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Association between the age-adjusted Charlson Comorbidity Index and complications after kidney transplantation: a retrospective observational cohort study

Qin Huang[1†], Tongsen Luo[1†], Jirong Yang[1†], Yaxin Lu[2], Shaoli Zhou[1], Ziqing Hei[1*] and Chaojin Chen[1,2*]

Abstract

Background Complications following kidney transplantation elevate the risks of readmission and mortality. The aim of this study was to assess the association between the age-adjusted Charlson Comorbidity Index (ACCI) and postoperative complications among kidney transplant (KT) recipients.

Methods Between January 2015 and March 2021, a study involving 886 kidney transplant recipients at the Third Affiliated Hospital of Sun Yat-sen University was conducted. Postoperative complications were defined by the Clavien-Dindo Classification of Surgical Complications. Target Maximum Likelihood Estimation (TMLE) was employed to assess the association between ACCI and postoperative complications. The odds ratio (OR) was computed to determine the relationship between ACCI and postoperative complications. Subsequent interaction and stratified analyses were performed to assess the robustness of the findings.

Results Out of 859 KT participants ultimately included in the study, 30.7% were documented to have encountered postoperative complications. Participants with an ACCI value exceeding 3 exhibited a notably increased risk of postoperative complications following multivariable adjustment [aOR = 1.64, 95% CI [1.21,2.21], $p = 0.001$]. Congestive heart failure (OR = 16.18, 95% CI [1.98–132.17], $p < 0.001$), peripheral vascular disease (OR = 2.32, 95% CI [1.48–3.78], $p < 0.001$), and chronic obstructive pulmonary disease (OR = 6.05, 95% CI [2.95–12.39], $p < 0.001$) emerged as the top three preoperative comorbidities significantly linked to postoperative complications in ACCI.

Conclusion An ACCI value exceeding 3 preoperatively constituted a risk factor for postoperative complications among KT patients.

Keywords Kidney transplant, Postoperative complication, Risk factor, Age-adjusted Charlson comorbidity index, End-stage renal disease

†Qin Huang, Tongsen Luo and Jirong Yang contributed equally to this work.

*Correspondence:
Ziqing Hei
heiziqing@sina.com
Chaojin Chen
chenchj28@mail.sysu.edu.cn
Full list of author information is available at the end of the article

Introduction

Kidney transplantation (KT) is regarded as the most effective treatment for end-stage renal disease (ESRD). Compared to long-term dialysis, kidney transplantation significantly prolongs life expectancy and enhances quality of life [1, 2]. Owing to continuous innovation and improvement in surgical techniques for kidney transplantation, the survival rate of ESRD patients has significantly improved [3]. However, it is crucial to be aware of potential complications that negatively impact patients. These complications may lead to a diminished quality of life, increased likelihood of short-term postoperative readmission, elevated medical expenses, and potential life-threatening situations [4, 5]. Among the most frequent post-operative complications of kidney transplantation are graft failure (rejection, stenosis of the grafted renal vessels, thrombosis), cardiovascular complications (cardiac arrest, heart failure, arrhythmias), infectious complications (pulmonary infections, urinary tract infections), urological complications (ureteral stenosis), and neurological complications (peripheral neuropathy, cerebrovascular disease) [6–11]. Primarily, short-term causes of death after transplantation involve graft failure, cardiovascular disease, and postoperative infection. Cancer of the transplanted kidney or other organs has influenced long-term survival [12, 13]. A study reported the highest mortality rate in the first year after KT, which was more than 20% [12]. Another study also found a high mortality rate in the first year postoperatively, which has decreased from nearly 20% in the 1980s to less than 10% in the 2010s, and the author also showed that the highest mortality rate was found in the first three months [13]. Graft failure was undeniably the most common cause of death among KT recipients, and another common cause of death was cardiovascular disease: cardiovascular deaths accounted for 36% in patients with normal grafts, compared with 50% in patients with failed grafts [12–16]. The highest correlation factor for graft failure is delayed graft function (DGF), which is a unique manifestation of acute kidney injury framed within the transplant process [17].

However, there are no established definitions or severity ratings for describing complications. The Clavien-Dindo Classification (CDC) of Surgical Complications was updated in 2004 to provide a comprehensive and structured definition and classification of surgical complications [18]. This update influenced the International Classification of Surgical Complications, resulting in an elevated classification for life-threatening complications like acute respiratory distress syndrome (ARDS) requiring endotracheal intubation.

The Charlson Comorbidity Index (CCI) is a widely recognized and frequently cited tool for measuring comorbidities in clinical research. Studies have associated high CCI scores with early fracture-related complications in femoral fractures treated with cervical fixation [19]. Additionally, the Charlson Comorbidity Index has shown predictive value for short-term and long-term outcomes in patients with end-stage renal disease undergoing dialysis and kidney transplantation [20–24]. Furthermore, considering that age is a significant risk factor for postoperative complications across various procedures, a higher age-adjusted Charlson comorbidity index (ACCI) has also demonstrated a correlation with survival following kidney transplantation [24]. However, no studies have yet confirmed the association between ACCI and postoperative complications in kidney transplant recipients. Therefore, we selected the ACCI for further investigation to determine its association with postoperative kidney transplant complications.

In this study, we retrospectively evaluated the relationship between the ACCI and postoperative complications in kidney transplant patients.

Materials and methods

Study design and patient selection

This retrospective cohort study was approved by the Research Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University in Guangzhou, China (reference number: [2019] 02–609-02). Because all patient information is sourced from electronic health records (EHRs) and the patient's identity has not been identified, the informed consent form has been abandoned. After obtaining institutional review board approval for the study, we retrieved data from the electronic health record system for patients who underwent kidney transplantation at our two centers between 1st January 2015 and 31st March 2021. Patients with any of the following conditions were excluded from this analysis: (1) age < 18 years; (2) previous kidney transplantation; and (3) a combination of other organ transplants during cohort observation.

Data collection

Data collection was based on previous literature. All clinical data related to demographics, vital signs, detailed medical history, or perioperative variables associated with postoperative complications were collected from the EHR system. Clinical characteristics included age, gender, body mass index, smoking history, duration of illness, preoperative comorbidities of hypertension, diabetes mellitus, coronary artery disease, pneumonia and preoperative fever. Baseline laboratory values included white blood cell count, red blood cell count, hemoglobin, alanine aminotransferase, aspartate aminotransferase, creatinine, serum albumin and lipids. Perioperative variables included time

of surgery, preoperative electrolyte status, type of preoperative dialysis, duration of illness, the transfusion of red blood cells, and the preoperative use of anticoagulants or antiplatelet agents. We additionally collected donor data, including donor age, gender, BMI, donor source (DCD, donation of cardiac death or DBD, donation after brain death), ABO compatibility, ischemic times, and comorbidities such as hypertension and diabetes. Complications were identified by reviewing laboratory tests and discharge summaries within 30 days of transplantation.

Outcomes and exposures

The primary outcome of this study was the occurrence of postoperative complications. Postoperative complications were graded by the Clavien-Dindo Classification(CDC) of Surgical Complications, which categorizes complications into four grades based on the required interventions [18]. In the CDC of surgical complications, the complication 'renal insufficiency requiring dialysis' should be of particular concern in KT patients. Consequently, we introduced the concept of delayed graft function (DGF), which is defined as a serum creatinine level that remains elevated, unchanged, or decreases by less than 10% for three consecutive days within the first week following transplantation [25]. In this study, we documented patients diagnosed with DGF according to this definition who underwent postoperative dialysis as CDC IVa. The secondary outcome was the survival rate within 100 days after KT.

The primary exposure variable is the age-adjusted Charlson Comorbidity Index (ACCI). It is calculated based on 16 prevalent comorbidities. Based on disease severity, comorbidities are categorized into four groups: 1 point (myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, connective tissue disease, peptic ulcer disease, diabetes, and chronic obstructive pulmonary disease); 2 points (hemiplegia, moderate to severe chronic kidney disease, diabetic foot, solid tumor, leukemia, and malignant lymphoma); 3 points (liver disease); and 6 points (malignant tumor and AIDS). Additionally, the corresponding age group score was added (0 points for individuals under 50 years old; 1 point for those aged 51–60 years old; 2 points for those aged 61–70 years old; 3 points for those aged 71–80 years old; and 4 points for those aged 81 and older) [27]. Patients were stratified into two groups based on their ACCI scores: the low-score group (≤ 3 points) and the high-score group (>3 points). A score of >3 has been linked to an increased risk of mortality in other malignancies, as previously documented [26–28].

Statistical analysis

Continuous variables were reported as mean ± standard deviation (SD) or median and interquartile range (IQR). Categorical variables were presented as numbers and percentages. Statistical analyses were conducted using SPSS version 24.0 and R version 3.6.2 software (Vienna, Austria). Normality of baseline characteristics was assessed using the Kolmogorov–Smirnov test (K-S test). Two independent samples t-test or Wilcoxon rank sum (Mann–Whitney) test was used for quantitative data, and chi-squared test or Fisher exact test for qualitative data. A significance level of $P<0.05$ was considered statistically significant. Missing values for continuous and categorical covariates were imputed using means and modes.

The correlation between ACCI and postoperative complications in kidney transplant recipients was evaluated using targeted maximum likelihood estimation (TMLE), a semiparametric and bi-robust estimator enabling the utilization of diverse machine-learning models for a flexible and precise estimation of the exposure-outcome relationship [29, 30]. TMLE permits the existence of missing outcome variables within the raw data and compensates for them through inverse probability weighting, thus enhancing data utilization. Additionally, it adjusts for confounders related to the outcome, thereby more effectively mitigating bias arising from model misspecification. Based on clinical plausibility and existing literature reports, TMLE was employed to examine the adjusted relationship between ACCI and outcomes, including predefined confounders. Adjusted risk ratios (aORs) and corresponding 95% confidence intervals (CIs) were calculated independently.

To assess potential modifications to the association between postoperative complications and ACCI from other factors, interaction terms were incorporated into the regression model separately. These analyses included variables such as age, gender, BMI, pre-surgery conditions (e.g., coronary artery disease, diabetes, pneumonia, hypokalemia), preoperative dialysis type, use of anticoagulants or antiplatelet medications pre-surgery, red blood cell transfusions, preoperative levels of albumin and immunoglobulin, albumin, blood urea nitrogen, intraoperative factors (e.g., anesthesia duration, surgery duration, red blood cell infusion volume, blood loss, urine output) and donor information(e.g., donor age, gender, BMI, donor source, ischemic times, comorbidities such as hypertension and diabetes).

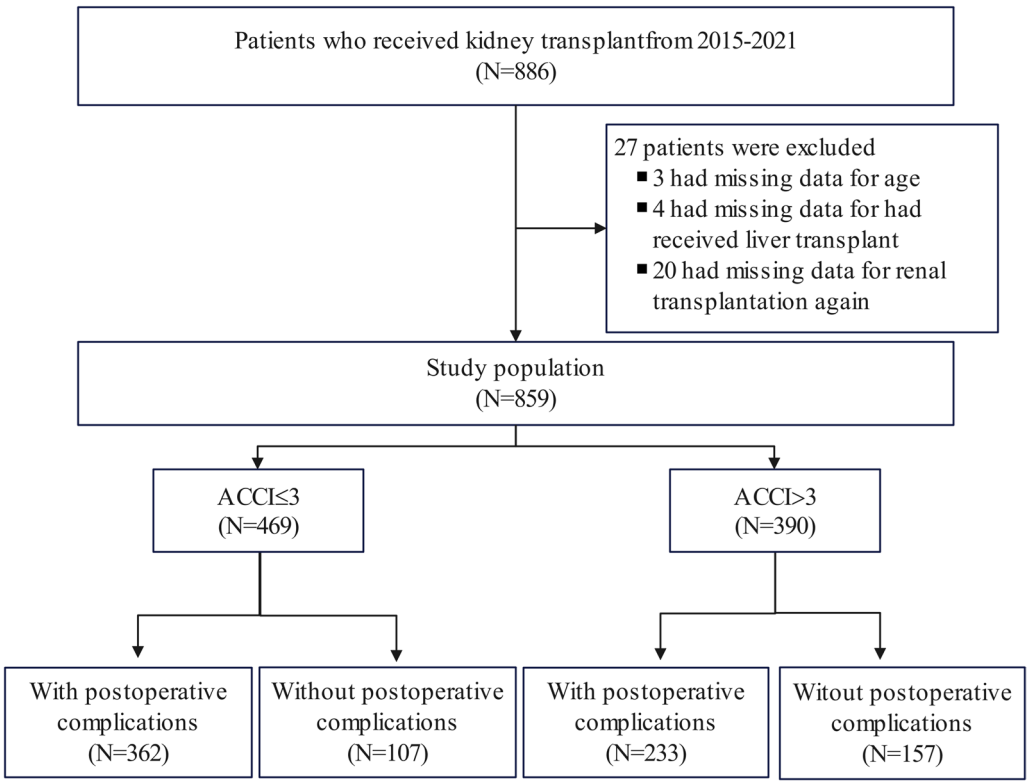

Fig. 1 Flow chart

Result

Study cohort and baseline characteristics

A total of 859 patients were ultimately retrieved in the study (Fig. 1). There were 469 patients (54.60%) in the ACCI ≤ 3 group and 390 patients (45.40%) in the ACCI > 3 group. The baseline characteristics for the two groups were illustrated in Table 1. The study cohort comprised 593 males (69.03%) and 266 females (30.97%), with a median age of 43 (IQR, 34—51) and a median BMI of 22.27 (IQR, 20.08—24.57). Patients in the ACCI > 3 group had higher BMI, blood urea nitrogen, triglycerides, and cholesterol, as well as lower hemoglobin count and albumin levels (all $p < 0.01$). More patients in the ACCI > 3 group had preoperative comorbidities, including coronary artery disease, pneumonia, and diabetes mellitus (all $p < 0.001$). A higher proportion of patients in the ACCI > 3 group was taking anticoagulants or antiplatelet drugs before surgery (23.45% vs 36.67%, $p < 0.001$), as well as receiving RBC infusions (1.92% vs 4.36%, $p = 0.043$) and immunoglobulin infusions (8.10% vs 13.85%, $p = 0.007$). All patients included in the study were ABO compatible. Only the difference in age of donor (44, IQR [33;53] vs 47.0, IQR [36;54], $p = 0.015$) was statistically significant between the two groups.

Patients with preoperative conditions including coronary heart disease (5.68% vs 2.18%, $p = 0.014$), pneumonia (23.11% vs 6.55%, $p < 0.001$), hypokalemia (11.36% vs 6.55%, $p = 0.024$), anticoagulant or antiplatelet drug use (37.50% vs 25.88%, $p = 0.001$), and red blood cell transfusion (6.44% vs 1.51%, $p < 0.001$) exhibited higher likelihood of postoperative complications compared to those without such complications (sTable 1). Patients experiencing postoperative complications demonstrated lower preoperative albumin levels (43.55, IQR [39.83; 46.70]) compared to those without complications (43.90, IQR [40.60;47]; $p = 0.002$), and higher proportion preoperative received albumin infusion (97.73% vs 94.12%, $p = 0.034$). In comparison to patients did not subject to dialysis, those undergoing preoperative peritoneal dialysis or hemodialysis had higher incidence of postoperative complications (7.20% vs 60.23% vs 32.58%, $p < 0.001$).

The distribution of patients populating each category of the ACCI is shown in Table 2. The most common comorbidity was diabetes (273, 31.78%), followed by diabetes with end-organ damage (92, 10.71%), mild liver disease (84, 9.78%), and peripheral vascular disease (82, 9.55%). sTable 2 presents the frequency of ACCI scores. As all included patients were in the end-stage renal disease

Table 1 Baseline clinical characteristics and outcomes of patients categorized by ACCI

Characteristics	Total($N=859$)	ACCI ≤ 3 ($N=469$)	ACCI >3 ($N=390$)	*P* value
Demographics				
Age(y) [1]	43[34;51]	36[30;42]	52[47;58]	<0.001
Gender[2]				0.577
Male	593(69.03%)	320(68.23%)	273(70.00%)	
Female	266(30.97%)	149(31.77%)	117(30.00%)	
BMI[1]	22.27 [20.08;24.57]	21.61 [19.57;23.98]	22.98 [20.78;25.26]	<0.001
History of smoking[2]	82(9.55%)	41(8.74%)	41(10.51%)	0.380
History of drinking[2]	25(2.91%)	14(2.99%)	11(2.82%)	0.886
Coronary Artery Disease[2]	28(3.26%)	2(0.43%)	26(6.67%)	<0.001
Hypertension[2]	763(88.82%)	413(88.06%)	350(89.74%)	0.436
Diabetes mellitus[2]	273(31.78%)	56(11.94%)	273(70.00%)	<0.001
Pneumonia[2]	100(11.64%)	17(3.62%)	83(21.28%)	<0.001
Preoperative characteristics				
Hyperkalemia[2]	111(12.92%)	72(15.35%)	39(10.00%)	0.334
Hypokalemia[2]	69(8.03%)	39(8.32%)	30(7.69%)	0.024
Types of preoperative dialysis[2]				0.176
Nodialysis required	74(8.61%)	48(10.23%)	26(6.67%)	
Hemodialysis	558(64.96%)	301(64.18%)	257(65.90%)	
Peritoneal dialysis	227(26.43)	120(25.59%)	107(27.44)	
Taking anticoagulants or antiplatelet drugs before surgery[2]	253(29.45%)	110(23.45%)	143(36.67%)	<0.001
Infusion of RBC befor esurgery[2]	26(3.03%)	9(1.92%)	17(4.36%)	0.043
Infusion of ALB before surgery[2]	818(95.23%)	4442(947.12%)	376(96.41%)	0.142
Infusion of immunoglobulin before surgery[2]	92(10.71%)	38(8.10%)	54(13.85%)	0.007
White blood cell count[1]	6.76[5.62;8]	6.77[5.71;7.91]	6.75[5.55;8.10]	0.326
Hemoglobin count[1]	111[97;124]	112[98;126]	109[97;122]	0.005
Platelet count[1]	198[162;251]	195[162;242.75]	205[162;261]	0.399
PT[1]	12.80[12.30;13.30]	12.80[12.30;13.30]	12.80[12.30;13.20]	0.708
APTT[1]	36.90[34.20;39.50]	37.20[34.10;39.70]	36.70[34.20;39.20]	0.299
Albumin[1]	43.80[40.30;46.80]	44.60[40.90;47.50]	42.70[39.40;45.80]	<0.001
Creatinine[1]	965.50[765.75;1,180.25]	1,023[817.25;1,235]	886.50[698.25;1,098.50]	<0.001
Blood glucose[1]	5.15[4.63;6.06]	4.98[4.50;5.53]	5.50[4.80;6.78]	0.436
Total bilirubin[1]	4.74[3.56;6.62]	5[3.79;6.82]	4.50[3.34;6.28]	0.652
Blood urea nitrogen[1]	21.16[16.45;27.25]	20.95[16.47;26.49]	21.31[16.26;28.02]	<0.001
Triglyceride[1]	1.45[1.04;2.13]	1.36[1.03;1.95]	1.55[1.06;2.37]	0.002
Cholesterol[1]	4.33[3.68;5.09]	4.25[3.64;4.95]	4.45[3.75;5.24]	0.005
Low-density lipoprotein cholesterol[1]	2.34[1.83;2.96]	2.32[1.82;2.91]	2.36[1.83;3.02]	0.318
Intraoperative characteristics				
Intraoperative infusion of red blood cells[2]	152(17.69%)	67(14.29%)	85(21.79%)	0.004

Table 1 (continued)

Characteristics	Total(*N* = 859)	ACCI ≤ 3 (*N* = 469)	ACCI > 3 (*N* = 390)	*P* value
Intraoperative blood loss not less than 200ml[2]	342(39.81%)	179(38.17%)	163(41.79%)	0.280
Intraoperative urine volume not exceeding 100ml[2]	445(51.80%)	250(53.30%)	195(50%)	0.335
Duration of surgery[1]	195 [170;225]	186.50 [165;215.75]	203 [173.75;235.50]	0.001
Duration of anesthesia[1]	270[235;310]	259.5[230;300]	280[245;315.25]	0.001
Donor information				
Age (y)[1]	45[35;53]	44 [33;53]	47 [36;54]	0.015
Gender[2]				0.902
Male	680 (79.16%)	372 (79.32%)	308 (78.97%)	
Female	179 (20.84%)	97 (20.68%)	82 (21.02%)	
BMI[1]	22.86 [20.81;24.80]	22.86 [20.76;24.55]	23.03 [21.16;24.97]	0.334
Allograft sources[2]				0.478
DCD[2]	544 (63.33%)	302 (64.39%)	242 (62.05%)	
DBD[2]	315 (36.67%)	167 (35.61%)	148 (37.95%)	
Ischemic times(h)[1]	8.65[6.90;11.10]	8.80 [7.00;11.08]	8.50 [6.80;11.43]	0.621
Hypertension[2]	246 (28.64%)	129 (27.51%)	117 (30.00%)	0.421
Diabetes mellitus [2]	37 (4.31%)	22 (4.69%)	15 (3.85%)	0.544
Prognosis				
In-hospital mortality[2]	17(1.98%)	3(0.64%)	14(3.59%)	0.006

1.Continuous variables are expressed as the median (interquartile range); 2.Categorical variables are expressed as a number (%). RBC, red blood cell; *ALB* Albumin, *PT* prothrombin time, *APTT* activated partial thromboplastin time, *ACCI* age-adjusted Charlson comorbidity index, *DCD* donation of cardiac death, *DBD* donation after brain death

Table 2 Breakdown of ACCI categories and frequency of patients populating each category

Scores	Conditions	n	%
Assigned weights for disease			
1	Myocardial infarction	3	0.35
	Congestive heart failure	8	0.93
	Peripheral vascular disease	82	9.55
	Cerebrovascular disease	8	0.93
	Dementia	0	0
	Chronic obstructive pulmonary disease	38	4.42
	Connective tissue disease	12	1.40
	Ulcer disease	42	4.89
	Mild liver disease	84	9.78
	Diabetes	273	31.78
2	Hemiplegia	0	
	Moderate/severe renal disease	859	100
	Diabetes with end-organ damage	92	10.71
	Any tumor	6	0.70
	Leukemia	0	0
	Lymphoma	0	0
3	Moderate or severe liver disease	6	0.70
6	Metastatic solid tumor	0	0
	Acquired immune deficiency syndrome	0	0
Assigned weights for age			
1	For each decade over age 40 years (up to 4 points)		

category prior to surgery, the minimum ACCI score was 2, with most patients scoring either 2 or 4 (617, 71.83%).

Intraoperative characteristics and prognosis

Patients in the ACCI > 3 group received more red blood cell infusions (14.29% vs 21.79%, $p = 0.004$), experienced longer durations of surgery (186.50, IQR [165; 215.75] vs 203, IQR [173.75; 235.50]; $p = 0.001$) and anesthesia (259.50, IQR [230; 300] vs 280, IQR [245; 315.25]; $p = 0.001$, Table 1).

In comparison to patients without complications, whose experienced postoperative complications exhibited a higher percentage of individuals with intraoperative urine output less than 100ml (59.85% vs 48.24%, $p = 0.002$), longer durations of anesthesia (275, IQR [236; 318] vs 265, IQR [235; 305]; $p = 0.011$) and longer durations of surgery (200, IQR [172; 235] vs 192, IQR [165; 220]; $p = 0.015$). Patients experiencing postoperative complications exhibited a higher postoperative hospitalization mortality rate (5.30% vs 0.50%, $p < 0.001$, sTable 1).

The incidence and distribution of postoperative complications

In the study, a total of 264 kidney transplant patients encountered postoperative complications (sTable 1). Based on the Clavien-Dindo Classification of Surgical Complications, the highest incidence was observed in grade IV (158; 18.39%), while the lowest was in grade I (26; 3.03%; Table 3). 249 patients (28.99%) in our cohort developed DGF postoperatively, of whom 115 patients (13.39%) required dialysis after surgery, which was the most prevalent postoperative complication (CDC IVa). Another postoperative complication with a high incidence was pneumonia requiring antibiotic treatment after surgery (CDC II).

Relationship between ACCI and postoperative complications

The study included 469 patients (54.60%) in the ACCI ≤ 3 group and 390 patients (45.40%) in the ACCI > 3 group. In comparison to patients without postoperative complications, patients with postoperative complications showed a higher proportion of preoperative ACCI > 3 (59.47% vs 39.16%, $p < 0.001$, sTable 1). Patients with ACCI > 3 exhibited a higher in-hospital mortality rate compared to those with ACCI ≤ 3 (3.59% vs 0.64%, $P = 0.006$, Table 1).

Subsequent correlation analysis revealed that patients with ACCI > 3, as opposed to those with preoperative ACCI ≤ 3, faced an increased risk of postoperative complications (aOR = 1.64, 95% CI [1.21,2.21], $p = 0.001$; Table 4) following multivariate adjustment. Moreover, the influence of BMI > 28, coronary artery disease, diabetes, pneumonia, hypokalemia, peritoneal dialysis type, duration of anesthesia and intraoperative urine volume ≤ 100ml significantly altered the association between preoperative ACCI and postoperative complications (all interactions $p < 0.001$). Additionally, the gender of donor, allograft sources and ischemia time were also significant influences on the correlation between ACCI and postoperative complications (all interactions $p < 0.001$).

The linear combination of the main effects and interaction terms of preoperative ACCI revealed a significant correlation between ACCI > 3 and postoperative complications. The interaction between preoperative ACCI and postoperative complications was stronger among specific patient subgroups: BMI > 28 [aOR (95% CI), 18.97 (9.31, 38.62) vs. 5.37 (3.60, 7.99), $p < 0.001$], anesthesia time ≥ 300 min [aOR (95% CI), 7.02(1.98, 24.83) vs. 2.91(1.94, 4.37), $p = 0.044$], non-coronary heart disease patients [aOR (95% CI), 119.59 (16.42, 871.27) vs. 3.7 (0.08, 179.84), $p < 0.001$], non-diabetes patients[aOR (95% CI), 60.04 (20.94, 172.13) vs. 3.57 (0.65, 19.7), $p < 0.001$], patients without preoperative dialysis [aOR (95% CI), 19.98 (7.84, 50.93) vs. 1.10 (0.49, 2.47), $p = 0.005$ & 8.81 (3.91, 19.84), $p < 0.001$], and patients with intraoperative urine volume > 100ml [aOR (95% CI), 18.79 (5.68, 62.17) vs. 5.42 (0.8, 36.64), $p < 0.001$; Table 4]. Furthermore, the correlation between the ACCI and postoperative

Table 3 Detailed information of postoperative complications according to the Clavien-Dindo Classification

Grade	System	Disease	*N* (%)	
I	cardiovascular system	atrial fibrillation (reversible after correcting potassium ions)	9 (1.05%)	26 (3.03%)
	respiratory system	pulmonary atelectasis requiring physical therapy	2 (0.23%)	
	nervous system	temporary confusion of consciousness, no need for treatment	0 (0)	
	Other	open wound infection at the bedside	15 (1.75%)	
II	cardiovascular system	tachyarrhythmias requiring beta-blockers	0 (0)	115 (13.39%)
	respiratory system	pneumonia requiring antibiotic treatment	104 (12.11%)	
	nervous system	TIA, anticoagulant therapy is required	2 (0.23%)	
	digestive system	infectious diarrhea requiring antibiotic treatment	30 (3.49%)	
	urinary system	urinary tract infection requiring antibiotic treatment	6 (0.70%)	
	other	same as I, but combined with cellulitis, requiring antibiotic treatment	7 (0.81%)	
IIIa	cardiovascular system	pacemaker implantation is required for severe chronic arrhythmia	0 (0)	47(5.47%)
	nervous system	see grade IV		
	urinary system	ureteral stricture after kidney transplantation requires stent implantation	31 (3.61%)	
	other	a closed noninfective wound dehiscence was observed	15 (1.75%)	
IIIb	nervous system	see grade IV		
	digestive system	the anastomotic leak required reoperation	0 (0)	
	urinary system	ureteral stricture after kidney transplantation requires surgical treatment	13 (1.51%)	
	other	the wound was infected to an enterocele	0 (0)	
IVa	cardiovascular system	low output syndrome due to heart failure	22 (2.56%)	158 (18.39%)
	respiratory system	respiratory failure, requiring tracheal intubation	12 (1.40%)	
	nervous system	ischemic stroke/intracerebral hemorrhage	18 (2.10%)	
	digestive system	necrotizing pancreatitis	0 (0)	
	urinary system	DGF with dialysis	115 (13.39%)	
IVb	cardiovascular system	same as Iva, combined with renal failure	12 (1.40%)	
	respiratory system	same as Iva, combined with renal failure	2 (0.23%)	
	nervous system	same as Iva, combined with hemodynamic instability	7 (0.81%)	
	digestive system	ischemic stroke/cerebral hemorrhage with respiratory failure	19 (2.21%)	
	urinary system	same as Iva, combined with hemodynamic instability	0 (0)	
d	cardiovascular system	cardiac dysfunction after myocardial infarction (Iva-d)	17 (1.98%)	

complications was stronger in recipients when the donor was male, the ischemia time exceeded 10 h, and the allograft sources were from donation after circulatory death (DCD) (all interactions $p<0.001$).

ACCI was identified as a risk factor for DGF requiring dialysis, a specific complication following KT (OR = 1.43, 95% CI [0.96, 2.11], $p=0.043$, sTable 3). Coronary artery disease (OR = 2.71, 95% CI [1.16, 6.30], $p=0.016$), hypokalemia (OR = 2.31, 95% CI [1.28, 4.15], $p=0.004$), use of anticoagulants or antiplatelet drugs (OR = 2.05, 95% CI [1.37, 3.07], $p<0.001$), infusion of red blood cells (OR = 3.63, 95% CI [1.58, 8.35], $p=0.001$) and albumin (OR = 1.16, 95% CI [1.13, 1.20], $p=0.010$) were associated with DGF requiring dialysis (sTable 3). Intraoperative urine volume not exceeding 100 ml was linked to a higher risk of DGF requiring dialysis. (OR = 2.37, 95% CI [1.56, 3.62], $p<0.001$). In terms of donor information, ischemic times (OR = 1.08, 95% CI [1.03, 1.14], $p=0.001$), BMI (OR = 1.07, 95% CI [1.01, 1.14], $p=0.019$), and hypertension (OR = 1.81, 95% CI [1.21, 2.72], $p=0.004$) would increase the risk of DGF requiring dialysis. In contrast, allograft sources (DCD or DBD) were not significantly associated with DGF requiring dialysis (OR = 1.20, 95% CI [0.79, 1.82], $p=0.386$).

Further analysis of the relationship between various components in ACCI and postoperative complications of kidney transplantation highlighted the five preoperative comorbidities most strongly associated with postoperative complications. These included congestive heart failure (OR = 16.18, 95% CI [1.98–132.17], $p<0.001$, Table 5), cerebrovascular disease (OR = 6.85, 95% CI [1.38–34.39], $p=0.006$), chronic obstructive pulmonary disease (OR = 6.05, 95% CI [2.95–12.39], $p<0.001$), peripheral vascular disease (OR = 2.32, 95% CI [1.48–3.78], $p<0.001$), and mild liver disease (OR = 1.80, 95% CI [1.14–2.85], $p=0.011$). These findings emphasize the

Table 4 The relationship between ACCI with postoperative complications before and after model adjusted

Characteristics	Unadjusted model[a]		Full adjusted model[b]		*p* value[c]
	OR	95%CI	OR	95%CI	
ACCI > 3 with postoperative complications	2.28	(1.70,3.06)	1.64	(1.21, 2.21)	0.001
Gender					0.357
Male	2.61	(1.54,4.44)	1.94	(0.79, 4.79)	
Female	2.15	(1.50,3.07)	2.61	(0.57, 12.05)	
BMI[d]					
18–28	2.98	(0.78,11.33)	5.37	(3.60, 7.99)	-
< 18	2.31	(1.68,3.17)	4.03	(2.09, 7.76)	0.346
> 28	1.39	(0.41,4.72)	18.97	(9.31, 38.62)	< 0.001
Hemoglobin count					0.503
< 100	2.67	(1.55,4.61)	2.64	(1.41, 4.94)	
≥ 100	2.12	(1.49,3.01)	2.04	(0.52, 8.08)	
Albumin					0.029
< 35	1.85	(0.56,6.13)	0.79	(0.20, 3.1)	
≥ 35	2.27	(1.68,3.09)	3.80	(0.24, 60.84)	
Duration of anesthesia(min)					0.044
< 300	1.97	(1.37,2.83)	2.91	(1.94, 4.37)	
≥ 300	2.83	(1.67,4.81)	7.02	(1.98, 24.83)	
Duration of surgery(min)					0.060
< 240	2.19	(1.57,3.06)	3.64	(2.39, 5.53)	
≥ 240	2.42	(1.24,4.75)	7.34	(2.32, 23.16)	
Coronary Artery Disease					< 0.001
NO	2.20	(1.63,2.98)	119.59	(16.42, 871.27)	
YES	1.17	(0.07,20.72)	3.7	(0.08, 179.84)	
Diabetes mellitus					< 0.001
NO	2.54	(1.74,3.71)	60.04	(20.94, 172.13)	
YES	2.05	(1.04,4.04)	3.57	(0.65, 19.70)	
Pneumonia					< 0.001
NO	1.78	(1.28,2.46)	0.08	(0.02, 0.26)	
YES	2.66	(0.92,7.73)	1.22	(0.13, 11.33	
Hypokalemia					< 0.001
NO	2.12	(1.55,2.89)	0.09	(0.03, 0.26)	
YES	4.67	(1.67,13.02)	1.28	(0.17, 9.79)	
Types of preoperative dialysis[d]					
No dialysis required	3.67	(1.24,10.87)	19.98	(7.84, 50.93)	-
Hemodialysis	2.02	(1.39,2.93)	1.10	(0.49, 2.47)	0.005
Peritoneal dialysis	2.59	(1.49,4.49)	8.81	(3.91, 19.84)	< 0.001
Taking anticoagulants or antiplatelet drugs before surgery					0.357
NO	2.10	(1.46,3.01)	1.94	(0.79, 4.79)	
YES	2.31	(1.36,3.92)	2.61	(0.57, 12.05)	
Infusion of RBC before surgery					0.114
NO	2.23	(1.65,3.02)	11.86	(2.11, 66.74)	
YES	1.92	(0.36,10.29)	3.19	(0.11, 91.69)	
Infusion of ALB before surgery					0.291
NO	2.18	(0.38,12.58)	0.54	(0.02, 13.73)	
YES	2.25	(1.67,3.05)	1.31	(0.01, 172.95)	
Infusion of immunoglobulin before surgery					0.033
NO	1.99	(1.45,2.72)	0.39	(0.10, 1.56)	
YES	5.45	(2.11,14.11)	1.56	(0.11, 22.33)	
Intraoperative infusion of RBC					0.800
NO	2.28	(1.64,3.16)	2.14	(0.74, 6.14)	
YES	2.23	(1.10,4.53)	2.38	(0.35, 16.03)	
Intraoperative blood loss					0.101
≤ 200ml	2.15	(1.46,3.16)	1.70	(0.57, 5.08)	
> 200ml	2.46	(1.54,3.91)	2.97	(0.51, 17.3)	
Intraoperative urine volume					< 0.001
≤ 100ml	2.39	(1.61,3.55)	18.79	(5.68, 62.17)	
> 100ml	2.29	(1.46,3.6)	5.42	(0.80, 36.64)	
Age of donor (y)					0.468
< 50	2.22	(1.53,3.21)	3.18	(2.02, 5.03)	
≥ 50	2.36	(1.43,3.88)	4.12	(1.30, 13.01)	
Gender of donor					< 0.001
Male	2.23	(1.56,3.20)	1.55	(0.56, 4.31)	
Female	3.63	(1.76,7.48)	2.95	(0.54, 16.28)	
BMI of donor[d]					
18–28	2.36	(1.73,3.23)	1.29	(0.87, 1.93)	-
< 18	1.28	(0.33,4.95)	0.38	(0.21, 0.70)	0.002
> 28	2.00	(0.57,7.06)	1.97	(1.01, 3.81)	0.507
Allograft sources					< 0.001
DCD	2.57	(1.54,4.28)	27.13	(6.61, 111.42)	
DBD	2.16	(1.50,3.11)	5.98	(0.68, 52.45)	
Ischaemic times(h)					< 0.001
< 10	1.68	(1.03,2.73)	0.64	(0.20, 2.08)	
≥ 10	2.70	(1.85,3.93)	5.20	(3.32, 8.14)	
Hypertension of donor					0.066
NO	2.23	(1.56,3.20)	1.55	(0.56, 4.31)	
YES	2.36	(1.39,4.01)	2.95	(0.54, 16.28)	
Diabetes mellitus of donor					0.979
NO	2.24	(1.66,3.03)	3.25	(0.45, 23.54)	
YES	4.00	(0.58,27.41)	3.17	(0.07, 151.26)	

a.Using Univariate Logistic model; b. Using Targeted Maximum Likelihood Estimation model, adjusted Age, Gender, BMI, Coronary Artery Disease, Diabetes mellitus, Pneumonia, Hypokalemia, Types of preoperative dialysis, Taking anticoagulants or antiplatelet drugs before surgery, Infusion of RBC before surgery, Infusion of ALB before surgery, Infusion of immunoglobulin before surgery, Albumin, Blood urea nitrogen, Duration of anesthesia, Duration of surgery, Intraoperative infusion of RBC, Intraoperative blood loss, Intraoperative urine volume, allograft sources, ischemic times, age of donor, gender of donor, BMI of donor, and hypertension or diabetes mellitus of donor. c. p-interaction, comparison of OR values for stratified populations using Z-test; d. Z-test was used to compare the OR value of Types of preoperative dialysis and different stratifications of BMI

Table 5 Most predictive factors of ACCI

Conditions	Postoperative complications	
	OR(95%CI)	*p* value
Congestive heart failure	16.18(1.98,132.17)	< 0.001
Peripheral vascular disease	2.32(1.48,3.78)	< 0.001
Cerebrovascular disease	6.85(1.38,34.39)	0.006
Chronic obstructive pulmonary disease	6.05(2.95,12.39)	< 0.001
Mild liver disease	1.80(1.14,2.85)	0.011
Diabetes	1.35(0.99,1.83)	0.065
Diabetes with end-organ damage	1.69(1.08,2.62)	0.020

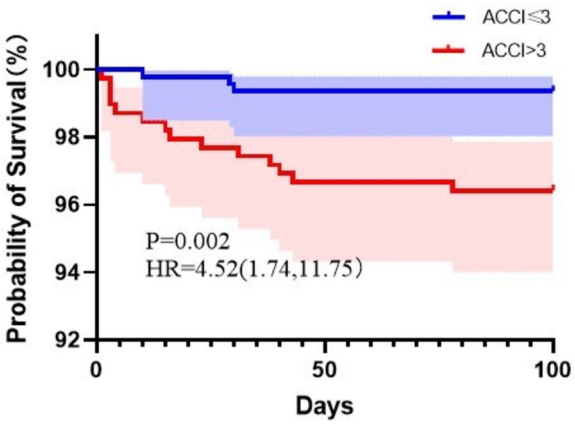

Fig. 2 Kaplan–Meier curve. *Survival probability is plotted on the Y-axis against postoperative time on the X-axis. Different color stands for different index scores. ACCI, age-adjusted Charlson Comorbidity Index

significance of considering these specific comorbidities when evaluating the risk of postoperative complications post kidney transplantation.

Survival analysis

In the study, 17 (1.98%) patients died during hospitalization after kidney transplantation, and a higher mortality rate was associated with postoperative complications ($p < 0.001$, Table 1). Further analysis through survival curve analysis showed that patients with ACCI > 3 had significantly lower 30-day, 50-day, and 100-day survival rates compared to those with preoperative ACCI ≤ 3 (HR = 4.52, CI [1.74, 11.75]; $p = 0.002$; Fig. 2). These findings indicate that a higher ACCI score is linked to reduced survival rates following kidney transplantation, highlighting the importance of thorough preoperative risk assessment and management to enhance patient outcomes.

Discussion

In this retrospective observational study, we observed that a preoperative ACCI > 3 significantly elevated the risk of postoperative complications in renal transplant patients, with an adjusted odds ratio (aOR) of 1.64 (95% CI 1.21–2.21). Additionally, patients with ACCI > 3 exhibited notably lower 30-day, 50-day, and 100-day survival rates compared to those with preoperative ACCI ≤ 3.

Patients with end-stage renal disease undergoing renal transplantation often present with multiple underlying conditions before surgery, such as renal hypertension, anemia, and heart disease [31]. When multiple comorbidities coexist concurrently before surgery, the prognosis for KT patients becomes uncertain. The age-adjusted Charlson Comorbidity Index is a valuable tool for evaluating a patient's overall health status and predicting prognosis based on their comorbidities [32].The study results indicate that an ACCI score > 3 is a risk factor for postoperative complications in kidney transplant patients. According to the ACCI scale, the baseline ACCI score for all renal transplant patients is 2, without factoring in any other comorbidities. The patients with ESRD and age > 50 all had a ACCI score of 3 at baseline. According to the study, an ACCI score exceeding 3 (≥ 4) preoperatively constituted a risk factor for postoperative complications, indicating that the KT patients over 50 years old but no more than 60 years old, without other comorbidity were not associated with high risk of postoperative complications, except that they had one or more preoperative comorbidity to make the ACCI score exceeding 4. Some results suggest that age is an independent risk factor of postoperative complications and mortality for KT recipients, with an elevated risk of mortality in KT recipients over 60 years of age [33, 34]. To avoid ambiguous confusion, we conducted a ROC curve analysis of ACCI scores and postoperative complications in our dataset (sFigure 1), revealing a cut-off value of 3.5. Thus, we emphasized that the preoperative ACCI score exceeding 3 (≥ 4) means that constituted a risk factor for postoperative complications. Additionally, we reviewed relevant literature, which indicated that an ACCI greater than 3 is associated with a high risk of postoperative complications or death [26]. Therefore, in combination with our results, ACCI > 3 is risk factor for postoperative complications in KT patients.

Older patients with a multitude of comorbidities, encompassing cardiovascular disease, respiratory conditions, diabetes, or cancer, may experience heightened mortality following KT [35]. While advancing age is a recognized high-risk factor for prognosis in KT, certain studies have indicated that adolescents who undergo kidney transplantation exhibit a less favorable long-term

prognosis than their older counterparts, primarily due to suboptimal medication adherence [36, 37]. These results emphasize the critical need for the development of tailored risk assessment and management approaches grounded in age, comorbidities, and other pertinent factors to enhance the prognosis of renal transplant recipients.

ACCI is based on a comprehensive analysis of multiple evaluation indicators. The aim of this study was to identify one that can be used to predict all renal transplant surgery-related complications, not just only one transplant-related complication such as delayed renal function recovery, although transplant-related complications are very important and very common in such patients. However, due to the long-term renal dysfunction in KT patients, usually combined with systemic diseases such as hypertension and cardiovascular disease, there is a great risk of complications in various organs after surgery. These complications are usually related to the preoperative systemic condition of the patients. The scoring criteria of ACCI covers the assessment of comorbidities in various organs, so it has advantages in predicting the risk of various postoperative complications during the perioperative period. ACCI is a valuable tool for the assessment of patient comorbidities and is associated with both long-term and short-term outcomes [38]. It has been shown to be associated with an increased risk of post-hip fracture mortality in the elderly [39] as well as complications and 30-day mortality after surgery in general surgery patients [40]. In addition, Analyzing the internal components of ACCI is relatively important for the influence of postoperative complications, which is conducive to our preoperative targeted intervention for kidney transplant patients. Consequently, we conducted a correlation analysis of its internal evaluation factors. Our analysis revealed that patients with congestive heart failure, cardiovascular and cerebrovascular diseases and chronic obstructive pulmonary disease (COPD) before surgery are the primary three risk factors associated with a heightened risk of postoperative complications (Table 5).

Cardiovascular disease (CVD) is recognized as a major contributor to morbidity and mortality in patients with end-stage renal disease (ESRD) undergoing hemodialysis [41, 42]. The decline in renal function among ESRD patients results in the accumulation of substances that are inadequately excreted by the kidneys, leading to the formation of uremic toxins in the body. These biologically active uremic toxins can have detrimental effects on the cardiovascular system by influencing the function of cells such as white blood cells, endothelial cells, smooth muscle cells, and platelets, thereby contributing to the progression of cardiovascular disease [43]. In addition, chronic hypoxia resulting from lung diseases such as COPD is associated with the onset and progression of chronic kidney disease (CKD) [44]. Studies have indicated that COPD heightens the mortality risk in mid to late-stage CKD patients, particularly among elderly and male individuals [45]. The research conducted by Brian D. Kent et al. has further corroborated that COPD is linked to increased mortality rates and reduced success rates of kidney transplants in end-stage renal disease patients, aligning with our own finding [46]. Consequently, implementing targeted preoperative interventions to enhance cardiopulmonary function in kidney transplant patients may prove beneficial in mitigating postoperative complications. Moreover, while preoperative diabetes mellitus in kidney transplant patients does not inherently elevate the risk of postoperative complications (OR = 1.35, 95% CI [0.99–1.83], $p = 0.065$, Table 5), the likelihood of such complications significantly rises in the presence of end-stage organ damage due to diabetes (OR = 1.69, 95% CI [1.08–2.62], $p = 0.02$, Table 5). Therefore, individuals undergoing kidney transplantation with concurrent diabetes should prioritize vigilant long-term blood glucose management to avert diabetes-related complications.

The acquisition of the ACCI is a straightforward and efficient process. For patients undergoing kidney transplantation, healthcare providers can simply gather medical history and examination data prior to surgery to calculate the ACCI score, without necessitating additional tests or imposing a significant medical burden. Moreover, by integrating the ACCI calculation into the electronic medical record system, the score can be automatically generated by identifying relevant keywords and subsequently verified by clinicians, enhancing the ease of use. The Age-Adjusted Charlson Comorbidity Index (ACCI) is systematically organized and demonstrates consistent performance across diverse healthcare facilities and geographic areas. These characteristics highlight the practicality and broad applicability of the ACCI in assessing the risk of postoperative complications in KT recipients.

There are two definitions of delayed graft function (DGF): one indicates a need for dialysis within one week of surgery, while the other refers to a serum creatinine level that remains elevated, unchanged, or decreases by less than 10% for three consecutive days during the first week after transplantation [25]. Since the first definition is more subjective and associated with physician judgment, the second definition is more commonly used. According to this second definition, DGF occurred in 249 patients (28.99%) in our study data. Not all patients with DGF required dialysis, so the patients ultimately included

in the analysis were those who developed DGF and required dialysis, corresponding to the CDC classification of class IVa ($n=115$, Table 3). To further investigate whether the 115 cases requiring dialysis were associated with the ACCI score, we consult the original data and discovered that 15.64% (61/390) of patients developed DGF and required dialysis in the ACCI > 3 group, whereas only 11.51% (54/469) of patients were in the other group. The analysis of the ACCI concerning the presence or absence of the complication, conducted using the Mann–Whitney U test for independent samples, revealed a statistically significant difference between the two groups (OR = 1.43, 95% CI [0.96–2.11], $p=0.043$, sTable 3). This suggests that higher ACCI scores are associated with an increased incidence of DGF requiring dialysis. Certainly, additional risk factors for DGF include ischemia time, organ quality, donor age, ischemia–reperfusion injury, organ source (living or deceased), HLA, ABO factors and calcineurin inhibitors [47–52]. In the study, we also found that longer ischemic times, higher BMI of donor, and donor combined hypertension were risk factors for DGF requiring dialysis (sTable 3).

This study has several limitations. Firstly, retrospective analysis inherently leads to miss data. Besides summarizing medical records, we incorporated perioperative examinations into the preoperative ACCI calculations and postoperative complication statistics to mitigate this bias. Secondly, some patients may have only 1–2 comprehensive and systematic examination results postsurgery. Hence, the postoperative examination findings are not treated as independent variables but rather as a reference for identifying postoperative complications. Lastly, while perioperative cardiac arrest due to electrolyte imbalance is not uncommon in end-stage patients, this specific complication classification is not encompassed in our study.

Conclusion

The presence of a preoperative ACCI score greater than 3 was identified as a potential risk factor for postoperative complications in kidney transplant patients. By utilizing the ACCI score, we can proactively identify high-risk individuals who are likely to experience postoperative complications following kidney transplant surgery.

Abbreviations

ACCI	Age-adjusted Charlson Comorbidity Index
KT	Kidney transplant
TMLE	Target Maximum Likelihood Estimation
OR	Odds ratio
ESRD	End-stage renal disease
DCD	Donation of cardiac death
DBD	Donation after brain death
CDC	Clavien-Dindo Classification
DGF	Delayed graft function
ARDS	Acute respiratory distress syndrome
EHRs	Electronic health records
AIDS	Acquired Immunodeficiency Syndrome
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular disease
CKD	Chronic kidney disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-024-03888-1.

Supplementary Material 1.

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Authors' contributions

CC and ZH: Conceptualization; Data Curation; Project Administration; Resources; Supervision; Writing – Review & Editing; QH, TL and JY: Conceptualization; Formal Analysis; Investigation; Methodology; Writing – Original Draft Preparation; Writing – Review & Editing; YL: Formal Analysis; Methodology; SZ: Conceptualization; Data Curation.

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Data Availability

The data that support the findings of this study can be made available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

This retrospective cohort study was approved by the Research Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University in Guangzhou, China (reference number: [2019] 02–609-02). Because all patient information is sourced from electronic health records (EHRs) and the patient's identity has not been identified, the informed consent form has been abandoned.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Anesthesiology, Guangdong Province, The Third Affiliated Hospital of Sun Yat-Sen University, No. 600 Tianhe Road, Guangzhou 510630, China. [2]Center for Big Data and Artificial Intelligence, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, People's Republic of China.

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