INTRODUCTION

Epidemiological studies in the literature provide conflicting conclusions regarding the risk of myocardial infarction (MI) in people diagnosed with congenital hemophilia A (HA). Furthermore, a survey of studies highlighted potential methodological limitations across a wide array of publications.1,6

As a result, the question of whether HA protects from MI remains inconclusive.

The aim of this study was to assess the risk of MI in people with hemophilia A (PwHA) compared with individuals with no evidence of HA.

METHODS

Pharmaco-epidemiological approach

Initially, a traditional pharmaco-epidemiological approach was conducted using the US Truven MarketScan Commercial Database and/or Medicare Supplemental Database.

• A cohort of PwHA was identified based on the following criteria:
  - A confirmed diagnosis of congenital HA between Jan 1, 2000 and Sept 30, 2017; – 33 claims for HA within 365 consecutive days; and
  - Continuous enrollment with insurance coverage for the 6 months after diagnosis of HA.

• All individuals were also required to be male, and have no evidence of a diagnosis of von Willebrand disease (VWD), hemophilia B, acquired HA, or MI prior to their first HA diagnosis.

• A cohort of individuals with no evidence of HA in the study period was then randomly selected from the MarketScan database and frequency matched to the HA cohort by age, sex, insurance type, region, enrollment duration, diabetes status, and hypertensive status at a 1:3 ratio.

• High relative risk estimations using the pharmaco-epidemiological approach prompted further investigations considering concomitant medications.

These results led to the revision of methods underlying cohort identification to the machine-learning approach.

Machine-learning approach

• For this approach, the inclusion criteria for the study were further refined to include participants with:
  - ≥1 medical or pharmacy claim for factor VIII (FVIII) therapy, activated prothrombin time (APTT) complex concentrate, or activated factor VIIa therapy; or
  - ≥1 medical or pharmacy claim for FVIII therapy and no diagnosis of VWD; or
  - ≥1 medical or pharmacy claim for desmopressin and ≥1 medically-attended visit with a diagnosis of HA in the same claim or drug; or
  - ≥1 medically-attended visit with a HA diagnosis.

• The earliest data for fulfilling any of these inclusion criteria was deemed the individual’s index date.

• Participants also had to have 6 to 12 months of continuous insurance enrollment prior to study entry in order to participate.

• An HA classification algorithm4,5 set to 98.5% specificity and 77.8% sensitivity was adapted and applied to the aforementioned refined cohort.

RESULTS

Pharmaco-epidemiological approach

• Based on the defined criteria, 3337 people with congenital HA were identified (Table 1).

• The crude incidence rate of MI in this cohort was estimated to be 1.08 (95% confidence interval (CI): 0.88–1.30) per 100 person-years. Relative to the matched cohort of individuals with no evidence of HA (n=16,684), an unadjusted IRR of 1.71 (95% CI: 1.67–1.75) was estimated (Table 3).

• These high relative risk estimations prompted further investigations into concomitant medications, which revealed evidence of misclassification bias with a large proportion of participants having been prescribed anticoagulants and a low frequency of hemophilia drug utilization.

Machine-learning approach

• The use of the machine-learning approach identified 3145 individuals with a 25% probability of being true PwHA; ten were excluded as they had a previous history, leaving a final cohort of 3144 PwHA (Table 2).

• The crude incidence rate of MI was calculated to be 0.25 (95% CI: 0.15–0.34) and 0.22 (95% CI: 0.18–0.27) per 100 person-years in the HA and non-HPA population (n=15,873), respectively, yielding an unadjusted IRR of 1.34 (95% CI: 1.07–1.67; Table 3).

• The adjusted IRR was estimated to be 1.31 (95% CI: 0.85–2.00; p<0.002), indicating that there was no evidence to suggest a difference in the rate of MI in the HA population versus a matched non-HPA control (Table 3).

• This study highlights the importance of validating cohort selection methods.

• While every effort was taken to mitigate for the effects of confounders and biases, the risk ratios should be interpreted in the context of the limitations of a secondary data use study.

• No evidence of a different risk of MI in PwHA relative to non-HPA counterparts was observed in this analysis; however PwHA should be made aware of cardiovascular risks and have access to services to reduce actionable cardiovascular risk factors (e.g. support to stop smoking, reduce hypertension, treat obesity etc.).

REFERENCES


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DISCLOSURES

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