ACUTE KIDNEY INJURY – EXPERIMENTAL

EARLY BIOMARKERS OF ACUTE KIDNEY INJURY AFTER RENAL SYMPATHETIC DENERVATION IN PIG

Dong Won Lee1, Jeong-Su Kim2, Il Young Kim1, Harin Rhee3, Min Jung Kim1, Eun Young Seong2, Sang Heon Song3, Soo Bong Lee1 and Ihm Soo Kwak3

1Pusan National University School of Medicine, Internal Medicine, Yangsan, Republic of Korea, 2Pusan National University School of Medicine, Cardiology, Yangsan, Republic of Korea, 3Pusan National University School of Medicine, Internal Medicine, Busan, Republic of Korea

Introduction and Aims: Renal sympathetic denervation is available and implemented as a strategy for the treatment of resistant hypertension and is currently under clinical investigation. In the aspect of chronic safety, renal function, as assessed by serum creatinine, eGFR (MDRD), and cystatin C was reported to be unchanged from baseline at 6 months. We investigated whether RDN might cause subtle inflammation and subclinical damage in the early phase of acute kidney injury.

Methods: Female pigs were divided into 6 groups; normal control (group A), Sham-operated control (group B), contrast media control (group C), and renal sympathetic denervation groups subdivided into 3 groups according to the time of sacrifice; immediately (group D), 1 week later (group E), and 2 weeks later (group F) after renal sympathetic denervation. We checked interleukin (IL)-1α, 1β, 18, 6, 10, tumor necrosis factor-α (TNF-α), cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), caspase-1, apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC), and nucleotide-binding oligomerization domain, leucine-rich repeat and pyrin domain containing protein3 (NLRP3) as early biomarkers of inflammation and acute kidney injury.

Results: There were no significant changes in group B and C compared to group A. BUN, serum creatinine, cystatin C, urine protein/creatinine ratio, and urine albumin/creatinine ratio showed a tendency to increase in group D and E and then decrease in group F with no statistical significance. Pro-inflammatory cytokines, IL-1β, 18 increased in group D and E (p<0.05 vs. A), and decreased in group F (p<0.05 vs. D, E) significantly. Caspase-1 activity, ASC, and NLRP3 expressions were also increased in group D (p<0.05 vs. group A), and decreased in group E and F (p<0.05 vs. group D).

Conclusions: In conclusion, RDN did not cause clinically significant damages on kidneys. However RDN can induce the activation of pro-inflammatory cytokines, caspase-1 and NLRP3 inflammasome, and then finally but transiently self-limited acute kidney injury.