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Prediction model for acute kidney injury after coronary artery bypass grafting: a retrospective study

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Abstract

Background Acute kidney injury (AKI) after coronary artery bypass grafting (CABG) is associated with a less favorable outcome. The aim of this study is to investigate the incidence, mortality and risk factors of AKI after CABG, and to establish a risk prediction model.

Methods From January 2016 to June 2018, 541 patients who underwent CABG were enrolled. The clinical characteristics were collected to calculate the incidence and mortality of AKI after CABG. Patients were divided into AKI group and non-AKI group according to the statistical data. The differences of preoperative, intraoperative and postoperative variables between the two groups were comparatively analysed. The risk factors of AKI were obtained by binary logistic stepwise regression analyses using related factors as independent variables.

Results The incidence of postoperative AKI in 541 patients was 27.9% (151 cases). The in-hospital mortality in AKI group was higher than that in non-AKI group (5.30% vs 0.00%, $P<0.001$). Single factor analysis showed that the risk factors for postoperative AKI including age, BMI, hypertension, cardiac insufficiency, eGFR, serum uric acid level, CABG combined valve operation, cardiopulmonary bypass (CPB), operation time, aortic cross-clamping time, CPB time, mechanical ventilation time and postoperative low cardiac output syndrome. Multivariate regression analysis suggested that age ($P=0.006$, OR 2.323), BMI ($P=0.004$, OR 2.495), hypertension ($P=0.032$, OR 1.712), eGFR ($P=0.002$, OR 3.054), CPB time ($P=0.024$, OR 1.007) and postoperative low cardiac output syndrome ($P=0.010$, OR 2.640) were independent risk factors for AKI.

Conclusions AKI is a common complication after CABG and is related to multiple perioperative factors. It is suggested that early recognition of these risk factors and interventions should be carried out in clinical practice. The risk prediction model can be used as a simple tool for predicting postoperative AKI.

Keywords Acute kidney injury · Coronary artery bypass grafting · Risk factor · Prognosis

Introduction

Coronary artery bypass grafting (CABG) is one of the main surgical methods for coronary heart disease. It is the preferred treatment for patients with severe multiple vessel diseases and complicated coronary artery diseases in revascularization [1, 2], which plays an important role in improving patients' living quality and prolonging their life span. The number of patients receiving CABG has gradually increased in recent years. However, acute kidney injury (AKI) following CABG is a common, serious complication resulting in increased morbidity, mortality, and medical expenditure [3]. Depending on the various definitions of AKI, 12–50% of patients who have undergone CABG developed AKI, and among which 2–11.2% patients with an increased mortality rate require renal replacement therapy (RRT) [4]. Depending on the various definitions of AKI, 12–50% of patients who have undergone CABG developed AKI, among which 2–11.2% patients with an increased mortality rate require renal replacement therapy (RRT) [4]. The occurrence of AKI involves a series of complex pathophysiological mechanisms, which may be related to

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different clinical risk factors [5]. Therefore, the analyses of risk factors for AKI after CABG are helpful to strengthen the monitoring and prevention of high-risk groups, and to improve the prognosis of patients as far as possible.

At present, there are few studies on the risk factors of AKI after CABG. In this study, We explored the risk factors of AKI based on the analysis of clinical data, to quench the ignitions of the disease and to reduce postoperative complications.

Patients and methods

Study design and patient population

All patients who received CABG in Nanjing First Hospital between January 2016 and June 2018 were retrospectively enrolled in this study, including patients undergoing on-pump CABG (ONCAB), off-pump CABG(OPCAB), CABG combined valve operation, aortic aneurysm operation or other surgical interventions (such as left atrial myxoma enucleation, cardiac tumor removal, etc.). Patients with chronic renal failure who had undergone long-term dialysis and patients with incomplete clinical data after surgery were excluded.

Data collection and definitions

Demographic data (age, sex, height, weight and previous history) and operation conditions were recorded for all the patients. We examined the correlations between preoperative, intraoperative and postoperative variables and AKI after CABG. Categories of preoperative risk factors of AKI included patients' general conditions, preoperative comorbidities and laboratory data. For intraoperative variables, we investigated emergency operations, type and time of operations, combined operations, cardiopulmonary bypass (CPB), aorta cross-clamping time and number of bypass graft during surgery. Postoperative situations included hypotension, insufficiency of circulation blood, congestive heart failure, low cardiac output syndrome, reoperation, mechanical ventilation time, ICU duration, and Hospital stay, etc. Risk factors related to patients, heart and operation were defined according to EuroSCORE II [6]. The morbidity and mortality of AKI after CABG were evaluated. According to statistical data, the patients were divided into AKI group and non-AKI group. Differences of clinical data between the two groups were analyzed. And multivariable logistic regression modeling was used to identify the risk factors of AKI.

Based on the KDIGO Clinical Practice Guideline for Acute Kidney Injury [7], AKI was defined as any of the following: increase in serum creatinine (Scr) ≥ 0.3 mg/dl (26.5 μmol/l) within 48 h or increase in Scr ≥ 1.5 times baseline in 7 days or urine volume < 0.5 ml/kg/h for 6 h.

Urine output and Scr level were routinely measured and the data collected in our medical records.

Baseline creatinine level was defined as the preoperative value obtained closest to the date of the operation (within 7 days before the operation). The preoperative estimated glomerular filtration rate (eGFR) was calculated by CKD-$EPI_{scr-cys}$ equation [8]. Proposed KDIGO staging of AKI [7]: stage 1 was defined as increase in Scr to 1.5–1.9 times baseline or ≥ 0.3 mg/dl (26.5 μmol/l, or urine output < 0.5 ml/kg/h for 6–12 h. Stage 2 was defined as increase in Scr to 2.0–2.9 times baseline or urine output < 0.5 ml/kg/h for ≥ 12 h. Stage 3 was defined as increase in Scr to 3 times baseline or ≥ 4.0 mg/dl (353.6 μmol/l) or initiation of RRT, or urine output < 0.3 ml/kg/h for ≥ 24 h or anuria ≥ 12 h.

Statistical analysis

Statistical analyses were performed using SPSS Version 19. Normal distribution measurement data were summarized as mean and standard deviation, and independent sample *t* test was used for comparison between groups. Skewed distribution measurement data were represented by M (P25, 75), the Mann–Whitney *U* test was used in the comparison between two groups, and Kruskal–wallis test was used for multi group comparison. *P* values less than 0.05 were considered as statistical difference. Risk factors for AKI were preliminary assessed using univariate analysis, and significant variables were substituted subsequently into multi-factor logistic regression analysis.

Results

Characteristics of the study population

A total of 541 patients with a mean age of 66.97 ± 9.02 years, including 400 (73.94%) men and 141 women (26.06%) were investigated. The preoperative renal functions of all patients were generally normal, with all estimated glomerular filtration rate (eGFR) ≥ 30 ml/min/1.73 m^2, mean eGFR 89.56 ± 25.01 ml/min/1.73 m^2. All baseline characteristics and concomitant diseases are listed in Table 1. Patients were divided into AKI group and non-AKI group according to their postoperative renal functions. No significant differences were observed in sex, rate of preoperative diabetes, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, miocardial infarction, cardiac surgery and percutaneous coronary intervention (PCI) among the two groups. Compared to the patients without AKI, those with AKI were older, had higher level of body mass index (BMI), higher frequency of hypertension and cardiac insufficiency.

Table 1 Preoperative demographic data and clinical characteristics of all patients

Variable	All patients ($n = 541$)	AKI ($n = 151$)	Non-AKI ($n = 390$)	P value
Age (years)	66.97 ± 9.02	70.09 ± 8.37	65.77 ± 8.98	**< 0.001**
Gender, male (%)	400 (73.94%)	109 (72.19%)	291 (74.62%)	0.564
BMI (kg/m^2)	24.79 ± 3.31	25.38 ± 4.06	24.57 ± 2.94	**0.026**
Hypertension, *n* (%)	364 (67.28%)	118 (78.15%)	246 (63.08%)	**0.001**
Diabetes mellitus, *n* (%)	168 (31.05%)	54 (35.76%)	114 (29.23%)	0.141
COPD, *n* (%)	39 (7.21%)	10 (6.62%)	29 (7.44%)	0.743
Cerebrovascular disease, *n* (%)	54 (9.98%)	15 (9.93%)	39 (10%)	0.982
Miocardial infarction, *n* (%)	43 (7.95%)	13 (8.61%)	30 (7.69%)	0.724
Cardiac insufficiency, *n* (%)	177 (32.72%)	61 (40.40%)	116 (29.74%)	**0.018**
Cardiac surgery, *n* (%)	3 (0.56%)	1 (0.66%)	2 (0.51%)	1.000
PCI, *n* (%)	49 (9.06%)	13 (8.61%)	36 (9.23%)	0.821
Hemoglobin (g/l)	130.97 ± 16.00	127.70 ± 16.78	132.24 ± 15.52	0.316
PT (min)	11.91 ± 1.17	12.02 ± 1.13	11.86 ± 1.18	0.172
Scr (μmol/l)	79.63 ± 22.49	88.96 ± 27.68	76.02 ± 18.97	**< 0.001**
eGFR (ml/min)	89.56 ± 25.01	79.79 ± 28.05	93.34 ± 22.66	**< 0.001**
Uric acid (μmol/l)	341.09 ± 110.37	373.21 ± 126.83	328.74 ± 100.84	**0.002**
Bilirubin (mmol/l)	11.49 ± 5.68	11.41 ± 5.33	11.52 ± 5.82	0.839
Cholesterol (mmol/l)	4.16 ± 1.18	4.11 ± 1.01	4.18 ± 1.24	0.088
Triglyceride (mmol/l)	1.70 ± 1.30	1.78 ± 1.53	1.67 ± 1.20	0.186
Albumin (mmol/l)	39.83 ± 4.51	39.39 ± 3.10	40.00 ± 4.93	0.105

Bold values indicate $P < 0.05$

It is suggested that the history of advanced age, obesity and cardiovascular disease may be related to postoperative AKI. In terms of preoperative laboratory indicators, no substantial differences were observed in the mean level of hemoglobin, prothrombin time (PT), bilirubin, cholesterol, triglyceride and albumin among the two groups. However, the mean value of serum Scr and uric acid of AKI group were higher than that of non-AKI group. Correspondingly, the eGFR level in AKI group was significantly lower than that in non-AKI group. All these suggested that baseline renal function and uric acid level can affect the prognosis of kidney.

Surgical data

Of the 541 patients, 131 (24.21%) received OPCAB, 256 (47.32%) with ONCAB, 93 (17.19%) with CABG combined valve surgery, 61 (11.28%) with CABG combining other operations (left atrial myxoma extirpation, ligation of left atrial appendage, etc.). Of all the patients, 410 (75.79%) received CPB, the average time of which was 93.63 ± 37.16 min (7–375 min). The blocking time of the ascending aorta was between 4 and 185 min and the mean time was 61.40 ± 26.86 min during the operation. The number of bypass vessels was 1–6, with an average of 3.08 + 1.10. Details related to the surgery are shown in Table 2. There was no significant difference observed in the rate of emergency and combined operation, as well as in the number of bypass vessels during AKI and non-AKI patients. The aortic cross-clamping time and cardiopulmonary bypass time in AKI group were longer than those in non-AKI group, but there was no significant difference between the two groups. The operative time in AKI group is significantly longer than that in non-AKI group. Moreover, AKI ratio increased significantly in patients undergoing CPB and CABG combined with valve surgery.

Postoperative complications and outcomes

Postoperative acute renal failure occurred in 151 patients, accounting for 27.91% of the total number. Most of them were classified into stage 1 according to the KDIGO criteria (Fig. 1). In this study, all 151 patients with AKI had an elevated Scr level within 48 h after operation, which reached the diagnostic criteria of AKI. Among them nine cases (5.96%) had postoperative oliguria, which met both the Scr diagnostic criteria and the urine volume diagnostic criteria of AKI. $N = 8$ sufferers were treated with RRT, accounting for 5.30% of AKI cases. Scr decreased and urine volume increased in 110 patients (72.85%) within 2 weeks after operation, among which 77 (50.99%) had their renal function recovered to baseline level before discharge. 16 patients (10.60%) were discharged from hospital with no improvement in renal function. Eight patients (5.30%) died in hospital.

Compared with non-AKI group, patients in AKI group had higher incidence of postoperative insufficient circulating blood volume and low cardiac output syndrome, higher frequency of reoperation. The mechanical ventilation time, ICU duration and hospital stay in AKI group were also significantly higher than those in non-AKI group (Table 3). Furthermore, the mortality of AKI patients was significantly higher than that of non-AKI patients ($P<0.001$), suggesting that patients with AKI had poorer prognosis than non-AKI patients.

Logistic regression analysis for AKI

All variables in Tables 1, 2 and 3 were substituted into the single-factor logistic regression analysis. It showed that the risk factors for postoperative AKI include age, BMI, hypertension, cardiac insufficiency, eGFR, serum uric acid level, CABG combined valve operation, CPB, operation time, aortic cross-clamping time, CPB time, mechanical

Table 2 Clinical features of surgery

Variable	All patients (*n* = 541)	AKI (*n* = 151)	Non-AKI (*n* = 390)	*P* value
Emergent/urgent operation, *n* (%)	8 (1.48%)	4 (2.65%)	4 (1.03%)	0.314
Combined with valve surgery, *n* (%)	93 (17.19%)	34 (22.52%)	59 (15.13%)	**0.041**
Combined with other operations, *n* (%)	61 (11.28%)	19 (12.58%)	42 (10.77%)	0.550
OPCAB, *n* (%)	131 (24.21%)	24 (15.89%)	107 (27.44%)	**0.005**
CPB, *n* (%)	410 (75.79%)	127 (84.11%)	283 (72.56%)	**0.005**
Operation time (h)	3.88 ± 1.10	4.10 ± 1.21	3.80 ± 1.05	**0.007**
Aortic cross-clamping time (min)	61.40 ± 26.86	66.65 ± 31.37	59.60 ± 24.35	0.057
CPB time (min)	93.63 ± 37.16	99.33 ± 46.35	91.13 ± 31.91	0.072
Number of bypass vessels	3.08 ± 1.10	3.06 ± 0.99	3.09 ± 0.97	0.769

Bold values indicate $P<0.05$

Fig. 1 Postoperative AKI staging

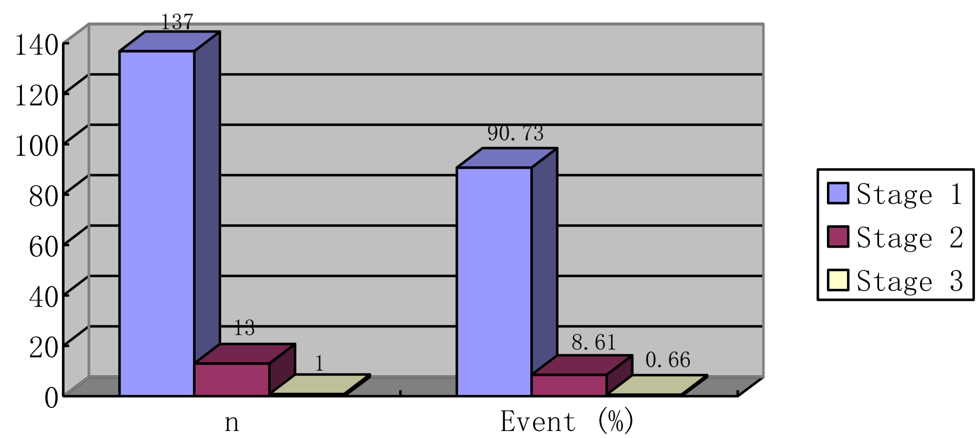

Table 3 Postoperative complications and outcomes

Variable	All patients (*n* = 541)	AKI (*n* = 151)	Non-AKI (*n* = 390)	*P* value
Mechanical ventilation time (h)	21.60 ± 55.80	30.98 ± 67.15	18.00 ± 50.40	**0.032**
Hypotension, *n* (%)	49 (9.06%)	13 (8.61%)	36 (9.23%)	0.821
Insufficient circulating blood volume, *n* (%)	318 (58.78%)	97 (64.24%)	221 (56.67%)	**0.022**
Low cardiac output syndrome, *n* (%)	43 (7.95%)	21 (13.91%)	22 (5.64%)	**0.001**
Congestive heart failure, *n* (%)	27 (4.99%)	10 (6.62%)	17 (4.36%)	0.278
Reoperation, *n* (%)	42 (7.76%)	6 (3.97%)	36 (9.23%)	**0.040**
ICU duration (h)	46.9 ± 73.8	63.17 ± 84.20	40.55 ± 68.39	**0.004**
Hospital stay (days)	23.00 ± 10.28	25.87 ± 15.72	22.08 ± 7.09	**0.045**
Hospital mortality, *n* (%)	8 (1.48%)	8 (5.30%)	0 (0.00%)	**< 0.001**

Bold values indicate $P<0.05$

Table 4 Univariate logistic regression analysis for AKI

Predictive factors	*β*	*W*	OR	95% CI	*P* value
Age	0.868	10.646	2.382	1.414–4.012	0.001
BMI	0.76	8.127	2.139	1.268–3.609	0.004
Hypertension	0.739	10.959	2.093	1.352–3.241	0.001
Cardiac insufficiency	0.471	5.568	1.601	1.083–2.367	0.018
eGFR	1.658	28.596	5.251	3.870–9.606	0.000
Serum uric acid	0.841	14.007	2.318	1.492–3.599	0.000
Combined with valve surgery	0.489	4.124	1.613	1.017–2.613	0.042
CPB	0.694	7.705	2.001	1.226–3.265	0.006
Operation time	0.242	8.131	1.274	1.079–1.505	0.004
Aortic cross-clamping time	0.008	4.223	1.008	1.000–1.016	0.040
CPB time	0.006	4.051	1.006	1.000–1.011	0.044
Mechanical ventilation time	0.004	4.483	1.004	1.000–1.007	0.034
Postoperative low cardiac output syndrome	0.994	9.548	2.702	1.438–5.076	0.002

Table 5 Multivariate conditional logistic regression analysis for AKI

Predictive factors	*β*	*W*	OR	95% CI	*P* value
Age	0.843	7.570	2.323	1.274–4.234	0.006
BMI	0.914	8.251	2.495	1.337–4.657	0.004
Hypertension	0.537	4.592	1.712	1.047–2.799	0.032
eGFR	1.117	9.475	3.054	1.500–6.218	0.002
CPB time	0.007	5.096	1.007	1.001–1.013	0.024
Postoperative low cardiac output syndrome	0.971	6.577	2.640	1.257–5.543	0.010

ventilation time and postoperative low cardiac output syndrome(Table 4).

Then the above 13 variables were selected into logistic stepwise regression model, suggesting that age, BMI, hypertension, eGFR, CPB time and postoperative low cardiac output syndrome were independent risk factors for AKI (Table 5).

Then the logic regression equation was obtained: logit $P = 0.843 \times \text{age} + 0.914 \times \text{BMI} + 0.537 \times \text{hypertension} + 1.117 \times \text{eGFR} + 0.007 \times \text{CPB time} + 0.971 \times \text{postoperative low cardiac output syndrome} - 2.837$.

Discussion

AKI after CABG has been a prominent clinical disorder which worsens the prognosis and increases the fatality rate, and the research on its pathogenesis is still in progress in recent years. Various criteria for AKI may lead to discrepant research results in clinical approaches [9, 10]. The recommendations of KDIGO on AKI are based on an exhaustive evidence-based review of the literature and provide welcome guidance on practice for clinicians [11]. The KDIGO standard was used in this study to find that the incidence of AKI after CABG was nearly 30%. Therefore, the study of its risk factors has important guiding significance for clinical practice. According to the KDIGO criteria, we found that 137 cases were classified into stage 1, which accounted for 90.73% of the total number of AKI, suggesting that most of the AKI were mild renal impairment cases. It is helpful for the early diagnosis and intervention of AKI.

Surgical risk assessment system is of great significance for perioperative management, and the risk of the patients can be actively intervened through the preoperative assessment. The European system for cardiac operative risk evaluation II (EuroSCORE II) was improved on the basis of EuroSCORE [6]. Research suggests that EuroSCORE II calculation was superior to EuroSCORE and Society of Thoracic Surgeons (STS) score [12], it not only better predicts the mortality risk of CABG [13], but also well applies to Chinese patients [14]. The operative risk factors in this study were based on the related projects of EuroSCORE II, and the specific conditions of the patients were comprehensively reflected.

This research shows that the risk of postoperative AKI increases in elderly patients. One reason may be the relative poor basic renal function in elderly patients. According to the literature, the renal function gradually decreases with the aging of the patient [15], whose viewpoint is also confirmed by this study. We found that the mean eGFR was 100.53 ± 34.4 ml/min/1.73 m^2 for patients aged less than 60 years old, mean eGFR 86.66 ± 23.79 ml/min/1.73 m^2 for those aged 60–80 years, and 74.70 ± 24.08 ml/min/1.73 m^2 for more than 80 years. On the other hand, elderly patients with multiple underlying diseases are more likely to have a lower organ compensation, which may be another important reason for poor renal prognosis.

BMI is found to be an independent risk factor for AKI after CABG. Previous studies have shown that obesity can lead to glomerular hypertension, and its pathological presentations indicate glomerular hypertrophy and focal segmental glomerulosclerosis (FSGS) [16]. Excessive activation of renin-angiotensin system (RAS) in obese patients leads to renal hemodynamic changes and then aggravates renal impairment [17]. Obesity is also closely related to atherosclerosis (including renal vessels). CABG operation aggravates the renal arterioles ischemia, leading to the occurrence of AKI.

Hypertension has been reported as an independent risk factor for AKI after cardiac surgery [18]. Persistent hypertension can increase glomerular capsular pressure, leading to glomerular fibrosis and renal arteriosclerosis. Even if the preoperative renal function was normal, there may be renal parenchyma ischemia and nephron deficit. Thus lead to increased risks of postoperative AKI [19]. Similarly, it is found in this study that the incidence of AKI in hypertensive patients was significantly higher than that in non-hypertensive patients despite that there was no statistically significant difference in their basic renal function. Therefore, tight control of hypertension may be essential to reduce the incidence of AKI after CABG.

The trend of eGFR calculated by CKD-EPI$_{scr-cys}$ equation was roughly the same as that of Scr, Both were used to estimate the preoperative renal function. Consequently, they need not to be put together in multi-factor research. We found that preoperative eGFR was an independent risk factor for AKI after CABG, which was similar to previous studies [20].

Prolonged CPB can lead to systemic inflammatory response and ischemia–reperfusion injury, resulting in the occurrence of AKI [21]. In this study, although CPB itself is not an independent risk factor for AKI after CABG, the CPB time is, of which the OR value is 1.007, thus the above mechanism is verified. Therefore, in clinical operation, the occurrence of AKI will be to some extent reduced by shortening the CPB time.

Low cardiac output syndrome (LCOS) is also a common complication after CABG [22], which can lead to renal hypoperfusion, resulting in oliguria and acute kidney injury [23]. It is reported that the risk of postoperative LCOS can be reduced by preoperative intra-aortic Balloon Pump (IABP) [24]. The use of levosimendan may improve postoperative low cardiac output and reduce the need for RRT [25].

There are several limitations to this study. First, the number of patients was small and derived from a single center, and thus the results may not be directly extrapolated to other patient populations. Second, we did not analyze the use of contrast agent, mainly because all patients had undergone coronary angiography for more than a week before operation, basically passed the crisis of contrast-induced nephropathy [26]. Third, almost all patients were prescribed with various doses of vasoactive agents (including nephrotoxic drugs) to maintain the cardiovascular system after surgery, therefore the effects of vasoactive agents and nephrotoxic drugs on AKI were not involved in the study. Finally, considering that the number of coronary artery lesions shown by coronary angiography was approximately the same as that of vessels transplanted, we did not incorporate this factor into the study.

Conclusions

The incidence of AKI after CABG is quite high and correlated with various factors during the perioperative period. Early recognition of these risk factors and interventions are helpful to reduce the incidence of AKI after CABG and improve the prognosis of patients. Further studies are needed to conduct long-term follow-ups for the patients after CABG, to explore the effect of AKI on long-term survival after CABG.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of retrospective study, formal consent is not required.

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