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Frequency and prognostic impact of acute kidney injury in patients with acute pulmonary embolism. Data from the RIETE registry☆

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ABSTRACT

Rationale: Acute kidney injury (AKI) is associated with a poor outcome. Although pulmonary embolism (PE) may promote AKI through renal congestion and/or hemodynamic instability, its frequency and influence on outcome in patients with acute PE have been poorly studied.
Methods: The frequency of AKI (defined according to the "Kidney Disease: Improving Global Outcomes" definition) at baseline and its influence on the 30-day mortality was evaluated in patients with acute PE from the RIETE (Registro Informatizado Enfermedad TromboEmbolica) registry. We used multivariate analysis to assess whether the presence of AKI influenced the risk for 30-day death.
Results: The study included 21,131 patients, of whom 6222 (29.5%) had AKI at baseline: 4385 patients (21%) in stage 1, 1385 (6.5%) in stage 2 and 452 (2%) in stage 3. The proportion of patients with high-risk PE in those with no AKI, AKI stage 1, AKI stage 2 or AKI stage 3 was: 2.8%, 5.3%, 8.8% and 12%, respectively ($p < 0.001$). After 30 days, 1236 patients (5.9%) died. Overall mortality was 4% in patients with no AKI, 8.4% in AKI stage 1, 14% in AKI stage 2 and 17% in AKI stage 3 (all $p < 0.001$). AKI was independently associated with an increased risk of all-cause death at 30 days (odds ratio = 1.25; 95%CI: 1.02–1.54).
Conclusions: One in every 3–4 patients with acute PE had AKI at baseline. The presence of AKI independently predicted 30-day mortality. This study suggests that AKI may deserve to be evaluated as a prognostic factor in patients with acute PE.

1. Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE) constitute manifestations of venous thromboembolism (VTE) which is a common disorder associated with significant morbidity and mortality. Pulmonary embolism (PE) is a frequent cause of cardiovascular death [1]. In patients with acute PE, the presence of arterial hypotension (defined as systolic blood pressure [SBP] levels below 90 mm Hg) is associated with an increased risk of death at day-30. Patients with mild hypotension (SBP levels between 90 and 100 mm Hg) or right ventricular failure also have a worse survival rate [2].

Acute Kidney Injury (AKI) is defined by an abrupt decrease in kidney function and is associated with adverse short-term and long-term outcomes even in the case of mild and reversible AKI [3–8]. AKI is a broad

Abbreviations: AKI, acute kidney injury; *CKD*, chronic kidney disease; CKD-EPI, Chronic Kidney Disease - Epidemiology Collaboration; COPD, Chronic obstructive pulmonary disease; CrCl, creatinine clearance; CVP, central venous pressure; *DOAC*, Direct oral anticoagulants; *DVT*, Deep vein thrombosis; *eGFR*, Estimated glomerular filtration rate; *ICD*, International Classification of Diseases; *KDIGO*, Kidney Disease: Improving Global Outcomes; *LMWH*, Low molecular weight heparin; *MDRD*, Modification of the Diet in Renal Disease; *PE*, pulmonary embolism; *RIETE*, Registro Informatizado de la Enfermedad TromboEmbolica; *SBP*, systolic blood pressure; *SCr*, serum creatinine; *s-PESI*, simplified pulmonary embolism severity index; *VKA*, Vitamin k antagonist; *VTE*, venous thromboembolism.

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clinical syndrome encompassing various etiologies, including specific kidney and extra-renal diseases. Renal macrocirculatory [9,10] or microcirculatory hypoperfusion [11,12] is believed to be a major mechanism promoting renal dysfunction. Both shock and renal congestion -increasing interstitial edema, interstitial pressure and ultimately decreasing renal perfusion– are frequent during the course of PE and might lead to AKI [13–17]. Prevalence and prognostic impact of reduced kidney function has been already evaluated in acute PE, but with various definitions which may mix acute and chronic renal dysfunction [18–21].

While these studies support the hypothesis of renal dysfunction associated with VTE, none were specifically designed to assess the prevalence of AKI or its impact on outcome. The Registro Informatizado de la Enfermedad TromboEmbolica (RIETE) registry is an international, multicenter, observational, prospective registry of consecutive patients with objectively confirmed symptomatic acute VTE. The rationale and methodology of RIETE has been already published elsewhere. The aim of the current study was to assess the influence of PE severity on the risk for AKI. Secondary objectives were to assess the incidence and prognostic impact of AKI in this setting.

2. Materials and methods

2.1. Data collection

The RIETE database is an ongoing, international (see acknowledgement for countries and centers), multicenter, prospective cohort of consecutive patients presenting with symptomatic VTE confirmed by objective tests initiated in March 2001 in Spain, and externalized in others countries since 2006 [22]. Participating physicians ensure that eligible patients are consecutively enrolled. Patients were excluded only if they were currently participating in a therapeutic clinical trial with a blinded medication and a planned follow-up <3 months. Participants were contacted for information if follow-up appointments are missed.

All patients provided informed consent to their participation in the Registry, according to the requirements of the ethics committee within each hospital. To study the outcomes of patients, RIETE did not impose experimental intervention and attending physicians determined management according to the clinical practice of each participating hospital. The participating centers completed the diagnostic evaluation and imaging as standard at their hospital.

The manuscript was prepared according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for the communication of observational studies [23].

The following information were collected: demographic data, symptoms on presentation, type of symptomatic VTE, types and results of diagnosis methods, risk factors for VTE, and therapeutic management for both the acute phase and the subsequent 3 months. During follow-up, any signs or symptoms suggesting VTE recurrences, bleeding complications, and any other adverse events were noted.

Data were recorded on to a computer-based case report form at each participating hospital and submitted to a centralized coordinating center through a secure website. To ensure the validity of the information entered into the database, one of the specially trained monitors visited each participating hospital and compared information in 25 to 50 randomly chosen patient records with the information entered into the RIETE database. For data quality assessment, monitors assessed 4100 random records from all participating hospitals that included 1,230,000 measurements. These data showed a 95% overall agreement between the registered information and patient records. RIETE also used electronic data monitoring to detect inconsistencies or errors and attempted to resolve discrepancies by contacting the local coordinators.

2.2. Patient entry criteria

Adult patients with acute PE confirmed by objective tests (pulmonary angiography, lung scintigraphy, or helical computed tomography scan) and enrolled in the RIETE database were included. Patients without serum creatinine (SCr) levels measured at admission were excluded.

PE severity was defined according to ESC guidelines [24]. Shock or systemic systolic blood pressure (SBP) levels < 90 mm Hg identified high-risk PE patients. Patients with s-PESI (simplified Pulmonary Embolism Severity Index) = 0 were classified at low risk and the remaining patients were considered to be at intermediate risk. Intermediate risk patients were subclassified according to the presence or absence of hemodynamic instability (SBP levels 90 to 100 mm Hg), because of its potential impact on renal function.

2.3. Acute kidney injury definition

AKI was defined according to the "Kidney Disease: Improving Global Outcomes" (KDIGO) definition [25]. Baseline serum creatinine levels was back-calculated from theoretical renal function according to MDRD equation and in accordance with international KDIGO guidelines (Supplemental Table S1) [25]. According to KDIGO guidelines, AKI severity was staged on the following criteria: stage 1: increase in SCr levels to ×1.5 times "baseline" Scr or ≥0.3 mg/dl (≥26.5 (μmol/l)) increase; stage 2: increase of >2.0–2.9 times "baseline" Scr; stage 3: increase of >3.0 times "baseline" Scr or more than or equal to ×4.0 mg/dl (×353.6 μmol/l).

AKI severity (using KDIGO criteria) was assessed according to PE severity, in patients with low-risk, intermediate risk and high-risk PE (using ESC/ERS guidelines).

2.4. Data analysis

The results are reported as median and interquartile range or number (%). Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables were compared using the nonparametric Wilcoxon signed-rank test, the Mann–Whitney *U* test, or the Friedman test.

Survival and occurrence of major bleeding were assessed using Kaplan-Meier curves and differences across pre-specified stratification group assessed using log-rank test.

We performed conditional logistic regression analyses to identify variables statistically and significantly associated with outcome and AKI, as measured by the estimated odds ratio (OR) and 95% confidence interval (95% CI). Variables yielding p values < 0.20 in the univariate analyses or considered clinically relevant were entered in a forward stepwise logistic regression model. Non–log-linear continuous variables were dichotomized. The covariates were entered in the model with critical entry and removal p values of 0.20 and 0.1, respectively. Multicollinearity and interactions were tested. The Hosmer–Lemeshow test was used to check the goodness of fit of the logistic regression. Correlation between continuous variables was performed using Spearman's correlation coefficient. All tests were two-sided, and p values < 0.05 were considered statistically significant. The statistical tests were performed using the IBM SPSS 13 software package (IBM, Armonk, NY, USA).

3. Results

3.1. Baseline characteristics of PE patients, according to AKI presence and severity

Among the 66,625 patients of the RIETE registry with VTE at inclusion, data regarding PE (with or without concomitant DVT) were evaluable for 21,131 patients who were included in this study (Supplemental Fig. S1). Table 1 reports the clinical characteristics. Overall, 6222 (29.5%) had some degree of AKI at baseline: 4385 patients (21%) had stage 1 AKI, 1385 (6.5%) AKI stage 2 and 452 (2%) had stage 3 AKI. Overall, patients with AKI were significantly older, and more likely to have comorbidities (chronic heart failure, atrial fibrillation, diabetes mellitus or anemia) than those with no AKI. The proportion of patients with AKI (and its severity) progressively increased according to the severity of PE. The proportion of patients with high-risk PE was: 2.8%, 5.3%, 8.8% and 12% in patients with no AKI, AKI stage 1, AKI stage 2 and AKI stage 3, respectively (p < 0,001). AKI patients were more likely to receive unfractionated heparin as initial therapy than patients without AKI.

Table 2 presents the baseline characteristics independently associated with AKI. The risk of AKI increased steadily with increasing severity of PE (Table 2). After adjustment for confounders, the odds ratio (OR) for AKI was of 1.65 (95%CI: 1.51–1.79) in patients with s-PESI ≥ 1 and SBP levels ≥ 100 mm Hg; 2.09 (95%CI: 1.79–2.44) in patients with s-PESI ≥ 1 and SBP levels between 90 and 100 mm Hg; and 3.86 (95% CI: 3.26–4.56) in patients with high-risk PE, compared to low risk patients (s-PESI 0). Other predictive factors were age over 65 years (OR = 4.84; 95% CI: 4.44–5.28), chronic heart failure (OR = 1.57; 95% CI: 1.42–1.73), atrial fibrillation (OR = 1.30; 95% CI: 1.18–1.44) and anemia (OR = 1.39; 95% CI: 1.29–1.48). In contrast, recent surgery, CT scan diagnosis, trauma, female gender and chronic lung disease were significantly associated with a lower risk of AKI (Table 2).

The Hosmer–Lemeshow test for predictive factors at AKI inclusion indicated goodness-of-fit χ^2 of 15.984 (p = 0.043), and an area under the curve of 0.748 [95% CI, 0.741–0.755]) (Supplemental Fig. S2).

3.2. Predictors of mortality and bleeding at 30 days

After 30 days, 1236 patients (5.85%) died. Overall mortality (Supplemental Table S2 and Fig. 1) increased in AKI patients: the highest severity of AKI was associated with the highest mortality rate (4% in no AKI, 8.4% in AKI stage 1, 14% in AKI stage 2, 17% in AKI stage 3, all p <

0.001). Similarly, AKI influenced other outcome variables, including the rate of fatal PE (0.78% in no AKI, 2.8% in AKI stage 1, 5.3% in AKI stage 2, 6.4% in AKI stage 3, all $p < 0.001$) or fatal bleeding (0.22% in no AKI, 0.55% in AKI stage 1, 0.94% in AKI stage 2, 1.1% in AKI stage 3, all $p < 0.01$). Finally, the rate of major bleeding (Supplemental Table S2 and Fig. 2) also increased with the presence and severity of AKI (1.5% in no AKI, 3% in AKI stage 1, 3.6% in AKI stage 2, 5.3% in AKI stage 3, $p < 0.001$).

After adjustment for confounders (Supplemental Table S3) including initial severity of PE, AKI was independently associated with an increased 30-day all-cause mortality (OR = 1.25; 95%CI: 1.02–1.54). Model fit for predictive death at day 30 was assessed by using Hosmer-Lemeshow goodness-of-fit test, which showed a χ^2 of 10.447 ($p = 0.235$) (Supplemental Fig. S3). The area under operating characteristic curve of 0.817 [95% CI, 0.801–0.834].

4. Discussion

To our knowledge, this is the first study evaluating the frequency and the prognostic impact of AKI (according to KDIGO classification) in patients with acute PE. In some degree, AKI was found at baseline in almost one in every three patients with PE, being more frequent and severe in patients with severe PE. Moreover, AKI was an independent risk factor for death at 30 days. Compared to general population, the prevalence of AKI is significant in PE patients. Most of previous studies focused on chronic kidney disease, while we assess the frequency of AKI according to the international guidelines.

There are very few data about the frequency and severity of AKI in patients with PE, despite these patients seem to be at high risk of AKI. In a recent retrospective cohort study of 7588 patients admitted for PE [26], AKI was found in 372 (4.9%). This lower frequency may be explained because AKI was defined according to the International Classification of Diseases, Ninth Revision (ICD-9), when all our patients were assessed for AKI according to KDIGO guidelines. On multivariate analysis, massive PE was found to be an independent risk factor for AKI (OR: 2.92; CI 95%: 2.28–3.76, $p < 0{,}001$). No assessment of AKI nor PE severity were provided [26]. In our study, the risk of AKI also increased with PE severity, with an up to 4-fold higher risk in the high-risk group (3.86 95%CI [3.26–4.56]). This result is consistent with our hypothesis, as the proportion of patients with severe AKI increased with the severity of PE.

In PE patients, venous congestion may occur because of an increased central venous pressure (CVP) secondary to ventricular failure

Table 1
Baseline characteristics of PE patients according to AKI presence and severity.

Patients, (n = 21.131)	No AKI (14,909)	AKI (6222)		
		AKI 1 (4385)	AKI 2 (1385)	AKI 3 (452)
Clinical characteristics				
Female gender	7703 (52%)	2151 (49%)†	894 (65%)‡	265 (59%)†
Age (mean years ± SD)	64 ± 17	77 ± 11‡	79 ± 9.7‡	76 ± 13‡
Age > 65 years	8214 (55%)	3796 (87%)‡	1274 (92%)‡	374 (83%)‡
Past history of VTE	2154 (14%)	677 (15%)	191 (14%)	58 (13%)
Underlying disorders				
Chronic heart failure	1160 (7.8%)	743 (17%)‡	298 (22%)‡	96 (21%)‡
Chronic lung disease	2218 (15%)	784 (18%)‡	229 (17%)	69 (15%)
Severity of the PE				
sPESI = 0	5524 (37%)	820 (19%)‡	200 (14%)‡	68 (15%)‡
sPESI ≥ 1 and SBP levels ≥ 100 mm Hg	8262 (55%)	3069 (70%)‡	958 (69%)‡	300 (66%)‡
sPESI ≥ 1 and SBP levels [90–100 mm Hg]	703 (4.7%)	262 (6.0%)‡	105 (7.6%)‡	30 (6.6%)
High-risk PE (SBP < 90 mm Hg)	420 (2.8%)	234 (5.3%)‡	122 (8.8%)‡	54 (12%)‡
Risk factors for AKI				
Exposures				
Sepsis	20 (0.13%)	7 (0.16%)	4 (0.29%)	7 (1.5%)‡
Trauma	611 (4.1%)	122 (2.8%)‡	44 (3.2%)	13 (2.9%)
Recent surgery	1842 (12%)	311 (7.1%)‡	83 (6.0%)‡	39 (8.6%)*
Arterial surgery	53 (0.36%)	17 (0.39%)	8 (0.58%)	1 (0.22%)
CT scan diagnosis (%)	13,338 (89%)	3516 (80%)‡	925 (67%)‡	254 (56%)‡
Susceptibilities				
Atrial fibrillation	1197 (8.0%)	660 (15%)‡	251 (18%)‡	77 (17%)‡
Liver cirrhosis	54 (0.36%)	7 (0.16%)*	4 (0.29%)	0
Chronic liver insufficiency	127 (0.85%)	25 (0.57%)	7 (0.51%)	6 (1.3%)
Diabetes mellitus	1978 (13%)	741 (17%)‡	233 (17%)‡	98 (22%)‡
Cancer	3502 (23%)	1045 (24%)	299 (22%)	105 (23%)
Anemia	4665 (31%)	1662 (38%)‡	656 (47%)‡	269 (60%)‡
Initial therapy				
LMWH	12,564 (84%)	3614 (82%)†	1134 (82%)*	345 (76%)‡
Mean LMWH doses/kg/day	180.2 ± 40	177 ± 41‡	168 ± 44‡	157 ± 51‡
Unfractionated heparin	1120 (7.5%)	496 (11%)‡	190 (14%)‡	78 (17%)‡
Fondaparinux	416 (2.8%)	65 (1.5%)‡	8 (0.58%)‡	6 (1.3%)
Thrombolytics	354 (2.4%)	159 (3.6%)‡	38 (2.7%)	16 (3.5%)
DOACs	331 (2.2%)	14 (0.32%)‡	2 (0.14%)‡	0‡
Long-term therapy				
Vitamin K antagonists	9245 (62%)	2900 (66%)‡	879 (63%)	254 (56%)*
LMWH	3740 (25%)	1032 (24%)*	329 (24%)	118 (26%)
Mean LMWH doses/kg/day	154.9 ± 44.8	147.3 ± 49.9‡	141.9 ± 49.1‡	133 ± 48.5‡
DOACs	1306 (8.8%)	125 (2.9%)‡	18 (1.3%)‡	4 (0.88%)‡

Values are expressed as median (IQR), count (percentage) or mean ± standard deviation.
AKI Acute kidney injury, *VTE* venous thromboembolism, *PE* pulmonary embolism, *sPESI* simplified pulmonary embolism severity index, *SBP* systolic blood pressure, *CT* computerized tomography, *LMWH* low molecular weight heparin, *DOACs* direct oral anticoagulants.
* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.001$.

Table 2
Multivariate analysis of predictive factors for AKI at inclusion.

	OR (95%CI)	p
Patients, N		
Clinical characteristics		
Female gender	0.81 (0.76–0.86)	<0.001
Age > 65 years	4.84 (4.44–5.28)	<0.001
Underlying disorders		
Chronic heart failure	1.57 (1.42–1.73)	<0.001
Chronic lung disease	0.77 (0.70–0.84)	<0.001
Severity of the PE		
sPESI = 0	Ref.	
sPESI ≥ 1 and SBP levels ≥ 100 mm Hg	1.65 (1.51–1.79)	<0.001
sPESI ≥ 1 and SBP levels [90–100 mm Hg]	2.09 (1.79–2.44)	<0.001
High-risk PE (SBP < 90 mm Hg)	3.86 (3.26–4.56)	<0.001
Risk factors for AKI		
Exposures		
Sepsis	1.80 (0.90–3.61)	0.098
Trauma	0.76 (0.63–0.91)	0.003
Recent surgery	0.54 (0.48–0.61)	<0.001
CT scan diagnosis	0.38 (0.35–0.41)	<0.001
Susceptibilities		
Atrial fibrillation	1.30 (1.18–1.44)	<0.001
Liver cirrhosis	0.43 (0.21–0.85)	0.015
Chronic liver insufficiency	0.74 (0.50–1.10)	0.133
Diabetes mellitus	1.02 (0.93–1.11)	0.733
Anemia	1.39 (1.29–1.48)	<0.001

AKI Acute kidney injury, *PE* pulmonary embolism, *sPESI* simplified pulmonary embolism severity index, *SBP* systolic blood pressure, *CT* computerized tomography.

[15,27–29]. Sudden pressure overload in the pulmonary circulation due to PE may lead to acute right ventricular dysfunction along with tricuspid regurgitation. As a consequence, central venous pressure rises and may lead to renal congestion then injury [30]. In patients with underlying cardiopulmonary disease (COPD), the hemodynamic impact will be manifested for lower levels of pulmonary vascular obstruction [31,32]. Additionally, cardiogenic shock and subsequent renal hypoperfusion may occur. Several other mechanisms may be involved in the development of AKI (contrast injection for CT scan, bleeding, recent surgery, cancer) [25]. Moreover, the development of AKI may also influence the outcome, as AKI is currently known to expose patients to heart and/or lung failure [33]. In a prospective cohort study including 220 consecutive patients with acute PE, 47% had a decreased glomerular filtration rate (GFR) [18]. Additionally, GFR decreased steadily with increasing degree of PE severity, suggesting a correlation between the importance of renal failure and the severity of PE [18]. Kostrubiec et al. also suggested that outcomes were poorer in patients with persistent renal dysfunction lasting >72 h [34]. Therefore, particularly in hemodynamically stable patients who are

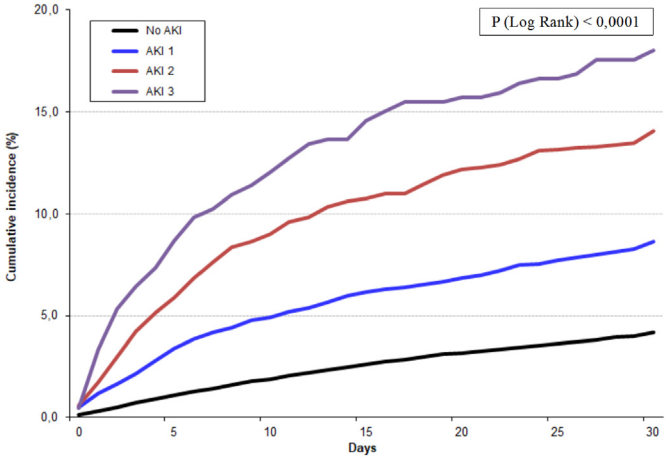

Fig. 1. Kaplan–Meier 30-day survival curves; Patients without AKI and patients with different stages of AKI according Kidney Disease: Improving Global Outcomes (KDIGO) classification.

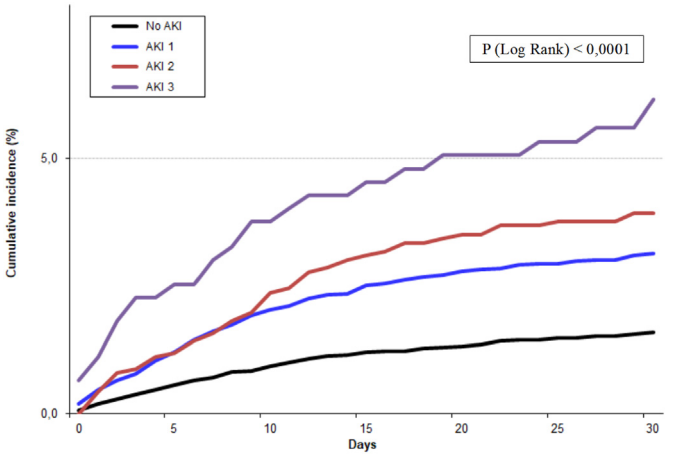

Fig. 2. Kaplan–Meier 30-day major bleeding; Patients without AKI and patients with different stages of AKI according Kidney Disease: Improving Global Outcomes (KDIGO) classification.

believed to be at low risk of death, markers of acute kidney injury might be additionally helpful in risk stratification, as signs of right ventricular dysfunction and worse outcome. These findings are new and possibly represent an important step forward in the interactions between the cardiopulmonary and renal systems during PE.

Similarly, the prognostic impact of AKI in this specific population has been poorly studied [18,19]. An independent association between AKI and mortality has been constantly demonstrated in different subsets of diseases [7,35]. AKI has been associated with an increased short- and long-term all-cause morbi-mortality [3–8], both AKI severity [5,6,8] and duration [36] being associated with poorer short-term and long term outcome. Our study found similar results in this particular setting, with a steadily increased in mortality with AKI severity (8.4% in AKI stage1, 14% in AKI stage 2 and 17% in AKI stage 3) and an independent association with poor outcome. Applying the Bradford–Hill criteria to evaluate the causality relationship between pulmonary embolism and AKI, most of them are validated. Moreover, AKI severity appears to directly reflect PE severity. These results are consistent with the hypothesis that AKI staging helps to identify patients with pulmonary embolism and with a poor prognosis. AKI may become part of the PE severity evaluation. A new predicting score using AKI stage could be developed to accurately define PE severity. It requires more study to validate his clinical utilities. Hence, we observed that patients presented worsened renal function, justifying intensified vigilance, for they may then suffer from a significant increase all-cause mortalities.

Renal failure is associated with an increased risk of bleeding under anticoagulant therapy [37]. Most of these data are based from patients with chronic renal failure, and are usually explain by a modified pharmacology of anticoagulant therapy. Moreover, AKI have also been linked to an increase risk of bleeding, mainly in the field of gastro-intestinal hemorrhage from the upper gastrointestinal tract [38–41]. Beside pharmacological modification of anticoagulant therapy due to AKI, the increase risk of bleeding may also be related to a potential hemostasis dysfunction.

We acknowledge several limitations to our study. First, prehospitalisation SCr levels were not known. Missing serum creatinine levels prior to the index event is a recognized problem in AKI research. While estimate baseline kidney function cannot truly be estimated, estimation was made using the Modification of Diet in Renal Disease (MDRD) formula as validated in KDIGO [25]. Although widely used, estimated creatinine clearance formula are unreliable in setting of AKI [42], these formula requiring steady-state serum creatinine to be used. It can lead to underestimation of the baseline serum creatinine and can exaggerate the apparent serum creatinine rise and causing an overdiagnosis of AKI and/or an overcall of AKI stage [43,44]. This assumption has limited applicability to usual

clinical practice, where a substantial proportion of patients with AKI have pre-existing CKD [45,46]. The rate of misclassification is largely attributable to patients with CKD [43]. Depending on the surrogate selected, this misclassification can occur bidirectional misclassification of AKI incidence, severity, and prognosis – either underestimating or overestimating the disease incidence, which, in turn, impacts the staging and associated mortality of presumed AKI. As consequences, their used is discouraged by experts [47]. Despite these limitations our study suggests AKI as an independent factor of bad outcome for patients with PE. Moreover, urine output which have been repeatedly identified as important part of AKI classification in epidemiology studies, has not been included because of a lack of data.

Our results although informative may therefore not help in assessing rate of patients that may be ineligible to LWMH. Additional studies assessing measured creatinine clearance levels are needed to clarify the impact of our findings on treatment modalities.

Furthermore, the prevalence of CKD stages may have been slightly underestimated. CKD has been reported as a predisposing factor for AKI [48,49]. Based on The Longitudinal Investigation of Thromboembolism Etiology (LITE) study, CKD has been clearly associated with an increased risk of VTE, particularly patients with stage 3/4 CKD [50]. Then, not having the proportion of patients with chronic kidney disease is a limit of our work. The proportion of anemia at admission in our study (41.6% in the AKI group, vs 31% in the non-AKI group) can indirectly suggest that CKD was more frequent in the AKI group than in the non-AKI group.

The study included many patients with relevant comorbidities, such as diabetes mellitus, chronic heart failure, chronic lung disease, advanced age, sepsis…, which are well known to affect kidney function themselves. However, the patients were included in the most important registry of VTE, worldwide, which represent accurately the current epidemiology of PE patients.

5. Conclusion

The risk of AKI increases with PE severity. AKI occurs in about one in three patients with PE, and is associated with an increased risk of mortality. The possible role of AKI in the prognosis evaluation of PE, in association with current recommended scores (sPESI) deserves further dedicated study.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.04.083.

Declaration of Competing Interest

None.

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