

Elucidation of the mechanism of tubulo-Interstitial injury in chronic kidney disease by use of newly developed chronic renal ischemia model.



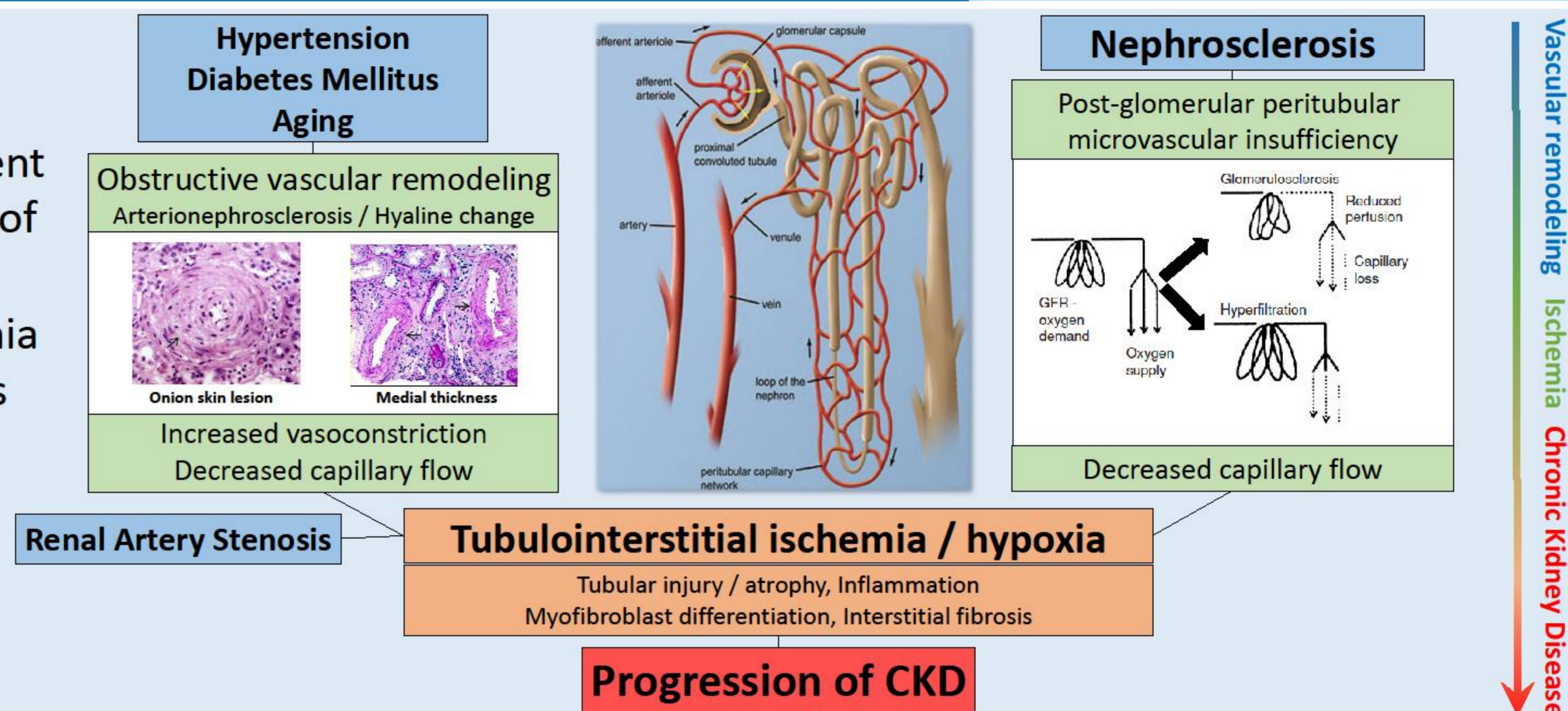
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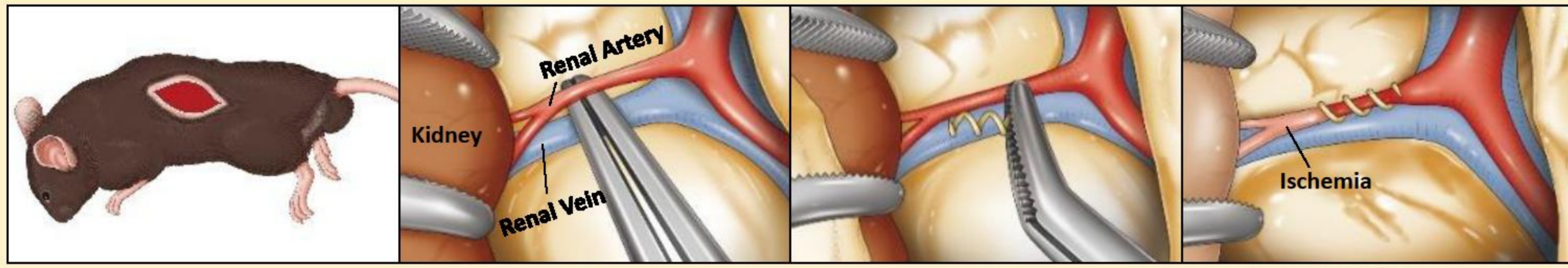
Introduction

- ▶ The renal ischemia plays an essential role in a development of chronic kidney disease (CKD); However the mechanism of renal injury needs further to be elucidated.
- ▶ Most of previous animal models to simulate renal ischemia have been ischemic-reperfusion injury model, which shows characteristics of acute kidney injury.
- ▶ To elucidate the progression of kidney dysfunction with chronic ischemia, we developed a novel chronic renal ischemia model using a titanium coil.



Methods

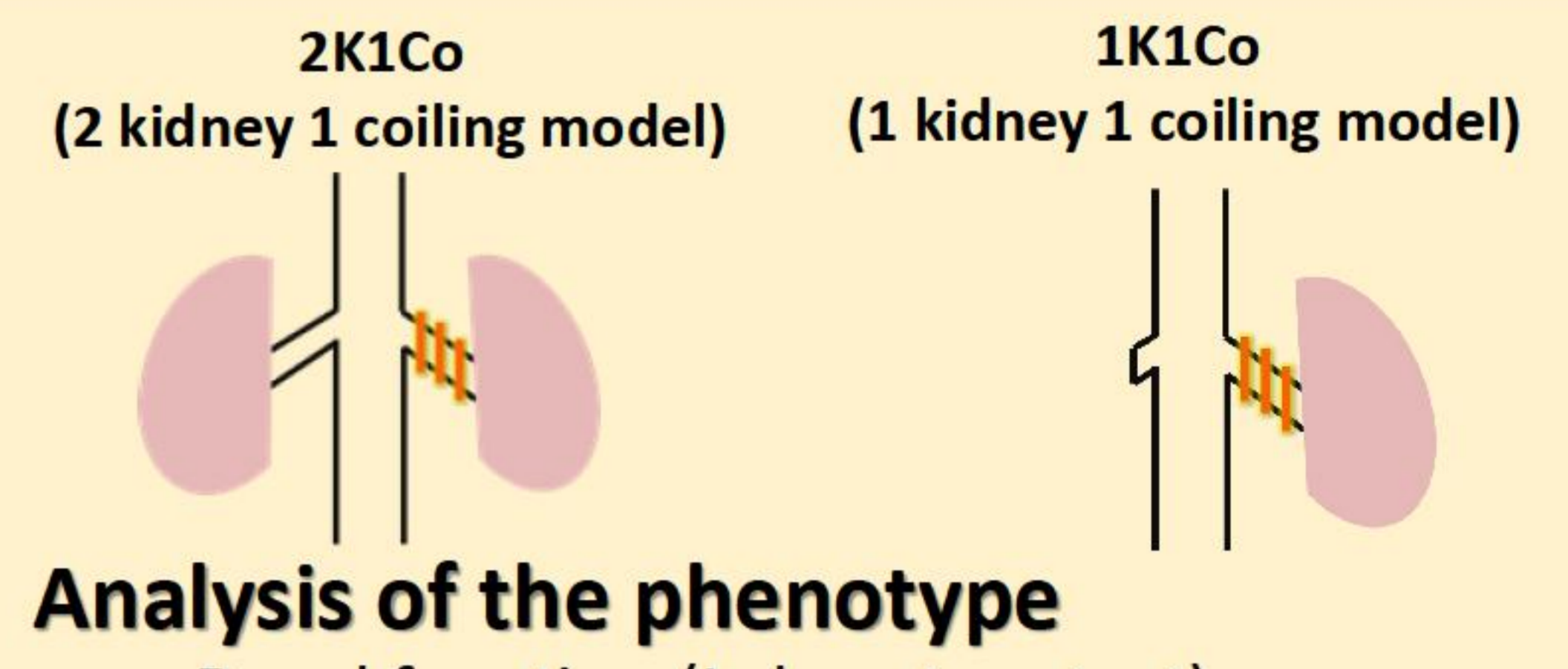
1K1Co (1 kidney 1 coiling model)



1. Anesthesia with somnopenyl (5mg/kg)
2. Nephrectomize the right kidney
3. Separate left renal artery from renal vein
4. Set a coil around left renal artery
5. Check the kidney bloodstream by a laser Doppler method.



After setting a coil around left renal artery without bleeding.
Titanium coil
Inside diameter : 0.17 - 0.28 mm



Analysis of the phenotype

- Renal function (Laboratory test)
- Blood pressure
- Kidney weight
- Pathology
- Changes of gene expression

Results

Sham: Sham operation performed.
1K0Co: Hemi-nephrectomy performed without coiling.
1K1Co 0.24: Renal artery coiling with a 0.24mm diameter coil after hemi-nephrectomy.
1K1Co 0.21: Renal artery coiling with a 0.21mm diameter coil after hemi-nephrectomy.

Blood Pressure

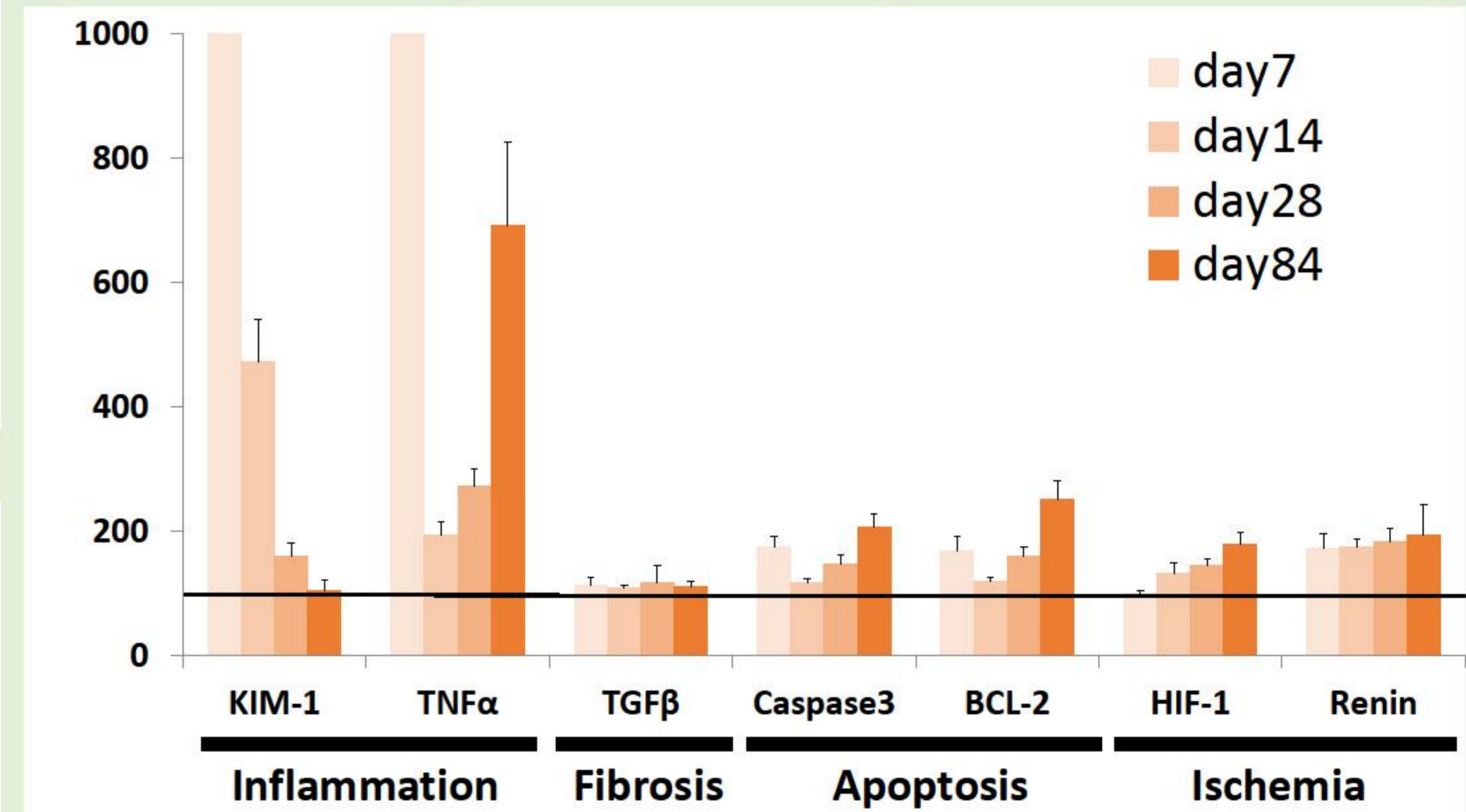
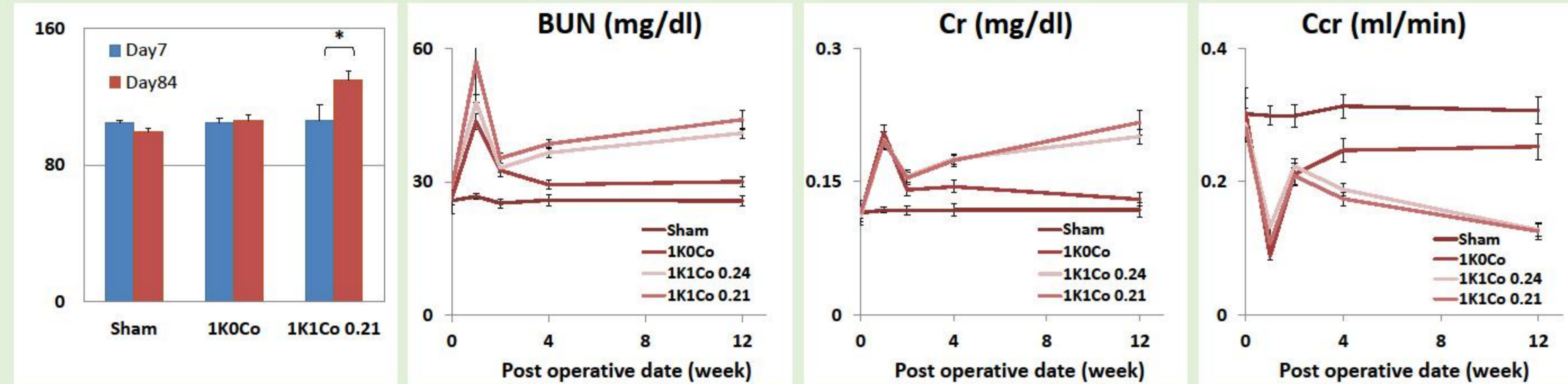
n = 8 in each group.
(* : p<0.05, ** : p<0.01)

Kidney Function

n = 16 in each group.
(* : p<0.05, ** : p<0.01)

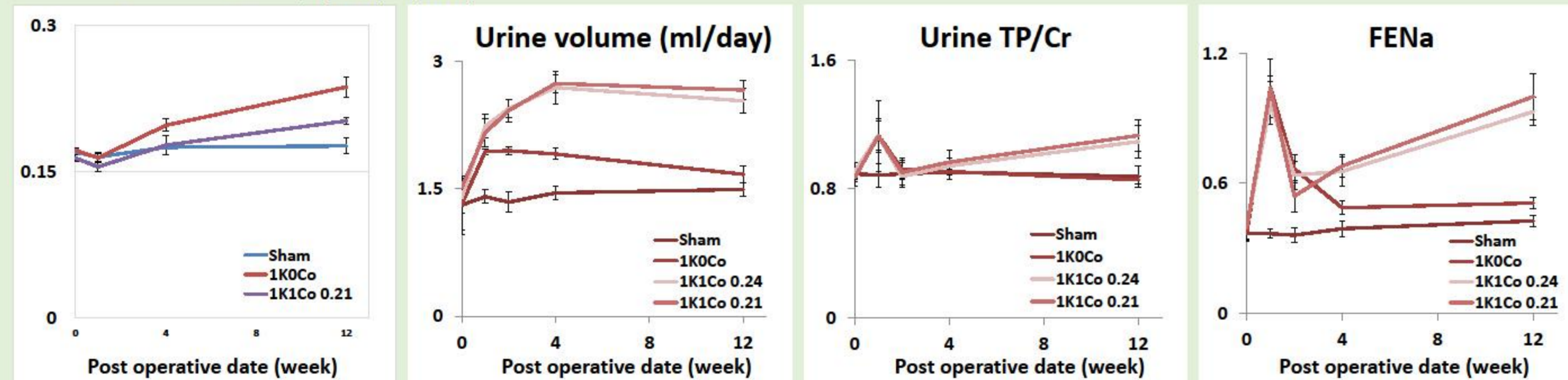
Gene Expressions

(qPCR, whole kidney, relative ratio compared with control kidney)

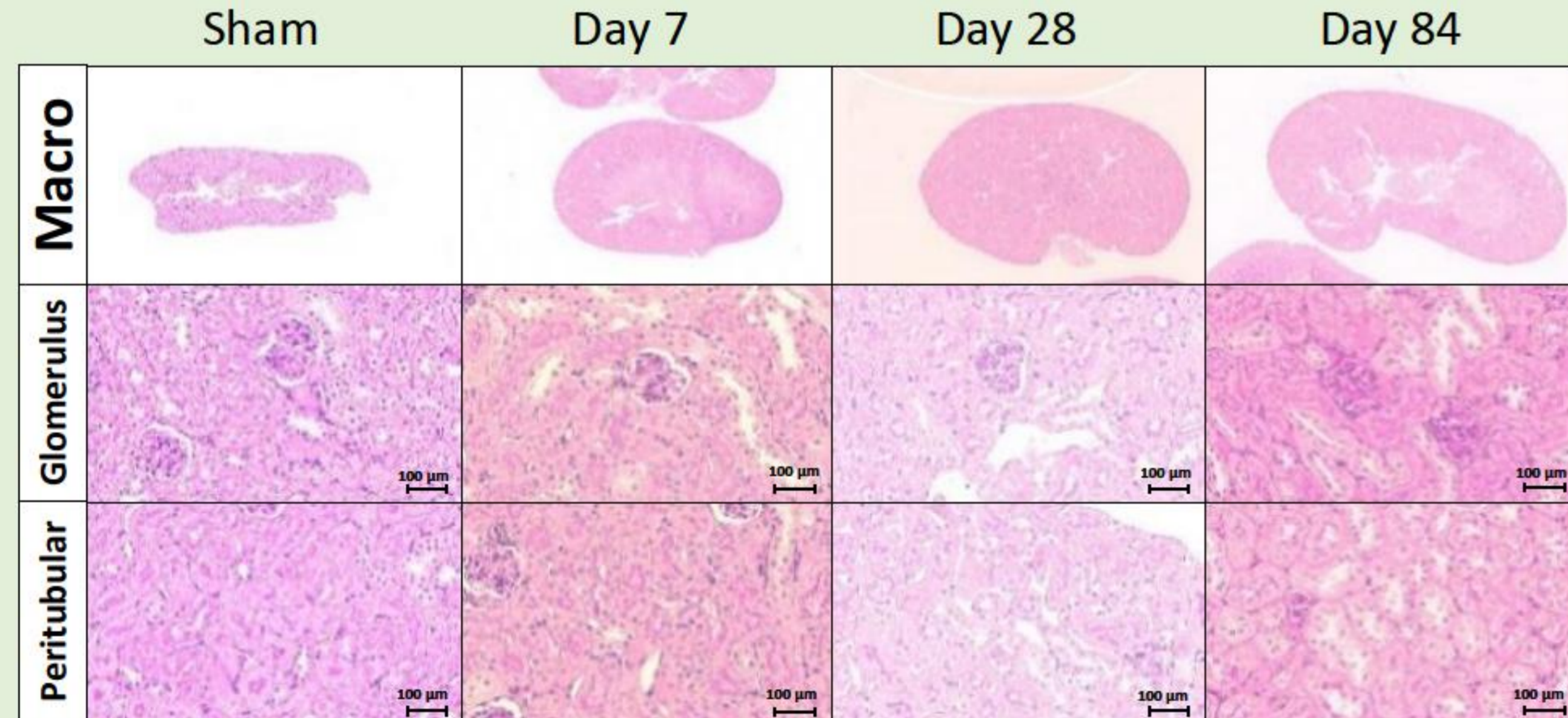


Kidney Weight

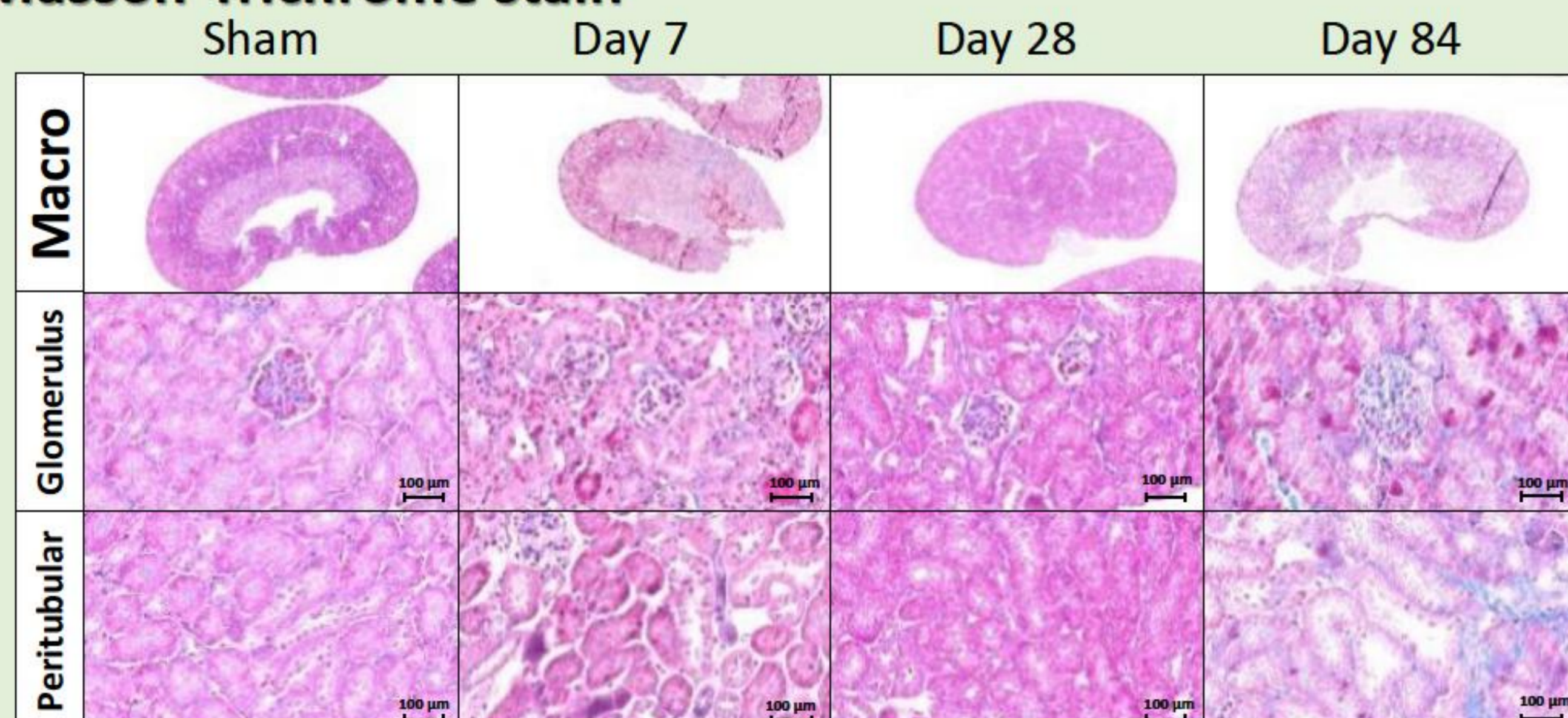
n = 12 in each group.
(* : p<0.05, ** : p<0.01)



Periodic acid-Schiff stain



Masson-Trichrome stain



Conclusions and Discussion

	1K0Co (hemi-nephrectomy)	1K1Co (hemi-nephrectomy+coiling)
Blood pressure	No change	Elevated
Kidney weight	Increased	No change (1K1Co 0.21,0.24) Decreased (1K1Co 0.17)
Survival Rate	No change	Decreased (1K1Co 0.17)
Renal Function	Transient worsening	Progressively deteriorating after transient worsening
Pathology	No change	Interstitial fibrosis and tubular atrophy (IFTA), and interstitial inflammation. Dilated tubules. Glomerular volume tends to be larger.

The novel renal ischemia model by means of renal artery coiling in mice constitutes characteristics of chronic renal ischemia observed in human diseases, including interstitial fibrosis, tubular atrophy, and interstitial inflammation.

