Incidence of Myopathy in Post COVID-19 Patients undergoing Statin Therapy

Jithin John BS[1], Eduardo Leon BS[1] , & Ramin Homayouni PhD[1]

[1]Oakland University William Beaumont School of Medicine, Oakland University, Rochester, MI

OAKLAND UNIVERSITY WILLIAM BEAUMONT

Introduction

Statin therapy is a widely used drug for cardiovascular diseases and has been shown to provide mortality benefits, especially in diseases like atherosclerosis. However, it is important to understand the safety of statin use in patients with COVID-19, given that statin-associated myositis has been well documented since its first use. This condition causes mitochondrial damage, cell death, and an associated increase in blood Creatinine Kinase (CK) levels. There has been little research regarding the risk factors associated with statin use in COVID-19 patients.

COVID-19 causes inflammation, which may result in muscle damage. Since statins also cause muscle damage, it is suggested that statins should be avoided in individuals with COVID-19 or in those at risk of exposure to the virus. However, recent literature has also suggested that statin use is protective against SARS-CoV-2 infection due to its antioxidant and anti-inflammatory properties.

While there are isolated case reports of COVID-19 causing myopathies such as rhabdomyolysis, the literature on concomitant statin use is scarce. Therefore, this analysis aims to examine the association between statin therapy and post COVID-19 cases myopathy. The results of this study may help guide physicians in improving both in-hospital and post-hospital care of COVID-19 patients.

It is hypothesized that using statin prior to SARS-CoV-2 infection will be associated with an increased risk of myopathy and increase in CK values, based on previous findings. Overall, this study is significant as little research has been conducted regarding statin use and myopathy in COVID-19 patients.

Aims and Objectives

Aim 1: To examine the association between statin use and COVID-19 diagnosis.

Aim 2: To investigate the association between statin use and myopathy after adjusting for gender, race, pre-COVID types of statin therapy, and severity of COVID-19.

Aim 3: To investigate the association between statin use and increase in blood CK values after adjusting for gender, race, pre-COVID types of statin therapy, and severity of COVID-19.

Methods

In this retrospective study, medical records were extracted from the Beaumont Health Epic electronic medical records (EMR). The inclusion criteria for the study are outlined in the figure below. For designation of "New Myalgia," the patient must not have had an ICD10 code for myalgia at any time prior to COVID-19. Patients were designated as increase in CK if their maximum CK value during the three months after COVID-19 was above their pre-COVID19 normal ranges (20-200 IU/L).

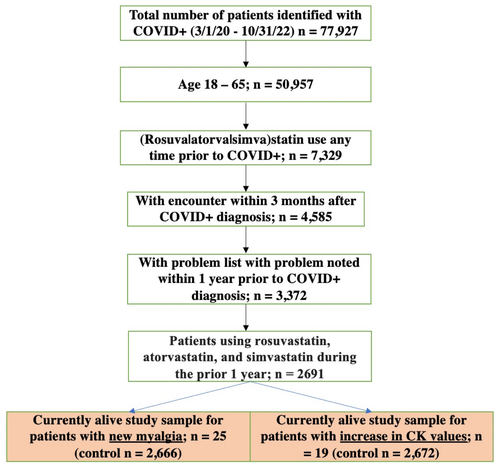

Figure 1: Consort diagram describing the inclusion criteria for the study population.

Results

Statin Use Before and After COVID-19

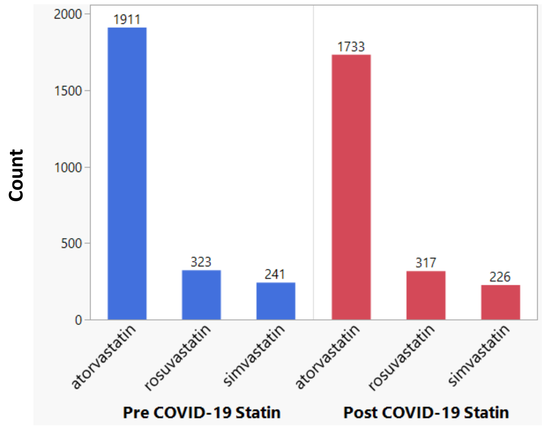

Figure 2: The number of patients on Statin therapy before (blue bars) and after (red bars) SARS-CoV-2 infection.

Incidence of New Myalgia

Table 1 Characteristics of Patients who did or did not develop Myalgia after SARS-CoV-2 infection.

	No New Myalgia	New Myalgia	p-value
Population, *n*	2666	25	
Age, *median (IQR)*	56 (10)	54 (16)	0.381[a]
Female, *n (%)*	1358 (0.51)	18 (0.72)	0.044[b]
Race, *n (%)*			0.669[c]
White or Caucasian	1605 (0.60)	17 (0.68)	
Black or African American	874 (0.33)	7 (0.28)	
Pre-COVID Statin use, *n (%)*			0.474[c]
Atorvastatin	1895 (0.77)	16 (0.67)	
Rosuvastatin	318 (0.13)	5 (0.21)	
Simvastatin	238 (0.10)	3 (0.12)	
Max CK values, *median (IQR), n*			
Pre-COVID (1 year)	119.0 (188.5) n=634	69.5 (22.5) n=6	0.073[a]
Post-COVID (3 months)	107.0 (217.0) n=411	129.0 (219.0) n=9	0.797[a]
Severe COVID, *n (%)*	1176 (0.44)	6 (0.24)	0.044[b]

[a]Wilcoxon Rank Sum test, [b]Fisher's Exact test, [c]Chi-square test. IQR: Interquartile range; SD: standard deviation; Dx: Diagnosis.

Table 2 Adjusted odds ratios for developing New Myalgia after SARS-COV-2 infection based on multivariable logistic regression.

Variable	Adj Odds Ratio	Lower 95% CI	CI Upper 95% CI	Wald p-value
Age [per unit year]	0.97	0.93	1.02	0.27
Gender [Female]	2.74	1.08	6.98	0.03
Race [Caucasian v. AA]	1.57	0.60	4.08	0.35
Pre-COVID statin therapy:				
[Rosuvastatin v. Atorvastatin]	1.67	0.60	4.68	0.32
[Rosuvastatin v. Simvastatin]	1.13	0.26	4.83	0.87
Severe COVID [Yes]	0.39	0.14	1.06	0.07

Increase in Blood CK Levels

Table 3 Characteristics of patients who did or did not have an increase in CK levels from normal levels after SARS-CoV-2 infection.

	No change in CK	Increase in CK	p-value
Population, n	2672	19	
Age, *median (IQR)*	56.00 (11.00)	58.00 (10.00)	0.113[a]
Female, *n (%)*	1368 (0.51)	8 (0.42)	0.494[b]
Race, *n (%)*			0.686[c]
White or Caucasian	1612 (0.60)	10 (0.53)	
Black or African American	873 (0.33)	8 (0.42)	
Pre-COVID Statin use, *n (%)*			0.606[c]
Atorvastatin	1898 (0.77)	13 (0.68)	
Rosuvastatin	319 (0.13)	4 (0.21)	
Simvastatin	239 (0.10)	2 (0.11)	
Max CK values, *median (IQR), n*			
Pre-COVID	117.0 (194.0) n=621	129.0 (89.0) n=19	0.586[a]
Post-COVID	102.0 (165.0) n=401	397.0 (288.0) n=19	0.0001[a]
Severe COVID, n (%)	n (0.56)	n (0.37)	0.106[b]
Post-COVID Myalgia Dx, *n (%)*	2630 (0.98)	18 (0.95)	0.264[b]

[a]Wilcoxon Rank Sum test, [b]Fisher's Exact test, [c]Chi-square test. IQR: Interquartile range; SD: standard deviation; Dx: Diagnosis.

Table 4 Adjusted odds ratios for elevated CK values after SARS-CoV-2 infection based on multivariable logistic regression.

Variable	Adj Odds Ratio	Lower 95% CI	CI Upper 95% CI	Wald p-value
Age [per unit year]	0.94	0.87	1.01	0.07
Gender [Female]	1.41	0.56	3.56	0.47
Race [Caucasian v. AA]	1.71	0.66	4.47	0.27
Pre-COVID statin use:				
[Rosuvastatin v. Atorvastatin]	0.51	0.16	1.59	0.24
[Rosuvastatin v. Simvastatin]	0.61	0.11	3.37	0.57
Severe COVID [Yes]	0.47	0.18	1.22	0.12

Conclusions

Using a multivariate linear regression model adjusted for age, race, gender and severity of COVID-19, we found no association between the type of statin therapy prior to SARS-CoV-2 infection and development of new myalgia or increases in blood CK levels from normal ranges (Tables 2 and 4).

In contrast, we found that development of new myalgia, but not an increase in CK level, after SARS-CoV-2 infection was significantly associated with female gender (adj OR 2.74, 1.08-6.98, 95% CI), irrespective of the type of statin therapy.

Lastly, we found that the severity of COVID-19, defined by hospitalization within 14 days of COVID-19 diagnosis, was not associated with an increase in new myalgia or elevated CK levels after infection.

In conclusion, we found no differences between the type of statin therapy (atorvastatin, simvastatin, and rosuvastatin) and the onset of new myalgia post-COVID19 or elevated CK levels from normal pre-COVID ranges. These findings are largely consistent with prior published data suggesting that statins may have a negative effect in COVID-19 patients.

Limitations

The study suffers from low number of observations for the target outcomes: new myalgia (27/2691) and elevated CK levels (19/2691). Thus the study is not powered to detect a small differences in statin therapy on these outcomes.

The small number of outcome observations may be due in part to our strict criteria for defining new myalgia or an increase in CK levels from normal ranges, thereby excluding individuals who already had myalgia or elevated CK levels prior to infection.

Lastly, the study was not designed to address the impact of statin use on developing myalgia and elevating CK levels after infection compared to a control population who was not on statin therapy prior the infection.

References

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