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MOLECULAR AND GENETIC PATHWAYS OF WOUND HEALING BY AGE IN RECONSTRUCTIVE AND PLASTIC SURGERY: A COHORT STUDY

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Abstract.

Despite advances in surgical techniques and perioperative care, postoperative complications – including impaired wound healing, pathological scarring, infection, and flap or graft failure – remain a significant clinical problem, adversely affecting patient outcomes and satisfaction while increasing healthcare costs.

The Aim *of this study is to evaluate age-dependent expression of the IL6, CCL2, MAPK1, MAPK8, IL10, MMP9, COL1A1 and COL3A1 in a cohort of women undergoing reconstructive and plastic surgery cohort, and to assess the molecular and genetic pathways involved in wound healing.*

Materials and Methods. *Ninety-five women participated in the prospective longitudinal cohort study and underwent reconstructive / plastic surgery. The mean age 35.48 ± 6.61 years (range: 19-57 years). All participants provided written informed consent prior to enrollment and subsequently underwent comprehensive demographic, clinical, instrumental, and laboratory assessments. The study was conducted in accordance with the principles of the Council of European Convention on Human Rights and Biomedicine. Ethical approval was obtained from the Biomedical Ethics Commission of Bukovinian State Medical University. Participants were stratified by age: <30 yr (24.21%), 30-39 years (44,21%), ≥40 yr (31.58%); and by the presence of postoperative complications: complicated cases (12.63%) and uncomplicated cases (87.67%). Transcriptional activity of IL6, CCL2, MAPK1, MAPK8, IL10, MMP9, COL1A1 and COL3A1 genes in peripheral blood was assessed by pathway-specific PCR array. Purified RNA was reverse-transcribed (RT) with a complementary DNA (cDNA). Statistical analysis was performed using Statistica 7.0 software (StatSoft Inc., USA) and Excel® 2016™. This study was conducted as part of an ongoing comprehensive Research Program of the Family Medicine Department at Bukovinian State Medical University «Improvement of diagnosis and prediction of hypertensive-mediated certain target organ damage and symptom control in comorbid pathology considering clinical-metabolic and molecular-genetic predictors» (State Registration No. 0124U002524; project period: 01 January 2024 to 31 December 2028).*

Results. *Women ≥40 yr undergoing plastic and reconstructive breast surgery are characterised by a high-risk molecular profile for postoperative complications. This profile encompasses increased pro-inflammatory activity, reflected by elevated IL6 gene expression (M = 0.75; p = 0.05); enhanced proliferative and regenerative processes, indicated by MAPK1 expression (M = 0.63); and activated stress-related signalling pathways, evidenced by MAPK8 expression (M = 1.64; p = 0.017). It is further distinguished by intensive extracellular matrix remodeling with accelerated collagen and matrix degradation, reflected by elevated MMP9 expression (M = 0.82; p = 0.002);); augmented fibrogenesis, manifested as a twofold increase in COL1A1 expression (M = 1.53; p_1 = 0.017), a comparatively modest increase in COL3A1 (1.69- and 0.75-fold), and a 2.55-fold upregulation of TGFβ1 2.55-fold (p = 0.041); and an immunosuppressive shift, reflected by a compensatory increase in IL10 expression (M = 0.22; p_1 = 0.05).*

A marked imbalance in the COL1A1/COL3A1 ratio (COL1A1 ≫ COL3A1) was identified, representing the molecular basis of fibrosis and hypertrophic scar formation. Women 30-40 yr, by contrast, exhibited the most balanced gene expression profile, which may correspond to an optimal tissue reparative potential.

Conclusion. *Women >40 yr undergoing plastic and reconstructive breast surgery exhibit a molecular profile associated with a high risk of postoperative complications. Women 30-40 yr demonstrate a more balanced gene expression profile, consistent with a more favorable reparative tissue response and wound healing.*

Key words: *Wound Healing; Gene Expression; Plastic and Reconstructive Breast Surgery; Inflammation; Women; Age; Tissue Response; Molecular and Genetic Mechanism; Regenerative Processes; Fibrogenesis.*

Introduction

Reconstructive and plastic surgery plays a crucial role in restoring form, function and quality of life in patients undergoing treatment for congenital anomalies, trauma, oncological conditions, degenerative diseases or aesthetic indications. The scale of these interventions is considerable: in the United States in 2015 alone, more than 1.5 million surgical procedures and over three million nonsurgical aesthetic interventions were performed [1]. Despite significant advances in surgical techniques, perioperative care, and biomaterials, postoperative complications remain a substantial clinical challenge. Impaired wound healing, excessive scar formation, surgical site infection, flap or graft failure, and chronic postoperative inflammation continue to adversely affect functional and aesthetic outcomes, increase healthcare costs, and compromise patient satisfaction [2-4].

Wound healing is a complex, tightly regulated biological process encompassing coordinated interactions among inflammatory mediators, immune cells, extracellular matrix remodeling, angiogenesis, and tissue regeneration [5; 6]. Dysregulation of any phase of this process process – particularly the inflammatory and matrix remodeling phases – may result in delayed healing, hypertrophic scarring, fibrosis, or wound dehiscence. Complications associated with implant-based breast reconstruction are broadly classified as either short-term or long-term [7]. Short-term complications are considered perioperative events that may jeopardize the success of the reconstruction, including seroma, haematoma, infection, and skin envelope necrosis. Long-term complications do not typically pose an immediate risk of reconstructive failure; however, they encompass

unfavorable aesthetic outcomes – such as implant malposition, contour deformities, and rippling – more serious reconstructive sequelae, including severe capsular contracture or animation deformity, and rare systemic conditions, such as breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) and breast implant illness (BII). Mounting evidence indicates that individual variability in postoperative outcomes cannot be fully explained by surgical factors alone, underscoring the importance of host-related biological determinants [8].

Genetic and molecular mechanisms are now recognised as key contributors to interindividual differences in tissue repair and susceptibility to postoperative complications [5; 9; 10]. Polymorphisms and altered expression of genes involved in inflammatory signaling, immune regulation, extracellular matrix turnover, and angiogenesis have been associated with abnormal wound healing and pathological scar formation [11-13]. Cytokines such as interleukin-6 (IL-6) and interleukin-10 (IL-10), chemokines including C-C motif chemokine ligand 2 (CCL2), mitogen-activated protein kinases (MAPK1, MAPK8), matrix metalloproteinase-9 (MMP9), and structural extracellular matrix proteins (COL1A1, COL3A1) are among the key molecular mediators implicated in these processes. Alterations in their expression or interaction networks may shift the balance between physiological repair and pathological remodeling [14-17].

The present study was therefore designed to investigate the molecular and genetic pathways involved in the wound healing and the development of postoperative complications in reconstructive and plastic surgery.

The aim of the study is to evaluate age-dependent expression of IL6, CCL2, MAPK1, MAPK8, IL10, MMP9, COL1A1 and COL3A1 genes in a cohort of women undergoing reconstructive and plastic surgery, and to assess the molecular and genetic pathways involved in wound healing.

Material and methods

Clinical material was collected at the Limited Liability Company «Bukovinian Centre of Plastic and Aesthetic Surgery» (Chernivtsi city, UA) between 2024 and 2025. A total of 95 women were enrolled in the prospective longitudinal cohort study and underwent reconstructive / plastic surgery. The mean age 35.48 ± 6.61 years (range: 19-57 years). All participants provided written informed consent prior to enrolment, after which a comprehensive assessment was performed, encompassing demographic and clinical evaluation, instrumental examination (breast ultrasonography or mammography), and laboratory investigations (complete blood count and biochemical analysis). The study was conducted in accordance with the principles of the Convention on Human Rights and Biomedicine of the Council of Europe, the fundamental requirements of Good Clinical Practice (1996), and the ethical standards for medical research involving human participants set forth in the World Medical Association Declaration of Helsinki. Ethical approval was obtained from the Biomedical Ethics Commission of Bukovinian State Medical University (BSMU).

Women were stratified by age: <30 yr (24.21%), 30-39 yr (44.21%), and ≥40 yr (31.58%); by the presence of postoperative complications: complicated cases (12.63%) and uncomplicated cases (87.67%); by type of reconstructive or plastic surgery: augmentation mammoplasty (69.47%), reduction mammoplasty (5.26%), mastopexy (6.32%), mastopexy with mammoplasty (9.47%), implant replacement (7.37%), and implant removal (2.11%); and by type of complication: retromammary seroma (2.11%), capsular fibrosis (6.32%), implant retroposition with breast shape change (3.16%), and implant rupture (1.05%). %). A total of 24.21% of women had a history of surgical interventions at other anatomical sites (caesarean section, ear, nose and throat surgery, and appendectomy), and 14.74% a history of concomitant chronic conditions (cystitis, pyelonephritis, Gilbert syndrome, bronchitis, and meniscus tear).

Transcriptional activity of IL6, CCL2, MAPK1, MAPK8, IL10, MMP9, COL1A1 and COL3A1 genes in the peripheral blood was assessed by pathway-specific polymerase chain reaction (PCR) array using the iTaq Universal SYBR Green Supermix SMX500 set (Thermo Fisher Scientific Inc., Bio-Rad Laboratories, Inc., USA). Total RNA was isolated from blood leucocytes using GeneAll® Hybrid-RTM Blood RNA kit (GeneAll Biotechnology Co., Ltd., Korea) according to the manufacturer's instructions. The purified RNA subjected to reverse transcription (RT) with the cDNA iScript™ gDNA Clear Synthesis Kit (Bio-Rad Laboratories, Inc., USA). RNA samples with integrity values ranging from –2.0 to 2.2 were included in the analysis, and all reactions were performed in triplicate. Relative messenger RNA (mRNA) expression of target genes was quantified using glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as the reference gene and normalized by the ΔΔCt method, as described previously [18; 19]. Fold changes in gene expression were calculated using the 2^–ΔΔCt formula.

Statistical analysis was performed using Statistica 7.0 software (StatSoft Inc., USA) and Excel® 2016™. Categorical variables were analysed by odds ratio (OR) with 95% confidence interval (CI) using the chi-square test (χ^2, df = 1); Fisher exact test was applied when expected cell frequencies were below 5 A multivariate logistic regression model was additionally employed. Differences between groups were evaluated using Student's *t*-test (two-tailed, equal variances assumed; reported as mean, M), one-way analysis of variance (ANOVA), Pearson chi-square test, or the Wilcoxon-Mann-Whitney *U* test when data distribution deviated from normality, as determined by the Shapiro-Wilk or Kolmogorov-Smirnov tests (Z-score; Me (Q1; Q3) with interquartile range – IQR). Statistical significance was set at $p < 0.05$.

This study was conducted as part of an ongoing Research Program of the Family Medicine Department at Bukovinian State Medical University «Improvement of Diagnosis and Prediction of Hypertension-Mediated Target Organ Damage and Symptom Control in Comorbid Pathology Considering Clinical, Metabolic, and Molecular Genetic Predictors» (State Registration No. 0124U002524; project period: 01 January 2024 to 31 December 2028).

Results and Discussion

The relative normalized mRNA expression levels (ΔΔCt) of IL6, MAPK1, MAPK8, MMP9, and TGFβ1 genes in peripheral blood, with GAPDH as the reference gene, are presented in Figure 1. Genes associated with inflammation, signal transduction, and extracellular matrix remodeling, accompanied by pronounced inter-individual variability, demonstrate predominantly low-to-moderate systemic expression. This expression pattern may reflect a balance between pro- and anti-inflammatory mechanisms, suggesting a predominantly local nature of molecular alterations that are not consistently reflected in circulating blood.

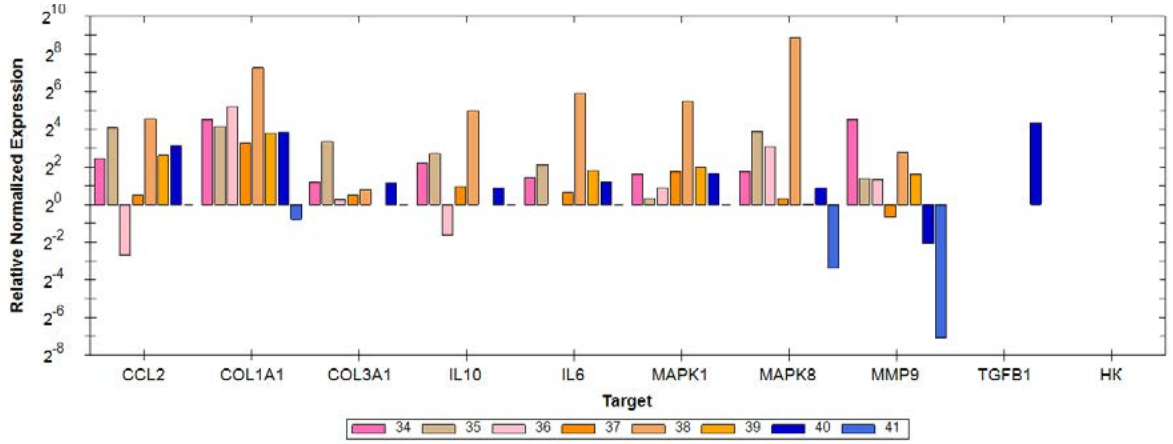

Figure 1. Relative normalized mRNA expression of genes *IL-6, CCL2, MAPK1, MAPK8, IL-10, MMP9, COL1A1, COL3A1, TGFβ1* in peripheral blood samples, using GAPDH as the reference gene (–2~2 LogN mRNA, ΔΔCt).

Normalised mRNA expression analysis of key immune-inflammatory, signalling, and matrix-remodelling genes revealed a clear age-dependent molecular response in women undergoing plastic and reconstructive breast surgery (Table 1). The most pronounced changes were observed in women >40 yr, indicating an increasing molecular predisposition to impaired tissue healing. In women <30 yr, the mean IL6 expression level was reduced (M = –0.70), suggesting a less pronounced inflammatory response. In the 30-40-yr group, a moderate increase – though remaining negative – was observed (M = –0.31), whereas women >40 yr demonstrated a marked elevation in IL6 expression (M = 0.75; p = 0.05), indicating age-related amplification of the pro-inflammatory activity. This finding reflects enhanced systemic inflammation associated with an increased risk of prolonged inflammation, seroma formation, and potential infectious complications [20; 21].

Table 1

Genetic-molecular panel of wound healing markers by level of normalized gene expression depending on the age of the operated women

Marker	mRNA level Expression, Me (Q1; Q3); M		
	<30 yr, n=12	30-40 yr, n=24	>40 yr, n=14
IL-6	0 (–2.21; 1.06); M: –0.70	0 (–0.49; 0.91); M: –0.31	0 (0; 1.69); M: 0.75 (p=0.05)
CCL2	–0.46 (–0.55; 1.84); M: 0.53	0.01 (–2.42; 0.88); M: –1.84	0 (–0.66; 1.79); M: 0.05
MAPK1	0.32 (–0.40; 1.12); M: –0.09	0 (–0.74; 1.05); M: 0.04	0.48 (–0.99; 1.43); M: 0.63
MAPK8	1.03 (–0.56; 2.70); M: 1.01	–0.45 (–2.57; 1.07); M: –0.66 (p=0.028)	0.78 (–0.18; 3.43); M: 1.64 (p_1=0.017)
IL-10	–0.82 (–3.96; 1.60); M: –0.87	–0.76 (–0.90; 0.23); M: –1.06	1.14 (–1.30; 1.30); M: 0.22 (p_1=0.05)
MMP9	–0.20 (–2.49; 1.54); M: –0.54	–0.72 (–3.13; 0.44); M: –1.73	0.83 (0.23; 1.81); M: 0.82 (p_1=0.002)
COL1A1	0.34 (–1.26; 2.46); M: 0.70	–0.63 (–1.71; 1.04); M: –0.40	0.55 (–0.22; 3.75); M: 1.53 (p_1=0.017)
COL3A1	0.80 (0.04; 2.05); M: 0.42	0.03 (0; 0.39); M: –0.04	0.72 (–0.60; 1.04); M: 0.71
TGFβ1	1.50 (1.25; 1.75) M: 1.50	0.80 (–1.10; 2.58) M: 0.72	3.82 (3.57; 4.07) M: 3.82 (p=0.041)

Note. p – significance of differences with group <30 years; p_1 – significance of differences with 30-40 yr group.

CCL2 gene expression exhibited the greatest variability in women <30 yr (M = 0.53) (Table 1). In the 30-40-yr group, a decrease in mean expression was observed (M = –1.84), possibly reflecting reduced chemotactic activity. In women >40 yr, expression values stabilized near zero (M = 0.05). Age-related activation of monocyte-macrophage recruitment may contribute to chronic inflammation, fibrotic processes, and imbalance of M1/M2 macrophage polarization [22].

MAPK1 expression demonstrated a gradual age-related increase, from near-neutral values in younger age groups to higher levels in women >40 yr (Me = 0.48; M = 0.63), reflecting enhanced proliferative and regenerative signaling. The most pronounced age-related differences were observed for MAPK8 (JNK): high expression was detected in women <30 yr (M = 1.01), significantly lower levels in the 30-40-yr group (M = –0.66; $p = 0.028$), and a subsequent significant increase in women >40 yr (M = 1.64; $p_1 = 0.017$), indicating age-related activation of stress-associated signaling pathways. The lowest normalized expression levels of MAPK1 and MAPK8 were observed in women 30-40 yr, which may reflect reduced cellular proliferation or stress signaling outside a conditionally optimal age range (<30 and >40 yr). Activation of the JNK pathway is associated with oxidative stress, apoptosis, and impaired angiogenesis [23], constituting a molecular basis for the risk of flap necrosis and delayed wound healing.

In women <40 yr, IL10 expression was reduced (M = –0.87 and –1.06, respectively), indicating limited anti-inflammatory compensation. Women >40 yr, by contrast, exhibited increased normalized IL10 expression (Me = 1.14; M = 0.22; $p_1 = 0.05$) (Table 1), likely representing an adaptive response to intensified inflammation. This may reflect a compensatory immunosuppressive response to excessive or chronic inflammation, which simultaneously limits effective antibacterial defense and promotes infectious complications [21; 24; 25].

MMP9 expression increased with age and reached its maximum in women >40 yr (Me = 0.83; M = 0.82; $p_1 = 0.002$), exceeding levels in younger women by 1.37- and 2.55-fold (M = –0.54 and –1.73, respectively). This finding indicates intensified collagen and extracellular matrix degradation, wound matrix instability, and an increased risk of seroma formation and tissue dehiscence.

Both COL1A1 and COL3A1 genes demonstrated increased expression in women ≥40 yr, particularly COL1A1, which increased approximately twofold (2.19 and 1.93, respectively), with a wide interquartile range (Table 1, Fig. 2). COL1A1 expression was lowest in women 30-40 yr (M = –0.40) and increased significantly in women >40 yr (Me = 0.55; M = 1.53; $p_1 = 0.017$), indicating age-related enhancement of fibrogenesis. In women <30 yr, relatively high COL3A1 expression was observed (M = 0.42), which decreased in the 30-40-yr group (M = –0.04) and increased again after 40 years (M = 0.71), consistent with changes in connective tissue remodeling phases. This pattern reflects activation of fibrogenesis and imbalance of the COL1A1/COL3A1 ratio (COL1A1 ≫ COL3A1), constituting the molecular basis of fibrosis and hypertrophic scarring.

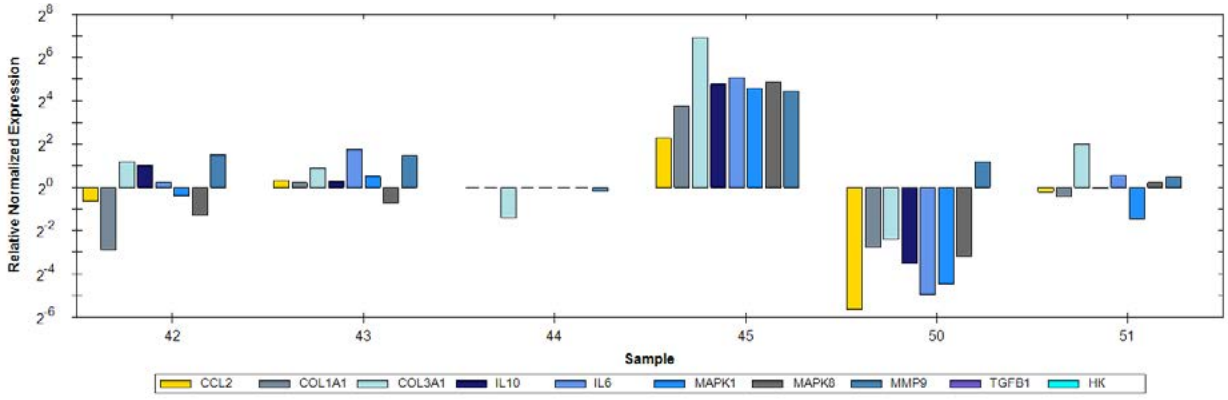

Figure 2. Relative normalized mRNA expression (ΔΔCt) of the studied genes in peripheral blood samples, with GAPDH as the reference gene.

In women <30 yr, TGFB1 gene expression was moderate and relatively stable (Me = 1.50; Q1-Q3: 1.25-1.75; M = 1.50), corresponding to physiological fibrogenic regulation and balanced tissue repair. In the 30-40-yr group, a decrease in central tendency was observed (Me = 0.80; Q1-Q3: –1.10 to 2.58; M = 0.72), accompanied by substantial expansion of the interquartile range, indicating heterogeneity of TGFB1 expression potentially related to hormonal fluctuations, metabolic factors, or individual differences in wound-healing regulation. In women ≥40 yr, TGFB1 expression increased 2.55-fold and nearly fivefold compared with younger groups ($p = 0.041$), with a narrow interquartile range (Table 1). In the majority of participants, transcriptional activity of TGFβ1 was not detected, possibly attributable to its transient expression, post-transcriptional regulation, or predominantly local (tissue-specific) activation not reflected in peripheral blood.

To provide an integrated assessment of molecular risk for postoperative complications, a Molecular Complication Risk Index (MCRI) was developed. The index is based on a weighted sum of normalized expression levels of genes involved in inflammation, stress signaling, and extracellular matrix remodeling (wound healing). Given that gene expression values are presented in folds (ΔΔCt), rank-based normalization was applied for each gene: low expression (Me ≤ Q1) = 0 points; moderate expression (Q1 < Me ≤ Q3) = 1 point; high expression (Me > Q3) = 2 points. The expected age-related stratification of postoperative complication risk is presented in Table 2.

Table 2

Expected age-related stratification of the risk of postoperative complications

Age	Molecular profile	Expected result of MCRI, points
<30 yr	Moderate inflammation, active ECM	5-8
30-40 yr	Balanced response	3-6
>40 yr	High activity of inflammation +MMP9 + MAPK8 + COL1A1 + TGFβ1	9-14

Note. ECM – extracellular matrix

According to MCRI values: 0-5 points indicate low risk of postoperative complications (physiological healing); 6-10 points indicate moderate risk (seroma formation, prolonged inflammation); MCRI ≥11 points indicate high risk (infection, necrosis, fibrosis, capsular contracture, etc). The highest MCRI values, corresponding to an unfavorable molecular profile, are associated with women >40 yr.

Following reconstructive breast surgery, tissues within the wound area frequently experience hypoxia. This condition activates hypoxia-inducible factor-1α (HIF-1α), a key transcription factor that regulates cellular adaptation to hypoxia and initiates the expression of genes involved in angiogenesis, metabolism, and cell survival [20; 26]. Under reduced oxygen tension, HIF-1α becomes stabilized and promotes the synthesis of vascular endothelial growth factor (VEGF), which is critical for neovascularization and tissue repair.

Dysregulation of this pathway – whether driven by chronic inflammation, oxidative stress, or comorbid conditions – may result in impaired tissue regeneration and fibrosis, thereby compromising wound healing and promoting pathological scarring. Under these conditions, the synthesis of transforming growth factor-β (TGF-β) is activated. TGF-β plays a dual role [27]: under physiological conditions, it stimulates cellular proliferation and tissue repair, enhances collagen synthesis (COL1A1, COL3A1), and suppresses extracellular matrix degradation through inhibition of matrix metalloproteinases (MMPs); during prolonged inflammation, however, excessive activation of TGF-β promotes pathological extracellular matrix accumulation, fibroblast activation, and the development of fibrosis [28; 29].

This mechanism is of particular relevance to wound healing following major surgical procedures and may be associated with increased tissue stiffness, contracture formation, and aesthetic complications after breast reconstruction [30].

Conclusion

Women ≥40 yr undergoing plastic and reconstructive breast surgery exhibit a molecular profile associated with a high risk of postoperative complications, characterised by enhanced pro-inflammatory signaling (IL6), activation of stress-related pathways (MAPK8), intensified extracellular matrix remodeling and collagen degradation (MMP9), increased fibrogenesis (COL1A1, TGFβ1), and a compensatory immunosuppressive response (IL10). The pronounced imbalance in the COL1A1/COL3A1 ratio constitutes a molecular basis for fibrosis and hypertrophic scar formation. Women 30-40 yr, by contrast, demonstrate a more balanced gene expression profile, consistent with a more favorable reparative tissue response and wound healing.

Prospects for further research. Include prospective validation of the proposed molecular risk index, investigation of tissue-specific gene expression dynamics, and assessment of personalised perioperative strategies aimed at reducing postoperative complications in high-risk age groups.

Contribution of co-authors to the preparation of the manuscript. L. Sydorchuk – *c*onceptualisation, writing (original draft), software, validation, supervision and project administration; R. Gumennyi – methodology, writing (review and editing), visualisation, and funding acquisition. All authors reviewed the final version of the manuscript and consented to its publication.

Conflict of interest. The authors declare no conflict of interest.

Use of Artificial Intelligence. No generative artificial intelligence tools were used in the preparation of this manuscript.

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НЕОНАТОЛОГІЯ, ХІРУРГІЯ ТА ПЕРИНАТАЛЬНА МЕДИЦИНА
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МОЛЕКУЛЯРНІ ТА ГЕНЕТИЧНІ ШЛЯХИ ЗАГОЄННЯ РАН ЗАЛЕЖНО ВІД ВІКУ У РЕКОНСТРУКТИВНІЙ ТА ПЛАСТИЧНІЙ ХІРУРГІЇ: КОГОРТНЕ ДОСЛІДЖЕННЯ

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Резюме.

Незважаючи на досягнення в хірургічних техніках та періопераційному догляді, післяопераційні ускладнення, включаючи порушення загоєння ран, патологічне рубцювання, інфекція та відторгнення клаптя або трансплантата, залишаються значною клінічною проблемою, негативно впливаючи на результати та задоволеність пацієнтів, одночасно збільшуючи витрати на охорону здоров'я.

Мета. Дослідити експресію генів IL6, CCL2, MAPK1, MAPK8, IL10, MMP9, COL1A1 та COL3A1 залежно від віку у когорті жінок, які перенесли реконструктивну та пластичну хірургію, а також оцінка молекулярних та генетичних шляхів, що беруть участь у загоєнні ран.

Матеріал та методи. У проспективному поздовжньому когортному дослідженні взяли участь 95 жінок, яким було проведено реконструктивну/пластичну хірургію. Середній вік 35,48±6,61 років (від 19 до 57 років). Всі жінки підписали інформовану згоду на участь у дослідженні, після чого їм було виконано комплекс демографічних, клінічних, інструментальних та лабораторних обстежень. Дослідження проводилося відповідно до принципів Ради Європи з прав людини та біомедицини. Етичне схвалення на проведення дослідження отримано від Комісії з біомедичної етики Буковинського державного медичного університету. Жінки були розподілені за віком: <30 років (24,21%), 30-39 років (44,21%), ≥40 років (31,58%); за наявністю ускладнень (наявні – 12,63%, без ускладнень – 87,67%). Транскрипційну активність генів IL6, CCL2, MAPK1, MAPK8, IL10, MMP9, COL1A1 та COL3A1 у периферичній крові досліджували за допомогою ПЛР-чипу, специфічного для певних шляхів. Очищена РНК пройшла зворотну транскрипцію (ЗТ) з кДНК. Статистичний аналіз проведено за допомогою програмного забезпечення Statistica 7.0 (StatSoft Inc, США) та Excel® 2016™. Дослідження було проведено в рамках поточної комплексної науково-дослідної програми кафедри сімейної медицини Буковинського державного медичного університету «Удосконалення діагностики та прогнозування гіпертонічного ураження певних органів-мішеней і контроль симптомів при супутніх захворюваннях з урахуванням клініко-метаболічних та молекулярно-генетичних предикторів» (державна реєстрація № 0124U002524; термін виконання: з 1 січня 2024 року по 31 грудня 2028 року).

Результати дослідження. Жінки віком ≥40 років, які перенесли пластичні та реконструктивні операції на молочній залозі, характеризуються високим молекулярним профілем ризику післяопераційних ускладнень, який включає підвищену прозапальну активність, що відображається збільшеною експресією гена IL6 (M = 0,75; p = 0,05), посиленням проліферативних та регенеративних процесів за експресію гена MAPK1 (M = 0,63) та активацію сигнальних шляхів, пов'язаних зі стресом, про що свідчить експресія MAPK8 (M = 1,64; p = 0,017). Цей профіль також характеризується інтенсивним ремоделюванням позаклітинного матриксу та посиленою деградацією колагену та матриксу, що відображається підвищеною експресією MMP9 (M = 0,82; p = 0,002), а також посиленим фіброгенезом з дворазовим збільшенням експресії COL1A1 (M = 1,53; p_1 = 0,017), більш помірним збільшенням COL3A1 (в 1,69 та 0,75 рази) та вираженою підвищеною регуляцією TGFβ1 у 2,55 разу (p = 0,041). Крім того, спостерігається імуносупресивний зсув, що відображається компенсаторним збільшенням експресії IL10 (M = 0,22; p_1 = 0,05).

Встановили помітний дисбаланс у співвідношенні COL1A1/COL3A1 (COL1A1 ≫ COL3A1), що відображає молекулярну основу фіброзу та утворення гіпертрофічних рубців. Натомість, жінки віком 30-40 років демонстрували найбільш збалансований профіль експресії генів, що може відповідати оптимальному потенціалу репарації тканин.

Висновки. Жінки віком понад 40 років, які перенесли пластичні, чи/ та реконструктивні хірургічні втручання на молочній залозі, демонструють молекулярний профіль, асоційований із високим ризиком післяопераційних ускладнень. Жінки віком 30-40 років демонструють більш збалансований профіль експресії генів, що відповідає сприятливішій репаративній відповіді тканин та загоєнню ран.

Ключові слова: загоєння ран; експресія генів; пластична та реконструктивна хірургія молочної залози; запалення; жінки; вік; тканинна відповідь; молекулярно-генетичний механізм; регенеративні процеси; фіброгенез.

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