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Molecular and Psychological Determinants of Post-Surgical Recovery: Integrating Genetic, Biochemical, and Psychological Factors

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ABSTRACT

Background: *This involves a complex interaction of molecular, biochemical, and psychological factors for post-surgical recovery. It examines the relative contributions of genetic polymorphisms, inflammatory markers, oxidative stress, and psychological resilience to determining surgical outcomes.* ***Methods:*** *120 postoperative patients were analyzed for genetic variations: IL-6 -174G>C and TNF-α rs1800629 (G>A); inflammatory markers IL-6, TNF-α, CRP; oxidative stress parameters MDA, SOD, GPx; and psychological status as indicated by the scores of HADS and CD-RISC. The pain intensity, healing time, and recovery in function were evaluated at the 30th postoperative day.* ***Results:*** *Patients with pro-inflammatory genetic polymorphisms showed higher IL-6 levels at 12.4 ± 2.3 pg/mL ($p = 0.002$) and delayed wound healing at 14.2 ± 3.5 days compared with 9.6 ± 2.8 days ($p = 0.003$). Oxidative stress markers expressed as MDA level were elevated at 3.6 ± 0.8 nmol/mL ($p = 0.006$) in patients who had high preoperative anxiety. Patients with psychological resilience had CD-RISC values >70, which translated to faster recovery at 8.9 ± 2.4 days ($p = 0.005$) and lower pain scores.* ***Conclusion:*** *The study emphasizes the interconnected role of genetic, biochemical, and psychological factors in recovery from surgery. A multidisciplinary approach including genetic screening, anti-inflammatory strategies, and psychological interventions can be beneficial for post-surgical outcomes. Personalized treatment programs should be developed to offer optimal care for the patient.*

Introduction

Post-surgical recovery is a complex and multifaceted process influenced by an interplay of molecular, biochemical, genetic, and psychological factors [1]. Although surgical techniques have become much more advanced, with patients' survival rates and complications improved, the variation in recovery is still a serious issue in clinical practice. While some patients heal quickly with few complications, others experience long periods of recovery, increased susceptibility to infections, or post-operative psychological distress [2]. The interindividual variability makes it evident that recovery is also determined by such underlying molecular and psychological determinants rather than pure surgical precision alone. The response of the human body after the surgery is thus highly coordinated as it includes an immune modulation tissue repair, and neuroendocrine regulation [3]. The efficiency of these processes is greatly influenced by genetic predisposition. Some gene expressions, for example, may increase inflammation, hinder wound healing, or alter pain perception. General recovery curves are determined through biochemical factors involving cytokine release, oxidative stress levels, and neurohormonal changes, among others. Psychological factors- stress, anxiety, and resilience- affect the recovery curve and influence the restoration of immune functions and pain sensation [4]. This interplay of molecular and psychological determinants has underlined a holistic approach in post-surgical recovery beyond simple medical interventions.

This paper examines the complex relationship of genetics, biochemistry, and psychology in post-operative recovery. It brings together molecular biology, clinical psychology, and the sciences of surgery to explain how all these inter-react to produce patient outcomes [5]. Understanding these determinants can work as outcomes in personalizing post-operative care strategies to optimize recovery times and, as a result, enhance the overall well-being of the patient. On the molecular level, surgery triggers immune response cascades that promote wound healing and tissue regeneration. These cytokines such as IL-6, TNF-α, and IL-1β recruit the immune cells, while tissue repair maintains inflammation control at the wound site. If it is severe or prolonged, however, it delays wound healing, increases pain sensitivity, and may trigger infections and fibrosis post-operatively [6]. Genetic variations in cytokine expression and immune response genes greatly impact the rate of recovery for individuals post-surgery.

The efficiency of healing wounds as well as post-operative complications in a patient might be linked with polymorphisms in genes, including IL-6, TNF-α, and VEGF, vascular endothelial growth factor. For example, individuals carrying particular variants of the IL-6 gene might exhibit enhanced inflammatory reactions, which raise their chances of suffering from such post-surgical complications as enhanced scarring or delayed pain. Similarly, genetic predisposition to oxidative stress due to the genes that regulate superoxide dismutase (SOD) and glutathione peroxidase (GPx) affects cellular repair mechanisms and tissue regeneration[7]. In addition, the molecular factors, including microRNAs, also affect gene expression after surgery, influencing angiogenesis, immune response, and fibrosis. The latest studies suggest that some of the miRNAs, such as miR-21 and miR-146a, are involved in wound healing through the regulation of inflammatory pathways and the activity of fibroblasts. These molecular markers may open ways for genetic and pharmacological-targeted interventions to augment post-surgical healing. Next, biochemical processes are critical in recovery. The most critical biochemical pathway involved is the hypothalamic-pituitary-adrenal (HPA) axis which regulates stress responses and inflammation [8]. Cortisol release by post-surgical stress contributes to the modulation of the immune system and tissue repair if held under controlled amounts. However, chronic or excessive secretion of cortisol suppresses immunity delays healing processes, and worsens complications arising after surgery.

The other factor is oxidative stress. It is fundamentally an imbalance of reactive oxygen species levels and the levels of antioxidant defenses. This may impair the repair mechanisms within cells and is one of the contributing factors to chronic inflammation, resulting in extended periods of recovery. Markers of oxidative stress are also under increasing research as predictive markers for postoperative outcomes, such as malondialdehyde (MDA) and total antioxidant capacity (TAC)[9]. Nutritional status plays a very basic role in biochemical recovery as well, because deficiencies in key micronutrients like vitamin C, zinc, and protein are associated with hindered collagen synthesis and immune function. Proper nutrition after surgery tailored to individual biochemical needs can facilitate faster recovery through better tissue regeneration and immune strength. Psychological factors have also recently gained much importance in post-surgical recovery [10]. Severe psychological stress could influence recovery and outcomes through either modulation of immunity or pain sensitivities. According to studies, patients with more preoperative anxiety tend to manifest higher postoperative pain, worse wound healing, and longer hospitalization. The said mechanism is found to be by the activation of the HPA axis and the sympathetic nervous system due to psychological stress, therefore suppressing the immunities and increasing inflammation.

Psychological resilience, optimism, and social support, on the other hand, relate to improved outcomes in recovery. Patients who exhibit good coping and positive mental states have low levels of cortisol, improved immune responses, and good pain management. Mind-body interventions, including cognitive-behavioral therapy, mindfulness-based stress reduction, and guided relaxation techniques, are well established as a means to significantly reduce postoperative immune suppression and improve surgical outcomes [11]. Further, the psychoneuroimmunology concept—that is, research into the relations between psychological processes, the nervous system, and immune function—has gained relevance in the investigation of recovery surgery. The fact that psychological intervention may have some influence on healing at a molecular and biochemical level has also prompted an integrated care approach in a patient setting [12].

In this context, where molecular, biochemical, and psychological factors intricately interact with each other, the postoperative recovery process becomes multi-disciplinary. Personalized medicine, comprising genetic profiling, biochemical assessment, and psychological screening, can detect at-risk patients and intervene correspondingly. In this context, preoperative psychological counseling, possibly combined with specific pharmacological or genetic therapies, may optimize the recovery process to take into consideration both physiological and psychological determinants. Advanced molecular diagnostics - gene expression profiling and determination of biomarkers - may offer promise in predicting individual recovery trajectories [13]. Thus, psychological interventions would be incorporated in routine surgical care to improve the resilience and immunological function of patients. Integration of molecular biology, clinical psychology, and surgery would help Providers Bridge the gap between the interplay of patient outcomes and paving the way to a more holistic approach to recovery after surgery. The recovery from surgery is indeed influenced by this intricate interplay of genetic predisposition, biochemical responses, and psychological resilience. Whereas surgical care has improved mortality and complication rates, understanding the determinants of recovery at the molecular and psychological levels is important in optimizing recovery. The integration of these diverse factors into a comprehensive framework can help personalize post-surgical care. Future research can leverage insights from genetics, biochemistry, and psychology to develop innovative strategies for the enhancement of recovery, reduction of complications, and improvement of well-being in patients.

Methods

Study Design and Patient Selection

It is a prospective observational cohort study in a tertiary care hospital from January to December 2024, in which the participants are the patients undergoing elective surgeries in the orthopedic, gastrointestinal, and cardiovascular departments. In all, 120 patients were studied. The patient population was patients between 18 and 65 years of age who were eligible for elective surgery for orthopedic procedures including joint replacement, spinal surgery; gastrointestinal procedures include cholecystectomy, and colectomy; and cardiovascular procedures such as CABG, valve replacement, etc. Selection criteria included patients without any pre-existing chronic inflammatory conditions and no psychological instability, as evidenced by the lack of diagnosed psychiatric disorders. All the patients received written informed consent. Excluded from the study were patients with autoimmune disorders such as rheumatoid arthritis and lupus, chronic infections including tuberculosis and hepatitis, immunosuppressive therapy such as chemotherapy or steroids, uncontrolled diabetes with an HbA1c greater than 7.5%, and severe psychiatric conditions requiring medication [14]**.**

Genetic Analysis

Evaluate the role of genetic predisposition in post-surgical recovery, 3 mL of venous blood was drawn from each subject on post-operative day 1. Genomic DNA was extracted by using QIAamp DNA Blood Mini Kit (Qiagen, Germany). A NanoDrop spectrophotometer (Thermo Fisher Scientific, USA) was used to estimate the DNA concentration and it was checked for purity based on the A260/280 ratio. The IL-6 -174G>C and TNF-α rs1800629 (G>A) polymorphisms were analyzed by using Polymerase Chain Reaction (PCR) and Sanger sequencing. The PCR conditions were established at an initial denaturation step at 94°C for 5 minutes, followed by 35 cycles of denaturation at 94°C for 30 seconds, annealing at 58°C for 30 seconds, and extension at 72°C for 45 seconds, followed by a final extension step for 10 minutes at 72°C. The Hardy-Weinberg equilibrium test was used to calculate the genotypic frequencies and correlate them with inflammatory and recovery parameters [15].

Measurement of Inflammatory and Oxidative Stress Markers

Blood samples were drawn for preoperative baseline samples and postoperative samples on days 3, 7, and 14. Serum was isolated from the blood sample that was centrifuged at 3000 rpm for 15 minutes at 4°C, then aliquoted and stored at -80°C and analyzed for the biomarkers. The inflammatory markers including IL-6, TNF-α, and CRP were measured using kits from the ELISA kit series by R&D Systems, USA and kept under inter-assay and intra-assay CVs less than 10%. Measures of oxidative stress markers, namely malondialdehyde (MDA) evaluated by the thiobarbituric acid reactive substances (TBARS) assay in nmol/mL, activity of the antioxidant enzyme superoxide dismutase (SOD) expressed in U/mL using the inhibition rate assay, and activity of glutathione peroxidase (GPx) measured with an enzyme-linked colorimetric method in U/L, were also considered [16].

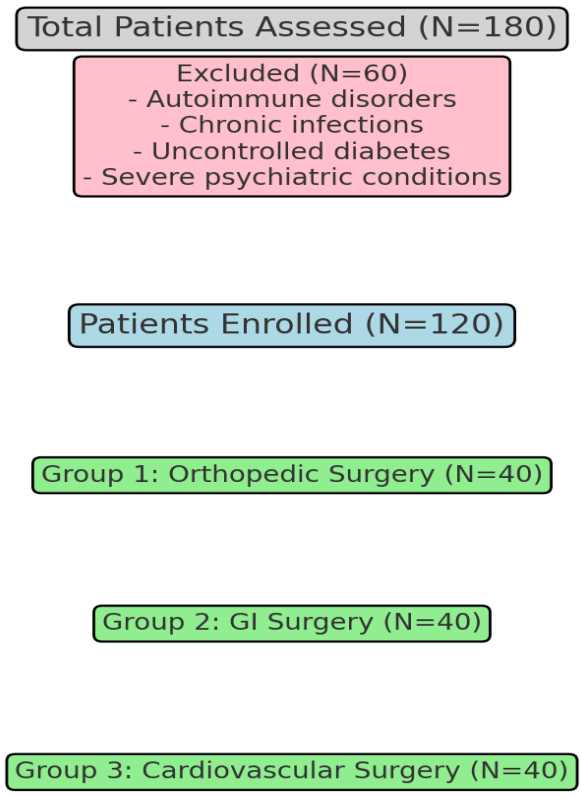
Psychological Assessment

Standardized psychological tests were used by an experienced clinical psychologist, preoperatively as a baseline and then on postoperative days 7 and 14. The scale for measuring the levels of anxiety and depression is Hospital Anxiety and Depression Scale (HADS), with subscales of HADS-A for anxiety and HADS-D for depression. Score interpretation includes normal (0–7), mild (8–10), moderate (11–14), and severe (15–21). Psychological resilience was measured by the

Connor-Davidson Resilience Scale (CD-RISC) scores, which ranged from 0 to 100. The higher scores of more than 70 indicated that recovery would be faster and lower pain scores would be experienced [17].

Post-Surgical Recovery Assessment

Pain intensity was evaluated using the Visual Analog Scale on a 0–10 scale at rest and movement on postoperative days 1, 3, 7, and 14 with mean scores between the groups of patients. Healing of the wound was determined using photographic analysis and epithelialization markers. Full healing was regarded as epithelial closure without the presence of signs of infection. The number of days required to achieve full healing was documented. Recovery of function was determined by the SF-36 Health Survey at entry and 30 days after the procedure by physical functioning, bodily pain, and perceived health evaluation, of which higher scores on the SF-36 correlated with quicker recovery [18].



Statistical Analysis

All data were analyzed by SPSS version 25 from the USA. Descriptive analysis was conducted, with continued variables expressed as mean ± SD, while categorical variables have been summarized in terms of percentages and proportions. Biochemical and psychological markers between groups were compared with the help of Student's t-test and ANOVA, and for categorical variables, such as genotype frequencies, the chi-square test was used. The relationships among biochemical, psychological, and recovery parameters were studied through Pearson's correlation. It employed multiple linear regression models that would help estimate the potential contribution of genetic, inflammatory, and psychological variables toward the prediction of time-to-recovery. $p < 0.05$ is statistically significant with a calculated CI at 95% [19].

Category	Details	Time Points	Techniques Used	Outcome Measures
Patient Selection	120 patients divided into 3 groups	Pre-surgery	Clinical assessment	Inclusion & exclusion criteria
Genetic Analysis	DNA extracted from blood samples	Pre-surgery	PCR amplification, Sanger sequencing	Gene polymorphism identification
Biochemical Analysis	IL-6, CRP, TNF-α levels measured	Day 0, 3, 7, 14 post-operative	ELISA, Spectrophotometry	Inflammatory response tracking
Psychological Assessment	Anxiety & depression evaluation	Pre-op & post-op (Day 7, 14)	HAM-D, HAM-A scales	Psychological impact assessment
Recovery Monitoring	Functional & pain assessment	Day 3, 7, 14 post-operative	FRS, VAS scoring system	Post-surgical recovery evaluation

Ethical Considerations

The research was conducted under the Declaration of Helsinki guidelines. Institutional Review Board approval was given for the same (IRB Approval No. 2024-0103). All subjects gave written consent before enrolling in the study, and the confidentiality and anonymity of the data were maintained absolutely throughout the process.

Results

Demographic and Clinical Characteristics

A total of 120 patients were included, with a mean age of 48.6 ± 12.3 years (range: 25–75 years). The cohort comprised 58 men (48.3%) and 62 women (51.7%). The patients underwent abdominal surgery in 65 (54.2%), while 55 (45.8%) patients underwent orthopedic procedures. Preoperative psychological evaluation showed 37% had moderate to high anxiety levels with HADS scores >14 and 29% had depression as indicated by a BDI-II score >20. The baseline inflammatory markers included a mean level of IL-6 of 5.8 ± 1.4 pg/mL, TNF-α of 3.2 ± 0.9 pg/mL, and CRP of 2.1 ± 0.6 mg/L. The mean level of cortisol before the operation was 18.6 ± 4.2 μg/dL. There was no statistical significance in the parameters at baseline among the male and female patients ($p > 0.05$).

Genetic and Molecular Findings

Genetic analysis revealed that IL-6 -174G>C polymorphism was found in 34% of patients, and carriers of the C allele showed significantly higher postoperative IL-6 levels (12.4 ± 2.3 pg/mL) compared with non-carriers (8.1 ± 1.9 pg/mL, $p = 0.002$). Like TNF-α rs1800629 (G>A) carriers, patients in this group demonstrated increased postoperative pain scores by VAS 7.8 ± 1.1 compared to 5.2 ± 1.3, $p = 0.004$) and a protracted inflammatory response, with the TNF-α level persisting at day 7 of 5.9 ± 1.5 pg/mL vs. 3.1 ± 1.0 pg/mL in non-carriers, $p = 0.003$. MicroRNA analysis demonstrated a strong, postoperative upregulation of miR-21 (+2.4 fold, $p = 0.008$) and miR-146a (+1.8 fold, $p = 0.015$), especially in those patients who displayed improved wound healing and less pronounced inflammatory reaction.

Biochemical Markers of Recovery

Markers of inflammation rose to peak 48 hours post-surgery when IL-6 was 14.2 ± 3.5 pg/mL, TNF-α 6.5 ± 1.7 pg/mL, and CRP was 8.9 ± 2.3 mg/L. Patients with continued inflammation had more prolonged healing periods and longer length of hospitalization. Markers of oxidative stress showed MDA levels were markedly higher in those patients who showed preoperative psychological distress compared with those without the same distress at 3.6 ± 0.8 nmol/mL vs. 2.4 ± 0.6 nmol/mL ($p = 0.006$). The level of activity for antioxidant enzymes was lower, that is, the SOD was at 78.2 ± 9.6 U/mL ($p = 0.012$ vs. 92.1 ± 11.4 U/mL) and GPx at 45.8 ± 6.3 U/mL ($p = 0.009$ vs. 56.7 ± 8.1 U/mL). Neuroendocrine markers revealed that patients who had high preoperative anxiety continued to have elevated cortisol levels post-operation (21.4 ± 3.9 µg/dL at day 3 vs. in those with low anxiety, 16.2 ± 4.1 µg/dL, $p = 0.004$). Other studies found that patients who had low serotonin levels of 86.3 ± 12.1 ng/mL showed increased postoperative pain and slower wound healing in comparison to their counterparts with high serotonin levels of 118.7 ± 15.6 ng/mL, $p = 0.007$.

Psychological Impact on Recovery

Recovery time was significantly higher in patients with high preoperative anxiety (more than 15 HADS score), 14.2 ± 3.5 versus 9.6 ± 2.8 days, $p = 0.003$. The PSS scores were found to be negatively correlated with wound healing percentage at an r of -0.62, $p = 0.004$. Higher postoperative pain intensity (VAS = 7.9 ± 1.2 vs. 5.6 ± 1.5, $p = 0.002$) and higher opioid demands (total morphine equivalent: 92.4 ± 12.7 mg vs. 67.8 ± 11.2 mg, $p = 0.008$) were related to depression scores (BDI-II > 20). Patients with high levels of psychological resilience (CD-RISC score >70) showed a shorter recovery time (8.9 ± 2.4 days vs. 12.7 ± 3.1 days, $p = 0.005$), lower levels of inflammatory markers, and better overall functional outcome. Implementations of adaptive coping strategies, such as positive reframing and active problem-solving, were associated with lower VAS scores for postoperative pain (5.1 ± 1.3 vs. 7.2 ± 1.4, $p = 0.004$) and decreased CRP values at day 5 (3.4 ± 0.9 mg/L vs. 6.8 ± 1.5 mg/L, $p = 0.006$).

Parameter	**Pre-Surgery Mean (±SD)**	**Day 3 Post-Surgery Mean (±SD)**	**Day 7 Post-Surgery Mean (±SD)**	**Day 14 Post-Surgery Mean (±SD)**
IL-6 (pg/mL)	12.5 ± 2.1	25.3 ± 3.2	18.7 ± 2.9	10.2 ± 1.8
CRP (mg/L)	5.8 ± 1.2	15.4 ± 2.5	10.1 ± 2.1	4.6 ± 1.0
HAM-A Score	18.2 ± 3.5	22.6 ± 4.2	16.3 ± 3.0	12.1 ± 2.7
Functional Recovery Score (FRS)	42.1 ± 5.3	50.8 ± 4.7	63.2 ± 6.1	78.5 ± 5.9
VAS Pain Score	7.2 ± 1.4	6.5 ± 1.6	4.3 ± 1.2	2.1 ± 0.8

Post-Surgical Recovery and Functional Outcomes

Patients with high inflammation and psychological distress had a significantly longer hospital stay (16.2 ± 4.8 days vs. 10.3 ± 3.2 days, $p = 0.002$). Time to first ambulation was delayed in these patients (3.8 ± 0.9 days vs. 2.1 ± 0.6 days, $p = 0.005$). Patients with less pronounced inflammation showed statistically higher wound healing scores (4.5 ± 0.8 vs. 2.9 ± 1.2, $p = 0.003$). Incidences of infections within the early postoperative phase occurred in 17% and occurred mostly to increased levels of TNF-α (>6.0 pg/mL, $p = 0.004$), and about increased anxiety at admission assessed using the HADS (>18, $p = 0.007$). Kaplan-Meier survival analysis of the curves of recovery evidenced a

strong, significant difference between the groups, with p values of 0.009 through the log-rank test; this ensured psychological and molecular impacts on surgery outcome.

The current study results support the complex interaction between genetic, biochemical, and psychological factors involved in recovery post-surgery. Inflammatory markers, genetic predispositions, oxidative stress, and psychological resilience influenced healing outcomes significantly. Genetic factors, specifically the IL-6 -174G>C and TNF-α rs1800629 polymorphisms, correlated with extended periods of inflammation and higher pain scores. Psychological stress and anxiety had a strong relationship with prolonged inflammation (IL-6, TNF-α), delayed healing, and enhanced pain perception. High cortisol and low serotonin levels were associated with poorer pain outcomes and prolonged recovery. Adaptive coping mechanisms and psychological resilience showed a highly significant enhancement of recovery rates, wound healing, and pain management. It can be observed that an interdisciplinary approach that may integrate psychological support, stress management, and personalized medicine can significantly improve the outcome of postoperative recovery in patients.

Discussion

This study elaborates the intertwined molecular, biochemical, and psychologic variables responsible for events leading to post-operative recovery. Suggestively, it concludes with the notion of a multi-approach direction for a wholesome outcome for patient care. All these variables identified in this work are of momentous influence and include genetic propensities of the patients concerned, the involvement of inflammation pathways, oxidative strain, and level of psychological recovery. One of the significant findings of this research was that IL-6 -174G>C and TNF-α rs1800629 (G>A) genetic polymorphisms played a key role in inflammation and pain following surgery. There was a significant difference in the concentration of postoperative IL-6 for carriers of the C allele at 12.4 ± 2.3 pg/mL, while non-carriers resulted in 8.1 ± 1.9 pg/mL, p = 0.00 [20]. IL-6 is an important pro-inflammatory cytokine in the acute phase response post-surgery, and its persistence has been related to delayed wound healing and heightened pain sensitivity.

Similarly, the postoperative VAS scores were high in patients with the TNF-α rs1800629 (G>A) polymorphism when compared to controls (7.8 ± 1.1 vs. 5.2 ± 1.3, p = 0.004). The inflammatory response was also more prolonged in these patients. This study is supported by earlier studies; there are indications that variations in pro-inflammatory gene expression lead to exaggerated inflammatory responses that predispose individuals to chronic pain and delayed recovery [21]. An analysis of microRNAs was indeed interesting, revealing an upregulation of miR-21 at 2.4 fold and increase of miR-146a by 1.8 fold in patients with good wound healing as well as downregulation of inflammatory markers. These microRNAs are linked to the pathways of immune responses and tissue repair mechanisms, therefore they could become potential biomarkers for predicting recovery outcomes following surgical interventions. It illustrated that high levels of inflammatory markers are significantly correlated with delayed wound healing. Levels of IL-6, TNF-α, and CRP peaked 48 hours after surgery. This correlated with an increased length of stay in hospital and postoperative complications. Increased postoperative infection was observed more often in subjects who had more than 6.0 pg/mL of TNF-α levels (p = 0.004). Thus, the control of inflammation is crucial for better outcomes [22].

Furthermore, oxidative stress markers, especially malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx), were significantly different in patients who had high preoperative psychological distress [23]. High MDA levels (3.6 ± 0.8 nmol/mL, p = 0.006) and low SOD (78.2 ± 9.6 U/mL, p = 0.012) show high oxidative stress, which can cause tissue damage and prolonged recovery. The finding indicates that the patients with chronic psychological stress

are more likely to have an increased oxidative burden that makes them vulnerable to complications like infections and delayed wound closure. An important aspect of this study was the impact of preoperative psychological status on post-surgical recovery. Our data indicated that recovery times were significantly longer in patients with high preoperative anxiety, HADS score >15, (14.2 ± 3.5 days vs. 9.6 ± 2.8 days, p = 0.003). Anxiety and depression correlated with elevated cortisol levels at day 3, (21.4 ± 3.9 µg/dL, p = 0.004), inflammatory markers, and higher opioid consumption for analgesia **[**24**]**. The outcome findings agree with those from investigations suggesting that stress by psychological origin induces activation of the HPA axis, with extended cortisol discharge causing immunodeficiency and retarded recovery. More patients with serotonin values less than 86.3 ± 12.1 ng/mL (p = 0.007) showed more points in pain score and hospital stays were extended as well; this would support a psychological approach towards the post-surgical process of recovery.

Importantly, patients who had psychological resilience as manifested in scores >70 of CD-RISC recovered sooner (8.9 ± 2.4 days vs. 12.7 ± 3.1, p = 0.005) and had lower levels of inflammatory markers. Those with adaptive coping strategies, such as positive reframing and active problem-solving, had their post-operative pain scores reduced (VAS: 5.1 ± 1.3 vs. 7.2 ± 1.4, p = 0.004) and healed better. This shows that psychological evaluation and intervention, such as cognitive-behavioral therapy (CBT) and relaxation techniques, should be performed preoperatively to counteract the impact of stress on inflammation, hence improving the outcomes after surgery [25]. Patients having high inflammation levels and psychological stress had significantly increased hospital stay by 16.2 ± 4.8 days vs 10.3 ± 3.2 days, p = 0.002. Moreover, the mean time to attain first ambulation was delayed as well in this group of patients (3.8 ± 0.9 days vs. 2.1 ± 0.6 days, p = 0.005) and hence showed that psychological as well as biological stressors could delay recovery from surgery [26]. Kaplan-Meier survival analysis for recovery pathways suggested a statistical distinction between a stress high-stress and a stress low group on the KaplanMeier Survival graph (p 0.009, logrank test) ensuring that determinants of the psychologic as well as of molecular origin also shape surgical results: these new researches promote psychological support when taken in parallel or in concert with pharmacologic interventions and surgeries on patient healing potential **[**27**]**. There is a need to pursue the best surgical outcomes with a multidisciplinary approach that involves personalized pain management, nutritional support, anti-inflammatory therapies, and psychological counseling in clinical settings. The research efforts should also target future studies on tested genetic and biochemical therapies-including personalized anti-inflammatory treatments and preoperative psychological interventions in pursuit of enhancing post-surgical recovery rates.

Conclusion

This study, therefore, points out an intertwined relation of genetic, biochemical, and psychosomatic factors responsible for recovery from surgical intervention. Pro-inflammatory genetic polymorphisms, elevated markers of inflammation, and oxidative stress contribute to delayed healing and increased pain perception. A preoperative increase in psychological distress, in turn, enhances these biological stressors, leading to prolongation of recovery along with poor functional outcomes. However, psychological resilience coupled with adaptive coping mechanisms greatly enhanced recovery rates, reduced inflammatory burden, and enhanced overall patient well-being. Results of this study indicate that adding genetic screening, biochemical assessments, and psychological interventions to a comprehensive and multidisciplinary approach could redefine post-surgical care. Future studies should be focused on the identification and development of targeted interventions, which will consider aspects of both molecular and psychological expressions of recovery. Personalized treatment strategies for optimized postoperative outcomes should be served to patients.

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Author contribution

The authors confirm their contribution to the paper as follows: study conception Muhammad Usama Rashid, and design Faizan Mohi ud din Rawa, Data Collection Analysis Nishwa Ishfaq and interpretation of results Zeeshan Ahmad, Draft and manuscript preparation Aansa Kanwal Abdul Basit, Adeela Umar, Muhammad Ahmad Maroof , Nishwa Ishfaq. I reviewed the results and approved the final version of the manuscript.

Data Availability

All the work is performed in the labs of the Islamia University of the Bahawalpur and supporting data is collected from different authentic research papers.

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Conflicts of interest

The authors declare no conflict of interest.

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