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Association of Statin with 1-Year Mortality in Patients with Infective Endocarditis

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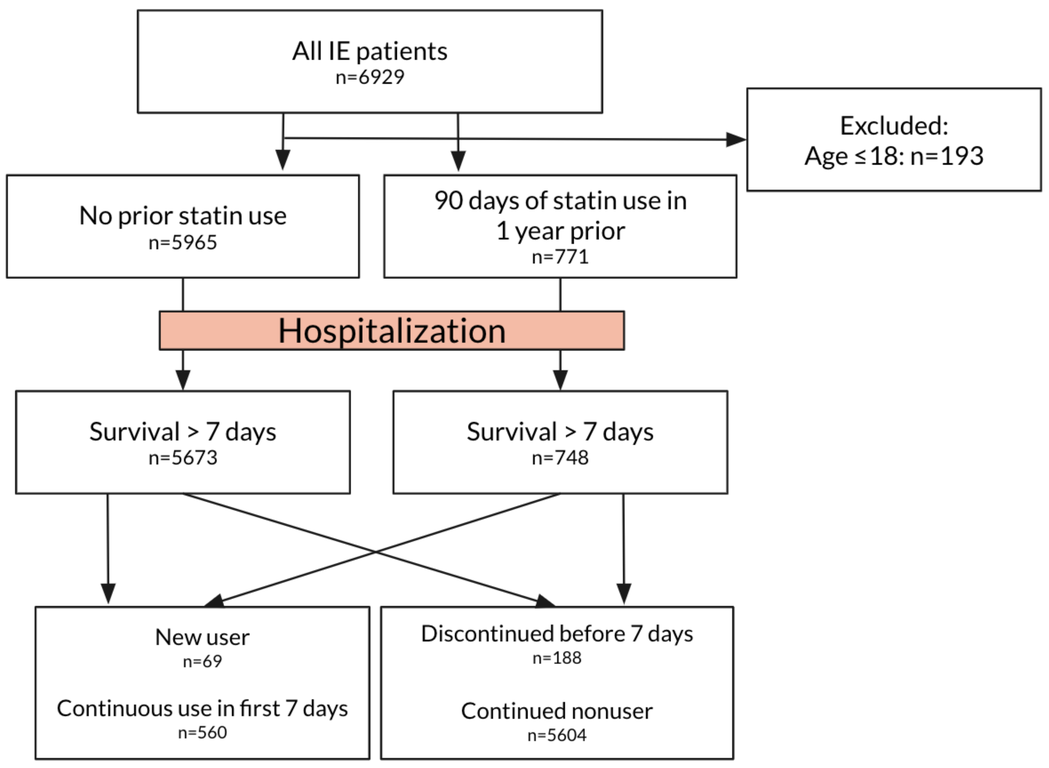
Introduction

- Infective endocarditis (IE) is associated with poor clinical outcomes despite improving diagnostic accuracy and treatment modalities
- Randomized controlled trials are difficult to perform for a diseases like infective endocarditis, where the incidence is <10/100000 person-years[1]
- Population based studies lack generalizability due to considerable geographic variability in underlying diseases and bacteriologies [1]
- We investigate into the efficacy of statin as an adjunctive therapy, overcoming the aforementioned considerations by including relevant variables

Methodology

- Adult patients diagnosed with IE from 1996 to 2019 were identified from a territory-wide clinical information registry via the use of ICD-9 codes
- Statin use post-admission is defined by 7 days of consecutive statin use. To allow for fair comparison, events in the first 7 days are censored
- We utilized **covariate balancing propensity scores** and **inverse probability of treatment weighting (IPTW)** to balance comorbidities, concurrent drug uses, bacteriological data and socioeconomic variables between treatment groups[2]
- Utilizing multivariable cox proportional hazards regression, we investigated if statin usage post-admission affects mortality.
- Additional outcomes are the risk of death caused specifically by IE, stroke and embolic events, for which statin's effect is determined through competing risk regression

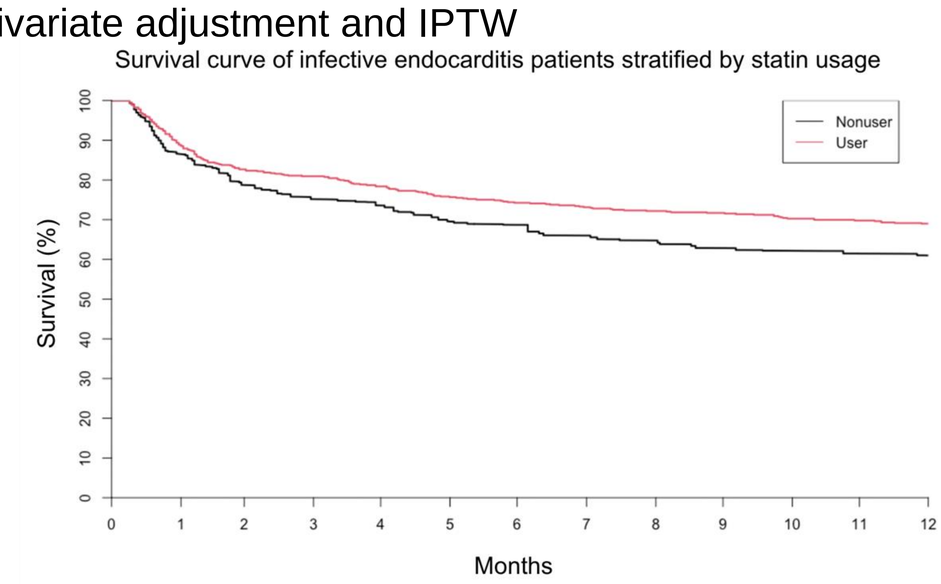
Figure 1 Flow diagram of all patients with infective endocarditis



Results

- Among 6727 adult patients (63% male, mean age 58.1), 629 patients had post-admission statin use among whom 69 are new users. Among those who survived 7 days (n=6421), 27.5% deceased within one year. (Figure 1)
- Post-admission statin use was at a **34% lower risk of mortality** from the seventh day onwards than nonusers after multivariable adjustment, including prior statin use (Figure 2, hazard ratio [HR]=0.66, 95% confidence interval [CI]=0.49-0.88, p=0.004)

Figure 2 Kaplan-Meier curves representing surviving population, with multivariate adjustment and IPTW



- Considering competing causes of deaths, the use of post-admission statin **only** significantly reduced **mortality attributable to IE** (Subdistribution HR [SHR]=0.49, 95% CI=0.26-0.95, p=0.034) but not other causes (SHR=0.76, 95% CI=0.56-1.04, p=0.09).
- **Simvastatin, atorvastatin, and rosuvastatin** all significantly reduced one year mortality (Table 1, Simvastatin: HR=0.70, 95% CI=0.52-0.94, p=0.018; Atorvastatin: HR=0.56, 95% CI=0.36-0.89, p=0.015; Rosuvastatin: HR=0.45, 95% CI=0.21-0.94, p=0.033).
- A **dose-dependent relationship** between reduction in mortality and statin use (HR=0.62, 95% CI=0.46-0.84, per unit defined dose[3] increase in daily dose, p=0.002)

Table 1. Hazard ratio associated with statin use stratified by formulation

Statin use	One year death count in nonusers	One year death count in users	Person-days of follow-up	Adjusted HR	p-value
No statin	5792	1571	1666496	1 (Ref)	-
Simvastatin	471	154	130433	0.70 (0.52-0.94)	0.018
Atorvastatin	122	33	35192	0.56 (0.36-0.89)	0.015
Rosuvastatin	29	7	8643	0.45 (0.21-0.94)	0.033
Fluvastatin	7	1	2210	0.64 (0.10-4.24)	0.647

- Among statin users, there was a 39% lower risk of **stroke** (SHR=0.61, 95% CI=0.40-0.95, p=0.03) within one year after the seventh day of admission
- Statin was not associated with embolisms other than stroke in a cohort of 6375 patients (SHR=1.10, 95%=CI 0.56-2.14, p=0.79)
- As a **negative control outcome**, statin use resulted in a 5% nonsignificant reduction in the risk of incident diagnosis of endocrine disorders other than those related to the pancreas (SHR=0.95, 95% CI=0.38-2.49, p=0.91)

Subgroup analysis

- Statin use was associated with lower mortality among patients who were **culture negative** (HR=0.47, 95% CI 0.23-0.99, p=0.046) and patients who were confirmed to have **methicillin resistant staphylococcus aureus (MRSA)** (HR=0.49, 95% CI=0.27-0.91, p=0.024), but not for other bacteria.
- Results are consistent across other subgroups by demographics and comorbidities

Conclusion

- Post-admission use of statin was associated with a lower risk of mortality and stroke in IE patients, independent of pre-admission use**.**

Reference

[1]Tleyjeh IM, Abdel-Latif A, Rahbi H, Scott CG, Bailey KR, Steckelberg JM, et al. A systematic review of population-based studies of infective endocarditis. Chest. 2007;132:1025-35.
[2]Imai K, Ratkovic M. Covariate balancing propensity score. Journal of the Royal Statistical Society: Series B (Statistical Methodology). 2014;76(1):243-63.
[3]WHO collaborating center for Drugs Statistics Methodology.

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