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Association between hospitalised vaso-occlusive crises and sickle cell disease-related organ damage in sickle cell disease patients aged 16 years and older using the french national health insurance database (SNDS)

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KEY FINDINGS & CONCLUSION

Key findings

Using the French national healthcare reimbursement database, we were able to identify a cohort of 17,726 SCD adult patients (≥16 years) hospitalized or with reimbursement of care for SCD between 2012 and 2018. Aside H-VOC, ACS was the most common SCD-related organ damage resulting in hospital admission, with 18.5% of patients coded as being admitted for experiencing an ACS event at least once. Patients with an annual rate of greater than 3 H-VOCs were compared with patients with an annual rate less than 1 H-VOC and had a notably 19, 17, 16 and 13 times increase in risk to have osteonecrosis, pulmonary hypertension, pulmonary embolism, or ACS during the FUP, respectively.

Limitations

An improved monitoring of women during pregnancy as well as an increase prevalence of sickle crisis during pregnancy could explain the over representation of women. A miscoding of SCD by obstetricians at time of pregnancy, with coding of SC Trait as having SCD with crisis could also be a possibility.

The main challenge of the study was the identification of SCD-related organ damage based on the medico-administrative database. Underestimations are anticipated. However, we believe it is unlikely that these underestimations would alter the magnitude or direction of the exposure-outcome relationship.

The interaction between age and H-VOC groups has been studied and suggests that the effect of VOC is still present in each age class.

Conclusion

Our study found, in a nationwide cohort in France, in a real-life setting, that patients frequently experiencing H-VOCs are at much greater risk of hospitalization for some SCD-related organ damage compared to patients rarely experiencing H-VOCs.

The highest associations with H-VOC were found for osteonecrosis, pulmonary embolism and pulmonary hypertension.

This could provide additional evidence to reinforce treatment of SCD patients with recurrent VOCs.

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INTRODUCTION

Patients with sickle cell disease (SCD) experience a wide range of complications thought to be due to the systemic impact of chronically inflamed vasculature, ongoing haemolysis, multi-cellular adhesion and ischemic damage [1].

One of the most impactful complications is the vaso-occlusive crisis (VOC).

Evidence of the relationship between VOC occurrence and the incidence of SCD-related complications is still emerging in very large cohorts of patients.

The objective of the study was to assess the association between hospitalised VOC rates and SCD-related organ damage in an exhaustive cohort of SCD adult patients in France.

Methods

Study overview and data sources

Retrospective observational cohort study using the French national health insurance's claims database (SNDS, Système National des Données de Santé)[2]. This database gathers participant level information on hospital records, primary and secondary care, and death.

Inclusion period and inclusion criteria

Between January 1st, 2012 and December 31st, 2018

- **Patients with SCD** (with either a hospital record or Long-Term Disease (LTD) status with diagnostic ICD-10 codes D57.0-2)
- **16 years and older**

The index date was defined as the first interaction with the healthcare system (whether it was related to their SCD or not). Participants were followed-up for at least one year and until the end of the study (December 31st, 2018).

Study outcomes

A **hospitalised VOC (H-VOC)** was defined as a hospital stay of **at least one night** with a primary or related diagnosis of SCD with crisis (D57.0), preceded by a transit through the emergency room (to avoid capturing SCD-related hospital stays for reasons other than VOCs).

The H-VOCs annual rate was defined as the total number of H-VOCs during the follow-up divided by the number of follow-up years until the event of interest.

Patients were categorised by the annual rate of H-VOCs they experienced into three groups: <1; 1 to <3; ≥3 H-VOCs per year.

Complications known to be experienced by patients with SCD and leading to a hospitalisation were identified during the follow-up using ICD-10 codes reported in the hospital discharge records.

Statistical analyses

Cox proportional hazards models with age as the time scale were used to study the association of the annualized rate of H-VOCs and the risk of complications, adjusted for sex.

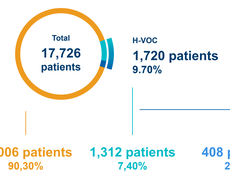
RESULTS

Study population

Patients were followed-up for 6 years (±1.8, median 7), on average.

Baseline characteristics

The mean age of the cohort was 35 years and 65% were women.
Patients with >3 H-VOCs were reported to be younger compared to those experiencing <3; and there were fewer patients in older age groups alive in the 1+ H-VOC categories.

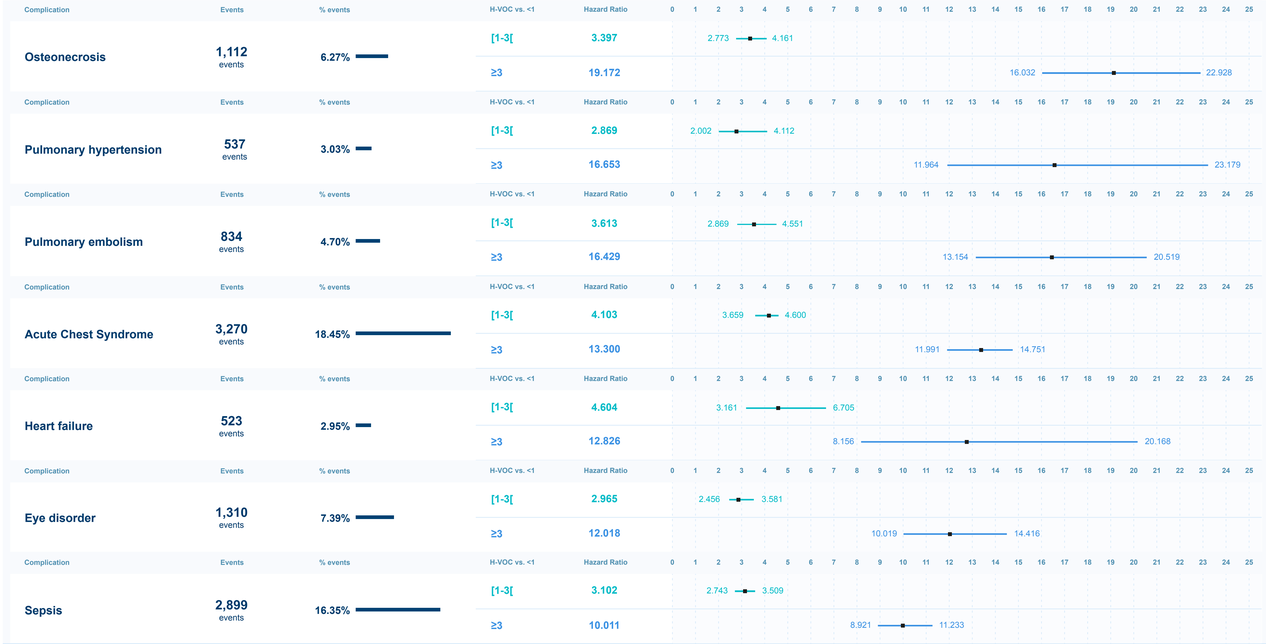


Sex	Total	<1 H-VOC	[1-3[H-VOC	≥3 H-VOC
Men	34.74% 6,158	33.32% 5,333 patients	48.25% 633 patients	47.06% 192
Women*	65.26% 11,568	66.68% 10,673	51.75% 679	52.94% 216

Age	Total	<1 H-VOC	[1-3[H-VOC	≥3 H-VOC
Mean (+/- SD)	35.0 years +/-15,8	36.3 years +/-15.8	23.8 years +/-9.0	21.3 years +/-7.0
16 to 29 years	43.13% 7,645	39.24% 6,281	76.37% 1,002	88.73% 362
30 to 39 years	24.71% 4,380	25.74% 4,120	16.92% 222	9.31% 38
40 to 49 years	14.19% 2,515	15.26% 2,442	5.26% 69	0.98% 4
50 to 59 years	9.30% 1,648	10.18% 1,630	1.22% 16	0.49% 2
60 years and more	8.68% 1,538	9.58% 1,533	0.23% 3	0.49% 2

* A high proportion partly due to several hospitalisations found in women while pregnant

Highest associations between hospitalised H-VOC rates and SCD-related organ damage in SCD patients



Other SCD-related organ damage

Complication	Events	% events
Acute Kidney Injury	2,175 events	12.27%
Gall stones	1,851 events	10.44%
Priapism among men	271 events	4.40%
Dialysis	688 events	3.88%
Central nervous system	667 events	3.76%
Kidney transplantation	181 events	1.02%
Liver	969 events	5.47%
Stroke	849 events	4.79%

Patients with recurrent H-VOC (1 to <3 H-VOCs per year)

are also significantly associated with stroke, acute kidney injury, priapism, gall stones, liver complications, central nervous system complications and dialysis.

Patients with ≥ 3 H-VOC

are at an even higher risk (with HR <10).

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Disclosures

Eleonore Herquelot, Ludovic Lamarsalle and Fanny Raguideau are employees of HEVA, a company contracted by Novartis to carry out the study.
Hannah Lennon was previously an employee of HEVA and is now an employee of IQVIA."
Miranda Bailey is employed by Novartis.
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