# The Safety and Economic Impact of Cefazolin vs. Nafcillin for Methicillin Susceptible *Staphylococcus aureus* Bacteremia

Lauren K. Flynt[1], Rachel M. Kenney,[1] Marcus Zervos,[1] Susan L. Davis[1,2]
[1]Henry Ford Hospital, Detroit, MI, [2]Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences

Address correspondence to:
Lauren Flynt, PharmD
lflynt1@hfhs.org

## Introduction

- Beta-lactams are superior to vancomycin for methicillin sensitive *Staphylococcus aureus* (MSSA) infections.
- Several studies have demonstrated first generation cephalosporins are non-inferior to that of semi-synthetic penicillins in terms of efficacy for MSSA bloodstream infections (BSI).
- Using cefazolin for patients with MSSA endocarditis is somewhat controversial due to the inoculum effect and is generally reserved for patients with penicillin allergy.
- Benefits of cefazolin include a lower drug acquisition cost, and a favorable adverse effect profile, particularly with respect to acute kidney injury.
- The purpose of this study was to evaluate the outcomes of infection, safety and economic impact of using cefazolin versus nafcillin in patients with MSSA BSI.

## Methods

**Study Design**
This was a retrospective cohort study approved by the institutional review board.

**Subjects**
The study included patients at Henry Ford Health System (a four hospital health system) from November 2013 to October 2015.

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| • ≥ 18 years of age<br>• 1 positive blood culture for MSSA<br>• Received ≥ 72 hours of nafcillin or cefazolin | • Patients on intermittent hemodialysis, continuous renal replacement therapy or any other for of renal replacement therapy<br>• Baseline Serum Creatinine (SCr) > 2 mg/dL<br>• Meningitis as source of infection |

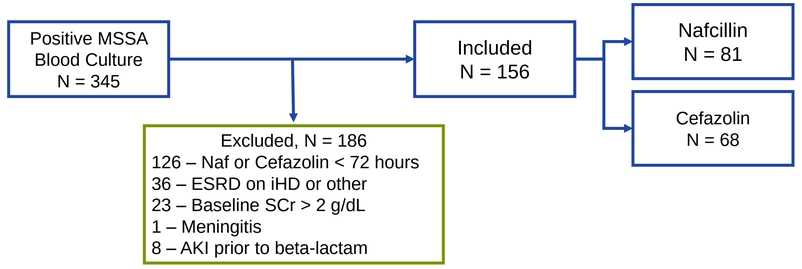
** If the patient was on both nafcillin and cefazolin at some point during therapy for MSSA bacteremia, then the initial beta-lactam > 72 hours was used to group the patient.

**Data Collection and Endpoints**
Data was collected from electronic medical records. Data collected at baseline included
- Patient characteristics: demographics, comorbid conditions.
- Infection characteristics: source of infection according to concomitant positive cultures or medical record documentation of diagnosis.
- Incidence of nephrotoxicity: defined as an absolute increase in SCr > 0.3 mg/dL in 48 hours or ≥50% from baseline SCr. (Baseline SCr was defined as immediate prior SCr in last 90 days or average SCr on days 1 and 2 from positive blood culture).
- Treatment duration and cost: total number of days and doses of beta-lactam therapy administered from an inpatient perspective. Drug cost was estimated based on average wholesale price (AWP).

**Analysis**
Categorical variables were compared with Pearson Chi square tests and continuous variables with Mann-Whitney-U. A multivariate logistic regression analysis was performed with variables identified in univariate analysis with P values were < 0.2 or considered clinically relevant. IBM SPSS version 21 (Chicago, IL) was utilized for statistical analysis. A decision analysis was used to assess the most cost-effective treatment using TreeAge software (Williamstown, MA).

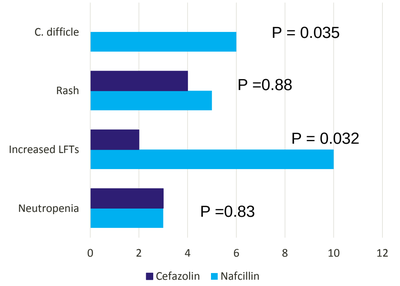
## Results

### Patient Characteristics

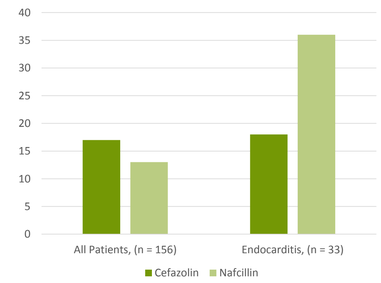



| Covariate | Cefazolin (N = 68) | Nafcillin (N = 81) | P value |
|---|---|---|---|
| Male, n (%) | 23 (33.8) | 47 (58) | 0.003 |
| Age, median [IQR] | 65 [61-68] | 54 [51-58] | < 0.001 |
| Comorbidities, n (%) | | | |
| Diabetes | 33 (44) | 29 (35.4) | 0.269 |
| Hypertension | 51 (68) | 49 (59.8) | 0.283 |
| Malignancy | 20 (26.7) | 17 (20.7) | 0.381 |
| Baseline SCr (mg/dL), median [IQR] | 0.93 [0.7-1.29] | 0.88 [0.74-1.03] | 0.242 |
| PITT bacteremia score ≥ 4, n (%) | 7 (9.4) | 13 (15.9) | 0.221 |
| Concomitant nephrotoxins, n (%) | | | |
| Acyclovir | 5 (7.4) | 3 (3.7) | 0.325 |
| Aminoglycosides | 5 (7.4) | 10 (12.3) | 0.313 |
| Loop diuretics | 26 (36.8) | 25 (30.9) | 0.447 |
| Vasopressor | 2 (2.9) | 8 (9.9) | 0.092 |

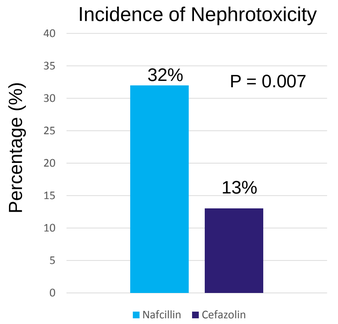
### Adverse Effects




### Clinical Failure



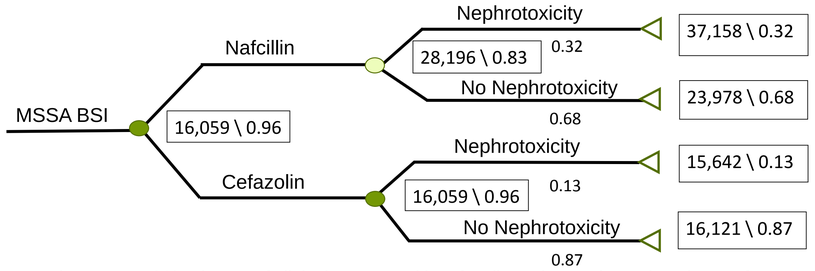

### Nephrotoxicity




| Variable | Crude OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|
| Nafcillin | 3.1 (1.3-7.2) | 2.7 (1.1-6.6) |
| Endocarditis | 3.3 (1.4-7.7) | 2.8 (1.2-6.8) |
| ICU Admission | 3.3 (1.5-7.3) | 2.9 (1.3-6.8) |
| PITT bacteremia score ≥ 4 | 0.85 (0.3-2.8) | Not tested |
| ≥ 1 Concomitant Nephrotoxin* | 1.03 (0.5-2.2) | Not tested |

*Concomitant nephrotoxin includes one of the following: acyclovir, aminoglycoside, loop diuretic, vancomycin, or vasopressor.

### Cost Comparison: Nafcillin vs Cefazolin for MSSA BSI




- There was a 96% chance of clinical success with cefazolin and an estimated total cost of $16,059 compared with 83% and $28,195 for nafcillin. Cefazolin was found to be dominant therefore the incremental cost effectiveness ratio could not be calculated

## Summary

- This study identified that first-generation cephalosporins may have a more favorable side effect profile due to less nephrotoxicity compared with nafcillin therapy.
- There is a lower average wholesale price for cefazolin than nafcillin; however, drug acquisition cost is a minor component on overall cost burden.
- Patients who experienced AKI had a longer length of stay in the intensive care unit, contributing to a larger difference in overall costs between the agents.
- Considering the safety profile and lower acquisition cost of cefazolin, it may be considered as a preferred therapy to nafcillin for patients with MSSA bacteremia without endocarditis or central nervous system involvement.

Disclosure Statement: The authors do not have any conflicts of interest in relation to the presentation of this data