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Dissecting the Triad of Distress: A Multivariate Analysis of Clinical, Surgical, and Sociodemographic Determinants of Quality of Life in Indonesian Breast Cancer Patients Undergoing Chemotherapy

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A B S T R A C T

Introduction: The assessment of health-related quality of life (HRQoL) is a paramount outcome in breast cancer survivorship, yet the interplay of disease-specific, treatment-related, and patient-level factors is not fully understood in Southeast Asian populations. This study aimed to comprehensively model the predictors of HRQoL and fatigue by simultaneously evaluating clinical, surgical, and sociodemographic variables among Indonesian breast cancer patients. **Methods:** A cross-sectional study was conducted with 102 female breast cancer patients undergoing chemotherapy at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. Data on clinical variables (AJCC stage, chemotherapy cycles, treatment intent), surgical procedures (breast and axillary surgery type), and sociodemographic characteristics were collected. HRQoL was assessed using the validated Indonesian versions of the Functional Assessment of Cancer Therapy-General (FACT-G) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaires. Bivariate correlations and a hierarchical multivariate linear regression analysis were performed to identify significant independent predictors of FACIT-F scores. **Results:** The cohort was characterized by advanced disease (Stage III/IV: 62.7%) and aggressive surgical management (Mastectomy: 75.5%; Axillary Lymph Node Dissection: 68.6%). In the multivariate analysis, several factors emerged as significant independent predictors of poorer HRQoL. These included advanced cancer stage (β = -0.41, $p < 0.001$), having undergone a mastectomy versus breast-conserving surgery (β = -0.28, $p = 0.002$), having had an axillary lymph node dissection versus sentinel node biopsy (β = -0.25, $p = 0.005$), and a higher number of chemotherapy cycles (β = -0.19, $p = 0.018$). The final model explained a substantial portion of the variance in HRQoL (Adjusted $R^2 = 0.58$). In contrast, sociodemographic factors including age, income, and education were not significant predictors in the final model ($p > 0.05$). **Conclusion:** HRQoL in this cohort is not determined by a single factor but by a triad of distress: the biological burden of the disease (stage), the physical and psychological morbidity of surgical treatment, and the cumulative toxicity of chemotherapy. These treatment-related realities powerfully override the influence of sociodemographic characteristics. These findings mandate a paradigm shift towards an integrated supportive care model that proactively addresses surgical morbidity alongside systemic side effects from the point of diagnosis.

1. Introduction

Breast cancer represents a formidable global health challenge, standing as the most frequently diagnosed malignancy and a principal cause of cancer-related mortality in women worldwide.[1] The epidemiology of breast cancer reveals a concerning trend, with a disproportionately escalating incidence and mortality burden in low- and middle-income countries (LMICs),

including Indonesia.[2] In 2020 alone, approximately 2.3 million women were newly diagnosed with breast cancer, a figure that underscores the urgent need for effective and holistic oncological care strategies on a global scale. Over the past several decades, the advent of multimodal treatment—a coordinated application of surgery, systemic therapy (chemotherapy, endocrine therapy, targeted agents), and radiation therapy—has markedly improved survival rates. This success has catalyzed a crucial evolution in the philosophy of cancer care, extending the focus beyond the traditional endpoint of mere survival to encompass the comprehensive well-being and health-related quality of life (HRQoL) of patients throughout their arduous cancer journey.[3]

Chemotherapy remains a central pillar of systemic treatment for breast cancer, employed across various settings: as neoadjuvant therapy to downstage tumors before surgery, as adjuvant therapy to eradicate micrometastatic disease post-surgery, and in a palliative capacity to control metastatic disease.[4] While its cytotoxic efficacy is indispensable for improving oncologic outcomes, chemotherapy is notoriously associated with a wide spectrum of acute and chronic toxicities that can profoundly impair a patient's HRQoL. Among these, cancer-related fatigue (CRF) is arguably the most pervasive, distressing, and functionally limiting symptom reported. CRF is a complex, multidimensional syndrome characterized by a persistent and debilitating sense of physical, emotional, and cognitive exhaustion disproportionate to recent activity, which is not ameliorated by rest.[5] Its pathophysiology is intricate, involving a complex interplay of pro-inflammatory cytokines, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, metabolic disturbances, and direct neurotoxic effects, all induced by both the underlying malignancy and its treatment.

The HRQoL of a breast cancer patient is shaped by a complex interplay of numerous factors. Clinical characteristics, such as the anatomical extent of the disease (stage), are known to be powerful determinants. A higher tumor burden in advanced stages is intrinsically linked to a greater systemic inflammatory response, paraneoplastic syndromes, and a heavier symptom load.[6] Concurrently, the intensity and nature of the treatment itself represent a major source of morbidity. Beyond the cumulative toxicity of chemotherapy, the surgical intervention—often the first and most definitive treatment step—carries its own significant and lasting impact. The type of surgery, ranging from breast-conserving surgery (BCS) with sentinel lymph node biopsy (SLNB) to a modified radical mastectomy with axillary lymph node dissection (ALND), has vastly different implications for a patient's physical functioning, body image, and emotional state.[7] Morbidities such as chronic pain, lymphedema, and restricted shoulder mobility are direct surgical sequelae that can severely compromise HRQoL for years after treatment completion.

Alongside these powerful disease- and treatment-related factors, sociodemographic variables—including age, socioeconomic status, educational attainment, and social support systems—are also postulated to modulate a patient's capacity to cope with their diagnosis and treatment, thereby influencing their perceived HRQoL.[8] In many Western healthcare systems, where patients often present with earlier-stage disease, these psychosocial and socioeconomic factors are frequently identified as significant modifiers of patient-reported outcomes. However, the relative contribution of these distinct domains—clinical, surgical, and sociodemographic—remains inadequately explored in resource-constrained settings like Indonesia. In such settings, patients often present with more advanced disease at diagnosis due to a combination of factors, including low awareness, cultural barriers, and limited access to screening programs, thus facing a greater biological burden from the outset. Furthermore, the Indonesian healthcare system, largely unified under the national health insurance scheme (BPJS Kesehatan), provides a relatively standardized pathway for core cancer therapies, which may moderate the influence of personal income on access to treatment.[9]

Understanding which factors are the primary drivers of patient well-being is paramount for designing effective, targeted, and resource-appropriate supportive care interventions. If disease stage is the dominant factor, efforts must be redoubled in public health campaigns for early detection. If surgical morbidity is a key independent predictor, then resources should be channeled towards rehabilitation, physiotherapy, and psychological support for body image issues. If chemotherapy toxicity is paramount, then aggressive symptom palliation protocols are needed.[10]

Therefore, the primary aim of this study was to dissect the complex interplay of predictors affecting HRQoL in a cohort of Indonesian breast cancer patients. The novelty of this research lies in its comprehensive, multi-domain approach, aiming to simultaneously quantify and compare the predictive power of (1) clinical disease characteristics (stage), (2) surgical treatment morbidity (type of breast and axillary surgery), (3) systemic treatment intensity (chemotherapy cycles), and (4) sociodemographic factors. We hypothesized that in a setting characterized by advanced disease presentation, the patient's HRQoL would be determined by a confluence of treatment-related morbidities, with the biological burden of the disease (stage) and the physical impact of its treatment (surgery and chemotherapy) emerging as dominant, independent predictors that would overshadow the influence of sociodemographic variables.

2. Methods

This study utilized a cross-sectional, descriptive-analytical design to investigate the determinants of HRQoL. Data were prospectively collected from patients attending the outpatient Surgical Oncology Clinic at Dr. Mohammad Hoesin General Hospital in Palembang, South Sumatra, Indonesia. This institution functions as a national tertiary referral hospital and is the primary center for comprehensive cancer care in the region, serving a diverse urban and rural patient population. The study was conducted over a two-month period, from June 1st, 2025, to July 31st, 2025. Ethical approval was obtained from the Institutional Review Board and the Ethics Committee of the Faculty of Medicine, Universitas Sriwijaya and the study was conducted in accordance with the principles of the Declaration of Helsinki.

The target population included all female patients with a histopathologically confirmed diagnosis of breast cancer who were undergoing chemotherapy. A total sampling technique was employed, wherein every consecutive patient who met the eligibility criteria during the study period was invited to participate to minimize selection bias. The inclusion criteria were: (1) Female, aged ≥18 years; (2) Confirmed histopathological diagnosis of breast cancer (any stage); (3) Having received at least one cycle of a chemotherapy regimen; (4) The last chemotherapy administration was within three months of the data collection date; (5) Ability to comprehend and independently complete questionnaires in Bahasa Indonesia; (6) Provision of written informed consent. The exclusion criteria were: (1) Presence of severe cognitive impairment or psychiatric conditions precluding reliable self-reporting; (2) Co-existing severe, uncontrolled systemic illnesses, such as congestive heart failure NYHA Class IV or end-stage renal disease, that could independently and profoundly affect HRQoL; (3) Inability to complete the questionnaires due to physical incapacitation; (4) Refusal to provide informed consent.

Based on these criteria, a final sample of 102 patients was enrolled. The sample size was deemed adequate for the planned correlational and multivariate regression analyses, calculated a priori to detect a medium effect size ($f^2 = 0.15$) with an alpha of 0.05 and a power of 80% for a model with up to eight independent variables.

Data were gathered using a two-pronged approach: a structured review of official medical records and the administration of validated self-report questionnaires. A trained research assistant, who was not involved in the patients' clinical care, approached eligible individuals in the clinic waiting area, provided a

detailed explanation of the study's purpose and procedures, and obtained written informed consent.

A standardized data extraction form was used to collect information from patients' medical records. Clinical data were: (1) Cancer Stage: Staging was based on the American Joint Committee on Cancer (AJCC) 8th Edition guidelines and recorded as Stage I, II, III, or IV; (2) Chemotherapy Frequency: Recorded as the total number of chemotherapy cycles the patient had received to date; (3) Treatment Intent: Categorized as Neoadjuvant (chemotherapy before surgery), Adjuvant (chemotherapy after surgery), or Palliative (for Stage IV metastatic disease). Surgical data were: (1) Type of breast surgery: categorized as breast-conserving surgery (BCS) or mastectomy; (2) Type of axillary surgery: categorized as sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND); (3) Sociodemographic data: collected via a structured interview; age: recorded in years and categorized (<40, 40-59, >59); education level: highest formal education completed (categorized as no school/elementary, middle/high school, university); monthly household income: self-reported and categorized based on the regional minimum wage (Low: <1.5 million IDR, Medium: 1.5-3.5 million IDR, High: >3.5 million IDR); Marital status: categorized as married or not married.

HRQoL was measured using the officially translated and validated Bahasa Indonesia versions of the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system instruments. Functional Assessment of Cancer Therapy-General (FACT-G, Version 4) is a 27-item core questionnaire that assesses HRQoL across four primary domains: Physical Well-Being (PWB, 7 items), Social/Family Well-Being (SWB, 7 items), Emotional Well-Being (EWB, 6 items), and Functional Well-Being (FWB, 7 items). Each item is rated on a 5-point Likert scale (0="Not at all" to 4="Very much"). The total FACT-G score ranges from 0 to 108, with higher scores indicating better HRQoL. Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, Version 4) includes the 27 items of the FACT-G plus a 13-item Fatigue Subscale (FS). The FS specifically measures the intensity of fatigue and its impact on daily functioning. The total FACIT-F score is the sum of the FACT-G and FS scores, ranging from 0 to 160. For all FACIT instruments, higher scores represent a better outcome (better HRQoL and less fatigue).

All data were coded and analyzed using SPSS Statistics Version 27.0 (IBM Corp., Armonk, NY). Frequencies and percentages were used for categorical variables. Means, standard deviations (SD), and ranges were calculated for continuous variables, including HRQoL scores. The non-parametric Spearman's rank correlation coefficient (rho) was used to assess the strength and direction of monotonic relationships between ordinal independent variables (stage, income, education) and the primary dependent variables (total FACT-G and FACIT-F scores). The point-biserial correlation was used for dichotomous variables. A p-value of <0.05 was considered statistically significant. To address the potential influence of the very small Stage I subgroup (n=2), the Spearman's correlation between cancer stage and FACIT-F score was re-calculated after excluding these two patients. A hierarchical multivariate linear regression analysis was performed to identify the independent predictors of HRQoL, using the total FACIT-F score as the continuous dependent variable. Variables were entered in blocks to assess their relative contribution: Block 1 contained sociodemographic variables, Block 2 contained the primary clinical variable (cancer stage), Block 3 contained surgical variables, and Block 4 contained the chemotherapy variable. This hierarchical approach allows for the assessment of how much additional variance is explained by treatment-related factors after accounting for patient-level characteristics. Standardized beta coefficients (β) were used to compare the relative predictive power of each variable. Collinearity diagnostics (Variance Inflation Factor, VIF < 5) were checked to ensure model stability.

3. Results

A total of 102 eligible patients were enrolled. The detailed sociodemographic, clinical, and surgical characteristics of the cohort are presented in Table 1. The mean age of participants was 48.7 years (SD ± 9.2). The cohort was predominantly from lower-to-middle socioeconomic strata, with 78.4% having completed high school or less and 78.5% reporting low-to-medium household incomes. Clinically, the patient population was defined by advanced disease at presentation. The majority of patients had Stage III (42.1%) or Stage II (35.3%) disease, with a significant proportion (20.6%) having Stage IV metastatic disease. Only 2.0% were diagnosed at Stage I. The treatment intent was primarily adjuvant (65.7%). Surgical management was correspondingly aggressive: 75.5% of patients underwent a mastectomy, and 68.6% had a full axillary lymph node dissection.

Table 1. Patient Cohort Characteristics (n=102)

Sociodemographic, Clinical, and Surgical Data from the Study Population

CHARACTERISTIC	CATEGORY	FREQUENCY (N)	PERCENTAGE (%)
Age (years)	< 40	28	27.5%
	40 - 59	57	55.9%
	> 59	17	16.7%
Education Level	No School / Elementary	39	38.2%
	Middle / High School	41	40.2%
	University	22	21.6%
Monthly Income (IDR)	< 1.5 Million (Low)	37	36.3%
	1.5 - 3.5 Million (Medium)	43	42.2%
	> 3.5 Million (High)	22	21.6%
Cancer Stage (AJCC 8th)	Stage I	2	2.0%
	Stage II	36	35.3%
	Stage III	43	42.1%
	Stage IV	21	20.6%
Type of Breast Surgery	Mastectomy	77	75.5%
	Breast-Conserving Surgery	25	24.5%
Type of Axillary Surgery	Axillary Lymph Node Dissection	70	68.6%
	Sentinel Lymph Node Biopsy	32	31.4%

The mean FACIT-F score for the entire cohort was 98.5 (SD ± 21.2), and the mean FACT-G score was 76.8 (SD ± 18.5), indicating a moderate level of HRQoL impairment and fatigue. As shown in Figure 1, a box-and-whisker plot of FACIT-F scores stratified by cancer stage revealed a clear negative trend. While there was distinct separation in the median scores between stages, there was also considerable overlap in the distributions, particularly between adjacent stages, reflecting the inherent variability in patient experiences.

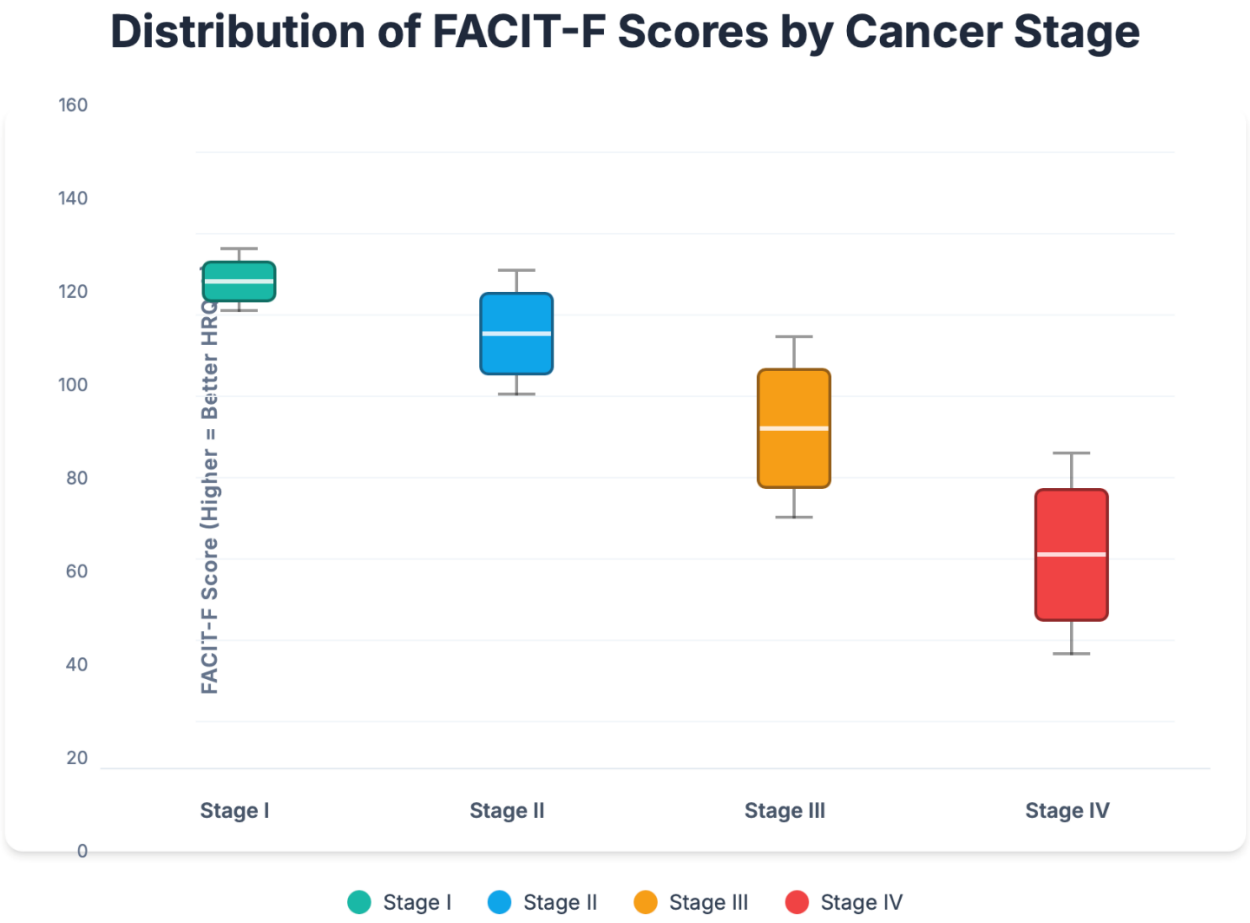

Figure 1. Distribution of FACIT-F scores by cancer stage. The plot illustrates a strong negative monotonic relationship, with median HRQoL scores decreasing as cancer stage advances. The interquartile ranges and whiskers show variability within each stage and some overlap between adjacent stages.

When stratified by key characteristics (Table 2), a consistent dose-response relationship was observed between advancing cancer stage and deteriorating HRQoL. Patients with Stage IV disease reported severely compromised quality of life (Mean FACIT-F: 61.2) compared to those with Stage II disease (Mean FACIT-F: 115.6). Similarly, patients who underwent mastectomy and ALND reported clinically and statistically significant lower mean HRQoL scores than those who received breast-conserving surgery and SLNB, respectively. In contrast, variations in mean scores across sociodemographic categories were minimal and showed no discernible pattern.

Table 2. Mean Health-Related Quality of Life (HRQoL) Scores

Stratified by Key Clinical and Surgical Characteristics (n=102)

CHARACTERISTIC	CATEGORY	N	MEAN FACIT-F SCORE (MAX 160)	MEAN FACT-G SCORE (MAX 108)
Cancer Stage	Stage I	2	138.5 (±5.1)	95.0 (±4.2)
	Stage II	36	115.6 (±10.2)	88.1 (±8.5)
	Stage III	43	92.3 (±14.8)	71.5 (±11.3)
	Stage IV	21	61.2 (±16.5)	53.4 (±12.1)
Breast Surgery	Breast-Conserving Surgery	25	111.4 (±13.3)	85.2 (±9.8)
	Mastectomy	77	94.1 (±22.6)	73.9 (±19.6)
Axillary Surgery	Sentinel Lymph Node Biopsy	32	113.8 (±12.1)	87.0 (±9.1)
	Axillary Lymph Node Dissection	70	91.7 (±22.1)	72.1 (±19.0)
Chemotherapy Cycles	< 4	70	105.1 (±18.9)	81.3 (±16.7)
	5 - 10	26	89.8 (±20.5)	69.9 (±15.4)
	> 10	6	65.3 (±19.3)	52.2 (±14.8)
Overall Mean		**102**	98.5 (±21.2)	76.8 (±18.5)

The Spearman's correlation analysis (Table 3) confirmed the profound negative impact of disease severity and treatment intensity on HRQoL. A strong, statistically significant negative correlation was found between cancer stage and both FACIT-F (ρ = -0.68, $p < 0.001$) and FACT-G scores (ρ = -0.65, $p < 0.001$). A sensitivity analysis excluding the two Stage I patients showed the correlation remained strong and highly significant (ρ = -0.66, $p < 0.001$), confirming the stability of this finding. Similarly, chemotherapy frequency showed a moderate negative correlation with HRQoL (FACIT-F: ρ = -0.42, $p < 0.001$). In stark contrast, none of the sociodemographic variables demonstrated a significant correlation with either HRQoL measure ($p > 0.05$ for all).

To determine the independent contribution of each domain, a hierarchical linear regression was performed (Table 4). Model 1, containing only sociodemographic variables, was not statistically significant and explained negligible variance (Adjusted R^2 = 0.02, p = 0.215). Model 2, which added cancer stage, resulted in a dramatic and significant increase in explanatory power (Adjusted R^2 = 0.47, $p < 0.001$). Cancer stage was a powerful predictor (β = -0.64, $p < 0.001$). Model 3, which added the surgical variables (Mastectomy vs. BCS; ALND vs. SLNB), further improved the model significantly (Adjusted R^2 = 0.55, $p < 0.001$). Crucially, both Mastectomy (β = -0.28, p = 0.002) and ALND (β = -0.25, p = 0.005) emerged as significant independent predictors of poorer HRQoL, even after controlling for stage. Model 4, the final model, added chemotherapy cycles. This led to a small but significant improvement (Adjusted R^2 = 0.58, $p < 0.001$). In this final comprehensive model, four variables remained as significant independent predictors of diminished HRQoL: advanced cancer stage, undergoing a mastectomy, undergoing an ALND, and a higher frequency of chemotherapy. Sociodemographic factors remained non-significant.

Table 3. Spearman's Correlation Coefficients (ρ)

Assessing the Relationship Between Predictors and HRQoL Scores

VARIABLE	FACIT-F SCORE (P)	P-VALUE	FACT-G SCORE (P)	P-VALUE
Clinical & Surgical Variables				
Cancer Stage	-0.68	<0.001	-0.65	<0.001
Chemotherapy Frequency	-0.42	<0.001	-0.40	<0.001
Sociodemographic Variables				
Age	0.08	0.421	0.11	0.273
Education Level	-0.09	0.368	-0.12	0.228
Income Level	-0.14	0.160	-0.15	0.133
Marital Status	-0.02	0.842	0.03	0.765

Correlation (ρ) Key:
- Negative Correlation
- Positive Correlation
- Not Significant

p-value Key:
- $p < 0.05$: Statistically Significant
- $p \geq 0.05$: Not Statistically Significant

Interpretation:
The length of the bar indicates the strength of the correlation (from -1 to +1). Longer red bars show a strong negative relationship (as one variable increases, the other decreases).

4. Discussion

This study was designed to construct a comprehensive predictive model for HRQoL in Indonesian breast cancer patients by dissecting the relative influence of clinical, surgical, and sociodemographic factors.[11] The findings provide a clear and compelling answer: patient well-being in this cohort is powerfully dictated by a triad of treatment-related distress—the biological burden of the disease, the morbidity of the required surgery, and the cumulative toxicity of chemotherapy. This confluence of factors effectively eclipses the impact of traditional sociodemographic characteristics, a finding that carries profound implications for the design and delivery of supportive oncology care in Indonesia and similar healthcare settings.

Our hierarchical regression analysis successfully disentangled the independent contributions of different facets of the cancer experience. The final model demonstrates that a patient's HRQoL is not a monolithic construct determined by "cancer" but is rather a composite outcome shaped by distinct, measurable insults.[12]

First, cancer stage remained a robust and powerful independent predictor of HRQoL, even after controlling for the type of treatment. This confirms the intrinsic negative impact of the biological burden of advanced disease. Progressing from Stage II to Stage III/IV is not merely a change in anatomical classification; it is a surrogate for increasing tumor volume, systemic inflammation, and metabolic derangement. The systemic release of pro-inflammatory cytokines such as IL-6, IL-1β, and TNF-α by tumor cells and the host immune response is a well-established mechanism underlying cancer cachexia, anorexia, pain, and, centrally, cancer-related fatigue.[13] These cytokines act on the central nervous system to induce "sickness behavior," a syndrome of lethargy, anhedonia, and social withdrawal that is directly captured by the PWB, EWB, and SWB subscales of the FACT-G. Therefore, the significant predictive power of stage in our final model reflects this escalating, non-removable biological hostility of the malignancy itself.

Table 4. Hierarchical Multivariate Linear Regression Analysis

Predicting Total FACIT-F Score (n=102)

VARIABLE	MODEL 1 (B)	MODEL 2 (B)	MODEL 3 (B)	MODEL 4 (FINAL) (B)	P-VALUE (FINAL)
Block 1: Sociodemographics					
Age	0.07	0.04	0.03	0.02	0.812
Education Level	-0.10	-0.05	-0.02	-0.01	0.905
Income Level	-0.15	-0.08	-0.04	-0.03	0.724
Block 2: Clinical Stage					
Cancer Stage	—	**-0.64***	**-0.45***	**-0.41***	**<0.001**
Block 3: Surgical Variables					
Mastectomy (vs. BCS)	—	—	**-0.31***	**-0.28***	**0.002**
ALND (vs. SLNB)	—	—	**-0.27***	**-0.25***	**0.005**
Block 4: Chemotherapy					
Chemotherapy Frequency	—	—	—	**-0.19***	**0.018**
Model Summary	0.02	0.47	0.55	0.58	—
Adjusted R^2	1.54	**24.1***	**21.8***	**19.5***	—
F-statistic	—	**0.45***	**0.08***	**0.03***	—
ΔR^2 (Change in R^2)					

Visual Key for Final Model (β) Coefficients

Note: The length and color of the bar visually represent the strength and direction of the variable's independent impact on HRQoL scores in the final model. Red indicates a negative impact (lower HRQoL). *p < 0.05

Second, and central to the novelty of this study, is the finding that surgical morbidity is a powerful, independent determinant of HRQoL. After accounting for the effect of stage, undergoing a mastectomy and an axillary lymph node dissection were both associated with a significant and substantial decline in HRQoL scores. This refutes any simplistic notion that the patient's experience is solely a function of their disease stage or chemotherapy. The surgical intervention leaves an indelible mark. A mastectomy, while oncologically necessary for many with advanced disease, is a source of significant psychological distress related to body image, femininity, and self-esteem, which directly impacts the Emotional Well-Being (EWB) domain. Axillary lymph node dissection, while crucial for regional disease control, carries a high risk of long-term morbidity, most notably lymphedema.[14] This chronic swelling of the arm leads to pain, recurrent infections, and profound functional impairment, severely impacting both the physical (PWB) and functional well-being (FWB) domains. The independent significance of these surgical variables in

our model underscores that the physical consequences of treatment are not just "side effects" but core drivers of the patient's overall suffering.[15]

Third, the cumulative toxicity of chemotherapy was also confirmed as a significant, independent predictor. Each additional cycle of cytotoxic agents inflicts damage on rapidly dividing healthy cells, leading to accumulating toxicities like myelosuppression (anemia, neutropenia), gastrointestinal mucositis, and peripheral neuropathy. Anemia, in particular, is a major contributor to fatigue by reducing oxygen-carrying capacity. The fact that chemotherapy frequency remained significant even after accounting for stage and surgery highlights the relentless, dose-dependent attrition that systemic therapy exacts on a patient's physiological reserves and functional status.[16]

Perhaps the most thought-provoking finding is the consistent lack of association between any sociodemographic variable and HRQoL in both bivariate and multivariate analyses. This finding, observed in the context of a robust model that accounts for disease and treatment severity, strongly suggests a threshold or "floor" effect. When the combined clinical burden—from advanced disease, major surgery, and intensive chemotherapy—is sufficiently severe, its profound physiological and psychological impact may create a level of distress that is not meaningfully altered by external sociodemographic advantages. The clinical imperative for survival and the severity of symptoms like intractable pain, debilitating fatigue, or functional limb impairment become the all-consuming aspects of a patient's existence.[17] In such circumstances, the potential benefits of a higher income or education—such as access to niche supportive therapies or a more nuanced understanding of the disease—may become marginal in the face of overwhelming biological and treatment-induced distress. Furthermore, the standardized care pathway provided by the Indonesian national health insurance system (BPJS Kesehatan) may level the playing field regarding access to core therapies, thereby reducing the influence of income on primary treatment, while strong communal and family support systems prevalent in the culture might buffer the effect of marital status.

The practical implications of these findings are profound. They advocate for a clinical strategy that moves beyond a stage-centric view to a multi-domain, morbidity-focused paradigm of supportive care.[18] (1) Integrated Pre- and Post-Surgical Rehabilitation: Given the independent impact of surgery, supportive care must begin before the operation. Pre-operative counseling should address body image concerns, and post-operative referral to physiotherapy must be standard practice to mitigate lymphedema and shoulder dysfunction; (2) Proactive Symptom Management: Resources should be intensely focused on symptom palliation protocols tailored not just to the chemotherapy regimen but also to the patient's surgical procedure and disease stage. Early and concurrent integration of palliative care services, focused on managing pain and fatigue, is essential for patients with advanced disease; (3) Holistic Assessment: Clinical assessments of patient well-being should routinely include questions about surgical sequelae (arm function, body image) in addition to chemotherapy side effects. Relying on performance status alone is insufficient.

The findings of this study must be interpreted in the context of several limitations. First, the cross-sectional design allows for the identification of significant associations but precludes any inference of causality. A longitudinal study would be required to track the trajectory of HRQoL over the course of the treatment continuum. Second, this was a single-center study conducted at a tertiary referral hospital, which may limit the generalizability of the findings to other types of hospitals or regions in Indonesia with different patient populations and resources.[19] Third, the use of a non-probability, total sampling technique, while pragmatic, may introduce selection bias. Fourth, despite our comprehensive model, there are other potential confounding variables not accounted for, such as patient comorbidities, pre-existing psychological conditions, and the specific level of

social support, which could also influence HRQoL. Finally, the very small subgroup of patients with Stage I disease (n=2) limited our ability to make robust statistical comparisons with this group, although a sensitivity analysis confirmed the stability of our primary correlation finding.[20]

5. Conclusion

In this cohort of Indonesian breast cancer patients, health-related quality of life is not determined by who the patient is (sociodemographics), but by what they are enduring. A triad of distress, comprising the biological burden of advanced disease, the distinct morbidity of extensive surgical intervention, and the cumulative toxicity of chemotherapy, collectively and independently predicts patient well-being. The powerful impact of these treatment-related realities renders the influence of sociodemographic factors statistically insignificant. This research fundamentally reframes the drivers of patient suffering in this context, advocating for a paradigm of care that prioritizes early diagnosis and integrates aggressive, proactive, and multi-domain supportive care—addressing surgical, systemic, and disease-related symptoms—as a non-negotiable standard for all patients with advanced disease.

6. References

1. Rafiei S, Souri S, Nejatifar Z, Amerzadeh M. Impact of physical activity on health perception and mental health in Iranian women with breast cancer. Support Care Cancer. 2025; 33(8): 701.
2. Altundag K. Physical activity and mental health in breast cancer: promising, but premature? Support Care Cancer. 2025; 33(9): 821.
3. Rigi Kooteh B, Mahdavi A, Mojahed A, Nadimi J, Rigi Motlagh A. Enhancing quality of life in Iranian women with breast cancer: the efficacy of psychological interventions. A meta-analysis. Mental Wellness. 2025; 3.
4. Kim EY, Shin S, Chang Y, Ryu S. Serum ferritin and iron-related biomarkers in relation to breast cancer risk by menopausal status: a prospective cohort study. Cancer Epidemiol Biomarkers Prev. 2025.
5. Fielder AM, Kim S, Ruterbusch JJ, Martin C, Gottschlich A, Schwartz AG, et al. Prescription and self-reported use of endocrine therapy among black hormone receptor-positive breast cancer survivors in the Detroit Research on Cancer Survivors cohort. Breast Cancer Res Treat. 2025.
6. Padamsee TJ, Phommasathit C, Swinehart-Hord P, Chettri S, Clevenger K, Rayo MF, et al. Patient-driven decisions and perceptions of the "safest possible choice": insights from patient-provider conversations about how some breast cancer patients choose contralateral prophylactic mastectomy. Psychol Health. 2025; 40(6): 1012–36.
7. Kim SJ, Arneja J, Christensen RAG, Anderson GM, Brooks JD. Trends in contralateral breast cancer and contralateral prophylactic mastectomy from 2009 to 2016. NPJ Breast Cancer. 2025; 11(1): 55.
8. Sun Y, Zhang F, Guo Q, Ma X. Comparison of local recurrence outcomes between breast conservation therapy and mastectomy for the treatment of breast cancer among young women: a systematic review and meta-analysis. Breast Care (Basel). 2025.
9. Fouad RA, Elgarhy SMA, El shazly SAM, Mohamed AAER. Effectiveness of discharge education plan for patients' care practices and anxiety levels post-mastectomy: a quasi-experimental study. Arch Breast Cancer. 2025; 12(3): 265–77.
10. Hyldebrandt HK, Stormorken AT, Vitelli V, Geirdal AØ, Grindedal EM. Experiences with risk-reducing mastectomy in Norwegian BRCA1/2 carriers without prior breast cancer. Fam Cancer. 2025; 24(3): 60.

11. Klimitz FJ, Chiarella LS, Huelsboemer L, Brown S, Boroumand S, Kochen A, et al. Area Deprivation Index (ADI) as a predictor of surgical complications in patients undergoing mastectomy. Clin Breast Cancer. 2025.
12. Abu-Hussein B, Elrosasy A, Samy H, Ali AS, Alijla SS, Bitar AN, et al. Efficacy and safety of S-ketamine in pain management for breast cancer patients undergoing modified radical mastectomy: a meta-analysis of randomized controlled trials. Clin Transl Oncol. 2025; 27(8): 3325–39.
13. Klimitz FJ, Diatta F, Freeman J, Schaschinger T, Brown S, Knoedler S, et al. The five-item Modified Frailty Index (mFI-5) predicts adverse short-term outcomes in patients undergoing mastectomy: a propensity score-matched analysis of 252,054 cases. Clin Breast Cancer. 2025; 25(6): e837-e845.e1.
14. Zhuo X, Meng Y, He Y, Lu H, Tang R, Li P, et al. Association analysis of family resilience with sleep quality and hope levels in post-modified radical mastectomy breast cancer patients. Support Care Cancer. 2025; 33(8): 746.
15. Scardina L, Petrazzuolo E, Accetta C, Carnassale B, D'Archi S, Di Leone A, et al. Surgical management of ipsilateral breast cancer recurrence after conservative mastectomy and prepectoral breast reconstruction: Exploring the role of wide local excision. Cancers (Basel). 2025; 17(17): 2881.
16. Lazarewicz MA, Wlodarczyk D, Lundgren S, Reidunsdatter RJ. Diversity in changes of HRQoL over a 1-year period after radiotherapy in Norwegian breast cancer patients: results of cluster analyses. Qual Life Res. 2019; 28(6): 1521–30.
17. Saiga M, Taira N, Kimata Y, Watanabe S, Mukai Y, Shimozuma K, et al. Development of a Japanese version of the BREAST-Q and the traditional psychometric test of the mastectomy module for the assessment of HRQOL and patient satisfaction following breast surgery. Breast Cancer. 2017; 24(2): 288–98.
18. Safar H, Mazanec SR. Relationship between symptom burden and HRQOL among Kuwaiti women recently diagnosed with breast cancer: a cross-sectional study. Asian Pac J Cancer Prev. 2023; 24(4): 1435–41.
19. Hao Y, Krohe M, Mazar I, Galipeau N, Foley C, Denise Globe, et al. Patient-reported outcomes in advanced breast cancer: inside the label and approval documents. Expert Rev Qual Life Cancer Care. 2016; 1(3): 197–205.
20. Armer JM, Feldman JL, Ostby PL, Thrift KM, Lasinski BB, Beck MS, et al. Simplifying evidence-based management of breast cancer-related lymphedema. Expert Rev Qual Life Cancer Care. 2016; 1(5): 389–402.