

The effect of the rising abdominal perfusion pressure on kidney Function assessed by the RIFLE criteria in critically ill patients with multiorgan dysfunction

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Abstract: Abdominal perfusion pressure (APP) is a novel, clinically measurable parameter to explain the circulatory compromise in the abdominal cavity, defined as the difference between the mean arterial pressure (MAP) and the intrabdominal pressure (IAP). Kidneys are especially vulnerable intrabdominal organ to the circulatory compromise and the third spacing in multiorgan dysfunction syndrome (MODS) patients. And this study was to evaluate the relationship of the APP to AKI assessed by RIFLE Patients and methods: 106 MODS patients were included in the study, routine laboratory investigations and vital signs were recorded and APP and RIFLE score were assessed daily for the first three days. Results: AKI patients had lower APP (86.3 ± 9.0 vs 78.4 ± 18.5 P 0.009). Patients with APP < 60mmHg showed worse RIFLE scores (O=0/18, R=1/6, I=2/27, F=13/39 p=0.03). APP was significantly correlated with urine output ($r=0.239$ P 0.013). Conclusion Low APP causes deterioration of kidney function and oliguria is the first and sensitive predictor.

Keywords: RIFLE, Abdominal Perfusion Pressure

1. Introduction

APP, similar to the familiar concept of cerebral perfusion pressure, is defined as the difference between the mean arterial pressure (MAP) and the IAP, and implies that as the IAP rises, the perfusion of organs or vessels in or near the abdomen falls even in the absence of a drop in MAP. [1], for IAH has been identified as a continuum of pathophysiologic changes beginning with regional blood flow disturbances and culminating in frank end-organ failure and the development of ACS [2].

The effects of increased IAP are multiple, but the kidney is especially vulnerable to increased IAP because of its anatomic position [5], and it is the most consistently described organ dysfunctions with oliguria being one of the earliest clinical signs of IAH [6].

IAH should be considered as a potential cause of acute kidney injury in critically ill patients; [5] and can be present at relatively low levels of intra-abdominal pressure (IAP). [1]

Although the means by which kidney function is impaired

in patients with ACS is incompletely elucidated, available evidence suggests that the most important factor involves alterations in renal blood flow. [5]

Until recently, there was a lack of consensus as to the best definition, characterization, and evaluation of acute renal failure. [7]

RIFLE is the first widely accepted AKI definition, validated in over half a million patients worldwide [8]

Such an acronym conventionally described 3 stages of progressively higher creatinine levels or decreased urine output flows (risk, injury, and failure) and 2 outcomes (loss of function and end stage kidney disease) [9].

2. Aim of the Study

Our study is to evaluate the relationship of the APP to AKI in the critically ill patients.

3. Patients and Methods

We studied 106 critically ill patients with MODS defined as

SOFA subscore of > 2 in at least 2 organ systems.

Patients with age less than 18 years and chronic renal failure were excluded.

In all patients we recorded MAP, temperature, heart rate, urine output (UO), bilirubin, creatinine, full blood count, arterial blood gases, sodium and potassium, lactate, Fluid gain, IAP and APP.

IAP was measured via the bladder, using the closed loop system repeated measurements technique [10] twice a daily.

IAH is defined as an IAP that was persistently 12 mmHg or greater [11].

APP is calculated as the difference between MAP and mean IAP.

Renal function was assessed by the RIFLE criteria using the first three stages [9], the estimated the serum creatinine (SCr) baseline was from the reversed Modification of Diet in Renal Disease equation [12].

- Risk: SCr increased 1.5 times or UO of <0.5 ml/kg/hr for 6 hours

- Injury: doubling of SCr or UO <0.5 ml/kg/hr for 12 hours
- Failure: tripling of SCr or SCr >4 mg/dl with an acute rise > 0.5 mg/dl OR UO below 0.3 ml/kg/hr for 24 hours

4. Statistical Analysis

Data was transferred to the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analyzed.

5. Results

Patients' mean age was 55.6±16.9; Based on the reason for ICU admission, there were 85 (80.2%) medical and 21 (19.8%) surgical, the mean APP was 79.7±17.5 and RIFLE 0 18(17%), R 7(6.6%), I 29(27.4%) and F 52(49.1%)

On admission, patients with low APP showed decline in renal function assessed by RIFLE criteria

Table 1. Relation of abdominal perfusion pressure on admission to RIFLE score.

Rifle on admission	APP on admission	P value	APP<60	APP>60	P value
0	86.3 ± 9.0	0.2	0(0)	18(20)	0.03
1	80.0 ± 14.3	NS	1(6.3)	6(6.7)	
2	82.0 ± 15.2		2(12.5)	27(30)	
3	76.2 ± 20.5		13(81.3)	39(43.3)	

A total of 106 patients were included, values are expressed as mean± standard deviation, APP abdominal perfusion pressure.

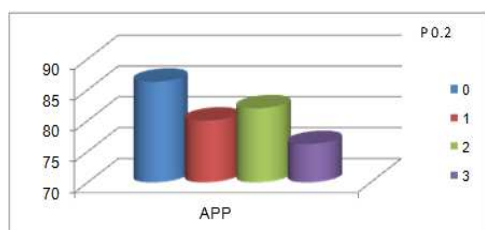


Figure 1. Relation of APP on admission to RIFLE score

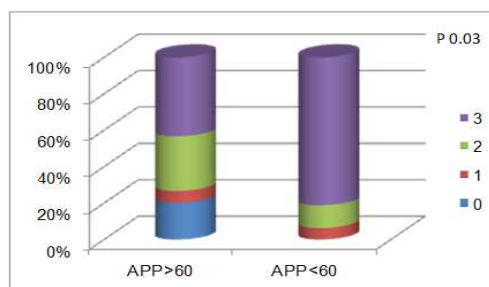


Figure 2. RIFLE on admission and abdominal perfusion pressure on admission cut off point 60 mmHg

APP was significantly lower in patients with [RIFLE >0]

Table 2. Relation of abdominal perfusion pressure on admission and with cut off point 60 mmHg to RIFLE >0 or =0 on admission

RIFLE>0	APP on admission	P value	APP<60	APP>60	P value
Yes	78.4 ± 18.5	0.009	16(100)	72(80)	0.07
No	86.3 ± 9.0	HS	0(0)	18(20)	

Table 3. Mean APP of the first three days and the RIFLE > and = 0 on day 3

RIFLE>0 on day 3	Mean APP mean±SD	P value
No	87.4±9.7mmHg	0.029
Yes	81±15.8 mmHg	

A total of 106 patients were included, values are expressed as mean± standard deviation number of cases, and figures in parentheses are percentages within APP > or< 60mmHg. APP abdominal perfusion pressure.

Table 4. Acute renal failure and APP on admission

RIFLE=F	APP on admission	P value	APP<60	APP>60	P value
Yes	78.1± 18.2	0.009	13(81.3)	39(43.3)	0.006
No	84.9± 12.7	HS	3(18.8)	51(56.7)	HS

The total population were included, values are expressed as mean± standard deviation (SD), APP abdominal perfusion pressure.

Patients with low APP on admission experienced higher incidence of acute renal failure.

A total of 106 patients were included, values are expressed as mean± standard deviation number of cases, and figures in parentheses are percentages within APP > or< 60mmHg. APP abdominal perfusion pressure.

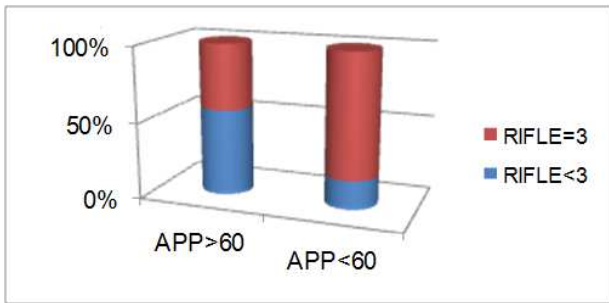


Figure 3. Acute renal failure and APP on admission cut off point at 60 mmHg

Table 5. Mean APP of the first three days and the RIFLE < and = 3 on day 3

		Mean APP mean±SD	P value
RIFLE =3 on day3	Yes	79 ± 17.3mmHg	0.037
	No	85.6 ± 11.4mmHg	

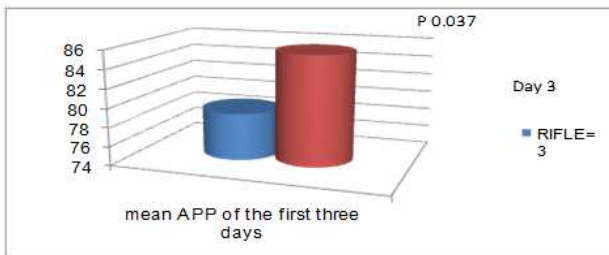


Figure 4. Mean APP of the first three days and the RIFLE < and = 3 on day 3

Table 7. Presence of Oliguria and APP

	APP	UO <0.5ml/hr		P	UO <0.3ml/hr		P
		Yes	No		Yes	No	
	Day 1	72.8±24.2	82.1±14	0.07	67.6±26.3	82.2±14	0.03
	Day 2	73.4±27.2	83.8±15.8	0.1	69±27.4	83.9±16.4	0.05
	Day 3	66.9±29	85.1±13.5	0.014	64.9±30.8	84.8±13.6	0.02

The total population were included, values are expressed as mean± standard deviation, APP abdominal perfusion pressure, UO, urine output

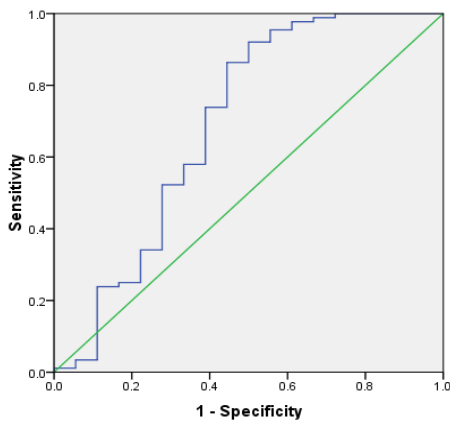


Figure 6. ROC curve for APP on admission to presence of oliguria less than 0.3ml/kg/hr

The total population were included, values are expressed as mean± standard deviation, APP abdominal perfusion pressure.

Urine output

On admission APP was significantly correlated with urine output.

Table 6. Urine output median and interquartile range between Patients with APP above and below 60mmHg

	Urine OutPut			Pvalue
	25 th percentile	median	75 th percentile	
APP >60mmHg	1287	2000	3100	<0.001
APP ≤60mmHg	212.5	350	1200	

A total of 106 patients were included, values are expressed as median and interquartile range.

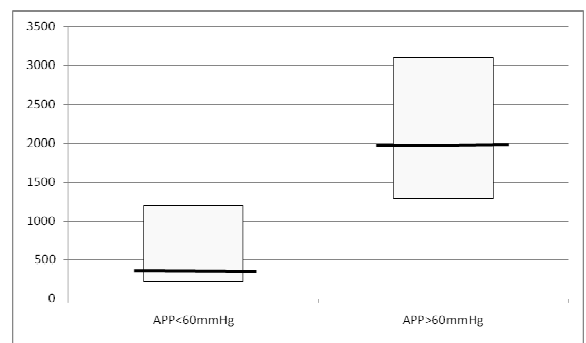


Figure 5. Urine output median and interquartile range between Patients with APP above and below 60mmHg

Predictors of ARF

Backward Stepwise logistic regression model was conducted to explore the significant predictors of ARF. Variables entered step 1 of the model was SIRS, APACHEII, Mean SOFA, MeanMAP and MeanAPP. Last step was significant($X^2 = 48.964$, $df=1$, $P<0.001$), R^2 ranged from 0.370 – 0.494. Only SOFA was the significant predictors as shown in the following table.

Table 8. Backward Stepwise logistic regression model to predict ARF.

	β	P value	OR	95% of OR	
				Lower	Upper
SOFA	0.485	<0.001	1.624	1.346	1.959
Constant	-4.475	<0.001	0.011		

AUC 0.690 (95% CI, 0.532 to 0.857 $p < 0.011$) Cut off point is at 75 mmHg with sensitivity of 73.9% and specificity of 61%

6. Discussion

APP is a parameter combining both the pathogenesis incriminated in renal dysfunction in acute critical care settings [1]. The cause of renal dysfunction in ACS is multifactorial [2], available evidence suggests that the most important factor involves alterations in renal blood flow [3] and decreased arterial visceral perfusion [1], while The presence of IAH as a risk factor for acute kidney injury (AKI) has been shown in many clinical settings. [3]

Increased IAP is caused by tissue oedema from generalized capillary leak [1] causing multiple effects, but the kidney is especially vulnerable to increased IAP because of its anatomic position. [3]

IAH causes compression of the inferior vena cava [4]. with subsequent increasing the hydrostatic pressure in the venous column, further impeding the venous return to the right heart chambers decreasing the cardiac preload. [5] and causing rise to renal venous congestion. [6]

The prognosis of AKI as a manifestation of IAH depends on the underlying pathology of IAH, early recognition, and timeliness of intervention. [7]

The systematic application of both IAH severity classes, as well as AKI stages (using RIFLE or AKIN [Acute Kidney Injury Network] criteria), may increase knowledge and awareness of the impact of earlier phases of IAH and less severe IAH on kidney function, as well as lead to more early and efficacious interventions. [3] as the impact of less severe IAH on AKI was virtually unrecognized.

In our study, Patients with AKI defined using the RIFLE classification RIFLE = 0 vs RIFLE >0, experienced significantly lower APP (78.4 ± 18.5 vs 86.3 ± 9.0 $p=0.009$), but the degree of injury assessed by RIFLE didn't show that statistical significance (RIFLE 0 = 86.3 ± 9.0 , 1 = 80.0 ± 14.3 , 2 = 82.0 ± 15.2 , 3 = 76.2 ± 20.5 $p 0.2$).

IAH should be considered as a potential cause of acute kidney injury in critically ill patient [3] In a cohort study of unselected ICU patients [9], IAH was an independent risk factor for the development of AKI, and IAP of 12 mm Hg was the most optimal cutoff for AKI defined using the RIFLE classification (sensitivity, 91%; specificity, 67%; area under the receiver operating characteristic curve, 0.85).

Restoration of APP using norepinephrine improves renal blood flow in bacteremic animals with IAPs up to 30 mm Hg, and maintaining a therapeutic APP may preserve renal blood flow in patients with intra-abdominal hypertension [8]

While using the cut off point APP > or ≤ 60 mmHg in our study, as it is considered to be an indicator of abdominal hypoperfusion since it correlated well with survival from IAH and ACS [10], it showed that inevitably all patients having APP lower than 60 mmHg had AKI but with non significant P value 0.07, while using renal SOFA subscore by Dorzi *et al*, the renal SOFA subscore was worse with APP cut off point 60mmHg but with non significant P value of 0.06 [10].

However in our study when we used the same cut off point but to discriminate the RIFLE=F, it was statistically significant ($p 0.006$)

Another study [9] investigated IAH and RIFLE F and it showed that the IAH can discriminate RIFLE F ($p < 0.0001$).

APP was an independent promoter of ARF [9] In our study, it showed strong relation between APP and presence of ARF, as APP was shown to be lower in RIFLE = F patients (78.1 ± 18.2 vs 84.9 ± 12.7 mmHg $p 0.009$)

In a study on liver transplant patients, IAH impaired renal function and was an independent risk factor for ARF after liver transplantation. [11]

Nice to mention that in our study, the mean APP of the first three days revealed highly significant relationship with AKI (RIFLE > 0) $p 0.029$ and the occurrence of acute renal failure too (RIFLE = F) $p 0.037$.

Dalino *et al* developed a logistic model including shock, IAH, APP, APACHE-II score, FG, surgical admission for ARF development. According to the level of significance, the stepwise analysis rated shock as most critical in the model for ARF development (RIFLE F), followed by IAH ($P < 0.002$) and low APP ($P < 0.046$). [9] but in our study APP didn't show that significant for predicting AKI, when we applied Backward Stepwise logistic regression model, using SIRS, APACHE, SOFA day1, MAP D1 and APP D1. As Only SOFA was the significant predictor ($p 0.001$).

Oliguria and anuria are common problems facing ICU clinicians caring for patients with AKI [12] and It is also valuable marker of kidney function and a criterion for diagnosing and staging acute kidney injury (AKI) [13].

The presence of anuria and increased intra-abdominal hypertension score are predictors of increased mortality [7].

Oliguria progressing to anuria and pre renal azotemia unresponsive to volume expansion is characteristic of renal dysfunction of ACS [2].

In our study the urine output was lower with lower APP ($p 0.013$), and even the cut off point of 60mmHg for APP was having highly significant lower urine output ($p < 0.001$).

In experimental studies carried out on euvolumic subjects, IAP of 20 mm Hg resulted in 75% reduction in glomerular filtration rate (GFR) and a pressure of 30 or above resulted in anuria. [2]

Interestingly here is, in an 137 patient study of critically ill, Oliguric patients without a change in serum creatinine had an intensive care unit mortality rate (8.8%) significantly higher than patients without AKI (1.3%), and similar to oliguric patients with an increase in serum creatinine (10.4%). [13]

When investigating oliguric criterion of RIFLE (< 0.5 ml/kg/hr and < 0.3 ml/kg/hr) in our study, it showed significant relation with the APP ($P 0.07$ and 0.03 respectively) but not when relating APP to RIFLE (which comprises also creatinine criteria) as it is turned to be non significant ($p 0.2$). That is because urine flow rate is a sensitive and specific biomarker that provides an early warning signal for impending renal dysfunction [13]

Despite that in an 81 septic shock patients study admitted to a surgical-medical ICU, it showed that abdominal perfusion pressure was negatively correlated with maximal serum creatinine ($P.001$, $r = 0.37$) [14]

Still urine output is a sensitive and early marker for AKI

and is associated with adverse outcomes in intensive care unit patients [13] and in one study the incidence of AKI increased from 24%, based solely on serum creatinine, to 52% by adding the urine output as a diagnostic criterion [13] and oliguric patients without serum creatinine changes had a significantly higher mortality rate than non-AKI patients (P 0.007). [13]

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