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GENOMIC BIOMARKERS FOR PREDICTING POSTOPERATIVE OUTCOMES IN GENERAL SURGERY: ADVANCES IN PRECISION SURGICAL CARE

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ABSTRACT:
Postoperative complications remain an important challenge in general surgery, with substantial variation in recovery and clinical outcomes among patients undergoing similar procedures. Conventional risk-prediction methods rely mainly on clinical, physiological, and procedural factors but may not fully capture individual biological susceptibility. Genomic biomarkers offer a promising approach for improving personalized postoperative risk assessment. This comprehensive review evaluates the potential of genomic biomarkers for predicting postoperative outcomes and examines their role in advancing precision surgical care. Relevant literature was reviewed using PubMed, ScienceDirect, and Google Scholar. Evidence was synthesized across genomic biomarkers, postoperative outcome prediction, pharmacogenomics, precision surgical applications, multi-omics, and emerging predictive technologies. Genomic variation, gene-expression signatures, immune and inflammatory profiles, and pharmacogenomic markers demonstrate potential for identifying patients at increased risk of adverse postoperative outcomes and variable treatment responses. Multi-omic approaches provide broader characterization of surgical stress and recovery. Integration of molecular biomarkers with clinical data, artificial intelligence, and predictive analytics may further strengthen individualized risk stratification, perioperative decision-making, and postoperative monitoring. Genomic biomarkers may complement conventional surgical risk assessment and facilitate personalized perioperative management. However, prospective validation, standardized assessment, population diversity, and effective clinical integration remain essential before widespread implementation.

KEYWORDS: Genomic biomarkers; Postoperative outcomes; General surgery; Precision surgical care; Pharmacogenomics

1. INTRODUCTION

Postoperative complications continue to be a serious problem in general surgery, as they result in delays to recovery, longer hospital stays, costs to healthcare, and affect the short- and long-term outcomes of the patients. Despite the advances in surgical techniques, anaesthesia, peri-operative monitoring, and post-operative care, there is still a lot of variation in how individual patients react to surgery. The recovery process of patients who have gone through similar procedures could be very different, which indicates that other factors besides clinical characteristics play a role in determining vulnerability to adverse outcomes. Prognostic biomarkers have therefore come to be a growing focus of attention, as they may provide other biological information to estimate the progression of the disease, treatment response, and clinical outcomes (Sah, 2025). This idea has given rise to ways of identifying patients who are at higher risk of developing complications after surgery before they actually occur in patient populations undergoing surgery.

The traditional surgical risk prediction models usually include the following factors: demographic variables, comorbidities, physiological variables, blood test parameters, severity of disease, and procedural variables. These factors are critical for the assessment of a patient's peri-operative status, but may not fully capture the biological diversity that underlies variability in surgical outcomes. New computational strategies have then been explored to enhance personalized prediction. Machine-learning methods, such as XGBoost, showed promise in that they could combine multiple patient variables to assess prognosis after surgery and could complement the information of traditional statistical models (Yan et al., 2022). Beyond breast cancer, AI is gaining traction in various surgical disciplines, including its ability to aid in risk prediction, clinical decision-making, surgical planning, and postoperative evaluation (Leivaditis et al., 2025).

With the advent of genomics, the concept of personalised perioperative medicine has been further extended. Genomic data has the potential to uncover biological differences that are not easily identifiable with routine clinical assessment,

such as inherited susceptibility, variations in molecular pathways, and differences in gene activity. Sequencing and molecular characterization have come a long way and have made genomic information increasingly relevant to the surgical decision-making process. For instance, genomic characterization has helped better understand the tumor heterogeneity in oral cancers, enabling better stratification of patients and surgical treatment (Saidak et al., 2021). The advances underscore a gradual shift from an anatomical and clinical evaluation to being biologically oriented in the surgical management of these conditions.

Genomic biomarkers can be either inherited genetic variants or polygenic scores, gene-expression patterns, or any other genome-derived pattern that is linked to susceptibility or clinical outcome. They have the potential to not only be important for the characterization of disease but also for predicting postoperative complications. Perioperative neurocognitive disorders have also been explored with genetic risk assessment, taking advantage of polygenic information and APOE-related traits to investigate how genetic differences between individuals can also contribute to differences in their vulnerability to PND (Thedim et al., 2025). These techniques can, in the future, supplement traditional pre-operative evaluation and assessment of a patient with an extra biological risk component.

Another type of promising biomarker is the gene-expression signature, which can capture the dynamic biological reaction to surgical stress. Applications of special interest include postoperative infections and sepsis where molecular changes can occur before evident clinical signs. Gene-expression profiling has shown promise in the identification of postoperative infection and sepsis prior to the onset of clinical symptoms, thereby making molecular signatures an attractive option to help identify patients at an earlier stage who are exhibiting adverse postoperative responses (Lukaszewski et al., 2022). Intensified surveillance and more timely clinical interventions in susceptible patients could be facilitated by earlier molecular identification.

The trend towards genomic prediction also represents a wider shift away from population-level risk assessment to precision surgical treatment. The efforts of precision approaches are focused on characterizing individual patients in a more complete way, combining molecular information with clinical characteristics, imaging information, physiological measurements, and other patient-specific information. In fact, finding a candidate biomarker does not automatically mean that this biomarker can be used in the clinic. Patients with advanced primary high-grade serous ovarian cancer have been a good example of the promise and ongoing challenge of developing biomarkers that can reliably predict surgical outcomes (Keunecke et al., 2022). Markers that are to be used in clinical practice need to be reproducible, validated independently, and shown to be valuable for providing information that goes beyond known clinical factors.

A correct prediction of the postoperative outcome might affect multiple steps of the surgical process. High-risk patient identification may benefit preoperative counselling, surgical strategy, perioperative optimisation, postoperative surveillance and follow-up planning. In oncology, there are more and more investigations of biomarkers together with predictive models to better stratify prognosis and provide individual treatment. The interest in using biomarkers in conjunction with predictive models has been increasingly observed in clinical practice, with a study of stage III breast cancer showing that the combination of both can enhance the prediction of survival and treatment outcomes (Obeagu & Obeagu, 2024). These principles could potentially also help to better assess postoperative outcomes in a more individualised fashion in general surgical populations.

With the integration of genomics into the realm of artificial intelligence and sophisticated predictive analytics, this shift could potentially be accelerated even more. Computational systems can handle complex relationships between different molecular, clinical, physiological and imaging variables and could aid in the development of individual prediction models (Leivaditis et al., 2025). Likewise, machine-learning algorithms compared to traditional regression models show the growing significance of data-driven approaches to predicting postoperative outcomes (Yan et al., 2022). If suitably validated, a combination of such technologies with genomics will help to create a more dynamic surgical risk assessment model that takes into account biological susceptibility and clinical status.

In this context, the present extensive review sets out to discuss recent developments in genomic biomarkers to predict postoperative outcomes in patients undergoing general surgery, and to explore the novel application of these in precision surgical care. The review emphasizes genomic and molecular markers linked with postoperative complications, the possibility of using these markers to predict the surgical outcome of a specific patient, and the use of pharmacogenomic data in perioperative and postoperative care. It also discusses the incorporation of genomic markers into clinical risk stratification and tailored surgical decision-making, and new technologies including multi-omics, enhanced genomic profiling, artificial intelligence and machine learning-mediated prediction. Lastly, the review highlights existing challenges, clinical challenges in translation, current research gaps and future prospects for the use of genomic biomarkers in the clinical setting with the ultimate goal of improving risk stratification and personalised perioperative management.

2. METHODOLOGY

This study uses a systematic review approach to explore how genomic biomarkers are used to predict postoperative outcomes in general surgery and the increasing importance of these in precision surgical care. The articles were selected from peer-reviewed research publications, comprehensive reviews, and scientific literature published primarily in the last decade, as well as important foundational studies to set the conceptual and clinical context of genomic risk prediction for surgical patients. A literature search was conducted on the major scientific databases such as Google Scholar, PubMed, and ScienceDirect. The terms used were: genomic biomarkers, genetic biomarkers, postoperative outcomes, postoperative complications, general surgery, surgical risk prediction, precision surgery, precision surgical care, pharmacogenomics, single-nucleotide polymorphisms, and genomic risk stratification. Various combinations and single terms were used to identify studies on the relationship between genomic variation and postoperative outcomes.

The literature search was focused on the following areas: genomic determinants of surgical outcomes, genetic susceptibility to postoperative complications, pharmacogenomic influences on perioperative management, and possible application of genomic information for personalized surgical risk assessment. Studies that focused on clinically relevant postoperative outcomes, such as surgical-site infection, impaired wound healing, anastomotic leakage, thromboembolic complications, postoperative inflammatory response, organ dysfunction, response to analgesics, length of hospital stay, readmission, and mortality, were given special attention. The selected literature was then grouped into 5 main themes: genomic biomarkers in relation to postoperative complications, genomic prediction of specific postoperative outcomes, pharmacogenomic biomarkers in perioperative and postoperative care, genomic biomarkers integrated into precision surgical care, and emerging genomic technologies and approaches. Themes were used to synthesize and interpret existing evidence and to appraise the potential of genomic biomarkers to contribute to the provision of personalised surgical care.

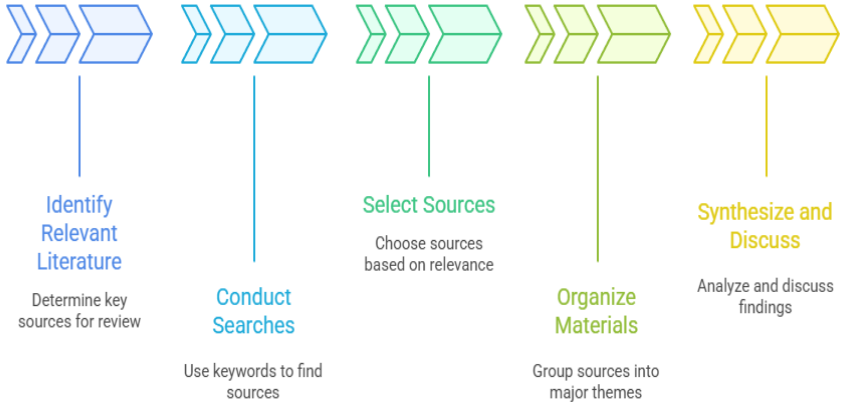

Figure 1. Overview of the Comprehensive Review Process

Figure 1 shows a general outline of the comprehensive review process followed in this study. It is carried out in 5 major stages: identification of literature relevant to genomic biomarkers and postoperative outcomes; systematic search of selected scientific databases with predefined search terms; selection of scientific sources suitable and relevant to the problem; classification of the selected literature into major thematic categories; synthesis and interpretation of the available evidence. The comprehensive review allowed an integrated view of the molecular, genomic, pharmacogenomic and clinical perspectives of the existing literature, and helped establish an integrated understanding of how genomic biomarkers can be used to better predict postoperative risk and advance the field of precision surgical care.

3. RESULTS

3.1 Genomic Biomarkers Associated with Postoperative Complications

There is growing interest in the use of genomic and molecular markers as markers of postoperative complications in individuals. Differences in inflammatory, immune, metabolic, and stress-response pathways may be responsible for some of the differences in surgical recovery and complication rates. Multimodal gene expression profiling has also shown that, in certain patients, immune responses to surgical trauma can help inform prognosis after surgery (Verdonk et al., 2021; Wenner et al., 2025). In surgical oncology and individualised perioperative care, molecular and genetic markers are also increasingly gaining significance (Minz et al. 2026; Zeng et al. 2024). Table 1 lists the main biomarker groups found in the literature reviewed.

Table 1. Major Genomic and Molecular Biomarkers Associated with Postoperative Complications

Biomarker Category	Biological Role	Postoperative Relevance	Reference
Genomic variation	Individual biological susceptibility	Variation in surgical outcomes	Minz et al., 2026
Inflammatory biomarkers	Regulation of surgical inflammation	Inflammatory complications	Wenner et al., 2025
Immune signatures	Perioperative immune regulation	Complications and recovery	Verdonk et al., 2021
Pharmacogenomic markers	Drug-response variability	Perioperative treatment response	Zeng et al., 2024
Molecular biomarkers	Patient-specific biological status	Personalized anesthesia and risk assessment	Nenadic et al., 2026

In summary (Table 1), postoperative risk seems to be due to a combination of molecular determinants, including genomic susceptibility, inflammatory, immune and pharmacological response, but not just one (Verdonk et al., 2021; Wenner et al., 2025). These biomarkers, therefore, can be used in addition to more traditional clinical markers in the field of individual surgical risk assessment (Nenadic et al., 2026; Zeng et al., 2024).

3.2 Genomic Biomarkers for Prediction of Postoperative Outcomes

Genomic and multi-omic methods have great potential to develop better prediction of perioperative outcomes by providing a biological difference that might not be reflected by traditional clinical risk factors. Multi-omic profiling of the perioperative immune response could yield data on biological responses to surgical stress in patients and may enable the identification of patients at higher risk for postoperative complications or altered postoperative immune responses (Verdonk et al., 2021). In the same fashion, molecular markers linked to inflammatory and metabolic responses could help to make more personalized risk assessments and recovery after surgery (Wenner et al., 2025).

There is also a study of predicting specific post-operative outcomes using biomarkers. Persistent post-surgical pain is one such important example, and multidimensional biomarker signatures may be used to identify patients who are more prone to the transition from acute to chronic post-surgical pain (Sluka et al., 2023). In general surgery, postoperative morbidity is multifactorial, comprising infectious, wound-related, thromboembolic, cardiopulmonary, and other complications, thus reinforcing the need for integrated approaches to individual risk assessment (Javed et al., 2023). There is also a rising role of molecular and genetic markers in cancer surgery, where molecular characterization could help with prediction of postoperative outcomes and prognosis (Minz et al., 2026). Together, these results indicate that integrated genomic and molecular profiles may offer a more holistic predictive strategy; however, these profiles need to be further clinically validated for their routine use in surgical risk-assessment models.

3.3 Pharmacogenomic Biomarkers in Perioperative and Postoperative Care

Pharmacogenomics is a vital bridge between genomic variation and personalised perioperative drug therapy. Genetic variation can affect how a patient reacts to certain anaesthetic and analgesic drugs, providing opportunities to tailor drug selection and dosage for individual patients (Nenadic et al., 2026; Zeng et al., 2024). Precision anesthesia in recent years is thus more and more incorporating molecular information with patient-specific physiological and clinical features (Lin et al., 2024). In Table 3, key applications are shown.

Table 3. Pharmacogenomic Applications in Surgical Care

Area	Clinical Relevance	Potential Application	Reference
Anesthetic response	Interindividual drug variability	Personalized anesthesia	Zeng et al., 2024
Analgesic response	Variable pain-control response	Individualized analgesia	Nenadic et al., 2026
Molecular diagnostics	Biological treatment differences	Perioperative risk assessment	Nenadic et al., 2026
High-risk anesthesia	Patient-specific risk	Precision anesthetic management	Lin et al., 2024

As demonstrated in Table 3, pharmacogenomic and molecular data can help in tailoring anesthetic and postanesthetic treatment (Nenadic et al., 2026; Zeng et al., 2024). They could fit into the traditional assessment well, especially in high-risk surgical groups (Lin et al., 2024).

3.4 Integration of Genomic Biomarkers into Precision Surgical Care

The use of genomic and molecular biomarkers in precision surgical care offers potential for more personalized risk stratification, surgical planning, and perioperative management. Integrating molecular data with clinical and physiological data could enhance the existing risk stratification before surgery and aid in more individualized predictions of surgical outcomes (Nirvik & Kertai, 2022). Predictive digital technologies can potentially support surgical decision-making by integrating patient-specific data, aiding treatment planning, and facilitating postoperative monitoring (Eitah et al., 2026).

There are many examples of surgical decision-making that is supported by biomarkers, such as precision oncology. For pancreatic cancer, molecular profiling has been studied as a way of further stratifying patients and stratifying patients for those potentially likely to benefit from surgical intervention (Dreyer et al., 2018). Of course, with the development of precision medicine, biological features have been combined with clinical staging and treatment strategies to provide more personalized treatment strategies in gastric cancer surgery (Wang et al., 2021). For head and neck oncology, the integration of diagnostic biomarkers with predictive models has further enhanced personalized surgical and peri-operative treatment planning opportunities (Kowalski et al., 2025). In aggregate, these advances suggest that the combination of conventional clinical data with emerging predictive technologies is likely to be the most clinically valuable when determining surgical care, as opposed to genomic and molecular biomarkers being used as stand-alone markers for surgical care.

3.5 Emerging Genomic Technologies and Future Approaches for Postoperative Risk Prediction

The opportunities of precision surgical risk assessment are growing with multi-omics, artificial intelligence (AI) and advanced predictive systems. Multi-omic technologies can provide a complex understanding of the biological response that occurs during the perioperative period, while AI can combine molecular and clinical data with the aim of creating predictive models (Negahi et al., 2025; Verdonk et al., 2021). These advances are increasingly applicable in the field of cancer surgery, emergency surgery, and personalized perioperative care (Lakshmanan et al., 2026; Malerba et al., 2026). The most significant developments are summarised in Table 5.

Table 5. Emerging Approaches for Postoperative Risk Prediction

Approach	Main Application	Future Potential	Reference
Multi-omics	Biological response profiling	Postoperative prediction	Verdonk et al., 2021
AI	Integrated data analysis	Personalized risk models	Negahi et al., 2025

Predictive digital tools	Surgical decision support	Real-time prediction	Eitah et al., 2026
AI-assisted surgery	Precision cancer surgery	Personalized management	Malerba et al., 2026
Precision technologies	Emergency surgical care	Individualized treatment	Lakshmanan et al., 2026

The integration of molecular profiling with computational and digital technologies in the future is likely to rely on the efforts of the following studies summarized in Table 5 (Eitah et al., 2026; Negahi et al., 2025; Verdonk et al., 2021). Precision approaches utilizing AI could also enhance the ability to convert complex patient information into tailored surgical plans, but this needs clinical validation and responsible implementation.

4. DISCUSSION

Based on these findings, genomic biomarkers show significant promise for enhancing postoperative risk assessment and moving towards precision surgical care. Surgical outcomes are affected by baseline patient factors, genetic vulnerability, disease biology, surgical stress, immune function, metabolic changes, and therapeutic sensitivity. The process of surgery triggers a series of endocrine, inflammatory, immune and metabolic events that differ from one patient to another and may impact the recovery process (Acharya et al., 2025). Therefore, genomic and molecular data can offer a further step in the biological dimension in the conventional risk assessment, especially if multiple types of biomarkers are accounted for simultaneously instead of using a single biomarker.

The advent of omics technologies has dramatically broadened the possibilities for elucidating this biological diversity. A variety of levels of the response to disease and surgical intervention can be captured using genomics, transcriptomics, proteomics and metabolomics. The advent of omics in surgery was a groundbreaking step towards taking surgery from the clinicopathological paradigm towards molecularly guided patient stratification (Beggs & Dilworth, 2015). More current multi-omic studies have the potential for compiling multiple biological layers into integrated predictive profiles. The experiences gained in other clinical domains also show how multi-omics and sophisticated computational approaches can aid in earlier detection of biological changes and better risk stratification (Alobaidi, 2025). These same concepts may be applied and validated to enhance perioperative prediction in surgical patients.

In oncological surgery, the value of the biomarkers is evident. Recurrence, response to treatment, resectability, and prognosis can be affected by tumor biology and thus molecular characterization is important for the individual treatment plan. For locoregional colorectal cancer, predictive and prognostic biomarkers are increasingly being assessed to better predict recurrence and to enhance treatment tailored to the cancer risk level of the patient (Cendra et al., 2025). Likewise, molecular-based precision neoadjuvant approaches for resectable non-small cell lung cancer (NSCLC) are increasingly being employed to inform treatment choice and to optimise multimodal treatment (Godoy et al., 2023). The ongoing shift towards personalised neoadjuvant management strategies to better select pancreatic cancer patients and optimise therapeutic response is evidenced by the recent development of agents targeting the receptors of the immune cells involved in cancer development and treatment (Wu et al., 2025). The progress of these developments shows that the potential for using biomarkers to affect not only the prognosis after surgery, but also pre-surgical decisions.

Another important discovery is that potential for biomarkers to assist in personalized postoperative symptom control. Surgical outcomes are highly variable and relate to biological, clinical and psychosocial factors. Research into biomarkers is in its early stages and a range of novel studies are trying to uncover biological markers for acute and chronic pain, which could lead to more personalized diagnosis and treatment (Mackey et al., 2025). The concept is gaining importance in surgical analgesia. Multimodal and patient-specific pain management strategies have increasingly become the norm in lung cancer surgery, aiming to minimize the unnecessary use of opioids while ensuring adequate pain control (Hwang, 2025). The incorporation of genomic or molecular markers along with clinical pain assessment may then help to provide more personalized postoperative care.

AI is one promising avenue to making sense of complex biomarker data and generate clinically relevant predictions. Genomic and multi-omic data sets can be complex, involving huge numbers of interacting variables, and at times difficult to analyze using traditional analytical approaches. AI-driven methods could aid in pattern recognition, risk stratification, and the incorporation of molecular data into imaging and clinical parameters. However, the challenges faced by surgical AI are still in the realm of data quality, interpretability, external validation, workflow integration, and ethical implementation (Mithany et al., 2023). AI's potential in metabolic and bariatric surgery is also highlighted by the perspectives of international experts, who emphasize the importance of careful validation, standardization, and responsible clinical implementation (Kermansaravi et al., 2025).

Outside the realm of general surgery, too, there are examples of the potential of integrated prediction. AI tools for glaucoma have potential applications across the continuum of disease management, including diagnosis, forecasting disease progression, and predicting surgical outcomes (Lan et al., 2025). Precision neuro-oncology at a higher level of technology is investigating the integration of genomic characterization, real-time multi-omics, artificial intelligence and gene-editing tools for personalized treatment of glioblastoma (Șerban et al., 2025). Such use can't be directly translated to the standards of general surgery at the present time; however, they show the direction surgical care may take with the use of genomics.

There are several hurdles to overcome before genomic markers can become commonplace tools for prediction after surgery. Biomarkers should be analytically reliable, reproducible in multiple cohorts, clinically meaningful in their predictive value and have demonstrated benefits in patient management. The processing of high-dimensional genomic data also poses challenges with respect to cost, infrastructure, computational skills, data privacy, and interpretation. Unfortunately, these limitations are not addressed by AI; a poorly representative dataset or an inadequate algorithm may instead give rise to further uncertainties (Kermansaravi et al., 2025; Mithany et al., 2023).

Large prospective surgical cohorts, an ethnically diverse patient population, a standard molecular sampling protocol, external validation, and incorporation of genomic data with existing clinical predictors should thus be the focus of future research. The most promising way forward would be a multimodal approach, merging the genomic and other omic biomarkers with clinical features, imaging, physiological measurements, and digital health data. This may turn postoperative prediction from a risk classification to a dynamic, biologically informed assessment. Finally, it is difficult to see how genomic biomarkers could supplant the normal surgical assessment of risk; instead, their main role might be to reinforce the traditional clinical information to enable earlier identification of risk, tailor perioperative management to the individual patient, and guide more effective postoperative care.

5. CONCLUSION

Predictive genomic biomarkers are an emerging opportunity in terms of predicting postoperative outcomes and precision surgical care. There is some current evidence to suggest that genomic variation, gene-expression patterns, pharmacogenomic markers and multi-omic signatures have valuable information regarding individual responses to surgical stress. These biomarkers can be used alongside traditional clinical risk factors to better identify patients who are at risk for complications following surgery, for changes in drug reactions, for chronic pain, for slow postoperative recovery, and/or for poor surgical outcomes. They could therefore help to better stratify, treat, monitor, and prevent patients in the perioperative setting. Combined with genomics, transcriptomics, proteomics, metabolomics, artificial intelligence, and sophisticated clinical informatics, there is growing potential to create more detailed and dynamic prediction models. The use of accessions in routine clinical care has been hindered, however, due to limited validation, population variability, analytical complexity, cost, data-integration needs, and interpretation and clinical applicability considerations. The need for future research is large prospective studies, a wide range of surgical cases, the standardization of biomarker assessment, and external validation of predictive models. Finally, genomic biomarkers should be used in conjunction with existing clinical evaluation. Their proper incorporation with clinical and technical data could help to improve the prediction of risks after surgery and play a significant role in the development of surgical care that is personalized, preventive, and precise.

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