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The construction of a digital intelligence early warning system for the whole process of acute lung injury in liver surgery based on cardiopulmonary interaction characteristics

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Digital Early Warning System for Acute Lung Injury in Liver Surgery.

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1. Research Background

1.1 Research Objectives and Significance

Acute lung injury (ALI) and the more severe acute respiratory distress syndrome (ARDS) are common postoperative complications of major liver surgery and liver transplantation, closely associated with significantly increased patient morbidity and mortality. Early warning systems based on interpretable machine learning models can identify abnormalities based on past patterns and current observations, issuing warning signals before hazards occur. These systems are considered highly valuable for precise prediction of clinical complications like ALI, which have sudden onsets and lack specific predictive indicators. This study aims to develop interpretable machine learning models using digital and intelligent methods, with cardiopulmonary interaction parameters as key features, to predict ALI in the perioperative period of liver surgery. Further, by integrating expert systems and iteratively optimizing them using information fusion technology, we aim to construct a digital and intelligent early warning system for ALI throughout the entire liver surgery process, meeting specificity and accuracy requirements and enabling early detection of high-risk ALI patients. Ultimately, we aim to establish an integrated platform for prevention, diagnosis, and treatment of ALI throughout the liver surgery process, centered on the ALI early warning system. This platform is designed to provide robust clinical decision support for healthcare professionals, reducing the incidence and mortality of ALI in the perioperative period of liver surgery.

1.2 Domestic and International Research Status

Domestic Research Status: While some progress has been made in ALI research for liver

surgery in China, large-scale clinical studies and effective predictive models remain insufficient.

International Research Status: ALI research for liver surgery is relatively advanced abroad, but challenges in predictive accuracy persist.

1.3 Research Conditions at Our Hospital

Data Resources: Beijing Tsinghua Changgung Hospital boasts rich clinical data resources, including a medical data center, electronic medical record systems, laboratory information systems, etc., providing ample data support for the research.

Technical Equipment: The hospital is equipped with advanced medical devices and technologies to meet data collection and analysis needs.

Professional Team: The research team comprises members with extensive clinical and research experience to ensure smooth research progress.

1. Research Objectives and Content

1.1 Research Objectives

Acute lung injury (ALI) and the more severe acute respiratory distress syndrome (ARDS) are common after major liver surgery and liver transplantation, and are closely linked to significantly increased patient morbidity and mortality. Severe liver dysfunction can lead to hemodynamic changes, coagulation abnormalities, and immune dysregulation, all of which can increase the risk of perioperative pulmonary complications, particularly ALI. Given the continuous and dynamic nature of ALI's pathophysiological process and its typically sudden onset, early warning systems are crucial. Such systems identify abnormalities based on past patterns and current observations, issuing warnings before hazards occur. A comprehensive early warning system can provide more effective perioperative coverage and clinical protection.

This study aims to develop interpretable machine learning models using digital and intelligent methods, focusing on ALI prediction in the perioperative period of liver surgery. It also aims to construct an ALI early warning system for the entire liver surgery process and establish an integrated ALI diagnosis and treatment platform for the entire liver surgery process, centered on the ALI early warning system. This platform will provide strong clinical decision support for medical professionals, with the goal of reducing the incidence and mortality of ALI in the perioperative period of liver surgery.

1.2 Research Content

1.2.1 Construction and Validation of Interpretable Machine Learning Models

Data Collection and Preprocessing

Literature Review: Systematically review domestic and international literature to understand the pathogenesis, risk factors, clinical manifestations, and pros and cons of existing predictive models for acute lung injury (ALI). This will provide a theoretical basis for data collection and model construction in this study.

Data Collection: Collect perioperative data from patients aged 18 and above who underwent major liver surgery at Beijing Tsinghua Changgung Hospital between June 2019 and May 2024. The data includes cardiopulmonary interaction parameters (e.g., pulse pressure variation, systolic pressure variation, stroke volume variation), preoperative baseline information (age, gender, weight, medical history), intraoperative information (surgery type, duration, anesthesia method, blood transfusion status), and postoperative information (complications, hospital stay, follow-up status).

Feature Selection: Use univariate and multivariate analyses to select features strongly associated with ALI occurrence as input variables for the machine learning (ML) model.

Model Development

Algorithm Selection: Develop interpretable ML models using six algorithms, including logistic regression, random forest, support vector machines, and neural networks, to enhance model accuracy and generalization.

Model Training: Split the dataset into training and validation sets. Train the model using the training set and optimize parameters through cross-validation to prevent overfitting.

Model Simplification and Optimization

Feature Importance Assessment: For the best-performing ML model, calculate the Shapley Additive Explanations (SHAP) values of input features to evaluate their importance.

Model Simplification: Select the top 20 features based on SHAP values to create a

simplified risk prediction model, improving interpretability and practicality.

Feature Weight Determination: Determine the feature weights in the simplified model for the entire major liver surgery process to support clinical decision-making.

Model Validation and Evaluation

Independent Test Set Validation: Validate the accuracy of the ML model using an independent clinical test set and evaluate its predictive performance using metrics such as sensitivity, specificity, accuracy, and ROC curve.

Interpretability Analysis: Conduct an interpretability analysis of the model's predictions, explaining the decision-making process and prediction basis to enhance clinical acceptance.

1.2.2 Construction and Clinical Validation of the Early Warning System

Construction of the Early Warning System

Expert System Development: Develop an ALI treatment expert system for the entire liver surgery process based on ML models. Integrate clinical guidelines, expert experience, and model predictions to form an ALI early warning system.

Logical Reasoning and Decision-Making Functions: Implement automatic logical reasoning and rapid clinical decision-making based on rules to provide real-time warnings and decision support for clinicians.

System Iteration and Optimization

Application of Information Fusion Technology: Use information fusion technology to integrate multi-source observational data, including vital signs, laboratory results, and imaging data, to enhance the accuracy and reliability of the early warning system.

System Optimization: Refine the early warning system based on clinical feedback and

actual application scenarios to improve system performance and user experience.

Clinical Validation and Evaluation

Expert Concept Validation Tests: Conduct concept validation tests for the iterated early warning system with clinical experts. Evaluate the system's probability predictions and perioperative suggestions, assessing dimensions such as consistency and acceptability through questionnaires.

Clinical Application Validation: Apply the early warning system in clinical practice, collect feedback from clinicians and patients, and evaluate the system's clinical value and effectiveness to further optimize its performance.

1.2.3 Establishment of an Integrated ALI Diagnosis and Treatment Platform

Theoretical Organization and Requirements Analysis

Theoretical Organization: Organize theories on the entire-process ALI early warning system, perioperative ALI diagnosis and treatment guidelines, expert consensus, case quality control, and knowledge retrieval needs in major liver surgery. Clarify the platform's functional positioning and construction goals.

Requirements Analysis: Communicate with clinicians, nurses, and managers to understand their actual needs and pain points in ALI diagnosis and treatment. This will provide a basis for platform design and development.

Data Center Construction and System Integration

Data Center Establishment: Establish a comprehensive data center for liver surgery wards to collect and integrate clinical, imaging, and laboratory data, providing data support for the platform.

Integration Interface Development: Develop integration interfaces to connect the entire-process ALI early warning platform and knowledge retrieval platform, enabling data sharing and interaction within a unified information system.

User Interface Design and Development

Interface Design: Create an intuitive and user-friendly interface with a simple and clear design style to facilitate quick adoption and operation by medical staff.

Function Implementation: Ensure medical staff can seamlessly access and operate all functions of the integrated system, including patient information queries, early warning result viewing, diagnosis guideline consultation, and knowledge retrieval.

System Testing and Optimization

Supervised Mode Testing: Conduct system testing and optimization in supervised mode with participation from clinicians and nurses. Comprehensive evaluation and feedback will be used to identify and resolve issues promptly.

Enhancing Safety and Effectiveness: Improve the safety and effectiveness of the entire-process ALI diagnosis and treatment platform through testing and optimization. Refine privacy protection mechanisms to ensure patient data security and privacy.

Training and Promotion

Comprehensive Training: Provide comprehensive training for medical staff, covering platform functions, operation methods, and clinical application cases, to ensure proficient use of the new system.

Application Promotion: Effectively implement the entire-process ALI diagnosis and treatment platform in practice. Enhance its adoption through promotion and demonstration,

offering robust support for the clinical management of liver surgery patients.

2. Research Protocol

2.1Study Design

This single - center cohort study has two phases: retrospective and prospective.

The retrospective phase analyzed patient data from June 2019 to May 2024 to develop and validate machine learning models.The prospective phase, starting December 2025, will enroll eligible patients. It will collect preoperative, intraoperative, and postoperative data, including cardiopulmonary interaction parameters and clinical blood samples. This data will assess the model's and early warning system's accuracy and effectiveness.

2.2 Study Population

Inclusion criteria: Patients aged ⩾18 years undergoing major liver surgery (e.g., resection of two or more liver segments, liver transplantation). Exclusion criteria:Patients declining participation, having comorbidities affecting outcome assessment, or having incomplete data records.

2.3Sample Size and Calculation

This study will enroll 2,497 patients to ensure adequate statistical power for external model validation. In major liver surgery, ALI incidence is approximately 4.1%.

Performance Indicator	Hypothetical Value	Target 95% Confidence Interval Width (Corresponding Standard Error)	Sample Size: Number of Study Participants (Events) Required

O/E	1	1 (0.245a)	390 (16)
Calibration Slope	1	0.2 (0.051)	2497 (103)
C-index	0.8	0.1 (0.0255)	1912 (79)
Standardized Net Benefit	0.53	0.2 (0.051)	2403 (99)

Assuming the linear predictor follows a skewed normal distribution, with an outcome event rate of 0.041.The required sample sizes, based on different model performance metrics, are shown above.

In summary, the minimum clinical sample size required for external model validation is 2,497 participants.

2.4Inclusion Criteria:

a. Aged ≥18 years; b. Scheduled for major liver surgery (e.g., resection of two or more liver segments, liver transplantation); c. Willing to participate and sign the informed consent form.

2.5Exclusion Criteria:

a. Patient refusal;

b. Presence of comorbidities that may affect outcome assessment; c

c. Incomplete recording of outcome measures;

d. Failure to follow up postoperatively;

e. Treating physician’s judgment that the patient is unsuitable for inclusion;

f. Participation in another study that may interfere with outcome assessment of this study.

2.6Intervention Methods:

This study involves no therapeutic interventions for participants; only their clinical data and samples will be collected.

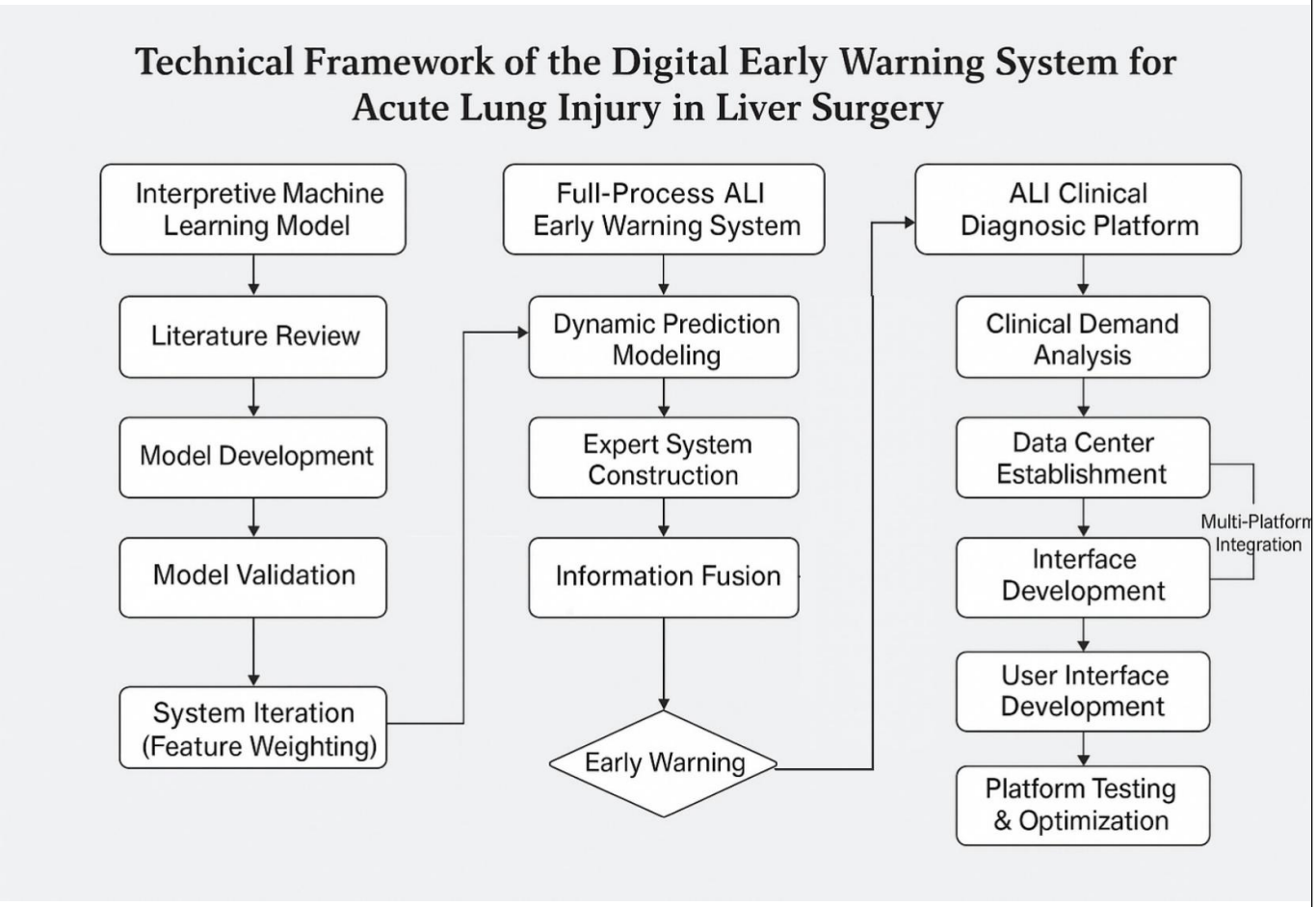
2.7 Observation Indicators and Follow-up Plan

Observation indicators include cardiopulmonary interaction parameters and relevant biomarkers in clinical blood samples. The follow-up plan involves assessing patients within seven days after surgery to collect information on their recovery and test results.

2.8 Statistical Analysis Methods

Data will be analyzed using R or SPSS, with analyses including descriptive statistics, correlation analysis, and regression analysis.

3. Flowchart



4. Evaluation Criteria

Primary outcome measure: Incidence of ALI within 7 postoperative days.

ALI diagnosis currently uses the Berlin definition of acute respiratory distress syndrome (ARDS):

a. Onset: Acute occurrence within one week of known injury or new/worsening respiratory symptoms;

b. Chest imaging (X-ray or CT): Bilateral pulmonary opacities not fully explained by effusion, atelectasis, or nodules;

c. Pulmonary edema cause: Respiratory failure not fully attributed to heart failure or fluid overload; if no related risk factors, objective tests (like Doppler echocardiography) are needed to exclude hydrostatic pulmonary edema;

d. Oxygenation:

Mild: With CPAP/PEEP >5 cmH_2O, 200 mmHg <PaO_2 /FiO_2 <300 mmHg;

Moderate: With CPAP/PEEP >5 cmH_2O, 100 mmHg <PaO_2 /FiO_2 <200 mmHg;

Severe: With CPAP/PEEP >5 cmH_2O, PaO_2 /FiO_2 <100 mmHg.Opportunities for improved clinical trial designs in acute respiratory distress syndrome Wick, Katherine D et al.

The Lancet Respiratory Medicine, Volume 10, Issue 9, 916 - 924

Secondary outcome indicators include postoperative recovery status, hospitalization duration, and complication incidence, among others.

5. Safety Reporting and Adverse Event Management

5.1 Definitions of Adverse Events and Serious Adverse Events

An adverse event (AE) is any unfavorable event occurring during the study that may impact the participant's well-being. A serious adverse event (SAE) refers to an event that results in death, is life-threatening, requires hospitalization or prolongs hospital stay, causes permanent or significant disability/damage, or leads to congenital anomalies/birth defects.

5.2 Management of AEs and SAEs

AEs will be promptly assessed and treated, with treatment plans adjusted if necessary. For SAEs, immediate emergency measures will be taken to ensure participant safety, and they will be reported to the ethics committee without delay.

5.3 Reporting Procedure

AEs and SAEs will be reported in accordance with hospital regulations and the requirements of the ethics committee.

6.Medical Ethics Risk Analysis

Ethical Issues: This study involves privacy protection and informed consent of participants.

Countermeasures: We will strictly adhere to ethical principles to ensure participant privacy and informed consent rights. Personal information and samples will be anonymized to

safeguard privacy. Throughout the study, we will fully respect participants' autonomy and voluntary participation.