REVIEW

The predictive value of metabolomic-related biomarkers in breast cancers: Current approaches in biotechnology

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Abstract

Breast cancer is the second most common cancer worldwide and is a leading cause of cancer-related mortality in women. The rising burden of breast cancer highlights the need for more accurate, non-invasive, and informative diagnostic tools. Despite the current advancements in medicine, predicting treatment response and patient prognosis remains challenging. It has thus become imperative to address the need for precise and reliable prognostic and diagnostic tools. Metabolic profiles, such as lipid processing and steroid hormone metabolism, have recently emerged as significant biomarkers in tumor biology, especially for early detection, prognosis, and therapy monitoring. This literature review explores the predictive value of serum lipid profiles and selected steroids as biomarkers in breast tumors. It shows their potential in improving diagnostic strategies and treatment planning in breast cancer management. These approaches offer valuable insights into tumor biology, metabolic changes, and hormone-driven pathways. Despite current challenges in sample preparation, data interpretation, and technical demands, recent advances such as high-resolution mass spectrometry, as well as spatial metabolomics and artificial intelligence, are helping to overcome these barriers. With continued research and technological progress, metabolomic-related biomarkers are expected to see broader use in clinical settings, supporting personalized treatment and improving outcomes for breast cancer patients.

Keywords: Metabolomics; Breast Cancer; Lipids; Biotechnology; AI

Introduction

Breast cancer is a significant contributor to cancer-related mortality among women, and it is the second most common type of cancer causing death among women worldwide (Menon et al., 2025). In the year 2022, breast cancer cases accounted for around 3 million cases worldwide, which is 13 percent of all the total cancer cases diagnosed (Giaquinto et al., 2022). Furthermore, in Georgia, according to IARC (International Agency for Research on Cancer) in the year 2022, the incidence report of cancer showed breast cancer as the number one cancer causing mortality among women, surpassing all other types of cancer in females in the Georgian population, a total of 1,730 new cases of breast cancer and 861 breast cancer-related deaths recorded in 2022 in Georgia by IARC. The risk factors of breast cancer include obesity, lack of physical exercise, hormone replacement therapy, menopause, risk increasing with age and family history of breast cancer (Petrović et al., 2021; Petrovic et al., 2017; Parveen Shaikh et al., 2023). About 90% to 95% of breast cancer cases are sporadic and only 5% to 10 % are due to identifiable genetic mutations ("Familial Breast Cancer," 2001). And, the most commonly associated genetic conditions are BRCA 1 and BRCA 2 caused by the mutations in the respective tumor-suppressing genes, BRCA 1 and BRCA 2; mutations in these can significantly increase the risk of epithelial malignancies, such as breast and ovarian cancer (Criscitiello & Corti, 2022; Freudenheim, 2020; Vinogradova et al., 2020). The other main subtypes of breast cancer are Luminal A: Hormone receptor-positive, human epidermal growth factor receptor (HER)-2 negative; Luminal B: Hormone receptor-positive, HER-2 positive; Basal-like: Hormone receptor and HER-2 negative; and HER-enriched: HER-2 positive, hormone receptor-negative (Menon et al., 2025). This classification helps to find a prognosis and tailor treatment according to the unique features of each cancer (Veerla et al., 2023). However, it does not provide information in predicting the disease progression or the response to the therapies of these subtypes.

Metastasis is considered the leading cause of this type of cancer. However, predicting metastasis at earlier stages of breast cancer before metastasis can help increase the survival rate. Unfortunately, breast cancer is often discovered and diagnosed later, after the metastasis. As a result, breast cancer is considered to have poor prognosis, even with the current clinical advances (Jafari et al., 2018; Park et al., 2022). For this reason, greater importance has been given in the recent years to recognize not just genetic predisposition of breast tumors but also certain other markers and its risk factors, to increase early screening and prevent the development of breast tumors. Therefore, it is imperative to have precise diagnostic methods, and the gold standard tools used nowadays are mammography and biopsy for the detection and diagnosis of breast cancer (He et al., 2020; Soori et al., 2022), but there has been an increasing need for a more non–invasive and early diagnosis, hence biomarkers come to aid in early detection and monitoring of the disease, as they have become invaluable for therapy and diagnosis (Moore et al., 2023).

Breast cancer widely varies in terms of the molecular and genetic characteristics, treatment responses, or even the potential aggressiveness and metastasis (Perou et al., 2000) and because of this varied heterogeneity there is a need for stronger and sensitive biomarkers.

In recent years, there has been a significant change in the prognosis of breast tumors due to the discovery of biomarkers and their application in providing initial diagnosis, insights for risk assessment, and targeted therapy, which could be serological, histological or genetic indicators. In Georgia, mammography and clinical breast examination are used for screening for breast cancer in women aged from 40 to 70, every two years (Irzaldy et al., 2024). Nevertheless, non-invasive

diagnostic methods have gathered greater attention as they could be relatively fast and painless for the detection and differentiation of many diseases. Hence, metabolomics and lipidomics are considered to be promising analytical methods as they represent direct and non-invasive techniques for diagnosis (Tan et al., 2020). Identifying the precise type of breast tumor developed is imperative and mainly reliant on histological and pathological markers, as it is necessary for therapeutic approaches and prognostic results (Smolarz et al., 2022).

Hormone receptor status (such as the estrogen receptor and the progesterone receptor), human epidermal growth factor 2 (HER2) are the primary breast tissue biomarkers in clinical practice as they help in pathological analysis and help determine the most suitable type of treatment approach for patients with breast cancer (Colomer et al., 2024), and additionally lipid species has been identified to be potential biomarkers for the early detection of breast cancer (Chen et al., 2016).

Therefore, understanding the mechanisms and the diagnostic efficiency of these biomarkers is considered crucial for identifying a more effective and dependable predictive tool in breast cancer management (Passaro et al., 2024).

An overview of metabolomics and lipidomic biomarkers

Metabolomics is the profiling of the chemical processes of metabolites, small substrates and products of a certain physiological metabolism (Idle & Gonzalez, 2007). Metabolomic biomarkers have great potential in the early diagnosis of cancer, identifying the precise subtypes, and tailoring precise treatment plans (Ghini et al., 2020; Salciccia et al., 2021). Tumor-specific metabolic profiles could help identify early stages of the tumor even before the symptoms present. Early metabolomic biomarkers have been evidently used in the diagnosis of prostate cancer (Salciccia et al., 2021), gliomas (Chou et al., 2021) and type 2 diabetes mellitus (Shahisavandi et al., 2023), while lipidomics have been used for a long time in risk prediction and therapeutic monitoring, more commonly for diabetes and cardiovascular diseases (Meikle et al., 2014). Metabolomics and lipidomics have shown the ability to predict and correlate with different disease and the enhanced metabolic and lipid adaptations in cancer cells compared to non-cancer cells shows that predicting metabolic and lipid biomarkers for cancer progression is more feasible (Rossi et al., 2022). For instance, lipidomics and metabolomics have been used to layout and interpret intratumor metabolic heterogeneity in gastric cancer (Sun et al., 2023).

Studies recently have shown the significance of understanding the metabolic usage in breast cancer, emphasizing the clinical relevance of metabolic stratification. Moreover, metabolic subtypes of human breast tumors have been identified, showing their potential for therapeutic implications and clinical significance (Iqbal et al., 2023). Also, a study recently on metastatic triple negative breast cancer showed how tumors adapt their metabolism depending on the tissues while holding their metabolic signatures, which is found to be critical in the understanding of the metastasis of breast tumor development, and additionally, this information collected from the metabolites provides useful insights about the therapeutic approach (Roshanzamir et al., 2022). And so, interactions between metabolic biomarkers with the cancer cells and their microenvironment have been considered to play a pivotal role in determining the therapeutic approaches, and finally, this highlights the importance of metabolic and lipids as biomarkers in breast tumor progression.

Role of selected steroid metabolites: A metabolomic perspective

Metabolomics, a quantitative study or analysis of metabolites such as small substrate molecules, biological end products, or resulting products after a pathophysiological process is found to hold

promising potential in precision medicine (Clish, 2015). The functional changes of the cancer cells and their progression are shaped by metabolic processes and their metabolites. These not only act as immediate indicators of disease processes but also provide a sensitive method in monitoring changes in biological systems, and so metabolites have been shown to be helpful in differentiating tumors from healthy tissue and in examining cellular activities both physiological and pathological (Griffin & Shockcor, 2004). Therefore, metabolomics is considered to be a potential pivotal tool in medicine in providing direct, feasible and precise molecular-level analysis, and new innovations in analytical methods. Both metabolomics and lipidomics, as biomarkers have been useful in monitoring progression of cancer cells, specifically breast tumor cells (Clish, 2015).

Metabolomics and its analytical studies involve a broad spectrum of small substrates, metabolic intermediates and metabolites, among which are mainly the selected steroid hormones that have evidently in recent years gathered application in the prognosis of breast tumor cell progression. Steroids such as estrogen, progesterone and androgens are important regulators of the normal physiology of breast tissue and have been involved in the progression of breast tumor cells. The levels and local synthesis of these steroid hormones provide insightful knowledge about the type of cancer cells developed in the breast tissue, prognosis, and the therapeutic interventions required (Valko-Rokytovská et al., 2021).

Considering the association of steroid hormones and risk factors of breast cancer is critical. For instance, women after menopause have adipose tissue as the main source to produce estrogen, a sex steroid hormone, and obese postmenopausal women have higher levels of endogenous estrogen and have an increased risk of breast cancer. It is also clear that breast cancer is a hormone-responsive cancer, which is why it is important to understand the association between steroid levels and breast tumors, as this will be insightful in the use of such steroid hormones as biomarkers (Kamińska et al., 2015).

Furthermore, breast cancer, due to its varying heterogeneity, has been distinguished into two main classification, one classification is done based on the molecular-characteristics and expression profiles of the tumor progression, and those subtypes are: (i) Luminal (A and B) (ii) basal-like estrogen receptor negative (ER -), progesterone receptor negative (PR -)and human epidermal growth factor receptor 2 negative (HER2-) also known as triple negative breast cancer (iii) Human epidermal growth factor receptor 2 (HER2) (iv) normal breast like (low expression of luminal epithelial genes and high expression of basal epithelial and non-epithelial genes) (v) claudin-low-expressed breast cancer (low expression of cell-cell junction proteins) (Prat et al., 2015; Valko-Rokytovská et al., 2021).

Likewise, the second clinical classification of breast cancer is based on steroid hormone receptor expression, as estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 expressions are not only crucial tools for the study of breast cancer but also are determined to be highly capable metabolomic biomarkers for understanding of the prognosis and survival of breast cancer cells (Iacopetta et al., 2012). Hence, the four more precise subtypes of breast cancer based on these biomarkers are: ER+/PR+/HER2-, ER+/PR+/HER2+, ER-/PR-/HER2+ and ER-/PR-/HER2-(Iacopetta et al., 2012). Furthermore, based on the subtype of breast cancer, the prognosis and the choice of therapy will differ. For instance, estrogen, which acts on its respective receptor, estrogen receptor, is considered to be an important etiological factor in breast cancer, and so, the therapies currently involve the inhibition of the estrogen receptor and cytochrome P450 19A1, also known as CYP19A1 or aromatase, which an enzyme that produces estrogen. Additionally, in recent

years, therapeutic strategies have started to focus on progesterone receptors and androgen steroid receptors and their respective ligands to manage the different subtypes of breast cancer (Africander & Storbeck, 2018).

Steroid metabolomics in breast cancer prognosis: A concluding perspective

The steroid hormones, which are structural derivatives of the cyclopentanoperhydrophenanthrene, play a key role in many of the physiological processes, and sex steroid hormones such as androgens, estrogens and progesterone are involved in the etiology of breast cancer. Each of these steroid hormones is synthesized to play a unique role in the living system (Petrović et al., 2021). For instance, progesterone plays an important role during pregnancy and the menstrual phases, while estrogen plays a key role in both sexual and reproductive health in women, impacting the endocrine, cardiovascular and metabolic systems and bone growth (Babiker, 2002; Imai et al., 2009). According to study, increasing BMI in postmenopausal women increases their breast cancer risk due to increased estrogens, particularly bioavailable estradiol (Liang et al., 2023). Moreover, weight increase and obesity have been considered as the most critical risk and prognostic factors for breast cancer in postmenopausal women. BMI and weight gain are associated with breast cancer risk in BRCA1 and BRCA2 variant carriers, with risk estimates generally consistent with those in the general population(Van Den Brandt et al., 2021). Based on the observational study, postmenopausal women have increased fat in different body segments, which is associated with an increased risk for breast cancer compared to premenopausal women (Cao et al., 2023). Notably, in premenopausal breast cancer patients, underweight is associated with a higher risk of HER2+ breast cancer, while overweight and obesity reduce the risk of ER + PR + breast cancer (Li et al., 2024).

These steroid receptors are expressed on breast cancer tissue and cause proliferation of the cancer cells. They are capable biomarkers in determining not just the prognosis but also the choice of therapy that is required. For instance, hormone therapy, for the estrogen receptor negative and progesterone receptor positive breast cancer, and similarly targeted therapy with trastuzumab for human epidermal growth factor 2 positive tumors (Schramm et al., 2015).

Specific steroids in the living system are synthesized locally in high concentrations during carcinogenesis (Caceres et al., 2016). Estrogens are known to increase their levels through local synthesis in human breast carcinoma, and understanding its synthesis is considered to be imperative, that is, estrogens are synthesized by aromatase that converts circulating androstenedione to estrone to estradiol with the help of additional enzyme such as 17β-hydroxysteroid dehydrogenase type 1 (17β-HSD1) in the breast cancer tissue. (McNamara et al., 2013; Takagi et al., 2010). And, so, reports show that there are high concentrations of intertumoral androgens and androgen-converting enzymes such as 17β-hydroxysteroid dehydrogenase type 5 (17β-HSD5) in breast cancer tissue (Suzuki et al., 2007).

As mentioned earlier in risk factors, women in the postmenopausal period have a high incidence of breast cancer development. That is, there are high chances for breast cancer to develop in women once the ovaries have concluded their function. In such cases, estrogen synthesis can cause high levels of estradiol in tumor cells, including increased intracellular estradiol. Because of this, there is an increase in the estradiol synthesis leading to low levels of peripheral estrogen in tumor cells (Miyoshi et al., 2001). Therefore, estrogen and estradiol are at higher levels in breast cancer tissues than in plasma. Furthermore, in postmenopausal women, extragonadal estrogen is a key contributor to the progression of breast cancer. Additionally, among estrogen-converting enzymes, aromatase is

considered the key estrogen synthase, which converts androstenedione and testosterone to estrone and estradiol, and aromatase has been seen to be expressed in breast cancer tissues. Moreover, this aromatase, expressed by breast tissue converts androgen precursors to estradiol, which plays a key role in menopausal women, as it leads to 70% of the estrogen receptor expressing breast cancer cells. Thus, inhibition of aromatase could be effective in the treatment of postmenopausal women with ER-positive breast cancer (Capper et al., 2016; Snell et al., 2018; Tilson-Mallett et al., 1983). Often, it is seen that estrogen receptors are expressed in invasive breast cancers in postmenopausal women and so is considered to make local estrogen production a key factor in tumor cell proliferation (Russo & Russo, 2006). On the other hand, androgens express antiproliferative effects on breast cancer through activation of the androgen receptors, and so, the androgen receptors are expressed in around 90% of breast cell carcinoma, eventually making it a good prognosis toll especially for the estrogen receptor positive breast cancers (Hammes & Levin, 2019; Hickey et al., 2012).

Steroid metabolomics is shown to be highly insightful in the prevention, prognosis and choice of treatment of cancers. Various types of steroids have been associated with common types of cancer, especially breast, prostate and endometrial cancers. It is considered as a promising approach in clinical cancer research.

Estrogen and its respective metabolites are closely associated with breast cancer, due to which increased levels of estrogen are used to characterize hormone-sensitive and hormone-receptor-positive breast cancers. Additionally, the most significantly used steroid biomarkers are estradiol, dehydroepiandrosterone and cortisol as they have a significant impact on androgen, estrogen and androstenedione metabolisms during cancer (N. H. Anh et al., 2019). Other steroid biomarkers include testosterone, androstenedione and dehydroepiandrosterone sulfate, which is used in postmenopausal women with elevated serum androgens to study their increased risk of breast cancer. This shows the high potential of steroid metabolomics in breast cancer prognosis, prevention and therapeutic strategies (Kaaks et al., 2005).

Lipidomic aspects of breast cancer and its role in prognosis

Lipidomics, the study of cellular lipids and their networks and pathways in biological systems. In lipidomics, the term lipidome, often used, refers to the lipids or lipid profiles in a cell, tissue or organ of a living system (Yang & Han, 2016). Lipidomics focuses on the identification of endogenous lipids and their metabolites, and the integral role of lipids in cellular structure, signaling pathways, and energy metabolism. Any abnormality observed with lipids is considered to have an insightful use in cancer, including breast cancer. In other words, by detecting even the subtle changes in the lipid profiles, lipidomics are capable of revealing the association of lipid metabolism changes with disease progression and therapeutic responses. Therefore, these analytical methods are both reliable and insightful in monitoring and providing prognosis for diseases (Ahluwalia et al., 2022; Kostara, 2023).

Lipids play a key role in forming the cell membrane and are vital to processes like energy production, plasma membrane repair and cellular transduction, all of which are contributed by specific lipid species such as sterols, glycerides and phospholipids (Horn & Jaiswal, 2019). In breast cancer, there is prominent remodeling of the lipid metabolism due to the metabolic demands and rapid proliferation of cancer cells, which increases during tumor progression (Hilvo et al., 2011; Suri et al., 2023). Additionally, lipolytic pathways in cancer cells enhance to metabolize the stored triglycerides and fatty acids, which are critical in cell division and invasion.

These changes are not just mere results of cancer but also take part in tumor progression and metastasis (Fu et al., 2021).

Recent lipidomic studies of samples of breast cancer patients have shown the association between the lipid profiles and the type of cancer and its tumor type. Additionally, the change in choline-containing compounds in tumor growth has also observed (Bathen et al., 2013; Mimmi et al., 2011). Furthermore, cancer cells have the ability to alter the microenvironment by secreting signaling molecules, causing cancer-associated fibroblasts and immune cell function to be impaired, leading to an increase in cancer cell progression, due to which many metabolic processes can be disrupted, including lipid metabolism in cancer cells (Liu & Cao, 2016). In cancer cells, lipid synthesis will be enhanced, consequently leading to the upregulation of fatty acids, cholesterol and phospholipids to promote cell growth. This results in the accumulation of lipid species in tumor cells, leading to the inactivation of immune mediators, providing a hospitable environment for the progression of cancer cells. These metabolic products of lipid biosynthesis in breast cancer cells become crucial in the analytical part of lipidomics (Fu et al., 2021; Petan, 2020). Therefore, lipidomics is considered to be a highly promising field in developing biomarkers for breast cancer, especially measuring or detecting the lipid synthesis patterns, remodeling and end products. Lipidomics provides useful insights on the metabolic state of tumors, prognosis and therapeutic strategies (Carmona et al., 2024).

Recent research shows that lipid metabolism varies across breast cancer subtypes, contributing to their distinct biological behavior and treatment response. For example, Luminal A and Luminal B subtypes often exhibit elevated levels of phosphatidylcholines and sphingomyelins, which are linked to increased membrane synthesis and proliferation (Hilvo et al., 2011). These lipid alterations may reflect the active hormone receptor signaling in luminal tumors.

In contrast, triple-negative breast cancer (TNBC), which is known for its aggressive growth and lack of hormone receptors, is associated with increased levels of ceramides and saturated fatty acids. These lipid classes are involved in inflammatory signaling, cell invasion, and immune evasion, all of which contribute to TNBC's poor prognosis (Carmona et al., 2024; Fu et al., 2021).

Moreover, cholesterol derivatives, especially oxysterols, have been found to interfere with estrogen receptor signaling, affecting tumor growth and response to endocrine therapy. These compounds are implicated in therapy resistance among ER-positive breast cancers and highlight the role of cholesterol metabolism in disease progression (Capper et al., 2016; Petan, 2020).

Use of lipid profiles and selected steroid hormones in association with lipidomics and metabolomics provide potential benefits in prognosis and breast tumor management, and for analysis several types of specimens are required. These include primary tumor samples, lymph node samples, plasma, urine and large samples of metastatic tumors from remote sites, all of which can be useful in clinical analysis (Ji et al., 2023; Rajkumar et al., 2022). However, these lipidomic and metabolic analytical methods face challenges in technical and methodological aspects, including careful suspension and quick processing of patient samples in dry ice to freeze and maintain the integrity of the lipidome and metabolome. And if any errors occur, it can lead to temperature fluctuations and affect the integrity of the sample. Hence, one of the flaws of the methods is the settings that the sample is prepared (Johnson & Gonzalez, 2012; Reis et al., 2021; Wagner-Golbs et al., 2019). Another one is that metabolites can be due to the diet, gut microbiota, and medications, which can affect patients individually (Hong et al., 2023). Additionally, to utilize lipid profiles and steroid hormones as predictive value, high-end instrumentation is required, such as high-resolution mass spectrometry, along with cooperation across many departments to

provide accurate and promising diagnosis (N. K. Anh et al., 2024). Moreover, one main challenge faced by both lipidomics and metabolomics is the difficulty in differentiating between immune and tumor cells from patient samples, and this flaw has been hoped to overcome through ongoing and future technological advances. Lastly, the promising potentials of using serum lipid profiles and selected steroids as predictive value for tumor progression outweighs its challenges.

Table 1: Comparison between traditional and metabolomic diagnostic approaches in breast cancer.

Aspect	Traditional Approaches	Metabolomics approach
Nature of Biomarkers	Structural or Genetic (Example: BRCA 1; BRCA 2; ER/PR status)	Functional, real-time data of small molecule metabolites (example: lactate, choline, amino acids)
Biological Information given	Mutations and receptor presence	Provides current tumor metabolism and microenvironment
Detection of Early-stage cancer	Moderately sensitive	Highly sensitive due to the detection of subtle metabolic shifts before structural changes occur
Subtype differentiation	Limited (requires multiple assays)	Effective in distinguishing subtypes based on metabolic signatures
Type of testing (Non-invasive or invasive)	Biopsy (Invasive) or Imaging (Non-invasive)	Urine, saliva (non-invasive), Blood - plasma or serum (Minimally invasive), tumor tissue, cerebrospinal fluid (invasive) and other serum components.
Technology used	Imaging, Immunohistochemistry, PCR, sequencing	Mass spectrometry, Nuclear Magnetic Resonance Spectroscopy, Machine learning integration
Application in Precision Medicine	Personalization is limited	Personalized therapy decisions can be provided based on metabolic results
Monitoring response to therapy	Delayed or later stage (example: tumor shrinkage)	Real-time monitoring of response to therapy

Emerging metabolomic technologies and future directions in breast cancer

In recent years, advances in metabolomic and lipidomic technologies have significantly improved our understanding of breast cancer biology (Table 1). These technologies allow for the detailed profiling of metabolites, which are the end products of cellular processes, and are increasingly used for disease diagnosis, prognosis, and monitoring.

The two most commonly used analytical platforms in metabolomics are mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy. Mass spectrometry, particularly when combined with liquid chromatography (LC-MS) or gas chromatography (GC-MS), provides high sensitivity and specificity in detecting a wide range of metabolites in complex biological samples, such as blood, urine, and tissue extracts (N. K. Anh et al., 2024; Clish, 2015).

NMR-based metabolomics, while slightly less sensitive than MS, has the advantage of being non-

destructive and highly reproducible, making it suitable for clinical applications (Bathen et al., 2013; Griffin & Shockcor, 2004). These platforms are now used to identify metabolic shifts specific to breast cancer subtypes, potentially providing earlier and more accurate diagnoses.

Integration of Multi-Omics

A major trend in cancer research is the integration of metabolomics with other omics technologies, including genomics, transcriptomics, and proteomics, within a systems biology framework. This approach helps uncover complex interactions between tumor metabolism and gene expression, allowing for a more holistic understanding of cancer heterogeneity (Passaro et al., 2024; Rossi et al., 2022).

Spatial metabolomics, a novel technique that combines imaging with metabolite detection, enables localization of metabolic changes within tumor microenvironments. This method has been used to reveal cell-type-specific metabolic remodeling in cancers such as gastric and breast cancer (Sun et al., 2023).

Artificial Intelligence and Predictive Modeling

With the rapid growth in metabolomics data, artificial intelligence (AI) and machine learning (ML) algorithms have emerged as essential tools for biomarker discovery. These models can analyze complex datasets to identify predictive metabolic signatures associated with prognosis, treatment response, and recurrence risk (Ghini et al., 2020; Salciccia et al., 2021).

Machine learning algorithms have already been applied to classify breast cancer subtypes based on metabolic profiles and to predict hormone receptor status using non-invasive serum samples (Iqbal et al., 2023).

Metabolomic profiling for predicting therapeutic response in breast cancer

Metabolomics provides not only an insightful prognosis but also acts as a tool for both deciding a more personalized therapy for the patients and monitoring therapeutic responses. Therefore, metabolomic profiling analyses the subtle signatures of tumor growth and its interaction with therapeutic interventions, helping clinicians in obtaining real-time data (Lin et al., 2024; Mei et al., 2023). In recent years, metabolomic profiling has emerged as a promising approach in predicting therapeutic responses in cancer treatment.

Notably, several recent studies have demonstrated that the use of metabolomics in relation to neoadjuvant chemotherapy has been found beneficial. Neoadjuvant chemotherapy is used for cancer patients in order to shrink the cancer cells and to optimize the effectiveness of the main treatments or surgery (Haddad & Goetz, 2015). It is crucially used in the initial downstaging of tumors before moving onto extensive treatment methods. However, difficulties have been faced in identifying factors that impact post-neoadjuvant chemotherapy and their rate of survival or treatment responses. The specific tumor and patient characteristics influence the responses to neoadjuvant chemotherapy, which is important in deciding further treatment planning. Therefore, a reliable and precise method is required to predict these responses. The vulnerability of the tumor to antitumor drugs and the development of the immunity of the patients determine the ability of breast cancer to be cured entirely and the rate of preventing metastasis, but these factors affect the responses of tumors and its eradication is challenging. Therefore, metabolomic approaches are considered to be insightful in aiding this challenge (Fang et al., 2025).

In a study in the year 2024, metabolomic approaches were used in relation with neoadjuvant therapy, and it was observed that increased levels of certain metabolites, such as histidine and lactate pre and post neoadjuvant chemotherapy were found to be connected to improving recurrence-free survival, although the increase in serine and taurine causes critically severe recurrence-free survival rate (Talarico et al., 2024).

Similarly, the responsiveness of cancer cells to an antitumor treatment that includes methotrexate is found to be modulated by catabolic pathways of histidine and its intake (Kanarek et al., 2018). Additionally, measuring the levels of serine after therapy is considered crucial, as increased concentrations of serine in the tumor microenvironment are found to promote the progression of tumor cells, as it has an immunosuppressive effect (Possemato et al., 2011; Sánchez-Castillo & Kampen, 2024). Furthermore, metabolomic approaches are used in planning target therapies. For instance, they are used to determine the suitability of hormone therapy or therapy with trastuzumab based on the type of breast cancer diagnosed (Schramm et al., 2015).

Clinical implementation and future prospects

Despite promising developments, clinical implementation of metabolomics in breast cancer faces several challenges. These include technical variability in sample handling, difficulty in standardizing metabolite quantification, and cost barriers for high-resolution equipment like LC-MS (Johnson & Gonzalez, 2012; Reis et al., 2021).

Nonetheless, ongoing research continues to push boundaries. Real-time metabolomic tools are under development to guide intraoperative decisions during tumor resection surgeries (Bathen et al., 2013); While point-of-care devices may soon enable rapid metabolite-based diagnostics at the bedside.

In the future, routine use of metabolomic biomarkers, such as lipid panels, steroid profiles, and specific metabolic signatures, may be integrated into standard clinical workflows. These biomarkers could support personalized treatment plans, early risk detection, and monitoring of therapy responses, contributing to more effective and precise breast cancer management (N. K. Anh et al., 2024; Carmona et al., 2024).

Thus, the integration of the use of metabolomics (specific steroid hormones) and lipidomics (lipid profiles) for the prognosis of breast cancer. Main risk factors such as increasing age, obesity, menopause and genetic mutations are highlighted, which can influence the hormone receptor expression and immunohistochemistry of the tumor, which can further help in the classification of breast cancer subtypes. It is suggested that the metabolite and lipid profile changes that occur during tumorigenesis in the breast become insightful in providing a highly sensitive method, precise prognosis, real-time data, and personalized therapeutic plans. Therefore, the combination of metabolomic and lipidomic methods is considered a promising approach in clinical medicine (Figure 1).

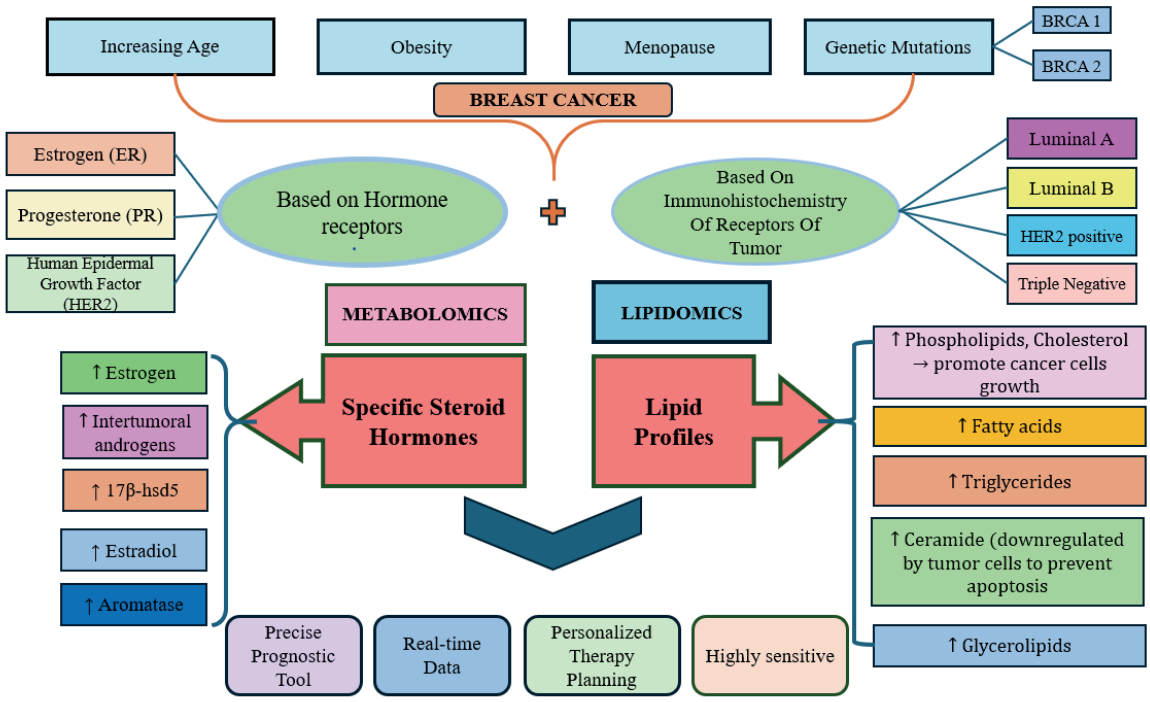

Figure 1. The significance of the metabolomic and lipidomic methods in clinical medicine.

Conclusion

In conclusion, the rising burden of breast cancer highlights the need for more accurate, non-invasive, and informative diagnostic tools. Lipid profiles and selected steroid hormones, supported by metabolomics and lipidomics, have emerged as promising biomarkers for early detection, prognosis, and therapy monitoring. These approaches offer valuable insights into tumor biology, metabolic changes, and hormone-driven pathways. Although there are challenges related to sample preparation, data interpretation, and technical demands, recent advances, such as high-resolution mass spectrometry, spatial metabolomics, and artificial intelligence, are helping to overcome these barriers. With continued research and technological progress, metabolomic-related biomarkers are expected to become more widely used in clinical settings, supporting personalized treatment and better outcomes for breast cancer patients.

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Conflict of interest

The authors declare no conflict of interest.

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Ethics committee approval

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Authors' contribution statement

Study conception and design: E.J., T.P., I.N.; **Data collection**: A.F.N., N.P.S., A.P.S., J.D.B., I.N.; **Analysis and interpretation of results**: A.F.N., E.J., T.P., N.P.S., A.P.S., J.D.B. I.N.; **Manuscript draft preparation**: A.F.N., E.J., T.P., N.P.S., A.P.S., J.D.B., I.N. All authors reviewed the results and approved the final version of the manuscript.

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