Perioperative Diabetes Insipidus in Patients Undergoing Off-Pump Coronary Bypass Grafting Surgery: A Study on Incidence, Related Factors and Clinical Significance

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Research article

Keywords: Diabetes insipidus, Perioperative, OPCABG

Posted Date: December 1st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-114656/v1

Abstract

Background

Perioperative diabetes insipidus (DI) is a serious complication occurring in patients undergoing off-pump coronary artery bypass grafting (OPCABG).

Methods

This was a retrospective study of 199 patients who underwent OPCABG surgery in Anzhen hospital, Beijing, China, between January 2019 to December 2019. Patients were divided into a DI(+) group and a DI(-) group according to perioperative urine condition. The incidence of perioperative DI in patients undergoing OPCABG surgery was calculated as the main outcome. Multivariable binary logistic regression analysis was used to identify independent prognostic factors of DI.

Results

Perioperative DI occurred in 43.2% (86/199) of these patients. Mean patient age was 62.5 ± 9.0 years, and 156 (78.4%) were male. Multivariable logistic regression analysis showed a correlation between BMI(OR=0.772, 95%CI[0.670-0.890], P□0.001), Crystal quantity(OR=1.001, 95%CI[1.000-1.001], P=0.008), perioperative Cr(OR=0.965, 95%CI[0.937-0.993], P=0.016). The DI(+) group had a significantly higher imbalance postoperative PH condition(41.9% vs 28.3%, P<0.05), higher median mechanical ventilation time than the DI(-) group (22.0 vs. 20.5, P<0.01) and higher median of ICU stay hours(27.0 vs 31.0, P=0.041).

Conclusion

Coronary artery disease(CAD) patients underwent OPCABG surgery were easy to have perioperative DI, which had a higher ICU stay and mechanical ventilation time than those without DI. BMI, Crystal quantity, perioperative creatinine was associated with the presence of DI. Prospective studies are needed to validate these findings.

Background

Off-pump coronary bypass grafting (OPCABG) surgery is an important therapy to treat CAD, the first pioneer of OPCABG surgery was Kolessov in the 1960s, the proportion of this treatment to treat CAD patients has been increasing in recent years[1]. In OPCABG surgery, the operation may cause significant fluctuations in the patients' hemodynamics. Maintaining blood pressure stability is essential in the perioperative of OPCABG surgery, therefore, it is very important to maintain a stable internal environment and fluid balance during the perioperative period[2]. Diabetes insipidus (DI) often occurs in OPCABG surgery, excessive urine production can exacerbate circulatory fluctuations. However, we often ignore the emergence of DI and risk factors for poor outcomes in patients undergoing OPCABG surgery. The role of perioperative DI in determining post-operative condition has not been evaluated, while there are seldom researches focus on the related factor of DI in patients undergoing OPCABG. In this research we detect the risk factors of DI in patients undergoing OPCABG surgery and the outcomes of these patients.

Materials And Methods

Study design

This retrospective study reviewed the charts of all CAD patients who underwent surgical treatment in Beijing Anzhen Hospital, China, between January 2019 to September 2019. Ethical approval for this study (Ethical Committee 2014023) was provided by the Ethical Committee of Beijing Anzhen Hospitals, Beijing, China (Chairperson Prof Yongxiang Wei) on 8 May 2014.

Setting

Beijing Anzhen Hospital, Beijing, China, from January 2019 to September 2019.

Patients

All patients diagnosed with CAD were included in this study. Inclusion criteria were (i) age 18–80 years and (ii) surgical treatment of OPCABG (iii) BMI 18–30 Kg/m^2. Exclusion criteria were (i) Combined with heart valve disease and requires valve replacement or repair (ii) Combined with heart failure, renal failure, uremia, primary aldosteronism (iii) surgical method was changed intraoperative.

Grouping

We defined intraoperative DI(+) as the speed of urine was greater than 2 ml/kg/h intraoperatively, postoperative DI(+) as the total amount of urine was greater than 3000 ml postoperatively within 24 hours. The DI (+) group of patients had both intraoperative DI(+) and postoperative DI(+), The DI (-) group of patients had both intraoperative DI(-) and postoperative DI(-), intraoperative DI(+) and postoperative DI(-) or intraoperative DI(-) and postoperative DI(+).

Data collection

Information regarding patient gender, age, history of hypertension (yes/no), type 2 diabetes (yes/no), body mass index (BMI), Blood routine (including hemachrome, white blood cells, platelet), Serum biochemistry (including AST, Creatinine, Na^+, K^+)

Intraoperative condition of the lowest temperature, maximal blood pressure, total infusion quantity, crystal quantity, colloidal quantity, blood loss, operating time, perioperative total urine volume were collected from the database. The speed of urine intraoperatively was calculated by total urine(ml)/body weight(Kg)/operating time(h).

Recovery condition of mechanical ventilation time, ICU stay, hospital stay was collected from the database

Serologic examination. Routine blood tests and biochemical, total volume of urine were monitored till 24 hours after surgery.

Anesthetic management

Patient vital signs were regularly monitored after hospital admission. All patients received standard anesthesia including 10 mg morphine i.v. before entering the operating room, and 5-lead ECG, pulse oximetry (SpO_2), blood pressure, central venous pressure (CVP) and bispectral index (BIS) monitoring. Anesthesia was induced using midazolam (3 to 5 mg), etomidate (150 to 300 μg kg^{-1}), sufentanil (1 to 3 μg kg^{-1}), and cis-atracurium (0.2 mg kg^{-1}) for muscle relaxation. Patient hemodynamics including systolic pressure, CVP and heart rate were maintained and fluid replenished as needed during induction. Sufentanil (0.5 to 1.5 μg kg^{-1}), propofol (2 to 5 mg kg^{-1} h^{-1}) and cis-atracurium (0.11 mg kg^{-1}) were administered to maintain a BIS value of 45 ~ 55.

Primary outcome and secondary outcome

Our primary outcome was the incidence of perioperative DI in patients undergoing OPCABG surgery to treat CAD. Our secondary outcomes including measurement of factors related to perioperative DI, extubation time, ICU duration, and activity of daily living scale score.

Statistical analysis

SPSS Statistics Desktop (version 21.0.0 for Mac OS, IBM, Armonk, NY, USA) was used for statistical analysis. Mean ± standard deviation was used to express continuous data, and frequencies were used to express categorical data. Normally distributed continuous variables were compared using a two-tailed Student's t-test. Wilcoxon rank sum testing was used for inter-group comparisons when parametric data were not normally distributed. χ^2 testing was performed to compare categorical variables. Multivariable binary logistic regression analysis was used to identify independent prognostic factors. A P value less than 0.05 indicated a significant difference. The sample size was calculated using a 1-sample, 1-sided test with a power of 0.99 and $\alpha < 0.05$. Formulas used are shown in the appendix.

Results

Baseline characteristics

247 of these patients planned to receive CABG and 234 patients planned to receive OPCABG. 35 additional patients were excluded (21 patients changed the operation style and received CABG which was planned to receive OPCABG, 5 patients was diagnosed chronic renal failure, 9 patients missing data in the case database). One hundred and ninety-nine cases were evaluable for this study(Graph 1.).

The result of primary outcome and secondary outcome

Eighty-six (43.2%) patients were DI (+). In all these patients, one hundred and twenty-six (63.3%) were male, their average age was 62.5 years. Their average speed of urine was 5.6 ± 3.3 ml/kg/h.

intraoperatively, the average total amount of urine was 3373 ± 1695 ml postoperatively within 24 hours in the ICU. In the DI(+) group, the average speed of urine was 7.0 ± 3.4 intraoperatively, the average total amount of urine was 4708 ± 1298 ml postoperatively. In the DI(-) group, the average speed of urine was 4.5 ± 2.7 ml/kg/h intraoperatively, the average total amount of urine was 2348 ± 1176 ml postoperatively. The percentage of imbalance postoperative PH condition ($P < 0.05$), duration of post-operative mechanical ventilation ($P < 0.01$), ICU stay ($P = 0.04$) was longer in DI (+) patients, compared to that of DI (-) patients (Table 1).

Table 1
Patients' demographics and clinical characteristics

index	DI(-)group	DI(+)group	OR(95%CI)	*P*
N(%)	113(56.8%)	86(43.2%)	-	-
General condition				
Age(year,mean ± SD)	62.5 ± 8.3	62.6 ± 9.9	1.001(0.970–1.033)	0.939
BMI (kg m-2)	26.99 ± 3.46	24.76 ± 2.94	0.766(0.680–0.863)	0.001
Male, n (%)	94(83.2)	62(70.1)	0.522(0.264–1.033)	0.060
Hypertension, n (%)	78(69.0)	49(57.0)	0.594(0.331–1.066)	0.080
Diabetes, n (%)	46(40.7)	29(33.7)	0.741(0.413–1.328)	0.314
Perioperative condition				
Hemachrome(g l-1)	142.2 ± 14.9	141.2 ± 13.6	0.946(0.990–1.019)	0.645
White blood cells (109 l-1)	7.2 ± 1.7	7.1 ± 1.8	0.972(0.893–1.027)	0.742
PLC(109 l-1)	235 ± 62	222.0(193.0,270.5)	0.999(0.994–1.003)	0.622
BNP(pg/mL)	70.0(31.0,167.0)	63.5(29.0,156.0)	0.999(0.997–1.001)	0.677
AST(IU/L)	22.0(18.0,27.8)	25.0(18.8,39.5)	1.010(0.996–1.023)	0.045
Creatinine (umol/L)	78.3 ± 20.4	69.8 ± 15.6	0.972(0.954–0.990)	0.002
Na (mmol/L)	139.8 ± 2.8	139.5 ± 2.2	0.956(0.856–1.068)	0.427
K (mmol/L)	3.9 ± 0.3	3.9 ± 0.3	1.129(0.459–2.773)	0.793
CVP (mmH2O)	7.8 ± 2.5	7.0 ± 3.0	0.896(0.986–0.997)	0.043
intraoperative condition				
The lowest temperature (°C)	35.5 ± 0.7	35.3 ± 0.8	0.611(0.414-0.900)	0.011

index	DI(-)group	DI(+)group	OR(95%CI)	*P*
Maximal BP(systolic,mm Hg)	157.4 ± 21.4	159.9 ± 22.6	1.005(0.993–1.018)	0.415
Maximal BP(diastolic,mm Hg)	78.4 ± 12.6	80.5 ± 10.4	1.016(0.991–1.041)	0.208
Total infusion quantity (ml)	2545 ± 713	2863 ± 1050	1.000(1.000-1.001)	0.012
Crystal quantity (ml)	1617 ± 666	2095 ± 1150	1.001(1.000-1.001)	0.001
Colloidal quantity (ml)	906 ± 498	769 ± 497	0.999(0.999-1.000)	0.056
Blood loss (ml)	708 ± 308	778 ± 347	1.001(1.000-1.002)	0.129
Operating time (min)	221 ± 43	208 ± 42	1.000(1.000-1.014)	0.039
Postoperative condition				
Hemachrome(g l-1)	106 ± 20	108 ± 20	1.004(0.990–1.019)	0.544
White blood cells (109 l-1)	11.6 ± 4.1	10.9 ± 4.1	0.957(0.893–1.027)	0.222
PLC(109 l-1)	187.0(150.0,223.0)	165.5(136.0,205.8)	0.996(0.991–1.001)	0.026
AST(IU/L)	22.0(18.0,31.0)	23.0(18.0,32.0)	0.999(0.995,1.003)	0.607
Creatinine (umol/L)	71.2 ± 22.6	64.3 ± 15.8	0.982(0.966–0.997)	0.017
Na (mmol/L)	140.5(139.1,142.0)	141.2(139.3,143.0)	0.998(0.989–1.006)	0.089
K (mmol/L)	4.2 ± 0.4	4.1 ± 0.5	0.733(0.396–1.354)	0.322
CVP (mmH2O)	8.1 ± 2.8	7.2 ± 2.8	0.887(0.798–0.987)	0.025
Recover condition				
7.35 < Postoperative PH < 7.45, n(%)	81(71.7%)	50(58.1%)	1.823(1.008–3.296)	0.046
Mechanical ventilation time	20.5(15.5,26.0)	22.0(18.8,41.9)	1.008(0.996–1.021)	0.009
ICU stay	27.0(21.9,50.6)	31.0(20.3,47.8)	1.003(0.994–1.012)	0.041

index	DI(-)group	DI(+)group	OR(95%CI)	*P*
Hospital stay	11.3 ± 3.4	12.4 ± 4.6	1.074(0.999–1.156)	0.558

Perioperative condition including: the lowest temperature, total infusion quantity, crystal quantity, operating time. Intraoperative and postoperative condition including: AST, creatinine and CVP were associated with the presence of perioperative DI (Table 1).

The result of Univariate analysis and Multivariable binary logistic regression

BMI (OR 0.772, 95%CI: 0.670–0.890, P < 0.01), Crystal quantity (OR1.001, 95%CI: 1.000-1.001, P = 0.008), Perioperative Cr (OR0.965, 95%CI: 0.937–0.993, P = 0.016) as related factors for DI (Table 2).

Table 2
Multivariable analysis of related factors for per-operative HO of AAD.(n = 497)

Variables	Crude analysis			Adjust analysis		
	OR	95%CI	*P*	OR	95%CI	*P*
BMI	0.772	0.670–0.890	▯0.001	0.718	0.590–0.874	0.001
Crystal quantity (ml)	1.001	1.000-1.001	0.008	1.001	1.000-1.002	0.010
Perioperative Cr	0.965	0.937–0.993	0.016	1.001	1.000-1.002	0.010

Adjust analysis: Add BMI, Hypertension, Diabetes, AST, Creatinine, CVP, The lowest temperature, Total infusion quantity, Crystal quantity, Colloidal quantity, Blood loss, Operating time, PLC into multivariable analysis

The occurrence of DI intraoperatively and postoperatively

The occurrence of DI was very high in the patients undergoing OPCABG surgery, during the period of operation, 175 patients’ speed of urine more than 2 ml/kg/h (87.9%, B + C in Graph 2.), during the period of ICU, the number of postoperative amount of urine more than 3000 ml was 125 (62.8, C + D in Graph 2.). The number of patients without DI was 14 (7.0%, A in Graph 2.)

Discussion

OPCABG surgery is an important therapy to treat CAD, as OPCABG surgery may improve long-term outcomes by reducing the rates of perioperative myocardial injury, stroke, and cardiac-related mortality, more and more patients receive this therapy[3]. However, OPCABG surgery is also known to cause a number of complications, including fluid, electrolyte, and acid-based imbalances[3]. The changes of these internal environment could cause DI which is a condition that the kidney are unable to conserve water[4]. DI is either due to deficient secretion of arginine vasopressin (AVP/ADH) (central) or to tubular unresponsiveness (nephrogenic). It has a high mortality and carries severe morbidity. DI after OPCABG surgery can lead to increased medication requirements. Predicting which patients are at high risks for developing DI can help direct services to ensure adequate care and follow-up.

The objective of this study was to retrospectively review our institution's data on patients undergoing OPCABG surgery and determine which clinical/laboratory variables are associated with DI in this patient population.

In our study, the occurrence of DI in the patients underwent OPCABG was very common, the percentage of patients suffered from DI perioperatively was 43.2%, the percentage of DI intraoperatively and postoperatively was 87.9% and 62.8%.

DI morbidity and mortality is mostly dependent on the electrolyte imbalance it produces, osmotic disturbances, acid base changes and the effect that has on end organ function. As it has shown in our results, the DI(+) group had a higher imbalanced postoperative PH condition than DI(-) group. We highly considered that the occurrence of DI was central DI due to the touch to aortic arch and left atrium of the heart and stimulating to the osmotic pressure receptor. Although the creatinine concentration was higher in the DI (-) group, both the concentration of these two group were in normal condition. After the occurrence of DI, fluid imbalance was further aggravated in patients with a low BMI compared to those with a high BMI[5]. In our study, there was significant difference between BMI in these two group (DI (-) vs. DI (+), 26.99 + 3.46 vs. 24.76 + 2.94).

DI is caused by insufficient production and secretion of antidiuretic hormone (ADH), or the inability of the kidney tubules to respond to ADH. ADH is a key factor to adjust kidney to conserve water. Secretion of ADH is primarily regulated by plasma osmolarity, but other factors such as left atrial distention, circulating blood volume, exercise, and certain emotional states can also alter ADH releasing[6].

The release of ADH directly acts on the kidney. Non-osmotic stimulus of ADH releasing is mediated through volume receptors located in the left atrium of the heart, aortic arch, and carotid artery. Osmotic stimulus of ADH release is mediated through osmoreceptors in the hypothalamus[7]. What's more, ADH were found to deficiency developed in patients undergoing aortocoronary bypass operations in some studies[8, 9]

The reason of DI in patients undergoing OPCABG may associated with both non-osmotic and osmotic stimulus of ADH. For non-osmotic of ADH, the operative procedures of OPCABG including changing the position of the heart always lead to touch to aortic arch and left atrium of the heart. For osmotic stimulus, Cerebral hypoperfusion can occur from intraoperative hypotension and declined cardiac output, Embolic strokes associated with the operation are predominantly attributable to thromboembolism and aeroembolism, these factors may restrict the function of hypothalamus[10].

For CAD patients underwent OPCABG surgery, the use of propofol and fentanyl can influence blood pressure, and the operator's operation on the heart also aggravates the difficulty of hemodynamic maintenance. The use of noradrenaline is very common in OPCABG surgery to maintain blood pressure. Adrenal hormone inhibits the synthesis and secretion of AVP, thus adrenal insufficiency can result in increased levels of AVP, which are then lowered following initiation of glucocorticoid replacement.

There were several limitations to this study. This was a retrospective study that needs independent validation. Patients evaluated here underwent OPCABG surgery by different operator and anesthetist, it is hard to avoid the influence caused by the operator and anesthetist. The use of drugs during perioperative period was not recorded very accuracy, there may be some factors of drugs associated with DI.

The occurrence of DI in patients undergoing OPCABG surgery is very common, prospective studies are needed to validate these findings and we need to focus more on this point.

Conclusion

About 43.2% of the CAD patients underwent OPCABG surgery had DI. Their recovery from surgery was slower than that of patients without DI. BMI, Crystal quantity, perioperative creatinine was associated with the presence of perioperative DI. Prospective studies are needed to validate these findings

Abbreviations

Diabetes Insipidus: DI

Off-Pump Coronary Artery Bypass Grafting: OPCABG

Coronary Artery Disease: CAD

Body Mass Index: BMI

Odds Ratio: OR

Confidence Intervals: CI

Creatinine: Cr

Intensive Care Unit: ICU

Intravenous:I.V.

Central Venous Pressure: CVP

Bispectral Index: BIS

Aspartate aminotransferase: AST

Arginine vasopressin: AVP

Antidiuretic hormone: ADH

Declarations

Ethics approval and consent to participate

This study was in agreement with the guidelines of the Ethics Committee of the Beijing Anzhen hospital.

Consent for publication

All patients gave verbal and written informed consent prior to enrollment.

Availability of data and materials

The dataset used and analyzed during the current study is available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors' contributions

YWY was responsible for the original idea, which was co-developed by all authors. All authors (PZ, ZJG, JKL, MJ, WPC amd YWY) developed the conception and design of this manuscript. PZ, ZJG, JKL and MJ validated the provision of study materials or patients and carried out all the data management and statistical analyses, which was supervised by YWY. PZ was responsible for writing the manuscript, which was critically revised by all co-authors. The authors read and approved the final manuscript.

Acknowledgements

None

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Figures

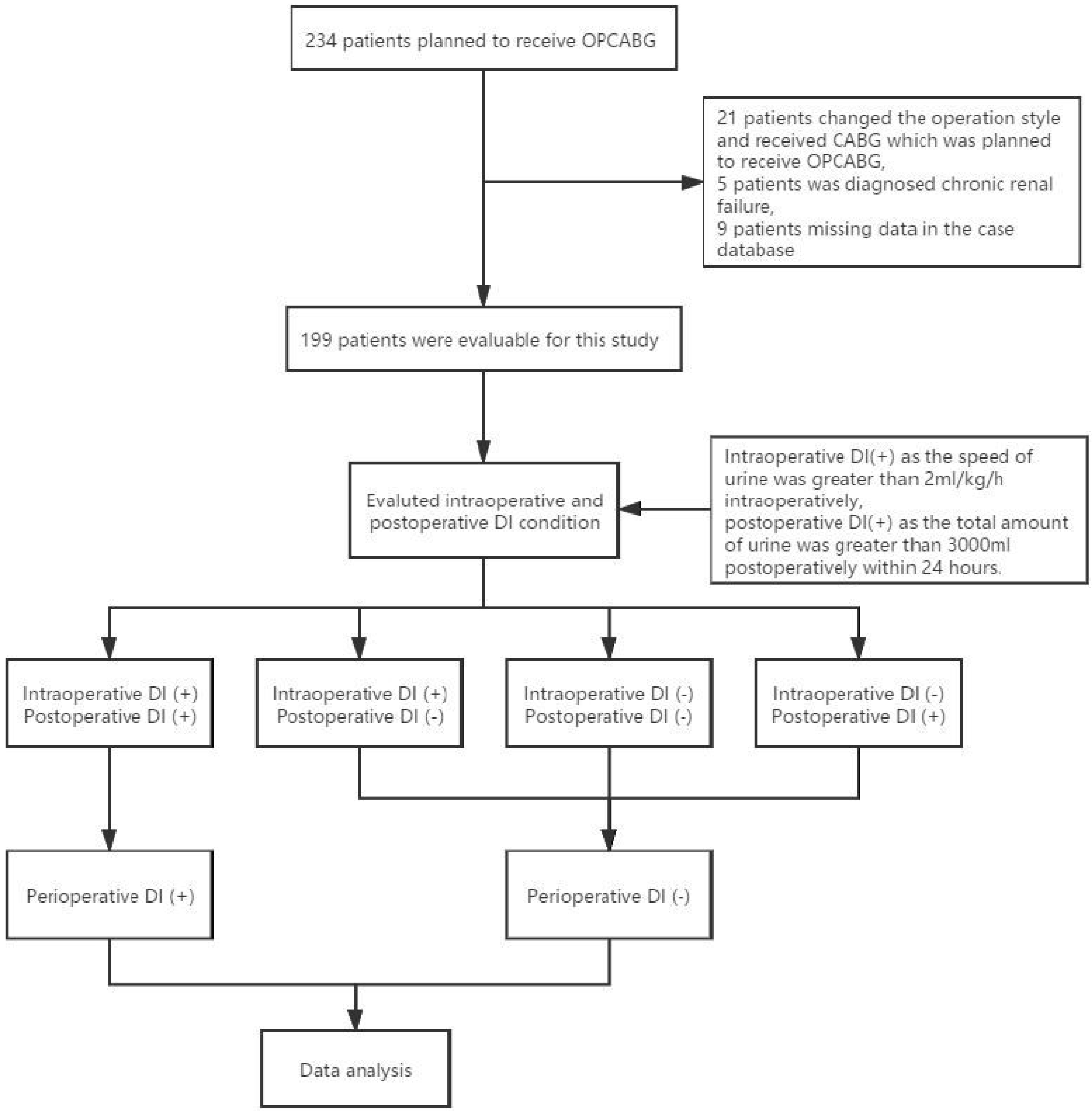

Figure 1

Patients selection of perioperative diabetes insipidus in patients undergoing OPCABG surgery.

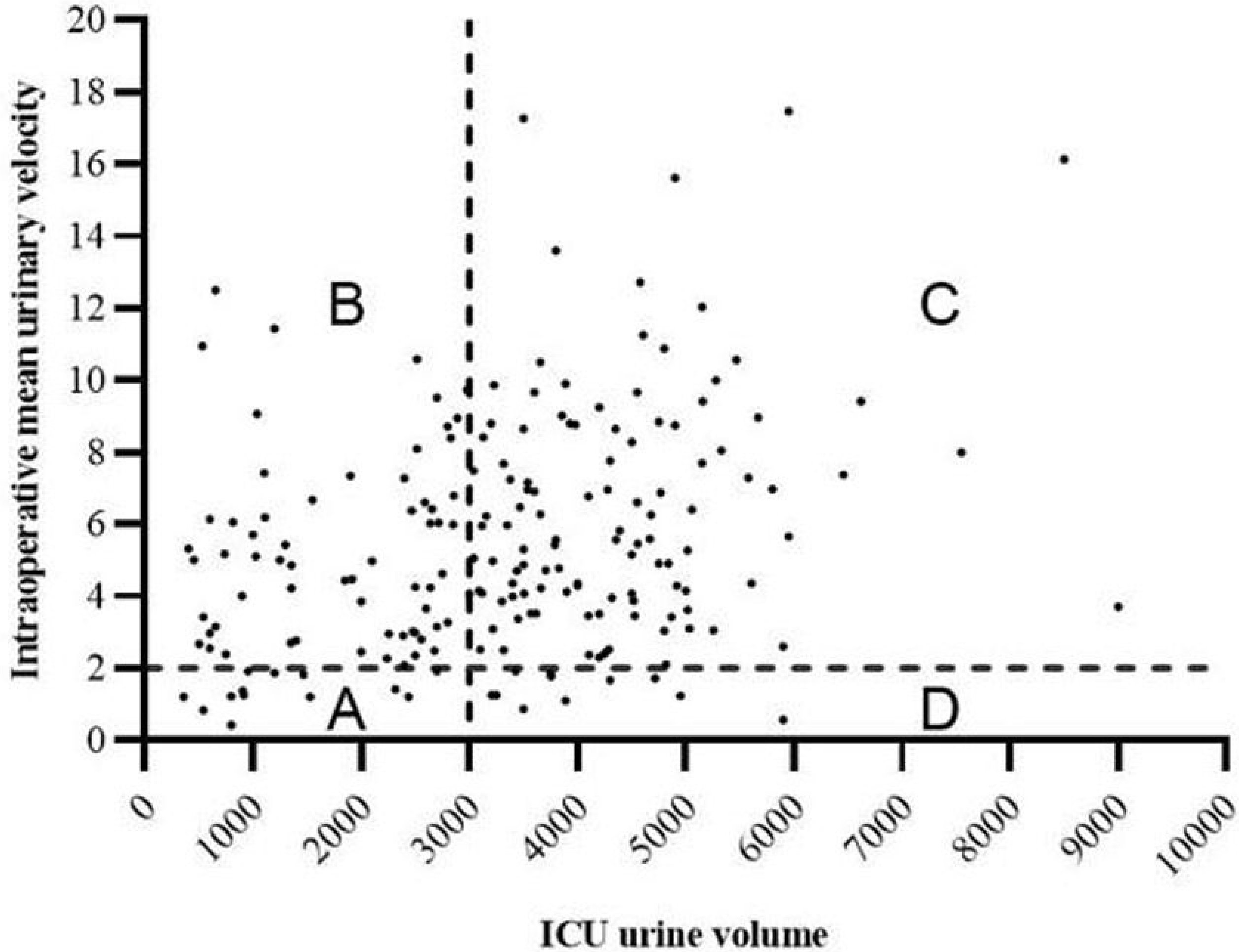

Figure 2

The occurence of DI intraoperatively and postoperatively.