【Invited Speech 1】

Dialysis and the Heart: Unraveling Cardiovascular Complications

Bengt Fellström

Dept of Nephrology, Uppsala University Hospital

Cardiovascular (CV) complications are very frequent in renal failure , especially in end stage renal disease and is one of the leading causes of premature death among renal patients . The CV risk increases gradually with reduced renal function. The mortality among renal patients, especially dialysis patients, is comparable to severe malignancies and dialysis patients die at high annual rate. A large number of risk

factors have been identified , whereas preventive treatment has been without success, so far. One of the leading causes seems to be the systemic inflammation

that renal patients are suffering from. Other contributing risk factors are hypertension, dyslipidemia, aberrations in calcium-phosphate metabolism, coagulation disturbances etc. We have recently demonstrated that leakage of troponins from the heart is a strong predictor of future severe CV complications.

As to preventive treatment, many means have been tried , but with limited success . Statins have been tried in several large scale clinical studies, but not been shown to have any beneficial effect on survival in dialysis patients. Only a modest effect on

atherosclerotic events in pre-dialysis patients could be demonstrated. It is true that a slight reduction in inflammation could be seen, tentatively related to the pleiotropic effects of statins, but that did not have any clear influence on CV events.

Recent studies using SGLT2 inhibitors have emerged and been demonstrated in multiple studies to have strong effects on CV disease in renal failure, even in advanced renal failure.

A next class of monoclonal antibodies are targeting cytokines, which are involved in the inflammatory pathway of the atherosclerotic process, also in patients with renal failure. That includes both compounds interfering with IL-1b (Canakinumab) and with IL6 (ziltivekimab and clazakizumab). The literature is overloaded with studies

showing strong relationships between CRP and IL6 and CV events in renal patients.

Phase 2b studies with both IL-6 MoAbs have demonstrated marked effects on hsCRP reduction along with reductions of Serum amyloid A, fibrinogen, serum

phospholipase A2 and Lp(a). The ZEUS Ph3 study (ziltivekimab) has now recruited roughly 6200 patients with CKD (GFR>15), who are now followed for CV events. The POSIBIL6 Ph3 study

(clazakizumab) is currently recruiting 2100 dialysis patients in a global RCT, and will follow up patients for an estimated four years.

Thus, there are ongoing approaches targeting both the sodium-glucose co-transporter system and the inflammation component in vascular disease in renal failure, which will lead to exciting years ahead, while awaiting the results from these studies on solid CV outcome endpoints. We hope that these studies will lead to more efficient means of preventing the high rate of CV complications and death among patients with severe renal failure.