International Journal of Research in Medical Sciences
Simour A et al. Int J Res Med Sci. 2019 Feb;7(2):410-416
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20190344

Original Research Article

Evaluation of intermittent hemodialysis conducted off-site on patients with renal insufficiency admitted in the intensive care unit of a developing country

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Received: 28 November 2018
Accepted: 29 December 2018

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ABSTRACT

Background: In most developing countries, the renal replacement therapy (RRT) in ICU is not performed locally. We designed this study to assess the intermittent hemodialysis (IHD) offsite intakes on survival in critically ill patients admitted with renal failure.
Methods: We prospectively analyzed all patients admitted to medical ICU with Acute Renal Failure (AKF) or Chronic Renal Failure (CKF) from February 2011 to September 2013. Patients were divided into two groups: those that received IHD in Hemodialysis Unit (IHD+) and those who did not (IHD-). Every patient IHD+ was matched to a patient IHD - using propensity score.
Results: 202 patients were included: 151 with ARF and 51 with CRF. 116 patients were matched (age: 48±18 years; 46F/70M; median serum creatinine: 51mg/l; IQR: 32-90 mg/l). The total number of dialysis sessions was 112 for 58 patients (1.8±1.4 session/patient). The median delay to initiate IHD was 5.5h (IQR: 2-8h) and median duration of transportation was 10 min (IQR: 10-15min) with 23.6% transportation incidents. Significant hypotension with tachycardia were reported during IHD. ICU mortality rate was the same in the both groups (58.6%). In multivariate analysis, CRF (RR=2.69; p=0.006), serum creatinine >50mg/l (RR=3.54; p=0.007) and requirement for vasopressors infusion (RR=1.8; p=0.041) were independent predictive factors for receiving IHD.
Conclusions: Our study doesn't show an improvement in survival in ICU patients who receive IHD offsite. The probability to require IHD offsite increases with CRF and the use of vasopressors.

Keywords: Intensive care unit, Intermittent hemodialysis, Renal failure

INTRODUCTION

Renal failure (RF) represents an over mortality and morbidity factor for the patients admitted in the intensive care unit.[1] Given the large prevalence of acute RF (ARF) in the intensive care setting, the resort to the technique of extrarenal purification (ERP) is often necessary and should allow the survival of the patient without harming the renal function's recovery or the other organs' failure. Hence, the optimization of ERP constitutes a major issue in critical illness. The availability of resources for management of acute kidney injury differs between developed and developing countries.[2] However, in the developing world, logistic and financial constraints still continue to be important considerations in the management of RF, especially in critically ill patients.[3]

In Morocco, only one study was interested in intermittent hemodialysis (IHD) and was conducted locally in an intensive care unit (ICU) that had dialysis facilities.[4] However, regarding the IHD that was conducted off-site, i.e. in the Hemodialysis unit on patients of ICU, no data has been reported in the literature despite being practiced in many countries including the developing ones.

The main objective of our study was to evaluate the input of IHD performed off-site on patients of RF who were admitted in an ICU. The secondary objective was to determine the predictive factors of the resort to IHD off-site.

METHODS

This is a prospective cohort study with matching, which was carried out in the Medical ICU during the period between February 2011 and November 2013. There were included all the adult patients of more than 17 years old who were hospitalized in ICU and who presented upon admission either acute renal failure (ARF) according to the RIFLE criteria or a chronic renal insufficiency (CRI). Many sociodemographic variables (age, sex, origin), clinical (temperature, heart rate (HR), respiratory rate (RR), systolic and diastolic arterial pressure (SAP/DAP), Glasgow coma score (GCS), biological (natrium (mmol/l), kaliemia (mmol/l), glycemia (g/l), bicarbonate (mmol/l), uremia (g/l), serum creatinine (mg/l), total protein (g/l), leukocytes (ilm/ mm^3), hemoglobinemia (g/dl), platelets ($/mm^3$) and reactive C protein (RCP; mg/l)), therapeutic (number of IHD sessions, indications, set up parameters, dialysate), and evolutionary were evaluated in addition to comorbidity (Charlson Comorbidity Index) and gravity (APACHE 2 (Acute Physiology and Chronic Health Evaluation 2) and LODS (Logistic Organ Dysfunction System)). Variables were studied in pre-dialysis, during dialysis, and post-dialysis: SAP/DAP, HR, LODS, use of mechanical ventilation, vascular filling, vasopressors, sedation and transfusion.

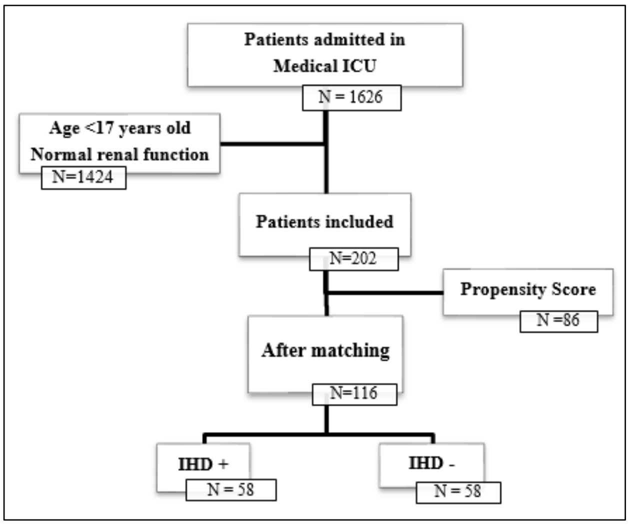
The parameters in relation to transport were also collected: duration of transport, incidents during transport, time between the indication and the beginning of the IHD session and reasons for the delay in starting the session.

Statistical analysis

Quantitative variables were expressed using the average ± standard deviation and the qualitative variables in actual numbers and percentages. Two groups have been characterized: the IHD group having benefitted from an intermittent hemodialysis (IHD+) which was conducted outside in the Nephrology-Hemodialysis unit, and the group which has not benefitted from IHD (IHD-). A propensity score was constructed to a multiple model of logistic regression in order to evaluate the probability that a patient be treated from IHD off-site. Each patient of the IHD+ Group was matched with a patient belonging to the HDI- Group having the closest propensity score. The two groups IHD+ and IHD- were compared before and after the matching and the main outcome was the mortality rate in ICU. The used statistical tests were: Wilcoxon test for the comparison of quantitative variables, Mc Nemar test for the comparison of qualitative variables, ANOVA for repetitive measurements and the conditional logistic regression for the identification of the predictive factors of the resort to IHD. The curves of survival were realized and compared using the log rank test. The data were written and analyzed using SPSS (Statistical Package for the Social Sciences; SPSS Inc.; version 13). A value of $p < 0.05$ is considered as statistically significant.

RESULTS

The number of admission to the Medical ICU during the study period involving all mixed pathologies was 1626 patients. In total, 202 cases were retained for the study, which makes 12.4% (IC95%: 7.9-16.9%). ARF according to the RIFLE definition was noticed in 152 patients (75.2%) which makes an incidence of 9.3% during the study period. Fifty patients presented a CRI including 22 (43.1%) which were already under renal replacement therapy before their admission. IHD off-site involved 28.7% (58/202) of the patients.



(IHD +: group with intermittent hemodialysis; IHD-: group without hemodialysis)

Figure 1: Flow chart of patients included in the study.

Among the 202 patients of renal insufficiency, 116 could be matched with the help of the propensity score with 58 in each group (Figure 1). The values of the propensity scores before and after the matching of the HDI+ and HDI-groups are represented in Figures 2 and 3. The average age of patients was 48±18 y (extremes: 17-87y) with a male predominance (46 females/70 males). The comorbidity index of Charlson was of an average of 3±2 (extremes: 0-8). The APACHE 2 and LODS scores were 24.1±6.5 (extremes: 7-46) and 6.8±2.2 (extremes: 3-16) respectively.

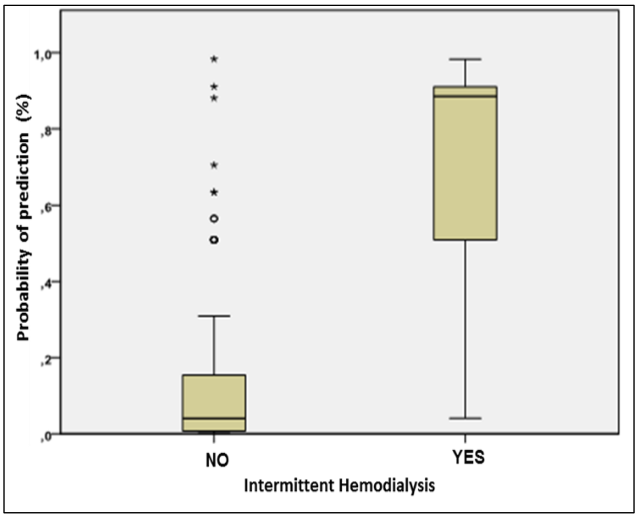


Figure 2: Propensity score before matching.

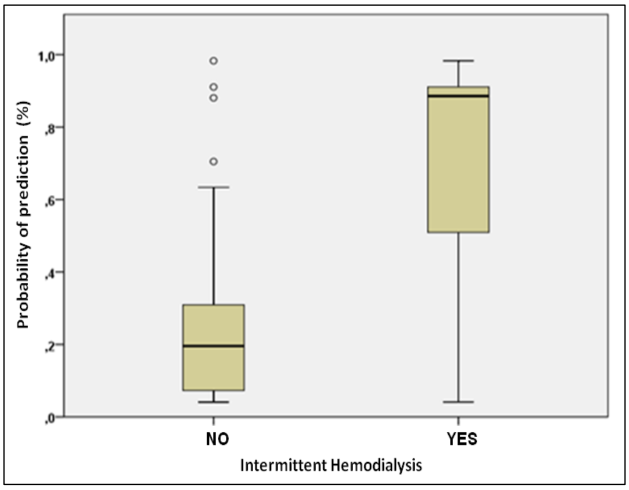


Figure 3: Propensity score after matching.

Among the 116 patients, 80.3% had one or many pre-existing diseases: CRI in 44% of the cases (n=51), acute arterial hypertension in 31% of the cases (n=36), diabetes mellitus in 29.3% of the cases (n = 34), systemic disease in 12.9% of the cases (n=15), ischemic cardiomyopathy in 6.9% of the cases (n=8), and hepatic cirrhosis in 6.9% of the cases (n=8).

The causes of hospitalization in intensive care were predominantly infectious pathologies (septic shock: 24% (n=28) and acute sepsis: 33% (n=38)). The types of RF were acute in 56% of the cases, chronic in 33.6% of the cases and acute in patients with chronic kidney failure in 10.3% of the cases. The comparison between the two groups IHD+ and IHD- is represented in Table 1.

In the IHD+ group, 112 sessions of dialysis were carried out. The number of IHD sessions carried out per patient was of an average of 1.8±1.4 (extremes: 1-8). Thirty two patients (55.2%) have benefitted from one IHD session, 14 patients (24.1%) from two sessions, 4 patients (6.9%) from three sessions and 8 patients (13.8%) from four or more sessions. The main indications of the first IHD session were hyperkalemia for 44.8% of the patients (n=26) and acute pulmonary edema for 32.8% of the patients (n=19). Regarding the overall carried out sessions, these proportions were respectively 32.1% (n=36) and 28.6% (n=32). The acute metabolic acidosis (HCO3- <10mmol/L) before IHD was the indication for eight patients (7.1%).

Table 1: Comparison of groups IHD + and IHD - (N=116).

Variables	IHD + n = 58 mean (SD) or %	IHD- n = 58 mean (SD) or %	p
Age, years	45 (19)	52 (16)	0.03
Chronic renal insufficiency	70.7	13	0.001
Cardiopathy	1.7	13	NS
APACHE 2	25 (7)	23 (6)	NS
LODS	7.3 (2.5)	6.4 (1.9)	0.047
Glasgow Coma score	11.8 (3.5)	12.4 (2.6)	NS
Kaliemia mmol/l	5.1 (1.2)	4.4 (0.9)	0.001
Uremia g/l	2 (1.1)	1.7 (0.8)	NS
Serum creatinine mg/l	88.3 (48.3)	49.9 (26.3)	0.0001
Haemoglobin g/dl	9.7 (2.8)	10.6 (3.1)	NS
Mechanical ventilation	67.2	48.3	0.039
Vasopressors	58.6	37.9	0.026
Nosocomial infection	27.6	24	NS
Length of stay days	7.4 (5.9)	5.9 (5.6)	0.028
Mortality	58.6	58.6	NS

IHD +: Group with intermittent hemodialysis; IHD -: Group without hemodialysis, APACHE 2: Acute Physiology and Chronic Health Evaluation; LODS: Logistic Organ Dysfunction System

The period between the indication and the start of the IHD session was an average of 8.2±10.2h [extremes: 1-48h; median: 5.5h; quartile: 2-8h]. The reasons for performing IHD sessions beyond 2h after its indication was: the absence of an available generator at the moment of indication (56%), the delay in inserting a catheter of dialysis (12%), the disagreement between the Nephrology and ICU teams about the indication to start IHD (8%), the lack of a portable ventilator for the intra-hospital transport (4%), the unavailability of an on-site intensive care specialist (4%), the delay of transport (4%), the absence of a nurse in the Hemodialysis unit (4%), the absence of an O_2 bottle for the transport (4%) and the extubation (4%).

The average duration of IHD sessions was 211±57min (extremes: 60-360min), the pump speed was 266±25ml/min (extremes: 121-300ml/min), the average conductivity was 141±3.9meq/l (extremes: 130-

150mEq/l), and the average temperature of dialysis fluid was 36.4±0.4°C (extremes: 35-37min). The used buffer was the bicarbonate (38±3.5mEq/l; extremes 17-43mEq/l) and for the calcium the used fluids were varying between 1.25mmol/l, 1.50mmol/l and 1.75mmol/l. The average quantity of ultrafiltration was 2136±1180ml (extremes: 0-4400ml).

During the 112 IHD, the analysis of SAP and DAP in pre, during and post IHD knew significant decreases during and after IHD (Table 2). However, the CR and the LODS increased significantly at the end of IHD: CR = 100±20b/min vs 105±24b/min (p = 0.03) and LODS = 7±2 vs 7.5±2.8 (p = 0.02).

The use of mechanical ventilation and vasopressors since admission to IHD+ group was respectively 67.2% and 58.6%. These values were 51.8% and 55.4% in pre-IHD; 52.7% and 59.8% during IHD; and 55.4 and 58% in post IHD (NS).

Table 2: Systolic and diastolic arterial pressures in pre, during and post IHD.

Variables	Pre IHD			During IHD		Post IHD	
	N	M±SD	extremes	M±ET	extremes	M±SD	extremes
SAP (mmHg)	112	143±30*†	85-260	115±36*	0-180	125.4±39†	0-220
DAP (mmHg)	112	74±17*	40-130	62±19*	0-110	67±27	0-250

M±SD: Mean±standard deviation; SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; *p<0.0001: p<0.001

The average duration of the patient's transport from the ICU to the hemodialysis unit was 15.8±18.7minutes [extremes: 5-120min; median: 10min; quartile: 10-15min]. After the dialysis session, the average duration of returning to the ICU was 16.6±16.9minutes [extremes: 5-80min; median: 10min; quartile: 10-15min].

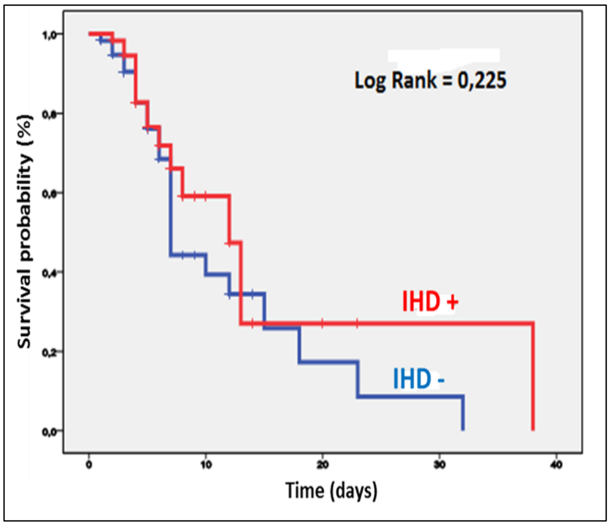
The occurrence of incidents during the transport was evaluated as 38 sessions. Nine incidents were noted (23.7%): out of order elevator (n = 3), disconnection of a thoracic drain (n = 2), falling with a head trauma (n = 1), removal of auto-pulsed adrenalin syringe (n = 1), depletion of the O_2 bottle (n = 1) and cardio-respiratory arrest (n = 1).

Table 3: Predictive factors for the use of IHD. Multivariate analysis.

Variables	RR (IC 95%)	P
Chronic renal insufficiency	2.69 (1.32-5.49)	0.006
Serum creatinine >50mg/l	3.54 (1.22-7.73)	0.002
Vasopressors	1.8 (1.02-3.18)	0.041

The predictive factors for the use to the off-site IHD of the univariate analysis are represented in Table 1. In the multivariate analysis, the patients who had more chances to benefit from off-site IHD were those who presented a CRI with serum creatinine >50mg/l and who necessitated the use of vasopressors (Table 3).

Regarding mortality in ICU, it was 58% (n=34/58) in each of the two groups (NS). This result is confirmed through the survival curves for IHD+ group and IHD- group (Figure 4).



(IHD +: group with intermittent hemodialysis; IHD-: group without hemodialysis)

Figure 4: Survival curves of the two groups.

DISCUSSION

In answer to our main objective, our study shows that there is a mortality statistically similar in the two groups. Regarding the secondary objective, the predictive factors of the resort to IHD off-site were the presence of a CRI, a serum creatinine >50mg/l and the use of vasopressors.

The incidence of RF in our study remains relatively low (9.3%) in comparison with the one described in the literature among critically ill patients and which varies according to the used definitions and the populations researched in the different studies: from 5 to 40%.[2,5-13]

According to the studies, RF requires an ERE technique in 20 to 70% of the cases.[7,14] All these studies are about the ERE performed within the ICU unlike our study in which the off-site IDH involved 28,7% of the patients. This value could have certainly been higher if performing ERE were not limited to the clinical instability of the patients who are difficult to be transported off-site, despite the fact that the severity of the patients' condition seems to be similar in both groups.

The comparison of the biological and clinical parameters of the two groups of patients involved in our study faces significant differences. Hence, RF was more acute in patients belonging to the IHD+ group, proven by uremia, serum creatinine, and kaliemia which were much higher than a much advanced RIFLE stage. This is probably explained by the fact that 72% of the patients in the IHD+ group were having CRI as opposed to 10% in the IHD- group. Unlike our work, the majority of studies dealing with dialysis in ICU exclude patients of CRI.[15-17] In Gaudry et al, 9.8% of the non-dialysis patients were having CRI as opposed to 12.1% in the dialysis group (p = 0.76).[14]

Hypertensions during the IHD constitute the most frequent complication.[18] The reported frequencies of the hypotensive episodes during the sessions varies according to the series between 20 and 52%.[4,19] In our study, the analysis of the variations in the arterial pressures of the IHD+ patients' group knows significant decreases which could be in relation to a bad tolerance of the extracorporeal circulation of the IHD circuit, to inadequate adjustments to the patient's condition often as a multiple organ dysfunction and/or to the hemodynamic instability of the patients.

The use of mechanical ventilation for critically ill patients necessitating an ERE varies between 37% and 88% and that to vasopressors between 25% to 82%.[4,14-16,20,21] These proportions constituted respectively 67.2% and 58.6% in our study and have not been significantly varied during and after dialysis in our patients. We observe as well that the actual number of the ventilated patients under vasopressors was statistically more important in the IHD+ group in comparison with the IHD- group.

Regarding the IHD indications, the issue of the initiation criteria of ERE on the patients admitted in ICU with an acute renal insufficiency remains very controversial.[22] Despite absence of specific research, the benefit of ERE in situations where the vital prognostic is involved seems reasonable, which explains the fact that many experts recommend resorting to it in the following situations : hyperkaliemia, metabolic acidosis, acute pulmonary edema refractory to medical treatment and lysis syndrome.[23] Vaara et al find out that an ERE which is deemed as preemptive, i.e. starting before the criteria of initiating ERE which are considered "classic", allows for a significant decrease of mortality by 48.5% (classic criteria group) to 29.5% (preemptive ERE group).[24] A matching of the preemptive ERE group patients with patients who have not benefitted from it find even a decrease in mortality in day 90 by 49.3% (no ERE group) to 26.9% (preemptive ERE group). The advanced explanation is that the ERE preemptive group benefitted from a better metabolic and hydric control. Ponce et al. widen their indications beyond the "classic" criteria by initiating IHD on 39% of the 231 involved patients including oliguria (diuresis at admission = 477±109ml/day) and in 23% of the cases including hyperuremia patients (uremia at admission at = 0.88±0.319g/l).[25] Gaudry et al indicate IHD even in front of the complications of an acute uremia, notably the encephalopathy, pericarditis, and the hemorrhagic syndrome.[14] In our study, the main indication of IHD was hyperkalemia in 44.8% of patients followed by acute pulmonary edema in 32.8% of patients and acidosis cases in 22.4% of patients. The classical character of our criteria for the IHD initiation testifies the difficulty of doing otherwise, given the alienation from the site where dialysis takes place and the unavailability of generators all the time due to the increased demand to the only Hemodialysis unit available in the hospital. Maoujoud et al who have a similar context to ours regarding the difference in performing IHD in ICU have indicated dialysis in 48.5% of the cases following an hyperkalemia, in 33.3% of the cases for an acute pulmonary edema and in 19% of the cases as a result of an acute acidosis.[4]

The setups performed for one IHD session can influence the hemodynamic tolerance and the prognostic of the patient. If the literature's data are numerous under the framework of chronic hemodialysis, they are much rare on intensive care patients. The adaptation of the dialysis prescriptions and setups for unstable patients would allow a decrease of the incidence of perdialytic hypotension from 20 to 30% thanks to optimized prescriptions.[26] Furthermore, except some specific setups, it seems that the prolongation of IHD sessions or the performance of shorter daily sessions would contribute in diminishing the occurrence of incidents.[27-29]

The offsite performance of IHD has exposed the patients of our study to complications of intra hospital transport (IHT). Every displacement was a real challenge for the medical team whose main objective was to ensure the continuation of care and the full-time surveillance outside ICU. The frequency of the complications linked to IHT varies from 6% to 45%.[30,31] This elevated risk is linked to the field and to the complexity of conditioning and to the extra renal purification techniques, particularly the ventilator ones.[30] It is not excluded that the morbi-mortality part attributable to transport be non-negligible, but given the weak actual number of evaluated transports, it is difficult to answer this particular point.

The finding of our study is that CRI patients and those who are hemodynamically unstable are those who were able to benefit from offsite IHD. These results could, on the one hand, be correlated to the fact that almost 71% of the IHD+ patients had a CRI, among whom 37.9% were already under extra renal purification treatment, and on the other hand to the severity of the admission of the observed organ system failures: respiratory, metabolic and hemodynamic. The absence of similar studies in the literature limits the discussion regarding the predictive factors of the resort to IHD.

Despite the performed developments to ameliorate the care for RF in ICU, mortality linked to dialysis remains very high, nearing 60%.[16] In fact, ERE is an independent risk factor of mortality in intensive care. This result is not yielded by our study because the resort to IHD and offsite enhancement does not seem to influence the improvement of patients. This could be explained by the number of patients included in the study (beta error), also by the difference in the severity of the organ failures between the two groups and perhaps by the dependence of dialysis indication on organizational parameters and techniques.

To our knowledge, our study is the only study conducted about offsite IHD although this should be a common practice in many developing countries. It therefore brings some clarifications about this practice, which we deem as precious. Moreover, the use of the propensity score has allowed us to estimate the effect of the IHD treatment while taking into consideration the unbalanced initial characteristics and to ultimately form two groups that are more comparable.

The big limitation of our study is the inclusion of CRI patients making our population heterogeneous. In fact, a quarter of all the included patients was having CRI, and this rate has reached 70.7% in the IHD+ group after matching. This has certainly influenced our results. But, beyond the existence of this underlying comorbidity, what we were more concerned about was to analyze the practice of IHD on intensive care subject who were distant from their natural site. The second limit could be the size of our sample which is probably limited in number although the number of the performed IHD sessions is not negligible. Third, the proportion and the profile of the IHD-group of patients who should have benefitted from ERE but who had not could not be analyzed nor the reasons behind that.

CONCLUSION

In conclusion, patients have benefitted from offsite IHD in our study and we have not found any improvements in survival. The probability of the use of hemodialysis was high under the presence of CRI and reliance upon vasopressors.

Unfortunately, we cannot omit the fact that during IHT, the intensive care patient is subject to a less secure environment, which enhances his/her vulnerability. Our work highlights a delay in initiating dialysis and incidents linked to transport. Despite being certainly practiced in the developing countries outside ICU's, data in the literature are inexistent in this domain.

Finally, in order to optimize the care in the area of RF which is a frequent entity in the intensive care environment, the availability of extra renal purification local facilities proves to be necessary. This is in addition to the training of the medical and paramedical team in order to be able to adapt to every situation while maintaining security and efficiency.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Simour A, Dendane T, Abidi K, Belayachi J, Madani N, Iraqi A, et al. Evaluation of intermittent hemodialysis conducted off-site on patients with renal insufficiency admitted in the intensive care unit of a developing country. Int J Res Med Sci 2019;7:410-6.