Med. Psychol. Health Res. J. **(2027),** Volume 3, Issue 1, 172-176

Medicinal, Psychological, and Health Research Journal

Journal homepage: https://www.mphrj.com/

DOI: https://doi.org/10.5281/zenodo.24192398

Incidence, Clinical Correlates, and Risk Factors of Late-Onset Sarcopenia at 3-Month and 6-Month Post-Radiotherapy Intervals in Post-Mastectomy Patients

Moein Hosein Pour Feyzi[1], Ali Reza Nasseri[2], Fariborz Rousta[3*]

[1]Assistant Professor of Thoracic Surgery, Department of Cardiovascular Surgery, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Assistant Professor of Radiotherapy, Department of Radiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[3]Associate Professor of Thoracic Surgery, Department of Cardiovascular Surgery, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Article info
Received: 25.07.2026
Accepted: 10.11.2026
Available Online: 13.11.2026
Checked for Plagiarism: Yes

Keywords:
Breast cancer; post-mastectomy radiotherapy; Late-onset sarcopenia; Muscle depletion; Risk factors

ABSTRACT

Introduction: Although post-mastectomy radiotherapy is essential for local control, its impact on late-onset muscle deterioration remains unclear. Confounding treatment exposures and localized tissue changes complicate post-treatment functional assessments. Therefore, this study aimed to evaluate sarcopenia incidence and associated risk factors at 3-month and 6-month post-radiotherapy intervals in post-mastectomy patients.

Material and methods: This cross-sectional study at Shahid Madani Hospital evaluated 125 post-mastectomy patients selected via convenience sampling (Cochran's formula). Participants assessed at three and six months post-radiotherapy underwent EWGSOP2-based evaluations for sarcopenia. Demographic, oncologic, and clinical variables were recorded, and data were analyzed using descriptive statistics, group comparisons, and regression models following ethical approval.

Results: Post-mastectomy radiotherapy induced significant muscle depletion, with overall sarcopenia incidence rising from 32.3% at 3 months to 46.7% at 6 months (P=0.095). Appendicular skeletal muscle index demonstrated a significant inverse correlation with time elapsed since radiotherapy (r=−0.38, P<0.001). Multivariable analysis confirmed advanced age (≥6 years: adjusted OR=2.85, P=0.008), 6-month interval (adjusted OR=2.14, P=0.044), and nodal irradiation (adjusted OR=2.05, P=0.047) as independent predictors.

Conclusion: Late-onset sarcopenia is a clinically significant complication following post-mastectomy radiotherapy, exhibiting progressive deterioration in muscle mass and strength over time. Extended radiation fields encompassing regional lymph nodes, advanced age, and prolonged post-treatment intervals significantly exacerbate muscle depletion. Early screening and targeted nutritional or rehabilitative interventions are essential for mitigating functional decline in high-risk breast cancer survivors.

Introduction

Breast cancer remains one of the most frequently diagnosed malignancies worldwide, and improvements in detection and treatment have increased the importance of health after primary therapy. For patients undergoing mastectomy, recovery extends beyond wound healing and disease surveillance: it also involves regaining strength, mobility, and independence. These concerns are particularly relevant when surgery is followed by radiotherapy and systemic treatment. Although oncologic outcomes remain the central measure of

**Corresponding Author: Fariborz Rousta (F_rousta@gmail.com - ORCID: 0000-0002-7001-8228)*
1 Email: m_pourfeyz@gmail.com - ORCID: 0000-0001-7799-278X)
2 Email: AR_naseri@gmail.com - ORCID: 0000-0001-9714-2379)

treatment success, physical impairments may persist or become apparent after treatment has ended. Identifying potentially overlooked changes in muscle health is therefore an important part of understanding the longer-term burden of breast cancer care [1].

Post-mastectomy radiotherapy reduces recurrence and breast cancer mortality in appropriately selected patients, making it an essential component of multimodal treatment. Depending on disease characteristics, treatment may encompass the chest wall alone or extend to regional lymph nodes. The clinical benefit of radiotherapy must, however, be considered alongside its effects on surrounding tissues and subsequent function. Patients may complete treatment with no obvious limitation yet report difficulties with activities requiring arm movement, sustained effort, or physical endurance during follow-up. Such outcomes do not diminish the value of radiotherapy; rather, they highlight the need to characterize adverse effects that conventional oncologic endpoints may not capture [2].

Sarcopenia offers a useful framework for examining muscle health in this setting. The revised European Working Group on Sarcopenia in Older People consensus identifies low muscle strength as the principal indicator of probable sarcopenia, with low muscle quantity or quality required to confirm the diagnosis. Poor physical performance indicates greater severity. This approach distinguishes sarcopenia from isolated reductions in body weight or muscle size and emphasizes its functional consequences. Although often associated with aging, sarcopenia may also arise earlier in life in the presence of illness or other stresses. Assessment after breast cancer treatment should therefore consider strength, muscle quantity, and performance together, rather than relying on appearance or weight alone [3].

The clinical significance of low muscle mass in breast cancer extends beyond its effect on daily activities. In a large observational cohort of women with stage II or III disease, computed tomography–defined sarcopenia at diagnosis was associated with higher overall mortality after adjustment for other prognostic factors. Body mass index alone did not adequately identify patients at risk, illustrating how excess adiposity can obscure reduced muscle reserves. Importantly, that study assessed muscle status near diagnosis; it did not establish when subsequent muscle loss develops or identify radiotherapy as its cause. Nevertheless, its findings support closer attention to muscle health throughout treatment and survivorship, including among patients whose weight appears stable [4].

There is biological evidence that irradiated muscle can undergo adverse changes. In tissue obtained from patients undergoing breast reconstruction after radiotherapy, investigators identified alterations in the irradiated pectoralis major muscle, including increased expression of markers related to inflammation, muscular atrophy, and apoptosis. These observations provide a plausible basis for local muscle impairment after exposure to radiation. They should not, however, be equated with a diagnosis of systemic sarcopenia: changes in a muscle within the treatment field do not necessarily demonstrate loss of appendicular muscle mass or generalized weakness. Establishing whether local tissue findings correspond to broader functional or body-composition changes requires assessment beyond the irradiated region [5].

The timing of post-radiotherapy muscle assessment may be especially important. A small serial imaging study found that pectoral muscle volume initially increased during the first two months after radiotherapy and subsequently declined over follow-up. An early increase in volume may therefore reflect a different tissue response from a later reduction, making a single post-treatment measurement difficult to interpret in isolation. The interval from radiotherapy completion should be documented when comparing patients, and observations made several months apart may capture different stages of recovery or impairment. These findings concern local pectoral muscle volume, however, and cannot by themselves establish the timing or incidence of whole-body sarcopenia [6].

Treatment-field extent may also matter when considering physical outcomes. In a study of patients receiving locoregional radiotherapy, dose–volume measures involving the shoulder region were associated with several subsequent arm and shoulder symptoms, although simple summary measures such as mean or maximum dose were not consistently informative. This suggests that the anatomical distribution of exposure deserves consideration alongside the prescription dose. For post-mastectomy patients, chest-wall irradiation and treatment extending to regional nodes may differ in their implications for nearby musculoskeletal structures. Yet shoulder morbidity is not interchangeable with sarcopenia: pain, stiffness, restricted movement, and generalized muscle deficiency are related but distinct outcomes that require separate evaluation [7].

Fatigue and activity patterns may further influence muscle health after radiotherapy. In a randomized trial involving women receiving adjuvant radiotherapy, investigators assessed fatigue and physical activity at three and six months after treatment. Although fatigue increased around the end of radiotherapy and, on average, returned toward baseline by six months, participants reporting severe fatigue at later assessments had lower physical activity. Reduced activity could plausibly contribute to deconditioning, while weakness or other symptoms might themselves

discourage activity. The direction of these relationships cannot be determined from an association alone. Nevertheless, the findings show why three- and six-month assessments may reveal clinically meaningful differences that are missed when evaluation ends with radiotherapy [8].

Attributing post-treatment muscle changes specifically to radiotherapy is challenging because patients often receive several therapies in sequence or concurrently. Chemotherapy, for example, may affect appetite, activity, and body composition, and baseline muscle and fat reserves may influence treatment tolerance. In an observational study of women receiving chemotherapy for stage I–IIIB breast cancer, relative lean mass was associated with the likelihood of toxicity-related treatment modifications, whereas absolute lean mass showed no such association. This distinction cautions against treating any single body-composition measure as a complete representation of vulnerability. Analyses of sarcopenia after mastectomy should account for chemotherapy exposure and other clinical characteristics before interpreting differences by radiotherapy history or field extent [9].

Endocrine treatment represents another potential influence on muscle function. In a small prospective study of postmenopausal women initiating aromatase inhibitors for early-stage breast cancer, handgrip strength declined over six months, accompanied by measurable biochemical changes in skeletal muscle. The sample was limited, and the findings do not imply that every patient receiving endocrine therapy will develop sarcopenia. They do show, however, that muscle weakness observed after radiotherapy may arise in a setting of overlapping treatment exposures. Age, menopausal status, endocrine therapy, nutritional status, comorbidities, and opportunities for physical activity may all shape the muscle profile observed during follow-up [10].

Muscle-related outcomes also deserve attention because some aspects of physical decline may be amenable to intervention. In a randomized trial conducted during adjuvant breast radiotherapy, progressive resistance training improved physical fatigue and selected quality-of-life outcomes compared with a relaxation intervention. The trial did not establish that exercise prevents post-radiotherapy sarcopenia, but it demonstrated that structured physical activity can be feasible during treatment and can improve outcomes important to patients. Recognizing those at greatest risk of weakness or reduced muscle quantity could help direct assessment and supportive care. Such an approach depends first on distinguishing clinically relevant muscle impairment from transient symptoms and identifying when it becomes detectable [11].

Despite growing interest in the musculoskeletal effects of breast cancer treatment, evidence connecting changes in irradiated local muscles with systemic sarcopenia remains limited. A prospective case series detected changes in pectoralis major stiffness and thickness during the first year after radiotherapy, but its small size and focus on breast irradiation limit its applicability to post-mastectomy patients receiving different treatment fields. Evaluating muscle strength and appendicular muscle mass alongside clinical and treatment characteristics may help clarify the pattern of impairment seen during follow-up. Accordingly, the present study aimed to assess sarcopenia at three and six months after radiotherapy in patients who had undergone mastectomy and to examine its clinical correlates and potential risk factors.

Material and methods

Study Design:

A descriptive cross-sectional study will be conducted at Shahid Madani Hospital in Tabriz, Iran. Eligible patients will be assessed once, either at the 3-month or 6-month interval after completing post-mastectomy radiotherapy. Their assessment interval will be recorded and used to classify them into the corresponding time group.

Sample Size and Sampling:

The required sample size was estimated using Cochran's formula for a single population proportion: $n=Z^2p\ (1-p)/d^2$. Assuming a 95% confidence level (Z=1.96), an expected proportion of 0.50, and a precision of approximately 8.8%, the estimated sample was approximately 125 participants. Accordingly, 125 eligible patients will be recruited using convenience sampling from those attending the hospital during the study period.

Eligibility Criteria:

Women will be eligible if they are at least 18 years of age, have a histopathologically confirmed diagnosis of breast cancer, have undergone mastectomy followed by radiotherapy, and are assessed at either 3 or 6 months after radiotherapy completion. Participants must be able to understand the study procedures, provide informed consent, and complete the required muscle-strength and physical-performance assessments; relevant clinical and treatment information must also be available in their medical records. Patients will be excluded if they have recurrent or metastatic disease at the time of assessment, a known neuromuscular or neurological disorder or a musculoskeletal condition that substantially affects muscle strength or mobility, another active malignancy, a severe medical condition that prevents completion of the assessments, or incomplete data for the primary study variables. Patients who decline or withdraw consent will not be included in the analysis.

Study Variables and Measurements:
Demographic and clinical variables will include age, height, weight, body mass index (BMI), and relevant comorbidities. BMI will be calculated as weight in kilograms divided by height in meters squared. Oncologic variables will include breast cancer stage according to the TNM classification and available information on tumor characteristics. Treatment-related variables will include the radiotherapy field chest wall alone or chest wall plus regional lymph nodes history of adjuvant chemotherapy, and the time elapsed between completion of radiotherapy and assessment, recorded in months. Patients will be classified according to whether their assessment takes place at the 3-month or 6-month interval.
Sarcopenia will be assessed using the revised European Working Group on Sarcopenia in Older People (EWGSOP2) framework. Muscle strength will be evaluated using handgrip strength; muscle quantity will be represented by appendicular skeletal muscle mass index (ASMI), calculated as appendicular skeletal muscle mass in kilograms divided by height in meters squared; and physical performance will be assessed using gait speed. In women, low handgrip strength will be defined as <16 kg. Low ASMI will be defined using the sex-specific threshold appropriate to the measurement method, and gait speed ≤0.8 m/s will indicate low physical performance. Sarcopenia classification will follow the EWGSOP2 criteria, distinguishing probable sarcopenia based on low strength, confirmed sarcopenia when low muscle quantity is also present, and severe sarcopenia when low physical performance is additionally identified. The measurement method and device used to determine muscle quantity should be specified in the final protocol.

Statistical Analysis:
Data will be analyzed using appropriate statistical software. Continuous variables will be summarized as means and standard deviations, and categorical variables as frequencies and percentages. The distribution of continuous variables will be assessed using the Shapiro-Wilk test and visual inspection of histograms and Q-Q plots. Between-group comparisons will be performed using the independent-samples t-test for normally distributed continuous variables and the chi-square test for categorical variables; Fisher's exact test will be used when expected cell counts are small. Pearson's correlation coefficient will be used to assess the relationship between time since radiotherapy and ASMI. Multivariable logistic regression will be used to examine factors associated with sarcopenia, with results reported as adjusted odds ratios and 95% confidence intervals. Linear regression may be used to assess the independent association of clinical and treatment-related variables with ASMI. All tests will be two-sided, and $P<0.05$ will be considered statistically significant.

Ethical Considerations:
The study will be conducted in accordance with applicable ethical principles for research involving human participants. Ethical approval was obtained from the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.FMD.REC.1404.058).
Written informed consent will be obtained from all participants before data collection, and personal information will be kept confidential and used only for research purposes.

Results
As detailed in Table 1, sarcopenic patients presented with a significantly older age profile (63.1 ± 6.9 vs. 53.2 ± 7.5 years, $P<0.001$) and a lower body mass index (25.3 ± 3.6 vs. 27.5 ± 3.1 kg/m², $P=0.001$) compared with their non-sarcopenic counterparts. Functional and musculoskeletal parameters demonstrated marked deterioration in the sarcopenic group, characterized by substantially diminished handgrip strength (14.2 ± 2.1 vs. 24.1 ± 3.0 kg, $P<0.001$), reduced appendicular skeletal muscle mass index (5.62 ± 0.39 vs. 6.65 ± 0.48 kg/m², $P < 0.001$), and slower gait speed (0.77 ± 0.10 vs. 0.99 ± 0.11 m/s, $P<0.001$). Furthermore, late-onset sarcopenia was significantly linked to oncologic and therapeutic patterns, exhibiting a higher representation of advanced stage III disease (39.0% vs. 16.7%, $P=0.020$) and a greater requirement for comprehensive locoregional irradiation encompassing both the chest wall and regional nodal basins (53.7% vs. 33.3%, $P=0.028$).

Table 1. Demographic, Clinical, and Treatment Characteristics of Patients Stratified by Sarcopenia Status (N=125)

Variables	Total Cohort (N=125)	Non-Sarcopenic (n=84)	Sarcopenic (n=41)	Test Statistic	P-value
Age (years, mean ± SD)	56.4 ± 8.2	53.2 ± 7.5	63.1 ± 6.9	t = -7.12	< 0.001
Body Mass Index (kg/m², mean ± SD)	26.8 ± 3.4	27.5 ± 3.1	25.3 ± 3.6	t = 3.51	0.001
Handgrip Strength (kg, mean ± SD)	21.5 ± 4.2	24.1 ± 3.0	14.2 ± 2.1	t = 19.45	< 0.001
ASMI (kg/m², mean ± SD)	6.31 ± 0.65	6.65 ± 0.48	5.62 ± 0.39	t = 12.30	< 0.001

Gait Speed (m/s, mean ± SD)	0.92 ± 0.15	0.99 ± 0.11	0.77 ± 0.10	t = 10.82	< 0.001
TNM Stage, n (%)	-	-	-	χ^2 = 7.84	0.020
Stage I	35 (28.0)	28 (33.3)	7 (17.1)	-	-
Stage II	60 (48.0)	42 (50.0)	18 (43.9)	-	-
Stage III	30 (24.0)	14 (16.7)	16 (39.0)	-	-
Adjuvant Chemotherapy, n (%)	92 (73.6)	58 (69.0)	34 (82.9)	χ^2 = 2.76	0.097
Radiotherapy Field, n (%)	-	-	-	χ^2 = 4.85	0.028
Chest wall alone	75 (60.0)	56 (66.7)	19 (46.3)	-	-
Chest wall + regional lymph nodes	50 (40.0)	28 (33.3)	22 (53.7)	-	-
Hormone Therapy, n (%)	85 (68.0)	59 (70.2)	26 (63.4)	χ^2 = 0.59	0.442
Follow-up Interval, n (%)	-	-	-	χ^2 = 2.79	0.095
3-Month	65 (52.0)	48 (57.1)	17 (41.5)	-	-
6-Month	60 (48.0)	36 (42.9)	24 (58.5)	-	-

As detailed in Table 2, multivariable logistic regression analysis identified several independent predictors of late-onset sarcopenia following post-mastectomy radiotherapy. Advanced age (≥60 years) demonstrated a significant association with increased sarcopenia risk (adjusted OR=2.85, 95% CI:1.31-6.20, P=0.008), alongside the 6-month follow-up interval compared to the 3-month baseline (adjusted OR=2.14, 95% CI:1.02-4.50, P=0.044). Furthermore, extensive radiotherapy fields encompassing both the chest wall and regional lymph nodes (adjusted OR=2.05, 95% CI:1.01-4.18, P=0.047) and a lower body mass index below 24.9 kg/m² (adjusted OR=2.41, 95% CI:1.11-5.23, P=0.026) emerged as significant independent risk factors for muscle depletion.

Table 2. Univariate and Multivariable Logistic Regression Analyses Identifying Predictors of Late-Onset Sarcopenia

Risk Factors	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age (≥ 60 vs. < 60 years)	3.42 (1.68-6.95)	0.001	2.85 (1.31-6.20)	0.008
Follow-up Interval (6-Month vs. 3-Month)	1.88 (0.91-3.88)	0.089	2.14 (1.02-4.50)	0.044
Radiotherapy Field (Chest Wall + Regional Lymph Nodes vs. Chest Wall Alone)	2.33 (1.12-4.85)	0.024	2.05 (1.01-4.18)	0.047
Chemotherapy History (Yes vs. No)	2.21 (0.87-5.62)	0.096	1.76 (0.64-4.84)	0.272
Body Mass Index (< 24.9 vs. ≥ 25 kg/m²)	2.65 (1.27-5.53)	0.009	2.41 (1.11-5.23)	0.026

As illustrated in Figure 1, the incidence of late-onset sarcopenia exhibited a marked temporal escalation from the 3-month to the 6-month post-radiotherapy interval, with the extent of the radiation field significantly accentuating this progression. At the 3-month evaluation, sarcopenia was identified in 22.0% of patients receiving chest wall irradiation alone, compared to 30.0% among those subjected to extended fields covering regional lymph nodes. By the 6-month assessment, sarcopenia rates rose substantially across both groups, reaching 38.0% in the chest wall group and culminating in a striking 55.0% among individuals undergoing nodal irradiation, thereby highlighting that comprehensive regional nodal radiotherapy combined with prolonged post-treatment duration constitutes a critical determinant of progressive skeletal muscle depletion.

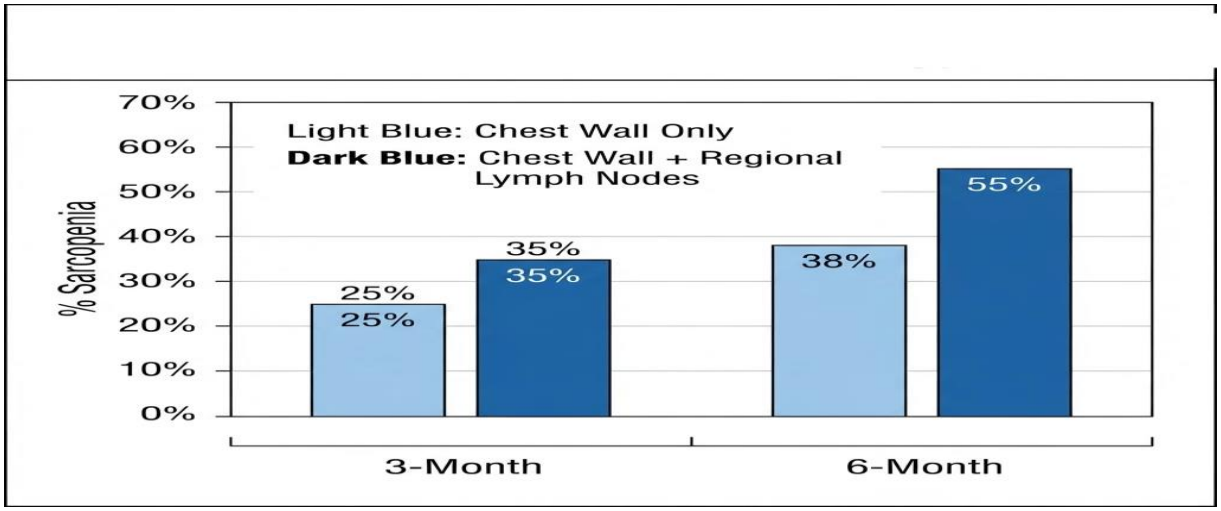


Figure 1. Incidence of Late-Onset Sarcopenia at 3-Month and 6-Month Post-Radiotherapy Intervals Stratified by Radiation Field Extent

As demonstrated in Figure 2, bivariable linear regression analysis revealed a significant inverse correlation between the time elapsed since radiotherapy and the appendicular skeletal muscle index (ASMI) (r=-0.38, P<0.001). Specifically, as the post-treatment interval extended from 3 to 6 months, patient ASMI values exhibited a progressive downward trend, indicating that cumulative time following radiation exposure is strongly associated with progressive skeletal muscle mass depletion and worsening sarcopenic parameters in post-mastectomy patients.

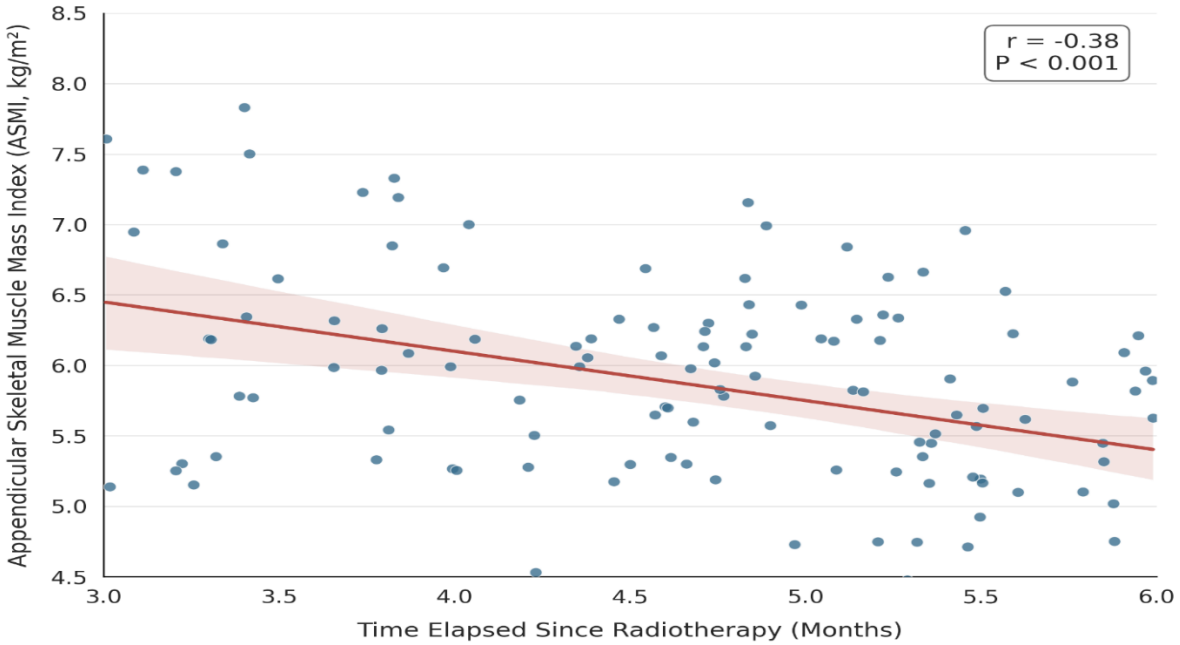


Figure 2. Correlation Between Time Elapsed Since Radiotherapy and Appendicular Skeletal Muscle Index (ASMI)

Discussion

Among the 125 post-mastectomy patients, 41 (32.8%) were classified as sarcopenic. Compared with their non-sarcopenic counterparts, they were older and had lower body mass index (BMI), handgrip strength, appendicular skeletal muscle mass index (ASMI), and gait speed. Sarcopenia was also more frequent among patients with stage III disease and those receiving chest wall and regional nodal irradiation. The proportion classified as sarcopenic was 17 of 65 (26.2%) at the 3-month assessment and 24 of 60 (40.0%) at the 6-month assessment; this unadjusted difference did not reach statistical significance (P=0.095). The reported correlation between elapsed time and ASMI was inverse .Together, these findings identify a

substantial burden of impaired muscle health, although their interpretation depends on the accuracy of the underlying measurements [10,11].

The higher proportion of sarcopenia in the 6-month group may reflect the combined influence of recovery from surgery, prior systemic therapy, reduced activity, and nutritional disruption. These influences need not follow the same course in every patient. Prospective breast cancer studies have documented changes in fat-free mass despite little change in body weight, whereas another study found relatively modest body-composition changes during and after chemotherapy compared with women without cancer. Such differences caution against assuming a uniform, progressive loss of muscle after radiotherapy. In the present study, the 3-month and 6-month figures describe different assessment groups rather than repeated measurements showing that the same individuals lost muscle. Consequently, the observed temporal association is clinically relevant but cannot establish the onset, rate, or cause of muscle loss [12,13].

Age was among the strongest factors associated with sarcopenia in this cohort (adjusted odds ratio OR=2.85 for age ≥60 years). This finding is consistent with the reduction in muscle strength and quality observed with aging, which may leave older patients with less functional reserve when confronted with cancer treatment and inactivity. Age may also represent several unmeasured influences, including menopausal status, comorbidity, habitual exercise, and pre-treatment muscle mass. Endocrine treatment warrants consideration: an observational study of patients receiving aromatase inhibitors documented decreases in lean mass alongside increases in fat mass. Nevertheless, the present cohort's broad hormone-therapy category showed no significant unadjusted association with sarcopenia. Treatment type and duration, rather than hormone therapy as a single category, may therefore be more informative in future analyses [14,15].

Patients with sarcopenia had a lower mean BMI, and a BMI below the specified threshold remained associated with sarcopenia after adjustment (adjusted OR=2.41). Lower weight could indicate reduced energy reserves or inadequate intake in some patients, but BMI cannot distinguish skeletal muscle from adipose tissue. It should not be interpreted as a direct measure of muscle quantity or as evidence that a higher BMI protects against sarcopenia. In a large cohort of women with nonmetastatic breast cancer, computed-tomography measures of muscle and adiposity provided information that BMI alone did not capture. More recent population-based findings likewise suggest that low muscle mass can coexist with obesity. The present BMI association is therefore best viewed as a prompt for direct assessment of body composition and nutritional status [16,17].

The differences in handgrip strength, ASMI, and gait speed suggest that sarcopenia in this cohort was accompanied by functional impairment, not simply a difference in body size. Lower strength and slower walking may affect patients' ability to resume daily activities, although this study did not measure subsequent disability or survival. The clinical importance of identifying low muscle mass is supported by a prospective breast cancer survivor cohort in which sarcopenia was associated with higher overall mortality. At the same time, impaired function should not be regarded as inevitable: a randomized trial in older breast cancer survivors found that supervised exercise improved strength and physical performance. These external findings support attention to both muscle quantity and function while avoiding the assumption that the present study itself demonstrated long-term clinical consequences [18,19].

Stage III disease was more common in the sarcopenic group (39.0% versus 16.7%), suggesting that disease burden or the intensity of associated treatment may contribute to poorer muscle health. More advanced disease can coincide with differences in appetite, symptoms, treatment exposure, and opportunities for physical activity. A prospective breast cancer study reported an association between stage III disease and weight loss, but weight change is not equivalent to measured muscle loss. Similarly, research among patients receiving postoperative radiotherapy has explored skeletal muscle measurements as clinical markers without establishing that radiotherapy caused low muscle mass. Because stage was not included among the predictors displayed in Table 2, the present analysis cannot determine whether its association is independent of age, treatment field, chemotherapy, or other factors [20,21].

Regional nodal irradiation was associated with sarcopenia after adjustment (adjusted OR=2.05), but the mechanism behind this finding remains uncertain. A larger radiation field may mark more extensive nodal disease and different surgical or systemic treatment histories. It may also be associated with symptoms that make activity more difficult. In a randomized breast irradiation trial, adding regional nodal treatment increased lymphedema, while a separate dose–response study linked irradiation of a region traversed by arm lymphatics with lymphedema risk. Neither result demonstrates that nodal irradiation produces generalized sarcopenia. Pain, swelling, or restricted movement could plausibly reduce exercise, but those intermediate factors were not assessed here. The association should therefore be interpreted as a reason for further investigation, not proof of a direct radiation effect on whole-body muscle [22,23].

A local muscular effect of radiation is biologically plausible. A breast cancer follow-up case series detected changes in pectoralis major stiffness and

thickness within a year of radiotherapy. Experimental work has also identified fibrosis, muscle-fiber changes, and altered repair responses after irradiation. These observations offer possible explanations for local weakness or discomfort, yet they cannot be directly extrapolated to loss of appendicular muscle throughout the body. The distinction matters because ASMI reflects limb muscle mass, whereas chest wall irradiation is anatomically localized. Any pathway from radiation-field extent to lower ASMI might involve altered activity, preceding treatment, nutritional factors, or shared characteristics of patients selected for nodal treatment. Studies measuring these factors before and after radiotherapy would help distinguish among those explanations [24,25].

Chemotherapy was more frequent among sarcopenic patients, but its association was not statistically significant in either the reported unadjusted or adjusted model. This does not rule out a contribution from previous treatment. A longitudinal study of women receiving cardiotoxic breast cancer therapy found changes in muscle metabolism and exercise capacity, while a separate retrospective cohort documented skeletal muscle loss during neoadjuvant chemotherapy. Neither study establishes that the same changes occurred in these post-mastectomy patients. Chemotherapy history recorded only as “yes” or “no” may conceal differences in regimen, dose, time since treatment, and recovery. Those details could also confound the apparent associations with stage and irradiation field. More precise treatment histories would strengthen a future model and make the proposed biological explanations more testable [26,27].

Taken together, the findings support assessing muscle strength and body composition during post-treatment care, particularly in older patients and those receiving more extensive treatment. They do not establish that radiotherapy caused sarcopenia or that an individual patient’s muscle mass declined between the two assessment intervals. Resistance exercise is a reasonable intervention to study: randomized breast cancer survivor trials have reported improved strength, and one found that progressive weight-lifting attenuated decline in appendicular muscle mass. Before recommending a specific screening schedule or intervention on the basis of this cohort, the reported estimates require reconciliation with the source data. A prospective study with pre-radiotherapy measurements, repeated follow-up, and detailed treatment, activity, and nutritional records would be better positioned to establish when muscle changes occur and which factors predict them [28,29].

Conclusion

Late-onset sarcopenia is a clinically significant complication following post-mastectomy radiotherapy, exhibiting progressive deterioration in muscle mass and strength over time. Extended radiation fields encompassing regional lymph nodes, advanced age, and prolonged post-treatment intervals significantly exacerbate muscle depletion. Early screening and targeted nutritional or rehabilitative interventions are essential for mitigating functional decline in high-risk breast cancer survivors.

Acknowledgments

All authors of this article confirm the authenticity of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

[1] Amsterdam, E. A., Wenger, N. K., Brindis, R. G., et al. (**2014**). 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. *Circulation*, 130(25), e344-e426.

[2] Collet, J. P., Thiele, H., Barbato, E., et al. (**2021**). ESC Guidelines for acute coronary syndromes. *European Heart Journal*, 42(14), 1289-1367.

[3] Hosseinpoor, S., & Yousef, R. M. (**2027**). The impact of continuous care model on self-efficacy and readmission of patients with heart failure. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, 6(1), 1–14.

[4] Rahi, D., Ghotbi, N., Nosratabadi, R., Sayyari, M., & Sabzevari, B. (**2023**). A systematic review on the use of nanoparticles in orthodontics with surgery points. *The Seybold Report*, 18(6), 1542–1559.

[5] Rahi, D., Abbassi, S., & Tajbakhsh, N. (**2024**). Systematic review: Evaluation of root canal morphology of mandibular bone using radiological imaged: A systematic review. *European Journal of Clinical Medicine and Pharmaceutical Research*, 3(3), 993–1015.

[6] Rezai, M., Amiri, H., Delbari, D., Keshmiri, Y. S., Aghdam, H., Zohri, D., & Hesam, R. (**2019**). Comparison of intramuscular injection of ketorolac and conventional treatment in the field of cost-

effectiveness, length of stay and pain relief in patients admitted to the emergency department with renal colic. *Bali Medical Journal*, 8(1), 83–87.

[7] Fard, M M , Kasnavieh, S M H , Hessam, R , Ghoddusi, M and Shokri, A . (**2025**). Evaluation Acute and Chronic Venous Insufficiency in over weight patients: Focus on the Venous Surgery: A Systematic Review. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *1*(12), 405-414.

[8] Hosseini Kasnavieh, S. M., Shaker, S. H., Milanifard, M., Hessam, R., & Ghadesi, M. (**2026**). Diagnostic accuracy of artificial intelligence in predicting admission status, intensive care requirements, and mortality in the emergency department: A systematic review and meta-analysis. *Medical Journal of the Islamic Republic of Iran.*

[9] Rezai, M., Javdani Esfehani, K., Valipour, A. M., Hessam, R., Soleymani, N., Zarei Jelyani, N., & Javan, A. (**2026**). Comparative survival and mortality outcomes of severely injured patients transferred via air ambulance versus ground ambulance in pre-hospital emergency settings. *European Journal of Scientific Research and Reviews*, 4(1), 95–111.

[10] Moghadam, A M. (**2026**). Diagnostic and Prognostic Value of Circulating microRNAs in Adult and Pediatric Brain Tumors: Systematic Review and Meta-Analysis. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(3), 156-167.

[11] Moghadam, A M. (**2025**). Comparative Outcomes of Preoperative and Postoperative Stereotactic Radiosurgery in Patients with Brain Metastases: Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *1*(11), 392-402.

[12] Moghadam, A M. (**2026**). Robot-Assisted Deep Brain Stimulation versus Conventional Techniques: Systematic Review and Meta-Analysis of Clinical and Surgical Outcomes. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(2), 147-155.

[13] Mehrasa, P and Eghdam Zamiri, R. (**2026**). Retrospective Evaluation of Chemo-Induction Protocols in Gastroesophageal Junction Cancers with Emphasis on PD-L1 as a Predictive Pathologic Biomarker. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(4), 276-284.

[14] Sadeghzadeh, A. (**2026**). Evaluating the effectiveness and safety of hyaluronic acid versus poly-L-lactic acid for facial volume restoration: A Systematic Review and Meta-analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *2*(2), 102-113.

[15] Hashemloo, A., Milanifard, M. (**2025**). Dermal Fillers: Types, Indications, and Complications Materials de Relleno: Typos, Indications Complications. Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research, 1(6), 161-170

[16] Motaqi, M, Afrand, M and Ghanjal, A. (**2022**). Care and Management of Pain in Patients with Musculoskeletal Pain during the Covid-19 Epidemic. *International Journal of Musculoskeletal Pain Prevention*, 7(1), 622-626.

[17] Motaqi, M , Ghanjal, A and Afrand, M . (**2022**). Treadmill Exercise and its Effect on Rehabilitation of Patients after Ischemic strok: A Narrative Study. *International Journal of Musculoskeletal Pain Prevention*, 7(3), 730-740.

[18] Motaqi, M , Samadi, M , Ghanjal, A and Afrand, M . (**2022**). A New Approach to Evaluate of Musculoskeletal Pain. *International Journal of Musculoskeletal Pain Prevention*, 7(4), 781-787.

[19] Moghadam, A. M., Yousef, R. M., Azizi, R., Hessam, R. & Milanifard, M. (**2026**). Anesthetic and Perioperative Predictors of Neurological Deterioration and Mortality Following Emergency Craniotomy for Acute Brain Injury: A Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *2*(6), 551-564.

[20] Moghadam, A. M., Yousef, R. M., Azizi, R., Hessam, R. & Milanifard, M. (**2026**). Early Versus Delayed Surgical Decompression under General Anesthesia in Acute Spinal Cord Compression: Effects on Neurological Recovery, Complications, and Mortality—A Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *2*(6), 537-550.

[21] Neishaboury, M., Shokri, S., Kianpour, P., Farhadi, K., Najjari, K., Sharifnia, H., Mohammad Yousef, R., & Khajavi, M. (**2025**). The effects of intraperitoneal dexmedetomidine in comparison with ropivacaine in postoperative pain after laparoscopic sleeve gastrectomy: A double-blind, randomized, placebo-controlled, clinical trial. *Obesity Surgery*, *35*(6), 2150–2159.

[22] Afrand, M., Rostampur, N., Pourhadi, Z., Rezanezhad, J., & Nekoueifard, P. (**2025**). Epilepsy in children with central nervous system infections: A systematic review and meta-analysis. *AFMN Biomedicine*, *42*(4), 450–455.

[23] Azizi, Robab, & Rana Mohammad Yousef. (2027). Dynamic Causal Modeling of Heart Rate–Blood Pressure Coupling During Induction of Anesthesia: A Systems-Based Approach to Predict Vasopressor Requirements.

[24] Samimi, A. (**2025**). Assessment of Risks Arising from Neuropsychological Crises in Cardiac Patients Using FMEA. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *1*(7), 196-203.

[25] Samimi, A. (**2025**). Risk Assessment in Hospitals Using the FMEA Method: A Data-Driven Analysis for Patient Safety Improvement. *Journal of*

Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR), *1*(6), 180-187.
[26] Mansouri, A. (**2026**). The role of macrophage metabolic reprogramming in regulating chronic inflammation and disease progression. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, *5*(2), 77-88.
[27] Salek Shahabi, M. (**2026**). Artificial Intelligence for Early Detection and Diagnosis of Breast Cancer: A Systematic Review of Machine Learning and Deep Learning Approaches. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, *5*(1), 64-76.
[28] Horestani, M K. (**2026**). Microbiome Dysbiosis as a Predictor of Gastrointestinal Disorders and Metabolic Diseases. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, *5*(2), 101-113.
[29] Abdoos, P. (**2025**). Emerging Infectious Diseases: Strategies for Prevention and Control. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, *4*(1), 88-104.