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Thrombosis Research 132 (2013) 671–675

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Renal failure as a risk factor for venous thromboembolism in critically Ill patients: A cohort study

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ARTICLE INFO

Article history:
Received 16 July 2013
Received in revised form 16 September 2013
Accepted 24 September 2013
Available online 29 September 2013

Keywords:
Critically ill
Acute kidney injury
Chronic kidney failure
Venous thromboembolism

ABSTRACT

Rationale: The relationship between kidney function and venous thromboembolism (VTE) in critically ill patients is not well studied. The main objective of this study was to evaluate this relationship in patients admitted to a medical-surgical intensive care unit (ICU).
Methods: This was a retrospective study of 798 patients admitted to a tertiary-care ICU and prospectively followed for the development of clinically suspected and radiologically diagnosed deep venous thrombosis or pulmonary embolism. Patients were divided based on admission creatinine and dialysis history into five groups: normal kidney function, RIFLE classes R, I and F (combined = acute kidney injury [AKI]) and endstage renal disease (ESRD). We compared VTE prophylaxis practices and VTE incidence in these groups and evaluated renal failure as a VTE risk factor using multivariate Cox regression analysis.
Results: Of the 798 patients, 27.2% had AKI and 10.1% had ESRD. Unfractionated heparin use was similar in the five groups but enoxaparin use was less frequent in AKI (13.4%) and ESRD (3.8%) patients compared with patients with normal kidney function (39.0%). VTE occurred in 7.6% of patients with normal renal function, 7.8% AKI patients and 2.5% ESRD patients ($p = 0.22$). The adjusted hazard ratios for VTE compared to patients with normal kidney function were 0.35 (95% confidence interval [CI], 0.08-1.47) for RIFLE class R, 1.19 (95% CI, 0.83-1.70) for RIFLE class I, 0.82 (95% CI, 0.59-1.14) for RIFLE class F and 0.71 (95% CI, 0.49-1.02, $p = 0.06$) for ESRD.
Conclusions: Neither AKI nor ESRD was an independent risk factors for critically ill patients.
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Introduction

Critically ill patients are at increased risk for venous thromboembolism (VTE) [1,2] during their stay in the intensive care unit (ICU). Additionally, many of them either have chronic kidney disease (CKD) or develop acute kidney injury (AKI) [3]. Studies that evaluated the relationship between the kidney function and VTE are scarce. A community-based population study of non-dialysis-dependent patients found that after adjustment for age, gender, race and center, the relative risk for VTE was 1.28 (95% confidence interval [CI], 1.02-1.59) for those with mildly decreased kidney function and 2.09 (95% CI, 1.47-2.96) for those with stage 3/4 CKD, compared with people with normal kidney function [4]. A large 1996 US cohort study found that end-stage kidney disease (ESRD) was associated with 2.1 increased risk of pulmonary embolism (PE) compared to the general population [5]. Whether kidney function is a risk factor for VTE in critically ill patient is not well studied. A prospective cohort study evaluated the incidence of proximal lower extremity deep venous thrombosis (DVT) in 261 critically ill patients using periodic ultrasonographic screening and found that ESRD, but not AKI, was associated with increased DVT risk (hazard ratio [HR], 3.7; 95% CI,1.2-11.1) [2]. PE was not evaluated in this study [2].

Because of the paucity of evidence, we evaluated the relationship between VTE and both AKI and ESRD using data from a prospective cohort of medical and surgical ICU patients followed for the development of VTE. Additionally, we reported the incidence of VTE and described VTE prophylaxis practices according to kidney function on ICU admission.

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http://dx.doi.org/10.1016/j.thromres.2013.09.036

Materials and Methods

Patients and Setting

This was a post-hoc analysis of data from a prospective observational cohort study performed to determine the incidence, predictors and outcomes of VTE in critically ill patients [6]. The cohort was comprised of 798 consecutive adult patients (age ≥ 18 years) admitted to the ICU of King Abdulaziz Medical City between July 2006 and January 2008 and expected to stay in the ICU for more than 48 hours. The ICU was a closed medical and surgical ICU staffed by board-certified critical care physicians 24 hours per day, 7 days per week. The hospital was a 900-bed tertiary-care academic center in Riyadh, Saudi Arabia, had been accredited by Joint Commission International and had its own thromboprophylaxis guidelines. These patients were followed for the development of VTE (both DVT and PE) during ICU stay and up to 5 days after ICU discharge to the wards. DVT was diagnosed by Doppler compression ultrasound of extremities and PE by spiral computerized tomography of the chest or lung ventilation-perfusion scans. These tests were ordered at the discretion of the treating intensivist when VTE was clinically suspected. Patients were excluded if they had any of the following: Do-Not-Resuscitate order or brain death within 24 hours of admission, chronic anticoagulation with warfarin or heparin, admission to the ICU with acute PE or DVT diagnosed on admission or within first 24 hours of ICU admission. The original study was approved by the Institutional Review Board of King Abdulaziz Medical City-Riyadh.

Data Collection

The following baseline information were noted: patients' demographics including age, gender, body mass index, Acute Physiology and Chronic Health Evaluation (APACHE) II [7], admitting diagnostic category (respiratory, cardiovascular, neurological, other medical illness, trauma and postoperative), admission Glasgow Coma Scale (GCS) score, admission creatinine, bilirubin, lactate, platelet count and International Normalized Ratio (INR) and pre-defined VTE risk factors. In addition, the following data were collected on a daily basis for a period of 30 days or until ICU discharge to the wards or mortality, whichever earlier: use of pharmacologic thromboprophylaxis (unfractionated heparin or low molecular weight heparin [enoxaparin]), the use of mechanical thromboprophylaxis (graduated compression stockings and intermittent pneumatic compression device), number and location of central lines, and requirement for mechanical ventilation and renal replacement therapy. The primary outcome of this study was the incidence of VTE among critically ill patients according to kidney function. The secondary outcomes were VTE prophylaxis practices, ICU and hospital mortality, ICU and hospital length of stay (LOS), and duration of mechanical ventilation.

Categorization of Patients According to Renal Function

For the purpose of this study, patients who had chronic renal failure requiring dialysis before ICU admission were classified as ESRD. The other patients were divided into four groups according to the RIFLE classification of kidney function. For this classification, baseline creatinine was estimated using back-calculation with the Modification of Diet in Renal Disease (MDRD) formula as per the following equation [8]: estimated baseline creatinine = $(GFR/[186 \times age^{-0.203} \times Sex \times Race])^{-0.867}$ (mg/dL), where the glomerular filtration rate (GFR) is the baseline GFR assumed to be 75 ml/min [9]; Sex = 1 if male and 0.742 if female; Race = 1.21 if black, otherwise Race = 1; and Age is in years. Patients were classified as having normal kidney function if admission creatinine was ≤1.5x estimated baseline creatinine. The other patients had AKI and were divided into RIFLE class R (Risk) if admission creatinine was >1.5x estimated creatinine but <2x, class I (Injury) if admission creatinine was ≥2x estimated baseline creatinine but <3x and class F (Failure) if admission creatinine ≥3x estimated baseline creatinine [9,10].

Statistical Analysis

Statistical analysis was performed using the Statistical Analysis Software (SAS, Release 8, SAS Institute Inc., Cary, NC, 1999, USA). Baseline characteristics and clinically relevant interventions of patients, as well as outcomes, in the five groups were summarized by providing the numbers and percentages for categorical variables and mean and standard deviation for continuous variables. The Chi-square test was used to assess differences among groups for categorical variables and ANOVA test for continuous variables. To evaluate if kidney function was a risk factor for VTE, proportional Cox regression analysis was performed with patients with normal renal function on ICU admission being the reference group. Baseline demographic and clinical characteristics that were significantly different among the patients with the different kidney function groups, VTE risk factors and thromboprophylaxis practices were entered in the model. These variables were age, gender, body mass index, admission APACHE II score, admission diagnostic categories, platelets count, INR, mechanical ventilation, bedridden status before admission, admission related to femur/hip fracture or surgery, presence and location of central venous catheter, use of oral contraceptives, history of venous insufficiency, presence of sepsis on admission, spinal cord injury, history of malignancy, history of congestive heart failure, history of recent surgery, history of previous PE or DVT, previous stroke, use of mechanical prophylaxis, use of unfractionated heparin and low molecular weight heparin for thromboprophylaxis. The results are presented as adjusted HRs with 95% CI. P-values < 0.05 were considered significant for all analyses.

Results

Baseline Characteristics and VTE Risk Factors

Of the 798 patients in the cohort, 37.3% had abnormal renal function on ICU admission, with 217 (27.2%) patients having AKI (8.0% RIFLE class R, 9.2% RIFLE class I and 10.0% RIFLE class F) and 10.1% having ESRD. Table 1 describes the characteristics of patients according to RIFLE classification. Patients with renal failure were older and had higher APACHE II score. Patients with renal failure were more likely to be admitted because of cardiovascular disease and sepsis and were less likely to be admitted postoperatively. Most patients required mechanical ventilation with no significant difference among the different groups. Renal replacement therapy was required during ICU stay for 4.0% of patients who had normal kidney function on admission, compared with 41.5% of with AKI patients (RIFLE classes R, I and F). Additionally, there were significant imbalances in other VTE risk factors among the three patient groups as described in Table 1.

Practices of VTE Prophylaxis

Table 2 describes thromboprophylaxis practices according to kidney function on ICU admission. The use of unfractionated heparin was similar in the five groups. Patients with renal failure received enoxaparin less frequently (13.4% of AKI patients and 3.8% of ESRD patients) compared with patients with normal kidney function (39.0%). Recent surgery, intracranial hemorrhage and other bleeding risks were the most common reasons cited for not administering pharmacologic prophylaxis. Graduated compression stockings were applied for similar proportions of patients in the different kidney function groups. However, there were more differences in the rate of application of intermittent pneumatic compression devices. Moreover, the percentage of patients

Table 1
Baseline characteristics and venous thromboembolism risk factors of patients in the cohort categorized according to renal function on admission to the intensive care unit.

	All patients N = 798	Normal kidney function N = 500	RIFLE class R N = 64	RIFLE class I N = 73	RIFLE class F N = 80	ESRD N = 81	P-value
Age (years), mean ± SD	50.2 ± 21.2	42.9 ± 20.9	60.5 ± 18.4	66.0 ± 14.0	61.8 ± 15.0	61.3 ± 13.1	<0.0001
Female gender, N (%)	263 (33.0)	125 (25.0)	32 (50.0)	34 (46.6)	38 (47.5)	34 (42.0)	<0.0001
Body mass index (Kg/m^2), mean ± SD	28.5 ± 10.2	27.1 ± 10.2	29.8 ± 8.7	31.7 ± 13.4	32.0 ± 9.2	28.8 ± 7.0	<0.0001
Admission GCS score, mean ± SD	8.6 ± 4.1	8.3 ± 4.0	8.3 ± 3.7	8.8 ± 4.2	9.0 ± 4.6	10.0 ± 4.2	0.03
APACHE II, mean ± SD	24.0 ± 9.0	20.2 ± 7.1	27.4 ± 8.3	30.9 ± 8.6	32.6 ± 8.0	30.0 ± 7.7	<0.0001
Admitting Diagnostic Category, N (%)							<0.0001
Respiratory	169 (21.2)	97 (19.4)	14 (21.9)	15 (20.6)	26 (32.5)	17 (21.0)	
Cardiovascular	246 (30.8)	95 (19.0)	26 (40.6)	39 (53.4)	37 (46.2)	49 (60.5)	
Neurological	57 (7.1)	36 (7.20)	7 (10.9)	5 (6.8)	5 (6.2)	4 (4.9)	
Other medical illness	36 (4.5)	12 (2.40)	9 (14.06)	3 (4.1)	79 (8.75)	5 (6.2)	
Non-operative Trauma	123 (15.4)	121 (24.2)	1 (1.6)	1 (1.4)	0 (0)	0 (0)	
Post-operative	167 (20.9)	139 (27.8)	7 (10.9)	10 (13.7)	5 (6.2)	6 (7.4)	
Trauma (nonoperative and postoperative), N (%)	226 (28.3)	214 (42.8)	4 (6.2)	3 (4.11)	2 (2.5)	3 (3.7)	<0.0001
Sepsis on admission, N (%)	321 (40.2)	131 (26.2)	41 (64.1)	49 (67.1)	47 (58.8)	53 (65.4)	<0.0001
Creatinine[**] (μmol/L), mean ± SD	159 ± 145	82 ± 26	146 ± 28	203 ± 39	393 ± 175	377 ± 174	<0.0001
Bilirubin[**] (μmol/L)), mean ± SD	58 ± 128	36 ± 75	67 ± 156	102 ± 186	84 ± 170	109 ± 188	<0.0001
Lactate (mmol/L), mean ± SD	3.3 ± 3.3	2.8 ± 2.4	3.9 ± 4.3	4.1 ± 3.6	4.5 ± 4.9	3.2 ± 3.7	<0.0001
Platelet count (10^9/L), mean ± SD	244 ± 156	259 ± 158	236 ± 151	215 ± 137	218 ± 160	212 ± 145	0.01
INR, mean ± SD	1.4 ± 0.7	1.3 ± 0.6	1.4 ± 0.5	1.7 ± 1.1	1.6 ± 0.8	1.6 ± 0.8	<0.0001
Bedridden for more 3 days before admission, N (%)	394 (49.4)	205 (41.0)	39 (60.9)	47 (64.4)	47 (58.8)	56 (69.1)	<0.0001
Congestive heart failure, N (%)	38 (4.8)	10 (2.0)	4 (6.2)	8 (11.0)	10 (12.5)	6 (7.4)	<0.0001
Active malignancy, N (%)	94 (11.8)	70 (14.0)	5 (7.8)	9 (12.3)	9 (11.2)	1 (1.2)	0.02
History of stroke, N (%)	106 (13.3)	49 (9.8)	14 (21.9)	14 (19.2)	14 (17.5)	15 (18.5)	0.004
Recent surgery, N (%)	243 (30.4)	193 (38.6)	9 (14.1)	18 (24.7)	13 (16.2)	10 (12.4)	<0.0001
Previous PE or DVT, N (%)	12 (1.5)	3 (0.6)	1 (1.6)	2 (2.7)	4 (5.0)	2 (2.5)	0.03
Femur/pelvic fracture or hip/knee replacement, N (%)	52 (6.5)	47 (9.4)	0 (0)	3 (4.1)	2 (1.2)	1 (1.2)	0.001
Spinal cord injury, N (%)	20 (2.5)	18 (3.6)	1 (1.6)	0 (0)	0 (0)	1 (1.2)	0.13
Central venous catheter[*], N (%)	595 (74.6)	356 (71.2)	49 (76.6)	58 (79.4)	66 (82.5)	66 (81.5)	0.07
Central venous catheter location, N (%)							
Femoral vein	342 (42.9)	172 (34.4)	26 (40.6)	36 (49.3)	57 (71.2)	51 (63.0)	<0.0001
Subclavian or internal jugular vein	525 (65.8)	315 (63.0)	46 (71.9)	50 (68.5)	59 (73.8)	55 (67.9)	0.25
Mechanical ventilation, N (%)	687 (86.1)	437 (87.4)	59 (92.2)	59 (80.8)	67 (83.8)	65 (80.2)	0.13
Renal replacement therapy, N (%)	191 (23.9)	20 (4.0)	16 (25.0)	24 (32.9)	50 (62.5)	81 (100)	<0.0001

APACHE, Acute Physiology and Chronic Health Evaluation; DVT, deep venous thrombosis; ESRD, end-stage renal disease; GCS, Glasgow Coma Scale; PE, pulmonary embolism; SD, standard deviation.

[*] includes hemodialysis catheters.

[**] To convert creatinine to mg/dl divide by 88.4, bilirubin to mg/dL divide by 17.1, lactate to mg/dl divide by 0.111.

who did not receive any form of thromboprophylaxis was similar in the five groups.

Outcomes of Patients

Table 3 describes the outcomes of the patients in the cohort according to their kidney function on admission to the ICU. VTE occurred in 38 (7.6%) patients with normal renal function, 17 (7.8%) AKI patients and 2 (2.5%) ESRD patients (p = 0.22). The incident rates of VTE were 3.6 per 1000 patient-days for patients with normal kidney function, 1.4 per 1000 patient-days for patients with RIFLE class R (incidence rate ratio with normal kidney function being the reference, 0.37; 95%CI, 0.09-1.55), 6.6 per 1000 patient-days for patients for RIFLE class I (incidence rate ratio, 1.82; 95%CI, 0.91-3.65), 3.7 per 1000 patient-days for RIFLE class F (incidence rate ratio, 1.02; 95%CI, 0.40-2.59) and 1.6 per 1000 patient-days for ESRD patients (incidence rate ratio, 0.44; 95%CI, 0.10-1.80).

Fig. 1 describes VTE incidence according to renal replacement therapy while in the ICU for different kidney function groups. For AKI patients, those who needed renal replacement therapy had similar VTE incidence compared to those who did not have it (8.9% and 7.1 respectively, p = 0.63).

On Cox regression analysis, AKI (RIFLE classes R, I and F) was not associated with increased VTE risk compared to normal kidney function (adjusted HR, 0.85, 95% CI, 0.47-1.54). The adjusted HRs for the different RIFLE classes were: 0.35 (95% CI, 0.08-1.47) for RIFLE class R, 1.190 (95% CI, 0.83-1.70) for RIFLE class I and 0.82 (95% CI, 0.59-1.14) for RIFLE class F. ESRD was associated with adjusted HR of 0.71 (95% CI, 0.49-1.02, p = 0.06) compared to normal kidney function.

Discussion

In this study, we did not find significant differences in VTE incidence in patients with AKI, ESRD or normal kidney function. In addition, renal replacement therapy while in the ICU did not seem to alter VTE incidence. On multivariate analysis, neither ESRD nor any of the RIFLE classes of AKI was an independent risk factor for VTE in critically ill patients during ICU stay.

Critically ill patients are at increased risk of VTE because of the presence of multiple predisposing factors [1]. However, renal function has not been well investigated in relationship to VTE development during critical illness. Renal dysfunction includes a myriad of conditions, such as nephrotic syndrome, AKI and ESRD. From pathophysiology point of view, nephrotic syndrome is associated with a hypercoagulable state and increased VTE risk (relative risk of PE, 1.39 and of DVT, 1. 72 compared to those who did not have this syndrome) [11]. ESRD is associated with both tendencies for bleeding and for thrombosis [12]. On one hand, it predisposes for bleeding diathesis, mainly due to abnormalities of primary hemostasis, in particular, platelet dysfunction and impaired platelet-vessel wall interaction [13]. On the other hand, it is associated with pro-thrombotic state due to increased levels of von Willebrand Factor, hyperfibrinogenemia, increased thrombin formation and activation of coagulation during hemodialysis [13]. Some of these physiologic changes are expected to affect AKI patients, but they are not well studied in this population. In addition, patients requiring

Table 2
Practices of pharmacologic and mechanical thromboprophylaxis according to kidney function. Pharmacologic prophylaxis includes the use of unfractionated heparin and enoxaparin.

	Normal kidney function N = 500	RIFLE class R N = 64	RIFLE class I N = 73	RIFLE class F N = 80	ESRD N = 81	P-value
Pharmacologic prophylaxis*, N (%)						
Unfractionated heparin	300 (60.0)	45 (70.3)	49 (67.1)	51 (63.8)	56 (70.0)	0.23
Low molecular weight heparin	195 (39.0)	11 (17.2)	10 (13.7)	8 (10.0)	3 (3.8)	<0.0001
No pharmacologic prophylaxis during stay in the intensive care unit	77 (15.4)	13 (20.3)	21 (28.8)	25 (31.2)	23 (28.4)	<0.0001
Cited reasons for not using pharmacologic prophylaxis, N (%)**						
Recent surgery	116 (23.2)	3 (4.7)	9 (12.3)	4 (5.0)	6 (7.4)	<0.001
Intracranial hemorrhage	111 (22.2)	5 (7.8)	4 (5.5)	0 (0)	3 (3.7)	<0.001
Other bleeding risk	81 (16.2)	26 (40.6)	32 (43.8)	31 (38.8)	27 (33.3)	<0.001
Mechanical prophylaxis, N (%)						
Graduated compression stockings	136 (27.2)	14 (21.9)	14 (19.2)	17 (21.2)	16 (20.0)	0.33
Intermittent pneumatic compression devices	169 (33.0)	28 (43.8)	25 (34.2)	15 (18.8)	18 (22.5)	0.005
No mechanical prophylaxis during stay in the intensive care unit	228(45.6)	28 (43.8)	37 (50.7)	49 (61.2)	47 (58.8)	0.03
Cited reasons for not using mechanical prophylaxis*, N (%)						
Pharmacologic prophylaxis	213 (42.6)	27 (42.2)	31 (42.5)	36 (45)	32 (39.5)	0.97
Lower extremity fracture	20 (4.0)	1 (1.6)	0 (0)	0 (0)	0 (0)	0.04
No prophylaxis, N (%)	38 (7.6)	4 (6.3)	7 (9.6)	12 (15.0)	11 (13.6)	0.12

* The same patient may have received unfractionated and low molecular weight heparin at different times during stay.
** Each patient could have more than one reason.

renal replacement therapy for AKI or ESRD will be exposed to an additional VTE risk due to vascular access [14].

The hematologic changes associated with renal dysfunction may affect physicians' decision to use VTE prophylaxis and/or choice of prophylaxis modality. This is supported by one study in which severe renal failure with glomerular filtration rate < 30 mL/min/m^2 was associated with increased risk of major bleeding and clinically relevant non-major bleeding combined (OR, 2.14; 95% CI, 1.44-3.20) on multivariate analysis [15]. A recent multinational cross-sectional study found that acute renal failure was associated with less use of thromboprophylaxis (aOR = 0.23, $p < 0.05$) [16]. However, another study that evaluated patients who had DVT found that thromboprophylaxis rates prior to DVT were similarly low in CKD and non-CKD patients (44.2% vs. 38.0%, $p = 0.06$) [17]. In our study the use of unfractionated heparin was similar in all groups regardless of kidney function. As expected, we found that low molecular weight heparin, enoxaparin, was less used in the renal failure groups, especially in ESRD patients. Renal failure is associated with decreased clearance of enoxaparin compared to normal renal function [18,19], which predisposes for acute bleeding. This has led the American College of Chest Physicians to recommend to avoid such an anticoagulant in the presence of renal impairment, to use a lower dose, or to monitor its anticoagulant effect [20]. However, this is not a class effect, as evidence suggests that dalteparin is not associated with increased bleeding risk due to bioaccumulation [21].

We found that the VTE incidence was not statistically different in the different kidney function groups. Patients with RIFLE class I had the highest VTE incidence (13.7%) and incidence rate (6.6 per 1000 patient-days) and ESRD patients to have the lowest incidence (2.5%). The risk of VTE in ICU patients with severe renal insufficiency receiving subcutaneous dalteparin was examined in a multicenter prospective cohort study. The study included 156 patients with a mean creatinine clearance of 18.9 ± 6.5 ml/min who underwent bilateral compression lower-limb venous ultrasound within 48 hours of study enrolment and twice weekly thereafter [22]. VTE was diagnosed in 15 (9.6%) patients within 48 hours of ICU admission and in 5.1% during ICU stay [22]. This study differs from our study as all patients were receiving dalteparin, while our study reflects a real-life practice with patients receiving different prophylactic regimens. Additionally, this study utilized screening ultrasounds, a strategy that is more sensitive in detecting DVTs than our approach, which was based on clinical suspicion. Nevertheless, the results of the two studies confirm that the risk of VTE in patients with renal insufficiency is considerable even with using thromboprophylaxis. Of note is that in our study AKI patients had higher INR and lower platelets compared to patients with normal kidney function, suggesting the presence of disseminated intravascular coagulation, and more central catheters in femoral vein than patients with normal kidney function. These factors may contribute to increased VTE risk. However, when controlling for imbalances in baseline characteristics and VTE risk factors, neither AKI nor ESRD was independently associated with VTE in ICU patients. These findings contrasted the findings of two studies that suggested that ESRD was a VTE risk factor [2,5]. One study was a large population-based cohort which found that ESRD was associated with 2.1 increased PE risk compared to the general population [5]. The other one was a prospective cohort of critically ill medical surgical patients which showed that ESRD was associated with increased DVT risk (HR, 3.7; 95% CI, 1.2-11.1) [2]. It also found that AKI was not a VTE risk factor [2], similar to what we found in our study. Additionally, a large retrospective study of 1,015,598 cancer patients from 133 U.S. medical centers between 1995 and 2003 found that these patients had a VTE rate of 4.1% and that renal disease as a co-

Table 3
Outcomes of patients in the cohort according to kidney function.

	Normal kidney function N = 500	RIFLE class R N = 64	RIFLE class I N = 73	RIFLE class F N = 80	ESRD N = 81	P-value
Venous thromboembolism, N (%)	38 (7.6)	2 (3.1)	10 (13.7)	5 (6.2)	2 (2.5)	0.056
PE and DVT, N (%)	2 (0.4)	1 (1.6)	1 (1.4)	0 (0)	1 (1.2)	0.59
DVT alone, N (%)	17 (3.4)	1 (1.6)	6 (8.2)	5 (6.2)	0 (0)	0.04
PE alone, N (%)	19 (3.8)	0 (0)	3 (4.1)	0 (0.0)	1 (1.2)	0.27
ICU Mortality, N (%)	68 (13.6)	21 (32.8)	25 (34.2)	30 (37.5)	27 (33.3)	<0.0001
Hospital Mortality, N (%)	125 (25.0)	33 (51.6)	38 (52.8)	49 (61.2)	47 (59.5)	<0.0001
ICU LOS (days), mean ± SD	16.7 ± 34.8	19.7 ± 25.3	17.5 ± 20.0	13.8 ± 17.4	12.3 ± 13.2	0.55
Hospital LOS (days), mean ± SD	75.8 ± 131.6	64.5 ± 75.9	56.8 ± 65.4	52.0 ± 65.6	81.0 ± 149.0	0.34
Mechanical ventilation duration (days), mean ± SD	9.9 ± 13.2	13.4 ± 13.61	10.1 ± 10.3	9.2 ± 10.2	6.3 ± 6.4	0.014

DVT, deep venous thrombosis; ESRD, endstage renal disease; ICU, intensive care unit; LOS, length of stay; PE, pulmonary embolism; SD, standard deviation.

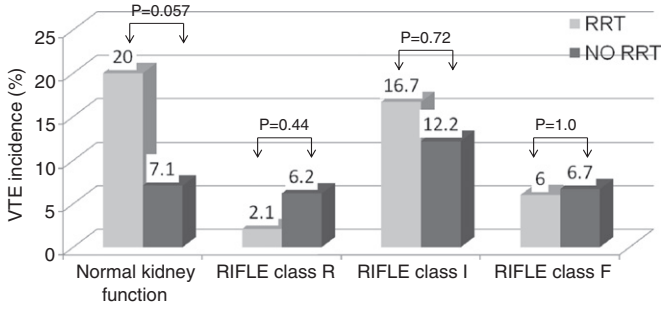

Fig. 1. Venous thromboembolism (VTE) incidence in patients with normal kidney function and acute kidney injury on admission to the intensive care unit according to the need for renal replacement therapy (RRT) during stay. RRT included conventional hemodialysis and continuous venovenous hemodialysis. There were 500 patients with normal kidney function on admission, 64 patients with RIFLE class R, 73 patients with RIFLE class I and 80 patients with RIFLE class F.

morbid condition was an independent predictor of VTE development (OR, 1.53; 95% CI,1.49-1.58) [23]. A community-based population study of non–dialysis-dependent patients found that after adjustment for age, gender, race, and center, the relative risk for VTE was 1.28 (95% CI, 1.02-1.59) for those with mildly decreased kidney function and 2.09 (95% CI, 1.47-2.96) for those with stage 3/4 CKD, compared with participants with normal kidney function [4]. Daneschvar and colleagues compared the profile of 268 CKD patients 4,307 patients with preserved kidney function who had DVT and found that CKD patients had upper extremity DVT more frequently than non-CKD patients (30.0% vs. 10.8%, $p < 0.0001$) [17]. Regarding PE, evaluation of the Nationwide Inpatient Sample found that patients with ESRD (527 per 100,000 persons) and CKD (204 per 100,000 persons) had higher have PE rates than those with normal kidney function (66 per 100,000 persons) [24]. Additionally, a prospective study of patients who had VTE showed that those with estimated glomerular filtration rate < 30 mL/min/1.73 m^2 were at increased risk of VTE recurrence (HR, 1.83; 95% CI, 1.03-3.25) [25].

The findings of this study should be interpreted in the light of its strengths and limitations. Among its strengths is the prospective data collection. Its limitations include the following: the study was conducted at one center; the sample size was small resulting in wide confidence interval in the results of regression analysis; we evaluated kidney function on ICU admission, however, we evaluated VTE incidence in patients who required renal replacement therapy during ICU stay; the investigation for DVT or PE was done only when clinically suspected by the treating ICU team, which may lead to the under-diagnosis of these conditions, however, this simulates day-to-day care in ICU as routine screening for DVT is not recommended for most critically ill patients [20].

In conclusion, we found that neither AKI nor ESRD was an independent risk factor for VTE in ICU patients. These patients should be treated as general ICU patients regarding practices of pharmacologic and mechanical VTE prophylaxis taking into consideration the bleeding risk and the guidelines for low molecular weight heparin use.

Conflict of Interest Statement

None.

Acknowledgements

Financial support: supported in part by Sanofi Aventis.

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