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## Renal Replacement Therapy and Cardiovascular Burden in Dialysis Patients

## **Study Description**

With substantial advances in understanding chronic kidney disease and uremic pathophysiology, innovative technologies and modern methods in renal replacement therapy have yet to be introduced. In view of the residual sub-optimal medical requirements of short intermittent dialysis, its medical responsibility is to update dialysis practice standards and propose new therapeutic solutions to increase the overall efficacy of dialysis sessions and reduce the therapy-induced stress burden.

When compared to age-matched general populations, patient experience remains a difficulty, with poorer quality of life and a greater focus on disease burden. To increase the social and economic burden of end-stage kidney disease (ESKD) management, these problems for patients, doctors, caregivers and health authorities require continuous study. Recently, these issues have been illustrated with a clear call to step away from a 'one-size-fits-all' approach to dialysis to offer more personalized treatment that combines patient goals and desires while also integrating quality and healthy therapy best practices.

## Modality of therapies and future options

Hemodialysis, which provides 12 h of treatment a week on a three-week basis, is currently considered the standard of care in Western countries for ESKD patients. Despite being popularised in previous decades as a balance between treatment effectiveness, patient responsiveness, acceptance, and economic viability, short treatment schedules are not ideal. Several experts have defined short treatment schedule pitfalls and limitations and have formed a causal correlation with poor results. In line with these clinical evidence, it has been postulated that dialysis-related pathology observed in long-term treated patients (e.g. cardiovascular disease, vascular calcification,  $\beta 2$ -microglobulin ( $\beta 2M$ ) amyloidosis and proteinenergy malnutrition) may represent a so-called 'residual syndrome' due to the incomplete restoration of the inner homeostasis environment.

Hemodialysis is a source of increased stress in the "unphysiological sense" of intermittent renal replacement therapy. The first stress is a 'biologic or cytokine storm,' which occurs when blood interacts with a dialyser membrane and its extracorporeal circuit, resulting in a disorder known as hemoincompatibility, which includes the activation of protein and cell systems in a cascade, as well as the release of numerous proinflammatory mediators.

The second stress is a 'biochemical stress' representing rapid biochemical changes that occur as a result of solvent, water and osmotic fluxes (e.g. disequilibrium syndrome ) with a strength

## **Luping Huang**\*

Department of Nephrology, Baylor College of Medicine, USA

#### \*Corresponding author:

Luping Huang, Assistant Professor of Medicine, Department of Nephrology, Baylor College of Medicine, USA
Illuang3@houstonmethodist.org

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that is directly related to the gradient of plasma-dialysate and operational conditions during the treatment (e.g. blood and dialysate flow). Given the suboptimal patient needs of short intermittent dialysis, it is our medical obligation to review dialysis practice standards and suggest new therapeutic options for increasing overall dialysis efficacy and reducing the stress burden caused by the therapy.

### Dialysis-induced stress reduction or prevention

These are important in the search for dialysis-induced cardioprotection. Functional imaging techniques (e.g. echocardiography, cardiac MRI) and the kinetics of cardiac biomarkers (e.g. troponin I) have shown that cardiocirculatory stress occurs early after extracorporeal initiation and worsens during treatment. Several factors contribute to cardiac stress (for example, modality, time, fluid control, and electrolytes); however, ultrafiltration rate is recognized as the most important. In short, ultrafiltration tends to contract volume, which is balanced by fluid retained in the extravascular space by vascular refilling. Vascular refilling processes rely mainly on the increase of circulating proteins and oncotic pressure, a condition that favors fluid moving back into the circulatory system. In other words, hypovolaemia results from the imbalance of ultrafiltration and refilling rates, with poor outcomes.

#### Reducing blood-extracorporeal circuit interaction

While significant progress has already been made with less reactive biomaterials, such as synthetic polymer hemodialysers, less bio reactive tubing content, and improved circuitry geometry, further progress is needed in the future.