Correlation of Statins Use with the Incidence of Venous Thromboembolism in Patients with Ankle Fracture

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Introduction/Purpose: Finding factors that can exacerbate or ameliorate the incidence of Venous thromboembolism (VTE) can affect the process of making decision on whether to start prophylaxis or not, especially when on the verge of whether to-give or not-to-give prophylaxis. Among each patient's profile, medications are of the most important factors influencing surgeon's decision on the prophylactic methods in VTE-vulnerable patients. Among medications, Statins were shown to reduce the incidence of VTE in patients who were receiving them for hyperlipidemia and cardiovascular conditions. However, none of the current VTE prediction methods, particularly in orthopaedic practice, have considered statins protective. Herein we aimed to determine any correlations between statin consumption and the incidence of VTE in ankle fractures and whether to include statins in prediction models of VTE.

Methods: In this case-control machine learning-based study, approved by the Institutional Review Board (IRB), the ICD and CPT codes were used to identify the patients who were diagnosed with ankle fracture in the Mass General Brigham database from 2004 to end of May 2021. After screening approximately 16,421 patients with ankle fractures, a total of 1,176 patients who were suspect VTE according to their signs and symptoms were recruited, 239 had confirmed VTE (case group) and 937 did not have VTE (controls). Forty-nine cases and 396 controls were statin users. Using a semi-automated machine learning-based algorithm, patients' demographics, past medical and surgical history, fracture characteristics and weber classification, and statin consumption status were obtained, and values were organized in a numerical analyzable manner in the dataset. We used chi-squared and Pearson correlation tests where applicable, and outcomes were displayed and interpreted using p-value (p<0.05 considered significant) and odds ratio (OR).

Results: The mean age and BMI in our case group were 55.1+-17.0 y/o and 30.0+-6.0, respectively; age and BMI in the controls were 69.4+-13.2 (p=0.09 vs. cases) and 29.2+-6.6 (p=0.12 vs. cases), respectively. Gender distribution is depicted in table 1. In addition, we found that in our population, a total of 239 patients had VTE, from which 49 (21%) were taking Statins and 190 (79%) were not. Out of the 937 patients who did not develop VTE, 396 (42%) were taking Statins whereas 541 (58%) were not. We found that patients taking statins had lower incidence of VTE after their ankle fracture, compared with patients not taking statins (OR=0.36, p <0.001). The distribution of statin users/non-users among cases and controls is shown in table 2. Moreover, using our machine learning algorithm, conditions that would necessitate the use of statins including cardiovascular diseases and hyperlipidemia showed negative significant correlation with VTE (p<=0.02).

Conclusion: Several studies have suggested that hyperlipidemic blood is prone to a greater generation of thrombin, endothelial dysfunction, and higher platelet activity. By disturbing these mechanisms, statins play a protective role against VTE. Herein, using machine learning algorithms together with statistical analysis, we found that Statins were significantly associated with a lower rate of VTE in patients with an ankle fracture. These findings can be considered in future prediction models that are built based on patient-specific factors. Knowing the protective effect of statins can also help clinicians with deciding on prophylaxis administration in at VTE-risk patients.
Table 1. Distribution of males and females in case and control groups.

| Gender | Case Group | Control Group | Total |
|--------|------------|---------------|-------|
| Female | 120 (50%)  | 633 (68%)     | 753   |
| Male   | 118 (50%)  | 305 (32%)     | 423   |
| Total  | 239        | 937           | 1176  |

*Case group: patients with ankle fracture who developed Venous Thromboembolism; Control group: Patients who did not develop Venous Thromboembolism.*

Table 2. Distribution of cases and controls based on statin consumption status.

| Statin Use       | Case Group | Control Group | Total |
|------------------|------------|---------------|-------|
| Statin Use       | 49 (21%)   | 396 (42%)     | 445   |
| No Statin Use    | 190 (79%)  | 541 (58%)     | 731   |
| Total            | 239        | 937           | 1176  |

*Case group: patients with ankle fracture who developed Venous Thromboembolism; Control group: Patients who did not develop Venous Thromboembolism.*