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Review of Breast Cancer Prognosis: MicroRNAs/lncRNAs, Obesity, The LPR6 Biomarker, and Night Fasting

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KEYWORDS

Breast cancer prognosis;
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Night fasting.

ABSTRACT:

Introduction: Prognosis is an important determining aspect in decision-making regarding the course of treatment needed and follow-up of breast cancer patients. The prognosis of breast cancer is challenging because of the heterogeneity of the disease. The growth of breast cancer is an infection that affects the world's well-being. Although Breast Cancer Growth Therapy continues to improve, survival in patients remains unacceptable because there is no direct evidence that can predict the course of the disease and the extent of Breast Cancer chemoresistance. As a result, specialists must strictly differentiate them in order to develop endurance further.

Objectives: This paper attempts to describe the prognosis of breast cancer from aspects related to hormones, namely LPR6 and microRNAs/IncRNAs biomarkers, as well as from aspects related to lifestyle, namely obesity and night fasting.

Methods: This writing audit review plans to outline four aspects of breast cancer prognosis. This study uses a literature review approach. This review summarizes the work in progress on image screening for Breast Cancer Guessing and includes articles from 2006 to 2021.

Results: The investigation of the articles found that LPR6 has an adverse influence on the growth of tumor invasion and thus may be an essential biomarker in breast cancer prognosis; Subtype characterization and breast cancer prognosis can be investigated by looking at microRNAs and IncRNAs so that scRNA-seq-based methods can be a good choice; Obesity correlates directly with breast cancer prognosis, BMI level correlates with increased estrogen receptors having an independent effect on breast cancer survival; Night fasting can be a consideration related to the prognosis of breast cancer, that night fasting can reduce the amount of glucose so that night fasting makes HbA1c fixation lower.

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1. Introduction

Breast cancer is prostate cancer with the most common malignancy among women worldwide, with an estimated 2,088,089 new cases and 626,679 deaths in 2018. Women in both made and agrarian nations are affected by dangerous breast development. However, breast cancer is more prevalent in developed countries, but the bet of death from this ailment is higher in developing countries. This situation happens from differences in treatment, compound replacement treatment, and conceptual models such as prime adolescent age, number of children, time of menarche, and empowerment components in developing countries. Also, there are contrasts in verification rates because of the receptiveness of mammography screening and clinical ideas to understand. [1].

Various stakeholders, including researchers, medical professionals, industrialists, and economists, want to implement optimal solutions for health [2]. Various avoidance techniques, including risk-recognizable proof and separation, screening, early location and determination, customized treatment, and biomarker ID, have been created in light of the significant frequency and death rates [3]. Medical procedure, radiotherapy, chemotherapy, designated treatment, and chemical treatment are the five principal therapies for Breast Cancer. However, the continuation of this treatment in patients with growing breast cancer remains inappropriate due to the absence of a reliable and valuable marker for predicting the course of the disease and the widespread chemoresistance of breast cancer. Accordingly, scientists should recognize valid Breast Cancer growth biomarkers and expected remedial focuses for illness treatment to further develop endurance [4]. Individualized findings and therapy, as well as atomically designated treatment, for Breast Cancer patients have become hotly debated issues. Specialists center progressively on further developing the general endurance rate and long-haul anticipation of Breast Cancer growth patients [4].

Breast cancer has four type based, namely Luminal A, Luminal B, HER2 Positive, and Triple-negative breast cancer (TNBC). Luminal A and Luminal B is the most widely recognized Breast Cancer subtype, representing 80% of all cases. Careful evaluation, chemotherapy, radiotherapy, and endocrine medications currently have merit in treating the luminal subtype. Despite the positive starting reaction to treatment, repeat, and metastases, growth drug obstruction stays the primary source of death in these patients [5]. In light of this squeezing need, new improvements in growing new restorative techniques for Breast Cancer patients are required [4].

Patients with early-stage breast cancer have a 99% 5-year survival rate, but only 24% have distant metastases, so early detection is critical [6]. Furthermore, despite receiving the same therapy, such as chemotherapy or neoadjuvant chemotherapy, some patients with the same TNM (Tumour, Node, Metastasis) stage may benefit from treatment. On the other hand, others have a high tumor recurrence or metastasis rate, making precise predictions about the therapy outcome for each patient difficult [7]. As a result, A study by Wang et al (2018) suggests that new markers are needed to improve breast cancer detection and prognosis [8].

Nearby treatment, chemotherapy, designated treatment, and endocrine treatment are possibilities for treating Breast Cancer growth. This treatment system impacts many things, similar as receptor status, the sort of cancer, the size of the growth, and metastases. Issues like triple-negative Breast Cancer, high-level Breast Cancer growth, and medication opposition make it challenging to utilize this treatment system [4].

Treatment options for breast cancer include targeted therapy, endocrine therapy, local therapy, and chemotherapy. Receptor status, tumor type, tumor size, and metastases impact this treatment plan. Problems such as triple-negative breast cancer, advanced breast cancer, and drug resistance hinder the adoption of this treatment strategy. Knowing the prognosis of breast cancer is part of the indicators of health services. Prognosis often determines the course of treatment determines the necessary investigations and follow-up of the patient. This paper tries to describe the breast cancer prognosis from aspects associated with hormones, especially LPR6 biomarkers and microRNAs/IncRNAs, as well as lifestyle factors in general, especially obesity and Night Fasting.

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2. Discussion

MicroRNAs/lncRNAs Related to Prognosis of Breast Cancer

Complex genetic and molecular changes lead to breast cancer, a complex disease. As a result, traditional clinicopathological factors cannot accurately predict a breast cancer patient's outcome. Identifying multi-gene prognostic factors for breast cancer has been the subject of several proposals for computational approaches. Consequently, brand-new clinical guidelines stress the significance of multi-gene assays in identifying patients who should receive adjunctive therapy [9]. Some genes tested are known cancer markers, crucial for determining a patient's prognosis [10].

Hereditary and genetic factors like gender, age, family history, and hormone therapy can all contribute to the development of breast cancer. Abnormal RNA gene expression is a critical factor in cancer development and one of its main characteristics. Non-coding RNA, such as lncRNA and miRNA, and protein-coding mRNA, are two of its many possible manifestations. Goodall & Wickramasinghe (2021) found that cancer alters RNA processing [11]. Different gene expressions (DGEs), for example, can have different effects on treatment and individual treatments [12].

A study used scRNA-seq data to find Epithelial to Mesenchymal Transition EMT-related signatures affecting breast cancer patients' clinical outcomes. The cancer subtype method works better when using miRNA data, whereas lncRNA data works as well as using mRNA alone. Based on a thorough comparison of 35 computational methods using miRNA/lncRNA data for breast cancer subtypes and prognosis in 19 breast cancer data sets [10]

A new approach to breast cancer prognosis known as scPrognosis is proposed based on scRNA-seq data. Based on Median Absolute Deviation (MAD), Switch-like Differentiation of genes in different stages of EMT (SDE), and NETwork in EMT (NET) measurements, scPrognosis stated that breast cancer signs using an integrative model, a process by which scPrognosis is used to integrate three measures to sequence genes, resulting in three measures of the gene namely MAD, SDE and NET. This model goes through integration in three steps 1) Their median absolute deviation at the expression level; 2) Their differentiation in different EMT stages; 3) Their role in dynamic gene coexpression networks in EMT.

We empirically compared our method to existing ones on four breast cancer data sets. The results showed that the scRNA seq-based method is valuable and practical for predicting the outcome of breast cancer. According to Li et al., her method found markers that suggested a connection between EMT and clinical outcomes in breast cancer. Methods for subtyping breast cancer based on miRNA mRNA data performed better than mRNA-based methods like Prediction Analysis of Microarray 50 (PAM50) and IntClust. However, this method using only mRNA data did not perform better than the cancer subtype method using lncRNA data [10]. By combining genes, miRNAs, and lncRNAs, the prognosis for breast cancer appears to improve, and we can better understand biological mechanisms. Because a variety of molecular mechanisms, including gene mutations, are responsible for the heterogeneity of breast cancer [13], miRNA guideline [14], regulation of lncRNA [15], or lncRNAs-related endogenous RNA competition [16]. Although some miRNAs/lncRNAs were not significantly associated with survival outcomes, several studies demonstrated the prognostic value of some miRNAs/lncRNAs [10]. Numerous studies have examined miRNA's role as a regulator of metabolic processes and carcinogenesis in breast cancer.

LPR6 Biomarker Related to Prognosis of Breast Cancer

Breast Cancer growth tissue with high LRP6 articulation has a lower general endurance rate. Breast cancer has four type based, namely Luminal A (Group 1), Luminal B (Group 2), HER2 positive (Group 3), Triple-negative breast cancer (TNBC) (Group 4). In comparison, patients with the development of luminal B-type breast cancer had lower rates when receiving LRP6. Regardless, patients with high LRP6 explanation and those with low LRP6 verbalization in other sub-nuclear sorts, particularly triple-negative Bosom Disease, do not generally have one-of-a-kind overall perseverance rates. Because our research suggests that LRP6 may be a crucial calculation for the event and movement of breast cancer growth, it is helpful for early determination and guessing to identify LRP6 articulation in breast cancer tissue tests. The discoveries of colorectal disease

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research [17]. LRP6 inhibitors can be utilized in Breast Cancer growth therapy and can act as a sub-atomic focusing on location for Breast Cancer treatment [4].

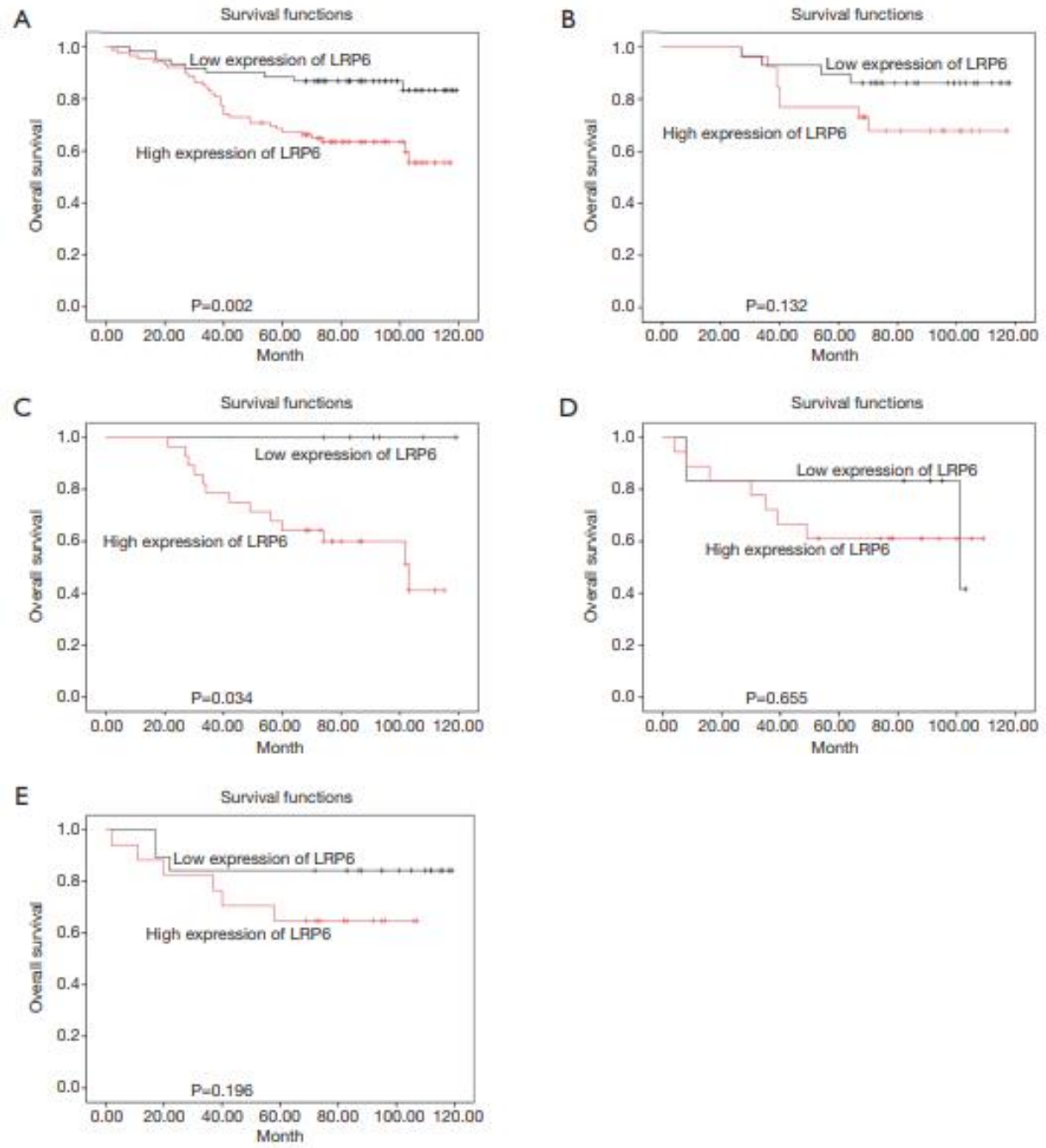

Figure 1. Analysis of the OS of all breast cancer patients and breast cancer patients of a particular subtype based on LRP6 expression by Kaplan-Meier curve.

The analysis of the Figure 1 examine the endurance pace of 150 breast cancer patients. Patients with high LRP6 articulation had a significantly lower endurance rate than patients with low LRP6 articulation. Articulation of the LRP6 (Figure 1A, P = 0.002) There was no significant difference in endurance (P > 0.05, Figure 1B) between luminal type A breast cancer growth patients with high LRP6 articulation and those with low LRP6 articulation

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when defining the examination by various subatomic types of breast cancer. In patients with luminal type B breast cancer growth, patients with high LRP6 articulation had a significantly lower endurance rate than those with low LRP6 articulation (P = 0.034, Figure 1C). There was no significant difference in general endurance between those with high LRP6 articulation and those with low LRP6 articulation in patients with triple-negative breast cancer or HER-2 overexpression (P > 0.05, Figure 1D and 1E) [4].

A constancy evaluation uncovered that high LRP6 verbalization in chest disorder tissue was conflictingly related to regular diligence. Patients with luminal type B breast cancer had lower regulatory levels when receiving LRP6; Regardless, patients with high LRP6 verbalization and those with low LRP6 explanation in other sub-nuclear sorts, particularly triple-negative chest dangerous development do not have generally novel overall perseverance rates. The disclosures recommended that LRP6 could be a colossal part, most importantly, an improvement of chest undermining improvement. Early finding and suppose are improved by distinguishing LRP6 enunciation in chest sickness tissue tests [4].

Obesity Related to Breast Cancer Prognosis

Obesity makes a negative impact on breast cancer's progression and outlook. There is much evidence to suggest that women with breast cancer who are overweight and physically inactive have a lower chance of surviving than women who are lighter and more active. Obesity is one of the few risk factors that can change the prognosis of breast cancer over time. As Recuperates information indicates, expanding actual work and bringing down muscle to fat ratio can be a sensible intercession to bring down insulin and leptin levels, possibly influencing Breast Cancer growth forecast [18].

Although it frequently measures obesity, the BMI does not provide information on body composition. The most common measurements for evaluating body fat distribution are waist circumference (WC) and waist-to-hip ratio (WHR). Larger tumors, decreased differentiation, increased lymph node invasion, and advanced disease are all associated with a BMI greater than 30 kg/m2 [19].

By controlling metabolic cycles, cell aggravation, and expansion motioning through pathways including adipokines, insulin-like development elements, cytokines, and estrogen flagging, heftiness, in principle, lead to breast cancer growth. The occurrence of adipogenesis and carcinogenesis involves many components because breast cancer patients can get rid of several miR due to comorbid obesity. No single miR can predict a figure or go probably as a lone biomarker. For different sorts of Breast Cancer and Breast Cancer growth with stoutness as a co-dismalness, various miR signature blends could give a particular arrangement of prognostic markers. Be that as it may, further examination and approval of this chance are required [3].

In Triple-Negative Breast Cancer (TNBC) and luminal-type Breast Cancer growth, high BMI is a prognostic variable [20]. Furthermore, in luminal Breast Cancer, waist-to-height *ratio* (WHtR) Is related to a more terrible forecast [21]. a meta-examination of 82 investigations included more than 200,000 individuals with Breast Cancer. This study uncovered that heavy patients had awful outright mortality (HR = 1.41, 95% CI 1.29-1.53) and more painful chest illness unequivocal mortality (HR = 1.35, 95% CI 1, 24-1.47) diverged from average weight patients [22].

By inhibiting Scavenger Receptor B-1 (SRB1), obesity causes overexpression of miR-24-3p, which reduces High Density Lipoprotein (HDL) uptake, lipid metabolism, and steroid intake. miR-24-3p overexpression increases breast cancer growth and proliferation by inhibiting p27Kip1 and BMI expression.

Leptin, a protein hormone produced by adipocytes, the placenta, and the mammary epithelium, takes the place of estradiol (E2) in most breast cancers [3]. Leptin as a protein with a sub-atomic load of 16kD encoded in the heftiness quality, controls metabolic cycles differently. Plasma levels of leptin are affected by BMI and estrogen awareness. According to various animal model tests, there is a link between increased breast cancer and leptin. Leptin levels in the plasma stream or articulations in breast cancer growth tissue have an increased association with breast cancer. The fact that hypoxia, Insulin like Growth Factor (IGF), estradiol, and insulin overexposure

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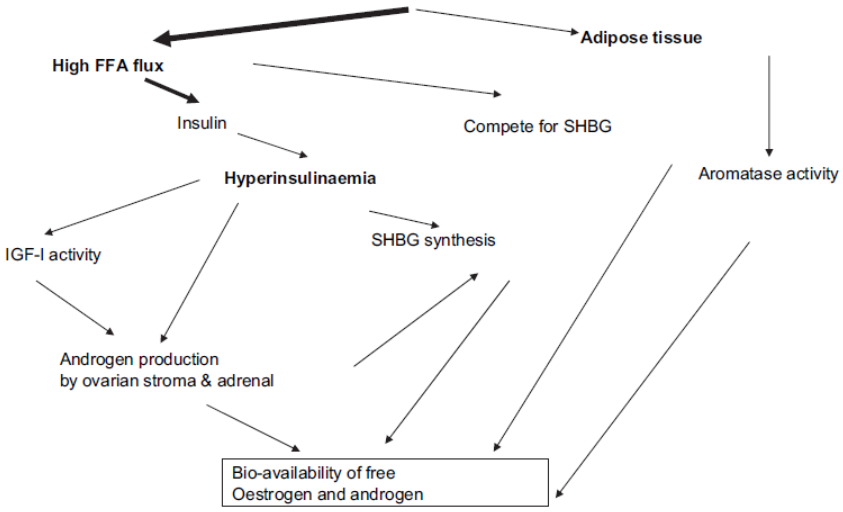

Figure 2. Incidence and prognosis of breast cancer result from obesity and hormonal changes.

are also directly related to poor breast cancer survival may explain the overexpression of leptin and leptin receptors in breast cancer tissue [23].

BMI and estrogen receptor levels have independent effects on breast cancer survival, according to a four-year follow-up cohort study of 1169 breast cancer patients. However, only in women without positive axillary glands does BMI affect survival. 71 Recent studies cast doubt on these figures. The National Surgical Adjuvant Breast and Bowel Project clinical trial for ER-node negative breast cancer found that obese women had a lower disease-free survival rate than normal-weight women [18].

Regular aerobic exercise may be necessary to prevent disease recurrence in these women by preventing weight gain. The Attendant's Wellbeing Study gives the most strong proof that actual work prompts weight reduction and weight support and is related to improved results in Breast Cancer patients. Everyone, at the individual, political, physical, and social levels, must make dietary and lifestyle changes to reduce the risk of obesity-related postmenopausal breast cancer. Weight the board through dietary and way-of-life changes ought to be a fundamental part of Breast Cancer follow-up for ladies [18].

Postmenopausal patients with higher BMI are at increased risk of peripheral adipose tissue estrogen synthesis. Since expanded aromatase action can instigate and invigorate strange mammary cell development, diminished sex chemical-restricting globulin might be answerable for the unfortunate Breast Cancer visualization. In postmenopausal women, aromatase inhibitors may not fully benefit women with a higher BMI [24].

Various studies prove that type 2 diabetes is an independent risk factor for breast cancer, and type 2 diabetes also occurs due to obesity. The world's leading causes of morbidity and mortality are diabetes and breast cancer. Patients with both diabetes and breast cancer had poor outcomes. An important question is how antihyperglycemic drugs affect breast cancer patient's chances of survival. Whether strict or remiss, glycemic control can impact Breast Cancer growth prognosis [25].

Due to concerns about toxicity, older women with a higher BMI may be able to tolerate comorbidities and lower chemotherapy doses. Mitogenic hormones, insulin-like growth factor, and insulin levels may be higher in women with a higher BMI (Figure 2). In addition, paracrine interleukin-6, tumor necrosis factor-alpha secretion, and developing a pro-inflammatory microenvironment can encourage tumor growth [21]. The above description is still relevant enough to conclude that obesity, menopause, and breast cancer prognosis are

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linked. However, whether BMI affects the prognosis of breast cancer is still up for debate.

The Mediterranean diet is one of the recommendations for a preventive type of diet. The Mediterranean diet is another option for lowering breast cancer incidence and improving prognosis. According to some similar studies, there is a corresponding decrease in risk. The Mediterranean diet consists primarily of olive oil, vegetables, raw grains, fruits, fish, legumes, cereals, legumes, and wine in moderation [26].

Aerobic exercise has long been a recommended sport to help control weight and improve abnormal metabolic conditions such as fasting blood sugar, HDL, and Triglyceride TG levels. Women who eat healthy meals and have an excellent lifestyle can survive breast cancer. Based on the prospective study of 1,490 women, the previous statement found that eating fruit and vegetables at least five per week and walking for 30 minutes six days a week significantly increased survival [19].

Night Fasting Related to Breast Cancer Prognosis

Glucose regulation, inflammation, obesity, and lack of rest are some breast cancer risk factors that improve outcomes with irregular fasting regimens. In 2122 ladies without diabetes mellitus, the US Public Wellbeing and Sustenance Assessment Study discovered that drawn-out evening fasting was related to critical upgrades in glycemic control. A more broadened evening fasting season was associated with cutting down C-responsive protein levels (CRP). Ladies should consume under 30% of their everyday energy after 5 p.m. for unfortunate Breast Cancer results like glucose guideline, irritation, heftiness, and rest [27]. Glycemic control biomarkers fundamentally improved among 2122 ladies without diabetes mellitus after more expanded evening fasting, as indicated by information from the US Public Wellbeing and Nourishment Assessment Review. C-responsive protein (CRP) levels were fundamentally lower during more extended night-time fasting. Information from in vivo experiment using rodents and people supports the speculation that more extended fasting stretches can reduce disease risk and further develop malignant growth results Ladies should consume under 30% of their daily energy after 5 p.m [28].

Significantly longer sleep duration was associated with extended nightly fasting and eating more frequently. Eating at odd times, like late at night, can impact metabolic factors like glucose regulation and disrupt sleep patterns [28]. Following previous research findings, circadian misalignment indicates an association with an increased risk of various types of cancer. Which demonstrated a link between the routines of night shift workers and an increased risk of breast cancer [29].

A similar report indicates that broadening irregular fasting around evening time may be a simple and feasible method for eliminating Breast Cancer repeat. In this encounter of patients with early-stage breast cancer, longer daily fasting stretches would result in lower HbA1c fixation and more extended rest periods. We estimated that intercessions to increment daily fasting spans could lessen type 2 diabetes, cardiovascular infection, and different tumors, given the connection between daily fasting, glycemic control, and rest [29]

3. Conclusion

There are four conclusions that are found based on each aspect of the prognosis. First, LPR6 biomarker can be a molecular targeting site for breast cancer therapy. Survival analysis showed that the overall survival rate of tumor patients with high LRP6 expression was significantly lower than that of patients with low LRP6 expression. LRP6 is an independent risk factor for breast cancer and is negatively correlated with breast cancer prognosis. LRP6 could be a valuable biomarker for poor breast cancer prognosis because it plays a critical role in tumor growth, migration, and invasion. Second, microRNAs and IncRNAs play a role in characterizing breast cancer subtypes and prognosis, so the scRNA-seq-based method is a good and valuable method for breast cancer prognosis. Third, Obese women have a lower disease-free survival rate than women of average weight. BMI and estrogen receptor levels have independent effects on breast cancer survival. A high BMI correlates with increased plasma leptin, a protein hormone produced by adipocytes, placenta, and mammary epithelium, displacing estradiol (E2) in most breast cancers. Fourth, night fasting is a simple and feasible method to eliminate recurrent breast cancer. Eating late at night can affect metabolic factors such as the amount of glucose regulation and disrupt sleep patterns. So that through, night fasting makes lower HbA1c fixation and longer resting time.

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4. Recommendation

Our recommendation for further research is to look at the prognostic model for breast cancer by optimally looking at it through a more independent population, for example in young and elderly patients.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approvals

The work does not need any ethical approval.

Data Availability

All the data pertaining to the manuscript has been provided in the manuscript.

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