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Effect of Body Mass Index (BMI) on Prognosis, Response to Therapy, and Surgical Outcomes in Various Subtypes of Breast Cancer: A Systematic Review

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Abstract: *Breast cancer management is increasingly complicated by the global obesity crisis. While elevated Body Mass Index (BMI) worsens prognosis, its exact effect on treatment response and survival across subtypes remains unclear. This systematic review evaluates how BMI impacts prognosis, pharmacological efficacy, and oncoplastic surgical outcomes to support personalized Evidence-Based Medicine (EBM). Following PRISMA guidelines, we conducted a qualitative narrative synthesis using the PICO framework to search databases up to 2026. We included observational studies and retrospective RCT analyses that correlated baseline BMI in adult women with overall survival, pathological complete response, and surgical complications. Because BMI cut-offs varied across studies, we assessed methodological quality using the Newcastle-Ottawa Scale (NOS) and applied a descriptive analytical approach to synthesize the findings.*
Keywords *:* Body mass index; breast cancer; surgical output; prognosis; therapeutic response.

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INTRODUCTION

Breast cancer is the malignant with the highest incidence rate in women globally and has a highly heterogeneous clinical and biological nature (Dauccia et al., 2025) (Dauccia et al., 2026). On the other hand, obesity has become a global public health problem that continues to increase in prevalence (Borremans et al., 2025) (Xande et al., 2025) (Abdul & Province, 2025). Increased Body Mass Index (BMI) or obesity has been widely recognized as one of the major risk factors, not only for the development of breast cancer incidence, but also triggers a poorer prognosis in various subtypes of r molecules (Borremans et al., 2025)(Yoon et al., 2025) Nonetheless, the exact mechanisms of how BMI affects a patient's treatment response and survival are still not fully understood and often show contradictory results depending on the specific subtype and the therapy modality given (Dauccia et al., 2025; Borremans et al., 2025).

In early-stage breast cancer with *positive Human Epidermal Growth Factor Receptor 2*

(HER2) receptors, obesity or high BMI (≥25 kg/m^2) have been shown to be associated with *worse Invasive Disease-Free Survival* (iDFS), *Distant Recurrence-Free Interval* (DRFI), and *Overall Survival* (OS) (Dauccia et al., 2025). This group of patients is also known to have higher rates of chemotherapy discontinuation due to toxicity intolerance, which can contribute to suboptimal clinical outcomes (Dauccia et al., 2025). Meanwhile, in postmenopausal ER-positive/HER2-negative (ER+/HER2-) subtype breast cancer, obesity parameters were able to modify the prognostic value of progesterone receptors (PgR) (Lee et al., 2025). Negative PgR status is known to be a strong predictor of poorer survival, but this negative effect is significantly only seen in obese patients and is not found in patients with normal BMI (Widhi et al., 2024) (Lee et al., 2025).

The impact of BMI also varies on more aggressive clinical presentations, such as *Inflammatory Breast Cancer* (IBC) (Borremans et al., 2025). In IBC patients, higher BMI is associated with older age at diagnosis and an increase in *the number of stromal tumor infiltrating lymphocytes* (sTIL) (Borremans et al., 2025). Specifically in the ER-/HER2+ subgroup, increased BMI was also correlated with a higher risk of metastasis at diagnosis, although BMI in general was not shown to significantly affect the achievement of *Pathological Complete Response* (pCR) or overall survival in IBC populations (Borremans et al., 2025).

In addition to influencing tumor biology, body composition also interacts in a complex way with pharmacokinetics and efficacy of systemic therapies (Nys et al., 2025)(Liu et al., 2026)(Biganzoli et al., 2025). In the realm of advanced endocrine therapy for postmenopausal ER+ patients, the prognostic value of BMI is highly dependent on the type of previous adjuvant endocrine therapy (such as *Selective Estrogen Receptor Modulator*/SERM or *Aromatase Inhibitor*/AI) as well as its mode of administration (Biganzoli et al., 2025). This *second-order interaction* suggests that adiposity status can alter the effectiveness of estrogen blockade, making the personalization of BMI-based endocrine therapy a rational clinical consideration (Biganzoli et al., 2025)

In addition, high BMI is often a concern related to increased intolerance and toxicity of systemic therapies, which forces early discontinuation of chemotherapy and potentially provides suboptimal clinical outcomes (Machado et al., 2026)(Durkin et al., 2022)(Dauccia et al., 2025) However, recent clinical evidence suggests that oncoplasty techniques such as *therapeutic mammoplasty* remain safe to perform in patients with high BMI (≥30 kg/m^2) without significant differences in the rate of surgical wound complications or the delay time of adjuvant therapy (chemotherapy or radiotherapy) compared to patients with normal BMI (Alotaibi et al., 2026)(Moen et al., 2021)(Alejandro et al., 2026)(Adwall, 2025).

Based on the heterogeneity of interactions between BMI and the above clinicopathological characteristics, pharmacological responses, and surgical outcomes, a comprehensive review is needed(Post et al., n.d.)(Yang et al., 2025) Therefore, this *Systematic Literature Review* aims to evaluate and summarize the latest evidence on the influence of Body Mass Index (BMI) on prognosis, therapeutic efficacy, and surgical outcomes in various subtypes of breast cancer, in order to provide the basis for *Evidence-Based Medicine* (EBM) in efforts to personalize oncology management (Lee et al., 2025; Dauccia et al., 2025;Alotaibi et al., 2026).

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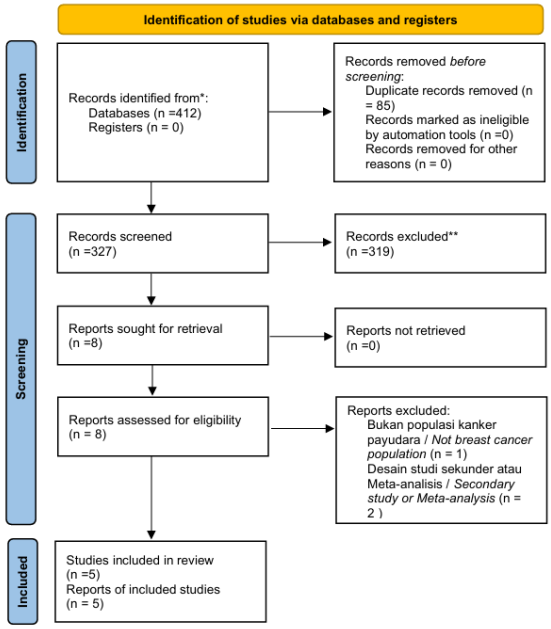
RESEARCH METHODS

This study is designed as a *systematic literature review* with a qualitative narrative synthesis approach that refers to the standard guidelines *of Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). This approach was chosen to comprehensively evaluate clinical outcomes, given the majority of the available primary literature in the form of large-scale multicenter retrospective cohort studies drawn from national registry databases as well as hospital medical records (Page et al., 2021).



A comprehensive literature search is conducted through major electronic academic databases to identify cutting-edge articles published up to 2026, to ensure the novelty of clinical data evaluated in the oncology literature. The search strategy was formulated using the PICO (*Population, Intervention/Exposure, Comparison, Outcome*) framework combined with Boolean operators. Keywords used include: ("Breast Cancer" OR "Breast Neoplasms") AND ("Body Mass Index" OR "BMI" OR "Obesity" OR "Overweight") AND ("Prognosis" OR "Survival" OR "Treatment Outcome" OR "Surgical Complications"), which have been shown to be effective in capturing cohort studies as well as *post-hoc analyses* of relevant phase III clinical trials.

The literature selection process was based on specific inclusion criteria that included primary observational studies and retrospective analysis of randomized controlled clinical trials, with adult female populations diagnosed with breast cancer of various subtypes, including ER+/HER2-, HER2-positive, and *Inflammatory Breast Cancer* (Biganzoli et al., 2025; Dauccia et al., 2025). Primary exposure is limited to the evaluation of Body Mass Index (BMI) or adiposity at diagnosis, with outcomes in the form of objective clinical parameters such as *Overall Survival* (OS), *Pathological Complete Response* (pCR), to surgical complications and adjuvant therapy delay time (Alotaibi et al., 2026; Borremans et al., 2025). Systematic review articles, meta-analyses, case reports, and *in vitro* studies are set as exclusion criteria to avoid bias and prevent duplicate data (*double* counting).

The literature that escaped the search process was evaluated for the quality of its methodology to assess risk *of bias*, especially since the majority of eligible studies were retrospective in design or were secondary data from previous clinical trials (Biganzoli et al., 2025; Lee et al., 2025). The assessment was conducted using the *Newcastle-Ottawa Scale* (NOS) standard instrument which included an evaluation of the study population selection, comparability of adjustments to confounding variables (such as age and stage of tumor), and objectivity of clinical outcome measurements(Soltanifar et al., 2021). Only literature with medium to high methodological quality was included in the final data extraction stage.

Data from the literature that met the inclusion criteria were systematically extracted into a standardization matrix that included the study design, sample count, molecular subtype, *cut-off* classification of BMIs used, as well as key findings related to clinical outcomes. Given the significant heterogeneity in the definition of the BMI cut-off point between studies, such as the use of the BMI limit of ≥ 25kg/m^2 for obesity criteria according to the Asia-Pacific guidelines (Lee et al., 2025) compared to the BMI limit of ≥ 30kg/m^2 in the European and American populations (Alotaibi et al., 2026; Borremans et al., 2025) then quantitative meta-analysis is not possible. Therefore, the data synthesis is focused on an analytical descriptive approach to compare and evaluate the impact of BMI on tumor biology, pharmacotherapy response, and surgical outcomes of oncoplasy in a structured manner (Biganzoli et al., 2025; Dauccia et al., 2025).

RESULTS AND DISCUSSION

Table 1. Article Data Mapping Results

Author & Year	Study Design	Population & Subtypes	Sample Count (N)	Therapy Modalities	Key Findings
Lee et al. (2025)	Cohort retrospective multicenter	Postmenopausal Patients, ER+/HER2- Breast Cancer	10.125	Therapy Endocrine	PgR-negative *status* is a strong predictor of OS and poor RFS only in obese patients (BMI ≥25 kg/m^2). This negative impact is not significant on patients with BMI <25 kg/m^2.
Dauccia et al. (2025)	Post-hoc *analysis* of phase III randomized clinical trials (APHINITY)	HER2-positive early-stage breast cancer	4.787	Adjuvant chemotherapy + HER2 blockade (Single/Dual)	Overweight/obese patients had a higher rate of chemotherapy discontinuation (14% vs 9%). High BMI is associated with independently worse iDFS, DRFI, and OS outputs.
Alotaibi et al. (2026)	Retrospective review	Breast Cancer undergoing *Therapeutic Mammoplasty* (TM)	73	Surgical Oncoplasty (*Therapeutic Mammoplasty* & Contralateral Reduction)	There was no significant difference in injury complications between the BMI <30 (33%) and BMI ≥30 (32%) groups. There was no significant

Author & Year	Study Design	Population & Subtypes	Sample Count (N)	Therapy Modalities	Key Findings
					delay in initiation of adjuvant therapy due to high BMI.
Biganzoli et al. (2025)	Retrospective analysis of phase III clinical trials (SOLE)	Postmenopausal patients, ER+/HER2-, Lymph Node Involvement positive	3.606	Extension of adjuvant endocrine therapy (5 years of *continuous vs intermittent* letrozole)	The prognostic value of BMI depends on the type of previous endocrine therapy (SERM or AI) as well as the mode of administration of *letrozole*. Obesity lowers the risk of DRFI in *continuous letrozole* but increases risk on intermittent administration.
Borremans et al. (2025)	Multicenter retrospective cohort study	*Inflammatory Breast Cancer* (IBC)	536	Chemotherapy Neoadjuvant (NACT)	High BMI correlates with increased *stromal tumor infiltrating lymphocytes* (sTIL) and a high risk of metastasis at diagnosis in the ER-/HER2+ subgroup. BMI did not significantly affect pCR or *survival* outcomes in general.

Characteristics of the Evaluated Study

Based on the literature selection process, this systematic review synthesizes five primary studies consisting of a multicenter retrospective cohort study and *a post-hoc analysis* of phase III clinical trials. The overall study involved tens of thousands of breast cancer patients from various molecular subtypes, ranging from postmenopausal ER+/HER2- positive, early-stage HER2-positive, to aggressive clinical presentations such as *Inflammatory Breast Cancer* (IBC) (Biganzoli et al., 2025; Borremans et al., 2025; Dauccia et al., 2025; Lee et al., 2025). The grouping of patients is based on the Body Mass Index (BMI) at diagnosis, where its impact on tumor biology, survival, therapeutic efficacy, and surgical outcomes is evaluated (Alotaibi et al., 2026; Biganzoli et al., 2025).

Effect of BMI on Tumor Biology and *Survival*

The impact of obesity on breast cancer prognosis has proven to be not universal, but rather highly dependent on molecular subtypes and hormone receptor profiles. In patients with early-stage HER2-positive breast cancer, *overweight* or obese status (BMI ≥25 kg/m^2) was independently associated with poorer survival, including decreased *Invasive Disease-Free Survival* (iDFS), *Distant Recurrence-Free Interval* (DRFI), dan *Overall Survival* (OS) (Dauccia et al., 2025). In contrast, in the postmenopausal ER+/HER2- subtype, BMI acts as an *effect modifier* to the prognostic value of the progesterone receptor (PgR) (Lee et al., 2025). It is known that the absence of PgR (*PgR-negative*) expression is a strong predictor of poor survival, but this lethal effect was only significantly realized in obese patients (BMI ≥

25kg/m^2) and was not found in patients with normal BMI (Lee et al., 2025).

In more aggressive cases such as *Inflammatory Breast Cancer* (IBC), obesity exhibits a unique interaction with the tumor microenvironment. High BMI in IBC patients is strongly correlated with increased age and high *stromal numbers of tumor infiltrating lymphocytes* (sTIL) at diagnosis (Borremans et al., 2025). In the ER-/HER2+ subgroup, an increase in BMI is also in line with a significantly higher risk of metastasis at the beginning of diagnosis (Borremans et al., 2025). Interestingly, despite the biological aggressiveness of the tumor due to obesity, survival analyses (DFS and OS) in the IBC population in general did not show a statistically significant difference between obese patients and patients with normal BMI (Borremans et al., 2025).

Impact of BMI on Pharmacological Therapy Efficacy (Chemotherapy and Endocrine)

Adiposity and increased BMI directly affect the pharmacokinetics as well as the patient's tolerability to systemic therapy(Reytor-González et al., 2025). In the adjuvant chemotherapy regimen for the HER2-positive subtype, patients with *overweight* and obesity categories were recorded to have a higher rate of *chemotherapy discontinuation* than patients with normal BMI (14% versus 9%) (Dauccia et al., 2025). Early discontinuation of therapy is strongly suspected to be one of the main contributors to low *survival* in the obesity group (Dauccia et al., 2025). However, in the administration of neoadjuvant chemotherapy (NACT) for IBC patients, differences in BMI did not significantly affect the achievement of a *Pathological Complete Response* (pCR), indicating that chemotherapy resistance in IBC may be more influenced by tumor intrinsic factors than adiposity (Borremans et al., 2025).

In the context of extended *endocrine therapy* for postmenopausal ER+ breast cancer, the interaction between BMI and external therapies is much more complex. The prognostic value of obesity is highly dependent on the type of adjuvant endocrine therapy previously received (either SERM, *Aromatase Inhibitor*/AI, or a combination thereof) and the mode of *administration of advanced letrozole* (Biganzoli et al., 2025). For example, in patients who were previously treated with a combination of SERM and AI, obesity conditions were able to reduce the risk of *distant recurrence* if the patient received *letrozole* continuously, but actually increased the risk of recurrence if *letrozole* was given intermittently (Biganzoli et al., 2025). This fact confirms that estrogen blockade strategies should be personalized by taking into account the peripheral estrogen source of adipose tissue in postmenopausal obese patients (Biganzoli et al., 2025).

Effect of BMI on the Exterior of Oncolasty Surgery

In the surgical field, a high BMI is often associated with poor wound healing and an increased risk of complications. However, a retrospective evaluation of *the Therapeutic Mammoplasty* (TM) technique—a breast conservation oncoplasty surgical technique with extensive tumor resection and tissue reduction—proves the opposite (Alotaibi et al., 2026). The rate of wound complications in patients with severe obesity (BMI ≥30kg/m^2) was 32%, a figure that was not significantly different from the group of patients with BMI <30 kg/m^2 which was at the level of 33% (Alotaibi et al., 2026). More importantly, the minor complications that arise do not cause significant delays to the initiation of advanced adjuvant therapy, thus concluding that TM is a highly safe and oncologically relevant surgical technique for breast cancer patients with high BMI (Alotaibi et al., 2026).

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Study Limitations and Clinical Implications

This systematic review demonstrates that BMI parameters cannot be underestimated in precision oncology, but the conclusions drawn should take into account the methodological limitations of the primary literature. One of the main limitations is the heterogeneity in the definition of the *cut-off* point of obesity. Some literature using European databases classifies obesity at a BMI figure of ≥ 30 kg/m^2 (Alotaibi et al., 2026; Biganzoli et al., 2025; Borremans et al., 2025), while studies on Asian populations refer to the WHO Asia-Pacific criteria with a BMI limit of ≥ 25kg/m2 for obesity (Lee et al., 2025). In addition, because most studies use retrospective cohort design and *post-hoc* analysis, the dynamics of post-diagnosis *weight fluctuation* are rarely well documented (Dauccia et al., 2025). Despite these limitations, the results of the synthesis confirm the need to integrate nutritional status and BMI into multidisciplinary management algorithms, both when predicting the effectiveness of pharmacological therapy, determining surgical techniques, and stratifying the survival risk of breast cancer patients (Alotaibi et al., 2026; Biganzoli et al., 2025; Borremans et al., 2025; Dauccia et al., 2025; Lee et al., 2025).

CONCLUSIONS AND SUGGESTIONS

Body Mass Index (BMI) significantly yet heterogeneously impacts breast cancer outcomes depending on molecular subtypes, hormone receptors, and treatments. While obesity worsens survival in early HER2+ and specific ER+/HER2- subtypes, increases chemotherapy discontinuation, and alters endocrine therapy efficacy, a BMI ≥ 30 kg/m^2 remains safe for oncoplastic surgeries like therapeutic mammoplasty. Consequently, integrating anthropometric parameters into risk stratification algorithms is crucial for personalizing oncology management. Future prospective studies must evaluate weight dynamics, employ comprehensive body composition metrics, and investigate obesity's interaction with the tumor microenvironment to uncover novel therapeutic targets.

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