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QUANTITATIVE RISK ASSESSMENT IN PERIOPERATIVE SURGERY: A BIOMATHEMATICAL APPROACH TO ENHANCED RECOVERY AND PATIENT-CENTERED OUTCOMES

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ABSTRACT
The dynamic aspects of surgical stress, physiological response and recovery still complicate perioperative risk assessment especially when patient-centered outcomes are considered more important than fixed endpoints. A biomathematical model of perioperative trajectory is presented involving the combination of surgical stress, inflammatory dynamics and physiologic reserve into a time-resolved dynamical system. Enhanced Recovery After Surgery (ERAS) adherence is implemented as a continuous control input, which allows measuring quantitatively the effect of interventions on the risk of complications, recovery time, and quality-of-recovery measures. The hazard-based formulation of the time-varying physiological states is used to map time-varying physiological states to postoperative risk, and cumulative complication probability to vary with the current recovery processes. The simulations have shown that higher levels of ERAS adherence lead to faster inflammatory resolutions, maintenance of physiologic reserve and a significant decrease in individual and population-wide complication risk. Virtual cohort analyses also indicate that ERAS compliance changes risk distributions and reduces patient recovery time with heterogeneous patient groups, and inter-patient variability should be considered. Recovery measures compared to complication measures alone are more sensitive to intervention intensity, and recovery time and quality-of-recovery measures are more sensitive than complication measures. The suggested framework gives a mechanistic basis to quantitative perioperative decision support and sets the course of direction towards individual and adaptive recovery plans that are based on systems-level modeling.

KEYWORDS: Perioperative risk assessment; biomathematical modeling; enhanced recovery after surgery; dynamical systems; patient-centered outcomes; virtual cohorts

1. INTRODUCTION

Perioperative surgical care is a high-risk phase of patient management, which is dynamically complex due to interacting physiological perturbations, clinical decision-making, and recovery trajectories. Even with significant improvements in surgical technique and perioperative procedures, postoperative complications and retarded recovery is still common especially in patients with heterogeneous background health conditions and different reactions to surgical stress. Although the traditional perioperative assessment tools prove to be effective in terms of stratification of the population, they are rather fixed in terms of the nature and are not adequately designed to detect the changing physiological condition of the individual patient during the perioperative time frame (White et al., 2020). Modern perioperative practice is becoming more focused on patient-centered outcomes, such as quality of recovery, functional restoration, and time to physiological stability, and less on isolated binary outcomes, such as morbidity or mortality (Roberts et al., 2021). This change is indicative of a larger understanding that recovery is a multidimensional, dynamic process that is subject to surgical, baseline reserve, inflammatory, and perioperative interventions. Nevertheless, the current risk assessment models mostly do not combine these dimensions into a single quantitative framework that can produce time-dependent forecasts (Ajitsaria et al., 2018).

The ERAS programs have become one of the major paradigms in the contemporary perioperative medicine, with the inclusion of multimodal interventions to alleviate surgical stress, lessen inflammation, and speed up recovery. Organized reviews of ERAS use show that it is widely used in all types of surgery, and is regularly linked with better outcomes, but adherence and efficacy remain highly variable (Zhang et al., 2022). It is important to note that ERAS protocols are not one-sided interventions but rather dynamic processes, which depends on patients, the physiological impact of which is

manifested over time and interacts with personal predisposition. The ERAS systems further measure the postoperative recovery to emphasize the issue of the static outcomes measures. Recovery is non-linear, physiological, functional, and experiential, which varies during the postoperative period and is challenging to measure by conventional means (Bowyer and Royse, 2020). The programs to improve the compliance with the components of ERAS, such as the digital reminder and protocol reinforcement, also focus on the variability of the perioperative routes but also indicate the need to have predictive tools that can aid in the measurement of the effects of interventions (Gopwani et al., 2023).

Simultaneous advancements in digital health and patient-generated data streams have increased the perioperative outcome measurement scope by allowing continuous and high-resolution measurement of recovery-related variables (Jayakumar et al., 2020). Randomized trials of specific perioperative interventions also help to demonstrate that patient-centered recovery is affected by specific physiological modulations, including metabolic optimization, which proves the significance of mechanistic knowledge (Wang et al., 2021). Likewise, the more general approaches to perioperative care, such as multimodal blood management and respiratory care, prove that the bundles of interventions can significantly redefine the postoperative pathways (Althoff et al., 2019; Misseri et al., 2023). In spite of these developments, a serious disjunction is still evident between clinical intuition and quantitative modeling. Majority of perioperative research presents results in a retrospective manner or examines discrete interventions without placing them in a mechanistic and time dependent model that can be used to provide predictive information. Computational systems biology provides a conceptual framework to fill this gap because it models biological processes as interacting dynamical systems that are externally controllable (Yue & Dutta, 2022). In this paradigm, the physiological responses like inflammation, stress, and recovery may be modeled as a coupled process that changes over time.

The growing use of in silico experimentations and virtual patient groups also testifies to the viability of these practices in biomedical studies. Computational trial models can be used to study the effects of interventions, uncertainty, and heterogeneity systematically without the ethical and logistical limits of large-scale clinical trials (Viceconti et al., 2021). These procedures provide an effective approach to study the interactions between patient variability and intervention intensity in perioperative settings to determine the risks and recovery. Statistically speaking, dynamic risk modeling demands the abandonment of the concept of the independent prediction scores in favor of hazard based and multistate equations that explicitly represent the time dependent physiological states and overlapping outcomes. Mechanisms Best-practice guidelines of the prediction model assessment focus on calibration, discrimination, and interpretability, which are all advantageous in being mechanistically grounded (Steyerberg et al., 2010). Competing-risk and multistate models also present formalities of interconnecting changing patient conditions to clinically important occurrences (Putter et al., 2007). Systems-oriented approaches have been championed at a more abstract conceptual level in the analysis of complex clinical syndromes, such as trauma and inflammation, where delayed responses and nonlinear feedback dominate system behavior (An et al., 2008). The progress of biological data integration and data-driven predictive engineering highlights the need to integrate mechanistic structure and data-driven understanding to obtain robust and interpretable models (Gligorijević and Pržulj, 2015). The future perspectives of digital twins in cardiovascular and perioperative medicine also show the translational potential of personalized and dynamic modeling systems (Corral-Acero et al., 2020). It is on this background that the current research formulates a biomathematical framework of quantitative perioperative risk assessment that explicitly incorporates surgical stress, inflammatory dynamics and physiologic reserve into a time resolved dynamical system. The proposed model will close the gap between patient-centered clinical goals and mechanistic quantitative modeling through the integration of the ERAS adherence as a continuous control input and physiological trajectory mapping to hazard-based complication risk and recovery measures. This work aims to illustrate the benefits of dynamic systems perspective in developing more insight into perioperative risk, recovery, and intervention-dependent outcomes through representative patient simulation and virtual cohort analysis.

2. METHODOLOGY

2.1 Overall Modeling Rationale

Perioperative period is extreme physiological transitions, which is instigated by surgical trauma, systemic inflammatory activation and loss and recovery of physiologic reserve. These mechanisms are nonlinear, dynamic, and interdependent and therefore, the risk scores at any given time are not adequate in the illustration of the vulnerability to postoperative complications that vary over time. To overcome this weakness, we have come up with a mechanistic biomathematical model where perioperative risk is a product of interacting coupled physiological subsystems developing with time.

The purpose of the modeling was not to create a detailed organ-scale model of physiology, but rather to create a low-dimensional interpretable systems model capable of relating the properties of surgery, patient heterogeneity and interventions during perioperative care with clinically meaningful outcomes. The use of Enhanced Recovery After Surgery (ERAS) strategies was explicitly integrated as a control input, which allowed to explore the intervention-dependent modulation of risks and the course of recovery in a quantitative manner.

2.2 State Variables and Physiological Interpretation

Three major dynamic state variables were used to represent the perioperative system. Surgical stress, S(t), is the cumulative neuroendocrine, metabolic and hemodynamic disturbance caused by operative trauma. The inflammatory response, which is represented by I(t), is the systemic immune activation, such as the cytokine signaling and the amplification of inflammation. The physiologic reserve was modeled indirectly by a latent reserve potential variable h(t) that enables the dynamics of reserve to vary without imposing biological restrictions.

In order to make sure that physiologic reserve is limited to a biologically significant range, the reserve potential was transformed to a constrained reserve variable H(t) through a logistic transformation,

$$H(t) = \frac{1}{1 + e^{-h(t)}}, \quad (1)$$

where $H(t) \in (0,1)$. In this formulation, values of $H(t)$ near unity correspond to high functional reserve, while values approaching zero indicate severe depletion. This transformation prevents nonphysical negative reserve values and stabilizes numerical simulations.

2.3 Surgical Stress Forcing and ERAS Control Representation

Surgical trauma was modeled as an exogenous forcing function $u(t)$ acting on the stress variable. The function was defined as a rectangular pulse,

$$u(t) = \begin{cases} A, & t_0 \le t \le t_0 + D, \\ 0, & \text{otherwise}, \end{cases} \quad (2)$$

where A represents the relative invasiveness of the surgical procedure and Drepresents operative duration. This abstraction captures the temporally localized nature of surgical insult while allowing procedure severity to be modulated continuously. ERAS adherence was modeled as a continuous control input $E(t) \in [0,1]$, representing the cumulative intensity of multimodal perioperative interventions. Rather than assuming instantaneous implementation, $E(t)$ was defined as a ramp function that increases gradually during the early perioperative period, reflecting real-world delays in mobilization, nutritional optimization, and analgesic effects. Higher values of $E(t)$ correspond to greater adherence and more effective mitigation of stress-induced inflammatory burden.

2.4 Governing Dynamical System

The temporal evolution of surgical stress was governed by the first-order linear equation

$$\frac{dS}{dt} = u(t) - k_S S, \quad (3)$$

where $k_S > 0$represents the rate at which stress resolves following surgical insult. Larger values of k_S correspond to faster physiological stabilization.

The inflammatory response evolved according to

$$\frac{dI}{dt} = \alpha S + \beta I \left(1 - \frac{I}{I_{\max}}\right) - k_I I - \eta E(t) I, \quad (4)$$

where α quantifies the degree to which surgical stress activates inflammation, β governs nonlinear inflammatory self-amplification, and $I_{\max}$ represents saturation of inflammatory capacity. The parameter k_I denotes the intrinsic resolution rate of inflammation in the absence of intervention, while η quantifies the effectiveness of ERAS-mediated inflammatory suppression. The term $\eta E(t) I$ therefore captures the intervention-dependent acceleration of inflammatory resolution.

The reserve potential evolved according to

$$\frac{dh}{dt} = r_h (h_{\text{set}} - h) - \gamma_h S - \delta_h I, \quad (5)$$

where r_h represents the rate at which reserve potential recovers toward a baseline set-point h_{set}. Parameters γ_h and δ_h represent depletion of reserve due to surgical stress and inflammation, respectively. Through Equation (1), this dynamics translates into bounded reserve trajectories that reflect depletion during acute stress and gradual recovery thereafter.

2.5 Quantitative Risk Modeling

Perioperative complication risk was formulated using a time-dependent hazard function,

$$\lambda(t) = \lambda_0 \exp(aI(t) + bS(t) - cH(t)), \quad (6)$$

where λ_0 is a baseline hazard rate. Parameters a and b represent the multiplicative contributions of inflammation and stress to instantaneous risk, while parameter c captures the protective effect of physiologic reserve. This formulation allows transient physiological derangements to translate directly into elevated complication risk, while recovery of reserve reduces vulnerability.

The cumulative probability of experiencing at least one postoperative complication by time T was defined as

$$P(T) = 1 - \exp\left(-\int_0^T \lambda(t)dt\right) \quad (7)$$

This probabilistic mapping provides a direct quantitative link between mechanistic state trajectories and clinically interpretable risk estimates.

2.6 Patient-Centered Outcome Metrics

Postoperative recovery time was defined as the earliest postoperative time point at which both reserve and inflammation met predefined recovery criteria. Specifically,

$$\tau_{\text{rec}} = \inf\{t \ge t_{\text{post}} : H(t) \ge H^* \text{ and } I(t) \le I^*\}, \quad (8)$$

where t_{post}denotes the end of surgery plus a minimum postoperative buffer period, and $H^*$and I^*represent clinically meaningful thresholds for functional reserve and inflammatory resolution. This definition emphasizes functional recovery rather than instantaneous physiological normalization.

A scalar quality-of-recovery (QoR) proxy was additionally computed at the end of the simulation horizon,

$$\text{QoR}(T) = \omega_H H(T) - \omega_I I(T) - \omega_S S(T), \quad (9)$$

where ω_H, ω_I, and ω_S are weighting coefficients reflecting the relative importance of reserve preservation, inflammatory burden, and residual stress.

2.7 Numerical Implementation and Verification

The equations of ordinary differential equations (Equations 3–5) were numerically solved with the help of Python (version 3.10) and standard scientific libraries. A high relative and absolute tolerance adaptive Runge-Kutta solver (solve-ivp, RK45) was used to achieve numerical accuracy. The simulation time was set to 72 hours and the time resolution was adequately fine to resolve perioperative transition. Systematic verification Model verification involved verifying that the model was numerically stable, that all state variables were bounded, and that the model behavior was qualitatively plausible over a large parameter space. The logistic transformation of reserve made sure that there was no simulation that would be outside of biology admissible limits.

2.8 Virtual Cohort Construction

A virtual cohort of 500 synthetic patients was created to assess the behavior of the population. Multiplicative modifiers on the parameters of the baseline models were used to introduce patient heterogeneity (variation in frailty (reserve set-point), inflammatory sensitivity, invasiveness of surgery, and compliance to the ERAS). The sampled modifiers were physiologically plausible to form a diverse yet controlled synthetic population. The virtual patients were simulated separately on the same governing equations and numerical procedures. Cumulative complication probability (Equation 7), postoperative recovery time (Equation 8), and quality-of-recovery proxy (Equation 9) were obtained and saved in a synthetic dataset to be used in statistical analysis and visualization in accordance with each simulation.

2.9 Reproducibility and Transparency

Every equation, definition of parameters, numerical procedures and outputs of the simulations were clearly defined. The virtual cohort dataset and computational workflow were maintained in such a way that reproducibility and future calibration of the model using empirical clinical data may be achieved.

3. RESULTS

3.1 Perioperative Forcing Functions and Model Inputs

The temporal structure of the perioperative inputs used across all simulations is shown in Figure 1. Surgical insult was represented by a finite-duration stress pulse $u(t)$, corresponding to the operative window, while ERAS adherence was modeled as a time-dependent control function $E(t)$ that increased gradually during the early perioperative period. This definition is indicative of the locality of surgical trauma and the gradual adoption of improved recovery measures. The forced functions were fixed at a baseline level and changed only when expressly comparing the effects of interventions, which thus isolates the effect of ERAS adherence and patient-specific parameters on perioperative dynamics.

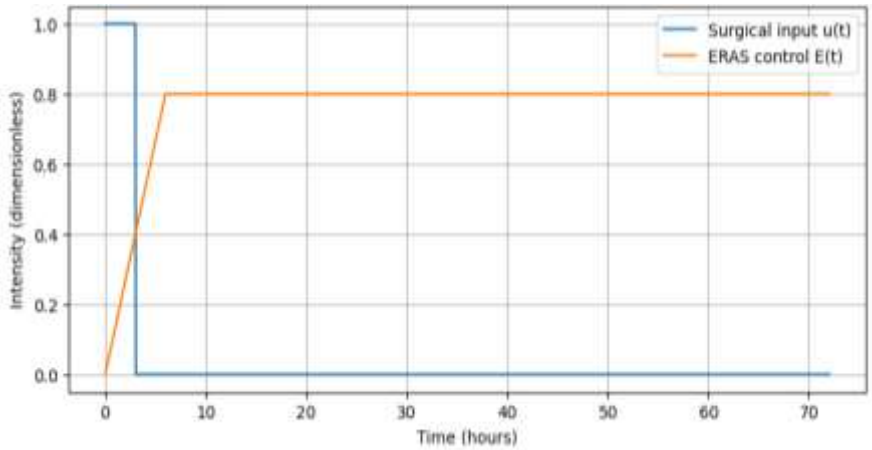

Figure 1. Perioperative forcing functions: surgical stress $\mathbf{u(t)}$and ERAS control $\mathbf{E(t)}$.

3.2 Baseline Perioperative Dynamics in a Representative Patient

The temporal evolution of surgical stress $S(t)$, inflammatory response $I(t)$, and bounded physiologic reserve $H(t)$ for a representative baseline patient is shown in Figure 2. Surgical stress rose rapidly during the operative period and decayed exponentially thereafter. The inflammatory process was delayed and peaked in reaction to the activation of stress before finally calming down during the postoperative phase. Physiologic reserve showed a short-term loss that was associated with peak stress and inflammation and then restored gradually to baseline. The formulation of the logistic reserve ensured that the physiologic reserve did not exceed the biologically permissible range (0,1) at any point in the simulation, and did not deplete nonphysically or recover indefinitely.

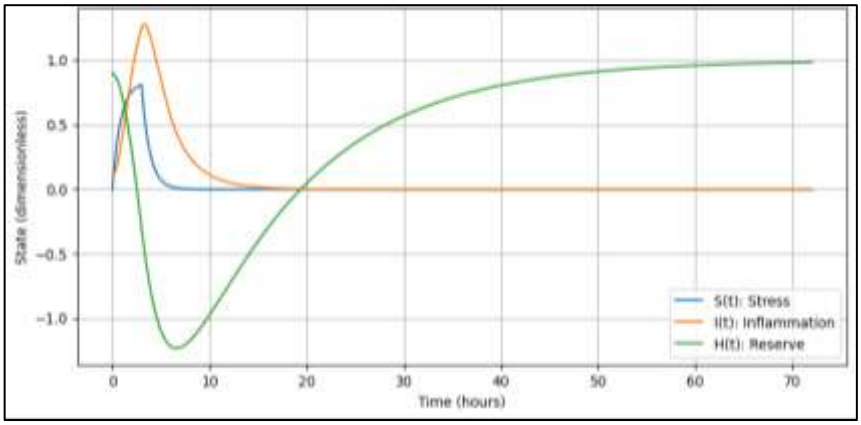

Figure 2. Baseline perioperative trajectories of surgical stress S(t), inflammatory response I(t), and bounded physiologic reserve H(t) for a representative patient.

3.3 Stability and Boundedness of Reserve Dynamics

Reserve dynamics were re-formulated to achieve numerical stability and physiological plausibility in terms of a logistic transformation of an unconstrained reserve potential. The resulting bounded reserve curves are indicated in Figure 3, which indicates steady depletion and recovery without numerical divergence. In all simulations, physiologic reserve was always kept within the range of 0 to 1 at different stresses, inflammation, and ERAS conditions, which confirms the soundness of the bounded formulation.

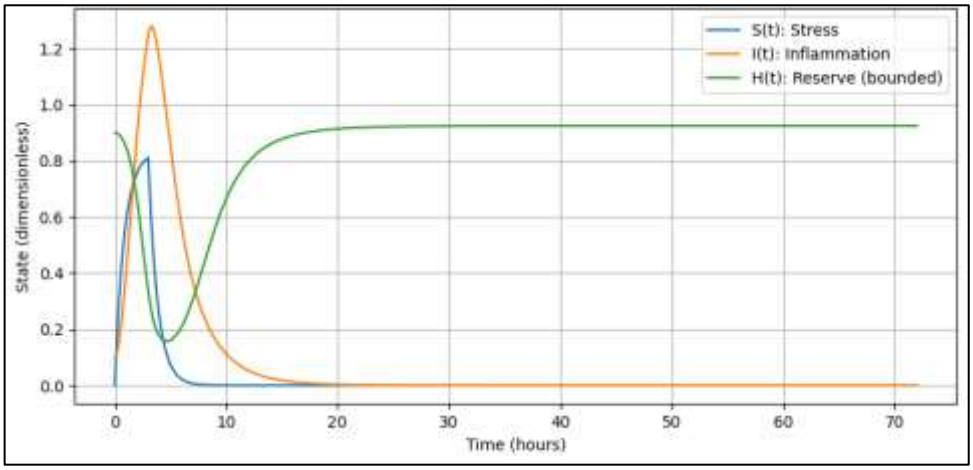

Figure 3. Perioperative trajectories illustrating bounded physiologic reserve dynamics following logistic transformation.

3.4 Time-Dependent Hazard and Accumulation of Complication Risk

Physiological trajectories were mapped to quantitative risk using the hazard-based formulation. The instantaneous complication hazard $\lambda(t)$is shown in Figure 4. The highest levels of hazard were observed in times of high stress and inflammation and reduced hazard as inflammatory load was overcome and physiologic capacity restored.

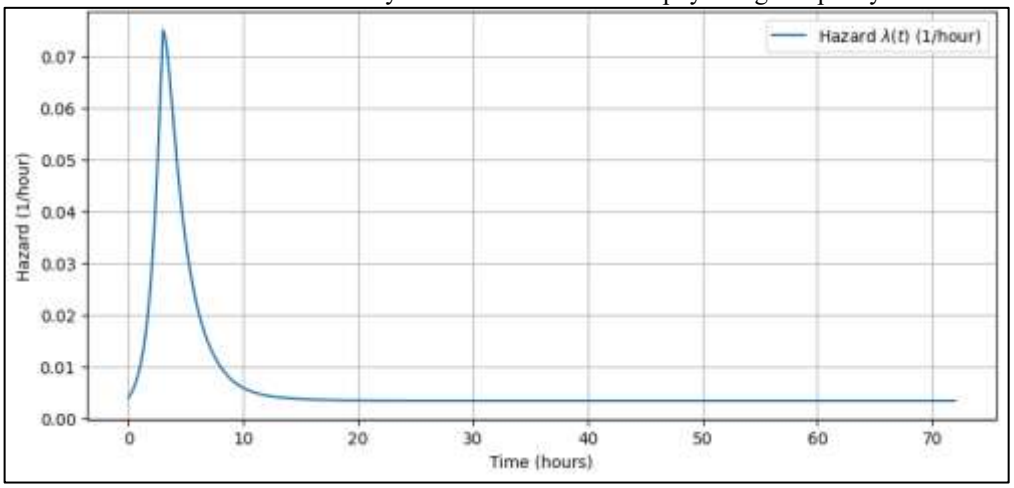

Figure 4. Instantaneous complication hazard λ(t) over the perioperative period.

Figure 5 presents the cumulative probability of the occurrence of postoperative complications. The greatest rate of risk accumulation was in the first days after surgery, which is associated with physiological vulnerability. With the recovery of reserves the slope of the cumulative risk curve became less, which implies less hazard instantaneously with time.

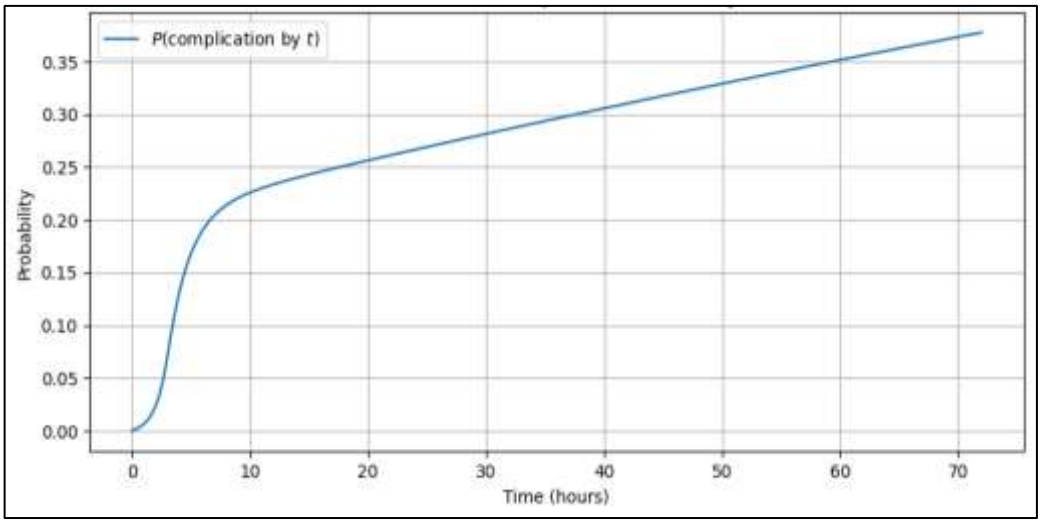

Figure 5. Cumulative probability of postoperative complications over time for the baseline patient.

3.5 ERAS-Dependent Modulation of Individual Risk and Recovery

The quantitative effect of ERAS adherence was considered by comparing low ERAS (E=0.2) and high ERAS (E=0.9) situations in the same patient and surgical operation. Figure 6 reveals the inflammatory and reserve paths in these two conditions. Great adherence to ERAS led to the quicker inflammatory resolution and the restoration of physiologic reserve earlier than the one in low adherence to ERAS. These differences in physiology were directly converted into outcome differences that were clinically significant. At low levels of ERAS adherence, the probabilistic cumulative time to any postoperative complication of the 72 hours was 0.6316 and recovery thresholds were not achieved even within the simulation horizon. High ERAS compliance, on the other hand, decreased the cumulative probability of complication to 0.3651 and produced a postoperative recovery time of 13 hours. There was also a significant improvement in quality-of-recovery proxy at 72 hours with high ERAS adherence.

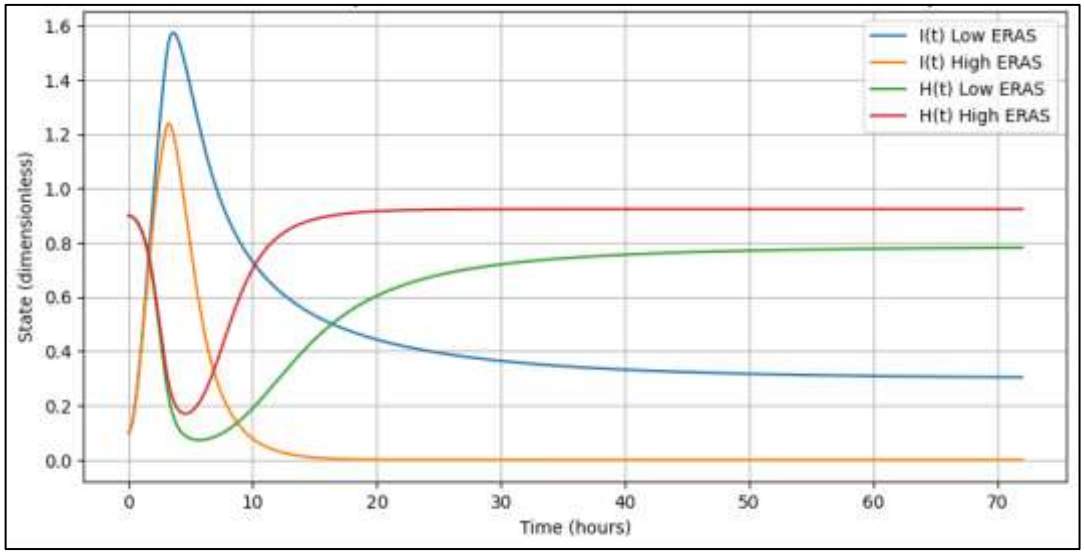

Figure 6. Inflammatory response and physiologic reserve trajectories under low and high ERAS adherence.

The results of the cumulative complication probabilities are illustrated in Figure 7, which indicates that there is continued difference in risk accumulation between the ERAS conditions.

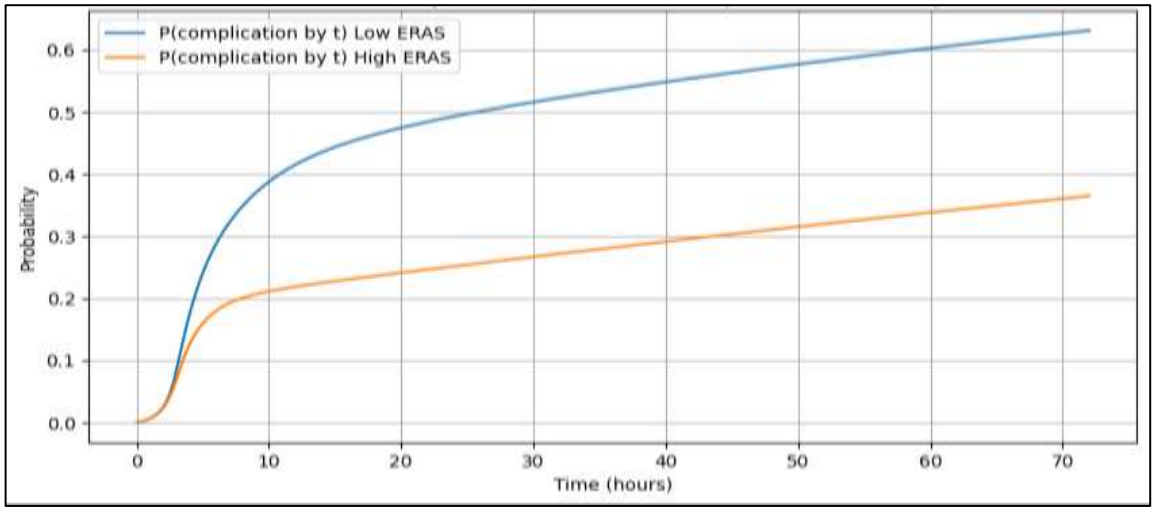

Figure 7. Cumulative complication probability for low versus high ERAS adherence.

Table 1. Predicted outcomes for a representative patient under low and high ERAS adherence.

ERAS adherence level	P (complication by 72 h)	Postoperative recovery time (h)	QoR proxy at 72 h
Low ERAS (0.2)	0.6316	Not achieved within horizon	0.5691
High ERAS (0.9)	0.3651	13.0	0.9241

3.6 Virtual Cohort Characteristics and Outcome Variability

The simulation of 500 synthetic patients was made to test behavior in the population. The cohort included frailty, inflammatory sensitivity, surgical severity and ERAS adherence heterogeneity. Table 2 reports descriptive statistics of patient characteristics and the simulated outcomes. There was also a significant heterogeneity in the predicted risk of complication, postoperative recovery time, and quality-of-recovery, which were the summed effects of patient heterogeneity and intervention intensity.

Table 2. Summary statistics of virtual cohort characteristics and outcomes (N = 500).

Variable	Mean	SD	Min	10%	25%	Median	75%	90%	Max
Frailty	0.996	0.148	0.578	0.802	0.889	1.002	1.084	1.200	1.417
Inflammatory sensitivity	0.985	0.194	0.458	0.730	0.845	0.998	1.114	1.221	1.578
Surgical severity	0.987	0.241	0.700	0.700	0.700	1.000	1.300	1.300	1.300
ERAS adherence	0.614	0.194	0.120	0.350	0.473	0.623	0.771	0.861	0.950
P(complication)	0.422	0.097	0.269	0.304	0.348	0.407	0.488	0.548	0.892
Recovery time (h)*	18.06	8.05	9.95	11.99	13.40	15.58	19.66	26.15	69.55
QoR proxy	0.903	0.082	−0.093	0.866	0.894	0.920	0.936	0.950	0.972

*Recovery time computed only for patients reaching recovery thresholds within 72 h (468/500).

3.7 Distribution of Complication Risk Across the Cohort

Figure 8 illustrates the cumulative postoperative complication probabilities distribution among the virtual cohort. The distribution was right-skewed and unimodal, which means that there was a group of high-risk patients although the average risk was moderate. This heterogeneity was a natural occurrence as a result of variability in parameters of patients without changing the model structure.

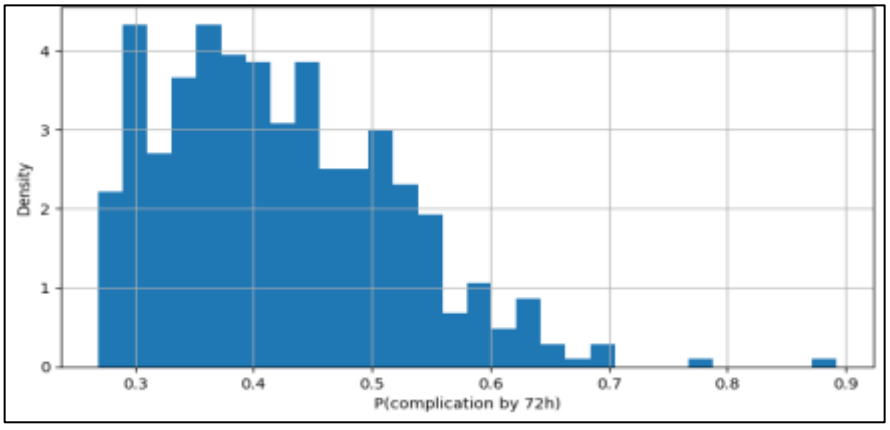

Figure 8. Distribution of predicted cumulative postoperative complication probabilities across the virtual cohort.

3.8 Population-Level Impact of ERAS Adherence

The cohort was stratified into high and low-ERAS groups depending on the median value of adherence to ERAS to make an assessment of the impact of ERAS adherence at the population level. Figure 9 represents the resulting risk distributions. The larger the ERAS adherence, the greater the shift to the left of the complication risk distribution, which implied the reduced predicted risk in the population.

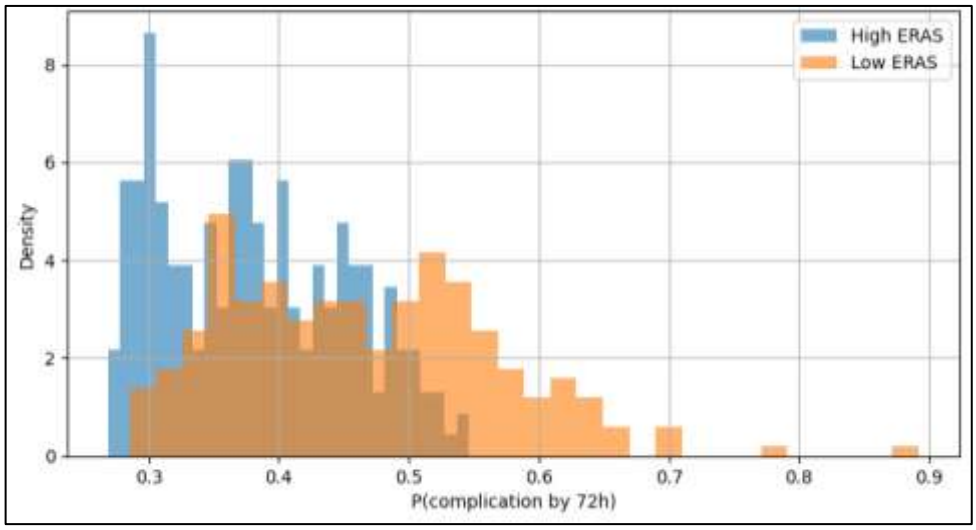

Figure 9. Comparison of complication risk distributions between low and high ERAS adherence groups.

Table 3 shows mean results of the two ERAS strata, showing a lower probability of complication, shorter recovery period, and better quality-of-recovery in the high-ERAS group.

Table 3. Mean outcomes stratified by ERAS adherence level.

ERAS group	N	Mean ERAS	Mean P(complication)	Mean recovery time (h)*	Mean QoR proxy
High ERAS	250	0.777	0.3813	14.22	0.9179
Low ERAS	250	0.451	0.4636	22.25	0.8872

3.9 ERAS Adherence and Patient-Centered Recovery Dynamics

Figure 10 demonstrates the correlation between the ERAS compliance and postoperative recovery duration of the virtual cohort. Increased ERAS compliance was linked to reduced and less fluctuating recovery time, and decreased compliance often led to delay in recovery or to not achieving recovery targets during the period of simulation.

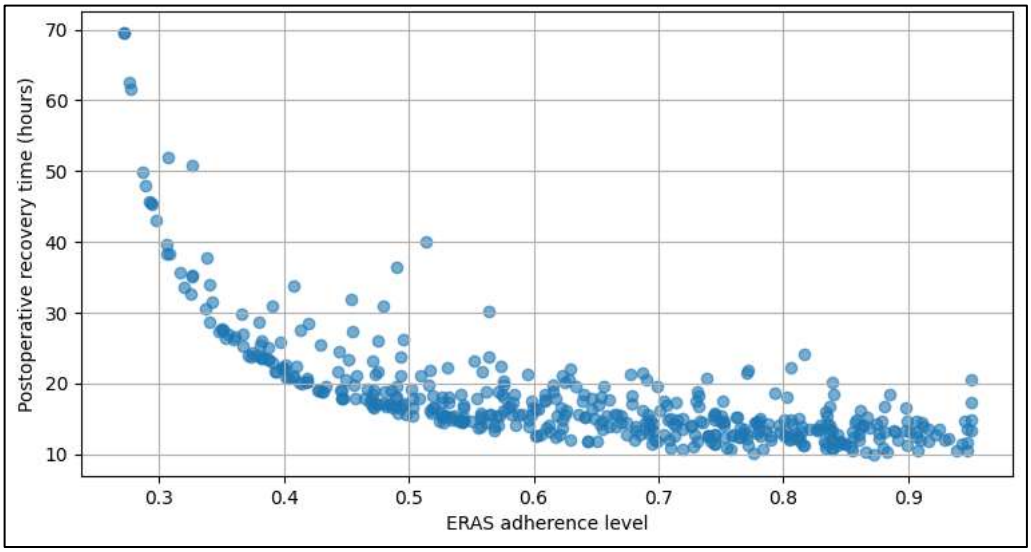

Figure 10. Postoperative recovery time as a function of ERAS adherence across the virtual cohort.

Quantitative associations between ERAS adherence and key outcomes are summarized in Table 4. ERAS adherence exhibited a strong negative monotonic association with recovery time (Spearman $\rho = -0.7691$) and complication probability ($\rho = -0.5043$), and a positive association with quality-of-recovery.

Table 4. Correlation between ERAS adherence and simulated outcomes.

Outcome	Spearman ρ	Pearson r
P(complication by 72 h)	−0.5043	−0.5631
Recovery time (h)	−0.7691	−0.6872
QoR proxy	0.2140	0.4103

3.10 Integrated Comparison of Individual- and Cohort-Level Outcomes

The individual-patient and cohort level key findings are summarized in Table 5, which depicts a steady decrease in the risk of complications and a postoperative recovery acceleration depending on the ERAS in all simulation scales.

Table 5. Integrated overview of individual- and cohort-level outcomes.

Analysis scale	ERAS condition	Key findings
Individual	Low ERAS (0.2)	High risk (0.63), no recovery within 72 h
Individual	High ERAS (0.9)	Reduced risk (0.37), recovery at 13 h
Cohort	Low ERAS group	Right-shifted risk distribution
Cohort	High ERAS group	Left-shifted risk distribution
Population trend	Increasing ERAS	Reduced risk and faster recovery

DISCUSSION

The paper provides a biomathematical framework that defines perioperative risk/recovery as a dynamic time-dependent process influenced by surgical stress, inflammatory response, physiologic reserve, and enhanced recovery interventions. The findings reveal that the outcomes of post operation occur as a consequence of interaction between physiological trajectories instead of fixed risk factors before operation, which gives rise to the importance of mechanistic modeling in perioperative care. Individual and population-level simulations demonstrated that an increased ERAS adherence increases the rates of inflammatory resolution, physiologic reserve, and cumulative complication risks. ERAS modulation was found to be more sensitive to recovery time and quality-of-recovery measures compared to complication probability individual, suggesting that dynamic recovery measures present a more comprehensive patient-centered data than binary endpoints. ERAS compliance started to change at the cohort level with the shift in the risk distributions, decreasing variability in recovery time, and the need to consider the heterogeneity of patients.

The hazard-based risk formulation offers a natural connection between the changing physiology and time-dependent risk of complication, as is expected by the traditional principles of survival and competing-risk analysis (Austin and Fine, 2017). Even though the current study pooled postoperative complications, it is easy to generalize the modeling structure to multistate or competing-risk models. The high reliance of recovery on the compliance with ERAS is consistent with the evidence that prolonged perioperative interventions can significantly change the course of postoperative recovery, such as digitally-assisted activity programs that enhance functional recovery (Lafaro et al., 2020). Methodologically, the framework is focused on interpretability and parsimony, but in clinical practice, parameter identifiability and observability of latent physiological states will need to be given careful consideration in the future (Raue et al., 2009). Theoretically, the treatment of ERAS compliance as a continuous control input places the perioperative care in a paradigm of predictive engineering, where interventions are aimed at balancing the physiological systems to achieve desirable results instead of being administered in the form of a fixed protocol (Şimsimsek et al., 2023).

A number of shortcomings must be mentioned. The model was tested on synthetic data and coarse-grained physiological models and complications were considered as a single aggregate output. The compliance of ERAS was also a scalar variable, but the real-life protocols are not homogenous. The next generation of work must be on empirical calibration, inclusion of competing-risk structures, and combination with longitudinal clinical and digital health data to make personalized and adaptive perioperative care possible. Overall, this study shows that a time-resolved and biomathematical method can be used to improve the knowledge of perioperative risk and recovery and offer a quantitative basis of patient-centered intervention-conscious perioperative decision support.

CONCLUSION

The present study introduces a biomathematical model of quantitative assessment of perioperative risk that conceptualizes surgical recovery as a dynamic process, which is governed by interacting physiological processes and interventions that are subject to modulation. The model combines surgical stress, inflammatory response and physiologic reserve in a time-resolved dynamical system, which takes the model beyond the static risk scores and offers mechanistic information on how perioperative trajectories change over time. By introducing enhanced recovery after surgery (ERAS) adherence as a continuous control input, it is possible to explicitly quantify intervention-dependent effects on the risk of complications, recovery time and patient-centered quality-of-recovery outcomes. The outcomes of the simulation of representative

patients as well as virtual cohorts indicate that greater adherence to ERAS always mitigates the inflammatory load, physiologic reserve, cumulative complication risk, and speed of postoperative recovery, as well as effective inter-patient variability. The mapping of physiological states to time-dependent risk based on the hazard further demonstrates how temporary periods of vulnerability may be detected and possibly be interfered with. Even though the framework was tested with synthetic data and simplified physiological representations, it provides an empirical-calibration-flexible framework in the future, as well as integrates competing-risk structures and longitudinal clinical and digital health data. On the whole, the work contributes to the use of biomathematical modeling in perioperative medicine and facilitates the creation of individual, adaptive, and patient-centered decision-support systems in surgical care.

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