IRB Proposal
Title: Predicting Acute Kidney Injury in Acute Decompensated Heart Failure (ADHF)

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A. Study Purpose and Rationale

Acute kidney injury as evidenced by an increase in serum creatinine is frequent in patients hospitalized for acute decompensated heart failure (ADHF)[1,2]. However, it is common knowledge that creatinine is elevated non-specifically and cannot distinguish real kidney damage (i.e. from ATN) from unapparent kidney damage (i.e. form prerenal azotemia). Neutrophil gelatinase-associated lipocalin (NGAL) is generated from the collecting duct by damage signals. Multiple studies have shown that higher plasma and urine NGAL (>100ng/ml) correlate with ATN from ischemia, sepsis, nephrotoxins and obstructive uropathy, while low NGAL (<100ng/ml) reflect non damaging serum creatinine rise (3). The purpose of this study is to investigate whether NGAL is can distinguish and predict pre-renal azothemia from acute kidney injury (AKI).

B. Study Design and Statistical Analysis

The propose study will be design as an observational prospective cohort study. We seek to enroll adult patients (age>18) admitted to New-York Presbyterian Columbia Medical Center for ADHF. Eligible participants (as identified below) who consent to participate will be enrolled in the study. All subjects will be asked to provide about 3ml of blood and urine, in addition to routine daily labs (BMP, Mg). Samples will be store under standard procedure, to be analyzed at a further date. We seek to enroll at least 195 participants. This number was determined using t-test for group means to show a 50ng/ml difference in urine NGAL levels between patients developing pre-renal azothemia and AKI, assuming 38% of patients admitted with ADHF develop worsening renal function (4). This number of participants will afford the study a 80 power at $p<0.001$.

AKI will be defined in accordance with criteria established by the Acute Kidney Injury Network (5): an abrupt (within 48 hours) absolute increase in serum creatinine ≥ 0.3 mg/dL, a percentage increase in serum creatinine ≥ 50% (1.5-fold from baseline), or documented oliguria ≤ 0.5 mL/kg/hr for >6 hours. Pre-renal azothemia defined as resolution of kidney function within 3 days with the administration of intravenous volume repletion or discontinuation of diuretics(5).

Standard t-test will be use to determine differences of mean NGAL levels, at different time points, between patients with prerenal azothemia and AKI.

C. Study Procedure

All subjects will be asked to provide about 3ml of blood and urine daily while hospitalize. These samples are in addition routine daily labs (BMP, Mg), as determined by primary hospital provider. Potential harm to participants is minimal, as they will already be undergoing blood draws as part routine care. As mentioned samples for NGAL assay will

be obtained at enrollment (admission) and daily until discharge. Once collected samples will be immediately processed, aliquoted, and stored at -80□F until sample analysis. NGAL will be measured by a research enzyme-linked immunosorbent assay (Cat. No. KIT 036, BioPorto Diagnostics, Gentofte Denmark). A 2000-fold dilution will be used to bring concentrations of each sample within the 100-fold sensitivity range of the assay, 10 to 1000 pg/mL. All laboratory analyses will be performed with investigators blinded to renal function.

Study is expected to last one and half years to achieve full enrollment. Subjects are expected to participate during the length of their hospital stay, approximately 3-8days.

D. Study Drugs

No medication or medications will be analyzed during this study.

E. Medical Devices

No device will be analyzed during this study.

F. Study Questionnaires

Participants will not be asked to fell questionnaires

G. Study Subjects

We seek to enroll adult patients (age>18) admitted to New-York Presbyterian Columbia Medical Center for ADHF. To be eligible patient will need to be diagnose with ADHF by the admitting physician with plan to receive in hospital diuretic therapy. Patient receiving renal replacement therapy (hemodialysis or peritoneal dialysis) prior to admission or patient unable to provide written consent will be excluded from study.

H. Recruitment of Subjects

Patients admitted to the cardiac nursing floors will be screen using the electronic medical record for the diagnosis of acute heart failure. Primary clinician caring for patient will be inform of intent to enroll patient and asked to confirm patient is suitable for the study, as per CPMC policy. Patient will be approach by a trained research assistance and will be asked to sign a written consent once study protocol and potential harms are explained.

I. Confidentiality of Study Data

All patients will be provided with a unique study code numbers. All labs studies collected will be marked with the unique patient identifier number that will differ from patient's hospital medical number. Master key for identifier number will be stored in encrypted computer file. In no publications or public presentations will information be available which could identify individual patients or their families.

J. Potential Conflict of Interest

None of the investigators have a proprietary interest in BioPorto Diagnostic or other NGAL measuring assays. There is no conflict of interest to disclose.

K. Location of Study

NYPH-Columbia University Medical Center, Milstein Building

L. Potential Risks

Minimal. There is a small possibility that a patient would receive an extra venipuncture.

M. Potential Benefits

Subjects may not benefit directly as a result of participation in the study. The potential benefits to society include establishing whether NGAL is an important biomarker of clinical outcomes in AKI in patient's ADHF.

N. Alternative Therapies

Not applicable

O. Compensation to Subjects

None

P. Cost to Subjects

None

Q. References

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3. Eugenia S, Antje E, Saban E, Ralph K, et al. Urinary Neutrophil gelatinase-associated lipocalin distinguishes pre-renal from intrinsic renal failure and predicts outcome. Kid Int. 2011:80;405
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5. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11(2):R31.