

Complications associated with central venous access devices in patients with hemophilia A: a secondary claims-based analysis

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INTRODUCTION

Background

- Adequate venous access is a vital aspect of caring for patients with hemophilia A (PwHA). In cases where peripheral venepuncture is not possible, central venous access devices (CVADs) facilitate the safe and effective infusion of factor concentrates.¹
- However, the use of CVADs is associated with an increase in potential complications, the most frequent of which are infections and thrombosis. These complications increase morbidity and may have a detrimental impact on patient management.²

Study objective

- To evaluate the incidence of complications associated with CVADs in PwHA.

METHODS

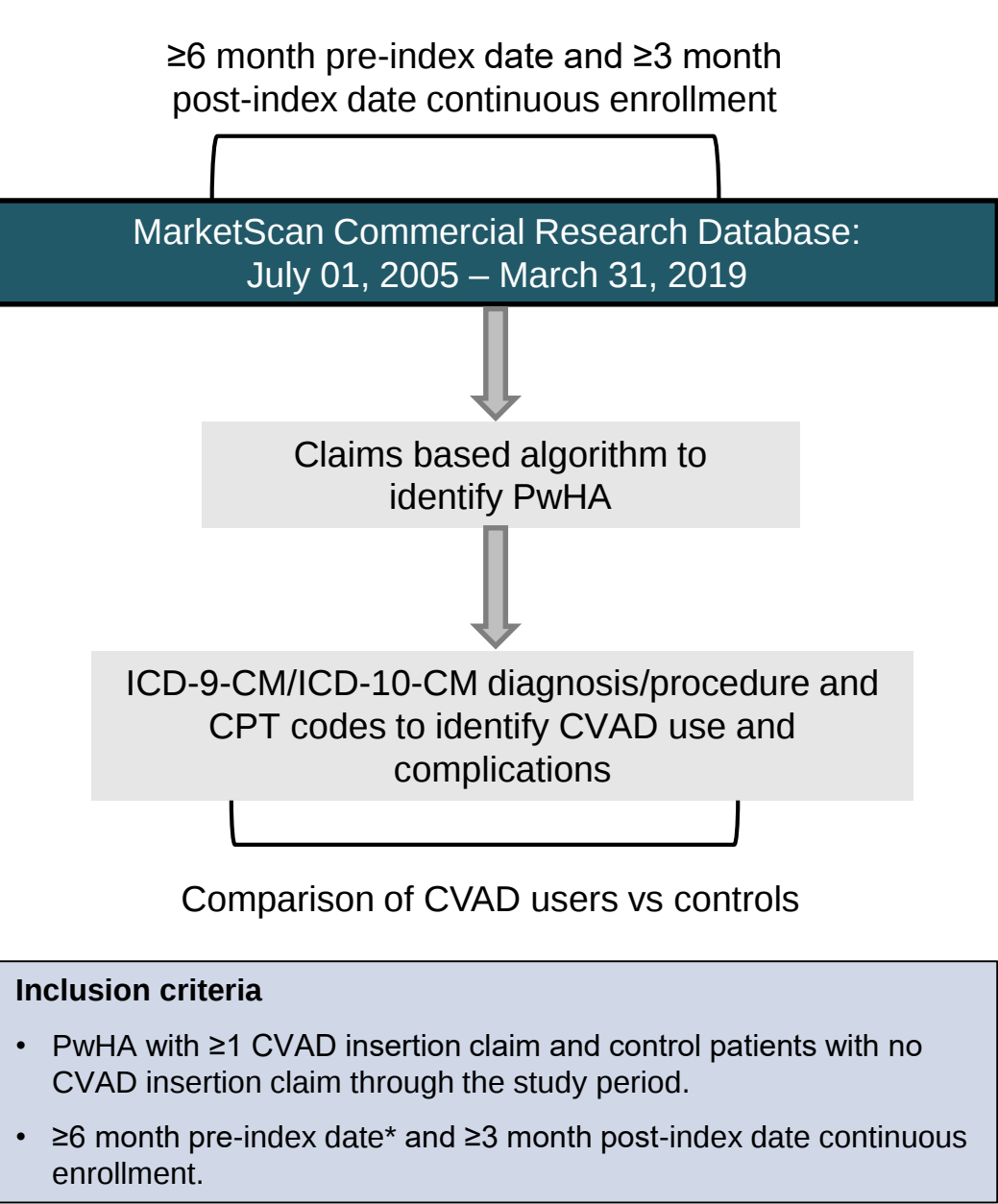
Participants

- This retrospective cohort study was conducted using claims data from the US-based MarketScan Commercial Research Database.
- The study cohort comprised PwHA and included patients with ≥1 CVAD insertion claim and control patients with no CVAD insertion claim.
- Information on the patients' baseline demographics and clinical characteristics was collected, including their Elixhauser comorbidity score, which is a measure of patient comorbidity based on ICD-9-CM and ICD-10 diagnosis codes found in administrative data.³

Analysis

- Hemophilia A (HA) was identified using a previously validated claims-based algorithm.⁴
- CVAD use and complications (all-cause infections, thrombosis, hematoma and mechanical failure) were identified using ICD-9-CM/ICD-10-CM diagnosis/procedure and current procedural terminology (CPT) codes.
- Incidence and rates of complications among CVAD cases were compared with controls (no evidence of CVAD use), and evaluated using Cox proportional-hazards models (adjusted for age, region, comorbidity score, and insurance type; **Figure 1**).

Figure 1. Analysis design.



*The index date was defined as the first date of port insertion for CVAD cases and first HA diagnosis for controls during the study period.

PwHA were followed until first outcome, plan switch or over a 2-year post-index period.

CPT, current procedural terminology; CVAD, central venous access device; HA, hemophilia A; PwHA, patients with hemophilia A.

RESULTS

Patient demographics

- Baseline demographics and Elixhauser comorbidity score of the study cohort (N = 862), are shown in **Table 1**.

Table 1. Patient demographics and clinical characteristics.

Variable	No CVAD (n = 801)	CVAD (n = 61)	p value
Age, mean±SD	25.9±17.4	4.7±5.3	< 0.0001
Male, n (%)	800 (99.9)	61 (100)	0.782
Health plan type, n (%)			
HMO	122 (15.2)	7 (11.5)	0.428
PPO	543 (67.8)	45 (73.8)	0.334
Other health plans	136 (17.0)	9 (14.8)	0.654
Region of the USA, n (%)			
North east	149 (18.6)	5 (8.20)	0.041
South	273 (34.1)	19 (31.1)	0.641
North central	204 (25.5)	17 (27.9)	0.679
West	165 (20.6)	19 (31.1)	0.053
Unknown	10 (1.2)	1 (1.6)	0.556
Elixhauser score, mean±SD	0.45±0.8	0.85±0.63	< 0.0001

CVAD, central venous access device; HMO, health maintenance organization; PPO, preferred provider organization.

- Sixty-one (7%) PwHA had evidence of CVAD use.
- Compared with controls, PwHA with CVAD:
 - Were significantly younger (mean age±SD: 4.7±5.3 years vs 25.9±17.5 years; $p < 0.001$). Age-matching between groups was not feasible due to the small sample size; however, the Cox proportional-hazards models were age-adjusted.
 - Had significantly more comorbidities, reflected by a higher Elixhauser comorbidity score (mean±SD: 0.9±0.6 vs 0.5±0.8; $p < 0.001$).

Incidence of CVAD-related complications

- In the period after the first date of port insertion (post-index), outcomes commonly associated with CVAD insertion were all significantly higher in CVAD cases compared with controls (**Table 2**).
 - Hematomas were an exception, with no incidence of hematoma in CVAD cases vs 1.5% in controls.

Table 2. CVAD specific outcomes by CVAD status.

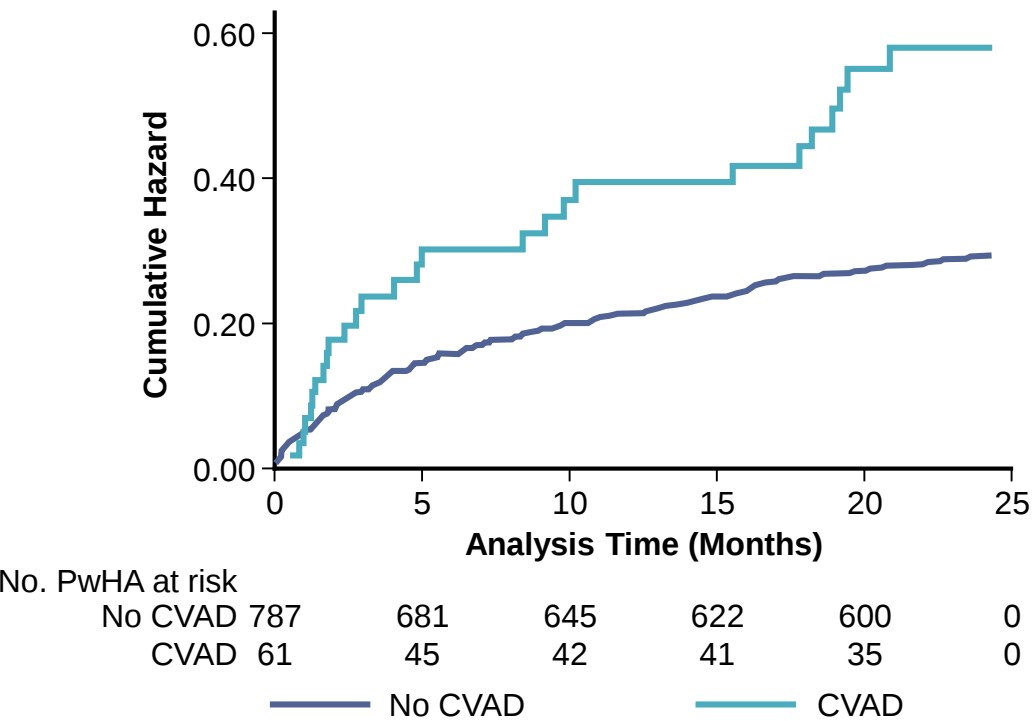
Variable, n (%)	No CVAD (n = 801)	CVAD (n = 61)	p value
Infection	214 (26.72)	27 (44.26)	0.003
Thrombosis	9 (1.12)	8 (13.11)	< 0.001
Mechanical failure	10 (1.25)	19 (31.15)	< 0.001
Hematoma	12 (1.50)	0 (0.00)	1
Composite AE score	231 (28.84)	40 (65.57)	< 0.001

AE, adverse event; CVAD, central venous access device. Composite AE score: incidence of any AE (infection, thrombosis, mechanical failure or hematoma).

Infections

- In the post-index period, a significantly higher proportion of PwHA with CVADs vs controls had all-cause infections (44.3% vs 26.7%; $p = 0.003$).
- CVAD cases had a higher rate (hazard ratio [HR] = 2.3; 95% CI, 1.5–3.6) of all-cause infections compared with controls (**Figure 2**).

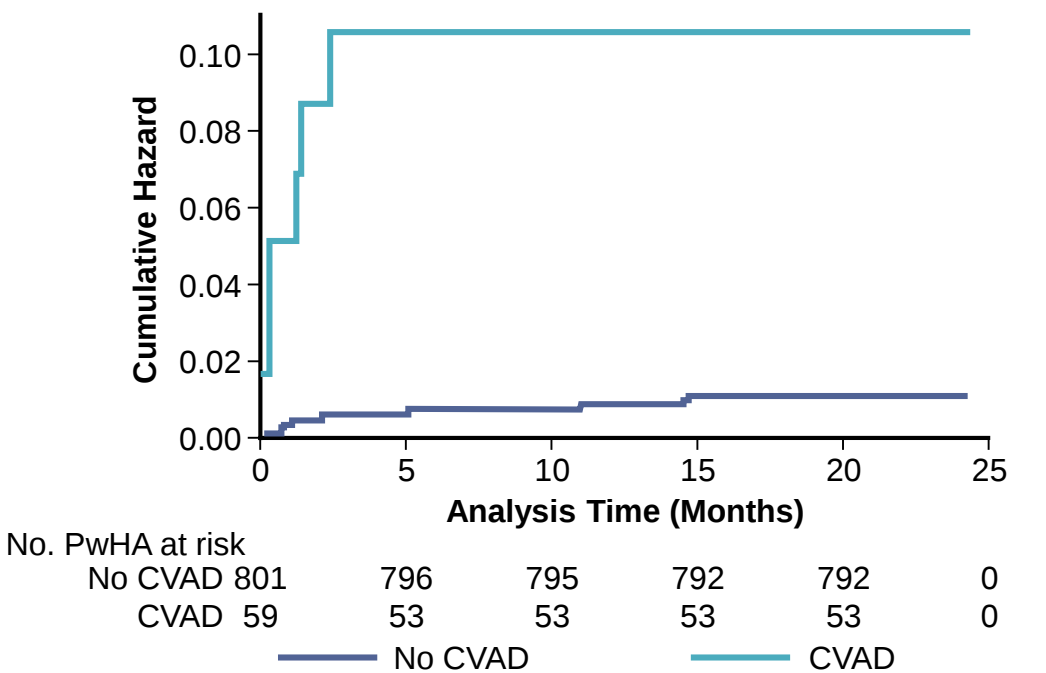
Figure 2. Cumulative hazard of infection by CVAD status.



Thrombosis

- A significantly higher proportion of CVAD cases vs controls had thrombosis in the post-index period (13.1% vs 1.1%; $p < 0.001$).
- CVAD cases had a higher rate (HR = 9.2; 95% CI, 2.4–35.6) of thrombosis compared with controls (**Figure 3**).

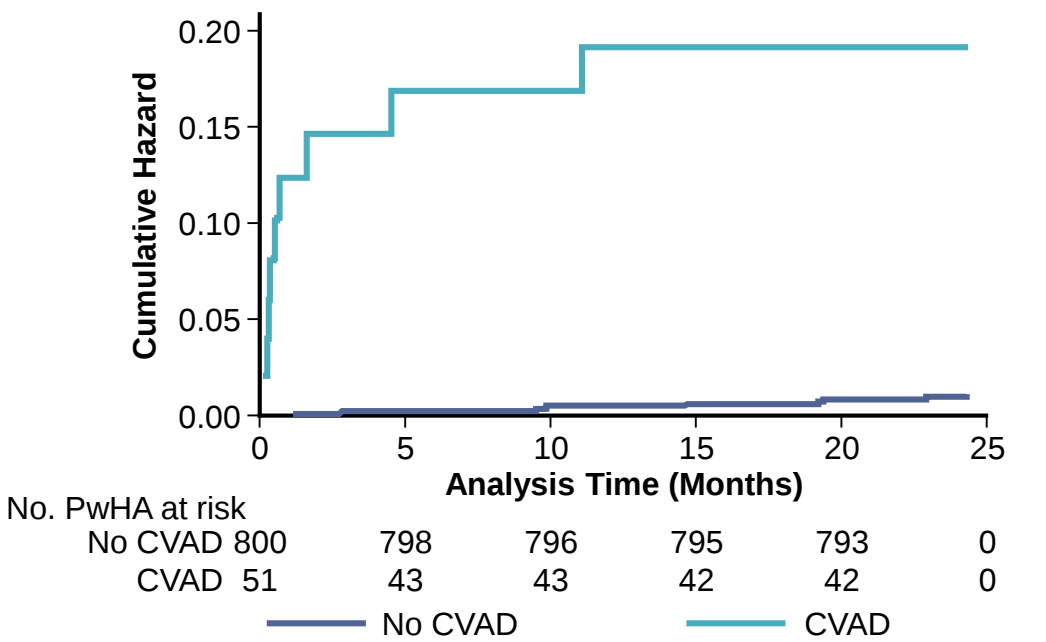
Figure 3. Cumulative hazard of thrombosis by CVAD status.



Mechanical failure

- A significantly higher proportion of PwHA with a CVAD experienced mechanical failure vs controls in the post-index period (31.1% vs 1.25%; $p < 0.001$).
- Mechanical failure was more common (HR = 7.9; 95% CI, 2.4–35.6) in CVAD cases vs controls (**Figure 4**).
 - The controls with mechanical failure (1.25%) may be due to the limitations of claims data in capturing CVAD use, causing a small number of CVAD users to be misclassified as CVAD non-users.

Figure 4. Cumulative hazard of mechanical failure by CVAD status.



Composite AE score

- CVAD cases had a significantly higher composite AE score vs controls in the post-index period, with 65.6% of PwHA with CVADs experiencing ≥1 of the named AEs, compared with 28.8% of PwHA without CVADs ($p < 0.001$).
- PwHA with CVAD use had a higher rate (HR = 3.3; 95% CI, 2.1–5.1) of occurrence of ≥1 of the specified AEs compared with PwHA without CVADs.

CONCLUSIONS

- This retrospective cohort study evaluates the incidence of complications associated with CVAD use in PwHA using claims data from 2005 through 2019.
- Results show that CVAD use in PwHA is associated with higher rates of complications, most notably all-cause infection and thrombosis.
 - PwHA with evidence of CVAD use are typically younger and have significantly more comorbidities than those with no evidence of CVAD use.
- These findings underscore the need for novel non-intravenous treatments which remove the requirement for CVADs.

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DISCLOSURES

CO: Employment with Genentech, Inc.; RK: Employment with Genentech, Inc.; AMP: Employment and shareholder of stock with F. Hoffmann-La Roche Ltd/Genentech, Inc.; EY: Employment with Genentech, Inc.; CSM: Employment with Genentech, Inc. IIA: Employment with Genentech, Inc.

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