Do Statins Reduce the Risk of Venous Thromboembolism after Ankle Fractures?

Nour Nassour, Bardiya Akhbari, Noopur Ranganathan, David Shin[1], Joseph Hasbrouck Schwab[2], Christopher W DiGiovanni[3], Daniel Guss, Hamid Ghaednia, Soheil Ashkani Esfahani[1]
[1]Massachusetts General Hospital, [2]MGH Dept. of Ortho Surg., [3]Mass General/Newton-Wellesley, F&A Ctr

INTRODUCTION: Venous thromboembolism (VTE) is a common complication in orthopaedic foot and ankle surgery and is often treated with prophylaxis to prevent occurrence of deep vein thrombosis (DVT) and pulmonary embolism (PE). Finding factors that can alleviate VTE incidence can aid decision making. Within a patient's profile, medications hold an important placeholder in terms of influencing the surgeon's decision on whether to administer prophylaxis to at-risk VTE patients. One such important medication are statins, which were shown to reduce the incidence of VTE in patients who were receiving them for hyperlipidemia and cardiovascular conditions. However, current VTE prediction methods, particularly in orthopaedic practice, have rarely considered statins protective. We hypothesized that receiving statins will reduce the need for VTE prophylaxis in trauma patients. 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 or apply them on the process of decision making for prophylaxis.

METHODS: In this case-control machine learning study, approved by the institutional review board, we used procedure (Current Procedural Terminology) and diagnosis (International Classification of Disease) codes to identify patients diagnosed with ankle fractures in the Mass General Brigham database from 2004 to 2021. After reviewing 16,421 patients, 239 cases were isolated who had developed VTE during 6 months after the fracture, and we included 937 patients who did not develop VTE after 6 months of their ankle fracture to our control group to reach a case to control ratio of 1:4. Within this population, 49 cases and 396 controls were statin users. In order to study the VTE-Statin correlation, we used chi-square and Pearson's 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 y/o and 29.2±6.6, respectively. Gender distribution is depicted in Table 1. In addition, we found that in our population, a total of 239 patients had VTE, of 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 a lower incidence of VTE after their ankle fracture, compared to 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 ($p \leq 0.02$).

DISCUSSION AND CONCLUSION:

In this study we see that patients taking statins are less prone to develop VTE after sustaining an ankle fracture. In fact, 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 can play a protective role against VTE. Using machine learning algorithms together with statistical analysis, we found that statins were significantly associated with a lower rate of VTE in patients with ankle fractures. This leaves us to wonder if statins could reduce the need for VTE prophylaxis.

Our findings on the correlation of statins with lower VTE incidence in ankle fractures can be also tested on other orthopaedic conditions, particularly traumas, and in future, can be useful in developing patient-specific prediction models for determining the risk of VTE and the use of prophylaxis. However, future studies on larger populations from different centers are highly suggested as well as clinical trials to prove the role of statins in reducing the rate of VTE or any possible synergistic effect with VTE prophylactic regimens.

Table 1. Distribution of males and females in case and control groups.

	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.

	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.