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REVIEW

Fertility preservation in women with BRCA1/2-related cancers: contemporary strategies, international recommendations, and a multidisciplinary approach

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ABSTRACT

Inherited mutations in the BRCA1/BRCA2 genes significantly increase the risk of breast and ovarian cancer in women of reproductive age, posing a clinical and socioeconomic challenge due to loss of fertility during cancer treatment and preventive interventions. The expansion of genetic testing programs is shifting the focus to proactive management of reproductive potential, requiring the integration of oncology, reproductive medicine, and medical genetics. The novelty of this review lies in its comprehensive synthesis of data on the impact of treatment and prevention of BRCA-associated cancer on fertility and a critical assessment of the effectiveness of fertility preservation strategies.

Purpose of the study. To summarize and analyze current advances, clinical guidelines, and unresolved issues related to preserving reproductive function in women carrying BRCA1/BRCA2 mutations.

Materials and methods. A systematic search of PubMed/MEDLINE, Embase, the Cochrane Library, and Web of Science was performed, along with an analysis of international guidelines (ESHRE (European Society of Human Reproduction and Embryology), ASCO (American Society of Clinical Oncology), ASRM (American Society for Reproductive Medicine), NCCN (National Comprehensive Cancer Network), ESMO (European Society for Medical Oncology)). Keywords: “BRCA1,” “BRCA2,” “fertility preservation,” “oocyte cryopreservation,” “embryo cryopreservation,” “ovarian tissue cryopreservation,” “PGT-M,” “PARP inhibitors,” and “chemotherapy gonadotoxicity.”, in the period of 2005–2025. Studies with incomplete data, duplicates, reviews of low methodological quality, and case series with fewer than 10 observations were excluded. Priority was given to meta-analyses, RCTs, large cohorts, and consensus reports.

Results. The included studies included cancer patients before and after treatment, BRCA carriers with and without prophylactic strategies, and IVF/ICSI cohorts with cryopreservation. Alkylating agents and taxanes have been shown to increase the risk of premature ovarian failure, while GnRH agonists partially reduce the risk of ovarian toxicity. The efficacy of oocyte and embryo cryopreservation in BRCA-positive women is comparable to the population-based efficacy with optimized stimulation (GnRH antagonists, letrozole-containing protocols). Ovarian tissue cryopreservation is applicable in urgently needed patients but requires oncoprotective assessment. PGT-M ensures the selection of mutation-free embryos. Multidisciplinary pathways improve the timelines of referrals and the completion rate of fertility preservation programs

Conclusion. Early identification of BRCA-positive women and the integration of a gynecologic oncologist, reproductive specialist, and geneticist enable personalized strategy selection: gamete/embryo cryopreservation, ovarian tissue, pharmacoprotection, and PGT-M. Standardized stimulation protocols and therapy timing, long-term safety and fertility data, and economic access models are needed. Improvements in biotechnology and patient pathways improve reproductive outcomes and quality of life.

Keywords: BRCA1, BRCA2, fertility, breast cancer, ovarian cancer, cryopreservation, oncoreproductology, preimplantation genetic diagnosis, multidisciplinary approach, hereditary cancer, ovarian reserve, reproductive counseling

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3.1.6. Онкология, лучевая терапия
ОБЗОР

Сохранение фертильности у женщин с BRCA1/2-ассоциированными опухолями: современные подходы, международные рекомендации и мультидисциплинарная тактика

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РЕЗЮМЕ

Наследственные мутации в генах BRCA1/BRCA2 существенно повышают риск развития рака молочной железы и яичников у женщин репродуктивного возраста, формируя клинический и социально-экономический вызов из-за потери фертильности на фоне противоопухолевого лечения и профилактических вмешательств.

Цель исследования. Обобщить и проанализировать современные достижения, клинические рекомендации и нерешенные вопросы по сохранению репродуктивной функции у женщин-носителей мутаций BRCA1/BRCA2.

Материалы и методы. Выполнен систематизированный поиск в PubMed/MEDLINE, Embase, Cochrane Library и Web of Science, а также анализ международных руководств Европейского общества репродукции человека и эмбриологии (ESHRE), Американского общества клинической онкологии (ASCO), Американского общества репродуктивной медицины (ASRM), Национальной комплексной онкологической сети (NCCN), Европейского общества медицинской онкологии (ESMO). Ключевые слова: «BRCA1», «BRCA2», «fertility preservation», «oocyte cryopreservation», «embryo cryopreservation», «ovarian tissue cryopreservation», «PGT-M», «PARP inhibitors», «chemotherapy gonadotoxicity». Период: 2005–2025 гг. Исключались работы с неполными данными, обзоры низкого методологического качества, серии случаев <10 наблюдений; приоритет отдавался метаанализам, RCT, крупным когортам и консенсусам.

Результаты. Включенные исследования охватывали онкологических пациенток до начала лечения и после него, носительниц BRCA с профилактическими стратегиями и без них, а также когорты ЭКО/ИКСИ с криоконсервацией. Показано, что алкилирующие агенты и таксаны повышают риск преждевременной недостаточности яичников, тогда как агонисты ГнРГ частично снижают риск овариальной токсичности. Эффективность криоконсервации ооцитов и эмбрионов у BRCA сопоставима с популяционной при оптимизации стимуляции (антагонисты ГнРГ, летрозол-содержащие протоколы). Криоконсервация овариальной ткани применима у срочных пациенток, но требует онкобезопасной оценки. PGT-M обеспечивает отбор эмбрионов без мутации. Мультидисциплинарные маршруты повышают своевременность направления и долю завершенных программ сохранения фертильности.

Заключение. Ранняя идентификация носительниц BRCA и интеграция онкогинеколога, репродуктолога и генетика обеспечивают персонализированный выбор стратегии: криоконсервация гамет/эмбрионов, овариальная ткань, фармакопротекция, PGT-M. Необходимы стандартизованные протоколы стимуляции и тайминга относительно терапии, долгосрочные данные о безопасности и деторождениях, а также экономические модели доступа. Совершенствование биотехнологий и маршрутизация пациентов улучшают репродуктивные исходы и качество жизни.

Ключевые слова: BRCA1, BRCA2, фертильность, рак молочной железы, рак яичников, криоконсервация, онкорепродуктология, преимплантационная генетическая диагностика, мультидисциплинарный подход, наследственный рак, овариальный резерв, репродуктивное консультирование

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BACKGROUND

BRCA mutations are hereditary variants in the BRCA1 (Breast Cancer Susceptibility Gene 1) and BRCA2 (Breast Cancer Susceptibility Gene 2) genes, which play a fundamental role in maintaining genomic stability through highly efficient homologous recombination-mediated DNA double-strand break repair mechanisms [1]. Dysfunction of these genes due to pathogenic variants leads to a significant decline in DNA repair capacity, which, in turn, markedly increases the lifetime risk of developing malignant neoplasms, most notably breast cancer (BC) and ovarian cancer (OC). According to current data, carriers of pathogenic BRCA1 variants have an estimated lifetime BC risk of 65–80 % and OC risk of up to 40–60 % [2], while for BRCA2 mutation carriers these estimates are 45–60 % and 10–20 %, respectively. Importantly, hereditary predisposition associated with BRCA1/2 mutations occurs in both women and men; however, the clinical impact is significantly greater in women due to their substantially higher baseline risk for associated cancers [3].

Identification of a pathogenic BRCA1/2 mutation warrants referral for specialized genetic counseling, which encompasses several key objectives. Primarily, counseling aims to provide the patient and her at-risk relatives with information on mutation-associated cancer risks, the molecular characteristics of the defect, as well as contemporary strategies for individualized surveillance, prevention, and early detection of malignancies. Additionally, when hereditary cancer predisposition is confirmed, counseling supports personalized therapeutic planning, including the discussion of risk-reducing surgical options. An essential component of counseling is evaluation of reproductive considerations and discussion of the risk of transmitting the mutation to future offspring, which requires collaboration with reproductive specialists and assessment of fertility preservation options [4].

The issue of fertility preservation is particularly relevant for young women of reproductive age who, due to their BRCA mutation status and early cancer diagnosis, may require intensive surgical treatment and/or aggressive systemic therapy. Systemic antineoplastic treatment, as well as risk-reducing salpingo-oophorectomy, is associated with a high risk of ovarian reserve depletion and premature menopause, thereby significantly limiting reproductive potential [5]. Hence, timely and comprehensive discussion of fertility preservation options must begin at the time of diagnosis, prior to initiation of anticancer treatment.

With the increasing number of identified BRCA mutation carriers, advancements in molecular genetic testing, and expanding opportunities in assisted reproductive technologies (ART), fertility preservation has gained substantial clinical and social significance [6]. Addressing this issue requires a multidisciplinary approach that integrates medical, ethical, legal, and psychological aspects, along with further research aimed at improving management strategies and quality of life for young BRCA-positive patients who are facing treatment with potential gonadotoxic effects [7].

International guidelines on fertility preservation in patients with BRCA1/2 mutations

The issue of fertility preservation in women with BRCA1/2 mutations is reflected in multiple international guidelines, including those of the European Society of Human Reproduction and Embryology (ESHRE)[1], the American Society of Clinical Oncology (ASCO)[2], the American Society for Reproductive Medicine (ASRM)[3], as well as leading oncological and genetic professional societies such as the European Society for Medical Oncology (ESMO)[4], the National Comprehensive Cancer Network (NCCN)[5], the International Federation of Gynecology and Obstetrics (FIGO)[6], the European Society of Human Genetics (ESHG)[7], and the American College of Medical Genetics and Genomics (ACMG)[8].

[1] European Society of Human Reproduction and Embryology (ESHRE) [Internet]. Available at: https://www.eshre.eu – *Editorial note.*
[2] American Society of Clinical Oncology (ASCO) [Internet]. Available at: https://www.asco.org – *Editorial note.*
[3] American Society for Reproductive Medicine (ASRM) [Internet]. Available at: https://www.asrm.org – *Editorial note.*
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[8] American College of Medical Genetics and Genomics (ACMG) [Internet]. Available at: https://www.acmg.net – *Editorial note.*

The modern multidisciplinary approach requires not only individualized reproductive preservation strategies, but also careful consideration of the specific genetic risks within this patient population [8].

According to the updated ESHRE and ASCO guidelines, all women of reproductive age with confirmed BRCA1/2 mutations, or those at high risk of carrying such mutations due to a burdened family history, must receive timely counseling on the possibilities and limitations of fertility preservation strategies. ASCO emphasizes that fertility preservation counseling should be offered to all patients before the initiation of potentially gonadotoxic therapy, regardless of the woman's ultimate decision regarding the use of preserved gametes or tissues in the future [9].

ESHRE highlights the importance of genetic counseling prior to *in vitro* fertilization (IVF) procedures and oocyte/embryo cryopreservation, as well as discussing the option of preimplantation genetic testing for monogenic disorders (PGT-M) in order to prevent transmission of the mutation to offspring. Both societies also recommend considering oocyte or embryo cryopreservation as the standard and most effective method, whereas ovarian tissue cryopreservation may be proposed only in exceptional cases with mandatory evaluation of the patient's oncological status and the potential risk of reimplanting tissue carrying a pathogenic mutation. ASRM also underscores the limitations of using autotransplanted ovarian tissue specifically in BRCA1/2 mutation carriers due to a theoretically increased risk of malignancy or micro-metastatic disease [10].

Several consensus documents (NCCN, ESMO) emphasize the necessity of integrating fertility preservation counseling into the decision-making process for oncological treatment planning, as well as ensuring multidisciplinary collaboration between oncologists and reproductive specialists.

Fertility preservation protocols should be considered for all reproductive-age patients prior to the initiation of chemotherapy or radiotherapy that may have a gonadotoxic effect, and also before prophylactic bilateral oophorectomy or adnexectomy recommended for BRCA mutation carriers as a preventive measure after the completion of childbearing. It is critically important not to miss the window of opportunity between diagnosis and the start of treatment.

Women carrying BRCA1/2 mutations differ not only in their baseline strategies of cancer treatment and prevention, but also in fertility preservation approaches. This patient group frequently demonstrates a reduced ovarian reserve already at the time of diagnosis, which necessitates early counseling and rapid decision-making regarding fertility preservation.

Methods for preserving reproductive potential in BRCA-associated diseases

Modern oncofertility offers a number of effective strategies for fertility preservation in women with BRCA mutations, which is particularly relevant given the unfavorable prognosis for natural reproductive function when aggressive treatment is required. The choice of method is individualized based on the oncological diagnosis, the time available before starting primary treatment, patient age, ovarian reserve, and reproductive plans [11].

Oocyte cryopreservation is a modern and widely accepted method of fertility preservation for women of reproductive age. The procedure involves controlled ovarian stimulation with gonadotropins, followed by transvaginal ultrasound-guided retrieval of mature oocytes and vitrification (ultra-rapid freezing), which ensures maximum preservation of the structural and functional potential of oocytes during long-term storage. This method is preferable for patients without a permanent partner or those not ready for fertilization at the time of diagnosis. Oocyte cryopreservation is considered effective and safe, and it is not associated with an increased risk of malignant transformation in BRCA mutation carriers [12].

In a study by Cobo A. et al., a comparative analysis of oocyte cryopreservation by vitrification was conducted in two groups: 5289 healthy women and 1073 women with cancer. Significant differences

were found between the cohorts. The post-thaw oocyte survival rate in healthy women was 91.4 %, whereas in cancer patients it was substantially lower at 81.2 %. Clinical pregnancy rates also differed: 65.9 % among healthy women versus 42.8 % among oncologic patients. The authors showed that in women aged up to 35 years inclusive, reproductive outcomes were significantly higher in the healthy cohort; however, after age 35 no statistically significant differences were observed, suggesting the dominant influence of age in the older group [13].

Regarding patients carrying BRCA1/2 mutations, a meta-analysis by Corrado G. et al. included six studies assessing mutation impact on fertility preservation outcomes. A total of 1848 patients were analyzed, 265 of whom carried BRCA mutations. Results were inconsistent: several studies reported reduced ovarian reserve and poorer response to stimulation, reflected by fewer retrieved oocytes and embryos, while others found no significant differences between carriers and non-carriers [14].

Another study by Corrado G. et al. compared *in vitro* maturation (IVM) outcomes between 57 patients with BRCA-mutation carriers and 277 controls. No significant differences in oocyte maturation were found. The mean maturation rate was 68.4 % in BRCA-positive patients versus 71.2 % in the control group (p = 0.287). Oocyte morphology quality was also comparable (82.1 % vs 84.5 %, p = 0.412). Subgroup analysis revealed no impact of mutation type (BRCA1 vs BRCA2) or age. Time to reach metaphase II was similar in both groups (24–26 hours), suggesting that BRCA mutations may not impair *in vitro* maturation, which is encouraging for fertility preservation programs [14].

Embryo cryopreservation is the method of choice for patients with a stable partner and/or defined reproductive plans. Embryos created via IVF are cryopreserved and stored until pregnancy is desired. This approach demonstrates the highest efficiency among assisted reproductive technologies but may require additional time, which is not always feasible in urgent cancer treatment settings [15, 16].

Ovarian tissue cryopreservation is an innovative and rapidly developing method, suitable for patients requiring immediate treatment or those for whom controlled stimulation is contraindicated. The technique involves laparoscopic retrieval of cortical ovarian tissue followed by cryostorage and potential autotransplantation after treatment. This may restore both fertility and endocrine function. However, in BRCA mutation carriers, the risk of reintroducing malignant cells remains a concern. Therefore, international guidelines consider ovarian tissue cryopreservation a limited option that requires careful individualized risk assessment and multidisciplinary counseling [17].

Use of gonadotropin-releasing hormone agonists (GnRHa) during chemotherapy is aimed at temporary suppression of ovarian function, reducing cytotoxic damage to follicles. GnRHa induce transient suppression of the hypothalamic-pituitary-gonadal axis, placing ovaries in a pharmacological “resting” state. Multiple meta-analyses confirm reduced risk of premature ovarian insufficiency and higher rates of spontaneous post-treatment pregnancy. Nevertheless, this method does not replace established cryopreservation protocols and is considered an adjunctive gonadoprotective strategy [18, 19].

Another option is the use of donor oocytes, which is considered a reserve strategy for women who have lost ovarian reserve due to treatment or who initially have a low likelihood of successful IVF with their own oocytes. Donor oocyte use enables the possibility of gestation and childbirth even in cases of complete loss of endogenous fertility, although it is associated with psychological, ethical, and legal considerations that must be discussed with prospective parents. In addition, the use of donor gametes fully eliminates the risk of transmitting a BRCA mutation to the offspring.

The development and creation of artificial or bioengineered ovaries represent one of the most promising areas of research. An artificial ovary is defined as a three-dimensional biocompatible scaffold populated with the patient’s own follicular cells and immature oocytes, or with donor-derived material.

Such constructs theoretically address the risk of malignant cell reintroduction and may allow restoration of both endocrine function and fertility. In the future, novel molecular targets for the pharmacological protection of the female reproductive system are being explored, and new agents are being developed that can selectively block apoptotic signaling pathways or exert cytoprotective effects directly on ovarian follicles [20].

It should be emphasized that timely referral of the patient to a reproductive specialist and the selection of an individualized fertility preservation strategy are essential components of the modern multidisciplinary approach to the management of women with BRCA mutations, helping to safeguard their reproductive autonomy and improve long-term quality of life.

Genetic screening for BRCA mutations to prevent transmission to offspring

The BRCA1 and BRCA2 genes are highly penetrant tumor suppressors. Mutations in these genes are inherited in an autosomal dominant pattern. This means that each pregnancy of a woman carrying a pathogenic mutation in BRCA1 or BRCA2 is associated with a 50 % risk of transmitting this mutation to the child, regardless of the child's sex. The mutations are transmitted equally through both the maternal and paternal lineage; the hereditary predisposition is determined by a homologous defective allele, and even a single altered gene copy substantially increases the risk of developing BRCA-associated malignancies [21].

Currently, a key tool for reducing the risk of transmitting a pathogenic BRCA mutation to offspring is preimplantation genetic testing for monogenic disorders (PGT-M). This method is used within IVF programs. At the blastocyst stage, biopsy of several trophectoderm cells is performed, followed by DNA analysis, which allows precise identification of the presence or absence of BRCA1/2 mutations in each embryo [22]. Based on these results, only embryos that have not inherited the mutation are selected for uterine transfer [23].

Another approach is analysis of BRCA mutations using umbilical cord blood. Cord blood is considered a potential source of DNA, especially in the neonatal period. It contains a sufficient number of nucleated cells to isolate genetic material for screening of known hereditary mutations, including BRCA1 and BRCA2. This approach can be applied, for example, to determine mutation carriage in a newborn as part of family genetic evaluation or by neonatology indications. In addition, cord blood testing has the advantage of non-invasive collection immediately after birth, ensuring both high safety and diagnostic value [24, 25].

Reproductive counseling for patients carrying BRCA mutations should include a discussion of the risk of transmitting the pathogenic allele to offspring, and information about modern possibilities of preimplantation genetic testing as an ethically and clinically meaningful method of interrupting autosomal-dominant transmission of cancer predisposition [26]. This provides families with the right to make an informed decision regarding the planning of healthy offspring.

Reproductive loss associated with BRCA-related therapy

Comprehensive treatment of malignant diseases in patients with BRCA mutations has a pronounced negative effect on reproductive function, primarily reflected in the state of the ovarian reserve and hormonal activity. Major components of contemporary anticancer therapy – chemotherapy, radiotherapy, and surgery – individually and collectively significantly increase the risk of premature ovarian insufficiency.

Chemotherapy is one of the leading causes of ovarian reserve depletion. Agents used in the treatment of breast and ovarian cancer have marked gonadotoxic effects. Toxicity is driven by direct damage to proliferating granulosa cells and induction of apoptosis in growing follicles [27]. The development of treatment-related amenorrhea (TRA) in oncology patients is determined by several interrelated factors, among which the most significant are patient

age, baseline ovarian reserve, and the presence of pathogenic BRCA variants.

Chemotherapeutic regimens containing cyclophosphamide, doxorubicin, and taxanes demonstrate high gonadotoxicity, inducing TRA in 83.6 % of cases, accompanied by a characteristic decline in anti-Müllerian hormone (AMH) levels, which in many patients shows partial recovery within three years after therapy completion. Age-stratified analysis of TRA risk reveals a clear correlation: patients over 35 years have a threefold higher probability of developing TRA. Recovery of reproductive function after TRA is generally favorable: menstrual cycles resume in about 70 % of patients within one year and in 90 % within two years after treatment. BRCA mutation carriers demonstrate additional features of reproductive aging, including earlier menopause by 1–3 years compared to the general population [28].

The baseline AMH level in BRCA carriers is of particular interest for ovarian reserve assessment. Numerous studies have attempted to determine whether women with germline pathogenic BRCA1/2 variants and diagnosed breast cancer have lower baseline AMH and/or a reduced response to controlled ovarian stimulation compared to non-carriers. However, available data show significant heterogeneity, contributing to difficulties in forming uniform clinical recommendations [29].

A major dilemma in contemporary oncology is the potential conflict between preserving fertility in young women and the urgency of initiating treatment. Fertility preservation procedures require time for planning and implementation and may delay chemotherapy, which could theoretically worsen oncological outcomes.

A retrospective study by Greer A. et al. involving 272 patients with stage 0–III breast cancer demonstrated that fertility preservation in 123 patients caused a mean treatment initiation delay of 10 days compared with controls (149 patients). Despite this delay, oncological outcomes were comparable: progression-free survival at three years was 85.4 % vs. 79.4 % (p = 0.411) and overall survival was 95.5 % vs. 93.5 % (p = 0.854) [30].

In modern reproductive practice, Random-Start ovarian stimulation is used, enabling initiation at any point in the menstrual cycle, which is particularly relevant for cancer patients requiring urgent treatment. In women with hormone-receptor–positive breast cancer, stimulation is combined with aromatase inhibitors to avoid supraphysiologic estradiol levels that may adversely affect disease progression. Thus, aromatase inhibitors are started concurrently with gonadotropins and continued for seven days after oocyte retrieval until estradiol falls below 50 pg/mL. The “double trigger” technique (combined hCG + GnRH agonist) is frequently used to optimize final oocyte maturation, especially in patients at risk for poor ovarian response due to BRCA-associated reduced reserve [31].

Hormone therapy usually does not directly damage the ovaries or suppress ovarian reserve. However, the standard treatment duration of 5–10 years significantly reduces reproductive potential due to age-related decline in fertility, limiting the likelihood of future pregnancy after therapy completion [32].

Radiation therapy, particularly irradiation of the pelvic or abdominal region, also adversely affects reproductive function. The ovaries are highly sensitive to ionizing radiation, and even relatively low doses may lead to irreversible follicular reserve damage. Ovarian dysfunction manifests as decreased estrogen levels, elevated FSH, and clinical signs of iatrogenic menopause. The nature and severity of damage depend on radiation dose and the volume of irradiated tissue [33, 34].

Surgical treatment of BRCA-associated malignancies often involves radical procedures such as bilateral oophorectomy (removal of the ovaries) or salpingo-oophorectomy (removal of the ovaries and fallopian tubes). Even when performed prophylactically, such procedures result in the immediate loss of ovarian function with the development of iatrogenic menopause, secondary amenorrhea, and inability to conceive naturally. Additionally, prophylactic mastectomy deserves particular attention. Although this intervention does not directly lead to loss of reproductive capacity, the breast plays

an important biological role in human reproduction. It is not only a symbol of femininity but also a key organ for breastfeeding, which directly affects mother–infant bonding, nutrition, and neonatal immune protection [35]. The loss of breast tissue is also frequently associated with significant psycho-emotional distress related to body-image alteration and perception of feminine identity, which may negatively influence future decisions regarding motherhood. The question of the feasibility and timing of preventive surgical interventions in women with identified pathogenic BRCA1/BRCA2 mutations, who have not yet completed their reproductive plans and have no clinical signs of malignancy, remains the subject of active scientific discussion and requires an individualized approach. Prophylactic mastectomy in carriers of pathogenic BRCA1/BRCA2 variants reduces the lifetime risk of breast cancer by approximately 90–95 %. Prophylactic bilateral salpingo-oophorectomy reduces the risk of ovarian and fallopian tube cancer by more than 80–90 % [36].

International clinical guidelines, based on consensus statements of leading oncological and genetic societies (NCCN, ESMO, SGO, ASCO, etc.), confirm that prophylactic bilateral mastectomy and/or bilateral salpingo-oophorectomy significantly reduce the risk of breast and ovarian cancer in BRCA mutation carriers. However, the optimal timing of such procedures, particularly for young women, remains a matter of debate. Early preventive surgery undoubtedly minimizes cumulative cancer risk but is associated with pronounced consequences for quality of life, fertility potential, psycho-emotional well-being, and hormonal balance. Several guidelines (NCCN, ESMO) indicate the possibility of delaying preventive surgery until childbearing is completed–typically until 35–40 years of age for BRCA1 carriers and 40–45 years for BRCA2 carriers, provided that stringent oncological surveillance is maintained [37].

Thus, all major components of the comprehensive treatment of malignant neoplasms in patients with BRCA mutations are associated, to varying degrees, with a risk of significant impairment of reproductive function. This necessitates early discussion, even before the initiation of specific anticancer treatment, of fertility preservation and individualized reproductive planning for each patient in this category.

CONCLUSION

The issue of fertility preservation in women with pathogenic BRCA1 and BRCA2 mutations is one of the most critical challenges at the intersection of oncology, reproductive medicine, and medical genetics. These patients belong to a population with an extremely high oncological risk, and modern treatment modalities – including surgical interventions, chemotherapy, and radiotherapy – are associated with the threat of ovarian reserve depletion and the development of premature menopause, which effectively leads to infertility, disrupts hormonal balance, and reduces long-term quality of life.

Comprehensive assessment of reproductive risks, thorough genetic counseling, and targeted patient education on available fertility preservation options constitute essential components of a multidisciplinary management approach. Current clinical guidelines emphasize the critical importance of early referral to reproductive specialists: timely optimization of diagnostic and therapeutic planning enables the implementation of effective oocyte or embryo cryopreservation strategies, providing the possibility of having a biologically related child even after completion of anticancer therapy. Furthermore, the active integration of preimplantation genetic testing for monogenic disorders (PGT-M) significantly reduces the risk of transmitting pathogenic BRCA mutations to offspring, which is ethically and clinically important for families with a burdened hereditary cancer history. A key direction for further development includes the improvement of biotechnological and pharmacological approaches to ovarian protection, including the creation of artificial ovaries and pharmacologic prevention of gonadotoxic effects associated with systemic therapy. The efficacy and long-term safety of these innovative strategies are currently the focus of intense scientific investigation,

highlighting the need for continued fundamental and clinical research.

Another essential task is the optimization of decision-making regarding risk-reducing surgeries (mastectomy, salpingo-oophorectomy) in BRCA mutation carriers who have not yet developed cancer. Current data support the possibility of delaying radical preventive interventions until after completion of reproductive plans, combined with dynamic specialized surveillance, which allows preservation of reproductive potential without a clinically significant increase in oncological risk, provided that individualized screening protocols are strictly followed.

Thus, the practical implementation of a multidisciplinary and personalized approach to the management of women with BRCA1/2 mutations, aimed not only at the prevention and timely treatment of malignant tumors but also at the preservation and restoration of reproductive health, must become a priority in modern clinical practice. Only such a comprehensive strategy – integrating medical, genetic, psychological, and ethical-legal aspects – can substantially improve quality of life and ensure informed reproductive decision-making for patients, supporting their right to motherhood and the well-being of future generations.

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