Vascular Function in Chronic Renal Failure

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Vita stråket 12, Sahlgrenska universitetssjukhuset, Göteborg
Fredagen den 14 mars 2014 kl. 13.00

av **Lisa Nguy**

Fakultetsopponent:
Professor Michael A. Adams, Queen's University, Kingston, ON, Canada

Avhandlingen baseras på följande delarbeten:

I. **Vascular function in rats with adenine-induced chronic renal failure**
Nguy L, Nilsson H, Lundgren J, Johansson ME, Teerlink T, Scheffer PG, Guron G.

Am J Physiol Regul Integr Comp Physiol. 2012 Jun 15;302(12):R1426-35.

II. **Rats with adenine-induced chronic renal failure develop low-renin, salt-sensitive hypertension and increased aortic stiffness**
Nguy L, Johansson ME, Grimberg E, Lundgren J, Teerlink T, Carlström M, Lundberg JO, Nilsson H, Guron G.

Am J Physiol Regul Integr Comp Physiol. 2013 May 1;304(9):R744-52.

III. **Adenine-induced chronic renal failure decreases aortic relaxation rate and alters expression of genes involved in vascular smooth muscle excitation-contraction coupling**
Nguy L, Shubbar E, Jernås M, Nookaew I, Lundgren J, Olsson B, Nilsson H, Guron G.

In manuscript

IV. **High NaCl intake exacerbates aortic relaxation defect in rats with adenine-induced chronic renal failure**
Nguy L, Shubbar E, Nilsson H, Guron G.

In manuscript

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Vascular Function in Chronic Renal Failure

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Abstract

A majority of patients with chronic kidney disease (CKD) die of cardiovascular (CV) disease before reaching end-stage renal disease. The causes of CV death in CKD are characterized by an excess of sudden cardiac deaths compared to the general population. Arterial defects that are typical in these patients are aortic stiffness and media calcifications. Maladaptive changes in vascular smooth muscle cells (VSMCs) take place in response to mineral metabolism disorders that develop with declining kidney function.

The aims of the present studies were: 1) to investigate the effects of chronic renal failure (CRF) on resistance arteries and aorta in rats with adenine-induced CRF (A-CRF); 2) to determine by which mechanisms A-CRF rats develop hypertension and to investigate whether reduced aortic relaxation rate is associated with increased aortic stiffness; 3) to investigate the presence of reduced relaxation rate in other conduit arteries and to elucidate underlying mechanisms of this vascular defect through gene expression analyses; and 4) to investigate the effects of a high NaCl intake on arterial functions and aortic relaxation rate in A-CRF rats.

We found that rats with A-CRF develop a reduced rate of relaxation, mainly in the thoracic aorta, but also in other major conduit arteries. This was associated with an increased aortic stiffness and was independent of vascular calcification. A-CRF rats developed salt-sensitive and renin-independent hypertension. High NaCl intake impaired relaxation in aortic VSMCs and augmented the reduction in aortic relaxation rate. Significantly altered expressions of several genes that are critically involved in excitation-contraction coupling of aortic VSMCs were found.

Our findings provide a possible link between CRF and the development of aortic stiffness, which in the future may unravel novel therapeutic targets. Such therapies have the potential to improve life expectancy not only in CKD but also in other patient groups.

Keywords: cardiovascular, chronic renal failure, hypertension

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