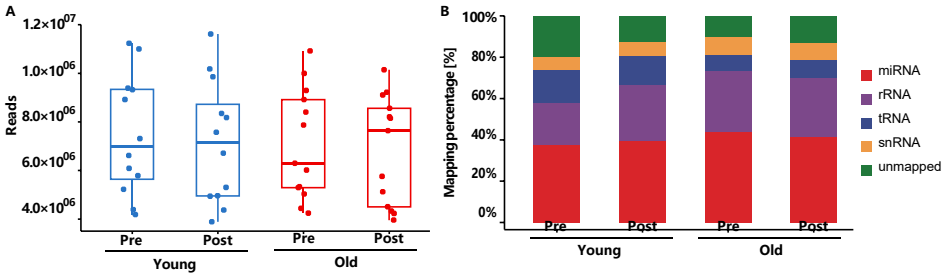
Supplement Materials

Detailed descriptions of the anesthesia process

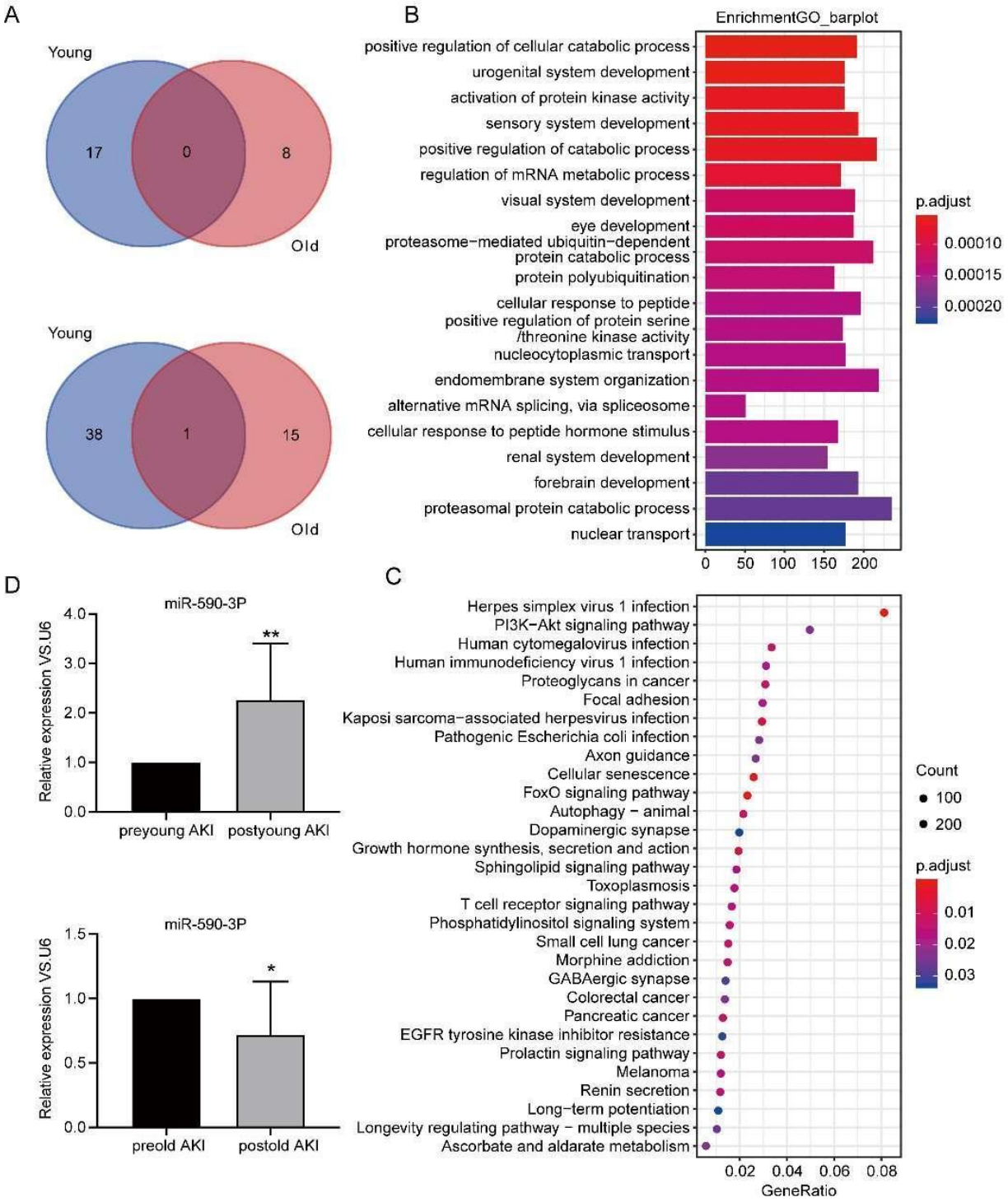
Anesthesia induction was performed with midazolam (approximately 40 mg kg^{-1}), sufentanil (approximately 3 μg kg^{-1}), propofol (1.5 mg kg^{-1}), and cisatracurium (0.5 mg kg^{-1}), and patients were orally intubated after relaxation. All the patients were given a central venous catheter through the right jugular vein. Anesthesia was maintained with sevoflurane (0.2-0.5 minimum alveolar concentration), propofol infusion (2-3 mg kg^{-1} h^{-1}) and dexmedetomidine (1 μg kg^{-1} h^{-1}) until CPB began, and volatile anesthetics were used again after CPB was withdrawn. Coronary artery bypass surgery was performed by median sternotomy. The CPB procedure began after heparinization of the arterial intubation of the ascending aorta and the intravenous intubation of the right atrium. Body temperature was maintained between 35°C and 37°C. The effect of heparin was reversed by protamine.

Detailed descriptions of the ultracentrifugation process

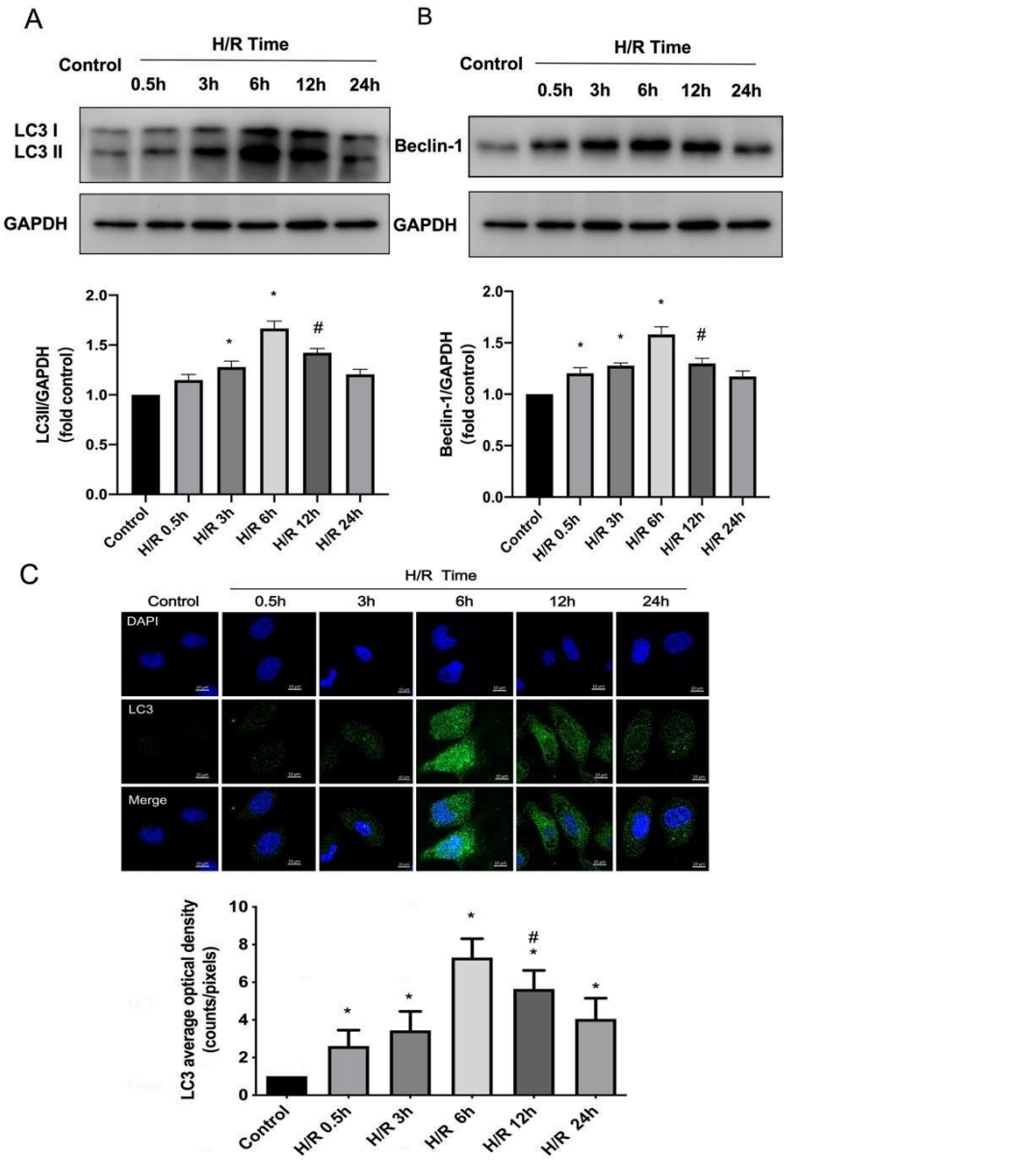
To separate the cell-derived exosomes, the supernatants of cell cultures were collected into 50-ml polypropylene tubes and centrifuged at 300 g for 10 min at 4°C to remove free cells. The supernatants were transferred to new centrifuge tubes, centrifuged at 2,000 g for 10 min at 4°C to remove cell debris, and then centrifuged again at 10,000 g for 30 min at 4°C to further remove cell particles. Then, the super clear supernatants were filtered with a 0.22-μm filter (Millipore-Sigma, USA) to remove dead cells and particles larger than 200 nm. Next, the exosomes were collected by centrifugation at 100,000 g for 70 min at 4°C. The supernatants were discarded, and the pellets were stored at 4°C for further experiments.



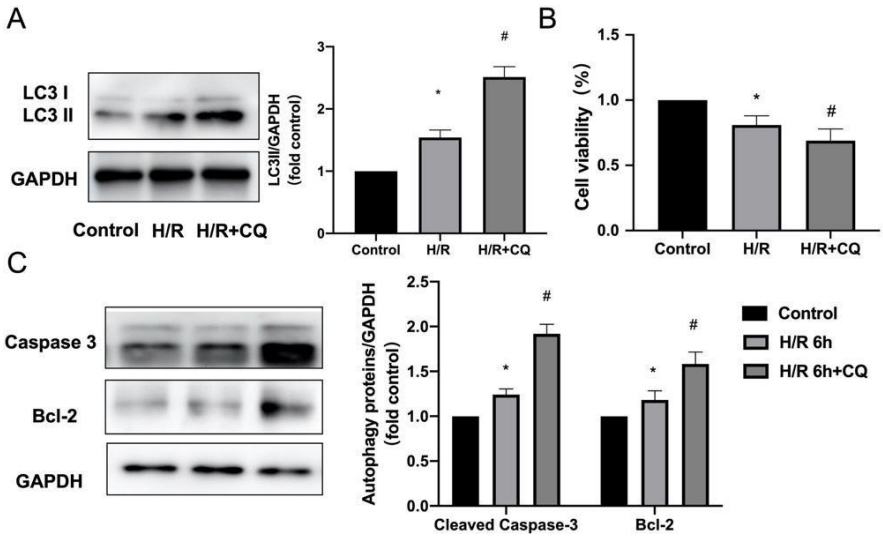
Supplementary Figure 1： Characterization of sequencing libraries. (A) Individual library sizes for exosome isolated from pre- and postoperative sera. No significant differences were detected between all time points and groups. (B) Mean relative mapping distributions for various classes of small RNA revealed a strong enrichment of miRNAs in circulating vesicles from all groups. Less than 0.2% of reads carried no adaptor or mapped to snRNA or snoRNA. rRNA, ribosomal RNA; Short, read less than or equal to 15 nt; snRNA, small nuclear RNA; tRNA, transfer RNA.



Supplementary Figure 2: (A) Differential regulation of miRNAs in young and elderly AKI patients. One miRNA showed signi fi cant downregulation after surgery in both groups. (B) GO functional enrichment analysis of target genes of hsa-miR-590-3p. (C) KEGG pathway enrichment analysis of target genes of hsa-miR-590-3p. (D) Hsa-miR-590-3p was expressed before and after surgery in both groups of patients as determined using RT–PCR. ∗ $P < 0.05$. AKI: Acute kidney injury; GO: Gene ontology; miRNA: microRNA.



Supplementary Figure 3: H/R induced autophagy *in vitro*. (A, B) Representative immunoblot images of LC3, Beclin-1, and GAPDH. (C) Representative images of LC3-positive puncta accumulation were obtained using confocal microscopy. *Scale bar* = 10 μm. The ratios of LC3 and Beclin-1 were quantified by densitometry based on immunoblot images from at least three independent experiments. The results are depicted as the ratio of the indicated proteins normalized to GAPDH. $N = 3$ for immunofluorescence staining. *Bar graphs* represent the mean ± SD. $^{*}P < 0.05$ *vs.* the control group; $^{\#}P < 0.05$ *vs.* the H/R 6 h group. H/R: Hypoxia/reoxygenation.



Supplementary Figure 4: Autophagy was significantly induced after H/R *in vitro* and inhibited the apoptosis of activated HK-2 cells. (A) Western blot analysis revealed that LC3 expression was upregulated in cultured HK-2 cells after IR injury and was further increased following treatment with CQ. (B) The cell viability in each group was determined by the CCK-8 assay. Cell viability was significantly decreased after H/R, while the cell viability of the H/R + CQ group was decreased significantly compared to that of the H/R group. (C) Western blot analysis revealed increased levels of cleaved caspase 3 and Bcl-2 in the HK-2 cells, but CQ treatment attenuated these increases. The data are expressed as the mean ± SD; $N = 4–5$ for Western blot, $^{*}P < 0.05$ *vs.* the control group; $^{\#}P < 0.05$ *vs.* the injury group. CCK-8: Cell Counting Kit-8; CQ: Chloroquine; H/R: Hypoxia/reoxygenation.

Supplementary Table 1. Comparison of intraoperative characteristics between young AKI and elderly AKI groups

Parameters	Young AKI ($n=12$)	Elderly AKI ($n=13$)	Statistics	*P* value
Anesthetics for maintenance during surgery				
Propofol, without volatile	3	2	–	0.645
Volatile, without propofol	1	2	–	>0.999
Volatile, with propofol	8	9	–	>0.999
Operative details				
Aortic cross-clamp time (min)	63.83 ± 9.30	65.31 ± 10.77	−0.365	0.718
Circulatory arrest time (min)	98.58 ± 12.21	101.54 ± 12.56	−0.596	0.557
AKI grade				
1	8	6	–	0.529
2	2	5	–	0.378
3	2	2	–	>0.999

Data are shown as *n* or mean ± standard deviation. AKI: Acute kidney injury.

Supplementary Table 2. MiRNAs information sheet expressed significantly after preoperative expression in young AKI patients

miRNAs	Log FC	*P* Value	Regulation
hsa-miR-548ax	9.62788	0.000583	up
hsa-miR-4467	-8.97443	0.002708	down
hsa-miR-423-5p	-2.88246	0.002929	down
hsa-miR-2110	-7.90793	0.003739	down
hsa-miR-200c-3p	8.061612	0.003763	up
hsa-miR-877-5p	-8.14668	0.004863	down
hsa-miR-449a	-6.43266	0.004948	down
hsa-miR-4732-5p	-3.53448	0.005166	down
hsa-miR-145-3p	-4.82447	0.007558	down
hsa-miR-22-3p	-2.81005	0.008149	down
hsa-miR-431-5p	5.574989	0.008261	up
hsa-miR-301a-3p	5.417528	0.009794	up
hsa-miR-151a-5p	-3.12251	0.011036	down
hsa-miR-374b-5p	5.706669	0.011294	up
hsa-miR-320a-3p	-2.58511	0.012724	down
hsa-miR-181c-3p	-7.88996	0.014655	down
hsa-miR-504-5p	7.770438	0.016112	up
hsa-miR-1290	-3.52073	0.017923	down
hsa-miR-99a-5p	-4.96536	0.019407	down
hsa-miR-99b-5p	-2.74279	0.02018	down
hsa-miR-6815-5p	-7.60393	0.02058	down
hsa-miR-3942-5p	-4.69864	0.022237	down
hsa-miR-542-3p	5.168403	0.02429	up
hsa-miR-1843	-4.37531	0.02496	down
hsa-miR-340-5p	3.223518	0.025329	up
hsa-miR-3064-5p	-7.19611	0.025974	down

hsa-miR-760	-7.10158	0.02742	down
hsa-miR-6868-3p	-7.08769	0.027626	down
hsa-miR-628-3p	-3.71876	0.028131	down
hsa-miR-493-5p	-7.04784	0.028271	down
hsa-miR-369-5p	5.699957	0.029114	up
hsa-miR-486-3p	-4.63078	0.029123	down
hsa-miR-125a-3p	-6.97661	0.029408	down
hsa-miR-642a-3p	4.894932	0.030321	up
hsa-miR-1537-3p	6.759074	0.030507	up
hsa-miR-4755-5p	-6.89682	0.030653	down
hsa-miR-10a-3p	-6.86302	0.0313	down
hsa-miR-3940-3p	-6.73498	0.033551	down
hsa-miR-30b-5p	4.394566	0.033941	up
hsa-miR-629-5p	-2.29818	0.034385	down
hsa-miR-1294	-3.62892	0.035485	down
hsa-miR-423-3p	-2.36136	0.036177	down
hsa-miR-502-3p	-6.52667	0.037438	down
hsa-miR-5187-5p	-6.11492	0.037484	down
hsa-miR-582-3p	-3.63448	0.037848	down
hsa-miR-769-3p	6.257686	0.039935	up
hsa-miR-542-5p	4.69105	0.040738	up
hsa-miR-3913-5p	-6.34138	0.041292	down
hsa-miR-590-3p	6.19281	0.041314	up
hsa-miR-1268b	-6.32097	0.041851	down
hsa-miR-378a-5p	6.152746	0.042191	up
hsa-miR-1246	-2.86045	0.043417	down
hsa-miR-3138	-6.23012	0.043757	down
hsa-miR-6805-5p	-4.69032	0.046478	down
hsa-miR-206	2.87779	0.048129	up

Supplementary Table 3. MiRNAs information sheet expressed significantly after preoperative expression in elderly AKI patients

miRNAs	logFC	*P* Value	Regulation
hsa-miR-628-5p	7.500165	0.002564	up
hsa-miR-7848-3p	7.311467	0.00375	up
hsa-miR-758-3p	6.460554	0.011859	up
hsa-miR-190b-5p	-6.96385	0.016738	down
hsa-miR-1303	-6.91101	0.016825	down
hsa-miR-202-3p	-6.9057	0.019599	down
hsa-miR-1299	5.038862	0.019643	up
hsa-miR-3614-5p	5.745355	0.021586	up
hsa-miR-1291	-6.42362	0.02715	down
hsa-miR-3143	-6.56449	0.02754	down
hsa-miR-449b-5p	-6.43986	0.030525	down
hsa-miR-381-3p	-6.3901	0.032402	down
hsa-miR-204-3p	-6.33482	0.03379	down
hsa-miR-2115-3p	-6.47949	0.033918	down
hsa-miR-212-5p	4.841204	0.036273	up
hsa-miR-2355-3p	-6.15206	0.039303	down
hsa-miR-4755-5p	-6.09492	0.041518	down
hsa-miR-193b-3p	4.720572	0.044261	up
hsa-miR-3124-5p	-6.15698	0.04472	down
hsa-miR-136-3p	-6.15444	0.04477	down
hsa-miR-1277-5p	4.632724	0.044795	up
hsa-miR-4772-5p	-6.08722	0.047888	down
hsa-miR-590-3p	-6.059	0.049	down
hsa-miR-616-3p	-5.89256	0.049142	down

Supplementary Table 4: miRNAs that vary significantly before and after surgery in both young and elderly AKI patients have the opposite miRNAs.

Group	miRNA	logFC	*P*-value	Regulation
Young AKI	hsa-miR-590-3p	6.193	0.041	up
Elderly AKI	hsa-miR-590-3p	–6.059	0.049	down

AKI: Acute kidney injury; FC: Fold change; miRNAs: microRNAs.