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RESEARCH ARTICLE

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Retrospective analysis of inferior vena cava collapsibility with point of care ultrasound and urine sodium and FENa in patients with early stage acute kidney injury

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ABSTRACT

Early stage acute kidney injury (AKI) is an independent risk factor for an increase in mortality. Accurate assessment of volume status is a major challenge during the early stages of acute renal injury. Determining volume status based on the history and physical exam lacks accuracy. Urine sodium and free excretion of sodium (FENa) provide objective evidence of intravascular volume status when interpreted carefully and is helpful to delineate prerenal from intrinsic renal failure. In recent years point of care ultrasound has been used to assess volume status. Our team conducted a retrospective chart review to assess the association of inferior vena cava collapsibility by point of care ultrasound (POCUS) and urine electrolytes (urine sodium, fractional excretion of sodium) during early stage AKI (Stage 1–2 of KDIGO guidelines). We reviewed 150 cases based on the provisional diagnosis. 36 patients met the criteria for further review. Using bivariate analysis, we found a strong association between >50% IVC collapsibility with FENa < 0.4% with an odds ratio 5.3 (CI 1.1–24.5, $p = 0.04$), and urine sodium <20 meq/dl with an odds ratio of 6.7 (CI 1.5–30, $p = 0.02$). Subsequently, multivariate analysis and Spearman correlation showed an inverse relation between IVC collapsibility and fractional excretion of sodium FENa ($\beta = -0.4$, $p = 0.001$) and ($r = -0.44$, $p = 0.01$). These findings suggest the role of POCUS and urinary markers in determining the intravascular volume status in AKI. POCUS is also valuable to assess volume status in cases of renal failure where urine studies are difficult to interpret.

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AKI; FENa; urine sodium; IVC collapsibility; point of care ultrasound

1. Introduction

Acute kidney injury (AKI) impacts lengths of hospital stay, cost of care, and overall mortality [1]. According to KDIQO guidelines, AKI is defined as any of the following. Rise in serum creatinine by 0.3 mg/dl above the baseline within 48 hours, increase in creatinine by 1.5–2.0 mg/dl presumed to have occurred within prior 7 days, or drop in urine output by 0.5 ml/kg/h within 6 hours [2]. In recent years the term pre-renal failure and ATN are discredited due to the difficulty in distinguishing one from the other due to the coexistence of each other. These terminologies of volume responsive and non-responsive acute kidney injury are coined to signify the role of accurate volume assessment and resuscitation in halting renal injury [3]. Renal hypoperfusion secondary to low intravascular volume status increases the susceptibility of the kidney injury. It has been hypothesized that accurate and timely assessment of patient volume status is critical in reducing the risk of renal insufficiency [4]. However, no randomized study evaluated the effects of volume resuscitation on progression of renal injury. Accurate assessment of volume status is challenging. A survey regarding volume assessment showed variable response among physicians at our institution (Figure 1). Most responses included history and physical examination findings to determine volume status. Volume assessment using POCUS has gained popularity in recent years. Determining inferior vena cava (IVC) collapsibility with POCUS is a reliable indicator for intravascular volume status [5,6]. Urine markers including urine Na, FENa, and FEurea are also helpful in determining volume status in appropriate settings [7,8] To our knowledge, no study has evaluated the relationship between IVC collapsibility and urine markers in the hypovolemic state. We conducted a retrospective review to determine this association between IVC collapsibility with POCUS and urine indices including urine sodium, FENa (fractional extraction of sodium), in patients with early stage AKI, i.e., (defined by stage 1 and 2 of KDIQGO guidelines).

2. Methodology

We used electronic medical records to conduct a retrospective chart review from our institution for the dates between January 2016 and July 2016. 150 cases were reviewed based on their provisional diagnosis such as acute renal failure, GI bleed, sepsis, severe diarrhea, and metabolic derangements (including hyponatremia,

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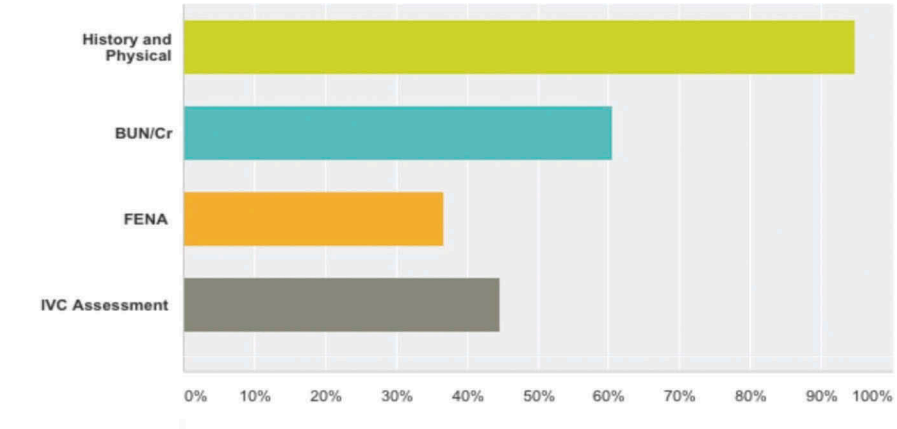

Answer Choices	Responses	
History and Physical	94.74%	36
BUN/Cr	60.53%	23
FENA	36.84%	14
IVC Assessment	44.74%	17
Total Respondents: 38		

Figure 1. Volume assessment survey response by the attending and residents.

hyperglycemia, and hypercalcemia). Cases were further selected on the basis of documented/imaging evidence of IVC collapsibility, same-day urine studies and serum chemistry. Data regarding IVC collapsibility were gathered from documentation of an attendant trained in performing POCUS. Significant inferior vena cava collapsibility was defined as more than 50 percent end inspiratory IVC collapse in spontaneously breathing patients. FENa less than 0.4% and Urine Na less than 20 percent was taken as indicative of low intravascular volume state. The cut-off value of FENa 0.4% was selected due to mild renal insufficiency in most of the cases.

2.1. Inclusion criteria

a) The presence of documented or imaging evidence of IVC assessment and same day urine indices (urine sodium and FENa) in cases meeting KDIGO stage 1–2 AKI. b) KDIGO stage 1–2 AKI is defined as an increase in serum creatinine by 0.3 mg/dl from baseline or rise in creatinine by 1.5-2.9 times from baseline. c) Patients at risk of developing kidney injury due to continued volume loss in conditions like diarrhea, polyuria due to hyperglycemia or hypercalcemia, or blood loss.

2.2. Exclusion criteria

a) Time interval of more than 12 hours between urine specimen collection and IVC assessment. b) Lack of documentation of IVC assessment. c) Unknown baseline creatinine and known kidney disease. d) Patients with history of severe pulmonary hypertension, chronic liver disease, congestive heart failure (EF < 30%), contrast-induced nephropathy and post renal failure were also excluded.

2.3. Statistical analysis

We used *t*-test analysis to determine the difference in mean IVC collapsibility in patients with FENa less than 0.4% and greater than 0.4%. Similarly, *t*-test was used to determine differences in mean IVC collapsibility in patients with urine sodium less than 20 meq/dl and urine sodium greater than 20 meq/dl. The odds ratio was calculated using a 4 × 4 table (Table 1 and 2). Subsequently, we applied linear regression and Spearman correlation to compare IVC collapsibility and FENa.

3. Results

104 out of 150 cases were excluded due to the lack of documented/digital data of IVC assessment, or lack

Table 1. A 4*4 table between urine sodium with IVC collapsibility.

	IVC Collapsibility <50%	IVC Collapsibility >50%
Urine sodium <20 meq/dl	4	16
Urine sodium >20 meq/dl	10	6

Table 2. Baseline characteristics of patients.

	Mean
Age	68.4 ± 17.4 years
Sex	50% male and 50% female
Serum creatinine (mg/dl)	1.7 ± 1.0
FeNa (%)	0.5 ± 0.4
IVC collapsibility (%)	70 ± 30%
Lactic acid	2.3 ± 1
Mean arterial pressure (mm of Hg)	70.5 ± 18

of same day urine studies. In 46 selected cases the average time separation duration between IVC assessment, serum chemistry, and urine studies was 2–3 hours. 10 cases were further excluded based on the exclusion criteria listed. A sample of 36 patients constituted 50% males (n = 18) and 50% females (n = 18). The mean age at the time of ultrasonography was 68.4 ± 17 years. The mean IVC collapsibility in all the patients was 70 ± 30%. The mean FeNa was 0.5% ± 0.4% in included cases (Table 3). The mean IVC collapsibility in patients with FeNa < 0.4% and FeNa > 0.4% was (83% vs. 59% p = 0.04). The mean IVC collapsibility in patients with urine sodium less than 20 meq/dl and urine sodium greater than 20 meq/dl was (82% vs. 54.7% p = 0.02). 16 out of 36 patients had FENa less than 0.4% meq/dl. Of those 16 patients, 3 patients had less than 50%, and 13 more than 50% IVC collapsibility. In 20 out of 36 patients with FENa greater than 0.4%, 11 patients had IVC collapsibility less than 50% and 9 greater than 50%. The odds ratio of more than 50% IVC collapsibility with low measured FeNa was 5.3 (CI 1.1–24.5, p = 0.04) (Table 4). Subsequently, multivariate analysis showed an inverse relation between IVC collapsibility and FeNa (β = −0.4, p = 0.001) and Spearman correlation (r = −0.44, p = 0.01) (Table 5). In 20 patients with urine sodium less than 20 meq/dl, patients had IVC collapsibility less than 50% and 16 greater than 50%. In 16 patients with urine sodium greater than 20 meq/dl, 10 patients had IVC collapsibility less than 50% and 6 greater than 50%. The odds ratio was similarly calculated using a 4 × 4 table. The odds ratio of greater than 50 percent IVC collapsibility with urine sodium less than 20 meq/dl was 6.7 (–CI 1.5 to 30, p = 0.02) (Figure 2).

4. Discussion

Renal hypoperfusion secondary to hypovolemia may coexist at different stages of AKI [4]. For that purpose, determining volume status and resuscitation is critical in reducing the risk of renal disease progression. Determining volume status in patients relies mostly on history and physical examination findings. However the evidence for using conventional methods is weak [9]. In previous studies physical signs including poor skin turgor, postural variation in blood pressure and heart rate, and dry oral mucosa were unable to accurately predict the volume status [10–12]. Despite the lack of evidence, these measures are commonly used in clinical settings. The survey at our institution showed similar findings where the majority of the physicians answered history and physical exam findings as a marker used for volume assessment (Figure 1). In recent years POCUS has gained popularity for determining volume status. Several studies have demonstrated the effectiveness and ease of using POCUS for volume assessment [5,6]. Studies have shown correlation of IVC assessment by POCUS with central venous pressure and invasive cardiac pressure measurement by right heart catheterization [6]. Determining volume status using POCUS is standard of care in ICU settings at our institution. We use greater than 50 percent collapsibility as cut-off for significant IVC diameter variation and fluid responsiveness in spontaneously breathing patients. Urinary electrolytes including urine sodium, FENa and FEurea are helpful markers of hypovolemia. Urine sodium less than 20 percent, and FENa usually less than 0.5–0.4 percent are indicative of hypovolemia [8]. In clinical settings timely collection of urine specimen and interpretation of urine studies after volume resuscitation are major constraints of using these markers accurately in cases of AKI. To

Table 3. A 4*4 table between FeNa (Free excretion of Na) with IVC collapsibility.

	IVC Collapsibility <50%	IVC Collapsibility >50%
FeNa < 0.4%	3	13
FeNa > 0.4%	11	9

Table 5. Correlation between FeNa and IVC collapsibility calculated using Spearman correlation index.

	FeNa	
	Beta	r
IVC collapsibility	−0.4 (p = 0.001)	−0.44 (p = 0.01)

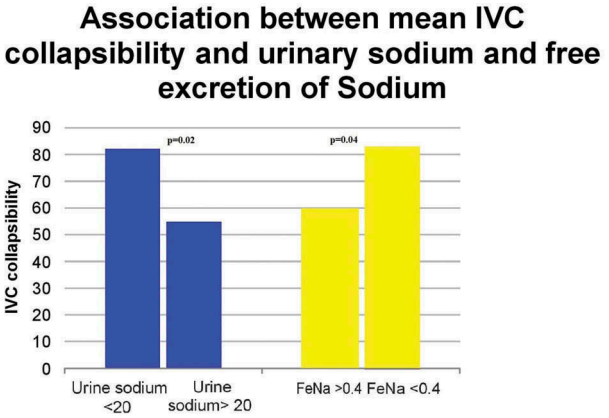

Figure 2. Association between mean IVC collapsibility and urinary sodium and free excretion of sodium.

Table 4. Comparing difference in mean collapsibility in subgroups of urine sodium and FeNa.

	Urine Sodium			FeNa		
	Urine sodium <20	Urine sodium >20	P value	FeNa < 0.4%	FeNa > 0.4%	P value
IVC collapsibility	82.0 ± 7.3%	54.7 ± 8.7%	0.02	83.0 ± 8.3%	59.0 ± 7.4%	0.04

our knowledge, no study has evaluated the correlation of IVC collapsibility against urinary markers in patients at risk for, or in early stages of, AKI. Our study showed an association of greater than 50 percent collapsibility with low calculated FENa. Multivariate analysis and Spearman correlation further strengthened correlation of high degree of IVC collapsibility with low calculated FENa. A similar association was noted with urine sodium and IVC collapsibility, where low urine Na (i.e., <20 meq/dl) was associated with more than 50 percent IVC collapsibility in cases of early stage AKI.

A closed loop circulatory system explains the physiologic association between urine electrolytes and IVC collapsibility. Due to a predictable changes between right atrial pressures and left ventricular diastolic pressures [13]. We believe that in hypovolemia, change in right atrial pressure and LVEDP alters hemodynamics causing increased sodium reabsorption by kidneys resulting in low urine Na and FENa and similarly causing increased IVC collapsibility. However, the only limitation with this concept is the presence of pulmonary HTN or valvular disease that results in unequal distribution of the pressures across the chambers of the heart making IVC collapsibility and urinary studies difficult to interpret [13]. We believe POCUS and urinary electrolytes increase the overall accuracy of the determining volume status. Findings from our study also suggest that POCUS can be used to predict renal hypo-perfusion (pre-renal component) during different stages of AKI, specifically in cases where urine studies are difficult to interpret due to timely urine collection after volume resuscitation, or in cases of false-positive results.

There are some limitations of our studies. Free excretion of urea is not included in the study due to the limited number of cases in which it was tested. In some cases there was no time distinction between performing POCUS and urine collection. Hence they were excluded from the study. Urine output criteria for AKI were not included due to the inaccurate documentation of urine output in the charts.

5. Conclusion

Our study demonstrates the association between urinary markers (including urine sodium and fractional excretion of sodium) and IVC collapsibility in patients in early stage AKI. We found an inverse correlation between IVC collapsibility and FENa using Spearman correlation. Together, POCUS and urinary markers can improve objective assessment of volume status, a major risk factor in progression of renal injury. POCUS, for its ready availability and ease of use is a favored tool to utilize in cases of hypovolemia causing renal hypoperfusion and difficult to interpret urine studies. Further prospective studies are required to assess the effectiveness of volume resuscitation based on the information from point of care ultrasound and urine electrolytes in AKI.

Disclosure statement

This is an IRB approved project. None of the participants in this study received any financial assistance. No authors had any conflicts of interest.

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