2019-11

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Cai, S

http://hdl.handle.net/10026.1/14654

10.1111/jan.14097
Journal of Advanced Nursing
Wiley

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Article type : Protocol

Incidence and risk factors of PostopeRativE Delirium in Intensive Care unit patients: a study protocol for the PREDICt study

Running head: Incidence and risk factors of postoperative delirium in intensive care unit patients

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This article has been accepted for publication and undergone full peer review (not applicable for Editorials) but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jan.14097

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Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;	Shining CAI, Mingzhi LV, Yuxia ZHANG
Involved in drafting the manuscript or revising it critically for important intellectual content;	Jos LATOUR, Yuxia ZHANG
Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content;	Yuxia ZHANG, Jos LATOUR
Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.	Ying LIN, Wenyan PAN, Jili ZHENG, Lihong CHENG, Jingjing LI

Funding Statement:

This study was funded by the Clinical Research Grant scheme of the Zhongshan Hospital, Fudan University in April 2018 (Grant No. 2018ZSLC08). The total amount of funding is 500,0000 RMB (equals to 72,257 US dollars).

Conflict of Interest

No conflict of interest has been declared by the authors.

Abstract

Aim: The aims of this study are 1) to determine the incidence of postoperative delirium among surgical Intensive Care Unit patients in China and identify risk factors, especially which are modifiable and have value for developing a prediction model; 2) to develop and validate a prediction model of delirium to recognize high-risk patients in surgical Intensive Care Units; 3) to investigate the short- and long-term outcomes of delirious patients and identify the predictors of patient outcomes.

Design: A single centre prospective cohort study.

Methods: Patients will be enrolled from three surgical Intensive Care Units in a tertiary teaching hospital. Delirium assessment and perioperative data will be collected throughout the hospitalization. Delirious patients will be followed up for 2 years. The study was approved by the ethics committee in May 2018 and was funded by the clinical research grant from Zhongshan hospital, Fudan University, Shanghai.

Discussion: Developing postoperative delirium can be a burden to patients both for the short- and long-term period. Due to the lack of effective treatments for postoperative delirium, prevention remains the best strategy. This study will provide an effective tool for early screening of high-risk

patients of postoperative delirium and provide a better understanding of the aetiology and outcome of delirium.

Impact: In clinical practice, a prediction model will offer an effective tool for ICU nurses to assess high-risk patients, which can support them to implement preventive strategies at the early stages to targeted patients. The follow-up results will help us better understand the impact of delirium on patients' long-term outcome.

Trial registration: The trial has been registered on US National Institutes of Health ClinicalTrials.gov (NCT03704324).

Keywords: delirium, intensive care unit, surgical patients, critical care, postoperative care, prediction model, nursing, protocol

1. INTRODUCTION

Delirium is an acute and fluctuating alteration of mental state characterized by a disturbance in attention, consciousness and cognition (A. P. Association, 2013). Postoperative delirium (POD) is a common postoperative complication that can occur in patients of any age(Aldecoa et al., 2017). The reported incidence of POD varies within a broad range due to different targeted population and different risk factors exposure(Smulter, Lingehall, Gustafson, Olofsson, & Engstrom, 2013). A meta-analysis including 26 studies reported an incidence of 4.0 to 53.3% in patients after orthopaedic surgery(Bruce, Ritchie, Blizard, Lai, & Raven, 2007). Critically ill patients admitted to Intensive Care Units (ICU) postoperatively had much higher incidence rates of POD compared with non-surgical ICU patients. Delirium affects up to 80% of mechanically ventilated adult patients in ICU and costs 4 to 16 billion dollars annually in the USA alone(Landro, 2011; Moyer, 2011). Postoperative delirium is associated with several negative outcomes, including increased mechanically ventilated days, hospital length of stay (LOS) and cost (Bellelli et al., 2014; Edelstein et al., 2004; Krzych et al., 2014; Witlox et al., 2010). Moreover, each day with a delirium is independently associated with an increased hazard of death by 10% (Ely et al., 2004). Delirium brings also great burden to patients and their families as the follow-up cognitive decline can persist for months to years hindering patients to return to their

previous quality of life and employment (Norman et al., 2016). Although few studies have focused on exploring relevant factors and developing strategies to prevent the occurrence of POD, the evidence gap remains and needs to be further explored.

1.1 Background

Given the high prevalence of POD among critically ill patients and its associated negative clinical outcomes, there is a growing body of research exploring related risk factors and predictors to prevent the occurrence of delirium at the early stage. Although the number of studies on delirium increased in the past decade, an evidence gap still exists in this area due to the heterogeneity of previous researches and their results. First, the incidence varies a broad range because the targeted population are different (Aldecoa et al., 2017). In China, up to now, no studies have investigated the incidence and risk factors of POD in surgical ICUs. Although there have been several studies exploring the potential risk factors of POD in ICU, most of these studies provide inconclusive evidence. The Benzodiazepine use and blood transfusion administration are the only two identified factors with strong evidence (Devlin et al., 2018). Hence, further studies are needed to focus on the aetiology of POD to find out modifiable and non-modifiable factors to verify presumed factors (Pandharipande et al., 2017).

Since there is lack of effective treatments for POD, prevention remains the best strategy. Studies have proven that preventive measures could help reduce the incidence, duration and severity of delirium (Inouye et al., 1999; Kalisvaart et al., 2005). However, if preventive measures including pharmacological, psychological or multicomponent interventions apply to all postoperative patients in ICU, they might be time and cost consuming and may also expose patients to unnecessary risk of adverse effects. Predictive models that include delirium risk factors can guide clinical practice to early prevention of high-risk patients.

We undertook a systematic review to identify validated prediction models for POD using PubMed, Embase, Medline and CINAHL. Ten prediction instruments were identified, of which only two were developed for ICU patients, named PRE-DELIRIC (van den Boogaard et al., 2012; van den Boogaard et al., 2014) and E-PRE-DELIRIC (Wassenaar et al., 2015). The PRE-DELIRIC model is designed to detect high-risk patients within 24 hours after ICU admission, while the E-PRE-DELIRIC model can be used during ICU admission. However, both models were developed in general ICU patients and not fully considering the impact of surgical patients. The other eight identified models were for hip surgery (Kalisvaart et al., 2006; Moerman et al., 2012), cardiac surgery (Koster, Oosterveld, Hensens, Wijma, & van der Palen, 2008; Rudolph et al., 2009), vascular surgery (Bohner

et al., 2003), non-cardiac surgery (Marcantonio et al., 1994) and general surgery (Dworkin, Lee, An, & Goodlin, 2016; Kim, Park, Kim, & Cho, 2016). Most of these models were developed based on preoperative data and did not target ICU patients.

Limited knowledge exists on the incidence, risk factors and outcomes of POD in the Asian population. So far, there is no delirium prediction model only for surgical ICU patients who may have high exposures to POD. In addition, limited studies have focused on long-term outcomes of delirious patients. Therefore, our PostopeRativE Delirium in Intensive Care unit patient (PREDICt) study can contribute to a deeper understanding of the incidence and risk factors of delirium in Chinese surgical patients during and after an ICU admission. The results of the PREDICt study can provide an evidence base for early identification of POD in surgical ICU patients that might improve clinical practice and ultimately long-term patient outcomes.

2. THE STUDY

2.1 Aims

The aim of the PREDICt study is to identify risk factors of postoperative delirium in surgical ICU patients and to develop a prediction model to assess the outcomes of delirious post-surgical patients.

The specific study objectives are:

1. to determine the incidence, severity and categories of POD in surgical ICU patients and investigate the modifiable and non-modifiable risk factors for the occurrence;

2. to develop and validate a risk model to predict POD in surgical ICU patients to identify high-risk patients.

3. to identify short- and long-term outcomes of POD patients and explore the predictors for long-term prognosis of patients who had POD in surgical ICU.

2.2 Study Design

This is a single-centre, prospective cohort study conducted at a tertiary teaching hospital in Shanghai, China. The trial has been registered at the US National Institutes of Health ClinicalTrials.gov (NCT03704324).

2.3 Setting

The study will be conducted in three surgical ICUs in XX hospital, Shanghai, China, which is the largest hospital in Shanghai with 2005 beds. In 2017, the hospital performed 98,146 surgical operations and the mean hospital length of stay after surgery was 5.95 days. The three ICUs are: 1)

Comprehensive surgical ICU with 28 beds and the ICU staff include 96 nurses and physicians. Approximately 50 postoperative patients per week are admitted, including thoracic surgery, general surgery, orthopaedic surgery, urological surgery and vascular surgery; 2) Cardiac surgical ICU with 39 beds and the ICU staff include 121 nurses and physicians This ICU admits around 100 postoperative patients per week; 3) Liver surgical ICU with 25 beds and the ICU staff include 56 nurses and physicians. This ICU admits around 80 postoperative patients per week.

2.4 Participants

Inclusion Criteria

Patients aged above 18 with a planned admission to the surgical ICU after a surgical procedure will be eligible for inclusion.

Exclusion Criteria

Exclusion criteria include preoperative delirium, dementia, patients who are unable to fully participate in delirium testing, including patients who are blind, deaf, illiterate or inability to understand Chinese.

Patients transferred from the ward directly to the ICU, not via the operation room, will be excluded. Surgical patients with an emergency or unplanned ICU admission are also excluded.

Patients will be recruited in two cohorts during two periods. The recruitment of the first cohort (developing cohort) will be from November 2018 - March 2019. The second cohort (validating cohort) will be recruited from June 2019 - December 2019. The study framework presented in Figure 1 described the recruitment of both cohorts, including the time frames and the data collection.

2.5 Sample size

The aim of the study is to characterize the incidence and profiles of POD in ICU. We calculated the sample size based on the POD guidelines of the European Society of Anaesthesiology (Aldecoa et al., 2017), the reported incidence varies from 3.6% to 53.3%. We used the lowest incidence 3.3% (Andersson, Gustafson, & Hallberg, 2001; Bruce et al., 2007) to estimate the sample size of 253 with a precision of 5% and confidence level of 95%. However, our study will also aim to identify risk factors of POD and develop prediction model. The rule of thumb in logistic modelling is that a minimum of 10 events per predictor variable (EPV) should be achieved based on simulation studies

(Vittinghoff & McCulloch, 2007). Therefore, we will target to recruit a minimum of 1000 patients to minimise the limitation of a small number of events of postoperative delirium.

2.6 Data collection

Delirium Assessment

The primary outcome will be the presence of POD in ICU which often occurs up to five days after surgery (Olin et al., 2005; Sharma et al., 2005). Each patient will be assessed for delirium on postoperative day 1 and continuing for five days or until discharge from ICU. The delirium-positive patients will receive continuing assessment until hospital discharge. When patients have sudden change in mental status or behaviours, more frequent screening will be conducted. Before delirium assessment, Richmond Agitation-Sedation Scale (RASS) (Sessler et al., 2002) will be used to initially estimate the mental state of patients. If patients' RASS scored -4 or -5, which means they can't response to voice, patients will not be screened for delirium until they regain consciousness. We defined patients with a POD if they have at least one positive screening during ICU stay. Two assessors will use instruments to interview medical staff caring for the patients and review the

patient's medical record of the past 24 hours. If the two assessors disagree with the results, a consensus panel consisting of two ICU physicians and one psychiatrist will make the final decision.

The Confusion Assessment Method for ICU (CAM-ICU) (Ely et al., 2001; Inouye et al., 1999) and the CAM-ICU-7 (Khan et al., 2017) will be used to detect delirium and delirium severity. The CAM-ICU is a validated and reliable tool to screen delirium and it needs 2-5min to be completed (Andrews, Silva, Kaplan, & Zimbro, 2015; van den Boogaard et al., 2009). The CAM-ICU-7 is a validated tool to assess delirium severity. It was derived from the CAM-ICU and RASS assessment with 4 items and a 7-point rating scale (Table 1), categorized as 0–2: no delirium, 3–5: mild to moderate delirium and 6–7: severe delirium (Khan et al., 2017). Both CAM-ICU and CAM-ICU-7 are easy to use and less burdensome for nurses to conduct (van Eijk et al., 2009).

Delirium can present as hyperactive, hypoactive and mixed forms based on the clinical presentation focused on psychomotor behaviour (Lipowski, 1983; Robinson, Raeburn, Tran, Brenner, & Moss, 2011). Hyperactive delirium is agitated and combative and often accompanied by hallucinations and delusions. Patients showing decreased alertness, motor activity and anhedonia raise suspicion for development of hypoactive delirium. Mixed delirium shows features of both conditions (Fong, Tulebaev, & Inouye, 2009; Meagher, O'Hanlon, O'Mahony, Casey, & Trzepacz, 2000).

Delirium subtype will be defined by CAM-ICU and RASS scores (Table 2). The Chinese version of the screening and assessment tools have been translated and published in the latest Chinese guideline by Chinese Medical Association Critical Care Medicine (CMACCM) Branch (Branch, 2018).

Over 6 months, all patients after surgery and ICU admission will be screened for delirium. Each unit will have designated research staff for the collection and entry of data for the study.

Demographic characteristic

The demographic variables and related information on potential risk factors identified by three systematic review (Gosselt, Slooter, Boere, & Zaal, 2015; Kassie, Nguyen, Kalisch Ellett, Pratt, & Roughead, 2017; Oh et al., 2015) and two guidelines (Aldecoa et al., 2017; Devlin et al., 2018) related to POD will be used. We will also include other variables based on clinical experience. The list of study variables and their timeframe are presented in Table 3. The demographic data will be collected at preoperative day 1 and postoperative day 1 to day 5 respectively.

The patient baseline data will be prospectively extracted from the medical records and entered into a database.

Preoperative baseline status

Patients who are awake before surgery and with a planned postoperative ICU admission will receive preoperative assessment by nurses. The health-related quality-of-life (HRQoL)，activities of daily living, anxiety and depression level, sleep quality before surgery, duration of fluid fasting, pain level and ASA class (American Society of Anaesthesiologists Classification) will be evaluated and recorded by nurses and anaesthetists. Ability of hearing and vision will be assessed during the interview with the patients. We will use the numeric rating scale (NRS) to assess pain level and the Modified Barthel Index to measure activities of daily living (Shah, Vanclay, & Cooper, 1989). The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) will be used to evaluate anxiety and depression level before surgery. Sleep quality will be assessed as good, average and bad according to patients' self-report. Patients' preoperative comorbidities will be assessed using the Charlson Comorbidity Index (CCI) (Charlson et al., 1986). Preoperative medications and examinations in the hospital will be extracted from the medical records. For liver surgery patients, the preoperative hepatic encephalopathy will be diagnosed and recorded by doctors; for cardiac surgery patients, the preoperative New York Heart Association (NYHA) functional classification will be evaluated and recorded by doctors.

Intraoperative risk factors

Intraoperative data will be collected from the information system used at the operation theatres, including date of surgery, surgical procedure, procedure urgency, type of anaesthesia, drug use, blood transfusion, operation time and arterial blood gas analysis. Occurrence of hypotension and duration will be recorded, which is defined as Mean Arterial Pressure <60mmHg. For cardiac surgery patients, duration of cardiopulmonary bypass, duration of cerebral perfusion (if any), number of bridge vessels (if it is Coronary Artery Bypass Grafting) and aortic cross clamp time will be collected.

Postoperative risk factors

Postoperative data will be collected from the medical information system and nursing documents, including APACHE II (Acute Physiology And Chronic Health Evaluation scoring system II) and/or EuroScore II (European System for Cardiac Operative Risk Evaluation II), blood transfusion, drug use, duration of intubation, sedation and pain level, reoperation, examinations, time and pattern of family visit, duration of extracorporeal life support treatment (including continuous renal replacement therapy, intra-aortic balloon pump and extracorporeal membrane oxygenation), comorbidities and length of surgical ICU stay and hospital stay. Vital signs and arterial blood gas analysis at ICU

admission will also be recorded. Critical care Pain Observation Tool (CPOT) will be used to assess pain level for intubated patients, the NRS will be used for non-intubated patients.

Short-term and long-term outcomes

Short-term outcomes are defined as duration of ICU stay, duration of hospital stay, hospital mortality and medical expense. Patients who had POD during ICU stay will be followed at 1 month, 3 months, 6 months, 12 months, 18 months and 24 months after hospital discharge. Patients will be asked the health state after hospital discharge via telephone or WeChat® (a most commonly used communication software in China). The mortality is defined as all-cause death postoperatively. The readmission is defined as all-cause readmission to hospital after initial discharge. The reason of readmission will also be recorded.

At 6 months, 12 months and 24 months, delirious patients will be invited to the hospital to revive mental assessment by Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). The HRQoL will be evaluated using the 12-Item Short Form Health Survey (SF-12) (Ware, Kosinski, & Keller, 1996). The questionnaire consists of 12 questions categorised into eight domains (physical function, role physical, bodily pain, general health, vitality, social function, role emotion and mental health). This generic instrument is shown to be valid and reliable in the Chinese

population (Lam, Lam, Fong, & Huang, 2013). The SF-12 will be investigated online by sojump (website, 2018). The baseline of HRQoL will be evaluated for all participants before surgery.

2.7 Data management

All the data will be entered and stored in the Research Electronic Data Capture (REDCap), which will be securely locked, and password protected. It is supported and maintained by the Evidence-based centre of Fudan University. Data management and analysis, including data audit, import and tracking will be done by the biostatisticians in the centre. Each patient will be given a study identification number; all paper files will be imported to the database once completed.

2.8 Statistical analysis

The incidence of POD will be described by the percentage – number of patients diagnosed with delirium after surgery divided by the total number of patients recruited in the study. The POD profile will be presented by delirium duration, delirium severity, delirium subtypes and associated outcomes. Delirium duration and severity, delirium subtype, associated outcomes and perioperative data recoded will be summarized using descriptive statistics including mean, SD, median range and frequency tables.

For developing the prediction model, we will use univariate logistic regression to assess the association between each potential determinant and the two groups (presence or absence of delirium). We will include determinants which are statistically or clinically significant and exclude a prevalence rate below 10%. Then we will use bootstrap resampling to model the prediction of POD given the included determinants using a multivariate logistic regression analysis (Moons et al., 2015; Steyerberg et al., 2001). We will use bootstrapping techniques to adjust for overfitting—that is, for overly optimistic estimates of the regression coefficients of the risk factors in the final model. Missing data will be handled using a multiple imputation procedure among the potential determinants. We will estimate the prediction ability of the model to discriminate between patients with and without delirium by using the area under the receiver operating characteristics curve (AUROC). The prediction model will be applied to the validation sample for the external validation. We will estimate the model performance by building a new AUROC.

The impact of delirium on short-term outcomes will be compared between patients' presence and absence of delirium. Delirium duration and severity will be divided into groups and associated outcomes will be compared between groups. Continuous variables will be compared using the Student's t-test or the Wilcoxon rank-sum; categorical variables will be compared by Pearson's X^2 test

or Fisher's exact test. The long-term outcomes including mortality, readmission and HRQoL will be compared among POD patients. Univariate and multi logistic regression will be used to find out predictors of associated outcomes.

2.9 Ethical considerations

This study was approved by the Hospital Ethics Board in May 2018 (B2018-071). The study will be conducted in accordance with the International Council for Harmonization and Good Clinical Practice principles. The study will adhere to the ethical principles stated in the Declaration of Helsinki (W. M. Association, 2018).

All patients will receive written and verbal information of the study before surgery. Written informed consent will be obtained before surgery. Patient have the right to withdraw from the study at any time. Data collection will be stopped, and patients' record will be deleted from the database if a patient withdraws from the study.

2.10 Validity, reliability and rigour

In this study, we will use several instruments including CAM-ICU, CAM-ICU-7 and SF-12. The validity and reliability will be tested with the baseline data. The consistency test of CAM-ICU between different auditors will be tested before the study. Furthermore, we will report the results of

the cohort study following the STROBE statement (von Elm et al., 2014) and report the prediction model according to TRIPOD statement (Collins, Reitsma, Altman, & Moons, 2015).

3. DISCUSSION

POD can cause a burden to patients both short-term and long-term. Although patients will be recovered from their surgeries, families of patients with POD can experience difficulties with their beloved once by the mental symptoms of delirium. As a consequence of both the complex ICU environment and isolation from families in the ICU, patients who underwent major surgeries tend to have higher possibilities to present delirium during ICU stay (Pipanmekaporn et al., 2015). To our knowledge, no studies have been performed to develop a prediction model of delirium for surgical ICU patients. The PREDICt study expects to develop a delirium prediction model for surgical ICU patients based on comprehensive investigation of potential predictors. In clinical practice, the prediction model resulting from our study might offer an effective tool for ICU nurses to detect high-risk patients, which can inform nurses to implement preventive interventions at the early stage and pay more attention to targeted patients. We expect that this tool can contribute to the reduction of the incidence of POD in ICU and improve quality of life after ICU discharge.

Our study will reveal the associated outcomes, especially the long-term outcomes of patients with delirium in the ICU period. To better understand the impact of delirium on long-term outcomes, we will determine the associated values and predictors of mortality, readmission and HRQoL. Our findings will provide an understanding of different types and severity of delirium on the outcomes of different kinds of patient populations. These findings will be useful for further intervention studies to improve long-term outcomes of delirious patients.

3.1 Limitations

The study has several limitations. First, although we plan to recruit a large sample in our study, it's a single centre which may lower the representativeness of the results. Patients recruited in this study are from a large tertiary hospital, patients tend to have more serious disease and undergo more complicated surgeries than patients in general hospitals. Second, we are using CAM-ICU and CAM-ICU-7 to detect delirium and assess its severity twice a day, both instruments have high sensitivity and specificity. However, as delirium status changes over time, it's difficult to exactly depict the profile of delirium progression. Third, we acknowledge that the study only includes surgical patients with a planned ICU admission. Surgical patients with an unplanned or urgent postoperative ICU admission are excluded and can be at risk of POD (Wassenaar et al., 2015). We

aim to study this specific group of patients in a follow-up study (Pandharipande et al., 2017). Lastly, the prediction model developed in the PREDICt study will not be externally validated among a large sample from another population, which will be conducted in a follow-up study.

4. CONCLUSION

POD is a frequent complication in patients admitted to an ICU postoperatively, which is associated with morbidity and can be a burden to patients and their families. This study will offer a prediction tool to recognize high-risk patients in ICU which can provide a reference for ICU nurses to implement prevention strategies. Furthermore, the study will identify short-term and long-term outcomes of delirium patients and explore predictors of long-term outcomes.

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Table 1 The Confusion Assessment Method for the ICU-7 Delirium Severity Scale

Items	Grading
1. Acute onset or fluctuation of mental status	0 for absent
Is the patient different than his/her baseline mental status? or Has the patient had any fluctuation in mental status in the past 24 hr as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/Sedation-Agitation Scale), Glasgow Coma Scale, or previous delirium assessment?	1 for present
2. Inattention	0 for absent (correct: ≥8)
Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand." Read letters from the following letter list in a normal tone 3 s apart. "SAVEAHAART" (Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A.")	1 for inattention (correct: 4-7) 2 for severe inattention (correct: 0-3)
3. Altered level of consciousness	0 for absent (RASS: 0)
Present if the actual RASS score is anything other than alert and calm (zero)	1 for altered level (RASS: >1, <1) 2 for severe altered level (RASS: >1, < -1)
4. Disorganized thinking	
Yes/no questions 1. Will a stone oat on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail?	
Errors are counted when the patient incorrectly answers a question.	

Command: Say to patient "Hold up this many fingers" (Hold two fingers in front of patient). "Now do the same with the other hand" (Do not repeat number of fingers)

An error is counted if patient is unable to complete the entire command.

ICU = Intensive Care Unit; RASS = Richmond Agitation-Sedation Scale;

Table 2 Classification and definition of delirium subtype

Delirium subtype	CAM-ICU	RASS
Hyperactive	positive	+1 ~ +4
Hypoactive	positive	0 ~ -3
Mixed	positive	both

CAM-ICU = Confusion Assessment Method for Intensive Care Unit;

RASS = Richmond Agitation-Sedation Scale

数据录入表单	Perioperative 术前访视 (1)	Intraoperative 术中情况 (2)	Postoperative in ICU 术后 ICU (3)	Postoperative in ward 术后 病房 (4)	Postoperative 1 month 出院 1个月 (5)	Postoperative 3 month 出院 3个月 (6)	Postoperative 6 month 出院 6个月 (7)	Postoperative 12 month 出 院12个月 (8)	Postoperative 18 month 出 院18个月 (9)	Postoperative 24 month 出 院24个月 (10)
Demographic characteristic 一般人口学资料	✔									
Baseline Status 术前基本情况	✔									
Health related quality of life 健康质量调查	✔						✔	✔		✔
Delirium 谵妄			✔	✔			✔	✔		✔
Lab Tests And Examination 实验室和影像学检查	✔		✔							
Surgical Factors 手术因素		✔								
Postoperative Vital Signs Icu Admission 入ICU生命体征			✔							
Postoperative blood gas analysis 入ICU血气			✔							
Condition Severity 疾病严重程度			✔							
ICU Sleep quality ICU睡眠质量			✔							
External Support 体外医疗支持			✔							
Medical Support 术后医疗支持			✔							
Blood Support 输血支持			✔							
Reoperation Possibility 再次手术可能性			✔							
Perioperative Complications 围手术期并发症	✔		✔							
Medication Use 药物使用情况	✔	✔	✔							
Mortality 死亡情况			✔		✔	✔	✔	✔	✔	✔
Readmission 再入院					✔	✔	✔	✔	✔	✔
MMSE 精神状态评估							✔	✔		✔
General report 患者情况报告			✔							

Table 3 Flow chart depicting the patients' timeline during the study.

MMSE = Mini-Mental State Examination; ICU = Intensive Care Unit

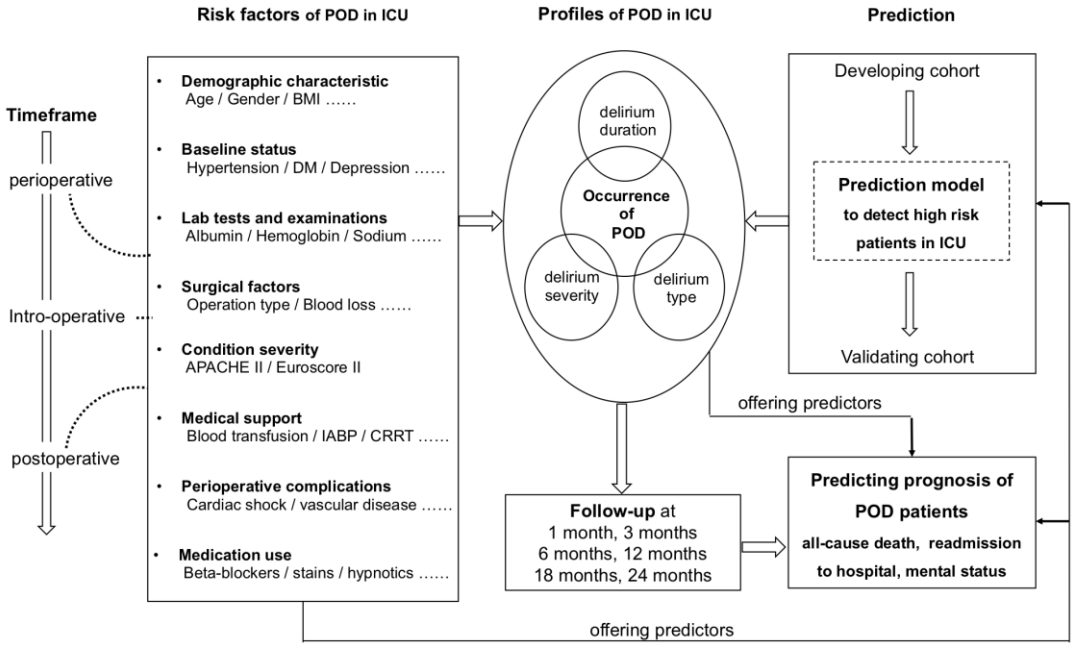

Figure 1 study framework