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Bedside ultrasound measurement of the inferior vena cava and its relation to intravascular volume status among hemodialysis patients

1. Study Purpose and Rationale

An integral component of the management of critically ill patients in intensive care units (ICUs) and emergency departments (EDs) is assessment of intravascular volume status to determine appropriate therapies for resuscitation, including the administration of intravenous fluid. Inferior vena cava diameter (IVCd) and IVC collapsibility index [IVCCI, (IVCd in end expiration –IVCd in end inspiration)/IVCd in end expiration], a measure of respirophasic variation in IVCd, are two such indicators that may assist in the elucidation of volume status and fluid responsiveness (1). Utilization of bedside ultrasound to determine IVCd and IVCCI is appealing given its noninvasive nature and rapidity with which this study may be completed. However, the reliance on IVC measurement in determining therapeutic regimens for the management of shock is considered controversial, particularly among those who cite that there is little high quality evidence supporting this strategy.

Although multiple studies exist supporting the notion that relatively small IVCd and increased respirophasic variation indicate hypovolemia and fluid responsiveness (2-5), these studies are often small, involving less than one hundred patients, and of questionable consistency due to use of different cut off values of IVCd for correlation to volume status (6). A recent metanalysis performed by Dipti et. al examined the role of IVCd in determination of volume status among adult ED patients in hypovolemic shock. Only 5 prospective studies met inclusion criteria, involving 189 controls and 86 cases. The authors found that IVCd in end expiration was similarly low among subjects identified as hypovolemic by clinical status (clinical assessment of shock and/or hypotension – SBP <90-100 depending on the study) (7). Yet, interestingly, the IVCd in two out of the five studies correlating with hypovolemia would have constituted euvolemia in the remaining three studies (6-7). The authors attribute this finding to likely differences in IVCd among different races/ethnicities, a finding that is not well characterized in the current literature (7). Thus, there are many unknowns regarding baseline IVCd including differences in racial/ethnic groups, gender, patient size, among others.

One flaw of many of these studies is the lack of a gold standard to which to compare volume status. Often, these studies rely on clinical signs such as prolonged capillary refill, decreased skin turgor, or hypotension to identify hypovolemia (3-5, 13). These are imperfect measures given the poor reproducibility of physical findings and that blood pressure is often maintained up until a blood volume loss of greater than or equal to 40% due to homeostatic mechanisms to maintain perfusion pressure (8). On the other hand, correlation with central venous pressure (2) is invasive requiring the placement of a central line, which is associated with well known complications of bleeding and infection (9). One novel group in which these studies may be performed are in hemodialysis (HD) patients in whom the investigator is able to compare changes in IVCd and IVCCI pre- and post-dialysis and correlate measurements with the precise amount of volume removed during dialysis. Existing studies often focus on relating IVCd to dry weight or intra-dialysis symptoms of excessive fluid removal including hypotension and chest pain (10-12) rather than specifically analyzing the relationship between IVC measurements and volume status.

In this current study, we intend to measure IVCd and IVCCI pre- and post-HD to precisely determine how these measurements change with fluid removal to assess whether IVC measurements are truly representative of intravascular volume status. Also, we aim to increase current knowledge regarding variation in IVCd and IVCCI in response to volume changes according to race/ethnicity, gender, age, and body habitus. We hypothesize that IVCd and IVCCI do correlate with intravascular volume status; specifically, that as volume is removed during HD, the IVCd should decrease and IVCCI should increase. In addition, we believe that these measurements vary greatly among individuals of differing demographics, and are thus more useful when assessed as a trend rather than as absolutes.

2. Study Design and Statistical Analysis

This investigation entails a prospective observational study in which IVCd and IVCCI will be assessed pre- and post-HD via bedside ultrasound. Data will be analyzed using student's paired T-test. To obtain an alpha level of .05 and power of 80%, we will enroll 63 subjects. This is based upon a proposed standard deviation of 2.75 mm given that measurements of IVCd post-HD may increase by 1 mm or decrease by up to 10 mm due to actual change in diameter and reproducibility error, and an effect size of 1 mm reduction of IVCd per liter removed.

3. Study Procedures

Using portable ultrasound, the investigators will examine maximal IVCd, measured at the end of expiration, and respirophasic variation by comparing IVCd at the end of expiration to IVCd at the end of inspiration using M mode with the ultrasound probe in the subxiphoid long axis position at the level of the hepatic veins while the patient is in a supine position. Prior to quantitative measurement, the investigator will qualitatively classify the IVC as "large" vs. "small" and qualitatively classify respirophasic variation as "present" vs. "absent" prior to HD and post-HD. The investigators will then quantitatively measure IVCd and IVCCI through use of electronic calipers pre-HD and post-HD. At the time of ultrasonagraphy (pre- and post-HD) vitals and weight will be recorded. All IVC measurements will be confirmed by the principal investigator, a pulmonary critical care specialist, who will review saved de-identified images at a later time, and a third impartial party will adjudicate disagreements in measurements/qualitative assessments. All post-HD IVC measurements will take place within one hour following completion of HD to prevent fluid reaccumulation and, thus, distortion of IVCd. The gathering of these measurements pre- and post-HD is expected to take approximately 15 minutes each and will not interfere with the patients' hemodialysis sessions.

Data will be abstracted from subjects' medical charts, including height, documented dry weight, weight pre- and post-HD, gender, race/ethnicity, and co-morbidities. Determination of co-morbidities will take place via patients' problem list, review of notes, and pertinent labs/tests, such as transthoracic/transesophageal echocardiography.

This study will likely take place over several weeks in order to obtain the required number of participants, and some participants may undergo ultrasound measurements a maximum of three times during distinct hemodialysis sessions to provide more data points. However, the majority of participants will only participate during one distinct HD session.

4. Study Drugs or Devices

Not applicable

5. Study Instruments

Commercially available ultrasound probe will be used to obtain measurements of IVCd and IVCCI pre- and post-HD in each study participant.

6. Study Subjects

Inclusion Criteria

Invited participants will include all end stage renal disease patients at the Columbia University Dialysis Center outpatient facility at 60 Haven Ave. undergoing three times per week HD who are greater than 18 years of age, able and desire to provide consent, within 3 kg of their documented dry weight at the end of their last dialysis session immediately prior to enrollment, and those who do not meet exclusion criteria.

Exclusion Criteria-

Patients with documented pulmonary hypertension as indicated by pulmonary artery resting pressure greater than 25 mm Hg, right sided heart failure (primary or secondary), on mechanical ventilation, and those with cirrhosis will be excluded from this study.

7. Recruitment
   A total of 63 subjects will be recruited from Columbia University Dialysis Center. Eligible participants will be identified by HD staff who will inform subjects of the study. Patients will only be contacted by the researcher once the researcher has been notified that the patient is amenable to learning more about the study.

8. Informed Consent Process
   Once identified by staff, the researcher will contact eligible subjects at CU Dialysis Center. The research protocol will be thoroughly explained with adequate time for questions. A Spanish version of the IRB consent form will also be available, and the investigator will utilize the assistance of a Spanish phone translator for Spanish speaking only patients. Once patients provide consent, they will undergo non-invasive measurement of IVC via ultrasound as described under "Study Procedures." Data will also be abstracted from patients' charts. No post-study contact is intended or expected.

9. Confidentiality of Study Data
   All patients will be assigned a unique identification number under which all pertinent data, including imaging, will be saved. Consent forms will be secured in a locked file cabinet in CUMC. All study data will be stored on secure network folders. Only study investigators will have access to data.

10. Privacy Protections
    All patients will be assigned a unique identification number under which all pertinent data will be saved. Only the investigator and principal investigator will have access to study data.

11. Location of the Study
    All ultrasound measurements will take place at Columbia University Dialysis Center at 60 Haven Avenue. The study investigators will undergo credentialing as this facility is run by DaVita Dialysis, a private company.

12. Potential Risks
    Minimal risks are associated with this investigation including, but not limited to:
    - Potential discomfort secondary to pressure of the ultrasound probe while obtaining measurements
    - Potential loss of secure data; however, precautions will be taken to prevent this as stated in "Confidentiality of Study Data"

13. Data and Safety Monitoring
    Given the low level of personal risk to individual subjects, no data and safety monitoring board will be established.

14. Potential Benefits
    As with most research, there is the intangible benefit of enhancing scientific knowledge. In this case, subjects' participation will assist with clarifying the utility of IVC measurement in determining volume status and fluid responsiveness. There is no expected direct benefit to the individually enrolled patient.

15. Alternatives
    This study entails prospective data collection to determine baseline characteristics of IVC in end stage renal disease patients on HD and does not include any study-specific therapeutic measures. Thus, the alternative is not to participate in the study.

16. Compensation to Subjects
    No compensation will be offered to participants.

17. Costs to Subjects

No additional costs will be incurred by subjects for participation in this study.

Sources

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