

The Influence of Age and Comorbidities on Breast Cancer Treatment in Young and Elderly Women: A Comparative Retrospective Study

Asmae Hamdan¹, Salma El baz², Oumaima Eddarif³, Hanan El kacemi⁴,
Tayeb Kebdani⁵, Khalid Hassouni⁶

^{1,2,3,4,5,6}Department of Radiotherapy Oncology, National Institute of Oncology, Mohamed V University, Rabat, Morocco

Abstract:

Introduction:

Breast cancer is the most commonly diagnosed cancer in women worldwide, affecting women of all ages. Therapeutic management of breast cancer should be tailored to numerous factors, with age playing a crucial role. Treatment decisions vary significantly between young and elderly women, influencing clinical outcomes and quality of life. Younger women often face more aggressive treatments but may refuse them due to concerns about toxicity, pregnancy, and future fertility. Elderly women may refuse treatments due to perceived aggressiveness, limited life expectancy, and multiple comorbidities. This study aims to compare treatment acceptance and refusal between young and elderly women with breast cancer.

Materials and Methods:

This retrospective descriptive study included all women diagnosed with localized breast cancer between January 2019 and December 2021 at the National Institute of Oncology in Rabat. The study included 257 women under 40 years old and 117 women aged 70 and older, meeting specific inclusion criteria. Data collected included age at diagnosis, tumor characteristics, indicated treatments (surgery, radiotherapy, systemic treatment), and therapeutic follow-up consultations.

Results:

The study found that 17.77% of patients were under 40 years old, while 8.09% were 70 years and older. Young patients often had fewer comorbidities (8.94%) compared to elderly patients (68.37%). Comorbidities in elderly patients were more diverse, particularly in cardiovascular and endocrine categories. Both groups predominantly had left-sided, non-specific type ductal carcinoma, with T2 stage being most common. Young women had a higher rate of lymph node involvement and more aggressive tumor grades. Treatment refusal was higher in the elderly group, particularly for chemotherapy, radiotherapy, and adjuvant endocrine therapy.

Conclusion:

Elderly women with breast cancer have a higher prevalence of comorbidities and are more likely to refuse various treatments compared to younger women. Treatment refusals in elderly patients are influenced by comorbidities, making treatments riskier and less acceptable. Optimizing therapeutic strategies to improve personalized patient care requires addressing the unique needs and concerns of both young and elderly women with breast cancer.

Keywords: Age, Comorbidities, Breast, cancer, Treatment

Introduction:

Breast cancer is the most commonly diagnosed cancer in women worldwide (1), which can affect them at any age, and therapeutic management should be tailored according to numerous factors, among which age plays a crucial role. It represents a major public health issue globally. Therapeutic decisions can significantly vary between young and elderly women, thus influencing clinical outcomes and quality of life. Local modalities and systemic anticancer therapies lead to improved survival outcomes for patients, including disease-free survival and overall survival (2).

In young women, although treatments are often more aggressive and intensive, treatment refusal can occur. These refusals are mainly motivated by fear of toxicities associated with therapies, as well as considerations related to pregnancy and future fertility. Young patients, often of childbearing age, must juggle between fighting cancer and their family aspirations, which can complicate therapeutic choices.

On the other hand, in elderly women, treatment refusal is frequently related to advanced age. Elderly patients may perceive treatments as being too aggressive or inappropriate given their limited life expectancy and the presence of multiple comorbidities. This perception not only influences their willingness to follow medical recommendations, but also the approach of practitioners who may hesitate to offer intensive treatments due to increased risks of complications.

This comparative retrospective study aims to describe the differences between young and elderly women with breast cancer in terms of acceptance or refusal of treatment. The objective is to provide insights to optimize therapeutic strategies and improve personalized patient care.

Materials and methods:

This is a retrospective descriptive study conducted over a period of 3 years, including all women with localized breast cancer diagnosed between January 2019 and December 2021 at the National Institute of Oncology in Rabat. This institute is the largest national oncology center in Morocco and is a collaborator of the International Atomic Energy Agency (IAEA). He recruits the largest number of patients.

Our study includes 1446 female patients diagnosed with localized breast cancer. The selection was then limited to young women under 40 years old and women aged 70 and older who met the inclusion criteria. We therefore selected 257 women out of a total of 301 women under 40 years old and 117 women out of a total of 188 women aged 70 and older.

The inclusion criteria were as follows:

- Patients with localized breast cancer
- Patients over 18 years old
- Patients under 40 years old or over 70 years old
- Patients without contraindications to indicated cancer treatment
- Normal geriatric assessment for elderly women
- Having a complete diagnosis

The exclusion criteria were as follows:

- Patients aged 40 years and younger than 70 years
- Patients with medical contraindications to cancer treatment
- The presence of psychiatric or cognitive disorders

The information collected from medical records for this retrospective analysis includes age at diagnosis, tumor characteristics, type of indicated treatment (surgery, radiotherapy, systemic treatment), therapeutic follow-up consultations.

Results:

We describe two groups of patients: the first, called the young group, includes patients aged less than 40 years, and the second, named the elderly group, includes women aged 70 years and older.

The group of young women consists of 257 patients, representing 17.77% of the total number of patients with localized breast cancer, compared to 117 women aged 70 and over, which is 8.09%. The age of patients in the young group ranges from 25 to 39 years, with a median of 36, while for the elderly group, ages range from 70 to 88 years, with a median of 74.

209 patients in the young group (81.32%) came from an urban area, compared to 66 patients in the elderly group (56.41%). The majority of the young group had a secondary level of education (47.85%), while the majority of the elderly group were uneducated women (82.90%) (Table 1).

Table 1: Descriptive and comparative table of socio-demographic characteristics of young patients under 40 years old (Total sample = 257) vs elderly patients aged 70 and over (Total sample = 117)

	Young groups (N=257)		Elderly groups (N=117)	
	Sample size	%	Sample size	%
<i>Place of residence</i>				
<i>Urban area</i>	209	81,32	66	56,41
<i>Rural area</i>	48	18,67	51	43,58
<i>Marital status</i>				
<i>Married</i>	166	64,59	86	73,50
<i>Single</i>	51	19,84	2	1,70
<i>Divorced</i>	38	14,78	7	5,98
<i>Widowed</i>	2	0,77	22	18,80
<i>Education level</i>				
<i>Not educated</i>	34	13,22	97	82,90
<i>Primary school</i>	89	34,63	16	13,67
<i>Secondary school</i>	123	47,85	3	2,56
<i>Higher education</i>	11	4,28	1	0,85

We note that comorbidities were present in 23 patients in the young group (8.94%) compared to 80 patients in the elderly group (68.37%). Comorbidities were present in 1 patient in the young group (7.00%) compared to 23 in the elderly group (19.65%), in 2 patients in the young group (1.16%) compared to 21 in the elderly group (21.36%), in 3 patients in the young group (0.77%) compared to 21 in the elderly group (17.94%), and more than 3 comorbidities in 11 patients in the elderly group (9.40%) compared to 0% in the young group.

We observe the presence of at least two comorbidities in nearly half of the elderly group (48.71%), while the majority of young women have only one comorbidity (7.00%)

Diabetes was the most common in the young group, while high blood pressure (HBP) was the most common in the elderly group. In second place, diabetes and HBP exchanged their positions respectively. We also observed the association of diabetes and HBP in 5 patients in the young group, representing 4.27%, and 29 patients in the elderly group, representing 24.78%. Other comorbidities are less represented in both groups, but elderly patients show a greater diversity of comorbidities, especially in cardiovascular and endocrine categories. Patients aged 70 and older have a much higher prevalence of comorbidities compared to patients under 40, with a greater diversity and higher frequency of multiple comorbidities (Table 2).

Table 2: Descriptive and comparative table of comorbidities in young patients under 40 years old (Total sample = 257) and patients aged 70 and older (Total sample = 117)

	Young groups (N=257)		Elderly groups (N=117)	
	Sample size	%	Sample size	%
<i>Comorbidities</i>				
Yes	23	8,94	80	68,37
Non	234	91,05	37	31,62
<i>Number of comorbidities/patient</i>				
1	18	7,00	23	19,65
2	3	1,16	25	21,36
3	2	0,77	21	17,94
>3	0	0,00	11	9,40
<i>Type of comorbidities</i>				
Hypertension	7	2,72	62	52,99
Diabetes	12	4,66	35	29,91
Other cardiovascular	2	0,77	23	19,65
Other endocrine	3	1,16	26	22,22
Bronchopulmonary	2	0,77	6	5,12
Other cancer	1	0,38	1	0,85
Others	3	1,16	33	28,20

The most common location was the left breast, with a percentage exceeding 50% in both groups. Non-specific type ductal carcinoma was the most common in both groups. Lobular carcinoma was quite common in the elderly, with a percentage of 23.93%. The most common T stage was T2 in both groups, present in nearly 2/5 of the young group and in over half of the elderly group. Lymph node involvement was positive in 46.30% of cases in the young group, compared to only 17.94% in the elderly group. The most common SBR grade was II in the young group (44.35%) and I in the elderly group (42.73%). The most common molecular profiles are luminal B in the young group and luminal A in the elderly group (Table 3).

Table 3: Comparative tables of the characteristics of primary tumors in young patients under 40 years old (Total number = 257) and patients aged 70 and over (Total number = 117)

	Young groups (N=257)		Elderly groups (N=117)	
	Sample size	%	Sample size	%
<i>Location</i>				
<i>Right</i>	135	52,52	62	52,99
<i>Left</i>	118	45,91	53	45,29
<i>Bilateral</i>	4	1,55	2	1,70
<i>Histological type</i>				
<i>Non-specific type ductal carcinoma</i>	239	92,99	87	74,35
<i>Lobular carcinoma</i>	12	4,66	28	23,93
<i>Others</i>	6	2,33	2	0,77
<i>T stage</i>				
<i>T1</i>	59	22,95	29	24,78
<i>T2</i>	99	38,52	61	51,13
<i>T3</i>	38	14,78	21	17,94
<i>T4</i>	61	23,73	6	5,12
<i>Lymph node involvement</i>				
<i>Yes</i>	119	46,30	21	17,94
<i>Non</i>	138	53,69	96	82,05
<i>SBR Grade</i>				
<i>I</i>	52	20,23	50	42,73
<i>II</i>	114	44,35	47	40,17
<i>III</i>	91	35,40	20	17,09
<i>Molecular profile</i>				
<i>Luminal A</i>	56	21,78	48	41,02
<i>Luminal B</i>	122	47,47	40	34,18
<i>HER2 positive</i>	32	12,45	24	20,51
<i>Triple negative</i>	47	18,28	5	4,27

From a therapeutic perspective, surgery, essential in treatment, including total mastectomy or lumpectomy, as well as axillary lymph node dissection or sentinel lymph node biopsy, was performed in all young women and in 97.43% of elderly individuals. Regarding chemotherapy, it was administered in adjuvant or neoadjuvant settings in 87.93% of cases, even though it was recommended in 91.43% of patients. It was applied in 24.78% of elderly patients, although it was indicated for 44.44% of them. Adjuvant radiotherapy, with or without lymph node irradiation, according to a standard or hypofractionated schedule, was applied in 72.37% of young women although it was recommended in 72.76% of them. For the elderly group, it was used in 61.53% of patients even though it was indicated for 71.79%. As for Adjuvant endocrine therapy, it was administered in 67.31% of cases even though it was recommended in 69.26% of the young group. It was administered in 24.78% of elderly patients, even though it was indicated for 44.44% of them. Regarding anti-HER2 treatment, it was administered in

19.45% of cases even though it was recommended in 20.62% of the young group. It was administered in 26.49% of elderly patients, although it was indicated for 31.62% of them (Table 4).

Table 4: Descriptive and comparative table of treatment characteristics in young patients under 40 years old (Total sample = 257) and patients aged 70 and over (Total sample = 117)

	Young groups (N=257)		Elderly groups (N=117)	
	Sample size	%	Sample size	%
<i>Surgery</i>				
<i>Indicated</i>	257	100,00	117	100,00
<i>Performed</i>	257	100,00	114	97,43
<i>Chemotherapy</i>				
<i>Indicated</i>	235	91,43	52	44,44
<i>Administered</i>	226	87,93	29	24,78
<i>Radiotherapy</i>				
<i>Indicated</i>	187	72,76	84	71,79
<i>Administered</i>	186	72,37	72	61,53
<i>Adjuvant endocrine therapy</i>				
<i>Indicated</i>	178	69,26	88	75,21
<i>Administered</i>	173	67,31	74	63,24
<i>Anti-HER2 treatment</i>				
<i>Indicated</i>	53	20,62	37	31,62
<i>Administered</i>	50	19,45	31	26,49

In the young group, none of the 257 patients refused surgery, compared to 3 out of 117 (2.56%) elderly patients. Chemotherapy was refused by 9 out of 235 young patients (3.82%) and by 23 out of 52 elderly patients (44.23%). Radiotherapy was refused by 1 out of 187 young women (0.53%) and by 12 out of 84 elderly women (14.28%). For adjuvant endocrine treatment, 5 out of 178 young women (2.80%) and 14 out of 88 elderly women (15.90%) refused it. Finally, anti-HER2 treatment was refused by 3 out of 53 young women (5.66%) and by 6 out of 37 elderly women (16.21%) (Table 5).

In conclusion, it emerges from this comparison that patients aged 70 and over have a much higher prevalence of comorbidities compared to patients under 40, with a greater diversity and higher frequency of multiple comorbidities. Furthermore, it is observed that women aged 70 and older generally refuse the various treatments offered more frequently than those under 40. This trend is particularly pronounced for chemotherapy, radiotherapy, and adjuvant endocrine therapy, where refusals are significantly higher in the older group. These refusals may be influenced by the increased presence of comorbidities in this age group, making treatments more risky or less acceptable.

Table 5: Descriptive table of refusal percentages for treatment in women under 40 and women aged 70 and older

	Younger groups		Elderly groups	
	Sample size	%	Sample size	%
<i>Surgery</i>	0/257	0,00	3/117	2,56
<i>Chemotherapy</i>	9/235	3,82	23/52	44,23
<i>Radiotherapy</i>	1/187	0,53	12/84	14,28
<i>Adjuvant endocrine therapy</i>	5/178	2,80	14/88	15,90
<i>Anti-HER2 treatment</i>	3/53	5,66	6/37	16,21

Women aged 70 and older, especially those with comorbidities, more frequently refuse certain breast cancer treatments compared to women under 40. Refusal of surgery is particularly notable only in older women with comorbidities (3.75%). The refusal of chemotherapy is 21.73% in young women with comorbidities and around 20% in elderly women, regardless of comorbidities. Refusals of radiotherapy and adjuvant endocrine therapy are also higher in elderly patients, especially those with comorbidities, reaching 10% and 12.5% respectively. Anti-HER2 treatment is refused by a small proportion of patients, but more pronounced in young women with comorbidities (8.69%) and elderly women with comorbidities (6.25%) (Table 6).

Table 6: Descriptive table of refusal percentages of treatment in young patients under 40 years old and elderly patients 70 years and older, based on comorbidities

	Younger groups Without comorbidities (N=234)		Young groups with comorbidities (N=23)		Elderly groups without comorbidities (N=37)		Elderly groups with comorbidities (N=80)	
	Sample size	%	Sample size	%	Sample size	%	Sample size	%
<i>Surgery</i>	0/234	0,00	0/23	0,00	0/37	0,00	3/80	3,75
<i>Chemotherapy</i>	4/234	1,70	5/23	21,73	7/37	18,91	16/80	20,00
<i>Radiotherapy</i>	1/234	0,42	0/23	0,00	4/37	10,81	8/80	10,00
<i>Adjuvant endocrine therapy</i>	1/234	0,42	4/23	17,39	4/37	10,81	10/80	12,50
<i>Anti-HER2 treatment</i>	1/234	0,42	2/23	8,69	1/37	2,70	5/80	6,25

Discussion :

The discussion on the impact of age and comorbidities on breast cancer treatment reveals significant challenges in optimizing therapeutic strategies.

Elderly women often receive less aggressive treatment or less frequently receive standard treatment than younger women worldwide (3) (4). Age is an independent risk factor for not receiving effective anticancer treatments (5). The vast majority of studies(6) (7), have shown that being elderly was a significant factor

for refusal. This situation highlights the clinical challenge related to decision-making, balancing between undertreatment and overtreatment of elderly patients.

By examining more closely the differences in therapeutic approach between young and elderly patients, it is evident that surgery remains the cornerstone of breast cancer treatment for all age groups. However, elderly patients aged ≥ 70 years at the time of diagnosis were less likely to undergo breast-conserving surgery than younger patients (8). Furthermore, while most women eligible for anti-estrogen treatment received it, adjuvant radiotherapy, chemotherapy, and/or trastuzumab were used infrequently (9). A study, involving over 120,000 women, showed that advanced age was associated with decreased rates of breast surgery, axillary surgery, and radiotherapy (10). Another study involving over 50,000 patients aged over 65 years demonstrated that increasing age is associated with decreased rates of chemotherapy. Chemotherapy administration rates for stages I and II decrease from 80% for women aged 67-69 to <10% for women over 85 (11).

Comorbidities also play a crucial role, elderly patients, even without comorbidities, had an increased risk of dying from breast cancer, despite higher mortality from other causes (8). The higher prevalence of comorbidities in elderly patients, such as hypertension and diabetes, further accentuates the challenges in managing their treatment. It has been shown that the presence of comorbidities influences treatment choice, adoption and toxicity, cancer and non-cancer survival, quality of life, and cost of care (12) (13) (14) (15). A study has shown that hypertension, diabetes, coronary artery disease, or strokes were associated with older age and not receiving chemotherapy and radiotherapy (16). Another study has shown that as the number of chronic diseases increases, the chances of reporting a lower quality of life and poorer emotional health after treatment also increase (17).

Furthermore, elderly patients are often less educated and may have less access to medical information, influencing their treatment decisions. They are also more likely to refuse treatment, often due to the presence of comorbidities and a perceived reduced life expectancy.

Young patients, on the other hand, often have to consider fertility concerns and worries about the long-term effects of treatments on their reproductive health. Communication between patients and healthcare professionals, as well as ongoing patient education about treatment options, can contribute to better adherence to therapeutic recommendations and improved clinical outcomes.

Conclusion:

This study highlights significant differences between young women and elderly women with breast cancer in terms of socio-demographic characteristics, comorbidities, and treatment behaviors. It is crucial to take these differences into account to adapt therapeutic strategies and improve personalized patient care, considering not only age but also the specific expectations and constraints of each group.

In conclusion, age and comorbidities are determining factors in breast cancer treatment decisions. Therapeutic strategies should be personalized taking into account not only the chronological age of the patients, but also their overall health status and personal preferences. Adapting treatments based on these variables would better meet the specific needs of patients, thus optimizing clinical outcomes and quality of life.

References

1. Ferlay J, Ervik M, Lam F et al. Global Cancer Observatory: Cancer Today. Available at: <https://gco.iarc.fr/today/>. [accessed on 01/05/2021].

2. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca P, Poortmans I, Rubio T, Zackrisson S, Senkus E. Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2019; 30:1194–1220.
3. Wyld, L., Garg, D. K., Kumar, I. D., Brown, H., & Reed, M. W. (2004). Stage and treatment variation with age in postmenopausal women with breast cancer: compliance with guidelines. *British journal of cancer*, 90(8), 1486–1491. <https://doi.org/10.1038/sj.bj>.
4. Lavelle, K., Todd, C., Moran, A., Howell, A., Bundred, N., & Campbell, M. (2007). Non-standard management of breast cancer increases with age in the UK: a population based cohort of women > or =65 years. *British journal of cancer*, 96(8), 1197–1203. <https://doi.org/10.1038/sj.bj>.
5. Enger, S. M., Thwin, S. S., Buist, D. S., Field, T., Frost, F., Geiger, A. M., Lash, T. L., Prout, M., Yood, M. U., Wei, F., & Silliman, R. A. (2006). Breast cancer treatment of older women in integrated health care settings. *Journal of clinical oncology*.
6. Gaitanidis, A., Alevizakos, M., Tsalikidis, C., Tsaroucha, A., Simopoulos, C., & Pitiakoudis, M. (2018). Refusal of Cancer-Directed Surgery by Breast Cancer Patients: Risk Factors and Survival Outcomes. *Clinical breast cancer*, 18(4), e469–e476. <https://doi.org/10.1016/j.clbc.2018.04.001>.
7. Chen, S. J., Kung, P. T., Huang, K. H., Wang, Y. H., & Tsai, W. C. (2015). Characteristics of the Delayed or Refusal Therapy in Breast Cancer Patients: A Longitudinal Population-Based Study in Taiwan. *PloS one*, 10(6), e0131305. <https://doi.org/10.1371/journal.pone.0131305>.
8. Derks MGM, van de Velde CJH, Giardiello D, et al. Impact of Comorbidities and Age on Cause-Specific Mortality in Postmenopausal Patients with Breast Cancer. *Oncologist*. 2019 et [doi:10.1634/theoncologist.2018-0010](https://doi.org/10.1634/theoncologist.2018-0010), 24(7):e467-e474.
9. Cyr, A., Gillanders, W. E., Aft, R. L., Eberlein, T. J., & Margenthaler, J. A. (2011). Breast cancer in elderly women (≥ 80 years): variation in standard of care?. *Journal of surgical oncology*, 103(3), 201–206. <https://doi.org/10.1002/jso.21799>.
10. Bastiaannet, E., Liefers, G. J., de Craen, A. J., Kuppen, P. J., van de Water, W., Portielje, J. E., van der Geest, L. G., Janssen-Heijnen, M. L., Dekkers, O. M., van de Velde, C. J., & Westendorp, R. G. (2010). Breast cancer in elderly compared to young.
11. Schonberg, M. A., Marcantonio, E. R., Li, D., Silliman, R. A., Ngo, L., & McCarthy, E. P. (2010). Breast cancer among the oldest old: tumor characteristics, treatment choices, and survival. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*.
12. Lee L, Cheung WY, Atkinson E, Krzyzanowska MK (2011) Impact of comorbidity on chemotherapy use and outcomes in solid tumors: a systematic review. *J Clin Oncol* 29(1):106–117. <https://doi.org/10.1200/JCO.2010.31.3049>.
13. Søgaard M, Thomsen RW, Bossen KS, Sørensen HT, Nørgaard M (2013) The impact of comorbidity on cancer survival: a review. *Clin Epidemiol* 5(Suppl 1):3–29. <https://doi.org/10.2147/CLEP.S47150>.
14. Crouch A, Champion VL, Von Ah D (2022) Comorbidity, cognitive dysfunction, physical functioning, and quality of life in older breast cancer survivors. *Support Care Cancer* 30(1):359–366. <https://doi.org/10.1007/s00520-021-06427-y>.
15. Ng HS, Koczwara B, Roder D, Chan RJ, Vitry A (2020) Patterns of health service utilisation among the Australian population with cancer compared with the general population. *Aust Health Rev* 44(3):470–479. <https://doi.org/10.1071/AH18184>.

16. Nechuta S, Lu W, Zheng Y, et al. Comorbidities and breast cancer survival: a report from the Shanghai Breast Cancer Survival Study. *Breast Cancer Res Treat.* 2013 et doi:10.1007/s10549-013-2521-2, 139(1):227-235.
17. Arneja J, Brooks JD (2021) The impact of chronic comorbidities at the time of breast cancer diagnosis on quality of life, and emotional health following treatment in Canada. *PLoS ONE* 16(8): e0256536. <https://doi.org/10.1371/journal.pone.0256536>.