Aqp2 may affect the occurrence of acute kidney injury after cardiopulmonary bypass

Yingjie Xiao
First Affiliated Hospital of Anhui Medical University
Yanli Li
First Affiliated Hospital of Anhui Medical University
Wenpeng Dong
First Affiliated Hospital of Anhui Medical University
Long Gui
First Affiliated Hospital of Anhui Medical University
Xu Yu
First Affiliated Hospital of Anhui Medical University
Min Lin (ahykdxlinm@163.com)
First Affiliated Hospital of Anhui Medical University https://orcid.org/0000-0002-4886-1497

Research article

Keywords: Aquaporin 2, Acute kidney injury, Cardiopulmonary bypass

Posted Date: August 31st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-64448/v1

Abstract

BACKGROUND

Acute kidney injury (AKI) is one of the most important postoperative complications of cardiac surgery, and despite complete recovery of renal function after surgery, AKI is independently associated with high mortality within 10 years after surgery. Experiments show that Aquaporin 2(AQP2) is associated with postoperative AKI. Results of AQP2 release patterns after acute kidney injury have not been the same in different studies.

METHODS

We selected all patients undergoing extracorporeal circulation surgery, collected their urine samples before and after surgery, centrifuged at 3000 rpm for ten minutes, and detected the expression of AQP2 in urine by ELISA.

RESULTS

Most of the patients without AKI showed an upward trend of AQP2, while the patients with AKI showed a downward trend of AQP2. Patients with lower AQP2 levels before surgery have a lower chance of developing AKI.

CONCLUSION

AQP2 can be used to predict and prevent postoperative AKI.

Background

Since the discovery of Aquaporin (AQP), the role of AQP protein in water transport and tissue edema formation in different tissue cells has received significant attention. AQP proteins are a family of membrane proteins responsible for the rotation of water inside and outside the cell and some other small molecular substances. It can increase the water permeability of cell membranes, thereby driving the transport of water under the action of osmotic pressure. A total of 13 AQP proteins have been found in mammals (0–12). It is widely distributed in organs such as red blood cells, kidneys, lungs, brain and eyes(1)

The kidney is an organ that maintains water balance in the body. Its main function is to regulate the concentration and dilution of urine, and to regulate water reabsorption through different AQPs. Of the 13 aqp (AQP0-AQP12) currently found, nine aqp (AQP1-8 and AQP11) were detected in human kidneys. Dysfunction of AQPs, especially AQP1-4, can cause disorders with water balance. Among them, AQP2 is

the most researched aquaporin, which is mainly expressed in the main cells of the renal junction tubules and collecting tubules. It is one of the most important channel proteins involved in regulating urine concentration. Rojek A et al.(2) after genetic research, compared with wild mice, AQP2-deficient mice lost weight and increased their urine output ten-fold in adulthood. Moreover, the urine output decreased significantly after dehydration, and urine osmotic pressure did not change significantly. Human water balance is critical and cannot be compensated by other mechanisms. In fact, the expression of AQP2 in rats increased under water-restricted conditions, while the expression of AQP2 decreased in conditions of water overload(3). The water reabsorption function of AQP2 is mainly regulated by arginine vasopressin (AVP)(7). There is no circadian rhythm in the secretion of AQP2(4).AVP is a hormone released from the posterior pituitary, which can stimulate the expression of AQP2 in the apical plasma membrane(5, 6). When AVP stimulation was removed, AQP2 returned to the cytoplasm and restored the cell impermeability(7). In normal animals, the opposite effect could be observed by using AVP antagonists(8).

In addition to AVP, there are also some factors including osmotic pressure, inflammation, insulin, aldosterone / prostaglandin and other factors that also affect AQP2 transcription, transport and post-translational modification(9). A study in the 20th century showed that higher levels of insulin can reduce urinary excretion(10). The water permeability of the isolated medullary collecting duct was increased after insulin infusion(11) Using mpkCCD (CL4) cells(12), it can be proved that insulin can induce a slight increase in AQP2 abundance in whole cells(13).

Acute kidney injury (AKI) is one of the most important postoperative complications of cardiac surgery, and despite complete recovery of renal function after surgery, AKI is independently associated with high mortality within 10 years after surgery(14). In AKI caused by ischemia-reperfusion, AQP2 decreases after acute kidney injury(15). A recent study showed that aquaporin-2 contained in urine extracellular vesicles in patients after renal transplantation Significantly reduced on the first postoperative day, accompanied by high urine volume and low osmotic pressure. Since then, AQP2 levels have gradually increased to control levels on the 6th day(16).However, some studies have pointed out that the content of aquaporins in urine is significantly increased after extracorporeal circulation(17). Therefore, the purpose of this study is to further determine the relationship between AQP2 and the occurrence of AKI after cardiopulmonary bypass, and to provide us with directions for further prevention and treatment of AKI.

Although it has been found that some indicators such as cystatin C(18), neutrophils(19), urinary uromodulin(20), α 1-antitrypsin(21) and urinary IL-18(22) can predict the occurrence of AKI, creatinine is still the gold standard. As a result, we have no recognized indicators to judge AKI in the early stage. And we have not found an effective way to intervene the occurrence of AKI. In this context, we chose aquaporins for further study.

According to relevant literature reports,aquaporin-2 was detectable in the urine in both soluble and membrane-bound forms(23). Membrane bound AQP2 is mainly located in a structure called exosomes(24). However, due to the complexity of exosomes separation, it is not easy to apply in clinical

practice. Therefore, this paper attempts to directly detect the content of AQP2 in urine after ordinary centrifugation.

Methods

Patients and protocol

This study was approved by the local ethics committee of the first affiliated hospital of Anhui medical university. The patients were prospectively observed at the First Affiliated Hospital of Anhui Medical University (Hefei, Anhui, China) from December 2019 to April 2020. All patients participating in the study obtained informed consent to participate in the study. We included all patients undergoing CPB during this period. Patients with one of the following characteristics were excluded: severe systemic infection or inflammation, end-stage renal failure or hemodialysis, cardiogenic shock, diabetes ,and the use of tolvaptan in preoperative and postoperative clinical procedures.

Urine samples were collected before, after and 24 hours after surgery. All samples were immediately centrifuged at 3000 rpm for 10 minutes, and the samples were stored at -80 ° C before analysis. U-AQP2 was measured using a sandwich ELISA kit(Jianglai Biological Company, Shanghai, China), and U-AQP2 was specifically detected with high sensitivity, minimum detection concentration is less than 1.0 pg / ml. Intra-assay coefficient of variation and inter-assay coefficient of variation are less than 9% and 11%, respectively. The test procedures are in accordance with the instructions. All measurements were performed by a technician who did not understand the group. Record the preoperative, intraoperative, and postoperative conditions of each patient, including demographic and clinical information, age, weight, gender, and preoperative medications. CPB, aortic occlusion time, and renal function were recorded. Record the patient's blood gas before, during and after the operation.

Operative Technique And Management

All patients were intravenously anesthetized according to a standard protocol using sevoflurane (1%), propofol (2.0 mg / kg), midazolam (0.1 mg / kg), rocuronium (1 mg / kg), and sufentanil (10 μg / kg) induced anesthesia. The method of maintaining anesthesia is continuous intravenous injection of propofol (4–12 mg / kg / h) during extracorporeal circulation, intermittent intravenous infusion of sufentanil citrate (total amount not exceeding 8–30 μg / kg), intermittent intravenous Rocuronium bromide (0.2–0.5 mg / kg).

All patients established a cardiopulmonary bypass at room temperature (35–36 ° C) after a midline incision of the sternum. Extracorporeal circulation uses roller pumps (Sarns, 3M, USA), membrane oxygenators (Medtronics, USA), ultrafilters (Solin, Italy), and arterial filters (Senko Medical Devices Co., Ltd., Tokyo, Japan). Pre-fill with saline (1000 mL), hydroxyethyl starch (500 mL), furosemide (1 ml), heparin (1 ml), and ulinastatin (500,000 u). After ACT ≥ 400 s, the transfer started. According to the length of the operation, the cardiac cardioplegic solution was Delnido cardioplegic solution (each

1000 ml matrix solution contains 20% mannitol 16.3 ml, 50% magnesium sulfate 4 ml, 4% sodium bicarbonate 13 ml, 15% potassium chloride 13 ml, lido 13 ml of caine, the above crystals are mixed with autotrophic blood and 4: 1) or HTK arrest solution (containing histidine, tryptophan and ketoglutarate). Heart beats back automatically after aorta opens.

All patients were routinely used furosemide and spironolactone according to urine volume after surgery, to ensure that the output was slightly greater than the input. All patients routinely use cardiotonics to maintain normal blood pressure.

Statistics

Statistical analysis using IBM SPSS statistics version 26. Graphing with Graphpad prism 8. Statistical analysis of urinary AQP2 preoperatively, postoperatively and 24 h postoperatively in 52 patients. All data meet the normal distribution after passing the K-S normal test. Comparing differences between groups using Mann-Whitney U Test. The correlation coefficient between the two samples was calculated by Person Correlation.All statistical tests were two-tailed tests, $p < 0.05$, which was statistically significant.

Results

Baseline characteristics and the clinical course

The study group consisted of **52** patients who underwent CPB. No patient received tolvaptan before surgery. There were no deaths or Secondary surgery. The evaluation standard of AKI is based on KDIGO which includes: a) an increase in serum creatinine by ≥ 0.3 mg/dl (≥ 26.5 μmol/l) within 48 h;b):an increase in serum creatinine to ≥ 1.5 times baseline within the previous 7 days;c) urine volume ≤ 0.5 ml/kg/h for 6 h.20 of them had postoperative acute kidney injury. Furosemide diuresis was routinely used in all patients during surgery.

The groups' baseline characteristics and operative and postoperative parameters are shown in Table 1. We divided into two groups based on whether the patient had acute kidney injury. We compared the two sets of data in Table 2. The results show that compared with the non-AKI group, the AKI group is older, with more male patients, longer CPB time, and AQP2 shows different trends. Age and history of hypertension are also considered as risk factors for acute kidney injury after surgery. Interestingly, gender may also affect the occurrence of AKI.

Table 1
Baseline characteristics, operative, and postoperative parameters in the study

Baseline characteristics	
Sex(M/F)	26/26
Age(years)	54.5[43-62.5]
Hypertension (%)	8(15.4)
Creatinine(μmol/L)	66.0[54.0-78.1]
Aqp2(ng/ml)	263.55[170.12-346.42]
Operative parameters	
CPB duration(min)	133.0[89.0-192.2]
Aortic Occasion Time(min)	80.0[45.5–131.0]
Postoperative parameters	
Aqp2 Difference(ng/ml)	0.75[-22.98-24.73]
Creatinine Difference(μmol/L)	12.15[0.70-37.28]
AKI(yes/no)	20(38.5)/32□61.5□
Continuous data are presented as medians [interquartile range], whereas categorical data are presented as total number of the incidents (percentage)	

Table 2
Aqp2 comparison between two groups divided by aki

AKI		
	no	yes
sex(M/F)**	12(37.5)/20□62.5□	14(70)/6□30□
Age(year)*	52[32–61]	56[50–66]
Hypertension(%)	3(9.4)	5(25)
Aqp2 Preoperative(ng/ml)	230.25[152.22-318.68]	284.55[193.90-498.53]
CPB duration(min)**	113[86–162]	184[126–249]
aqp2 Difference(ng/ml)***	9.97[-8.24-28.84]	-13.90[-25.95-0.76]
Continuous data are presented as medians [interquartile range], whereas categorical data are presented as total number of the incidents (percentage)		
*:p < 0.1; **:p < 0.05; ***:p < 0.01		

Aqp2 Indicator

Postoperative AQP2 increased in the non-AKI group, while postoperative AQP2 decreased in the AKI group. In addition, we also found that the reduced level of AQP2 may be related to the degree of kidney damage(Fig. 1). The more severe the kidney damage, the more obvious the decrease in AQP2. The pre-operative AQP2 content of female patients is lower than that of male patients, Patients with postoperative renal injury also had lower levels of AQP2 than patients without postoperative renal injury. (Fig. 2)

Discussion

Our study evaluated changes in AQP2 before and after surgery. Different from previous research results(17), We found that the trend of AQP2 changes during surgery is not the same. And the change trend of AQP2 is related to the change trend of creatinine 24 h after operation. The more severe the kidney damage, the higher the reduction in AQP2. Unlike Masahiro Fujii, t AQP2 does increase in some patients after operation, but the amount of AQP2 in patients with AKI is reduced after operation. We analyzed the AQP2 level of patients before surgery and found that patients without AKI had lower AQP2 levels than patients with AKI. It seems that the changes in AQP2 are inextricably linked to the occurrence of postoperative AKI.

Based on the above results, we seem to think that lower levels of AQP2 can reduce the incidence of postoperative AKI. When kidney function is impaired, it will protect its own function by reducing the content of AQP2.We further explore the cause of this phenomenon. We know that lactic acid can reflect the perfusion of peripheral microcirculation during surgery(25). As surgery time increases, lactic acid gets higher and higher. This suggests that the kidneys may face poor blood perfusion. As we mentioned before, the lack of AQP2 will lead to increased urine output. The kidney may improve its perfusion by reducing AQP2.

But this does not explain the problem of elevated AQP2 in non-AKI patients. We make reasonable guesses about this result. In the early stage of the operation, after the aorta was blocked, the patient's blood pressure dropped rapidly. At this time, the kidney thought that the body had acute shock. Therefore, the main measures for the kidney to cope with this are to increase the content of AQP2, increase the reabsorption of water, and reduce the discharge of urine. At this stage, the kidneys have not suffered substantial damage. With the prolonged ischemia, kidney damage becomes more severe, and the focus of the kidney shifts from improving shock to protecting its own function. We did not retrieve the literature related to the changes of AQP2 in the early stage of shock to verify this conclusion.

At the same time, our results also show that gender may also affect the occurrence of AKI. Male patients seem to be more prone to AKI than female patients. Our data results do not show a significant difference in the extracorporeal circulation time of male patients and female patients. In addition, female patients have lower AKI levels than male patients before surgery. We investigated the data and found that AQP2 is

indeed affected by estrogen. However, the research results given by different scholars are not the same. Tingskov SJ et al.'s results show that estrogen antagonist tamoxifen can reduce AQP2 downregulation(26). However, studies by Kim SO et al. have shown that estrogen can increase AQP2 expression in the bladder(27). Our research seems to support the former.

Cheema et al. reported that urine osmolality and renal AQP2 phosphorylation were increased in ovariectomized female rats. Repletion of estradiol increased urine output, decreased urinary osmolality and reduced AQP2 mRNA expression and protein phosphorylation. In addition, estradiol treatment of mpkCCD cells reduced AQP2 at both mRNA and protein levels. Further study revealed that mice lacking ERα displayed significant increases in AQP2 protein compared with wild-type controls, indicating that ER α can inhibit the expression of AQP2(28) .

Therefore, women are more able to cope with prolonged ischemic strokes than men. The reason of this phenomenon is not clear, but it will provide ideas for our future research and surgery if it's indeed caused by estrogen. We can give patients estrogen drugs before surgery to increase the content of renal aquaporins in patients to reduce or avoid the occurrence of postoperative AKI.

In addition, when traditional diuretics are less effective for postoperative patients, we often use tolvaptan to ensure the patient's urine output. Tolvaptan is a vasopressin type 2 receptor antagonist that has a diuretic effect and inhibits the reabsorption of water in the renal collecting duct without increasing electrolyte loss. It can reduce the expression of AQP2.This means that a decrease in renal aquaporin after surgery is beneficial for renal function recovery. Therefore, according to the results of this experiment, in addition to the use of estrogen, we may be able to use tolvaptan to reduce the AQP2 content of the kidney before surgery to reduce the incidence of AKI.

Conclusion

In summary, we found that AQP2 plays a vital role in renal function during and after surgery. In the early stage of cardiopulmonary bypass, due to a decrease in perfusion pressure, the kidneys reduce water discharge by increasing the content of AQP2. As kidney damage increases, the kidney protects its function by reducing AQP2. We can use AQP2 to predict whether the patient will have AKI after surgery. More importantly, we may be able to prevent the occurrence of postoperative AKI by controlling the changes in AQP2. Lower levels of AQP2 before surgery can reduce the incidence of AKI. These results provide us with ideas to prevent the occurrence of postoperative AKI: reduce the general level of AQP2 by estrogen drugs or tolvaptan before surgery. It also provides us with new research directions: improve animal experiments to clarify the effect of estrogen and tolvaptan on preventing postoperative AKI.

The limitation of this article is that this is a single-center study with a small sample size. Failed to compare under different cardiopulmonary bypass machines. Further investigation using a multicenter design with appropriate sample size of consecutive patients undergoing different types of cardiac surgery, including high-risk or complex surgical cases, is needed. Further research is needed to compare different intubation methods, different extracorporeal circulation machines, and intraoperative care. And

we did not continuously monitor the patient's AQP2 during operation. We only compared the changes of AQP2 before and after operation. Moreover, due to technical limitations, our current experiments can not prove whether AQP2 is secreted by renal cells or originated from ruptured and necrotic kidney cells.

Abbreviations

AQP Aquaporin

AKI Acute kidney injury

CPB Cardiopulmonary bypass

AVP arginine vasopressin

Declarations

Ethics approval and consent to participate

This study was approved by the local ethics committee of Anhui Medical University□The patients/participants provided their written informed consent to participate in this study.

Consent for publication

Not applicable

Availability of data and materials

The raw data supporting the conclusion of this manuscript will be made available by the authors ,without undue reservation, to any qualified researcher.

Competing interests

The authors declare that they have no competing interests.

Funding

The research was funded by individuals.

Authors' contributions

Yingjie Xiao designed and wrote the manuscript. Yingjie Xiao and Yanli Li participated in the implementation of CPB. Yingjie Xiao, Long Gui and Xu Yu participated in the data collection. Yingjie Xiao and Wenpeng Dong participated in the data analysis. Min Lin designed and supervised the experiments and wrote the manuscript.

Acknowledgements

Thanks to all the staff of Department of Cardiology and macrovascular surgery of the First Affiliated Hospital of Anhui Medical University for their support to this experiment.

References

1. King LS, Kozono D, Agre P. From structure to disease: the evolving tale of aquaporin biology. Nature reviews Molecular cell biology. 2004;5(9):687–98.
2. Rojek A, Fuchtbauer EM, Kwon TH, Frokiaer J, Nielsen S. Severe urinary concentrating defect in renal collecting duct-selective AQP2 conditional-knockout mice. Proc Natl Acad Sci USA. 2006;103(15):6037–42.
3. Murillo-Carretero MI, Ilundain AA, Echevarria M. Regulation of aquaporin mRNA expression in rat kidney by water intake. Journal of the American Society of Nephrology: JASN. 1999;10(4):696–703.
4. Sasaki S, Ohmoto Y, Mori T, Iwata F, Muraguchi M. Daily variance of urinary excretion of AQP2 determined by sandwich ELISA method. Clin Exp Nephrol. 2012;16(3):406–10.
5. Ren H, Yang B, Ruiz JA, Efe O, Ilori TO, Sands JM, et al. Phosphatase inhibition increases AQP2 accumulation in the rat IMCD apical plasma membrane. American journal of physiology Renal physiology. 2016;311(6):F1189-f97.
6. Lei L, Huang M, Su L, Xie D, Mamuya FA, Ham O, et al. Manganese promotes intracellular accumulation of AQP2 via modulating F-actin polymerization and reduces urinary concentration in mice. American journal of physiology Renal physiology. 2018;314(2):F306-f16.
7. Brown D. The ins and outs of aquaporin-2 trafficking. American journal of physiology Renal physiology. 2003;284(5):F893–901.
8. Hayashi M, Sasaki S, Tsuganezawa H, Monkawa T, Kitajima W, Konishi K, et al. Expression and distribution of aquaporin of collecting duct are regulated by vasopressin V2 receptor in rat kidney. J Clin Investig. 1994;94(5):1778–83.
9. Hasler U, Leroy V, Martin PY, Féraille E. Aquaporin-2 abundance in the renal collecting duct: new insights from cultured cell models. American journal of physiology Renal physiology. 2009;297(1):F10-8.
10. DeFronzo RA, Goldberg M, Agus ZS. The effects of glucose and insulin on renal electrolyte transport. J Clin Investig. 1976;58(1):83–90.
11. Magaldi AJ, César KR, Yano Y. Effect of insulin on water and urea transport in the inner medullary collecting duct. Am J Physiol. 1994;266(3 Pt 2):F394-9.
12. Hasler U, Mordasini D, Bens M, Bianchi M, Cluzeaud F, Rousselot M, et al. Long term regulation of aquaporin-2 expression in vasopressin-responsive renal collecting duct principal cells. J Biol Chem. 2002;277(12):10379–86.

13. Bustamante M, Hasler U, Kotova O, Chibalin AV, Mordasini D, Rousselot M, et al. Insulin potentiates AVP-induced AQP2 expression in cultured renal collecting duct principal cells. American journal of physiology Renal physiology. 2005;288(2):F334-44.
14. Hobson CE, Yavas S, Segal MS, Schold JD, Tribble CG, Layon AJ, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation. 2009;119(18):2444–53.
15. Asvapromtada S, Sonoda H, Kinouchi M, Oshikawa S, Takahashi S, Hoshino Y, et al. Characterization of urinary exosomal release of aquaporin-1 and – 2 after renal ischemia-reperfusion in rats. American journal of physiology Renal physiology. 2018;314(4):F584-f601.
16. Oshikawa-Hori S, Yokota-Ikeda N, Sonoda H, Ikeda M. Urinary extracellular vesicular release of aquaporins in patients with renal transplantation. BMC Nephrol. 2019;20(1):216.
17. Fujii M, Amitani R, Bessho R. Perioperative urinary excretion of aquaporin-2 dependent upon vasopressin in cardiac surgery. Heart and vessels. 2019.
18. Kararmaz A, Arslantas MK, Aksu U, Ulugol H, Cinel I, Toraman F. Evaluation of acute kidney injury with oxidative stress biomarkers and Renal Resistive Index after cardiac surgery. Acta chirurgica Belgica. 2019:1–9.
19. Weedle RC, Da Costa M, Veerasingam D, Soo AWS. The use of neutrophil lymphocyte ratio to predict complications post cardiac surgery. Annals of translational medicine. 2019;7(23):778.
20. Bennett MR, Pyles O, Ma Q, Devarajan P. Preoperative levels of urinary uromodulin predict acute kidney injury after pediatric cardiopulmonary bypass surgery. Pediatr Nephrol (Berlin Germany). 2018;33(3):521–6.
21. Du S, Tian J, Xiao Z, Luo Z, Lin T, Zheng S, et al. Serum alpha 1-antitrypsin predicts severe acute kidney injury after cardiac surgery. Journal of thoracic disease. 2019;11(12):5053–62.
22. Parikh CR, Mishra J, Thiessen-Philbrook H, Dursun B, Ma Q, Kelly C, et al. Urinary IL-18 is an early predictive biomarker of acute kidney injury after cardiac surgery. Kidney international. 2006;70(1):199–203.
23. Kanno K, Sasaki S, Hirata Y, Ishikawa S, Fushimi K, Nakanishi S, et al. Urinary excretion of aquaporin-2 in patients with diabetes insipidus. N Engl J Med. 1995;332(23):1540–5.
24. Miyazawa Y, Mikami S, Yamamoto K, Sakai M, Saito T, Yamamoto T, et al. AQP2 in human urine is predominantly localized to exosomes with preserved water channel activities. Clin Exp Nephrol. 2018;22(4):782–8.
25. Stammers AH, Mills N, Kmiecik SA, Petterson CM, Liu JL, Nichols JD, et al. The effect of electrolyte imbalance on weaning from cardiopulmonary bypass: an experimental study. The journal of extra-corporeal technology. 2003;35(4):322–5.
26. Tingskov SJ, Choi HJ, Holst MR, Hu S, Li C, Wang W, et al. Vasopressin-Independent Regulation of Aquaporin-2 by Tamoxifen in Kidney Collecting Ducts. Frontiers in physiology. 2019;10:948.
27. Kim SO, Song SH, Hwang EC, Oh KJ, Ahn K, Jung SI, et al. Changes in aquaporin (AQP)2 and AQP3 expression in ovariectomized rat urinary bladder: potential implication of water permeability in

urinary bladder. World J Urol. 2012;30(2):207–12.
28. Cheema MU, Irsik DL, Wang Y, Miller-Little W, Hyndman KA, Marks ES, et al. Estradiol regulates AQP2 expression in the collecting duct: a novel inhibitory role for estrogen receptor α. American journal of physiology Renal physiology. 2015;309(4):F305-17.

Figures

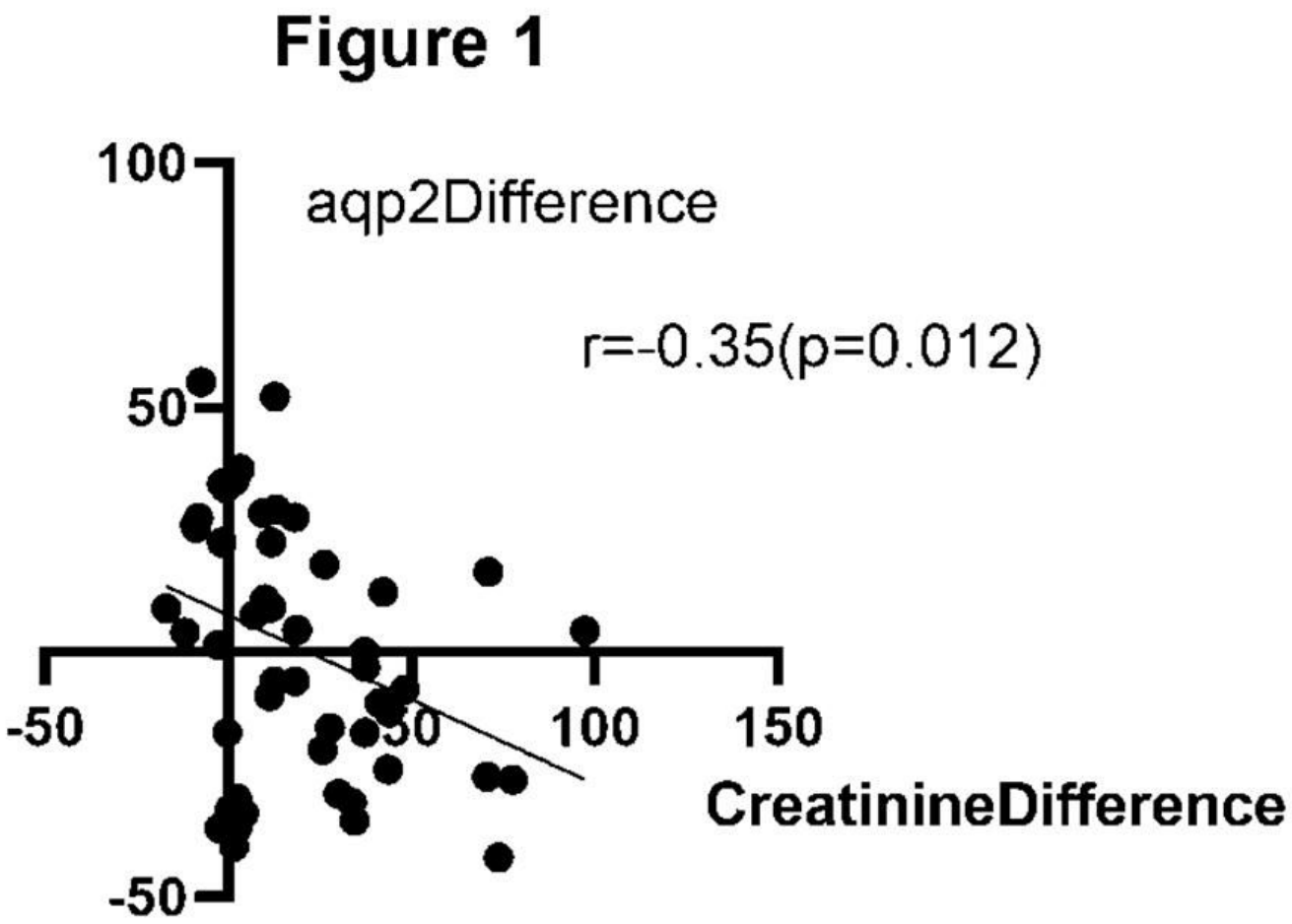

Figure 1

AQP2 changes with creatinine The change degree of AQP2 is negatively correlated with the change degree of creatinine. The data is verified by the person test. *p<0.05,**p<0.01,***p<0.001

Figure 2

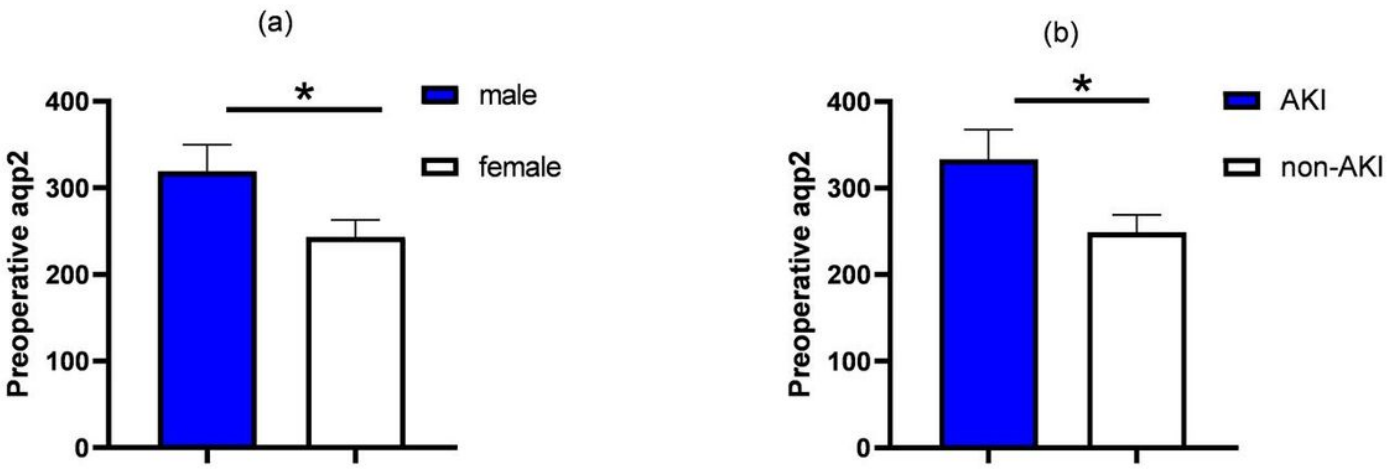

Figure 2

The expression level of AQP2 before operation under different groups The pre-operative AQP2 content of female patients is lower than that of male patients, Patients with postoperative renal injury also had lower levels of AQP2 than patients without postoperative renal injury. Date are presented as the mean±SEM(n>3 per group) and unpaired two-tailed Student's t-test were conducted; *p<0.05,**p<0.01,***p<0.001

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- GraphicalAbstract.jpg
- CentralPicture.jpg