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ORIGINAL ARTICLE

Outcomes of acute kidney injury depend on initial clinical features: a national French cohort study

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ABSTRACT

Background. Acute kidney injury (AKI) is a common condition that is associated with poor short- and long-term outcomes. The aim of this nationwide cohort study was to profile the long-term outcome of patients admitted for AKI in France.

Methods. Based on the comprehensive French hospital discharge database, all hospitalizations for an AKI episode were categorized in four groups according to the presence of at least one dialysis session [renal replacement therapy (RRT)] and according to the coding of AKI as the principal or associated diagnosis (PRINC_DIAG or ASS_DIAG).

Results. In this nationwide cohort of 989 974 patients (median age 77 years) hospitalized with AKI during the 2009–16 period, 422 739 (43%) patients died (235 572 during the first hospitalization) and 40 015 (4%) patients reached end-stage renal disease (ESRD) (5962 during first hospitalization) up to 31 December 2016. Patients without RRT and discharged from hospital had a cumulative incidence of ESRD that ranged from 5.3% (5.2–5.4) in the ASS_DIAG group to 28.7% (27.9–29.5) in the RRT-PRINC_DIAG group at 60 months. The cumulative incidence of death ranged from 31.0% (30.2–32.2) in the RRT-ASS_DIAG group to 45.5% (45.3–45.7) in the ASS_DIAG group. Initial clinical features were associated with outcome independent of comorbidities and age.

Conclusions. The death penalty of AKI is abysmal and AKI was an important predisposing factor to chronic ESRD. Our study strengthens the current recommendations for long-term follow-up of patients with AKI. The novelty of this study is to propose a clinical classification of AKI episodes that is easy to detect in administrative medical databases and that is strongly associated with immediate and long-term outcomes.

Keywords: acute kidney injury, cohort study, end-stage renal disease, medico-administrative database, survival

INTRODUCTION

Acute kidney injury (AKI) is a frequent condition, which is associated with poor outcomes [1–3] due to both high initial mortality and long-term risk of end-stage renal disease (ESRD) and death. Recent registry studies from the USA and Canada have linked AKI (including resolving AKI) with subsequent chronic kidney disease (CKD) and progression to ESRD [4–8]. Although European populations share many traits with those from North America, it is not known whether there is a similarly strong link between AKI and CKD on a larger scale. Measuring the real outcome of patients surviving AKI is the first step to facilitating appropriate referrals and informing organizations involved with long-term care goals [9].

The Kidney Disease: Improving Global Outcomes (KDIGO) initiative has provided a universal classification of AKI in three stages [10], based on rapid increase in serum creatinine and decrease in urine output. This approach is operational at the bedside and clinically sound: AKI staging improves both the diagnosis and prognosis stratification of AKI patients. At present, however, many countries do not cite KDIGO stages either in hospital discharge reports or in health insurance databases, making it difficult to make a granular estimation of the burden of AKI. On the other hand, medico-administrative databases provide social information and the clinical context in which AKI occurs, in particular, the analysis of comorbidities and associated organ failures. It is thus technically possible to sort patients with AKI as the main diagnosis from those with AKI diagnosed in a wider context. For example, a recent study in England, focusing on severe AKI requiring renal replacement therapy (RRT), found that in-hospital case fatality was higher when AKI was coded as a secondary (as opposed to primary) diagnosis [11].

The aim of this nationwide cohort study was to profile the long-term outcome of patients hospitalized for AKI in France,

depending on whether AKI was coded as primary or secondary diagnosis, and on the requirement (or not) for RRT.

MATERIALS AND METHODS

Population

All hospitalizations for an AKI episode between 2009 and 2016 were extracted from the comprehensive French hospital discharge database [Programme de Médicalisation des Systèmes d'Information (PMSI)], which makes anonymized data available for epidemiological studies and includes social, demographic and medical information about the diagnosis leading to admission, the underlying comorbidities and complications. AKI was defined either by a specific acute dialysis procedure (RRT) or, in accordance with the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD10), by its specific code in the PMSI. For each hospital stay, one principal diagnosis was coded and if necessary associated diagnoses. The principal diagnosis was the health problem for which the patient was admitted to the hospital. The associated diagnoses explained the increase of resources used during the hospital stay. Whenever the patient entered multiple units during his hospital stay, each unit coded as principal diagnosis the health problem that sent the patient to this unit. Therefore, AKI identified for the purpose of this study can be either a principal diagnosis or an associated diagnosis. Associated diagnoses are not listed hierarchically in the database. All hospitalizations were categorized into four groups (referred to as 'initial clinical features') as RRT-PRINC_DIAG, RRT-ASS_DIAG, PRINC_DIAG and ASS_DIAG according to the presence of at least one session of acute dialysis (RRT) and according to the coding of AKI as a principal diagnosis (PRINC_DIAG) or as the associated diagnosis (ASS_DIAG), as described above.

For each patient, the first hospitalization with AKI defined time zero. Patients with an anterior diagnosis of chronic ESRD in the database were excluded. To secure the exclusion of chronic ESRD patients from our analysis, we considered all information available in hospital discharges during the year 2008.

Data

Baseline information included age and gender, entry through the emergency unit, stay in an intensive care unit (ICU) and destination (home or home care facility), but not ethnicity (French laws prohibit recording of ethnicity in a database). Comorbidities were estimated using principal and associated diagnoses recorded during any hospitalization up to 1 year before the AKI episode (as given in the ICD, as above). Seven groups of former comorbidities were defined as diabetes, cardiovascular disease, cancer, dementia, pulmonary disease, hepatic disease and the presence of a former kidney or urinary system disease (ICD10 codes N0-N3). Hospital stays were grouped according to the final principal diagnosis retained at discharge (if multiple units) with differentiation according to the type as surgery or medical, or 'medical procedure' when it includes technical procedures like invasive radiological procedures.

Outcome

Incidences of in-hospital death and ESRD were analysed up to 31 December 2016.

Chronic ESRD was defined either by chronic RRT (requirement for chronic dialysis or renal transplantation) or by a specific diagnosis (principal diagnosis or associated diagnosis) during a hospital stay. All dialysis facilities are integrated in the national hospital medico-administrative database.

Deaths occurring during a hospital stay were identified—in France, around 58% of all deaths occur in a hospital. Information concerning death at home was not available. For each patient, the last hospitalization stay during the period (2009–16) was considered as the date of the most recent information. For outcome analyses, patients were censored at this date of latest available data, assuming that patients 'lost to follow-up' had the same risk of death as the others.

Statistical analysis

Baseline characteristics of the four groups of initial clinical features were expressed as frequencies and percentages in the overall population and according to the presence or not of previous CKD. They were compared using the chi-square test and logistic regression to adjust for age and gender.

The cumulative incidences of death and ESRD in each group were analysed with a subdistribution hazard (Fine and Gray) model to take into account the competing risks between those two outcomes. A subgroup analysis was done for patients who were alive and not on RRT at hospital discharge.

The effect of the initial clinical feature on death or ESRD was analysed with an adjusted cause-specific Cox proportional hazard regression censored at other outcomes. A sensitive analysis used a subdistribution model (Fine and Gray) in which persons experiencing the competing event are maintained in the risk set to account for the probability of their reaching the event of interest; but these results can only be applied to a population with similar rates of competing events [12]. All the models were adjusted for age, gender and comorbidities. Factors associated with outcomes according to the initial clinical feature were analysed with an adjusted cause-specific Cox proportional hazard regression censored at other outcome.

Results were reported, when appropriate, as subdistribution cumulative incidence rates or cause-specific hazard ratios (csHRs) with their 95% confidence intervals (CIs).

Statistical analyses were computed using SAS software, in particular the PHREG procedure and the %cuminc macro (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 989 974 AKI patients were identified between 1 January 2009 and 31 December 2016 in the French hospital medico-administrative database. Median age of the population was 77 years and 58% were male (Table 1). Around 91% of the patients came directly from home, 9% were transferred from another hospital, 56% entered the hospital via an emergency unit and only 49% went back home after the hospital stay. At least one comorbidity was recorded in the year preceding AKI in 50% of patients. Former cardiovascular disease and CKD

were diagnosed in 40% and 16% of patients, respectively. While hospital stays with no acute RRT were mainly classified as 'medical', 45% of the AKI as associated diagnosis + acute dialysis (RRT-ASS_DIAG) group were classified as 'surgical' and 55% of the AKI as principal diagnosis + acute dialysis (RRT-PRINC_DIAG) cohort were classified as 'medical intervention' (mainly due to the act of dialysis). As expected, 76% of hospital stays reporting AKI as principal diagnosis were classified in the group 'Diseases of the kidney and urinary tract'. Whenever AKI was an associated diagnosis, the hospital stay was classified as 'Diseases of the circulatory system' in 27% of cases and as 'Diseases of the respiratory system' in 13% (Table 1).

In-hospital death

During the whole study period, 422 739 (43%) patients died, including 235 572 patients during the first hospitalization for AKI (immediate mortality: 56%). The cumulative incidence of death at 60 months, considering ESRD as a competing risk, ranged from 46.4% (46.0–46.8) in the PRINC_DIAG group to 71.7% (71.3–72.1) in the RRT-ASS_DIAG group (Figure 1). When considering patients discharged from the hospital, the cumulative incidence of death (post-discharge mortality) at 60 months ranged from 31.0% (30.2–32.2) in the RRT-ASS_DIAG group to 45.5% (45.3–45.7) in the AKI as associated diagnosis, no RRT (ASS_DIAG) group (Figure 2). In the subgroup without former diagnosis of chronic kidney or urinary system disease, those cumulative incidences of death were similar, ranging from 30.2% (29.1–31.4) to 44.0% (43.8–44.2) (Table 2). In the group with a former diagnosis of chronic kidney or urinary system disease, those cumulative incidences were higher, ranging from 35.2% (33.0–37.4) to 53.4 (52.9–54.0).

Overall, RRT-ASS_DIAG patients had a higher risk of death (HR 1.9, 95% CI 1.9–2.0) as compared with RRT-PRINC_DIAG, while patients with AKI as PRINC_DIAG patients or ASS_DIAG not requiring dialysis had a lower risk using the cause-specific approach (HR 0.7, 95% CI 0.6–0.7 and HR 0.9, 95% CI 0.9–0.9, respectively) (Table 2). Those results were similar in all age groups. Using the sub-distribution approach, the ASS_DIAG patients had a higher risk than the RRT_PRINC_DIAG group, illustrating the fact that ESRD was an informative competing risk.

In the cohort overall, the risk of death increased with age, a previous history of cardiovascular disease, cancer, dementia, pulmonary or hepatic disease, and admission in ICU (Table 4). In contrast, risk of death was lower in women and in patients with a history of diabetes (Supplementary data, Table S1). The effect of older age on the risk of death was particularly significant for the PRINC_DIAG group (Table 3). In the RRT-ASS_DIAG group, the risk was lower in the presence of CKD or urinary system disease and cardiovascular disease.

ESRD

During the whole study period, 40 015 (4%) patients reached chronic ESRD, including 5962 (1.5%) during the first hospitalization for AKI (Figure 3). In the latter group, most patients had reached ESRD within weeks. When considering patients without ESRD discharged from hospital, the cumulative incidence of ESRD at 60 months ranged from 5.3% (5.2–5.4) in the ASS_DIAG group to 28.7% (27.9–29.5) in the RRT-PRINC_DIAG group (Figure 4). In the subgroup without a former diagnosis of chronic kidney or urinary system disease, those cumulative incidences of ESRD were slightly lower, ranging from 4.2% (4.1–4.3) to 25.4% (24.5–26.3) (Table 2). In the group with a former diagnosis of chronic kidney or urinary system disease, as expected, those cumulative incidences were much higher, ranging from 11.2% (10.9–11.5) to 42.5 (40.4–44.5).

Compared with RRT-PRINC_DIAG, PRINC_DIAG (HR 0.4, 95% CI 0.4–0.4), ASS_DIAG patients (HR 0.1, 95% CI 0.1–0.2) and RRT-ASS_DIAG (HR 0.4, 95% CI 0.4–0.5) patients were at lower risk of reaching ESRD (Table 2). This trend was also observed in each age group and according to the presence of a former diagnosis of chronic kidney or urinary system disease.

In the cohort taken as a whole, the risk of reaching chronic ESRD decreased with age, the presence of a cardiovascular disease, cancer, dementia, and pulmonary or hepatic disease and admission in ICU (Table 4). Conversely, the risk of ESRD was higher in men and in patients with a history of diabetes or a previous chronic kidney or urinary system disease (Supplementary data, Table S1). The effect of age on the risk of ESRD was in the opposite direction in the RRT_ASS_DIAG cohort (higher risk of ESRD in elderly patients) (Table 3). In the RRT_PRINC_DIAG group, diabetes was associated with a lower risk of ESRD.

DISCUSSION

In this nationwide cohort of 989 974 patients hospitalized with AKI during 2009–16, 422 739 (42%) patients died and 40 015 (3.4%) patients reached chronic ESRD during the follow-up up to 31 December 2016.

In the literature, hospitalizations for AKI are observed in heterogeneous groups of patients and are associated with very different outcomes. Recent classifications [Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE), Acute Kidney Injury Network (AKIN) and KDIGO] have been based on the dynamics of serum creatinine and urine output in an attempt to stratify the severity of renal injury. The stage classification does not take into consideration the patient comorbidities or the context of AKI. This classification is essentially adapted to an intensive care unit environment where AKI serves, among other organ failures, to identify patients at high risk of death. Our classification was based on diagnostic codes, and AKI was described as either a primary or an associated diagnosis, along with the need for dialysis. This would represent an alternative method of studying clinical trajectories and outcomes. In all age groups, initial clinical features were strongly associated with the risk of death or ESRD.

As in other studies, the immediate in-hospital mortality associated with AKI was abysmal (24%) [5]. In the study by Kolhe *et al.* [11], restricted only to AKI requiring dialysis and based on hospital discharge in England between 1998 and 2013, the in-hospital case-fatality increased from 30% in the period

Table 1. Description of the patients hospitalized for at least one AKI episode between 1 April 2008 and 31 December 2014

Initial clinical features	Total	RRT and AKI as principal diagnosis	RRT and AKI as associated diagnosis	AKI as principal diagnosis, no RRT	AKI as associated diagnosis, no RRT
Number of patients	989 974	27 922	89 903	152 285	719 864
Distribution of the patients (%)	100.0	2.8	9.1	15.4	72.7
Demographic characteristics					
Median age (years)	77.0	69.0	67.0	76.0	78.0
Male (%)	57.9	62.4	66.1	57.1	56.9
Former comorbidities before AKI episode (%)					
Kidney disease	16.1	18.3	11.7	19.4	15.8
Cardiovascular disease	39.8	38.4	39.5	37.3	40.4
Diabetes	14.3	19.3	14.6	14.8	14.0
Cancer	16.9	15.4	15.9	18.3	16.7
Dementia	5.9	1.7	1.1	6.0	6.6
Liver disease	4.3	5	6.8	3.3	4.2
Chronic respiratory disease	8.4	7.6	9.5	6.9	8.6
Index hospitalization: first hospital stay with an episode of AKI (%)					
Coming from home	91.1	87.6	85.5	93.3	91.5
Entry through emergency unit	55.5	55.4	43.8	59.5	56.1
Visit to an intensive care unit (%)	43.8	85.6	96.2	24.9	39.7
Mechanical ventilation	16.6	27.3	68.9	3.5	12.5
Use of catecholamines	22.5	42.0	83.9	5.6	17.6
Median of the Global Severity Score	47	53	64	34	41
Back home (%)	49.2	43.4	15.4	65.0	50.3
ESRD during first stay (%)	0.6	4.1	1.4	1.0	0.3
Death during first stay (%)	24.0	25.6	59.8	9.4	22.6
Type of hospitalization (%)					
Medical	71.2	19.5	47.1	87.9	72.7
Surgery	20.8	24.6	45.0	9.4	20
Medical procedure	5.2	54.9	5.9	2.0	3.5
Undifferentiated	2.8	1.0	2.0	0.7	3.9
Median of hospital stay duration (days)	10.0	20.0	19.0	7.0	10.0
Principal diagnosis at hospital discharge					
Disease of the circulatory system (%)	16.5	6.6	16.8	2.3	19.9
Including cardiac failure	6.3	2.0	2.3	0.9	8.2
Including shock conditions	2.7	1.7	7.6	0.3	2.6
Surgery of the circulatory system (%)	6.5	6.2	17.8	1.2	6.2
Including valve surgery	1.3	1.1	3.0	0.2	1.3
Including aneurysm surgery	0.9	1.2	3.1	0.2	0.8
Disease of the respiratory system (%)	10.7	3.3	13.4	1.1	12.7
Including respiratory failure	3.2	1.5	6.7	0.3	3.5
Including pneumopathy	3.6	0.9	3.5	0.4	4.4
Surgery of the respiratory system (%)	0.5	0.4	1.5	0.1	0.5
Including surgery of bronchial cancer	0.2	0.1	0.5	0.0	0.2
Disease of the digestive tract (%)	0.0	0.0	0.0	0.0	0.1
Including diarrhoea	0.5	0.1	0.1	0.2	0.7
Including intestinal obstruction	0.6	0.1	0.1	0.1	0.7
Surgery of the digestive tract (%)	3.7	2.7	9.8	0.8	3.6
Disease of the kidney and urinary tract (%)	18.4	54.3	1.6	80.2	6.0
Including acute kidney failure	13.1	52.0	0.0	75.5	0.0
Miscellaneous (%)	43.7	26.5	39.1	14.3	51.0
Including surgery procedure	10.1	15.5	15.9	7.3	9.7
Including medical procedure	30.6	10.2	21.1	6.3	37.7

1998–2008 to 41% in 2008–13. As in our study, overall prognosis was even more severe when AKI diagnosis was an associated diagnosis, which probably reflects those clinical situations in which AKI was one component of multi-organ failure. Other studies have shown that, even after discharge, death is more common than ESRD [13, 14], which is probably related to an increasing age (median age 77 years) and the presence of at least one comorbidity in 50% of patients before the AKI episode.

Regarding ESRD, Heung *et al.* [15], studying the Veterans Health Administration Database, found 1.3% of patients developing Stage 5 CKD within 1 year after discharge. In our study, the renal prognosis was even more pronounced (1.6% at hospital discharge and 3.7% long-term). As with death, evolution to ESRD was also more frequent when AKI was the primary diagnosis, especially when RRT was required. In the group with a former diagnosis of chronic kidney or urinary system disease the risk of ESRD was about 10 times higher than in the group without. For patients surviving AKI and discharged from hospital free of dialysis, long-term secondary progression to CKD—including ESRD—is now well acknowledged.

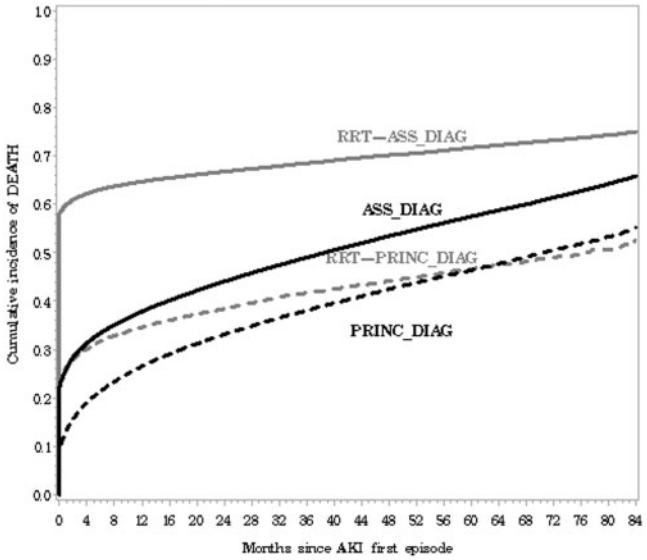

FIGURE 1: Cumulative incidence of death after the first episode of AKI, considering ESRD as a competing risk.

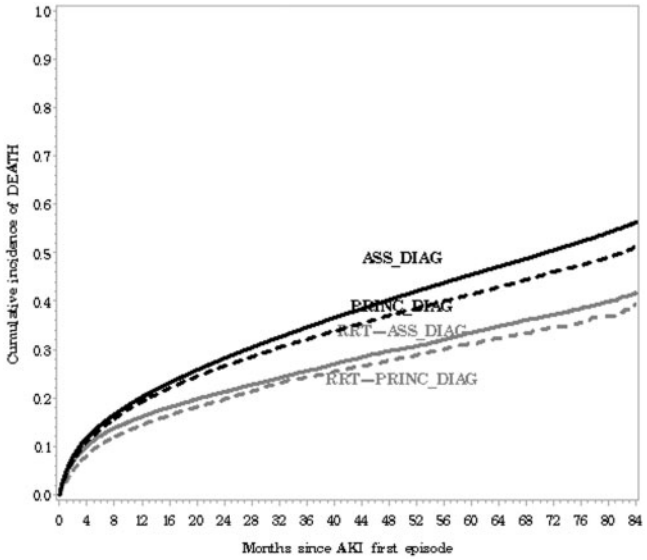

FIGURE 2: Cumulative incidence of death after the first episode of AKI, considering ESRD as a competing risk in patients discharged alive from hospital.

Even patients with a fully resolving episode of AKI were found to be at risk. Recently, the link between AKI and CKD has been emphasized, with a trend to consider both injuries as a single integrated syndrome [16, 17]. In contrast to other studies, however [5, 7], our results demonstrated that the association between initial clinical features and outcomes was almost identical, whether or not patients had a previous diagnosis related to urinary tract or kidney disease.

Similar to other studies, age and comorbidities were associated with a higher risk of death [11]. In our study, while increasing age, previous history of cardiovascular disease, cancer, chronic respiratory disease, liver disease or dementia were all independently predictive of a higher risk of death, they were also associated with a lower risk of ESRD. This contrasting pattern may reflect either a selection for starting chronic RRT in patients with a better prognosis (i.e. dialysis was proposed for patients who are more likely to survive) or be merely due to a competing risk (i.e. patients with more comorbidities would die before starting dialysis). Conversely, male gender, a history of kidney or urinary system disease or diabetes was associated with a higher risk of ESRD. Admission in an ICU, surrogate for the severity of illness, was associated to a higher risk of death and a lower risk of ESRD. Of note, some factors had a different impact according to initial clinical features. The characteristics of this elderly French population (median age 77 years) may question the generalizability of our results in other countries. However, trends were similar in each subgroups of age.

In our study, we extracted 40 015 patients with at least one AKI episode, which resulted in chronic RRT over the 8-year period (2009–16), which represents around 5000 patients/year. Since the number of new patients starting chronic RRT in France is around 10 000 patients/year we inferred that an AKI episode would constitute a historical event in as many as 50% of the ESRD incident patients collected in the French Renal Epidemiology and Information Network (REIN) registry during the same period [18]. This huge proportion is higher than the 25% with previous AKI history reported in the Medicare study for patients aged 67 years and older receiving treatment for ESRD [5]. At the very least, our findings strongly support the hypothesis of AKI as a marker of renal susceptibility that identifies high-risk patients more likely to progress to CKD and ESRD [17]. Another, non-exclusive explanation would be that AKI *per se* might trigger a subacute inflammatory and fibrogenic process that elicits progression to ESRD [19]. In recent years, experimental evidence has accumulated that tubular epithelial cells (the main victim of AKI) display cell cycle and metabolic abnormalities that compromise epithelial functions and promote fibrosis [20].

The major strength of our observational study was the national coverage obtained from the comprehensive French hospital discharge database and a long follow-up over 7 years. Our findings should, however, be interpreted in light of the following limitations. First, although administrative databases are completed by both doctors and administrative professionals, and hence represent high-powered resources for epidemiological research, the quality of the coding is questionable on such a large scale. In particular, it is reasonable to assume that some AKI episodes were actually confounded with an acute—that is, unplanned—start of RRT for ESRD. In addition, our study had no information on deaths occurring in the community, thereby underestimating overall mortality (42% of deaths in France). This limit was taken into account by censoring the follow-up of patients at the date of the last hospital stay available in the database. Second, less severe AKI episodes not leading to hospitalization were not captured in our hospital database analysis. Therefore, patients included in our study may not be representative of all AKI patients and would be expected to exhibit a more severe phenotype [21] and thus, worse outcomes. Because our classification was based on AKI as either principal or associated diagnosis, our results should now be externally validated in other countries to assess the pertinence and generalizability of

Table 2. Cumulative incidence of ESRD or death according to the former diagnosis of chronic kidney or urinary system disease with or without taking into account the event during the first stay

	Cumulative incidence of death						Cumulative incidence of ESRD					
	At Month 0		At Month 12		At Month 60		At Month 0		At Month 12		At Month 60	
Initial clinical features	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Without former diagnosis of chronic kidney or urinary system disease												
RRT and AKI as associated diagnosis	58.7	(58.4–59.0)	64.9	(64.6–65.2)	72.0	(71.5–72.4)	1.1	(1.1–1.2)	3.7	(3.5–3.8)	4.8	(4.7–5.0)
RRT and AKI as principal diagnosis	24.2	(23.7–24.8)	33.8	(33.2–34.5)	46.0	(45.1–46.9)	3.8	(3.6–4.0)	18.4	(17.8–18.9)	22.1	(21.4–22.8)
AKI as associated diagnosis, no RRT	22.2	(22.1–22.3)	36.9	(36.8–37.0)	56.3	(56.1–56.5)	0.3	(0.2–0.3)	1.6	(1.5–1.6)	3.5	(3.4–3.6)
AKI as principal diagnosis, no RRT	8.9	(8.7–9.1)	24.8	(24.6–25.1)	45.0	(44.5–45.4)	1.0	(0.9–1.1)	6.6	(6.5–6.8)	11.5	(11.3–11.8)
Subgroup of patients discharged from the hospital							Subgroup of patients discharged from the hospital without RRT					
RRT and AKI as associated diagnosis	–		15.4	(15.0–15.9)	33.0	(32.2–33.8)	–		6.3	(6.0–6.6)	9.3	(8.8–9.7)
RRT and AKI as principal diagnosis	–		13.4	(12.8–14.0)	30.2	(29.1–31.4)	–		20.3	(19.6–21.0)	25.4	(24.5–26.3)
AKI as associated diagnosis, no RRT	–		18.9	(18.8–19.1)	44.0	(43.8–44.2)	–		1.7	(1.6–1.7)	4.2	(4.1–4.3)
AKI as principal diagnosis, no RRT	–		17.7	(17.4–18.0)	40.0	(39.6–40.5)	–		6.3	(6.1–6.4)	11.7	(11.4–12.0)
With former diagnosis of chronic kidney or urinary system disease												
RRT and AKI as associated diagnosis	54.1	(53.1–55.0)	62.8	(61.8–63.7)	69.8	(68.7–70.8)	3.1	(2.8–3.4)	13.0	(12.3–13.6)	16.3	(15.5–17.2)
RRT and AKI as principal diagnosis	24.7	(23.6–25.9)	37.6	(36.2–39.0)	49.3	(47.5–51.0)	5.6	(5.0–6.2)	29.3	(28.0–30.7)	35.2	(33.6–36.8)
AKI as associated diagnosis, no RRT	22.3	(22.1–22.6)	42.6	(42.3–43.0)	63.6	(63.2–64.1)	0.4	(0.4–0.5)	4.2	(4.1–4.4)	9.1	(8.8–9.3)
AKI as principal diagnosis, no RRT	11.0	(10.7–11.4)	33.2	(32.6–33.8)	52.0	(51.2–52.9)	1.2	(1.1–1.4)	12.1	(11.6–12.5)	21.2	(20.6–21.9)
Subgroup of patients discharged from the hospital							Subgroup of patients discharged from the hospital without RRT					
RRT and AKI as associated diagnosis	–		20.4	(19.1–21.7)	36.6	(34.7–38.6)	–		23.0	(21.7–24.4)	30.9	(29.2–32.6)
RRT and AKI as principal diagnosis	–		18.5	(17.1–19.9)	35.2	(33.0–37.4)	–		34.1	(32.4–35.8)	42.5	(40.4–44.5)
AKI as associated diagnosis, no RRT	–		26.3	(25.9–26.6)	53.4	(52.9–54.0)	–		5.0	(4.8–5.1)	11.2	(10.9–11.5)
AKI as principal diagnosis, no RRT	–		25.3	(24.7–25.9)	46.7	(45.8–47.7)	–		12.3	(11.9–12.8)	22.8	(22.0–23.5)

Table 3. Association between initial clinical features and outcomes (csHR adjusted on gender, age and comorbidities)

		HRadj (95% CI) associated with the risk of ESRD or death		HRadj (95% CI) associated with the risk of ESRD		HRadj (95% CI) associated with the risk of death before ESRD	
Reference group: RRT and AKI as principal diagnosis							
All patients	RRT and AKI as associated diagnosis	1.50	(1.47–1.52)	0.37	(0.36–0.39)	2.08	(2.03–2.12)
	AKI as associated diagnosis, no RRT	0.71	(0.70–0.72)	0.11	(0.11–0.12)	1.01	(0.99–1.03)
	AKI as principal diagnosis, no RRT	0.61	(0.60–0.62)	0.31	(0.30–0.32)	0.74	(0.72–0.75)
0–20 years	RRT and AKI as associated diagnosis	1.03	(0.87–1.23)	0.18	(0.14–0.24)	2.43	(1.86–3.19)
	AKI as associated diagnosis, no RRT	0.49	(0.42–0.58)	0.08	(0.06–0.10)	1.19	(0.91–1.55)
	AKI as principal diagnosis, no RRT	0.20	(0.16–0.25)	0.17	(0.13–0.22)	0.16	(0.11–0.22)
20–40 years	RRT and AKI as associated diagnosis	1.20	(1.10–1.32)	0.24	(0.21–0.28)	3.24	(2.78–3.78)
	AKI as associated diagnosis, no RRT	0.52	(0.47–0.56)	0.10	(0.09–0.12)	1.53	(1.31–1.78)
	AKI as principal diagnosis, no RRT	0.55	(0.50–0.61)	0.29	(0.26–0.34)	0.64	(0.53–0.77)
40–60 years	RRT and AKI as associated diagnosis	1.49	(1.43–1.55)	0.34	(0.31–0.36)	2.30	(2.19–2.42)
	AKI as associated diagnosis, no RRT	0.75	(0.72–0.78)	0.14	(0.13–0.15)	1.20	(1.15–1.27)
	AKI as principal diagnosis, no RRT	0.64	(0.61–0.67)	0.36	(0.33–0.39)	0.75	(0.70–0.79)
60–80 years	RRT and AKI as associated diagnosis	1.56	(1.52–1.60)	0.43	(0.41–0.45)	2.08	(2.02–2.14)
	AKI as associated diagnosis, no RRT	0.72	(0.71–0.74)	0.13	(0.12–0.13)	1.01	(0.98–1.04)
	AKI as principal diagnosis, no RRT	0.62	(0.60–0.64)	0.33	(0.32–0.35)	0.71	(0.69–0.74)
>80 years	RRT and AKI as associated diagnosis	1.40	(1.35–1.45)	0.49	(0.44–0.54)	1.73	(1.65–1.80)
	AKI as associated diagnosis, no RRT	0.68	(0.66–0.70)	0.06	(0.06–0.07)	0.89	(0.85–0.92)
	AKI as principal diagnosis, no RRT	0.59	(0.57–0.62)	0.19	(0.18–0.21)	0.72	(0.69–0.74)
No former kidney disease							
All patients	RRT and AKI as associated diagnosis	1.53	(1.50–1.56)	0.31	(0.29–0.32)	2.10	(2.06–2.15)
	AKI as associated diagnosis, no RRT	0.73	(0.71–0.74)	0.10	(0.10–0.11)	1.02	(1.00–1.04)
	AKI as principal diagnosis, no RRT	0.61	(0.60–0.62)	0.30	(0.29–0.32)	0.73	(0.71–0.75)
With former kidney disease							
All patients	RRT and AKI as associated diagnosis	1.30	(1.25–1.36)	0.60	(0.56–0.65)	1.82	(1.73–1.91)
	AKI as associated diagnosis, no RRT	0.61	(0.59–0.64)	0.15	(0.14–0.16)	0.94	(0.90–0.98)
	AKI as principal diagnosis, no RRT	0.58	(0.56–0.61)	0.34	(0.32–0.36)	0.74	(0.70–0.77)

Table 4. Factors associated with the risk of ESRD or death (csHR) according to the initial clinical feature

	RRT and AKI as associated diagnosis		RRT and AKI as principal diagnosis		AKI as associated diagnosis, no RRT		AKI as principal diagnosis, no RRT	
HRadj (95% CI) associated with the risk of ESRD (cause specific)								
Age (years)								
≤20	1		1		1		1	
20–40	4.21	(3.31–5.34)	1.75	(1.39–2.19)	1.81	(1.58–2.08)	2.54	(2.16–2.99)
40–60	3.84	(3.09–4.77)	1.27	(1.03–1.58)	1.70	(1.49–1.93)	2.21	(1.89–2.57)
60–80	3.76	(3.03–4.65)	1.12	(0.91–1.39)	1.28	(1.13–1.45)	1.65	(1.42–1.92)
>80	4.09	(3.28–5.11)	1.15	(0.92–1.42)	0.68	(0.60–0.77)	1.01	(0.86–1.17)
Gender								
Female	1		1		1		1	
Male	1.12	(1.05–1.20)	1.14	(1.07–1.20)	1.25	(1.21–1.29)	1.30	(1.25–1.34)
Presence of comorbidities								
Kidney disease	3.84	(3.56–4.15)	2.36	(2.20–2.53)	3.35	(3.23–3.47)	2.67	(2.55–2.79)
Cardiovascular disease	0.76	(0.71–0.82)	0.81	(0.75–0.87)	0.81	(0.78–0.84)	0.79	(0.76–0.83)
Diabetes	1.19	(1.09–1.29)	0.86	(0.80–0.93)	1.40	(1.34–1.45)	1.17	(1.11–1.23)
Cancer	0.70	(0.64–0.77)	0.70	(0.64–0.76)	0.62	(0.59–0.65)	0.49	(0.46–0.52)
Dementia	0.68	(0.45–1.02)	0.59	(0.41–0.85)	0.28	(0.24–0.33)	0.35	(0.29–0.42)
Chronic respiratory disease	0.94	(0.84–1.05)	0.89	(0.79–0.99)	0.78	(0.74–0.83)	0.80	(0.74–0.86)
Liver disease	0.79	(0.69–0.91)	0.68	(0.58–0.79)	0.80	(0.74–0.86)	0.65	(0.58–0.72)
Visit to an intensive care unit	0.20	(0.18–0.21)	0.52	(0.49–0.56)	0.80	(0.77–0.82)	0.98	(0.94–1.02)
HRadj (95% CI) associated with the risk of death before ESRD (cause specific)								
Age (years)								
≤20	1		1		1		1	
20–40	0.95	(0.87–1.03)	0.69	(0.51–0.93)	0.84	(0.80–0.89)	2.30	(1.77–2.99)
40–60	1.35	(1.26–1.45)	1.45	(1.11–1.90)	1.64	(1.57–1.72)	7.23	(5.69–9.19)
60–80	1.62	(1.51–1.74)	2.08	(1.59–2.71)	2.04	(1.95–2.13)	10.59	(8.35–13.44)
>80	1.92	(1.79–2.07)	3.31	(2.54–4.32)	3.09	(2.95–3.23)	20.13	(15.86–25.54)
Gender								
Female	1		1		1		1	
Male	1.01	(0.99–1.03)	1.05	(1.01–1.09)	1.08	(1.07–1.08)	1.10	(1.08–1.12)
Presence of comorbidities								
Kidney disease	0.92	(0.90–0.95)	0.97	(0.92–1.03)	1.02	(1.01–1.03)	1.10	(1.07–1.13)
Cardiovascular disease	0.97	(0.95–0.99)	1.09	(1.04–1.15)	1.01	(1.00–1.02)	1.06	(1.04–1.09)
Diabetes	0.97	(0.94–0.99)	0.89	(0.84–0.94)	0.94	(0.93–0.95)	0.90	(0.88–0.93)
Cancer	1.19	(1.17–1.22)	1.55	(1.48–1.63)	1.81	(1.79–1.83)	2.21	(2.16–2.26)
Dementia	1.12	(1.02–1.23)	1.21	(1.02–1.42)	1.22	(1.20–1.25)	1.27	(1.22–1.33)
Chronic respiratory disease	1.16	(1.13–1.19)	1.30	(1.22–1.39)	1.23	(1.21–1.24)	1.20	(1.16–1.24)
Liver disease	1.25	(1.21–1.29)	1.73	(1.60–1.86)	1.60	(1.57–1.62)	1.55	(1.48–1.62)
Visit to an intensive care unit	1.71	(1.61–1.81)	1.50	(1.41–1.60)	1.32	(1.31–1.33)	1.16	(1.13–1.18)

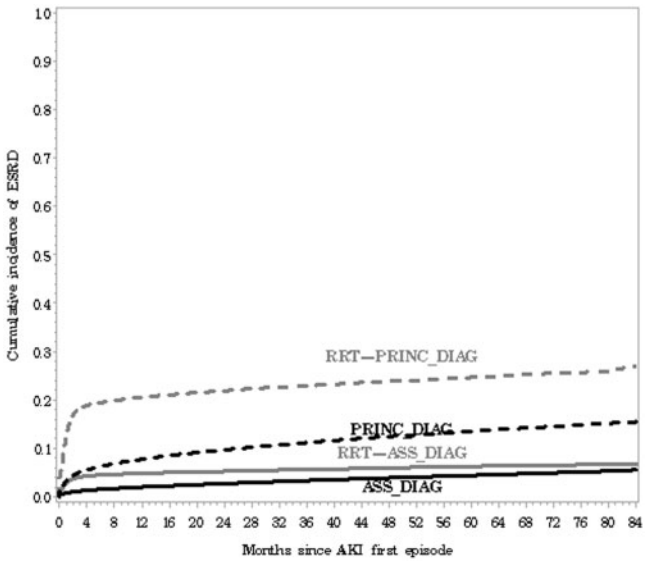

FIGURE 3: Cumulative incidence of ESRD after the first episode of AKI, considering death as a competing risk.

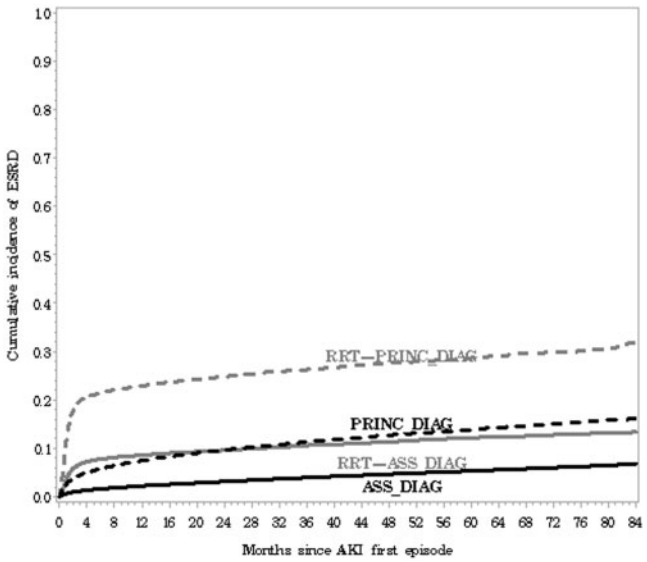

FIGURE 4: Cumulative incidence of ESRD after the first episode of AKI, considering death as a competing risk in patients without RRT discharged from hospital.

this classification. In fact, the means to classify AKI as primary or associated diagnosis may differ in different contexts including reimbursement policies. Finally, a major limit of our study was the lack of information on serum creatinine and urine output during hospitalization, which prevented us from applying and exploiting the KDIGO classification for comparison with other studies and exposed the study to the risk of low sensitivity [21]. However, our classification took into account the requirement for RRT. Besides, a recent study found that the long-term risk of renal decline was increased no matter how severe the AKI episode [14]. Further studies are now warranted to compare the performance of our classification with predicted long-term outcome to other classifications, including the KDIGO, AKIN or RIFLE.

Despite these limitations, our study did confirm the abysmal prognosis in patients experiencing an AKI episode, and strengthens the current recommendations for long-term follow-up of these patients. We advocate a clinical classification of such an episode that is very easy to detect in administrative medical databases and is associated with both immediate and long-term outcomes. This novel classification is based on the perceived primacy of AKI as a driver of the illness that brought the patient to the hospital and the need of acute RRT.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

AUTHORS' CONTRIBUTIONS

N.R. contributed to conception of the paper, analysis and interpretation of the data. O.M., A.H. and T.H. contributed to conception of the paper, interpretation of the data and drafting the article. C.C. contributed to conception of the paper, analysis, interpretation of the data and drafting the article.

CONFLICT OF INTEREST STATEMENT

None declared.

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ORIGINAL ARTICLE

Superior vena cava stenosis in haemodialysis patients with a tunnelled cuffed catheter: prevalence and risk factors

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ABSTRACT

Background. Although superior vena cava (SVC) stenosis may be a life-threatening complication of haemodialysis (HD) catheters, its prevalence and risk factors in HD patients are unknown. Our aim was to assess the prevalence and risk factors for SVC stenosis in HD patients with a tunnelled cuffed catheter (TCC) and to describe its clinical presentation.

Methods. In this single-centre, retrospective cohort study, all in-centre chronic HD patients carrying a TCC (1 January 2008–31 December 2012) were included ($n = 117$ patients, 214 TCC, 80 911 catheter-days). SVC stenosis was defined as a diameter reduction >50% on phlebography or computed tomography. Imaging was triggered by clinical SVC stenosis syndrome or vascular access (VA)-related concerns. We recorded demographics, conditions potentially influencing catheter permeability (medications, carriage of thoracic devices), number of TCCs, total duration of TCC carriage, previous arteriovenous VA and last (in use at time of stenosis detection) TCC details (location, diameter and length). VAs created while a TCC was still used were also recorded.

Results. An SVC stenosis was found in 11 patients (9.4%, 0.14/1000 catheter-days), which represents almost one-quarter of patients undergoing imaging, whatever the cause (11/45). Only two presented with clinically obvious SVC stenosis. The number of TCCs per patient was 2.64 ± 1.8 in the SVC stenosis group versus 1.75 ± 0.94 in the negative group ($P = 0.13$). On multivariate analysis (Poisson), diabetes {incidence rate ratio [IRR] 4.63 [confidence interval (CI) 1.2–17.8]; $P = 0.02$} and total duration of TCC carriage [IRR 1.47 (CI 1.2–1.8) per year; $P = 0.001$] were associated with SVC stenosis, whereas age had a slightly protective effect [IRR 0.96 (CI 0.91–1.01); $P = 0.01$]. Limitations are the retrospective design, detection and survivor bias.

Conclusion. SVC stenosis is not a rare condition, is mostly asymptomatic in the absence of a peripheral VA, is strongly associated with diabetes and is promoted by long TCC carriage. Age is slightly protective.

Keywords: catheters, central vein stenosis, haemodialysis, superior vena cava stenosis

INTRODUCTION

Central vein stenosis (CVS) [i.e. subclavian/innominate veins, superior vena cava (SVC)] is a significant cause of vascular access (VA) failure and causes significant morbidity in haemodialysis (HD) patients. Although the association of CVS with previous central venous devices has been known for decades [1, 2], its actual prevalence remains unknown and is likely