)	
Parity					
Nulliparous	9 (17.3%)	40 (22.6%)	13 (21.0%)	62 (21.3%)	0.587
Low Multiparous (1–4)	29 (55.8%)	91 (51.4%)	38 (61.3%)	158 (54.3%)	
Grand Multiparous (≥5)	14 (26.9%)	46 (26.0%)	11 (17.7%)	71 (24.4%)	

Table 2. **Distribution of clinical and histopathological characteristics of tumour by Oncotype DX risk group**

	Oncotype DX risk group			Total	*P*-value
	Low (*N* = 53)	Intermediate (*N* = 178)	High (*N* = 63)		
Histopathological Subtype					
Ductal	38 (71.7%)	147 (82.6%)	62 (98.4%)	247 (84.0%)	**0.010**
Lobular	12 (22.6%)	27 (15.2%)	1 (1.6%)	40 (13.6%)	
Mixed Ductal/Lobular	1 (1.9%)	1 (0.6%)	0 (0.0%)	2 (0.7%)	
Special Type (Pure)	2 (3.8%)	3 (1.7%)	0 (0.0%)	5 (1.7%)	
Tumour Focality					
Unifocal	43 (81.1%)	152 (85.4%)	49 (77.8%)	244 (83.0%)	0.310
Multifocal	7 (13.2%)	20 (11.2%)	13 (20.6%)	40 (13.6%)	
Multicentric	3 (5.7%)	6 (3.4%)	1 (1.6%)	10 (3.4%)	
Tumour Grade					
I	12 (23.1%)	38 (21.7%)	2 (3.2%)	52 (17.9%)	**<0.001**
II	37 (71.2%)	118 (67.4%)	35 (55.6%)	190 (65.5%)	
III	3 (5.8%)	19 (10.9%)	26 (41.3%)	48 (16.6%)	
Lymphovascular Invasion (LVI)					
Absent	43 (81.1%)	157 (88.2%)	45 (71.4%)	245 (83.3%)	**0.031**
Present	9 (17.0%)	18 (10.1%)	17 (27.0%)	44 (15.0%)	
Unknown	1 (1.9%)	3 (1.7%)	1 (1.6%)	5 (1.7%)	
Perineural Invasion					
Absent	40 (75.5%)	129 (72.5%)	46 (73.0%)	215 (73.1%)	0.617
Present	10 (18.9%)	45 (25.3%)	14 (22.2%)	69 (23.5%)	
Unknown	3 (5.7%)	4 (2.2%)	3 (4.8%)	10 (3.4%)	
T Stage					
T1	25 (47.2%)	80 (44.9%)	31 (49.2%)	136 (46.3%)	0.835
T2	28 (52.8%)	98 (55.1%)	32 (50.8%)	158 (53.7%)	
N Stage					
N0	41 (95.3%)	151 (95.6%)	52 (98.1%)	244 (96.1%)	0.688
N1mic	2 (4.7%)	7 (4.4%)	1 (1.9%)	10 (3.9%)	
Luminal Subtype					
Luminal A	41 (77.4%)	67 (37.6%)	4 (6.3%)	112 (38.1%)	**<0.001**
Luminal B	12 (22.6%)	111 (62.4%)	59 (93.7%)	182 (61.9%)	
Ki-67 proliferation index					
≤14%	44 (83.0%)	70 (39.3%)	4 (6.3%)	118 (40.1%)	**<0.001**
>14%	9 (17.0%)	108 (60.7%)	59 (93.7%)	176 (59.9%)	
Hormonal Receptor Status					
ER/PR Positive	53 (100%)	178 (100%)	63 (100%)	294 (100%)	N/A
ER + & PR -	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
ER - & PR +	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Table 3. **Association of treatment regimen received with the DX Oncotype risk groups**

Variable	Category	Low risk (*n* = 53)	Intermediate risk (*n* = 178)	High risk (*n* = 63)	Total	*P*-value
Chemotherapy Administration	Yes	1 (1.9%)	47 (26.4%)	60 (95.2%)	108 (36.7%)	**<0.001**
	No	52 (98.1%)	131 (73.6%)	3 (4.8%)	186 (63.3%)	
Hormonal Therapy (Overall)	Single	47 (88.7%)	126 (70.8%)	48 (76.2%)	221 (75.2%)	**0.029**
	Combine	6 (11.3%)	52 (29.2%)	15 (23.8%)	73 (24.8%)	
Hormonal Therapy (Premenopausal)	Single	15 (71.4%)	39 (48.1%)	13 (48.1%)	67 (51.9%)	0.148
	Combine	6 (28.6%)	42 (51.9%)	14 (51.9%)	62 (48.1%)	
Breast Surgery	Mastectomy	15 (28.3%)	38 (21.3%)	14 (22.2%)	67 (22.8%)	0.566
	Breast Conservative	38 (71.7%)	140 (78.7%)	49 (77.8%)	227 (77.2%)	
Axillary Procedure	Dissection	11 (20.8%)	41 (23.0%)	20 (31.7%)	72 (24.5%)	0.190
	Sampling	3 (5.7%)	12 (6.7%)	8 (12.7%)	23 (7.8%)	
	SNBX	39 (73.6%)	125 (70.2%)	35 (55.6%)	199 (67.7%)	
Clinical Risk Classification	Low Risk	25 (47.2%)	84 (47.2%)	20 (31.7%)	129 (43.9%)	0.091
	High Risk	28 (52.8%)	94 (52.8%)	43 (68.3%)	165 (56.1%)	
Hormonal Regimen	TAM	10 (18.9%)	37 (20.8%)	16 (25.4%)	63 (21.4%)	**0.037**
	TAM+Zoladex	5 (9.4%)	44 (24.7%)	9 (14.3%)	58 (19.7%)	
	AI	37 (69.8%)	89 (50.0%)	32 (50.8%)	158 (53.7%)	
	AI+Zoladex	1 (1.9%)	8 (4.5%)	6 (9.5%	15 (5.1%)	

Low clinical risk, potentially leading to undertreatment. Hormonal therapy regimens varied significantly across risk groups ($P = 0.037$). Aromatase inhibitors (AIs) were predominant in all risk groups. Tamoxifen use was higher in the high-risk group (25.4%) than in the low-risk group (18.9%). Adding Zoladex to AI and Tamoxifen was associated with increased Oncotype DX score and higher risk.

Ordinal regression analysis showed that **Ki-67 >14%** (aOR = 7.93; 95% CI: 1.57–40.1; $P = 0.012$) and **chemotherapy administration** (aOR = 37.5; 95% CI: 12.8–110; $P < 0.001$) were independent predictors of higher *Oncotype DX* risk categorisation. Several other variables, including **Grade 3 histology**, **Luminal B subtype**, and **comorbidities**, were significant in univariate analysis but lost significance after adjustment. The model demonstrated excellent fit (LR $\chi^2 = 194.63$, df = 13; $P < 0.001$) (Table 4).

In this study, only two deaths were recorded during follow-up. Based on the Kaplan-Meier survival curve (Figure 2), the 1-year and 5-year cumulative survival rates were the same at 99.3%. Comparison of survival in the Oncotype DX risk groups showed that the 5-year survival rate was 100% for patients with low and intermediate risk based on the Oncotype DX score, and 96.8% for the high-risk group (Figure 3). The 5-year survival rate in individuals with low and high risk according to clinical risk classification was 99.2% and 99.4%, respectively (Figure 4). The Log Rank test showed a statistically significant difference in survival distribution between risk categories based on the Oncotype DX score ($P = 0.025$). In contrast, no significant differences were observed according to clinical classification ($P = 0.863$) or between chemotherapy-treated and untreated patients ($P = 0.063$).

Discussion

The Oncotype DX assay calculates a Recurrence Score (RS) based on gene expression levels, which estimates the likelihood of cancer recurrence and the benefit of chemotherapy in combination with hormonal therapy. Higher RS values indicate a higher risk of distant recurrence and a greater likelihood of improved outcomes with chemotherapy.[16,17]

In this study, adjuvant chemotherapy was prescribed significantly more frequently to high-risk patients than to low- and intermediate-risk patients. In multivariate analysis adjusted for all covariates, chemotherapy was significantly associated with higher risk categorisation (aOR 6.76). Specifically, 95.2% of high-risk patients (RS ≥25) received adjuvant chemotherapy, while 26.4% of intermediate-risk and 1.9% of low-risk patients underwent chemotherapy. This treatment selection approach has been confirmed in previous studies. The present study used this identical risk stratification system. Treatment decision-making based on clinicopathological factors, including lymph node involvement, tumour size, tumour grading, receptor status, and HER2, has been widely applied in previous years. In the present study, clinical risk stratification was based on that described in the MINDACT trial, which involves classifying patients into low-risk and high-risk groups based on three main criteria: lymph node

Table 4. **Univariate and multivariate ordinal logistic regression analysis of Oncotype DX risk groups**

	Univariate analysis				Multivariate analysis			
Variable	**B**	**OR**	**95% CI**	***P*-value**	**B**	**OR**	**95% CI**	***P*-value**
Comorbidities (Present)	–0.575	0.56	(0.34–0.93)	**0.024**	–0.406	0.67	(0.37–1.20)	0.176
Histopathological Subtype								
Ductal	1.546	4.69	(0.83–26.6)	0.081	–0.115	0.89	(0.14–5.78)	0.904
Lobular	0.384	1.47	(0.24–8.99)	0.678	–0.779	0.46	(0.06–3.27)	0.437
Mixed	–0.341	0.71	(0.03–17.7)	0.835	–0.588	0.56	(0.02–16.96)	0.732
Tumour Grade								
Grade 3	2.263	9.61	(4.22–21.9)	**<0.001**	0.992	2.70	(1.08–6.73)	0.092
Grade 2	0.572	1.77	(0.95–3.30)	0.072	–0.096	0.91	(0.42–1.99)	0.811
LVI (Present)	0.619	1.86	(0.98–3.51)	0.056	–0.371	0.69	(0.32–1.49)	0.344
Luminal Subtype (Luminal B)	2.251	9.50	(5.17–17.4)	**<0.001**	–0.218	0.80	(0.16–3.93)	0.788
Ki-67 (>14)	2.496	12.1	(6.35–23.1)	**<0.001**	2.071	7.93	(1.57–40.1)	**0.012**
Chemotherapy (Yes)	4.209	67.3	(23.4–193)	**<0.001**	3.626	37.5	(12.8–110)	**<0.001**
Hormonal Therapy (Combined)	0.350	1.42	(0.84–2.40)	0.192	0.013	1.01	(0.53–1.93)	0.968
Clinical Risk (High)	0.416	1.52	(0.96–2.40)	0.077	–0.303	0.74	(0.40–1.38)	0.341

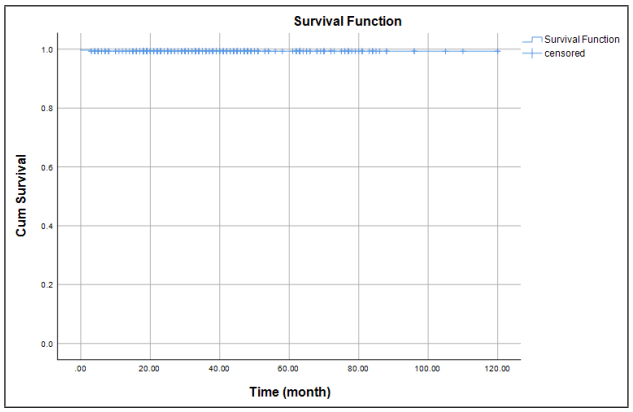

Fig. 2 **Kaplan-Meier survival curve for all breast cancer patients.**

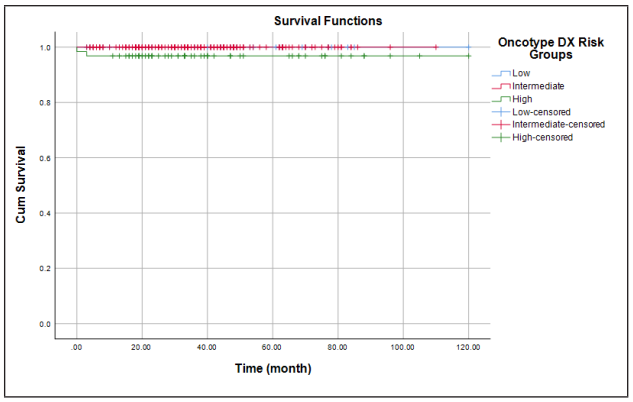

Fig. 3 **Survival function comparison based on Oncotype DX risk groups.**

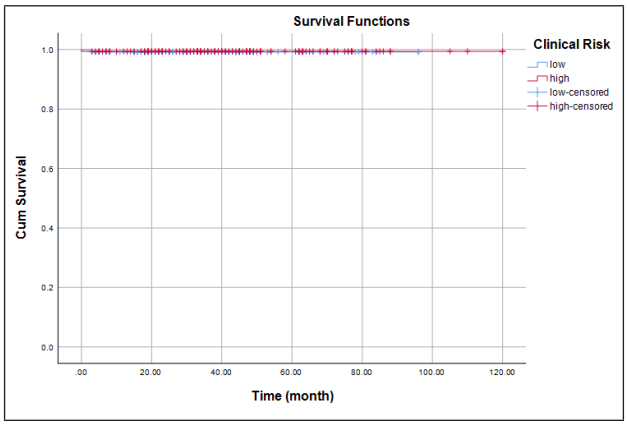

Fig. 4 **Survival function comparison based on clinical risk classification.**

involvement, tumour size, and tumour grade. Results revealed significant discordance between genomic and clinical risk stratification, with 52.8% of low Oncotype DX-risk patients classified as high clinical risk (suggesting possible overtreatment). In comparison, 31.7% of high genomic-risk patients were low clinical risk (indicating potential undertreatment). Survival analysis demonstrated that Oncotype DX-based risk stratification was significantly associated with patient survival, with higher risk correlating with increased mortality. While no significant association was observed between survival and conventional clinical risk classification.

The study by Schaafsma et al. showed that treatment decisions guided by Oncotype DX significantly extended breast cancer-specific survival (BCSS) compared to conventional decision-making.[18] These findings align with the present study's results, indicating that Oncotype DX more accurately predicts patient survival. The superior survival prediction demonstrated here ensures that patients needing advanced therapy receive it, while those who do not avoid overtreatment and its associated complications.

Livraghi et al. (2024) evaluated the Oncotype DX recurrence score (RS) in patients with early breast cancer of uncertain biological behaviour. They demonstrated that the RS test reclassified treatment recommendations in 15.9% of cases. This primarily led to reduced use of chemotherapy in intermediate-risk patients (RS 11–25) – a group historically lacking a clear chemotherapy benefit.[19] This finding is also consistent with the results of the present study.

In the present study, over half of patients classified as high clinical risk (who would typically qualify for adjuvant chemotherapy recommendation) were reclassified as genomic low-risk by Oncotype DX. In this category, chemotherapy is not indicated. Therefore, treatment decision-making using Oncotype DX can reduce unnecessary use of chemotherapy. Another study demonstrated an inverse relationship between the use of Oncotype DX and chemotherapy treatment. In other words, Oncotype DX-based treatment decisions led to decreased use of adjuvant chemotherapy.[18] Based on studies, chemotherapy works by targeting rapidly dividing cancer cells. Still, it may also affect healthy cells, leading to potential side effects, which underscores the importance of reducing its unnecessary prescription.[20]

Al-Zawi's study, which included 76 patients with early-stage breast cancer, found that 24% of patients eligible for adjuvant chemotherapy had a recurrence score of 26 or higher.[21] In the present study, 21.5% of patients had scores in the Oncotype DX high-risk group, and the majority received adjuvant chemotherapy. Previous studies have reported 13% to 28% of breast cancer patients with high RS.[21–23] The findings of the present study fall within this range. A study across 14 cancer centres in the UK found that chemotherapy was recommended for 15.3% of low-risk patients, 44.3% of intermediate-risk patients, and 92% of high-risk patients.[23] These results align with the findings of the present study, where chemotherapy use frequency in high-risk individuals was reported above 90%. However, in the present study, chemotherapy prescription in low-risk and intermediate-risk groups was significantly lower than in the study mentioned above, totalling less than 30% of patients. Given the patients' excellent survival, this is a promising sign and indicates that chemotherapy is prescribed only when essential at our center.

The NSABP-20 trial showed that patients with low RS (<18) derived no significant benefit from chemotherapy.[24] The TAILORx trial showed that patients with low recurrence scores (RS < 11) achieved excellent long-term outcomes solely with endocrine therapy, however, those with RS 11–25 had no added benefit from chemotherapy, high-risk patients, got significant benefit from chemotherapy.[17,25,26]

In our study, Ki-67% was associated with increased RS risk. Several studies reported similar findings.[27,28] The Ki-67% marker, used to measure cellular proliferation, provides valuable information about tumour growth rate.[29] Data analysis revealed a wide range of values, highlighting differences in tumour aggressiveness within the patient group. Higher Ki-67% typically indicates a faster-growing and potentially more aggressive tumour, which can influence treatment choices, particularly in determining the need for adjuvant chemotherapy in hormone receptor-positive, HER2-negative breast cancer cases. In the study by Al-Zawi et al., it was emphasised that the Oncotype DX recurrence score showed no correlation with the Ki-67 proliferation index.[13] This discrepancy in results may be due to the small sample size of that study (only 76 samples).

One limitation of this study is the relatively small sample size, which reduced the statistical power of the analysis, particularly about the relationship between the Recurrence Score and mortality outcomes. Specifically, because only two deaths are recorded in this study, results concerning patient survival and its association with the type of risk classification system should be interpreted with caution. Additionally, differences in unmeasured variables such as patients' economic status, psychological well-being, life style behaviors (such as diet, smoking and physical activity), social and family support and access to supportive therapies may have influenced the results. Furthermore, because the study is retrospective, recurrence data were not completely available, preventing statistically meaningful comparison between risk groups, restricting the ability to assess the predictive role of Oncotype DX in relation to recurrence. Thus, opening the way for further studies with lager sample size, prospective in type, and more advanced data collection to expand upon these findings.

Conclusion

The use of the Oncotype DX risk classification appears to be a more appropriate criterion for treatment decisions than conventional risk classification because of its superior prognostic prediction for patients with early breast cancer. Oncotype DX-guided treatment may reduce the administration of unnecessary adjuvant chemotherapy. The Ki-67 proliferation index is a strong predictor of Oncotype DX risk stratification and may be a suitable alternative when Oncotype DX is not available.

Ethical Approval

The study was approved by the ethics committee of the College of Medicine of the University of Sulaimani (No. on, 2024).

Acknowledgments

Not applicable.

Conflicts of Interest

The authors announce that they have no conflicts of interest.

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