Russian registry of Surgical OutcomeS — RuSOS: study protocol

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Nациональный регистр послеоперационных исходов — RuSOS: протокол исследования

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INTRODUCTION: Identification of risk factors that cause a high probability of an unfavorable outcome in the postoperative period is an urgent problem. The creation of national databases (registries) makes it possible to cover a certain patient population by identifying its risk predictors. Existing registries differ in the criteria for inclusion in the study, in the characteristics of the populations studied, and there is often no common view on the classification of postoperative outcomes. OBJECTIVE: Creation of a Russian national calculator for the risk of postoperative complications and mortality. MATERIALS AND METHODS: Two-level observational retrospective-prospective study. Setting: National multicenter study of surgical inpatients. Patients: Adult patients undergoing elective and emergency surgery. Types of interventions: obstetrics, gynecology, mammary gland, urology, endocrine surgery, maxillofacial surgery, orthopedics, traumatology, abdominal surgery, liver and biliary tract, thoracic surgery, vascular surgery, neurosurgery, cardiac surgery, other areas. RESULTS: The design was registered in the ClinicalTrials.gov database, the study was organized by the Federation of Anesthesiologists and Reanimatologists of Russia. Primary (30-day mortality, 30-day complications) and secondary (hospital mortality, hospital complications, length of stay in ICU, length of hospital stay, multiple organ failure (2 or more points on the SOFA scale), 90-day mortality, 90-day complications, post intensive care syndrome, readmission, 1-year mortality) outcomes; six primary and twelve secondary target points; criteria for inclusion, non-inclusion, exclusion. The required sample size and statistical analysis are described. The planned sample size to ensure the required power of the study is determined to be 60,800 observations for elective surgery and 20,000 observations for emergency surgery. The planned duration of the study is 2024–2028. CONCLUSIONS: The study has important scientific and medical-social significance; a Russian national calculator for the risk of postoperative complications and mortality will be developed. In the future, the developed calculator can become the basis for making medical decisions.

Abstract

Reферат

АКТУАЛЬНОСТЬ: Выявление факторов риска, обусловливающих высокую вероятность неблагоприятного исхода в послеоперационном периоде, является актуальной проблемой. Создание национальных баз данных (регистров) позволяет максимально охватить определенную популяцию пациентов, выявив характерные для нее предикторы риска. Как показывают данные литературы, существующие регистры различаются в критериях включения в исследование, в характеристиках изучаемых популяций, часто отсутствует единый взгляд на классификацию послеоперационных исходов.

ЦЕЛЬ ИССЛЕДОВАНИЯ: Создание российского национального калькулятора риска послеоперационных осложнений и летальности.

МАТЕРИАЛЫ И МЕТОДЫ: Двухуровневое обbservационное ретроспективно-проспективное исследование. Условия: национальное многоцентровое исследование пациентов хирургических стационаров. Пациенты: взрослые пациенты, подвергающиеся плановым и экстренным оперативным вмешательствам. Виды вмешательств: в акушерстве, в гинекологии, на молочной железе, в урологии и на почках, в челюстно-лицевой хирургии, в ортопедии и травматологии, на нижнем этаже брюшной полости, в гинекологии, на молочной железе, в урологии и на почках, в челюстно-лицевой хирургии, в ортопедии и травматологии, на нижнем этаже брюшной полости, на печени и желчевыводящих путях, на верхнем этаже брюшной полости, в торакальной хирургии, в сосудистой хирургии, в нейрохирургии, в кардиохирургии, в других областях (с обязательной конкретизацией).

РЕЗУЛЬТАТЫ: Разработанный дизайн был зарегистрирован в базе данных ClinicalTrials.gov, исследование организовано Федерацией анестезиологов и реаниматологов России. Определены первичные (30-дневная летальность, 30-дневные осложнения) и вторичные (госпитальная летальность, госпитальные осложнения, длительность пребывания в отделениях анестезиологии, реанимации и интенсивной терапии, длительность пребывания в стационаре, полиорганская недостаточность (2 балла и более по шкале SOFA (Sequential Organ Failure Assessment), 90-дневная...

KEYWORDS: hospital mortality, risk factors, concomitant diseases, registries, postoperative complications

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Introduction

Currently, the frequency of perioperative complications and mortality associated with surgery are minimized. Nevertheless, taking into account the significant number of surgical interventions performed worldwide (which is more than 300 million per year) [1], the total number of patients with complicated postoperative periods is high, and postoperative mortality ranks third in the structure of causes of death (7.7%), after coronary heart disease and stroke [2]. Moreover, even in discharged patients, complications that have developed can significantly reduce the quality of life and worsen the long-term prognosis [3]. To a greater extent, the aforementioned applies to high-risk patients, the identification of which is the priority task of anesthesiology.

Identification of risk factors that cause a high probability of an unfavorable outcome is currently unthinkable without comprehensive prospective population studies, which, on the one hand, allow us to assess the contribution of many variables to the risk of complications and mortality, and on the other hand, to maximize coverage of a certain population by identifying its characteristic predictors [4]. At the moment, several population-based studies and programs have been described in the literature, which have allowed the creation of national databases (registers) of postoperative outcomes. Such studies include several international (ISOS, EuSOS and ASOS) [5-7] and national ones, such as SweSOS [8] or ColSOS [9], which are at different stages of implementation. Of the national databases, the most well-known is the ACS-NSQIP database (the National Program for Improving the Quality of Surgical Care of the American College of Surgeons), which contains information on the outcomes of surgical treatment of more than 5 million patients from the United States since 1991 [10].

The obtained results of these studies often differ significantly, which was the result of a variety of approaches to the criteria for inclusion in the study, differences in the characteristics of the studied populations and the lack of a unified view on the classification of postoperative outcomes. When assessing mortality, the authors most often register a 30-day mortality, however, considering modern ideas about the role of perioperative factors and complications in the development of an unfavorable long-term outcome, it becomes obvious that it is necessary to determine the annual mortality. As the SweSOS national observational study showed, the mortality rate increases significantly over time, so the 30-day mortality rate was 1.8%, the 3-month mortality rate was 3.9%, and the 6-month and annual mortality rates were 5.0% and 8.5%, respectively [8].

There is also no unified approach to the registration of postoperative complications, and modern protocols include several systems, the most common of them are classification of the joint working group of ESA (European Society of Anesthesiologists, The European Society of Anesthesiologists) and EICM (European Society of Intensive Care Specialists, The European Society of Intensive Care Medicine) [11] and classification of ACS-NSQIP (National Program for Improving the Quality of Surgical Care of the American College of Surgeons, The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP)) [12]. Although they are similar in many ways (complications are grouped into blocks according to the nature of the disorders), differences are also present, and even the same complication may have a different definition. In addition, some significant outcomes are not included in these classifications, which determines their underestimation.

Of course, one of the advantages of creating an extensive population database is the registration of a large number of potential predictors of an adverse outcome, followed by an assessment of their individual contribution to the complex perioperative risk. The type of surgery itself is already a factor that largely determines the likelihood of complications (Table 1).

Objective

The goal is to create a Russian national calculator for the risk of postoperative complications and mortality.

Primary outcomes

1. 30-day mortality rate.
2. 30-day complications.

Secondary outcomes

1. Hospital mortality.
2. Hospital complications.
3. Duration of stay in the UARIT.
4. Length of hospital stay.
5. Multiple organ failure (2 or more points on the SOFA (Sequela Organ Failure Assessment) scale).
6. 90-day mortality rate.
7. 90-day complications.
8. Post intensive care (PIC) syndrome.
9. Repeated hospitalization.
10. Annual mortality.

Primary target points

1. Creation of a national register of postoperative outcomes in various fields of surgery.
2. Determination of the frequency and structure of outcomes after planned and emergency surgical interventions.
3. Identification of predictors of an unfavorable outcome.
5. Creation of calculators for the risk of postoperative complications and mortality in various fields of surgery and their integration into a single calculator.

6. Analysis of long-term results in patients with postoperative complications (90 days and a year after surgery).

Secondary target points

1. The role of concomitant diseases in the development of an unfavorable outcome.

2. The effect of age on primary and secondary postoperative outcomes.

3. The effect of the type of anesthesia on the course of the postoperative period.

4. The effect of oncological pathology and specific treatment on primary and secondary postoperative outcomes.

5. The impact of emergency surgery on the risk of an adverse outcome.

6. The effect of localization, access and duration of surgery on the postoperative outcome.

7. Assessment and validation of scales of surgical and anesthesiological risk of death (it is possible to list).

8. Assessment and validation of scales of surgical and anesthetic risk of primary and secondary outcomes.

9. Stratification of patients with high perioperative risk with details on cardiac, respiratory, neurological, renal, hepatic, hemostatic, infectious and others.

10. The influence of quality criteria for the implementation of FAR recommendations on the course of the postoperative period.

11. Analysis of the course of PIC syndrome in patients with complications and depending on the maximum score on the SOFA scale and the structure of PON in the postoperative period.


Inclusion criteria

A. Adult patients (age 18 and older) undergoing elective surgery performed with different access:

- in obstetrics;
- in gynecology;
- on the mammary gland;
- in urology and kidney surgery;
- in endocrine surgery;
- in maxillofacial surgery;
- in orthopedics and traumatology;
- on the lower floor of the abdominal cavity;
- on the liver and biliary tract;
- on the upper floor of the abdominal cavity;
- in thoracic surgery;
- in vascular surgery;
- in neurosurgery;
- in cardiac surgery;
- in other areas (with mandatory specification).
B. Adult patients (age 18 and older) undergoing emergency surgical interventions in these and other areas of surgery (for example, in purulent surgery).

Criteria for non-inclusion

1. Lack of informed consent of the patient.
2. Complications associated with the manipulations of an anesthesiologist-intensive care specialist.
3. Interventions without the participation of an anesthesiologist-resuscitator.

Exclusion criteria

1. Incomplete checklists.
2. Errors when filling out checklists.
3. Deviations from the Register protocol.

The design of the Register

The design of the Register is a two-level observational retrospective and prospective study.

The planned start date of the study is January 1, 2024.
The planned end date of the study is December 31, 2028.

First level

Basic checklist: filled in for all patients with postoperative complications. At the same time, the total number of patients operated on in a particular center is taken into account quarterly, taking into account their distribution by areas of surgery.

Based on the data from the basic checklist, answers will be received to the following target points (3 primary and 2 secondary):

1. Creation of a national register of postoperative outcomes in various fields of surgery.
2. Determination of the frequency and structure of outcomes after planned and emergency surgical interventions.
3. Analysis of long-term results in patients with postoperative complications (90 days and a year after surgery).
4. Analysis of the course of PIC syndrome in patients with complications and depending on the maximum score on the scale and the structure of PON in the postoperative period.
5. Analysis of the effectiveness of rehabilitation measures in patients with PIC syndrome.

Second level

Basic checklist plus additional checklist: filled in for all operated patients within one selected week on a quarterly basis.

The total number of patients operated on in a particular center is also taken into account quarterly, taking into account their distribution by areas of surgery.

Based on the data from the basic and additional checklists, answers to the most important target points (3 primary and 10 secondary) will be received:

1. Identification of predictors of an unfavorable outcome.
3. Creation of calculators for the risk of postoperative complications and mortality in various fields of surgery and their integration into a single calculator.
4. The role of concomitant diseases in the development of an unfavorable outcome.
5. The effect of age on primary and secondary postoperative outcomes.
6. The effect of the type of anesthesia on the course of the postoperative period.
7. The impact of oncological pathology and specific treatment on primary and secondary postoperative outcomes.
8. The impact of emergency surgery on the risk of an adverse outcome.
9. The effect of localization, access and duration of surgery on the postoperative outcome.
10. Assessment and validation of scales of surgical and anesthesiological risk of death (it is possible to list).
11. Assessment and validation of scales of surgical and anesthetic risk of primary and secondary outcomes.
12. Stratification of patients with high perioperative risk with details on cardiac, respiratory, neurological, renal, hepatic, hemostatic, infectious and others.
13. The influence of quality criteria for the implementation of FAR recommendations on the course of the postoperative period.

The basic and additional checklists are presented in Appendices 1 and 2.

Statistical analysis

The planned sample size for the second level is at least 108,000 in the estimated cohort and at least 54,000 in the validation cohort. The sample size was calculated taking into account the fact that at least 10 cases of postoperative complications per factor included in the final regression model are required. The sample size was calculated for each area of surgery, taking into account the known frequency of postoperative complications and mortality in elective and emergency surgery (Table 2).

The nature of the distribution of the studied indicators will be assessed using the Kolmogorov-Smirnov criterion. Continuous data will be presented as the median and interquartile range for the nonparametric distribution and as the mean and standard deviation for the parametric distribution. Categorical variables will be presented in the form of the number of patients and a percentage of the total number of patients.
To initially assess the association of the factor with postoperative complications, a single-factor analysis will be performed using the $\chi^2$ criterion and the Mann-Whitney or Kruskal-Wallis criterion. All variables with a reliable relationship identified in the univariate analysis ($p$ less than 0.05) will be included in the logistic regression if there is no colinearity between them (correlation coefficient less than 0.25). The logistic regression model will be carried out using a simultaneous inclusion procedure, in which the presence of complications and death will be a dependent variable. The criterion for excluding the factor will be set at a significance level of 0.05. Adjusted odds ratios and 95% confidence intervals will also be calculated.

The resulting predictive model will be evaluated in a validated group using ROC analysis and the Hosmer-Lemeshov criterion.

In relation to the development and validation of the obtained models and scales, such modern methodological approaches as:

- **TRIPOD** — Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (transparent reporting of a multiparametric prediction model for individual prognosis or diagnosis) [42];
- **PROBAST** — Prediction model Risk Of Bias ASessment Tool (a tool for assessing the risk of deviations from the initial accuracy of the forecasting model) [43];
- **SHAP** — SHapley Additive exPlanation (assessment of the contribution of each variable to the prediction of the model from the perspective of risk/benefit) [44];
- The Brier score — the Brier score is an indicator of the accuracy of predicting binary outcomes [45],

### Table 2. Minimum sample size for patients undergoing elective and emergency surgery

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<th>Emergency surgery</th>
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<td>2 000</td>
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<tr>
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<td>2 000</td>
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<tr>
<td>Maxillofacial surgery</td>
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<td>Neurosurgery</td>
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<td>Liver and biliary tract</td>
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<td>Thoracic surgery</td>
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<tr>
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<td>300</td>
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<td>Total number of patients</td>
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<td>20 800</td>
</tr>
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</table>

### Conclusion

For the first time in Russia, a multicenter study is planned to create a national registry to study the risk factors for an adverse outcome in elective and emergency surgery. This multicenter study will determine the role of disease predictors in the development of postoperative complications and death, as well as create a national model for assessing perioperative risk.

**Disclosure.** I.B. Zabolotskikh is the First Vice President of the All-Russian public organization “Federation of anesthesiologists and reanimatologists”; A.I. Gritsan is the Vice President of the Public Organization “Association of Critical Care of the Russian Federation.”
President of the All-Russian public organization “Federation of anesthesiologists and reanimatologists”; A.N. Kuzovlev is the Vice President of the All-Russian public organization “Federation of anesthesiologists and reanimatologists”, Deputy Director of Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitiology and K.M. Lebedinskiy is the President of the All-Russian public organization “Federation of anesthesiologists and reanimatologists”; E.M. Shifman is the Vice President of the All-Russian public organization “Federation of anesthesiologists and reanimatologists”. Other authors declare that they have no competing interests.

Author contribution. All authors according to the ICMJE criteria participated in the development of the concept of the article, obtaining and analyzing factual data, writing and editing the text of the article, checking and approving the text of the article.

Ethics approval. This study will be approved by the local Ethical Committees of the research centers included in the study.

Registration of the study. The study was registered in the international database https://clinicaltrials.gov under the auspices of the All-Russian Public Organization “Federation of Anesthesiologists and Reanimatologists” (principal investigator I.B. Zabolotskikh), study number NCT06146270.

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