

# EFFECT OF ANTIBIOTIC PROPHYLAXIS ON POST- OPERATIVE WOUND INFECTION IN CARDIAC SURGERY

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## ABSTRACT

Patients who underwent cardiovascular surgery were monitored for the emergence of infection after the procedure. Group received non-extracorporeal treatments, while Group had open-heart surgeries. Two groups were compared for infection rates after receiving preventive antibiotics. Starting one day before to surgery (period), patients (n = 253) were given ampicillin alone or in conjunction with gentamicin. In period B, 135 patients were given cefazolin alone or in conjunction with gentamicin beginning 30 minutes before induction. Patients in Group 1 had a 4.2 percent infection rate in Period A and a 3.5 percent infection rate in Period B, while patients in Group 2 had a 25.7 percent and an 18.7 percent infection rate. A total of 13% of people became infected. One to five sites of infection were present per affected individual. Most common were infections of the urinary tract, then those of the respiratory system, the skin, and the wounds. In both time periods, the vast majority of pathogens (47 out of 70 isolates) were Gram-negative rods (*Klebsiella* spp. and *Pseudomonas aeruginosa*). Gram-positive cocci were more common in period A wound infections than they were in period B. Three occurrences of fungal endocarditis were reported during period B, whereas none were reported during period A. There was a trend toward lower infection rates during cefazolin prophylaxis, but the results were not statistically significant.

**Keywords:** *antibiotic prophylaxis, cardiac surgery*

## INTRODUCTION

Antibiotic prophylaxis has been crucial in ensuring the safety of patients undergoing procedures such as heart surgery since the discovery of antibiotics. Nonetheless, despite worldwide efforts, the mechanisms of antibiotic prophylactic delivery remain largely unchanged 80 years later. When it comes to preventing surgical site infections (SSIs), anti-staphylococcal penicillin's or first/second-generation cephalosporins have been shown to be more effective than vancomycin in many cardiac surgery studies. This is especially true for SSIs caused by methicillin-susceptible staphylococci. It's possible that vancomycin's diminished bactericidal action and less-than-optimal penetration into mediastinal tissues during heart surgery under cardiopulmonary bypass explain this outcome. Despite this, when the period of dosage was kept constant across studies, researchers found little to differentiate between the two antibiotic protocols. Furthermore, investigations have shown that the time of vancomycin injection is important, with a higher risk of SSI in situations of delayed administration. Finally, vancomycin and gentamicin are used together in our facility to broaden the range of prophylaxis and specifically target Gram-negative bacterial infections. Interestingly, there haven't been many research comparing the effectiveness of cephalosporins to that of vancomycin and gentamicin.

Our single-center retrospective study's goal was to determine whether or not the antibiotic combination of vancomycin and gentamicin (VGA) is an effective replacement for cephalosporins (CA) in the prevention of SSI during cardiopulmonary bypass (CPB).

Antibiotic prophylaxis is guided by three main tenets: the antibiotic chosen, when it should be given for the first time, and how long the treatment should continue. Second-generation cephalosporins, in particular, have various benefits over other antibiotic options when it comes to making the decision of the antimicrobial agent. They are effective against both gram-positive and gram-negative bacteria and have a wide range of tissue penetration. In addition, people with penicillin allergies can use them safely because they have a low risk of negative effects. Although effective, cephalosporins have long been linked to a higher risk of *Clostridium difficile* infection. Studies have shown an increase in the use of second-generation cephalosporins in antibiotic prescriptions. Antibiotic prophylaxis with a second-generation cephalosporin is also advised for patients having heart surgery, according to the German Paul-Ehrlich-Gesellschaft e.V. (PEG).

There is a lack of consistency in the data from worldwide guidelines and recommendations for antibiotic prophylaxis in patients undergoing adult heart surgery about the length of the preventive regimen. Preoperative antibiotic prophylaxis, including supplemental use for lengthy procedures, is recommended in the 2011 American College of Cardiology Foundation/American Heart Association recommendation for coronary artery bypass graft surgery. Since the best length of prophylaxis is not delineated by the facts, even the PEG suggestion for the duration is based solely on consensus of the expert panel. For cardiothoracic surgeries, the panel recommends prophylaxis for no more than 24 hours beforehand. Neither a single dosage nor a regimen lasting more than 48 hours is generally recommended. Antibiotic prophylaxis is routinely used in all German heart surgery clinics, as proven by Gorski et al. in a statewide questionnaire given to all German heart surgery centers about antibiotic prophylaxis in adult cardiac surgery patients. However, there was wide variation in antibiotic prophylaxis duration strategies among adults undergoing heart surgery. Twenty-three percent use a one-time prophylactic dose, twenty-nine use it for 16 hours, twenty-seven use it for 24 hours, thirteen use it for 32 hours, and eight use it for 40 hours.

It is recommended by most standards that prophylaxis for cardiothoracic surgeries be limited to 48 hours at most. This provides an overview of the various worldwide recommendations for antibiotic prophylaxis for patients undergoing cardiac surgery.

Nosocomial infections following heart surgery have been reported at rates ranging from 2.7% to 26.8% in recent studies. They are major problems that cause a lot of harm, both physically and financially. Therefore, it is generally agreed that cardiac surgery patients should get perioperative antibiotic prophylaxis, however the optimal length of this treatment is still up for debate. Reduced toxicity, reduced selection of resistant organisms, decreased risk of *Clostridium difficile* infection, and decreased risk of postoperative complications have all contributed to a shift toward shorter doses of antibiotics for surgical prophylaxis. When compared to identical illnesses caused by antibiotic-sensitive organisms, hospital mortality rates are much higher when antibiotic-resistant infections occur. The danger of infection is increased, however, since cardiac surgery patients often leave the operating theater with indwelling chest catheters and central venous and arterial lines.

## **OBJECT**

1. Infections after heart surgery: a prospective investigation

2. Vancomycin and gentamicin (VGA), the antibiotic combination under investigation, might be a viable solution

## RESEARCH METHODOLOGY

"Cardiothoracic," "open," and "prophylactic." To create a list of trials suitable for meta-analysis, we used a bibliographic database (End-Note, version 1.2.1, Berkeley, California) on a Macintosh IIfx personal computer (Apple Inc., Cupertino, California) to cross-reference the citations from the articles found through this search and the major review articles in the field<sup>20</sup>. Traditional methods of literature searching and cross-referencing were used until no more references could be found. Included studies had to compare at least two antibiotic regimens (or placebo) where prophylaxis was administered preoperatively and extended for a brief period of time after the operation, and studies had to be published between 1960 and 1990 with a total sample size of at least 30 human patients. Furthermore, the authors had to supply enough information to assess the allocation and results of individual patients. The meta-analysis didn't include retrospective evaluations, unpublished data, or papers written in languages other than English. It also didn't include review articles, textbook chapters, case reports, abstracts, letters to the editor, editorials, or commentaries. Additional criteria for research exclusion were inadequate methodological explanation for design validation.

If all other criteria were satisfied, the principal authors were contacted to explain results. Each study was evaluated separately to establish if it fulfilled the inclusion criteria of the procedure. For each study, researchers extracted information on the incidence of main sternal wound and vascular (saphenous vein or internal mammary artery harvest site) infection. Mehta, Patel, and Greg<sup>26</sup>'s approach was implemented in the Epiinfo software package (USD, Inc., version 3.0, Stone Mountain, Ga.), which was utilized to calculate odds ratios and 95% precise confidence bounds. The visual technique provided by L'Abbe, Detsky, and O'Rourke was used to evaluate the consistency of treatment outcomes. The impact of investigator blinding, prophylactic duration, and antibiotic regimen on study combinability was analyzed using sensitivity analysis.

## DATA ANALYSIS

The literature search yielded more than 300 studies detailing viral outcomes in cardiothoracic procedures. Patients taking preventive antibiotics were studied 49 times, and the results of infectious complications were analyzed. Prospective design, random allocation of patients, and controlled comparison of at least two treatment regimens were the three inclusion criteria, which were satisfied by 28 studies examining 6759 patients. Fourteen of these studies, reporting on the outcomes of 4,404 patients, did not blind their investigators or failed to indicate how they did so. Twenty-one studies were ruled out because they did not satisfy the inclusion criteria outlined in the protocol. lack of randomization definition or use of a retrospective study descriptions of prophylaxis in the form of uncontrolled case series. Publication of duplicate abstracts or journal letters evaluating distinct treatment groups operated on by different surgical teams. German language publication of an analysis of using antibiotic creams topically rather than orally. F: Three studies' principal authors were contacted to clarify data.

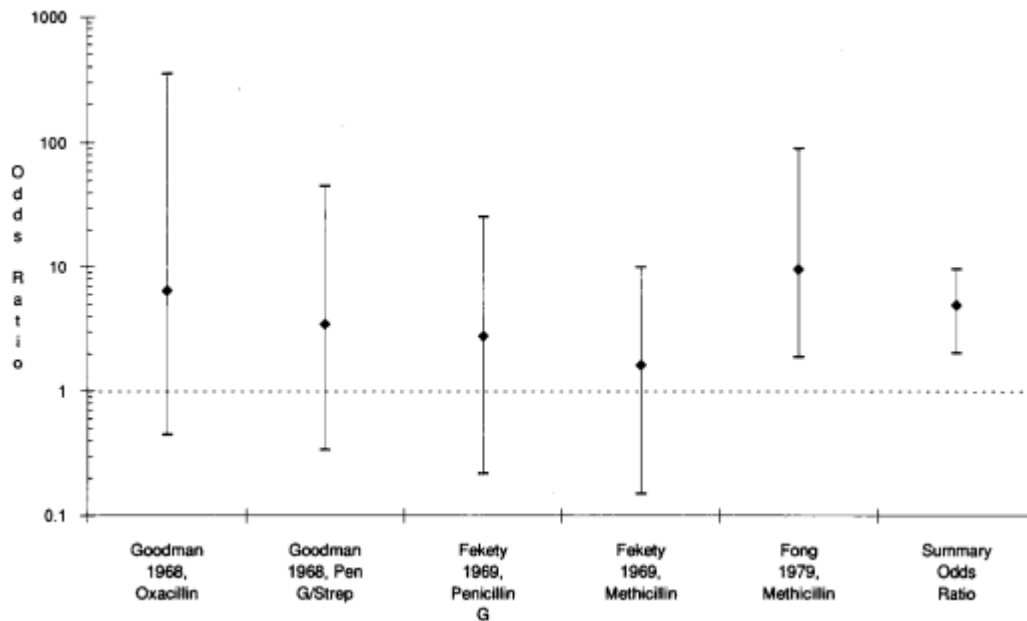
Studies where placebos were used. In all, 4 placebo-controlled trials including 405 patients were included in the meta-analysis.<sup>r</sup>- No information was provided to compare infection rates between wounds on the leg and those on the chest. Antibiotic prophylaxis' effect on the overall rate of infection in surgical wounds could be measured, nevertheless. In these investigations, wound infection rates in the placebo groups varied between 9.1% to 54.5%. Postoperative wound infection rates varied from 0% to 6.7% across all patient groups who received antibiotics,

demonstrating a consistent favorable treatment effect. The exact confidence intervals for the odds ratios, both for each individual and as a whole, are shown in Patients who received antibiotic prophylaxis had a statistically significant decreased risk of wound infection, with a summary odds ratio of 4.96 and lower and upper 95% precise confidence limits of 2.06 and 9.72, respectively. Comparatively, the wound infection rate dropped from around 20% to 25% in the placebo group to about 4% to 5% in the antibiotic group.

Prophylactic studies of varying lengths. There were four studies found that looked at the difference between short and lengthy courses of prophylactic antibiotics for a total of 466 individuals. All four trials employed cephalothin as the prophylactic cephalosporin, while one research used cephalothin in combination with kanamycin. In the short-term groups, doses and durations of cephalothin administration ranged from a single 1 gm dosage to 2 gm every 6 hours for 2 days. Two grams of cephalothin were given before surgery, and then either one or two grams were given every six hours for the next three days. Two of the trials were conducted before CABG was developed, and they did not track the incidence of infection in the legs. Two of the four trials showed a decreased risk of total wound infection in the short-duration therapy groups, but the difference was not statistically significant (summary odds ratio 0.89, lower 95% CI 0.28, upper 95% CI 2.75).

Prophylactic research comparing cephalosporin and ant staphylococcal penicillin combinations. Only six patient trials were found that directly compared the prophylactic use of an ant staphylococcal penicillin to that of a single cephalosporin; in five of these trials, the ant staphylococcal penicillin was coupled with either another penicillin or an aminoglycoside. Although no single trial attained statistical significance, results from five of the six suggested that patients treated with cephalosporin had fewer overall wound infections. Cephalosporin regimens appeared to be more effective than penicillin ones, with a summary odds ratio of less than . However, the precise 95% confidence intervals.

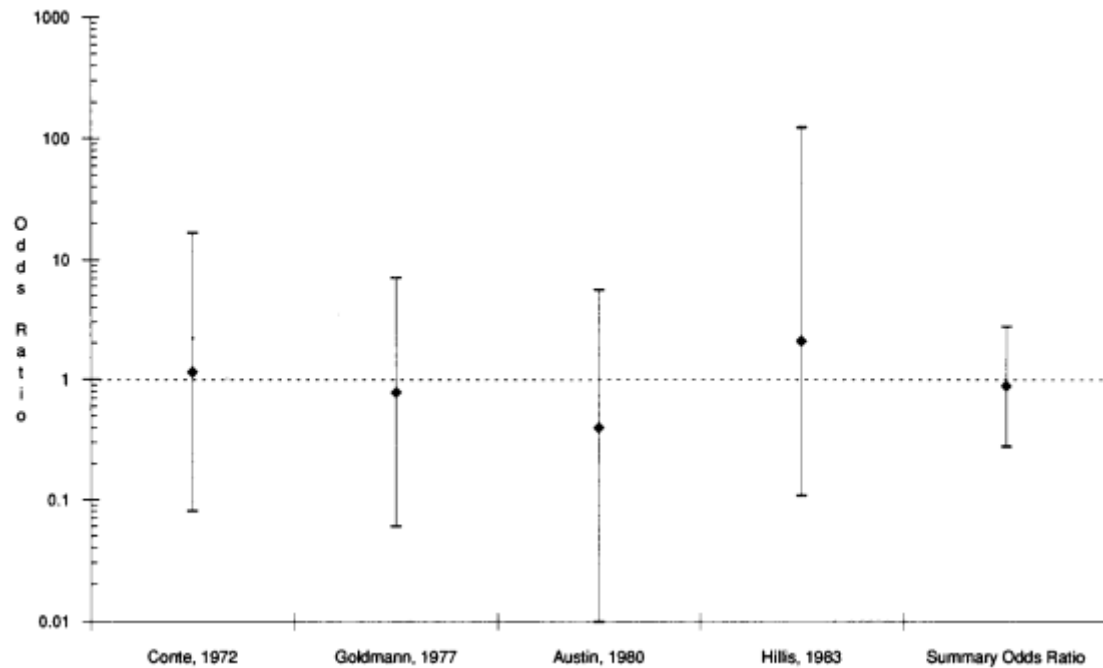
Research comparing cefazolin to cefamandole and cefuroxime. This meta-analysis includes results from six trials that directly compare cefazolin to either cefamandole or cefuroxime. Kaiser and colleagues removed patient data from their study if they used gentamicin as part of a prophylactic regimen using cefazolin or cefamandole. Since both Slama? and Gentry48 and their colleagues tested cefazolin, cefamandole, and cefuroxime in three-arm controlled trials, a total of eight comparison groups (2630 patients) were evaluated. After noticing a consistent pattern in favor of the second-generation cephalosporins, researchers pooled data from trials including cefamandole and cefuroxime. Patients treated with either cefamandole or cefuroxime did not fare differently, according to homogeneity tests. Patients treated with cefazolin had an overall wound infection rate between 2.5% and 16.7%, whereas those treated with cefamandole or cefuroxime had an infection rate between 0% and 13.5%.



**Fig. 1. Odds Ratios And 95% Exact Confidence Limits for Placebo-Controlled Trials of Prophylaxis in Cardiothoracic Operations**

The overall wound infection rate was lower in individuals treated with the second-generation cephalosporin in seven of the eight comparison groups. There were studies that measured sternum and leg wound infections. Seven out of eight treatment groups using either cefamandole or cefuroxime saw a decrease in sternal wound infection rates. In five of the eight groups given second-generation cephalosporin, the rate of infection in leg wounds decreased. Conklin and coworkers' research had a much higher overall wound infection rate than the other trials because of the high incidence of leg wound infections in both treatment groups.

Patients treated with cefuroxime fared worse than those treated with cefazolin for sternal wound infections, according to the study by Doubling and associates. In a meta-analysis comparing cefazolin to cefamandole and cefuroxime, no statistically significant differences were found between the infection sites of the sternum and the legs. However, a combined analysis of sternal and lower extremity wound infection rates produced a summary odds ratio of 1.58, with 95% precise confidence intervals of 1.03 and 2.45. This suggests that the use of a second-generation cephalosporin resulted in a one-and-a-half-fold reduction in total wound infection prevalence (to approximately 3%), despite the generally low wound infection rates found in cefazolin-treated patients (approximately 5% across the series) (Fig. 2).



**Fig. 2. Odds Ratios And 95% Exact Confidence Limits For short Versus Long Administration Of Antibiotic Prophylaxis In cardiothoracic Operations.**

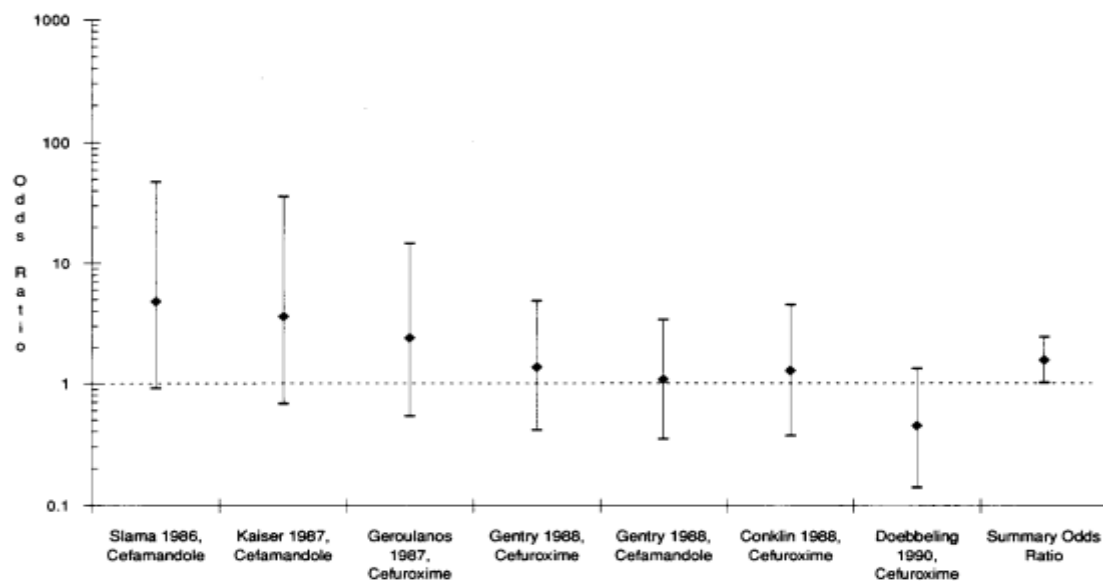
wound infection rates in the clindamycin group were lower for both the sternum and the legs. In a study including 512 patients, Gerolamo's et al. compared cefuroxime with ceftriaxone and found no significant differences in the overall wound infection rates (both 1.2%). When Kaiser and colleagues tested cefazolin and cefamandole, both of which included gentamicin, they discovered that the cefamandole/gentamicin group had significantly lower incidence of sternal and total wound infections. When comparing vancomycin with penicillin G, "Joyce and Schepisi" discovered that the vancomycin group had significantly fewer cases of wound infection overall. Unacceptably high sternal wound infection rates in the teicoplanin treatment group (21.5% to 28.0%) were found by Wilson and coworkers'"? evaluation of 517 patients receiving teicoplanin, in two dosage regimens, compared to a combination of flucloxacillin and gentamicin.

When results from multiple studies disagree with one another about the size or direction of an effect, when individual sample sizes are too small to detect an effect and label it statistically significant, or when a large trial would be too expensive and time-consuming to conduct, a meta-analysis can help. The rigorous, methodical, and repeatable nature of meta-analysis's subject review helps keep the "apples and oranges" dilemma of research integration at bay, but it's not without its detractors. Lack of statistical power, or the capacity to avoid error and reveal a difference between treatment groups where a difference genuinely exists, was the most significant methodological flaw in all published investigations of cardiothoracic prophylaxis.

The use of meta-analysis in these trials helps overcome the limitations of small sample numbers in previous research. The risk of postoperative infection following cardiothoracic surgery is low to begin with, and there is little room for improvement from one treatment protocol to the next. The sample size of 563 patients is estimated to be necessary to demonstrate a significant reduction in the clean surgical infection rate from 5% to 1% using the following parameters: power analysis ( $\alpha = 0.05$ ,  $\beta = 0.80$ ). The number of patients who may be enrolled in a study within a given time frame (often 1 to 2 years) once seemed to influence sample size. Incomplete reporting



of infections in individual patients was another major limitation of these investigations. The number of patients who had coronary artery bypass grafting (CABG), a prosthetic valve implanted, an atrial septal defect closed, or any combination of these procedures was seldom, if ever, reported.



**Fig. 3. Odds Ratios And 95% Exact Confidence Limits For Cefazolin Versus Cefuroxime Or Cefamandole Trials of Prophylaxis In Cardiothoracic Operations.**

different operations on the chest and heart. Neither elective nor emergency cardiothoracic procedures nor American Society of Anesthesiologists' preoperative morbidity classifications were used to stratify patients in any investigation. Whether or not postoperative infection rates change between CABG and valve repair is unclear given the available literature. Infection was defined quite differently between studies. Infections in the urinary system, genitourinary tract, and other organs were frequently reported using objective criteria, however these criteria differed from research to study. Antibiotic prophylaxis' impact on nosocomial infections, however, could not be assessed.

After randomization, different authors ruled invaluable a wide range of patient populations. The percentage of rejected patients varied between 0-31%. Minor protocol deviations were grounds for patient exclusion in certain research, whereas in another experiment no patients were removed from the study despite a 22% rate of protocol deviations. Some studies, especially those in which the principal investigator was not blinded, may have been affected by post hoc patient exclusions, which might distort the results. This may make the published studies of prophylactic outcome less relevant to actual practice, as the elimination of individuals who were "worst cases" may have predisposed to unfavorable findings. The severity of postoperative wound infections in these patients was thought to morally prevent any possibility of investigator bias in assigning infectious outcomes to a particular treatment group, hence blinding of investigators was not a requirement for study enrollment.

## CONCLUSION

Perioperative antibiotic prophylaxis for adult cardiac surgery patients can be reduced from 56 to 32 hours without increasing the risk of surgical site infection, nosocomial infection, or mortality, as shown by this observational study. This finding helps to reduce antibiotic resistance and healthcare costs. The incidence of SSI and associated

risk variables were consistent with the literature in this large, long-term cohort of consecutive patients. The most severely ill patients tended to employ VGA rather than CA. However, we did not discover evidence of an increased risk of SSI. Antibiotic prophylaxis was found to affect the microbial cultures of SSI in different ways. This means that VGA is a viable option for SSI avoidance. Additional research is required to verify these findings.

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