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Kidney Clinical Research Unit Buzz

A multidisciplinary team in nephrology care working together to deliver better treatments

New Study Alert Times 2!

Is salt build up a potential cause of heart disease in patient with chronic kidney disease?

Chronic kidney disease (CKD) is prevalent worldwide and affects around 10% of people living in developed health economies. As the kidney loses its function in patients with CKD, the kidneys are unable to filter toxins out of the blood as efficiently as those of healthy individuals. Arguably, sodium (salt) is the most relevant toxin in CKD and can build up in the kidneys of patients with CKD. Salt build-up has also been found to occur in the heart muscle tissue and could drive the development of scarring of the heart muscle tissue which contributes to heart failure.

Using sodium magnetic resonance imaging (MRI), we can measure the levels of salt in the heart muscle tissue of patients with CKD. We will examine whether the heart muscle tissue has high salt levels, and if so, whether this relates to any heart defects. The MRI images of healthy volunteers, CKD patients, and those on hemodialysis will be analyzed for levels of salt and the findings will then be compared to the cardiac biomarkers (proteins or enzymes that are released into the blood when the heart is damaged or stressed) and fibrosis (scarring) measured from each patient's proton MRI images to establish a possible correlation. This research has the potential to precede additional studies that may investigate the effect of diuretics (a drug that increases the production of urine) on the heart muscle tissue of CKD patients.

KIDNEY CLINICAL RESEARCH UNIT, VICTORIA HOSPITAL - July 2021 - Taylor Marcus, MSc, has launched a crowdfunding campaign to raise money for her project. The campaign is live on experiment.com. All donations will help the research team image and analyze the first few patients participants by covering the cost of MRI scan time and laboratory supplies.

Alteration of the corticomedullary gradient

The corticomedullary gradient is largely responsible for developing the gradients that are needed to concentrate urine (more solutes and less water). The ability of the kidneys to produce concentrated urine is a major determinant of the ability to survive the warm weather. When temperatures are high, we lose water through sweat, and so the kidneys retain water to maintain fluidity in the blood. The maintenance of a sodium (salt) gradient is a basic renal function, absolutely required for urine concentration because increased medullary sodium concentration increases the reabsorption of water into the kidney, to be redistributed in the blood. Therefore, physiologically there is a significant difference in the level of salt between the renal cortex and the medulla. We currently have no data on the corticomedullary gradient in patients with acute or chronic kidney disease.

We would like to develop a new marker of early renal failure and studying the alteration of the corticomedullary gradient could provide us with this information. Before we can provide a clear response to this question, we need to have some reference in chronic kidney disease and in the native and transplanted kidney. We need to know if the corticomedullary gradient is altered in patients with nephrolithiasis (kidney stones) or if we are able to measure it in patients with autosomal dominant polycystic kidney disease (ADPKD).

Many studies have shown the highly predictive value of interstitial fibrosis (inflammation and scarring of the kidney) in CKD, irrespective of the underlying nephropathy (a disease where the kidney is unable to remove waste products from your blood) leading to a decrease in the corticomedullary sodium gradient in either the native kidney or allograft. Corticomedullary gradient exploration would provide a relevant assessment of tubular dysfunction independently of glomerular damage and thus could be of prognostic value. Using sodium MRI we can take pictures and measure the salt content in the kidneys.

Leg Sodium-23 MRIs

One-year follow-up data from 52 hemodialysis and peritoneal dialysis patients revealed that larger skin sodium content in the leg is associated with cardiovascular disease and death. This means that sodium accumulation, whether due to or independent of fluid accumulation, is harmful and may contribute to explain the negative outcomes observed in patients undergoing kidney replacement therapy. New studies should focus on testing the effects of maintaining a healthy sodium balance in patients on dialysis, including dietary sodium restriction and sodium removal through dialysis.

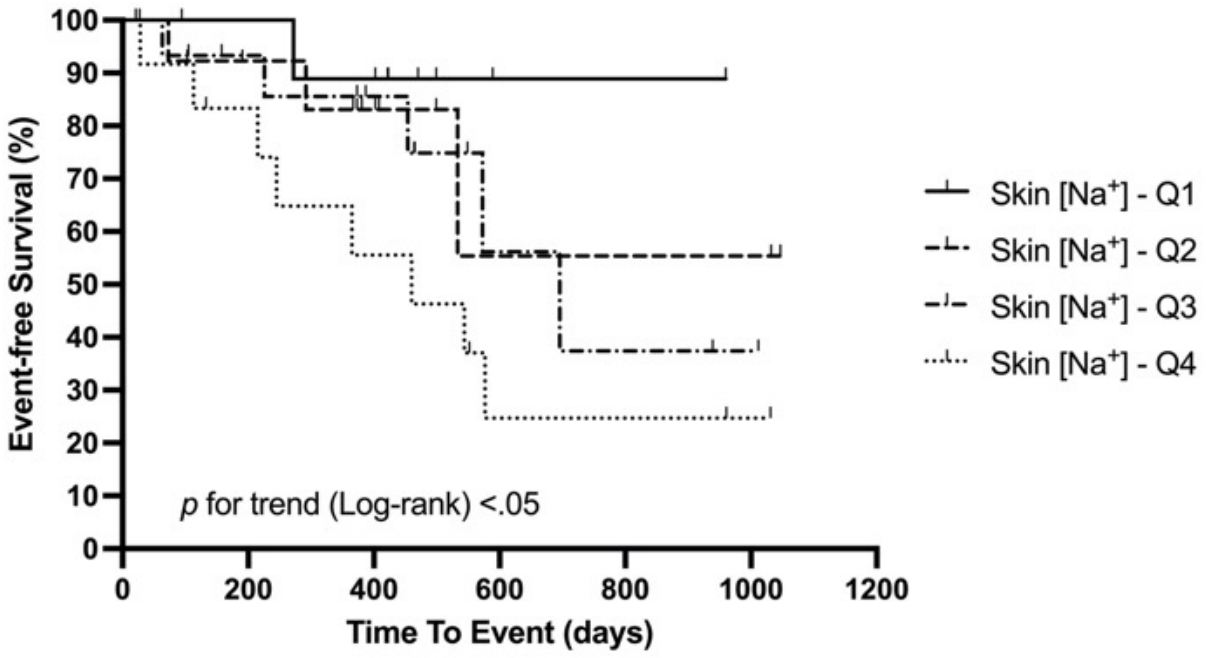
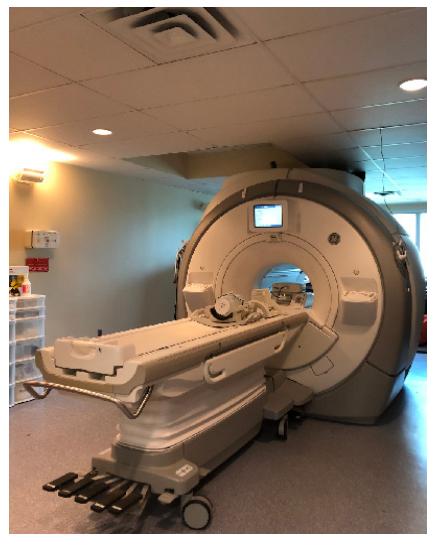


Figure: Event-free survival (cardiovascular events + death) in 52 dialysis patients (10 PD, 42 HD) after stratification according to skin sodium concentration (Skin [Na+]) quartile.



We also report our findings in children with kidney disease. We have currently scanned 18 healthy children and 17 pediatric patients with CKD. Preliminary analysis showed that the cause of kidney disease is associated with different levels of sodium accumulation. In particular, glomerular diseases causing nephrotic syndrome were associated with increased leg sodium content, whereas tubulo-interstitial diseases were associated with normal or reduced leg sodium content. Leg sodium content was more variable in kidney transplantation, possibly due to the influence of different immunosuppressant regimens on kidney sodium handling and tissue fluid physiology. The umbrella definition of “CKD”, therefore, encompasses several different kidney diseases with potentially very different kidney sodium handling.

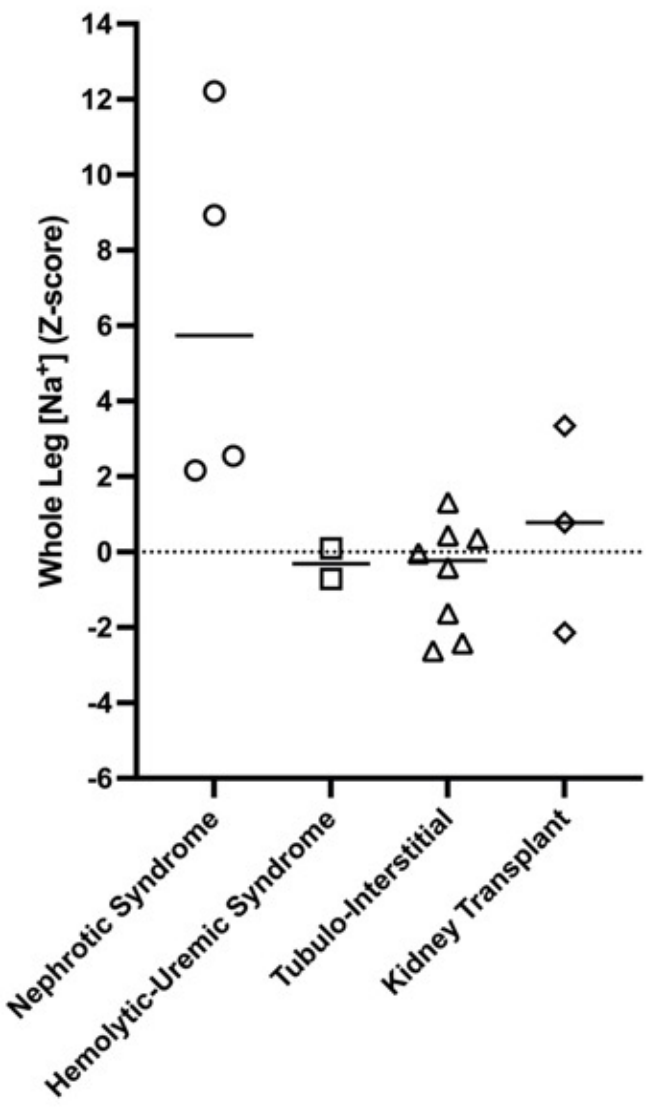


Figure: Standardized Z-scores for Whole-leg sodium concentrations ([Na+]) in pediatric chronic kidney disease patients were calculated from healthy children. The graph shows differential effects of kidney disease etiology on Whole-leg [Na+]. Z-scores ≥ +1.96 are considered above normal (sodium retention), and Z-scores ≤ -1.96 are considered below normal (sodium wasting).

Novel extracorporeal treatment to modulate hyperinflammation in COVID-19 patients

Some COVID-19 patients develop systemic hyperinflammation syndrome associated with shock, vasoplegia, respiratory failure, and even cardiopulmonary collapse. Mortality remains high among these very severe COVID-19 patients. We set up a clinical trial to propose a new treatment for very severe unstable COVID-19 patients in intensive care unit.

We propose to use slow low-efficiency daily dialysis (SLEDD) to provide an extracorporeal circuit and allow us to target this hyperinflammation using immunomodulation of neutrophils with a novel leukocyte modulatory device (L-MOD) to generate an anti-inflammatory phenotype but without depletion of circulating factors for patients with hemodynamics instability. The L-MOD is based on a platform of biomimetic membrane technology and uses an extracorporeal circuit in which blood passes over polysulfone fiber membranes in a localized low ionized calcium environment (Figure 1). The L-MOD may be able to mitigate the pro-inflammatory response.

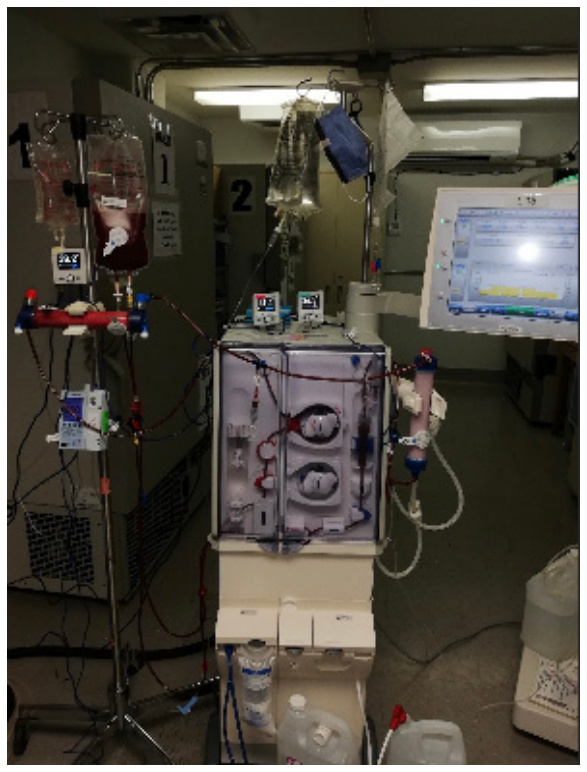


Figure 1 : SLEDD with LMOD device

SLEDD was performed twice, for approximately 12 hours, 2 days in a row to those particiapnts in the treatment group. Blood work was be collected on day 1, day 2, and day 5 of admission for both groups.

To date, we have included 11 patients in total, 5 in the control group and 6 receiving SLEDD. We have been able to show that the L-MOD allows for a significant decrease in vasopressive drug use compared to the control group, where vasopressive drug use tends to increase (Figure 2).

This new technique is safe. Mean arterial blood pressure remains stable and allows the decrease of vasopressor drug use during the dialysis, and white cells counts remains also stable compared to the control group (figure 3).

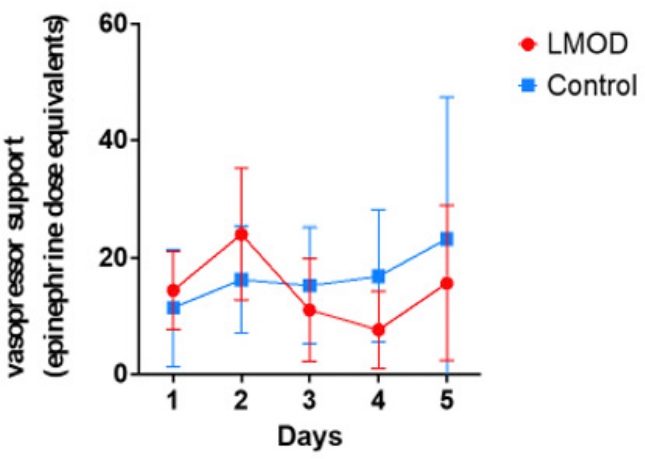


Figure 2: Changes of vasopressor drugs during the first 5 days (LMOD in red, Control in blue)

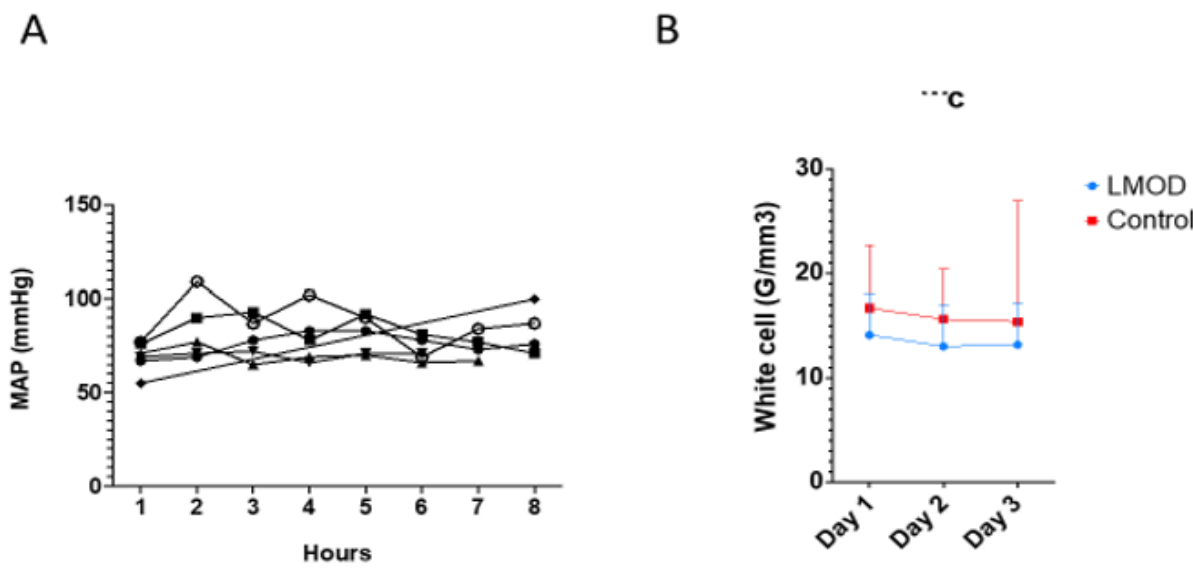


Figure 3: A. Mean arterial pressure for each LMOD patients remains stable during the treatment. B. White cells counts remains stable, in both groups.

Investigation of Electrophysiological Substrate of Arrythmia in Hemodialysis Patients

Our lab has studied changes in blood flow in different organs of hemodialysis patient. For this study, we were interested in the blood flow of the heart muscle and how we can improve patient's cardiac response to hemodialysis treatment. Exercise in the beginning of hemodialysis was used to condition the heart for the stress that the treatment would cause. We used computed tomography and echocardiography to evaluate this and found that particular components of the heart were more tolerant of dialysis when exercised. In addition to this, we wanted to determine whether this response is related to irregular heart rhythms in patients on hemodialysis treatment. To detect irregular heart rhythms, patients enrolled in this study have a small implantable loop recorder (heart monitoring device) placed directly under the skin near the heart. By doing this, we can study a patient's heart rhythm continuously for up to one year. Currently, seven patients have completed the CT imaging and four of these patients have had the loop recorder implanted and are being monitored.

Interdialytic peritoneal ultrafiltration in hemodialysis (iPUF-HD)

This is a study to test the efficacy and safety of additional fluid and sodium removal using peritoneal dialysis with a sodium-free high-dextrose (10%) solution in patients on hemodialysis.

The first patient completed the study procedures. The introduction of iPUF treatments improved dialysis tolerability and quality of life, facilitating fluid management. Out of 6 treatments, one episode of symptomatic hypotension was recorded, which was resolved by administering saline. One to two-hour long iPUF treatments were extremely efficient at sodium removal, with an average sodium removal of 2.2 grams, and fluid removal up to 0.7 liters after a one-hour treatment. Average glucose absorption from the solution was 35 grams, roughly the equivalent of one-and-a-half energy bar.

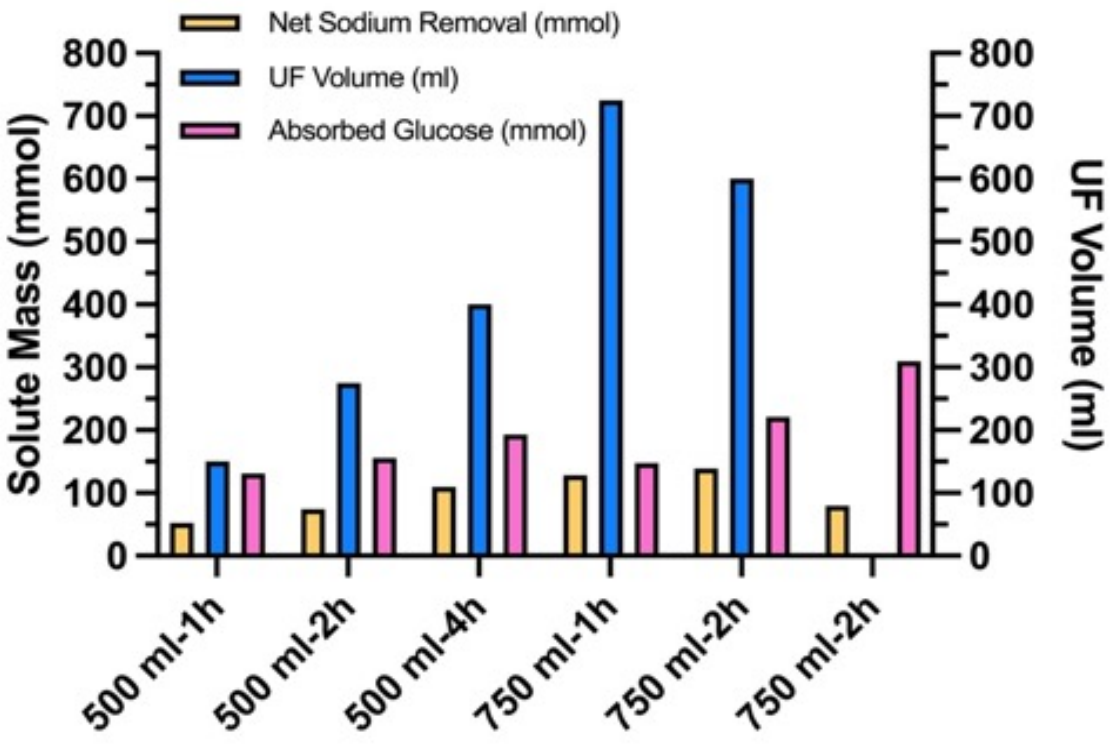
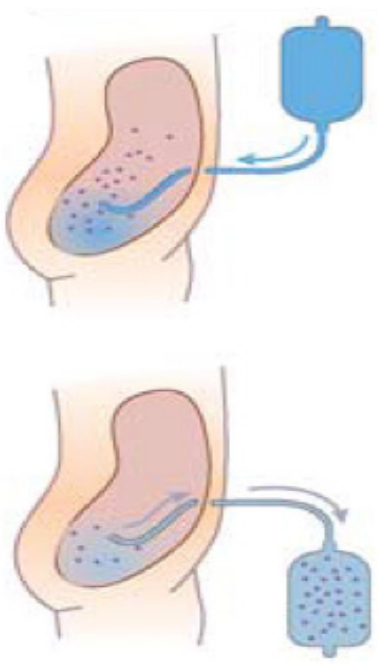


Figure: Summary of achieved sodium removal, ultrafiltration volume and absorbed glucose with varying 10% dextrose solution volume and dwell time.



Fluid Intake in Hemodialysis Patients

The aim of this study is to investigate how non-diabetic hemodialysis patients build up weight in-between dialyses. In particular, our interest surrounds the possibility that most of interdialytic weight gain may occur soon after hemodialysis, to compensate for intradialytic fluid removal as the result of “volemic thirst”. If this hypothesis is confirmed, a novel target to improve volume management in hemodialysis patients will emerge. Nine hemodialysis patients have currently completed the study procedures, and we are currently looking for 20 patients in total.

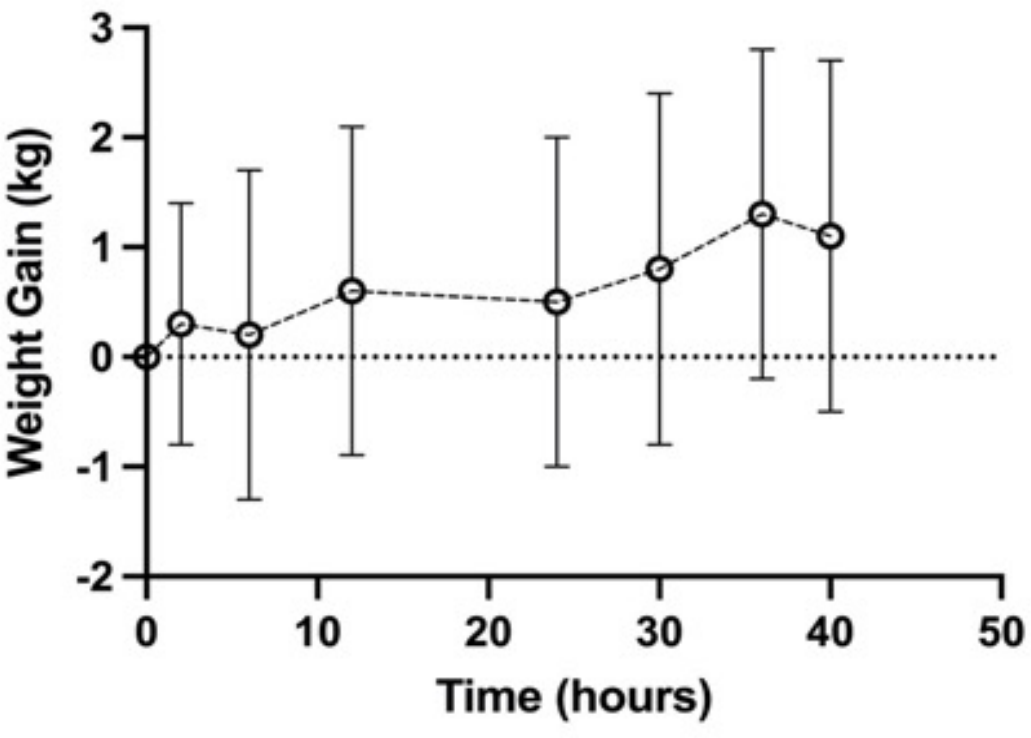


Figure: Weight gains during the first short dialysis interval reveal that more than 50% of the final weight gain is built-up within the first 12 hours after hemodialysis. (Error bars: SD)

Interventional Study to Assess the Effect of Extended Dialysis using the Theranova Dialyzer on Patient Reported Symptoms using the London Evaluation of Illness (LEVIL)

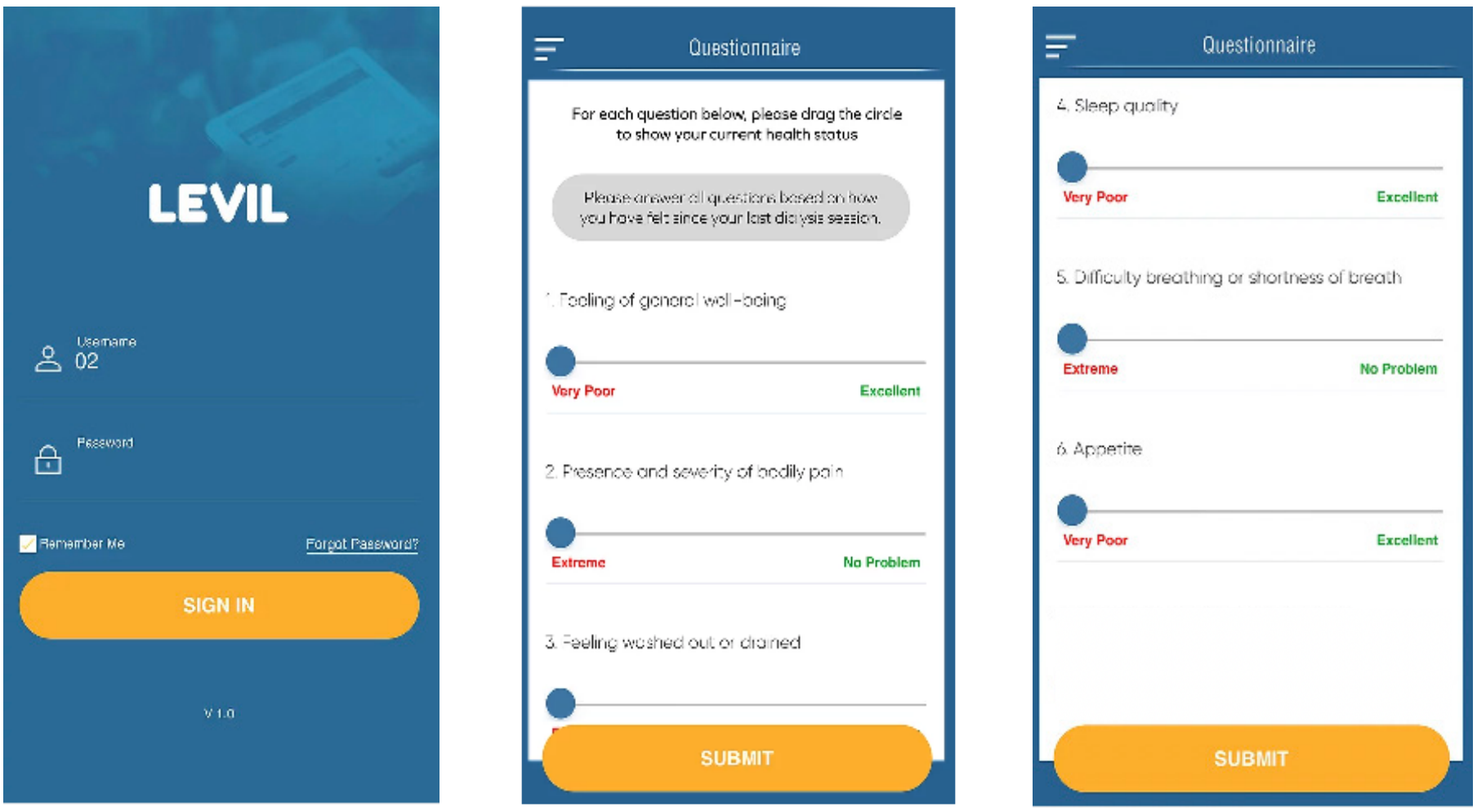
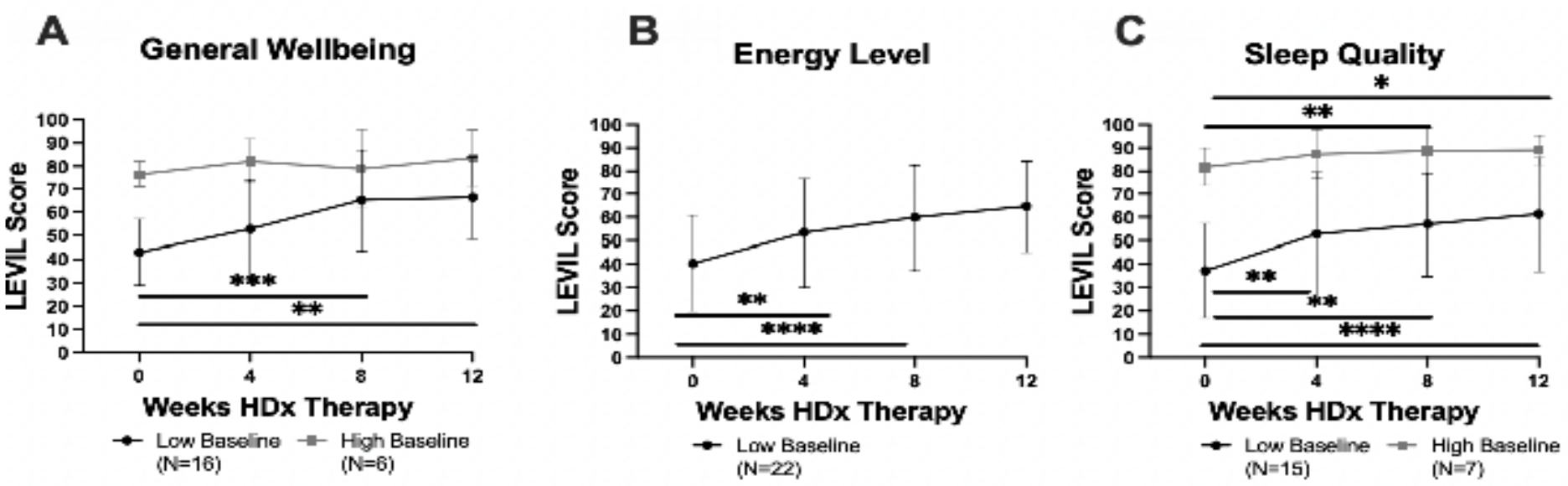


Figure: Participants answered six questions with each hemodialysis session using the LEVIL application, consisting of feeling of general well-being, presence and severity of bodily pain, feeling washed our or drained, sleep quality, difficulty breathing or shortness of breath, and appetite. Baseline symptoms were established after two weeks and participants continued with the questionnaire for the remaining 12 weeks.

12 weeks Theranova Dialysis Therapy



Panel A, General Wellbeing - Sixteen participants had a 'low' score at baseline which significatnly improved after both eight weeks and 12 weeks on the Theranova dialyzer.

Panel B, Energy Level - All participants suffered from a lack of energy and there was imporovement after both 8 and 12 weeks.

Panel C, Sleep Quality - Sixteen participants suffered from poor sleep quality and improvement in sleep was initially seen after just four weeks on the Theranova dialyzer.

Whats next? a 24-week extension with an 8 week wash out phase where patients return to their high-flux dialyzer while completing the questionnaire using the LEVIL application to asess the presence of any carry-over effects.