タイトル	Assessment of postoperative renal dysfunction requiring prolonged renal replacement therapy and the associated mortality rate
別タイトル	手術後の継続的な腎代替療法導入率ならびに死亡率の検討
作成者（著者）	古川, 力三
公開者	東邦大学
発行日	2020.03.15
掲載情報	東邦大学大学院医学研究科 博士論文.
資料種別	学位論文
内容記述	主査 : 小竹良文 / タイトル : Assessment of postoperative renal dysfunction requiring prolonged renal replacement therapy and the associated mortality rate / 著者 : Rikizo Kogawa, Ryoichi Ochiai / 掲載誌 : Toho Journal of Medicine / 巻号・発行年等 : 5(4):173-178, 2019 / 本文ファイル : 出版者版
著者版フラグ	ETD
報告番号	32661甲第937号
学位記番号	甲第642号
学位授与年月日	2020.03.15
学位授与機関	東邦大学
その他資源識別子	https://mylibrary.toho-u.ac.jp/webopac/TD35126739
その他資源識別子	info:doi/10.14994/tohojmed.2019-009
メタデータのＵＲＬ	https://mylibrary.toho-u.ac.jp/webopac/TD13001073

Original Article

Assessment of Postoperative Renal Dysfunction Requiring Prolonged Renal Replacement Therapy and the Associated Mortality Rate

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ABSTRACT

Introduction: Postoperative renal dysfunction requiring renal replacement therapy (RRT) is associated with a poor postoperative outcome. The aim of this study was to evaluate perioperative renal function among patients who required postoperative RRT.

Methods: This was a retrospective cohort study of Japanese patients who required RRT within 6 months of surgery at our institution over the previous 10-year period of observation. Following data were extracted from electronic patient records for analysis: preoperative renal function, incidence of RRT, recovery rate from RRT, and mortality rate at 6 months after surgery. Univariate and multivariate logistic regression analyses were conducted to determine the odds ratio (OR) for postoperative RRT dependence.

Results: Among 48677 patients who underwent surgery, 769 required RRT postoperatively. Of these latter patients, 159 did not receive RRT preoperatively. Therefore, the inductive rate of new RRT was 0.33% (159 of 48067 patients). The mortality rate was 42.1% (67 of 159) in patients who required new RRT. In patients who received new RRT without preoperative renal dysfunction, the recovery rate from RRT was 100% compared with 80.4% in patients with preoperative renal dysfunction. In multivariate analysis, the preoperative estimated glomerular filtration rate [adjusted OR = 0.76 (0.63-0.92), p = 0.005) was a significant risk factor for postoperative RRT dependence. The mortality rate related to multiple organ failure and sepsis in patients requiring postoperative RRT was 83.8%-90%.

Conclusions: Preoperative renal function is the most important factor influencing postoperative renal outcome.

Toho J Med 5 (4): 173–178, 2019

KEYWORDS: perioperative renal function, renal replacement therapy, mortality rate

Introduction

Perioperative acute kidney injury (AKI) is a well-recognized factor that increases the duration of postoperative stay in the intensive care unit (ICU), as well as increases the total length of hospitalization and risk of mortality. Moreover, perioperative AKI is associated with worse short- and long-term postoperative outcomes.[1–14] An

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DOI: 10.14994/tohojmed.2019-009

Received May 7, 2019: Accepted July 24, 2019
Toho Journal of Medicine 5 (4), Dec. 1, 2019.
ISSN 2189–1990, CODEN: TJMOA2

incidence of AKI of 1%-25% has been reported among hospitalized patients,[6–8, 15, 16] with the perioperative incidence estimated at 0.1%-43%.[2, 3, 10–12, 17] Specifically, the incidence of AKI was 1%-43% after cardiovascular surgery[2, 10] compared with 0.8%-7.5% after non-cardiovascular surgery.[12, 17]

Renal replacement therapy (RRT) is considered to be an important therapeutic strategy for the management of patients with AKI presenting with rapid injury and the deterioration of renal function. However, RRT itself is associated with worse postoperative functional renal outcomes.[10, 16] An incidence of AKI of 32% was reported among patients without a history of preoperative chronic kidney disease who were admitted to the ICU after surgery, with 6% of these patients requiring RRT. Complete or partial recovery from RRT was achieved in 97% of these patients, with the other 3% remaining RRT-dependent at the time of hospital discharge.[3] Although various studies have reported on the rate of postoperative AKI and the associated need for RRT and functional renal outcomes, only a few of these studies have specifically focused on Japanese populations. As the incidence of AKI and clinical outcomes after RRT are influenced by ethnicity,[18, 19] the determination of the predictive factors of postoperative renal prognosis in Japanese populations is important for identifying patients at risk for postoperative AKI and RRT, as well as in providing appropriate perioperative management to lower the risk and optimize postoperative renal function. Therefore, the aims of our study were as follows: (1) to determine the inductive rate of new RRT after surgery, (2) to evaluate the association between preoperative renal function and postoperative mortality and recovery from RRT, and (3) to identify the predictive factors of postoperative RRT dependence. Our retrospective analysis to address these aims was performed in a cohort of Japanese patients who received intraoperative anesthesia care at our department over a 10-year period of observation.

Methods

The study protocol was approved by the Ethics Committee of the Toho University Omori Medical Center, Japan (24-188, 25-30, 26-71, and 26-2639). Study data were collected from patients who underwent a surgical procedure, requiring intraoperative anesthesia management at our institution between April 1, 2004, and March 31, 2014, and required RRT within 6 months after surgery. Patients meeting these inclusion criteria were identified from our electronic medical records, and the following data were extracted for analysis: preoperative renal function, the incidence rate of RRT, recovery rate from RRT, and mortality rate at 6 months after surgery. Patients who received RRT preoperatively were excluded. Renal function was quantified using the estimated glomerular filtration rate (eGFR), which was adjusted for age, sex, and serum creatinine (Cr) level. Preoperative renal dysfunction was defined as an eGFR of <60 ml/min/1.73 m^2.

Continuous variables were analyzed using the Student's *t*-test, whereas categorical variables were analyzed using the chi-squared or Fisher's exact test. Univariate and multivariate logistic regression analyses were subsequently conducted to determine the odds ratio (OR) for postoperative RRT dependence. Variables with a p-value of <0.1 in univariate analyses were included in the multivariate analysis. All statistical analyses were performed using SPSS for Windows (version 24.0; SPSS Japan Inc., Tokyo, Japan). P-values of <0.05 were considered statistically significant.

Results

The patient flowcharts of the study are shown in Fig. 1, 2. Over the 10-year period of observation, 48677 patients underwent surgery at our department. Among these, 769 patients required RRT within 6 months of surgery. Of these latter patients, 159 did not receive RRT preoperatively. Therefore, the inductive rate of new RRT after surgery was 0.33% (159 of 48067 patients). The mortality rate was 42.1% (67 of 159) in patients who required new RRT postoperatively compared with 6.4% (39 of 610) in patients who had received RRT preoperatively ($p < 0.001$). The mortality rate was 47.4% (37 of 78) in patients who had not received RRT preoperatively and did not have preoperative renal dysfunction. For the 41 patients who survived in this group, the recovery rate from RRT at the time of discharge was 100%. By comparison, the mortality rate was 37.0% (30 of 81 patients) with a recovery rate from RRT of 80.4% (41 of 51) in patients who had not received RRT preoperatively and had preoperative renal dysfunction. Of note, in patients who had not received RRT preoperatively, preoperative renal dysfunction did not increase the mortality rate at 6 months after surgery ($p = 0.184$). However, the difference in recovery rate between the two groups was significant ($p = 0.002$).

In the groups classified according to preoperative renal function, the mortality rate related to multiple organ fail-

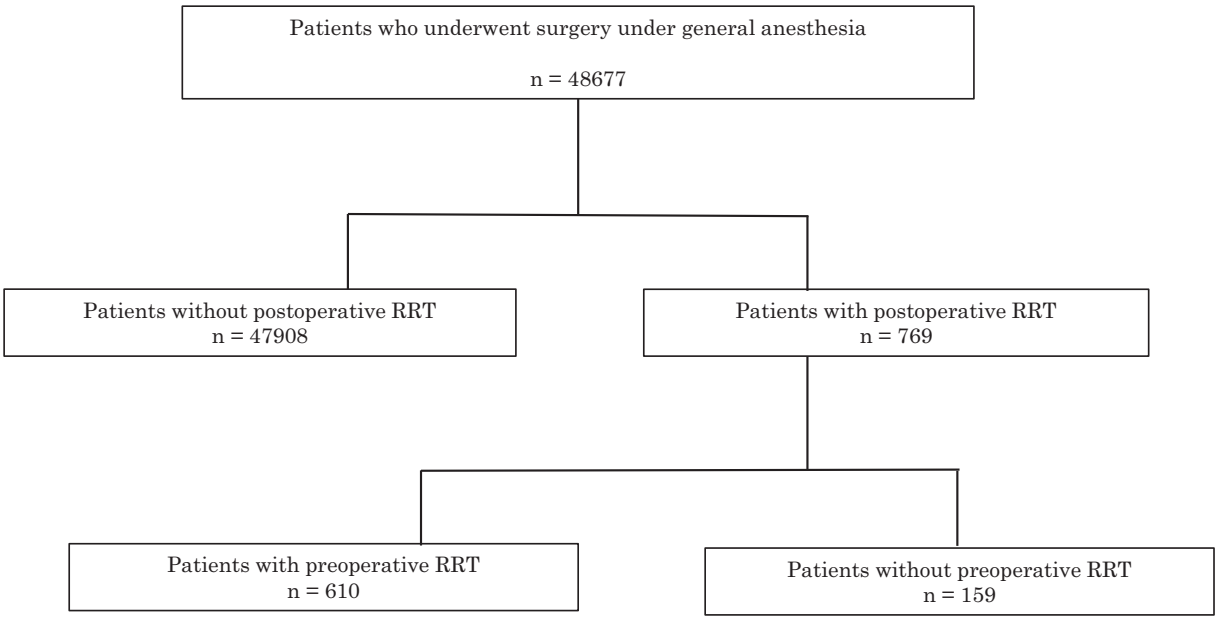

Fig. 1 Patient background in terms of perioperative renal replacement therapy (RRT).

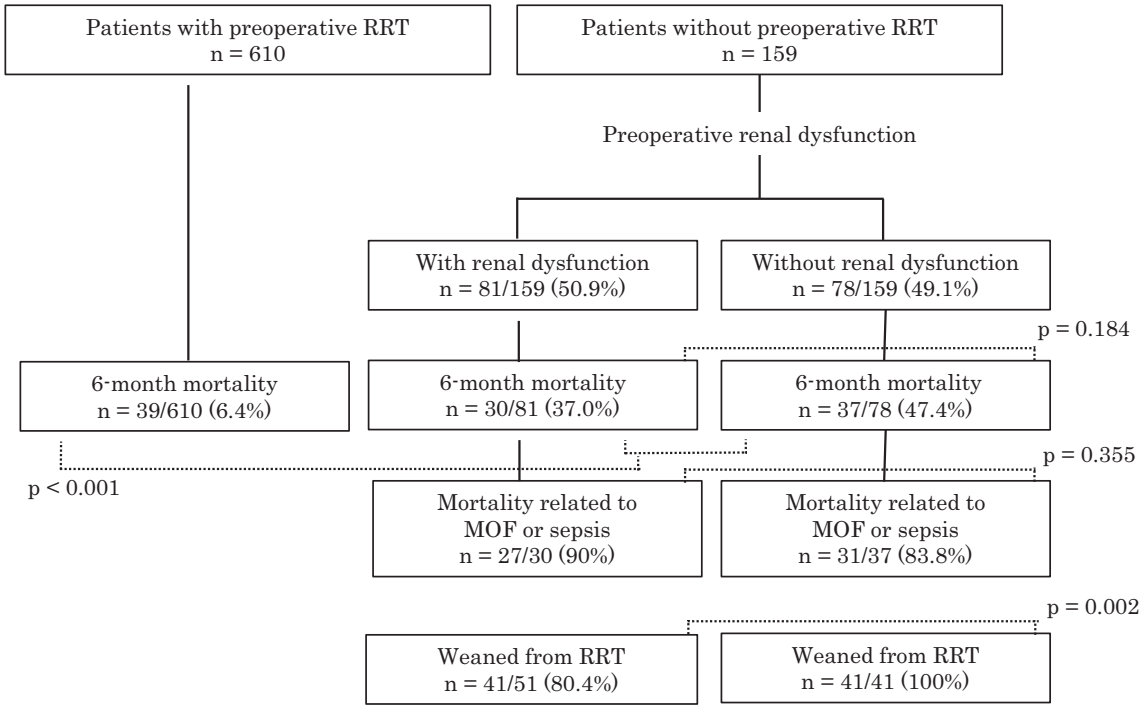

Fig. 2 Mortality and weaning rate among patients with postoperative renal replacement therapy (RRT). MOF: multiple organ failure.

ure (MOF) and sepsis was as follows: 83.8% (31 of 37) in patients without preoperative renal dysfunction and 90% (27 of 30) in patients with preoperative renal dysfunction. The difference between the two groups was not significant ($p = 0.355$).

Relevant demographic and health factors were compared between 82 patients who recovered from RRT and 10 patients who remained RRT-dependent at the time of discharge. The results of the univariate and multivariate analyses are provided in Table 1. The following variables were identified as significant in univariate analysis ($p < 0.1$): age, preoperative eGFR (basal eGFR), preoperative Cr

Table 1 Demographic and clinical factors

Parameter	Univariate analysis			Multivariate analysis		
	Weaned from RRT n = 82	Not weaned from RRT n = 10	p-value	Adjusted odds ratio	95% CI	p-value
Age, year, mean (SD)	64.6 (17.8)	75.3 (7.1)	0.063	1.14	0.92-1.41	0.225
Male, n (%)	50 (61)	7 (70)	0.426			
Emergent status, n (%)	52 (63)	3 (30)	0.046	0.35	0.03-4.90	0.434
preoperative Cr, mg/dl, mean (SD)	1.1 (0.7)	4.6 (2.2)	0.001			
preoperative eGFR, ml/min/1.73 m^2, mean (SD)	60.5 (27.4)	12.8 (6.6)	< 0.001	0.76	0.63-0.92	0.005
max Cr, mg/dl, mean (SD)	2.1 (2.0)	8.2 (1.9)	< 0.001			
last Cr, mg/dl, mean (SD)	1.1 (1.1)	6.3 (2.2)	< 0.001			
CPB use, n (%)	27 (32)	2 (20)	0.331			

RRT: renal replacement therapy, Cr: creatinine, eGFR: estimated glomerular filtration rate, CPB: cardiopulmonary bypass
basal Cr/eGFR: preoperative Cr/eGFR level
max Cr: perioperative highest Cr level
last Cr: Cr level at hospital discharge

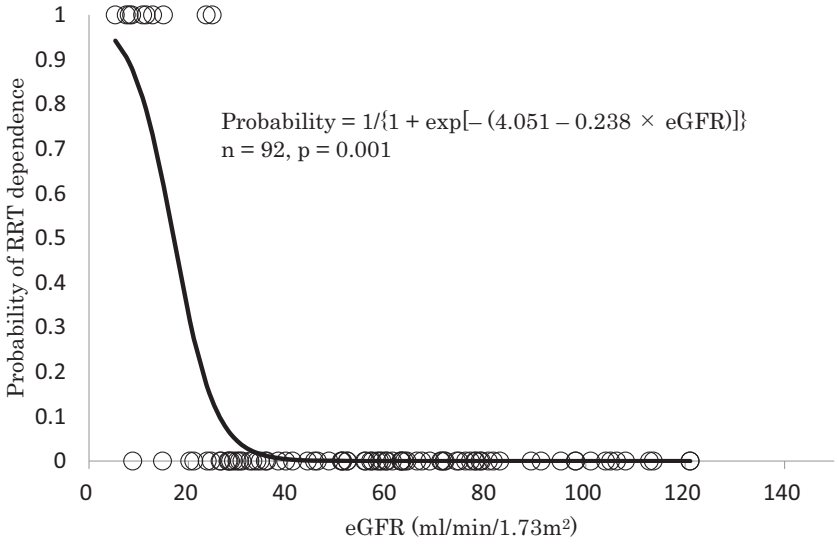

Fig. 3 Estimated glomerular filtration rate (eGFR) and the logistic regression model-estimated probability of renal replacement therapy (RRT) dependence.

(basal Cr) level, perioperative highest Cr (max Cr) level, Cr level at the time of discharge (last Cr), and emergent status of the surgery. Cr levels were excluded from multivariate analysis to prevent multicollinearity with eGFR. Multiple logistic regression analysis indicated that the basal eGFR [adjusted OR = 0.76 (0.63-0.92), p = 0.005] was a significant risk factor for postoperative RRT dependence. In the logistic regression analysis, the basal eGFR was found to be a significant predictor of postoperative RRT dependence (p = 0.001; Fig. 3), according to the following equations:

$$\text{probability} = 1/\{1+\exp[-(4.051 - 0.238 \times \text{basal eGFR})]\}$$

A 50% risk of postoperative RRT dependence was associated with a basal eGFR of 17.02 ml/min/1.73 m^2.

Discussion

We conducted a single-center, retrospective study to evaluate the association between preoperative renal function and the postoperative outcomes of the patients who had received new RRT postoperatively using data from our department of anesthesiology over a 10-year period of observation. The main findings of our study were as follows: the inductive rate of new RRT was 0.33%, with a mortality rate of 42.1% in patients who required new RRT

postoperatively. This mortality rate was markedly higher than the 6.4% rate in patients who had received RRT preoperatively. In patients who did not receive RRT preoperatively, preoperative renal dysfunction did not increase the mortality rate at 6 months after surgery. However, in univariate analyses, we identified the following predictive factors of postoperative RRT dependency at the time of discharge: preoperative Cr level, preoperative eGFR, perioperative highest Cr level, and Cr level at the time of discharge.

Previous studies have reported mortality rates of 42%-80% in patients with AKI requiring postoperative RRT,[5, 10, 13, 14, 16, 20, 21] with a perioperative range of 42%-72%.[20, 21] In comparison, the mortality rates at 6 months after surgery in our study were 47.4% in patients without preoperative renal dysfunction and 37.0% in patients with preoperative renal dysfunction. Although not statistically significant, the higher rate of mortality in patients without preoperative renal dysfunction may reflect the greater renal damage that affects the patient's progression from normal preoperative renal function to postoperative RRT.

Previous studies that evaluated perioperative renal function in patients with postoperative AKI have reported a higher risk of progression to chronic kidney disease and mortality in patients without preoperative renal dysfunction compared with patients with preoperative renal dysfunction.[5, 8] We confirmed this same paradoxical finding in our study.

The recovery rate from RRT in our study was 100% in patients without preoperative renal dysfunction compared with 80.4% in patients with preoperative renal dysfunction. Therefore, preoperative renal dysfunction was associated with a 19.6% rate of RRT dependence. Previous studies have reported a rate of progression to RRT dependence of 2.2%-3%,[2, 3, 17] which was lower than that in our study. Of note, patients with preoperative renal dysfunction were not included in these previous studies. Moreover, our findings on high increases in Cr level at the time of discharge from basal level among patients with RRT dependence indicate the need for continuous monitoring of Cr levels throughout the perioperative period.

Recent studies have demonstrated an association between small increases in serum Cr levels during hospitalization and worse long-term outcomes.[1, 4, 10] However, as Cr levels are influenced by age, sex, muscle mass, type of surgery, and perioperative therapy, including fluid therapy, the validity of using only Cr levels as a measure of real-time renal function has been criticized, and these factors should be carefully considered when making clinical decisions on care.[23, 24]

Furthermore, in multiple logistic regression analysis, we identified that the preoperative eGFR was a significant risk factor for postoperative RRT dependence. A 50% risk of postoperative RRT dependence was found to be correlated with a basal eGFR of 17.02 ml/min/1.73 m^2. Thus, we suggest that preoperative renal function is the most important factor related to postoperative renal outcome.

The mortality rate related to MOF and sepsis in patients requiring new RRT postoperatively was 83.8%-90% in our study. Therefore, MOF and sepsis after surgery are aggravating risk factors of mortality rate, regardless of preoperative renal function. The need for postoperative RRT reflects a high degree of physiological stress, which is an important factor in a patient's progression from postoperative status to a general status of morbidity, which includes MOF and sepsis.

Our study has several limitations. First, as mentioned above, we extracted detailed data on renal function only for patients who required new RRT postoperatively, excluding patients who had required RRT preoperatively and those who did not require RRT postoperatively. Thus, we could not estimate postoperative renal outcomes in all surgical patients. Second, with a study period of 10 years, the assessment of long-term outcomes was not possible for eligible patients recruited in the latter part of the period of observation. Therefore, we used mortality at 6 months after surgery as a measure of short-term outcome. Prospective observational studies will be needed to provide more details on the predictive factors of postoperative RRT and mortality. Although we identified that the preoperative eGFR level was a significant risk factor of postoperative RRT dependence, our study was conducted retrospectively; thus, we could not evaluate the direct mechanism of renal dysfunction. A prospective study evaluating the factors affecting perioperative renal function is required.

In conclusion, we assessed postoperative renal outcomes among patients who required RRT after surgery over a 10-year period in our institution. Although we advocate the general need for more advanced perioperative care to lower the risk in this clinical population, we identified preoperative renal dysfunction as a specific risk factor for non-recovery from RRT postoperatively.

Acknowledgements: None declared.

Conflicts of interest: None declared.

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