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Surgical Antibiotic Prophylaxis and Risk for Postoperative Antibiotic-Resistant Infections

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Abstract

Background—Antibiotic-resistant infections have high rates of morbidity and mortality and exposure to antibiotics is the crucial risk factor for development of antibiotic resistance. If surgical antibiotic prophylaxis (SAP) increases risk for antibiotic-resistant infections, prophylaxis may cause net harm even if it decreases overall infection rates.

Study Design—This retrospective cohort study included adults who underwent elective surgical procedures and developed infections within 30 post-operative days. Surgeries from multiple disciplines were included if SAP was considered discretionary by current guidelines. Postoperative antibiotic-resistant infections were defined as positive culture results from any site within 30 post-operative days showing intermediate or non-susceptibility across one or more antibiotic classes. SAP included use of antibiotics within any class and at any dose from one hour before first incision until the end of the operation.

Results—Among 689 adults with post-operative infections, 338 (49%) had post-operative resistant infections. Use of SAP was not associated with post-operative antibiotic-resistant infections (OR 0.99, 95% CI 0.67–1.46). This result remained robust when the SAP definition was extended to antibiotics given within 4 hours before first incision (OR 0.94, 95% CI 0.63–1.40) and when the follow-up window was narrowed to 14 days (OR 0.82, 95% CI 0.50–1.34). Prior

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antibiotic-resistant infections were associated with risk for post-operative antibiotic-resistant infections (OR 1.81, 95% CI 1.16–2.83).

Conclusion—Use of SAP was not associated with risk for post-operative antibiotic resistant infections in a large cohort of patients with post-operative infections. This provides important reassurance regarding use of surgical antibiotic prophylaxis.

INTRODUCTION

Surgical site infections (SSIs) are responsible for up to 20% of healthcare-acquired infections outside of the intensive care unit and are the most common cause of healthcare-acquired infections amongst surgical patients.(1) Surgical antibiotic prophylaxis (SAP) has been shown to decrease the risk of post-operative infections for a number of procedures across surgical disciplines.(2–4) For many procedures, however, the benefit of SAP is uncertain and the decision to use prophylaxis is at the discretion of the operating surgeon with a large degree of inter-operator variability.

Surgical antibiotic prophylaxis may lower overall infection rates but there is concern that it has the potential to cause harm. A single dose of SAP can increase antibiotic resistance within colonizing bacteria, and consequently SAP could contribute towards antibiotic-resistant infections.(5–7) In the United States, roughly 2 million people develop antibiotic-resistant infections each year. These infections are difficult to treat and have higher morbidity and mortality compared to non-resistant infections.(8, 9) Simultaneously, rates of post-operative infections for select procedures are low and have been getting progressively lower.(10–12)

If surgical antibiotic prophylaxis increases the risk for antibiotic-resistant infections, the potential harm of SAP may outweigh a modest overall reduction in rates of post-operative infections, particularly in procedures with traditionally low rates of post-operative infections. This study was performed to assess the relationship between use of SAP and development of post-operative antibiotic-resistant infections.

METHODS

Population

This was a retrospective cohort study. Adults 18 years old or more evaluated at an urban tertiary care hospital in New York were considered for the study if they had one of a specific list of elective surgical procedures between January 1, 2008 and December 31, 2016. We selected 2008 for the start of the study because it was the earliest date on which complete electronic data was available. For patients with multiple surgeries during the study period, only the first surgery was analyzed. We sought to include a broad list of different surgeries that encompassed as many surgical disciplines as possible and for which surgical antibiotic prophylaxis is considered discretionary according to current multi-society or specialty guidelines.(2, 5, 13–17) Surgical procedures were first identified by relevant coding (Supplementary Table 1), and then filtered using intelligent keyword searches to exclude situations in which multiple codes were used to describe various stages of a single operation (e.g., exploratory laparoscopy and partial pancreatectomy). The select surgical procedures

were also reviewed by a group of subject experts for accuracy and concordance with clinical practice behaviors.

Patients were included in the study if they had one of the pre-selected procedures and subsequently developed a post-operative infection within 30 days. Post-operative infection was defined as a post-operative culture from any site or fluid showing bacterial growth and speciation. Surveillance testing for colonization was not included in this definition. The cut-off of 30 days was chosen to balance the duration of the observed effect of single-dose antibiotics (up to 12 months)(18–20) with the assumption that any effect of antibiotics on bacterial resistance patterns would be likely to wane with the passage of time. To focus on incident rather than prevalent infections, patients who developed culture-positive infection within 24 postoperative hours were excluded. To ensure a minimum of follow-up time, patients were also excluded who died within 24 post-operative hours. This study protocol was approved by the institutional review board of Columbia University Medical Center.

Post-operative antibiotic-resistant infections

Post-operative antibiotic-resistant infections were defined as positive bacterial culture results from any site or fluid within 30 post-operative days showing intermediate susceptibility or non-susceptibility across one or more antibiotic classes using the clinical breakpoints from the . Clinical and Laboratory Standards Institute that were in effect at the time when the culture result was performed.(21, 22) Specialized cultures such as cultures performed from stool or vaginal samples were not included. In addition, the results of surveillance swabs or non-culture microbiological data (e.g., PCR or EIA results) were not included. All cultures were performed by a single clinical laboratory using standard techniques.

Primary exposure

The primary exposure was surgical antibiotic prophylaxis, defined as use of antibiotics within any class and at any dose given from 1 hour before first incision until the end of the operation. SAP was ascertained electronically from the provider order entry system; we captured antibiotics given in the pre-operative area as well as antibiotics given in the operating room. The cut-off of 1 hour was chosen based on current guidelines concerning the optimal timing for SAP and was further explored in sensitivity analyses.(5, 23, 24)

Covariates

Automated queries were used to retrieve demographic information, comorbidities using claims data (to compute the Charlson Comorbidity Index),(25, 26) and prior exposure to antibiotics and immunosuppressants (within 90 days of surgery). Immunosuppressants included steroids at a minimum dose of 5 mg of prednisone or equivalent, calcineurin inhibitors, antimetabolites, anti-tumor necrosis factor agents, and mycophenolate. Microbiological data from 90 days before each procedure was gathered including the originating site or fluid (e.g., urine), the organism, and the organism’s resistance pattern. Operative characteristics were captured including pre- and post-operative hospital admission and operative time. Hospital admission immediately before/after the index surgery was classified categorically based on whether there was an admission for ≥24 hours before the surgery or for ≥24 hours afterwards; we also examined whether there was an inpatient

hospitalization prior to the index surgery. Operative time was defined as the time from first incision until the time the patient left the room and was classified into approximate tertiles.

Statistical approach

Continuous variables were examined graphically so that appropriate cut-offs could be selected. Categorical variables were compared using the chi-squared test or Fisher's exact test when 5 or fewer events were expected in any category. The primary outcome was determined using logistic regression modeling to test risk for resistant versus non-resistant infections. We decided *a priori* that the multivariable model would include variables representing past exposure to antibiotics and representing operative time, because these variables are key potential confounders for the relationship between surgical antibiotic prophylaxis and post-operative antibiotic-resistant infections. To construct the final multivariable model, additional variables were tested stepwise and included if they had a significant independent relationship with the outcome of interest or if they altered the β-coefficient representing SAP by ≥10%. All analyses were performed using STATA statistical software version 14 (StataCorp, College Station, TX) at the $\alpha = .05$ level of significance.

Sensitivity analyses

The optimal dosing for surgical antibiotic prophylaxis is controversial.(23, 27) To test the robustness of our findings, we repeated the final model after extending the definition of SAP to include antibiotics given from 4 hours before first incision until the end of the procedure. Alternative follow-up timeframes and alternative definitions for antibiotic resistance have been used (22, 28, 29) so, as further tests of robustness, we repeated the final model with the follow-up window narrowed to 14 days and with post-operative antibiotic resistance re-defined as resistance in 3 or more antibiotic classes. To evaluate for the development of post-operative antibiotic resistance in a class-specific manner, we tested the 3 most commonly used prophylactic antibiotics for within-class post-operative resistance (e.g., use of cephalosporins and subsequent cephalosporin resistance). To further explore risk factors for post-operative urinary tract infections, we retrieved data related to the placement of indwelling urinary catheters intra-operatively or during the post-operative period. Selected stratified analyses and alternative cutoffs for continuous variables were also considered within the final model.

RESULTS

Population

There were 22,138 unique adults who had surgeries within the pre-selected categories between 2008 and 2016 and who met other inclusion criteria. Of these, 689 (3.1%) developed infections within 30 post-operative days and were analyzed.

Baseline and operative characteristics

Median time to infection was 10 days (IQR 5–19). Among those with post-operative infections, 550 (80%) subjects received surgical antibiotic prophylaxis. The most common classes of antibiotics used were cephalosporins, followed by piperacillin-tazobactam and gentamicin (Supplementary Table 2). Subjects who developed resistant compared to

nonresistant infections were more likely to have prior culture-proven infections (Table 1). The most common operations were cystoscopy, lymph node biopsy, and uncomplicated laparoscopic cholecystectomy (Table 2 and Supplemental Table 3). Most subjects did not require pre-operative hospital admission and most spent <24 post-operative hours in the hospital. Procedures were relatively brief with 56% of patients leaving the operating room within 2 hours after entering it.

Post-operative antibiotic-resistant infections

Urine was the most common culture source, accounting for 63% of all cultures (Table 3). The most commonly cultured organisms were *Escherichia coli*, *Enterococcus*, and *Klebsiella pneumoniae*. Among antibiotic classes, resistance was most often observed for penicillins, cephalosporins, and fluoroquinolones. Among organisms, high rates of resistance were seen within *Enterococcus* (72% of cultures showing resistance within ≥1 antibiotic class), *Proteus mirabilis* (70%), and *E. coli* (67%) (Supplementary Table 4).

Multivariable analysis

There was no difference in the rates of antibiotic resistance when we compared those who did versus those who did not receive surgical antibiotic prophylaxis (49% vs 47% respectively, p=0.68). In the final multivariable model, there was also no difference based on SAP after adjusting for potential confounders (OR 0.99, 95% CI 0.67–1.46, Table 4). The occurrence of a prior antibiotic resistant infection was the key predictor of a post-operative antibiotic resistant infection (OR 1.81, 95% CI 1.16–2.83).

Sensitivity analyses

We performed several tests to explore the robustness of our results. There was no change in the main result when the definition of surgical antibiotic prophylaxis was extended to include antibiotics received within 4 hours before first incision or during the operation (OR 0.94, 95% CI 0.63–1.40). There was also no change when the follow-up window was narrowed to 14 days (OR 0.82, 95% CI 0.50–1.34) or when the definition of resistant infections was narrowed to include only infections with resistance in ≥3 antibiotic classes (OR 1.53, 95% CI 0.90–2.60). There was no evidence of class-specific antibiotic resistance within the most-used antibiotic classes including cephalosporins (p=0.15), piperacillin-tazobactam (p=0.85), and vancomycin p=0.50). The relationship between SAP and resistant infections was unchanged when duration of prior hospitalization was organized into tertiles and included in the final model (OR 0.99, 95% CI 0.67–1.47). There was no change in the relationship of interest after excluding general surgical procedures (OR 1.07, 95% CI 0.67–1.69), or after excluding urological procedures (OR 0.98, 95% CI 0.61–1.56), or within the stratum of only urological or gynecological procedures (1.30, 95% CI 0.72–2.35). There was also no change after excluding cultures growing coagulase-negative *Staphylococcus* (OR 1.05, 95% CI 0.70–1.59). Finally, because many of the infections were urinary, we examined data related to the placement of indwelling urinary catheters. Again, no changes in the SAP-resistant infection relationship were seen when the presence or absence of an indwelling urinary catheter was included in the final model (OR 1.01, 95% CI 0.68–1.49).

DISCUSSION

In this large retrospective cohort study, use of surgical antibiotic prophylaxis was not associated with increased risk for post-operative antibiotic-resistant infection. This null finding was robust when SAP was operationalized differently, and also when the primary outcome was redefined to capture multi-drug resistant infections. There was no change in the relationship between SAP and post-operative antibiotic-resistant infection when results were stratified by type of surgical procedure, or after adjusting for known risk factors for infection such as the presence of an indwelling urinary catheter. The presence of prior antibiotic-resistant infection was the main predictor of post-operative antibiotic-resistant infection.

Previous studies have found that antibiotic use is associated with subsequent development of antibiotic resistance.(30–32) This finding is concerning because antibiotic-resistant infections are associated with increased morbidity and mortality, as well as longer and more expensive hospital stays.(9, 33) SAP is commonly used for procedures with relatively low risks for post-operative infection. If SAP is associated with even a slight increase in risk for post-operative antibiotic-resistant infections, this observation would become a significant factor in the risk-benefit equation for use of SAP. The lack of an association seen in this study provides important reassurance to surgeons who choose to use SAP for select procedures and also useful guidance for antibiotic stewardship programs seeking to minimize potentially harmful antibiotic use.

Single dose or short course antibiotics appear to have a lasting impact on the composition of the human gastrointestinal microbiome and on the development of colonization by antibiotic-resistant organisms.(34) Short course antibiotics decrease bacterial taxonomic richness and diversity within the distal gut for up to 12 months.(18, 19, 35, 36) Even single dose antibiotics seem to lead to increased rates of colonization with resistant organisms(7, 37) although there is some inconsistency between studies.(38) Notably, these studies have focused on changes in colonizing organisms rather than on the development of clinical infections with resistant pathogens. It is possible that although single dose antibiotics impact colonization with antibiotic-resistant organisms, this colonization does not develop into overt infection unless selective pressure from antibiotics is more prolonged.

The presence of a prior antibiotic-resistant infection was associated with increased risk for post-operative antibiotic-resistant infection. This is consistent with previous studies that support the utility of prior individual culture data in predicting subsequent antibiotic susceptibility patterns in both medical and Surg Infect (Larchmt).(39–41) Knowledge of an individual’s past culture data and related risk for antibiotic-resistant infection is a crucial part of appropriate antibiotic selection for a given patient.(40, 42, 43) A combined approach to SAP based on procedure-specific risks in conjunction with a patient’s own prior culture data could potentially serve to improve clinical outcomes.

Notably, the current study was restricted to patients who had culture-proven infections in the post-operative period (i.e., rates of SAP were compared in patients with antibiotic-resistant versus non-resistant infections rather than comparing rates in patients with antibiotic-

resistant infections versus no infections). We believe that this approach minimizes the potential for confounding due to baseline patient differences because it eliminates loss to follow-up and ensures relative homogeneity within the population (in all patients, there was some kind of postoperative infection). Additionally, our analysis accounted for the major factors likely to influence the risk of post-operative antibiotic-resistant infection and was performed within a large cohort.

Adherence rates to guidelines for SAP are 53% to 83% depending on which aspect of guidelines are being interrogated.(44, 45) Many surgeons use SAP when it is not indicated(46, 47) and many also fail to give antibiotics when they are indicated.(45) This study focused on procedures where use of SAP is considered discretionary according to current guidelines and on procedures with low baseline rates of post-operative infections; the results should not be generalized to types of procedures that were not included in the analysis. There are other limitations to the study. Although the study was large, we cannot completely exclude the possibility that use of SAP is associated with a modest increase in post-operative antibiotic-resistant infections. We took into account a broad variety of potential confounders but we were unable to assess the potential effects of socioeconomic status or post-operative adherence to follow up recommendations. This was a single center study, and it is possible that results could differ in a different patient population or hospital environment. Finally, our approach assumes that positive culture results in post-operative patients represent clinically relevant infections. This approach was chosen to address the underlying mechanistic question: is a single dose of SAP sufficient to cause antibiotic resistance? Alternative approaches should be considered in future studies.

CONCLUSIONS

Use of surgical antibiotic prophylaxis for low-risk procedures was not associated with risk for post-operative antibiotic-resistant infection in this large retrospective cohort of patients with post-operative infections. There was no association between SAP and antibiotic-resistant infection risk in multiple sensitivity analyses. A history of prior antibiotic-resistant infection was the main predictor of post-operative antibiotic-resistant infection risk. When SAP is used in patients with this history, antibiotics should be selected based on prior culture results. Such patients may also merit closer post-operative monitoring for infection. Fear of antibiotic resistance should not drive the decision whether or not to use SAP.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public health reports (Washington, DC: 1974). 2007 Mar-Apr; 122(2):160–6.
2. Nelson RL, Gladman E, Barbateskovic M. Antimicrobial prophylaxis for colorectal surgery. Cochrane Database Syst Rev. 2014 May 09.(5):Cd001181. [PubMed: 24817514]

3. Baum ML, Anish DS, Chalmers TC, et al. A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. N Engl J Med. 1981 Oct 01; 305(14):795–9. [PubMed: 7266633]

4. Hasselgren PO, Ivarsson L, Risberg B, Seeman T. Effects of prophylactic antibiotics in vascular surgery. A prospective, randomized, double-blind study. Ann Surg. 1984 Jul; 200(1):86–92. [PubMed: 6375599]

5. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt). 2013 Feb; 14(1):73–156. [PubMed: 23461695]

6. Roberts NJ, Douglas RG. Gentamicin Use and Pseudomonas and Serratia Resistance: Effect of a Surgical Prophylaxis Regimen. Antimicrob Agents Chemother. 1978 Feb; 13(2):214–20. [PubMed: 348094]

7. Khalil D, Hultin M, Rashid MU, Lund B. Oral microflora and selection of resistance after a single dose of amoxicillin. Clin Microbiol Infect. 22(11):949.e1–.e4.

8. Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011–2014. Infect Control Hosp Epidemiol. 2016 Nov; 37(11):1288–301. [PubMed: 27573805]

9. Neidell MJ, Cohen B, Furuya Y, et al. Costs of Healthcare- and Community-Associated Infections With Antimicrobial-Resistant Versus Antimicrobial-Susceptible Organisms. Clin Infect Dis. 2012 Sep; 55(6):807–15. [PubMed: 22700828]

10. Ruangsin S, Laohawiriyakamol S, Sunpaweravong S, Mahattanobon S. The efficacy of cefazolin in reducing surgical site infection in laparoscopic cholecystectomy: a prospective randomized double-blind controlled trial. Surg Endosc. 2015 Apr; 29(4):874–81. [PubMed: 25052130]

11. Chang WT, Lee KT, Chuang SC, et al. The impact of prophylactic antibiotics on postoperative infection complication in elective laparoscopic cholecystectomy: a prospective randomized study. Am J Surg. 2006 Jun; 191(6):721–5. [PubMed: 16720138]

12. Harmanli O, Boyer RL, Metz S, et al. Double-blinded randomized trial of preoperative antibiotics in midurethral sling procedures and review of the literature. Int Urogynecol J. 2011 Oct; 22(10): 1249–53. [PubMed: 21789661]

13. Bryson DJ, Morris DL, Shivji FS, et al. Antibiotic prophylaxis in orthopaedic surgery: difficult decisions in an era of evolving antibiotic resistance. Bone Joint J. 2016 Aug; 98-b(8):1014–9. [PubMed: 27482011]

14. Gynecologists ACoOa. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. Obstet Gynecol. 2009; 113:1180–9. [PubMed: 19384149]

15. Ottoline ACX, Tomita S, Marques MPC, et al. Antibiotic prophylaxis in otolaryngologic surgery. Int Arch Otorhinolaryngol. 2013 Jan; 17(1):85–91. [PubMed: 25991999]

16. Wolf JS Jr, Bennett CJ, Dmochowski RR, et al. Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. J Urol. 179(4):1379–90.

17. Avenia N, Sanguinetti A, Cirocchi R, et al. Antibiotic prophylaxis in thyroid surgery: a preliminary multicentric Italian experience. Ann Surg Innov Res. 2009 Aug 05.3:10. [PubMed: 19656389]

18. Zaura E, Brandt BW, Teixeira de Mattos MJ, et al. Same Exposure but Two Radically Different Responses to Antibiotics: Resilience of the Salivary Microbiome versus Long-Term Microbial Shifts in Feces. mBio. 2015 Nov 10; 6(6):e01693–15. [PubMed: 26556275]

19. Dethlefsen L, Huse S, Sogin ML, Relman DA. The Pervasive Effects of an Antibiotic on the Human Gut Microbiota, as Revealed by Deep 16S rRNA Sequencing. PLOS Biology. 2008; 6(11):e280. [PubMed: 19018661]

20. Buffie CG, Jarchum I, Equinda M, et al. Profound alterations of intestinal microbiota following a single dose of clindamycin results in sustained susceptibility to Clostridium difficile-induced colitis. Infect Immun. 2012 Jan; 80(1):62–73. [PubMed: 22006564]

21. (CLSI) CaLSI. CLSI Supplement M100. 27. 2017. Performance standards for antimicrobial susceptibility testing.

22. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for

acquired resistance. Clin Microbiol Infect: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2012 Mar; 18(3):268–81.

23. Hawn MT, Richman JS, Vick CC, et al. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. JAMA surgery. 2013 Jul; 148(7):649–57. [PubMed: 23552769]
24. Weber WP, Mujagic E, Zwahlen M, et al. Timing of surgical antimicrobial prophylaxis: a phase 3 randomised controlled trial. Lancet Infect Dis. 2017 Apr 03.
25. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5):373–83. [PubMed: 3558716]
26. Salmasian H, Freedberg DE, Friedman C. Deriving comorbidities from medical records using natural language processing. J Am Med Inform Assoc. 2013 Dec; 20(e2):e239–42. [PubMed: 24177145]
27. Classen DC, Evans RS, Pestotnik SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med. 1992 Jan 30; 326(5):281–6. [PubMed: 1728731]
28. Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. Infect Control Hosp Epidemiol. 2013 Jan; 34(1):1–14. [PubMed: 23221186]
29. Garner JS. The Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. Infect Control Hosp Epidemiol. 1996 Jan; 17(1):53–80. [PubMed: 8789689]
30. Bell BG, Schellevis F, Stobberingh E, et al. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. BMC Infect Dis. 2014; 14:13. [PubMed: 24405683]
31. Bidell MR, Opraseuth MP, Yoon M, et al. Effect of prior receipt of antibiotics on the pathogen distribution and antibiotic resistance profile of key Gram-negative pathogens among patients with hospital-onset urinary tract infections. BMC Infect Dis. 2017 Feb 28.17(1):176. [PubMed: 28241755]
32. McGowan JE. Is antimicrobial resistance in hospital microorganisms related to antibiotic use? Bull N Y Acad Med. 1987 Apr; 63(3):253–68. [PubMed: 3300827]
33. Paramythiotou E, Routsi C. Association between infections caused by multidrug-resistant gram-negative bacteria and mortality in critically ill patients. World J Crit Care Med. 2016 May 04; 5(2): 111–20. [PubMed: 27152254]
34. Blaser MJ. Antibiotic use and its consequences for the normal microbiome. Science (New York, NY). 2016 Apr 29; 352(6285):544–5.
35. Dethlefsen L, Relman DA. Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation. Proc Natl Acad Sci U S A. 2011 Mar 15; 108(Supplement 1):4554–61. [PubMed: 20847294]
36. De La Cochetière MF, Durand T, Lepage P, et al. Resilience of the Dominant Human Fecal Microbiota upon Short-Course Antibiotic Challenge. J Clin Microbiol. 2005 Nov; 43(11):5588–92. [PubMed: 16272491]
37. Archer GL, Armstrong BC. Alteration of staphylococcal flora in cardiac surgery patients receiving antibiotic prophylaxis. J Infect Dis. 1983 Apr; 147(4):642–9. [PubMed: 6601682]
38. Bloomfield MG, Page MJ, McLachlan AG, et al. Routine ertapenem prophylaxis for transrectal ultrasound-guided prostate biopsy does not select for carbapenem-resistant organisms: a prospective cohort study. J Urol. 2017 Mar 10.
39. MacFadden DR, Ridgway JP, Robicsek A, et al. Predictive utility of prior positive urine cultures. Clin Infect Dis. 2014 Nov 01; 59(9):1265–71. [PubMed: 25048850]
40. Linsenmeyer K, Strymish J, Gupta K. Two Simple Rules for Improving the Accuracy of Empiric Treatment of Multidrug-Resistant Urinary Tract Infections. Antimicrob Agents Chemother. 2015 Dec; 59(12):7593–6. [PubMed: 26416859]

41. Fong ZV, McMillan MT, Marchegiani G, et al. Discordance Between Perioperative Antibiotic Prophylaxis and Wound Infection Cultures in Patients Undergoing Pancreaticoduodenectomy. JAMA surgery. 2016 May 01; 151(5):432–9. [PubMed: 26720272]

42. Frakking FN, Rottier WC, Dorigo-Zetsma JW, et al. Appropriateness of empirical treatment and outcome in bacteremia caused by extended-spectrum-beta-lactamase-producing bacteria. Antimicrob Agents Chemother. 2013 Jul; 57(7):3092–9. [PubMed: 23612198]

43. Ortega M, Marco F, Soriano A, et al. Analysis of 4758 Escherichia coli bacteraemia episodes: predictive factors for isolation of an antibiotic-resistant strain and their impact on the outcome. J Antimicrob Chemother. 2009 Mar; 63(3):568–74. [PubMed: 19126669]

44. Bull AL, Russo PL, Friedman ND, et al. Compliance with surgical antibiotic prophylaxis--reporting from a statewide surveillance programme in Victoria, Australia. J Hosp Infect. 2006 Jun; 63(2):140–7. [PubMed: 16621135]

45. Miliani K, L'Heriteau F, Astagneau P. Non-compliance with recommendations for the practice of antibiotic prophylaxis and risk of surgical site infection: results of a multilevel analysis from the INCISO Surveillance Network. J Antimicrob Chemother. 2009 Dec; 64(6):1307–15. [PubMed: 19837713]

46. Graham HE, Vasireddy A, Nehra D. A national audit of antibiotic prophylaxis in elective laparoscopic cholecystectomy. Ann R Coll Surg Engl. 2014 Jul; 96(5):377–80. [PubMed: 24992423]

47. Wright JD, Hassan K, Ananth CV, et al. Use of guideline-based antibiotic prophylaxis in women undergoing gynecologic surgery. Obstet Gynecol. 2013 Dec; 122(6):1145–53. [PubMed: 24201674]

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Table 1

Baseline Characteristics, Stratified by Resistant vs NonResistant Postoperative Infection

Characteristic	All	Resistant infection		Non-resistant infection		p Value
		n	%	n	%	
Sex						.91
Male	286	141	49	145	51	
Female	403	197	49	206	51	
Age						.22
18 to 42 y	111	54	49	57	51	
43 to 60 y	170	74	44	96	56	
>60 y	408	210	51	198	49	
Race/ethnicity						.71
White	263	122	46	141	54	
Black	49	24	49	25	51	
Hispanic	170	88	52	82	48	
Other/unclassified	207	104	50	103	50	
Charlson Comorbidity Index						.44
0	337	167	50	170	50	
1	127	56	44	71	56	
≥2	225	115	51	110	49	
Prior exposure to antibiotics *						.99
No	526	258	49	268	51	
Yes	163	80	49	83	51	
Prior exposure to immunosuppressants *						.37
No	613	297	48	316	52	
Yes	76	41	54	35	36	
Inpatient hospitalization prior to the index surgery *						.35
No	664	328	49	336	51	
Yes	25	10	40	15	60	

Characteristic	All	Resistant infection		Non-resistant infection		p Value
		n	%	n	%	
Prior VRE colonization*						0.11
No	683	333	49	350	51	
Yes	6	5	83	1	17	
Prior MRSA colonization*						0.44
No	683	334	49	349	51	
Yes	6	4	67	2	33	
Prior culture-proven infection*						.04
None	487	231	47	256	53	
Sensitive	94	42	45	52	55	
Resistant ≥1 antibiotic class	108	65	60	43	40	

*Within the 90 days preceding surgery.

VRE, vancomycin-resistant Enterococcus faecium

Table 2

Operative Characteristics, Stratified by Resistant versus NonResistant Postoperative Infection

Characteristic	All	Resistant infection		Non-resistant infection		p Value
		n	%	n	%	
Preoperative admission for the index surgery						
No	503	242	48	261	52	.41
Yes	186	96	52	90	48	
Procedure type						
Endocrine surgery	27	14	52	13	48	
General surgery	3	83	51	81	49	
Gynecology	164	30	36	53	64	
Hand surgery	83	2	40	3	60	.12
Lymph node biopsy	5	77	47	88	53	
Orthopedic	165	15	58	11	42	
Otolaryngology	26	3	100	0	0	
Urology	216	114	53	102	47	
Operative time *						
<60 minutes	172	79	46	93	54	.40
60 to100 minutes	79	79	47	89	53	
>100 minutes	180	180	52	169	48	
Postoperative admission immediately after the index surgery						
No	344	163	47	181	53	.38
Yes	345	175	51	170	49	

* Defined as the time from first incision to when the patient left the room.

Table 3

Postoperative Culture Results

Characteristic	Total	
	n	%
Source		
Blood	75	11
Respiratory	30	4
Urine	432	63
Wound	67	10
Tissue/other fluid	85	12
Organism		
Acinetobacter	8	1
Escherichia coli	172	25
Enterobacter	38	6
Enterococcus	128	19
Klebsiella pneumoniae	72	10
Proteus mirabilis	27	4
Pseudomonas aeruginosa	37	5
Staphylococcus Aureus	52	8
Staphylococcus Epidermidis	21	3
Staphylococcus (coagulase negative)	71	10
Stenotrophomonas	2	0
Streptococcus Pneumoniae	38	6
Streptococcus (Group B)	37	5
Resistance pattern		
Amikacin	4	1
Aminoglycosides	42	6
Carbapenems	6	1
Cephalosporins (1st or 2nd generation)	95	14
Cephalopsporins (3rd or 4th generation)	47	7
Glycopeptides	15	2
Fluoroquinolones	109	16
Lincosamides	17	2
Macrolides	40	6
Monobactams	30	4
Nitroimidazoles	32	5
Penicillins	160	23
Penicillins/β-lactamase inhibitors	99	14
Polymixin	2	0

Characteristic	Total	
	n	%
Sulfa-based	91	13
Rifamycins	2	0
Tetracyclines	71	10

Table 4

Multivariable Model for Risk for Postoperative Antibiotic-Resistant Compared to Antibiotic-Sensitive Infection

Characteristic	Subjects with resistant infections/total exposed		Odds ratio (95% CI)
	n	%	
Surgical antibiotic prophylaxis			
No, N=139	66	47	Reference
Yes, N=550	272	49	0.99 (0.67–1.46)
Prior exposure to antibiotics *			
No, N=526	258	49	Reference
Yes, N=163	80	49	0.90 (0.62–1.31)
Prior culture-proven infection *			
None, N=487	231	47	Reference
Sensitive, N=94	42	45	0.95 (0.60–1.50)
Resistant ≥1 antibiotic class, N=108	65	60	1.81 (1.16–2.83)
Operative time †			
<60 minutes, N=172	79	46	Reference
60 to 100 minutes, N=168	79	47	1.05 (0.68–1.62)
>100 minutes, N=349	180	52	1.31 (0.89–1.93)

* Within the 90 days preceding surgery

† Defined as the time from first incision to when the patient left the room.