RESEARCH PROTOCOL

STUDY TITLE
Hand-carried ultrasound for ruling out hydronephrosis in acute kidney injury and acute kidney disease

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1. SYNOPSIS

<table>
<tr><td>Study Title</td><td colspan="2">Hand-carried ultrasound for hydronephrosis</td></tr>
<tr><td>Objective</td><td colspan="2">Determine if internal medicine trainees can rapidly and accurately rule out hydronephrosis using hand-carried ultrasound</td></tr>
<tr><td>Study Period</td><td colspan="2">Planned enrollment duration: 18 months
Planned study duration: 18 months</td></tr>
<tr><td>Number of Patients</td><td colspan="2">170</td></tr>
<tr><td>Study Treatment</td><td colspan="2">none</td></tr>
<tr><td>Study Design</td><td colspan="2">Prospective Observational</td></tr>
<tr><td>Inclusion and Exclusion Criteria</td><td colspan="2">List Inclusion and Exclusion Criteria for your study:</td></tr>
<tr><td></td><td>Inclusion Criteria:

1. Age >18 years

2. Acute kidney injury or acute kidney disease

3. Retroperitoneal ultrasound ordered or performed within the last 4 hours</td><td>Exclusion Criteria:

1. End-stage renal disease

2. History of kidney transplantation

3. Pregnant women

4. Prisoners

5. Patient unable to provide informed consent

6. Morbid obesity (BMI >40)

7. Current diagnosis of renal cell carcinoma

8. Rash overlying scanning area (left or right flank)</td></tr>
<tr><td>Measurements</td><td colspan="2">(1) Presence or absence of hydronephrosis on hand-carried renal ultrasound
(2) Severity of hydronephrosis (only when present) on HCU</td></tr>
<tr><td>Statistical Methodology</td><td colspan="2">Interobserver reliability/ kappa; Sensitivity, specificity, PPV and NPV of HCU performed by trainees compared to read by staff radiologist</td></tr>
</table>

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2. STUDY PROTOCOL

2.1 Background and Significance

Point-of-care ultrasound (POCUS) is an increasingly popular imaging modality that helps clinicians establish or rule out diagnoses, monitor therapy and provide real-time procedural guidance. The rapid availability, safety and low cost of POCUS have made it particularly useful in certain specialties, such as emergency medicine, critical care and trauma. The Focused Assessment with Sonography in Trauma (FAST) exam is a good example of the potential impact and wide applicability of POCUS in medical practice and is now performed worldwide and has supplemented CT as the first recommended imaging modality in the management algorithm of both stable and unstable trauma patients. POCUS is also gaining traction in medical education as an adjunct to physical examination, in the primary care setting, as well as in certain medical subspecialties.

Hand-carried ultrasound (HCU), a type of POCUS that displays images either on a smart phone or on a tablet, makes obtaining real-time imaging more portable and less cumbersome for providers who care for patients in different locations. In a study of 157 consecutive inpatients, trainee cardiologists using HCU were able to identify a normal echo in 94% and a normal EF in 100% of cases. This translated into significant reductions in cost and departmental workload.

Because renal structures are easily seen by ultrasound, enthusiasm for POCUS is increasing in the nephrology community, with terms such as “Point-of-care ultrasound in nephrology (POCUN) being recently carved out. POCUN has wide applications, including the assessment of volume status (inferior vena cava ultrasound, B-lines on lung ultrasound), hemodialysis access or obstructive kidney injury through the detection of hydronephrosis.

Renal ultrasonography is most commonly ordered for patients with acute kidney injury, with a main focus on identifying obstruction of the collecting system, a rare but potentially reversible cause of acute kidney injury. While data is lacking regarding the use of POCUS to identify hydronephrosis in an inpatient setting, data from emergency-use of POCUS demonstrates the validity of using POCUS to evaluate for hydronephrosis. In a prospective observational study of emergency department (ED) patients with suspected renal colic compared computed tomography (CT) results with POCUS and found that hydronephrosis on POCUS was predictive of a ureteral stone 88% of the time. These findings suggested that POCUS can be used to first detect hydronephrosis and aid physicians in identifying patients with renal colic[1]. Another prospective observational study of emergency physicians without prior training on renal ultrasonography who underwent a short training program and then evaluated patients with presumed renal colic, acute pyelonephritis or documented renal failure with POCUS. Results of POCUS were compared with radiologist-read ultrasound and found that hydronephrosis was detected in 100% of cases and accurately ruled out in 71% of cases[2].

2.1.1 Preliminary Data

None available

2.2 Objective

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Evaluate the accuracy of HCU in ruling out hydronephrosis in patients with a diagnosis of acute kidney injury (AKI) or acute kidney disease (AKD) in an inpatient setting. We anticipate potential cost savings for patients and for the healthcare system.

2.3 Patient Selection

2.3.1 Inclusion Criteria

Each subject must meet all of the following criteria:

1. Age >18 years
2. Acute kidney injury or acute kidney disease
3. Retroperitoneal ultrasound ordered or performed within the last 4 hours

2.3.2 Exclusion Criteria

Subjects will not be enrolled if any of the following criteria exist:

1. End-stage renal disease
2. History of kidney transplantation
3. Pregnant women
4. Prisoners
5. Patient unable to provide informed consent
6. Morbid obesity (BMI >40)
7. Current diagnosis of renal cell carcinoma
8. Rash overlying scanning area (left or right flank)

2.4. Study Design

Observational

2.4.1 Study Procedures

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The study team will identify potential participants based on inpatient orders placed in EPIC for a radiology-performed renal ultrasound. Once an order in EPIC has been placed for a renal ultrasound to be done by radiology on a patient that is admitted to Barnes Jewish Hospital, a team member will discuss the study with participants in person.

All patients that fit inclusion/exclusion criteria will be invited to consent and take part in the study
The recruiting investigator will meet individually with each patient and describe the study to them
Patients will either be in the emergency department, on the floor (South or North campus in BJH) or in the ICU. Investigator will spend the necessary time to explain the study to each patient and answer all questions.
Patients will be told that taking part in the study is purely voluntary and that they can decline to be involved. This will not affect their medical care.
Patients will be told that they can withdraw from the study at any time after enrolling.
Team member will make sure that patients interested in study participation are in a quiet area. Team member will review the consent and answer all study related questions.

Upon consent of patient, patient's age and gender with the assigned study code number will be recorded on enrollment log. Study code number, patient name and MRN will be written on bedside data collection sheet.

One non-invasive hand-carried renal ultrasound will be performed the following way:
MD performs right and left sided renal ultrasound and notes his findings on data collection sheet and places in envelope

Each enrolled patient will have the following ultrasound images recorded within 4 hours of completion of the radiology-performed renal ultrasound:
Right kidney longitudinal view
Right kidney mid transverse view
Left kidney longitudinal view
Left kidney mid transverse view

Each clinician will record their result (presence or absence of hydronephrosis, severity of hydronephrosis if present, technical ease or difficulty in obtaining ultrasound images) on a data collection form with the study number, patient name, date and time images were acquired, clinician initials, and comment section for any other observations. The clinician will place the completed form for their measurement in an envelope with the study number on the outside.

2.4.2 Minimization of Bias

There will be no specific gender or ethnic background for enrollment and the decision to approach for consent will be by convenience of team members.

2.4.3 Pre-Study Period

2.4.4 Study Period

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5/1/2019 to 10/31/2020

Methods:

2.4.6 Observations and Measurements

1. Presence or absence of hydronephrosis in the right kidney
2. Presence or absence of hydronephrosis in the left kidney
3. If hydronephrosis present: severity of hydronephrosis (mild, moderate, severe)
4. Time taken to obtain ultrasound images of both kidneys
5. Technical difficulty of study as rated by operator (easy, relatively easy, challenging, very challenging)

2.4.6.3 Primary Outcome Measures

1. Sensitivity, specificity, positive and negative predictive value of HCU compared to radiology read (blinded when obtaining data)

2.4.6.4 Secondary Outcome Measures

1. Duration of obtained measurement(s)
2. Interobserver reliability
3. Potential cost reduction

2.4.6.5 Statistical Methods

2.4.6.6 Sample Size

Assuming an alpha error of 0.05, marginal estimation error (d2) of 0.07, and prevalence of 90%, we determined that **170 patients** were to be included to detect a specificity of absence of hydronephrosis to be 90%.

2.5 Management of Intercurrent Events

2.5.1 Adverse Experiences

The investigator will closely monitor subjects for evidence of adverse events. All adverse events will be reported and followed until satisfactory resolution. The description of the adverse experience will include the time of onset, duration, intensity, etiology, relationship to the study intervention (none, unlikely, possible, probable, highly probable), and any treatment required.

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2.5.2 Premature Discontinuation

If a subject withdraws from the study, the subject will be replaced in order to provide the required number of evaluable subjects. Subjects will be withdrawn if the investigator decides that discontinuation is in the best interest of the subject, or the subject requests withdrawal from the study.

2.5.3 Potential Risks

There are minimal confidentiality risks. But all efforts will be made to minimize confidentiality risk such as: Renal ultrasound images conducted as part of the study will be conducted in private setting to the extent possible; Recruitment/consent will occur in a private setting; Participants will be able to ask questions in a private setting

2.5.4 Procedures to Minimize Potential Risks

There will be efforts to minimize breach of confidentiality risk, such as "minimum necessary" data collection, secured storage in redcap with password access.

2.5.5 Data and Safety Monitoring Plan

An expert colleague from the Department of Medicine, not involved in the study, will also be designated to serve in a monitoring capacity. Based on the small size and relatively low risks nature of the protocol, this person will review for adverse events once a month

3. HUMAN SUBJECTS RESEARCH

3.1 Protection of Human Subjects

The study will be conducted under appropriate Washington University Institutional Review Board protocols and consent forms approvals. The study will be conducted under the supervision of the PI, a Board-Certified and GCP-certified nephrologist, and a mentor with several years experience in the conduct of human volunteer studies.

3.2 Sources of Materials

3.2.1 List of Protected Health Information Collected for Study

Name
DOB
Hemodynamics (vital signs, laboratory values –Cr, HCO3, BUN)
Comorbidities (diabetes, hypertension, CHF, CKD etc.)
Results from recent limited or full retroperitoneal ultrasound

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3.2.2 Data Management

Paper data will be obtained by a research coordinator and placed in a sealed envelope. The envelope and paper data will be kept with the research coordinator during data acquisition and be digitally transcribed into Redcap. Paper data will be kept in a locked cabinet in the Renal Division Office where only research personnel would have access in order to maintain confidentiality.

3.3 Recruitment and Informed Consent

Recruitment will occur at Barnes Jewish Hospital where potential subjects will be approached by a team member. The study team will identify potential participants based on information received about orders placed for an inpatient renal ultrasound. A team member will discuss the study with participants in person.

All patients that fit inclusion/exclusion criteria will be invited to consent and take part in the study The recruiting investigator will meet individually with each patient and describe the study to them. Patients interested in study participation will have the opportunity to review the consent in a quiet area and study personnel will answer all study related questions.

3.4 Potential Benefits of the Proposed Research to the Subjects and Others

There is no benefit to individual subjects in this study. Society may benefit from a better understanding of the role of hand-carried ultrasound in the daily clinical care of patients.

3.5 Inclusion of Women

As a matter of operational policy, our studies of volunteers routinely and deliberately include equivalent numbers of women and men. To ensure sufficient enrollment of women, we typically close enrollment to men once their quota has been filled. This approach has been highly successful. However, the nature of the current study precludes enrollment of a set number of female or male patients since the main criteria for inclusion is acute kidney injury and having a renal ultrasound ordered. Women of childbearing potential are not excluded from our research protocols.

3.6 Inclusion of Minorities

All of our studies actively encourage the participation of minorities in the research. Our minority recruiting typically matches the demographic composition of the Washington University community from which subjects will be recruited (78% white, 21% Black, <1 % Hispanic).

3.7 Inclusion of Children

Children <18 yr will <u>not</u> be studied in these investigations because the research team is not trained in pediatrics and has no access to this patient population.

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4. REFERENCES

1. Leo, M. *et al.* Ultrasound vs. Computed Tomography for Severity of Hydronephrosis and Its Importance in Renal Colic. *West. J. Emerg. Med.* **18**, 559–568 (2017).
2. Javaudin, F. *et al.* Evaluation of a short formation on the performance of point-of-care renal ultrasound performed by physicians without previous ultrasound skills: prospective observational study. *Crit. Ultrasound J.* **9**, 8–11 (2017).

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