Thesis Project Portfolio

Urinary Extracellular Vesicle Diagnostic Tool Development - Computational Model for Dilution Determination

(Technical Report)

An Analysis of the Overrepresentation of African Americans in the Prescription of Hemodialysis Following a Diagnosis with End-Stage Renal Disease

(STS Research Paper)

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According to the CDC, approximately 37 million people in the United States have chronic kidney disease (CKD), and most are undiagnosed (*Chronic Kidney Disease Basics*, n.d.); this statistic suggests that 15% of the national population is unknowingly living with irreversible kidney damage. Symptoms of kidney failure typically are not exhibited until the damage has progressed to the "point of no return," in which the kidneys are in a state of failure and require medical intervention. CKD is nicknamed "the silent killer" due to this phenomenon, and there is currently no technology nor medical treatment to reverse CKD once they have reached the need for medical intervention. The current treatment modalities are dialysis, which can be hemodialysis or peritoneal dialysis, or a kidney transplant. Until there is a method for restoring kidney function once they are in a state of failure, the optimal solution is to prevent the kidneys from progressing to the point of kidney failure, which necessitates early diagnoses and treatments of diseases that lead to kidney damage, such as diabetes, hypertension, and lupus.

As detrimental and pervasive of an issue as kidney failure is in itself, the social impacts of kidney diseases are also devastating, which are accentuated by late diagnoses for patients with lower access to healthcare. Populations are not affected equally by kidney diseases, and examining current practices and statistics elucidates the extent to which kidney healthcare is riddled with disparities, particularly in the African American community (Norris et al., 2017). The creation of an earlier and more accessible diagnostic device could have profound social impacts that ameliorate existing discrepancies and foster more equitable medical care.

The challenges with current diagnostic methods for kidney diseases are that they are late-stage markers of kidney damage, unspecific to the site of kidney damage, and require extensive processing of the urine that hinders accessibility for patients to receive a kidney functionality

test. The aforementioned factors all likely contribute to why CKD is so prevalent, and they present the opportunity for a new diagnostic method to detect kidney damage that will address each of these weaknesses. This may be accomplished through looking from a new lens, particularly the potential use of nanoparticles in the body called urinary extracellular vesicles (EVs).

Urinary EVs are promising new kidney disease biomarkers that could be harnessed as a diagnostic tool for patients. EVs are membranous particles containing cell cargo with inherent biological information from the cells that they are released from and into the extracellular space (Svenningsen, 2020). EVs not bound to a specific location and can travel throughout the body via biofluids, including blood and urine (Urabe, 2020). The contents of EVs contain important biological information about the cell it came from and its conditions, and, thus, EVs containing content from kidney cells could be used to detect kidney damage that may not be symptomatic in the patient. The first major push for analysis of EVs as biomarkers began in 2018 (van Niel, 2018), and currently, they have been proved as early markers of kidney damage (Erdbrügger, 2021).

For my technical project, I seek to develop a microchip that contains antibodies conjugated to specific known biomarkers of kidney diseases that will capture EVs in the patient sample that bind to the antibody. Once the specific kidney extracellular vesicles are captured from the patient urine using an Exoview R100 machine, the disease state of the kidneys can be analyzed, and the patient can be informed about the health of specific portions of their kidneys. The goal is to make these custom antibody chips readily available and clinically routine since they only require a small volume and no processing time, and the hope is that this will allow patients to learn about any kidney damage early enough so that it may be treated before it progresses to CKD.

For the sociotechnical portion of this project, I have explored the prescription of hemodialysis for African American patients following a diagnosis of CKD and have sought to determine why this modality is chosen as opposed to other treatment options once the diagnosis has been made. African Americans constitute 13% of the United States population yet represent 40% of patients receiving dialysis (Umeukeje & Young, 2019). Of the three treatment modalities available, African American patients select hemodialysis at the greatest percent, and hemodialysis is considered to be the most painful, exhausting, and least conducive to a regular life. Hemodialysis also yields the shortest life-span of only about 5-10 years once treatments are begun (*Dialysis*, n.d.). There are several reasons for why African Americans may select hemodialysis even when they qualify for other treatment modalities, and these include the cost of each modality, lower medical literacy, and disparities within the organ transplant system. The elucidation of these reasons may serve to inform policymakers and doctors so that they can better explain and change practices to make the receipt of all treatment modalities more equitable for all patients.

After conducting work in both a scientific and social setting in the field of nephrology, it has been elucidated how devastating a CKD diagnosis is to patients, particularly the deterioration of the quality of life once hemodialysis is started. Had these projects been done in isolation, I am not sure that I would have understood the devastation that late diagnoses of kidney diseases create for patients. From the technical portion, I understood how non-specific the current diagnostic methods are, which demonstrated the need for a new diagnostic tool development to catch nephropathy earlier, but I would not have understood the complexities in the prescription and receipt of treatment in a social context. On paper and within scientific settings, the “worst case” treatment appears to be dialysis received at a clinic, but conducting research in a sociotechnical realm demonstrated the difficulties patients face with insurance and funding these

treatments as well as how limited the treatment options are for some patients due to persisting disparities. I also understood more for my sociotechnical research about the context for how diagnoses are typically made and why kidney damage goes undetected for such an extensive time, and this broader context of nephrology care was due to my technical project in which the diagnostic methods and physiology were integral to developing the diagnostic tool.

I hope that this research enables the prevention of CKD for many patients as well as an expanded opportunity for other treatment modalities following a diagnosis of CKD. The two projects complemented each other to hopefully foster a more inclusive and equitable patient opportunity for nephrology care.