Preoperative risk factors for delirium after major amputation: establishment of a nomogram

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Abstract

Background: To investigate the incidence and risk factors of postoperative delirium in patients with major limb amputation and to establish a nomogram prediction model.

Methods: This is a retrospective case-control study. Patients who underwent major limb amputation (limb amputation above ankle or wrist) in a medical center from January 2017 to December 2019 were selected as subjects. The patients were assessed for delirium using the Confusion Assessment Method (CAM). Patient demographic and clinically relevant data were collected, and independent risk factors were screened using univariate analysis and logistic multivariate regression analysis. Nomograms were constructed using independent risk factors. The validation of the nomogram was assessed by the concordance index (C-index), the receiver operating characteristic (ROC) curve, and calibration curves.

Results: A total of 120 patients with major amputation were included, and 46 patients developed postoperative delirium, with an incidence of 38.3%. Results of multifactorial logistic regression analysis showed that age, Barthel classification, admission to ICU (intensive care unit) after surgery, and postoperative albumin level were independent risk factors for the occurrence of postoperative delirium. The area under the receiver operator characteristics curve for the constructed model was 0.918(95%CI,0.869-0.967), and the regression model results were reliable.

Conclusion: The incidence of postoperative delirium is high in patients with major amputation, and the incidence of delirium is high in amputation patients with higher age, low Barthel index, postoperative admission to ICU, and low postoperative albumin. The nomogram model constructed based on these risk factors can better predict the occurrence of postoperative delirium after amputation and provide reference for early intervention treatment.

Background

In the United States, 185,000 people are expected to experience amputations each year [1],and a total of 3.6 million people are expected to be living with amputations by 2050 [2].In a US trial of 1002119 lower extremity amputees, the causes of amputation were 1. chronic ischemia (72%), 2. acute limb ischemia (ALI) (4%), 3. infection (15.1%), 4. tumor (1.2%), 5.trauma (3.6%), 6. other or any combination of these indications (4%), with 61.1%of patients having a combination of diabetes [3]. Amputation causes significant physical and psychological trauma to the patient and increases the risk of depression and anxiety [4].Delirium is an important complication in patients with amputation.

Delirium, also known as acute confusional state, is characterized by impairment of consciousness, cognitive function or perception, with an acute onset and an undulating course [5].Delirium costs more than $164 billion annually in the United States [6].POD(postoperative delirium) is common in hospitalized patients, with the incidence of postoperative delirium ranging from 2–72%, with a higher incidence in older patients [7].The main factors that cause delirium to occur include predisposing and precipitating factors, The more predisposing factors that are present, the fewer precipitating factors that are needed[8]. In the treatment of delirium, 30–40% of the cases are preventable [9],which provides a realistic basis for us to establish a predictive model.

In limb surgery, amputation is considered to be the last treatment, which is a double blow to the patient's body and psychology, especially in sudden trauma, acute limb ischemia, where patients have no psychological expectation and postoperative phantom pain, which may cause a high incidence of delirium. With the increase in the number of diabetic patients worldwide, patients with peripheral neuropathy will face an increased risk of amputation. Past literature suggests a high incidence of post-amputation delirium in vascular surgery [10],but it has not been studied in detail in amputation patients. Therefore, the aim of this study was to determine the incidence and risk factors of postoperative delirium in amputated patients and to create a nomogram. To provide a reliable and accurate theoretical basis for the prevention and treatment of postoperative delirium.

Method

Patients

This was a retrospective case-control study. All included cases were recorded in the Human Genetic Resources Center of the First Affiliated Hospital of Nanchang University, and received ethical approval from the review committee of the First Affiliated Hospital of Nanchang University. The medical records of patients who underwent major limb amputation[11] (above ankle or wrist) from January 2017 to December 2019 were reviewed. Inclusion criteria were as follows (I) undergoing major limb amputation (II) age over 18 years old. Exclusion criteria were as follows: (I) preoperative history of schizophrenia, epilepsy, Parkinson's syndrome, or dementia; (II) patients with multiple trauma resulting in damage to other systems; (III) patients with trauma resulting in cranial brain injury (e.g., subdural hematoma, spinal cord injury) with clear imaging evidence; (IV) patients with new cerebral infarction in the hospital; (V) Patients who are re-admitted for amputation for same limb. Specific inclusion and exclusion criteria are shown in(Figure 1).

Data collection

Baseline characteristics: In order to assess the risk factors for the development of postoperative delirium in amputated patients, baseline characteristics of all included patients were collected, including age, gender, marital status and comorbidities. In particular, details were recorded as to what caused the patient's amputation, the site of amputation. Comorbidities recorded included history of cardiovascular disease (hypertension, coronary artery disease, arrhythmia, heart failure, etc.), history of smoking and alcohol consumption, history of previous surgery, hearing and vision status, literacy level, and history of cerebral infarction. The Barthel index was scored when they were admitted to the ward. The Barthel index refers to: grading of self-care ability: 10 items were rated for eating, bathing, grooming, dressing, toileting, bowel control, urine control, bed and chair transfer, level walking, and stair climbing, and the scores were summed to give a total score. The scores of each item were summed to obtain the total score. A total score of < = 40 was considered as severe dependence, which required care from others; a total score of 41–60 was considered as moderate dependence, which required care from others; a total score of 61–99 was considered as mild dependence, which required care from others; and a total score of 100 was no dependence, which required no care from others[12].

Perioperative characteristics: preoperative factors: blood pressure value and classification measured for the first time on admission, random blood glucose value, HCT value, time from admission to the start of surgery. Intraoperative factors: ASA classification, type of anesthesia, duration of surgery, intraoperative blood loss, and whether blood was transfused. Postoperative factors: including serum potassium ion concentration, hemoglobin concentration, albumin level, white blood cell count, postoperative infection, and whether the patient was admitted to the ICU postoperatively. For serum potassium ion concentration, hemoglobin concentration, albumin level, and white blood cell count, we recorded preoperative levels and levels on the second postoperative day (patients mostly had delirium on the second postoperative day). As we were a retrospective case-controlled study, we also recorded the mode of payment for medical care, the number of days of hospitalization, and the cost of hospitalization.

Assessment of delirium

The Confusion Assessment Method (CAM) as the most useful bedside assessment tool for diagnosing delirium [13]。The CAM establishes a diagnosis of delirium based on the presence or absence of four features: dramatic changes in mental status accompanied by a fluctuating course, inattention, and disorganized thinking or altered level of consciousness[5](Figure 2)。Suspected symptoms of POD were assessed postoperatively on a daily basis by a physician who had systematically learned delirium assessment and a trained nurse according to the Confusion Assessment Method (CAM).The 3D-CAM [14] diagnostic tool was used for patients in the general ward and the CAM-ICU [15] diagnostic tool was used for patients in the intensive care unit (ICU). Both diagnostic tools are derivatives of CAM diagnostic tool.

Statistical analysis

Categorical variables were presented as frequencies and percentages, and continuous variables are expressed as medians (interquartile range [IQR]) or means (standard deviations). Between-group comparisons for categorical variables were performed using the chi-square test and Fisher's exact test if the expected frequency of more than 20% was less than 5. The Kolmogorov-Smirnov test was used to test normality for continuous variables, while between-group comparisons for continuous variables were performed using the Student's t test or the Wilcoxon rank sum test. Multi-factor logistic regression analysis was performed on variables that were statistically significant in the univariate analysis to determine the extent to which the variables were associated with the Odds ratio (OR) and 95% confidence interval (95% CI). Statistical analyses were performed using SPSS® version 26.0 (SPSS Inc., Chicago, IL, USA), and $P < 0.05$ were considered statistically significant. For the independent risk factors established by the multifactorial logistic regression method, a nomogram model was developed using the R software package "RMS" (http://www.r-project.org/). The predictive performance of the nomogram was measured by the coordination index (C-index) and calibration curves for 1000 Bootstrap samples to reduce overfitting bias. ROC curve analysis was used to calculate the optimal threshold value determined by maximizing the Jorden index (ie, sensitivity + specificity-1). The accuracy of the best cut-off value is assessed by sensitivity and specificity.

Result

A total of 180 patients were collected from January 2017 until December 2019 according to pre- defined inclusion and exclusion criteria, 67 patients were excluded, and a total of 120 amputated patients were included. There were 74 cases in the non-delirium group and 46 cases in the delirium group. The prevalence of postoperative delirium was 38.3%, with 36 males and 10 females, median age 67 years (IQR: 17), and delirium lasting 4 (IQR = 4) days.

The results of the univariate analysis of risk and prognostic factors are shown(Table 1).Age (P = 0.001), rapidity of amputation occurrence (P = 0.038), total number of surgeries (P = 0.009), the Barthel index(P = 0.011), VET (P < 0.001),blood glucose values on admission (P = 0.001), HCT on admission (P = 0.011),history of previous surgery (P = 0.021), hearing and vision status (P = 0.009), history of cerebral infarction (P = 0.020), history of cardiovascular disease (P = 0.044, anesthesia ASA classification (P < 0.001), type of anesthesia (P = < 0.001), intraoperative blood loss (P = 0.001), tracheal intubation (P < 0.001), infection (P = 0.001), and postoperative admission to the ICU (P < 0.001) ,preoperative hemoglobin (P = 0.015), postoperative hemoglobin (P = 0.002), postoperative white blood cell count (P = 0.005), preoperative albumin (P < 0.001), and postoperative albumin (P < 0.001) are risk factors for postoperative delirium.

Table 1
Basic characteristics of patients

Variable	No delirium(n = 74, 61.7%)	Delirium (n = 46, 38.3%)	Total(n = 120)	*P*-value	Odds ratio(CI95%)
Sex, male	61(82%)	36(78%)	97(80%)	0.572	1.303(0.519,3.276)
Age(IQR)	54(21)	67(17)	59(22)	**0.001**	1.046(1.017,1.076)
Reason of amputation					
trauma	20(27.1%)	20(43.5%)	40(33.3%)	0.134	2.000(0.855,4.681)
chronic ischemia	34(46.0%)	17(37%)	51(42.5%)	Ref	
infection	14(18.9%)	6(13%)	20(16.7%)	0.787	0.857(0.280,2.626)
others	3(4.1%)	3(6.5%)	6(5.0%)	0.654	2.000(0.364,10.980)
tumor	3(4.1%)	0(0%)	3 (2.5%)	0.544	0.667(0.549,0.809)
Duration of admission until surgery				**0.038**	2.217(1.038,4.738)
≤ 8 hours	23(31.1%)	23(50.0%)	46(38.3%)		
>8 hours	51(68.9%)	23(50%)	74(61.7%)		
Upper and lower limbs, lower limb	63(85.1%)	39(84.8%)	102(85%)	0.958	1.028(0.368,2.875)
Left or right limbs(left/right/both)	35/38/1	23/21/2	58/59/3	0.590	1.010(0.515,1.981)
Barthel index[c]				**< 0.001**	5.348(2.773,10.313)
100	4	0	4	Ref	
61–99	25	3	28	1.000	1.120(0.985,1.273)
41–60	32	11	43	0.560	1.344(1.128,1.601)
<=40	13	32	45	**0.011**	3.462(2.189,5.475)
VTE(IQR)	4(1)	6(1)	5(2)	**< 0.001**	2.499(1.668,3.745)
Blood glucose at admission(IQR)	6.06(3.9)	9.9(4.8)	7.39(4.25)	**0.001**	1.065(0.993,1.142)
HCT at admission(IQR)	0.309(0.130)	0.271(0.088)	0.284(0.114)	**0.011**	0.001(0.000,0.221)
Hospital stay(IQR)	17.5(15)	25(29)	20.5(20)	**0.012**	1.027(1.005,1.051)

IQR(interquartile range);VTE(venous thromboembolism); HCT(hematocrit); ASA (American Society of Anesthesiologists); ICU(intensive care unit); CI(Confidence interval); WBC (white blood cell); Hb (Hemoglobin);

Variable	No delirium(n = 74, 61.7%)	Delirium (n = 46, 38.3%)	Total(n = 120)	*P*-value	Odds ratio(CI95%)
Marital status, married	58(78%)	40(88%)	98(81.7%)	0.238	0.544(0.196,1.510)
Hospitalization expenses(IQR)	32079.5(24754)	94961(129705)		< 0.001	
Medical history					
alcohol	17(23%)	9(19.6%)	26(21.7%)	0.660	0.816(0.329,2.022)
Previous operation history	35(47.3%)	12(26.1%)	47(39.2%)	**0.021**	0.393(0.177,0.876)
Vision and hearing	21(28.4%)	24(52.2%)	45(37.5%)	**0.009**	2.753(1.277,5.935)
History of cerebral infarction	1(1.4%)	5(10.9%)	6(5%)	**0.02**	8.902(1.005,78.820)
Cardiovascular disease	15(20.3%)	17(37.0%)	32(26.7%)	**0.044**	2.306(1.011,5.258)
Classification of blood pressure at admision	47/21/6/0	30/13/3/0	77/34/9/0	0.947	0.920(0.510,1.659)
Classification of ASA(II/III/IV)				**< 0.001**	6.500(2.886,14.638)
II	29	1	30	Ref	
III	39	29	68	**< 0.001**	21.564(2.774,167.605)
IV	6	16	22	**< 0.001**	77.333(8.541,700.198)
Anesthesia				**< 0.001**	4.235(1.835,9.777)
general	34(45.9%)	36(78.3%)	70(58.3%)		
epidural	40(54.1%)	10(21.7%)	50(41.7%)		
Intraoperative blood loss(IQR)	200(100)	200(225)	200(200)	**0.001**	1.003(1.001,1.004)
surgery time(IQR)	90(45)	120(76)	90(45)	0.219	1.006(0.999,1.012)
Traches intubation	7(9.5%)	23(50%)	30(25%)	**< 0.001**	9.571(3.630,25.239)
Infection	16(21.6%)	24(52.2%)	40(33.3%)	**0.001**	3.955(1.776,8.806)
Enter to ICU	7(9.5%)	32(69.6%)	39(32.5%)	**< 0.001**	21.878(8.046,59.486)

IQR(interquartile range);VTE(venous thromboembolism); HCT(hematocrit); ASA (American Society of Anesthesiologists); ICU(intensive care unit); CI(Confidence interval); WBC (white blood cell); Hb (Hemoglobin);

Variable	No delirium(n = 74, 61.7%)	Delirium (n = 46, 38.3%)	Total(n = 120)	*P*-value	Odds ratio(CI95%)
Hemoglobin level(g/L)					
Preoperative Hb level(IQR)	101.5(43.5)	93.5(28.3)	100.3(38.5)	**0.015**	0.978(0.963,0.994)
Postoperative Hb level(IQR)	87.0(33)	75.0(28)	85.0(29)	**0.002**	0.961(0.940,0.982)
K+(mmol/L)					
Preoperative K+	3.87(0.49)	3.85(0.62)	3.87(0.54)	0.809	0.919(0.465,1.816)
Postoperative K+	3.93(0.47)	3.74(0.67)	3.86(0.56)	0.094	0.527(0.262,1.062)
White blood cell count(10*10^9/L)					
Preoperative WBC(IQR)	9.9(7.4)	10.24(7.36)	11.6(6.93)	0.314	1.041(0.982,1.103)
Postoperative WBC(IQR)	8.9(4.2)	18.9(6.37)	10.42(5.31)	**0.005**	1.140(1.035,1.255)
Albumin(g/L)					
Preoperative albumin	32.6(7.3)	27.9(4.9)	30.8(6.8)	**< 0.001**	0.894(0.839,0.953)
Postoperative albumin	29.9(5.0)	26.1(5.1)	28.5(5.4)	**< 0.001**	0.859(0.791,0.933)
IQR(interquartile range);VTE(venous thromboembolism); HCT(hematocrit); ASA (American Society of Anesthesiologists); ICU(intensive care unit); CI(Confidence interval); WBC (white blood cell); Hb (Hemoglobin);					

Numbers in bold: Statistically significant difference

Variables with $P < 0.05$ in the univariate analysis table were included in the multifactorial logistic analysis using stepwise forward regression analysis. The multifactorial model showed age (OR1.057, [95% CI1.013-1.103], P = 0.010), Barthel classification (OR3.113, [95% CI1.342-7.219], P = 0.008), postoperative ICU admission (OR14.905, [95% CI4.306-51.597] P < 0.001), and postoperative albumin (OR0.856, [95% CI0.753-0.974], P = 0.018) was an independent risk factor for the development of delirium and had the greatest impact on delirium(Table 2).

Table 2
Multivariate analysis of the variables

							95%CI	
	B	SE	Wald	df	*P*-value	OR	Upper	Lower
age	0.056	0.022	6.612	1	0.010	1.057	1.013	1.103
Barthel index	1.135	0.429	6.998	1	0.008	3.113	1.342	7.219
Enter to ICU	2.702	0.634	18.183	1	0.000	14.905	4.306	51.597
Postopertative albumin	-0.155	0.066	5.591	1	0.018	0.856	0.753	0.974

Independent risk factors (age, Barthel classification, postoperative admission to ICU, postoperative albumin) derived from a multifactorial logistic regression analysis were used to plot delirium prediction nomograms(Figure 3).The resulting model was internally validated using a bootstrap validation method (Bootstrap validation method).

The mixed test of the model coefficients (chi-square=76.974, $p<0.001$) suggested that the model passed the Omnibus test. The maximum likelihood ratio test showed a maximum likelihood logit value of 82.788, Cox & Snell R^2 value=0.473 and Nagelkerke R^2 value=0.643, both with R^2 values less than 1. All these results indicate that the model fits well and the obtained logistic model is statistically significant. The ROC curve was plotted using spss software(Figure 4),with an AUC(area under the curve) of 0.918, CI95 of 0.869–0.967, $p<0.001$, Jorden index of 0.697, sensitivity of 0.913 and specificity of 0.784, suggesting that the model works well. 1000 bootstrap calibration curves showed that the actual observed and predicted rates of the model there is good agreement between the probabilities (Figure 5).

Discussion

This study shows the predictive value of various preoperative and intraoperative risk factors for the occurrence of delirium after amputation surgery and establishes a nomogram. The incidence of postoperative delirium varies with the type of surgery, and several past publications have shown that the incidence of postoperative delirium in amputation patients is significantly higher than in other vascular surgical procedures and serves as an independent risk factor for postoperative delirium. [16][17][18][19].Through literature search, it is found that there are a few articles on various causes of postoperative delirium in amputated patients, so we separately study the postoperative delirium in amputated patients.

In this retrospective article, the incidence of delirium after amputation was 38.3%. The independent risk factors of postoperative delirium were determined by age, Barthel grade, entry into ICU and low serum albumin after operation. The nomogram is established according to four independent risk factors, and the test shows that the prediction effect of the model is good. The prognosis of patients with postoperative delirium is worse, and the occurrence of delirium indicates longer hospitalization time and higher hospitalization cost.

In our study, age was an independent risk factor for postoperative delirium, as has been previously reported in several papers [5][20]，Although a single factor can lead to delirium, usually delirium in the elderly is multifactorial [20]，Older patients are thought to be more susceptible to the reduced reserve capacity of the brain in the elderly and the gradual accumulation of permanent damage to neurons, dendrites, receptors and microglia[21],because of the link between aging and impaired physiological compensatory capacity to adapt to the physical stress of surgery when these patients already have coexisting conditions [22].Older patients are more vulnerable and present with more susceptibility factors compared to younger patients, and are more likely to suffer postoperative delirium with the same predisposing factors.

Barthel Index is also an independent risk factor for delirium. The Barthel Index is divided into 4 levels, which represent the patient's ability to take care of himself/herself in daily life[12].However, no significant correlation was found in the shin.et al article[23], possibly due to differences in the assessment tools used. When patients live their lives only through the help of others and lack autonomy. Especially in amputated patients, leg amputation leads to a reduced range of motion, confining the patient to the bed most of the time and diminished spatial perception. Patients with arm amputation have a reduced ability to take care of themselves and lose their basic life skills, especially in the short time after amputation, they are still unable to adapt to the way of life in the amputation state, which will increase the incidence of delirium[24].

Postoperative admission to ICU was the most significant independent risk factor in our study. Postoperative admission to ICU or not was done only after a systemic assessment. It represents a poorer current condition of the patient. However, the question of whether the ICU environment contributes to increased delirium risk in patients was not clarified in our study. Insomnia and constant exposure to light and noise are among the stressors for patients[25].Current guidelines suggest that [26], where possible, patients are given space and time for recognition and early access to their own families whenever possible. In the ICU environment, the inability to recognize day from night, disorientation and disturbance of the sleep-wake cycle, and the inability of family members accompany may lead to the occurrence of delirium.

Postoperative albumin is an independent risk factor for delirium after major limb amputation. The relationship between albumin levels and the development of postoperative delirium has been reported in different surgical populations. In a cohort study of elderly patients admitted to ICU for non-cardiac surgery, Dan-Fengzhang et al. [27] pointed out that lower albumin levels have a higher risk of delirium. Albumin has been hypothesized to be an overall biomarker of frailty and nutritional and functional abilities.[28] Weaker patients are more likely to develop delirium. At present, the pathophysiological mechanism of delirium caused by hypoalbuminemia is not clear. The possible reason is that it affects the metabolism of drugs and toxins, because albumin is the main transporter in plasma. The mechanism needs to be further studied.

Other factors are currently the subject of different conclusions in literatures. Different literatures still dispute whether postoperative infection is a risk factor for delirium[27][28][23].The pathophysiology of delirium remains incompletely elucidated, and given the complex multifactorial causes of delirium, each individual episode may have a unique set of component contributors; each group represents a discrete yet sufficient causal mechanism. Thus, a single cause or mechanism for psychosis may not be found[29].The systemic inflammatory response to sepsis can lead to a cascade of local (brain) neuroin flammation triggered by inflammatory cytokines, resulting in endothelial activation, impaired blood flow, and neuronal apoptosis. Neurological injury can lead to excessive microglia activation, resulting in a neurotoxic response and further damage to neurons[30].In the present study, the indicator of infection was bacterial culture results, and infection was a potential factor for delirium in the univariate analysis, but in the multifactorial analysis, the infection factor was corrected. Different literature gives contrasting conclusions as to whether the type of anesthesia is a risk factor for delirium[31].louis de Jong et al.[32]found that the type of anesthesia was not associated with the occurrence of delirium. Shin et al. et al.[23] found that ASA classification was not associated with delirium, but our study found that high ASA score was a risk factor for delirium in univariate analysis.

There are still some limitations of this study: firstly, this study is a retrospective chart- controlled study, which cannot fully ensure the credibility of all information, which may cause bias in the results to some extent; secondly, we used different diagnostic tools in assessing delirium in ICU wards and general wards, which may cause bias in the diagnosis of delirium; finally, the number of cases included in this study is small, and further validation of the model effect is needed at a later stage.

Conclusions

This study investigated the incidence and risk factors for delirium after amputation. We found that approximately 38.3% of elderly patients developed delirium after amputation. Among the perioperative variables, age, Barthel classification, admission to the ICU after surgery and postoperative albumin were significantly associated with the development of delirium. The nomogram achieved favorable effectiveness in predicting POD patients. Identifying risk factors for the development of postoperative delirium allows surgeons to implement interventions aimed at reducing the incidence delirium in this high-risk population, reducing the length and cost of hospitalization.

Abbreviations

CAM: confusion assessment method; C-index: concordance index; ROC: receiver operating characteristic curve; ICU: intensive care unit; ALI: acute limb ischemia; POD: postoperative delirium; HCT: hematocrit; 3D-CAM:3-minute diagnostic confusion assessment method; IQR: interquartile range; OR: odds ratio; CI: confidence interval; VTE: venous thromboembolism; ASA: American Society of Anesthesiologists; CI: Confidence interval; WBC: white blood cell; Hb: Hemoglobin; AUC: area under the curve;

Declarations

Ethics approval and consent to participate: This research was performed in accordance with the Declaration of Helsinki and approved by the First Affiliated Hospital of Nanchang University Ethic Committee. All included cases were recorded in the Human Genetic Resources Center of the First Affiliated Hospital of Nanchang University. All participants gave their informed consent in writing prior to inclusion in the study.

Consent for publication: Not applicable

Availability of data and materials: The datasets used during the current study are available from the corresponding author on reasonable request.

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Authors’ contributions

YC, TN, and JM contributed to the conception and design of the study. YC and ZP collected the data. YC and JZ performed the statistical analysis. YC wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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References

1. Owings MF, Kozak LJ. Ambulatory and inpatient procedures in the United States, 1996. Vital Health Stat 13. 1998;:1–119.
2. Ziegler-Graham K, MacKenzie EJ, Ephraim PL, Travison TG, Brookmeyer R. Estimating the Prevalence of Limb Loss in the United States: 2005 to 2050. Arch Phys Med Rehabil. 2008;89:422–9.
3. Kalbaugh CA, Strassle PD, Paul NJ, McGinigle KL, Kibbe MR, Marston WA. Trends in Surgical Indications for Major Lower Limb Amputation in the USA from 2000 to 2016. Eur J Vasc Endovasc Surg. 2020;60:88–96.
4. Nightingale S, Holmes J, Mason J, House A. Psychiatric illness and mortality after hip fracture. The Lancet. 2001;357:1264–5.
5. Marcantonio ER. Delirium in Hospitalized Older Adults. N Engl J Med. 2017;377:1456–66.
6. Leslie DL. One-Year Health Care Costs Associated With Delirium in the Elderly Population. Arch Intern Med. 2008;168:27.
7. Sasajima Y, Sasajima T, Uchida H, Kawai S, Haga M, Akasaka N, et al. Postoperative Delirium in Patients with Chronic Lower Limb Ischaemia: What are the Specific Markers? Eur J Vasc Endovasc Surg. 2000;20:132–7.
8. Inouye SK. Precipitating Factors for Delirium in Hospitalized Elderly Persons: Predictive Model and Interrelationship With Baseline Vulnerability. JAMA. 1996;275:852.
9. Inouye SK, Bogardus ST, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, et al. A Multicomponent Intervention to Prevent Delirium in Hospitalized Older Patients. N Engl J Med. 1999;340:669–76.
10. Visser L, Prent A, van der Laan MJ, van Leeuwen BL, Izaks GJ, Zeebregts CJ, et al. Predicting postoperative delirium after vascular surgical procedures. J Vasc Surg. 2015;62:183–9.
11. Peters EJG, Childs MR, Wunderlich RP, Harkless LB, Armstrong DG, Lavery LA. Functional Status of Persons With Diabetes-Related Lower-Extremity Amputations. Diabetes Care. 2001;24:1799–804.
12. Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. J Clin Epidemiol. 1989;42:703–9.
13. Wong CL, Holroyd-Leduc J, Simel DL, Straus SE. Does This Patient Have Delirium?: Value of Bedside Instruments. JAMA. 2010;304:779.
14. Marcantonio ER, Ngo LH, O’Connor M, Jones RN, Crane PK, Metzger ED, et al. 3D-CAM: Derivation and Validation of a 3-Minute Diagnostic Interview for CAM-Defined Delirium: A Cross-sectional Diagnostic Test Study. Ann Intern Med. 2014;161:554.
15. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in Mechanically Ventilated Patients: Validity and Reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). JAMA. 2001;286:2703.

16. Sasajima Y, Sasajima T, Azuma N, Akazawa K, Saito Y, Inaba M, et al. Factors Related to Postoperative Delirium in Patients with Lower Limb Ischaemia: A Prospective Cohort Study. Eur J Vasc Endovasc Surg. 2012;44:411–5.
17. Styra R, Larsen E, Dimas MA, Baston D, Elgie-Watson J, Flockhart L, et al. The effect of preoperative cognitive impairment and type of vascular surgery procedure on postoperative delirium with associated cost implications. J Vasc Surg. 2019;69:201–9.
18. van Eijsden W, Raats J, Mulder P, van der Laan L. New aspects of delirium in elderly patients with critical limb ischemia. Clin Interv Aging. 2015;:1537.
19. Visser L, Prent A, van der Laan MJ, van Leeuwen BL, Izaks GJ, Zeebregts CJ, et al. Predicting postoperative delirium after vascular surgical procedures. J Vasc Surg. 2015;62:183–9.
20. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. The Lancet. 2014;383:911–22.
21. Izaks GJ, Westendorp RG. Ill or just old? Towards a conceptual framework of the relation between ageing and disease. BMC Geriatr. 2003;3:7.
22. M.M. de Castro S, Ünlü Ç, B. Tuynman J, Honig A, van Wagensveld BA, Steller EP, et al. Incidence and risk factors of delirium in the elderly general surgical patient. Am J Surg. 2014;208:26–32.
23. Shin Y-H, Yoon JS, Jeon HJ, Kim YB, Kim YS, Park JY. Postoperative delirium in elderly patients with critical limb ischemia undergoing major leg amputation: a retrospective study. Korean J Anesthesiol. 2018;71:311–6.
24. Robinson TN, Raeburn CD, Tran ZV, Angles EM, Brenner LA, Moss M. Postoperative Delirium in the Elderly: Risk Factors and Outcomes. Ann Surg. 2009;249:173–8.
25. Pang PSK, Suen LKP. Stressors in the ICU: a comparison of patients' and nurses' perceptions. J Clin Nurs. 2008;17:2681–9.
26. Overview | Delirium: prevention, diagnosis and management | Guidance | NICE. https://www.nice.org.uk/guidance/cg103. Accessed 30 Sep 2021.
27. Rade MC, YaDeau JT, Ford C, Reid MC. Postoperative Delirium in Elderly Patients After Elective Hip or Knee Arthroplasty Performed Under Regional Anesthesia. HSS J ®. 2011;7:151–6.
28. Slor CJ, Witlox J, Adamis D, Jansen RWMM, Houdijk APJ, Gool WA, et al. The trajectory of C-reactive protein serum levels in older hip fracture patients with postoperative delirium. Int J Geriatr Psychiatry. 2019;34:1438–46.
29. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. The Lancet. 2014;383:911–22.
30. Hughes CG, Patel MB, Pandharipande PP. Pathophysiology of acute brain dysfunction: what's the cause of all this confusion? Curr Opin Crit Care. 2012;18:518–26.
31. Marcantonio ER, Goldman L, Orav EJ, Cook EF, Lee TH. The association of intraoperative factors with the development of postoperative delirium. Am J Med. 1998;105:380–4.
32. de Jong L, van Rijckevorsel V, Raats JW, Klem TMAL, Kuijper TM, Roukema GR. Delirium after hip hemiarthroplasty for proximal femoral fractures in elderly patients: risk factors and clinical outcomes. Clin Interv Aging. 2019;Volume 14:427–35.

Figures

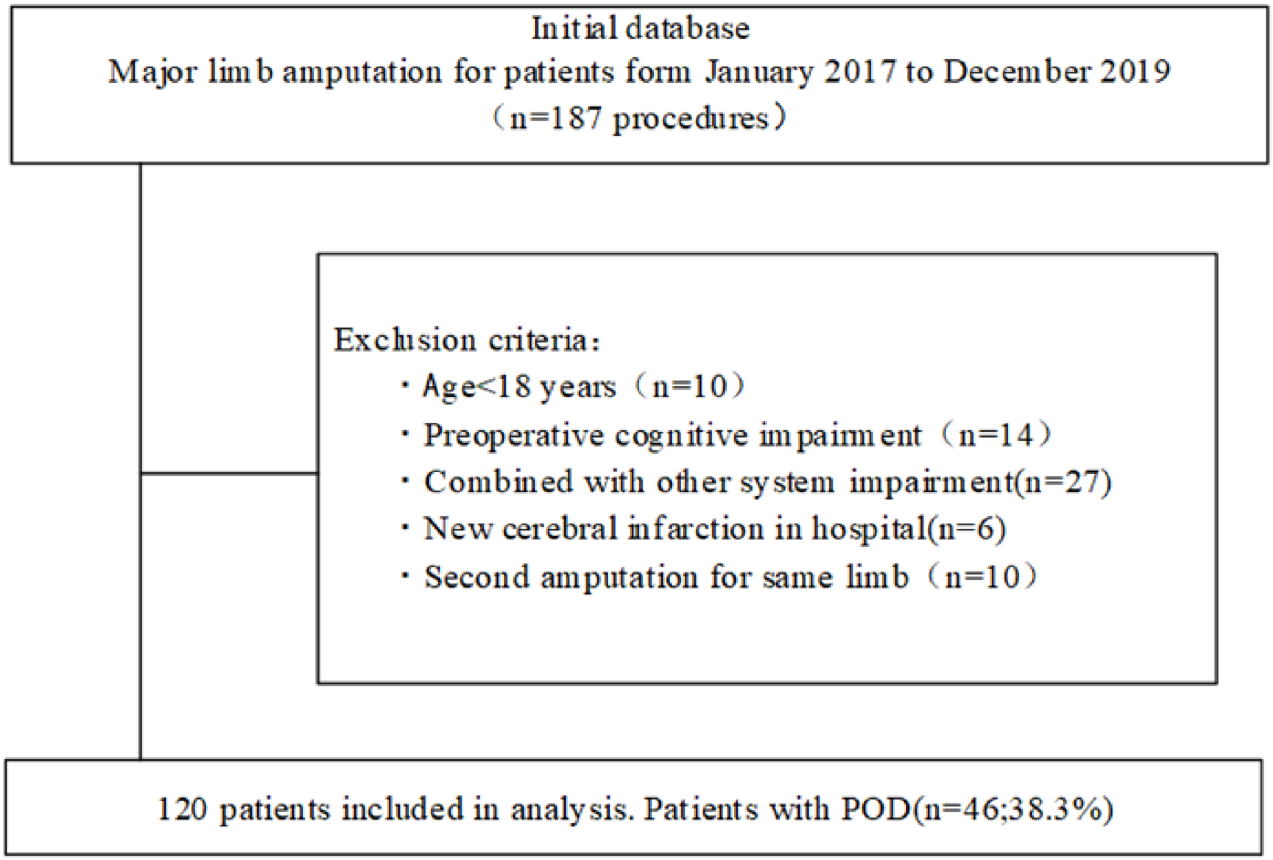

Figure 1

Inclusion and exclusion criteria

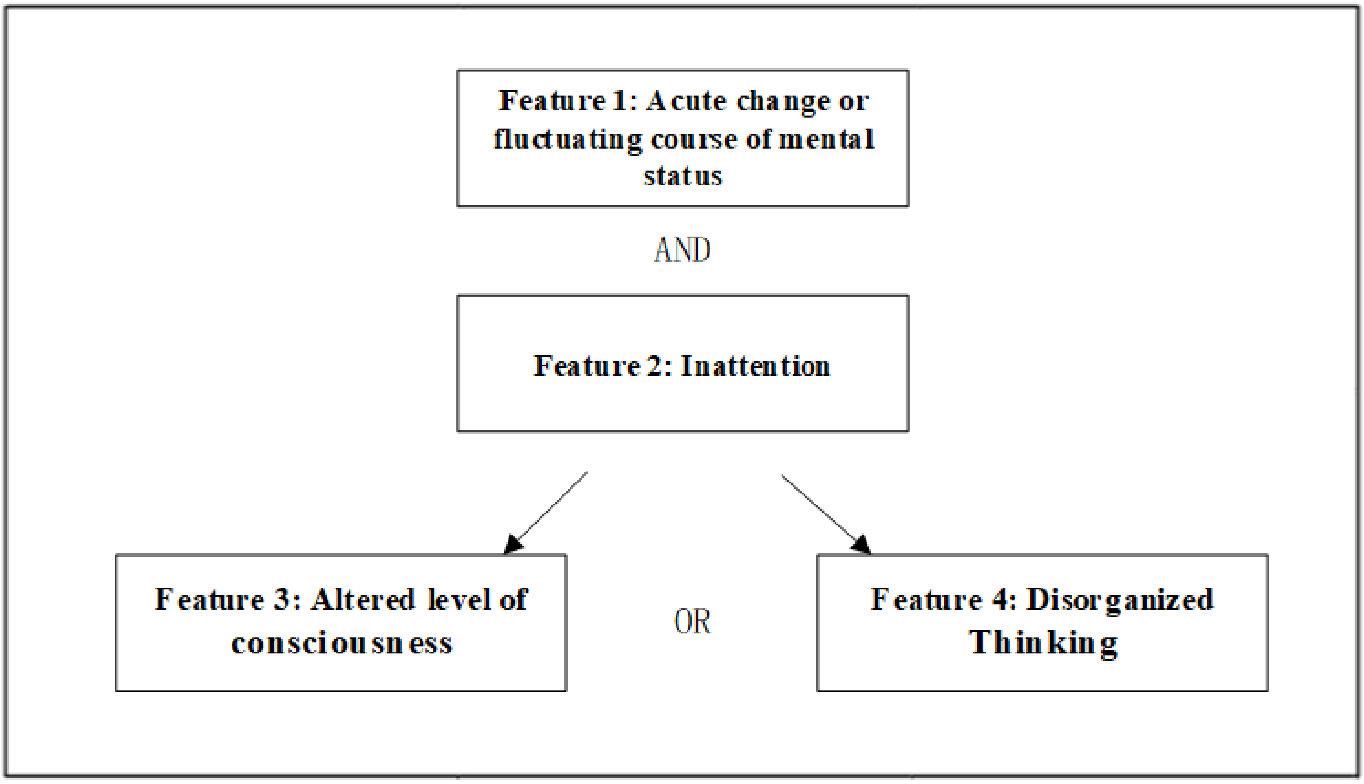

Figure 2

Diagnostic criteria of delirium

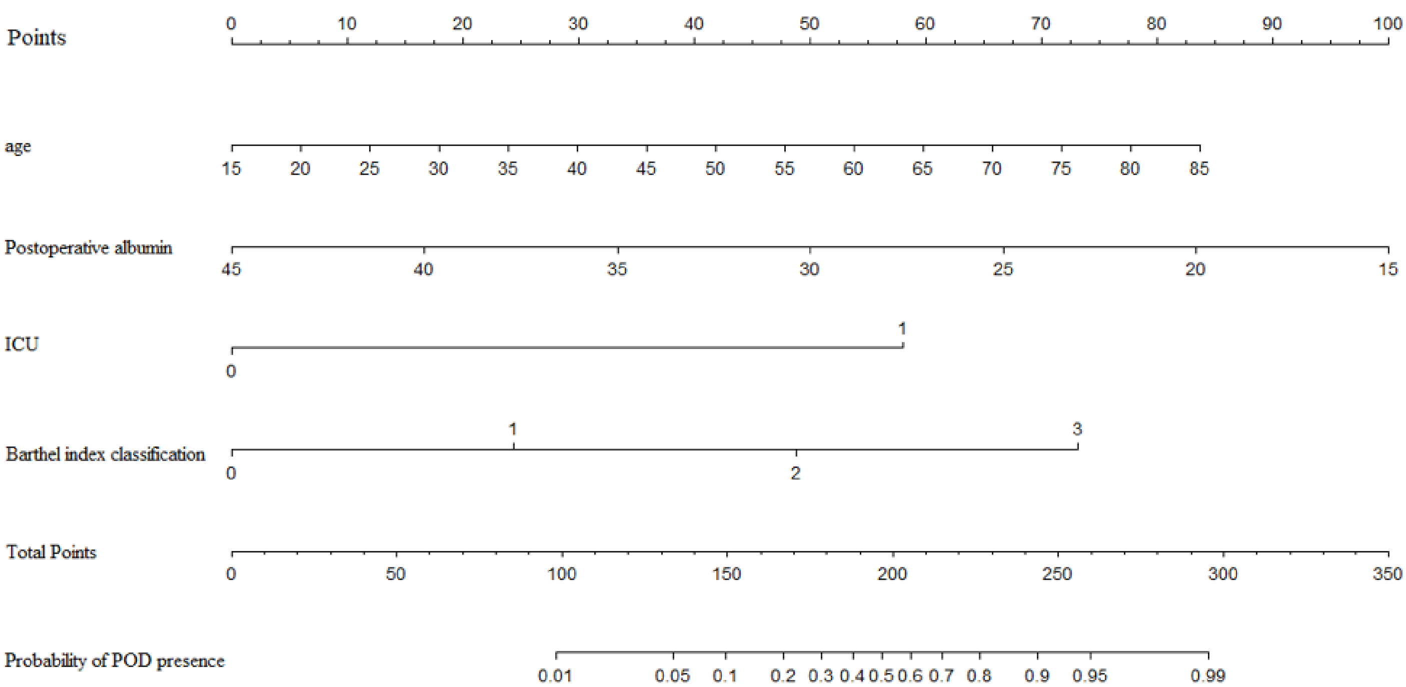

Figure 3

nomograma for delirium after major amputation

Barthel classification :0(100),1(61-99),2(41-61),3(<=40); ICU :0(no enter to ICU),1(enter to ICU).

To use the nomogram, find the position of each variable on the corresponding axis, draw a line to the points axis for the number of points, add the points from all of the variables, and draw a line from the total points axis to determine the POD probabilities at the lower line of the nomogram.

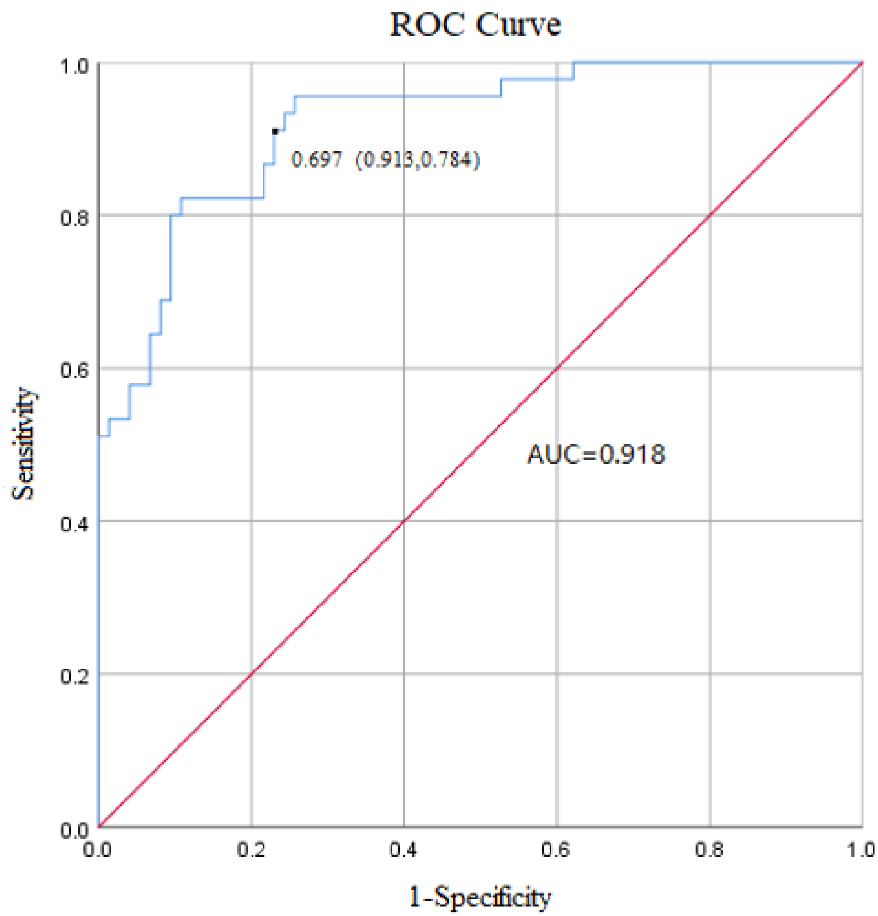

Figure 4

ROC curve for predicting the risk of delirium in amputated patients

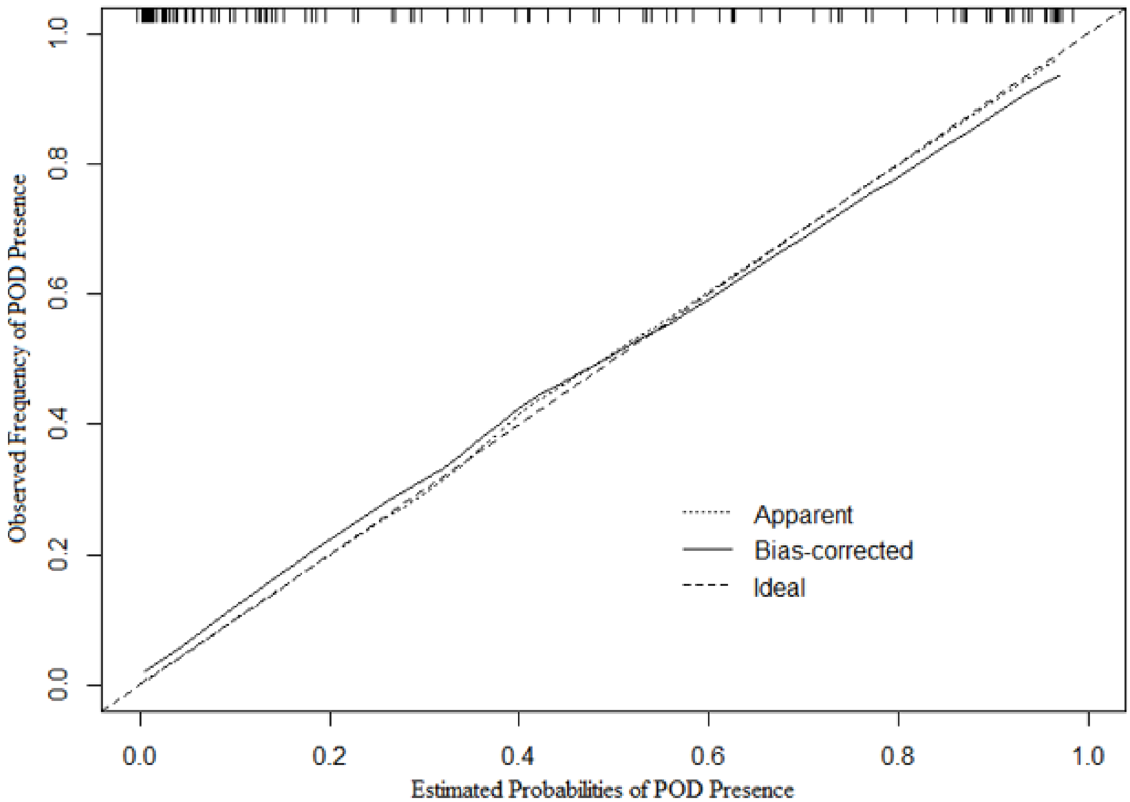

Figure 5

calibration curves