# How the COVID-19 pandemic changed postoperative infections in urology wards: A retrospective cohort study from two urology departments

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## Abstract

**Introduction:** We aimed to compare the rate of postoperative infection and drug-resistant organism (DRO) before and during the COVID-19 pandemic in urology departments.
**Methods:** A retrospective cohort study was carried out. Data from all elective surgical procedures carried out in two urology departments between April and June 2018 and the homologous period in 2020 were collected. Main outcomes were the number of postoperative infections during the pandemic and the number of DROs. Sample size was calculated based on a 50% relative reduction of infections during the pandemic. Variables were compared by Chi-squared test, and multivariable logistic regression was used to estimate predictors.
**Results:** A total of 698 patients undergoing elective surgery were included. The postoperative infection rate during the pre-pandemic period was of 14.1% compared to 12.1% during the pandemic (p=0.494). DROs were lower during the pandemic (92.3% vs. 52.4%, p=0.002). The pandemic period was the main predictor for reduced multidrug-resistant isolates, with an odds ratio of 0.10 (p=0.010, 95% confidence interval 0.016–0.57).
**Conclusions:** Postoperative infection rates were not significantly reduced during the COVID-19 pandemic, despite the adoption of enhanced infection preventive measures. There was, however, a decrease in the rate of DROs during this period, suggesting a secondary benefit to enhanced infection prevention practices adopted during the COVID-19 era.

## Introduction

Hospital-acquired infections (HAIs) represent a global healthcare crisis, contributing to patient morbidity and mortality.[1] According to the European Centre for Disease Prevention and Control (ECDC), HAIs represent a significant burden among infectious diseases and are increasingly caused by multidrug-resistant microorganisms.[2,3]

In response to the COVID-19 pandemic, hospitals had to reorganize wards, postpone elective procedures, and cancel non-urgent activities. Measures to limit the spread of the disease included restrictions to patient's visitors, avoidance of street clothes by healthcare professionals, frequent object disinfection, and improved hand hygiene — all protocols that were followed in both hospitals included in our analysis.[4] Some of these measures have been shown to lower the rate of HAIs;[5,6] however, little is known about the overall impact of the pandemic on nosocomial infections. Some reports observed an increase in HAIs, such as those associated with central lines.[7] Others postulate that while some types of HAIs may increase, surgical site infections might be lower, as surgical room turnover decreases.[8]

We hypothesized that the occurrence of postoperative infection during the pandemic would be lower, particularly in surgical departments, as a consequence of COVID-19 preventive measures. The objective of this study was to compare the rate of postoperative infections and patterns of antimicrobial resistance before and during the pandemic in urology departments.

## Methods

An observational, retrospective cohort study was carried out. Centers participating in this study were the Centro Hospitalar e Universitario do Porto, a university teaching hospital, and Centro Hospitalar Tâmega e Sousa, a secondary care hospital, both localized in the northern region of Portugal. Simulations from Pekar et al define the period between October and November 2019 as the plausible interval when the first case of SARS-CoV-2 emerged.[9] As such, data from 2018 were used as the control group; all elective surgical procedures between April and June 2018 and the homologous period in 2020 (encompassing the peak of the first wave) were collected through patient record consultation. Ambulatory surgical patients were not included in the analysis, as they tend to have a short exposure time to healthcare facilities and mainly included those admitted for simple scrotal or penile surgery, with low complication rates. Non-elective, urgent surgeries, such as ureteral stenting or nephrotomy tube placement, were excluded since they comprised of patients referred from other emergency departments (for lack of emergent urological care) who were subsequently transferred back to their original hospital, hindering data analysis.

### Definitions and variables

Patient data included age, sex, level of care (secondary care vs. university teaching hospital), postoperative in-hospital length of stay, American Society of Anaesthesiologist (ASA) score, type of procedure, perioperative antibiotic prophylaxis, preoperative urine cultures, perioperative use of medical devices, postoperative infections, microbial culture (including blood, urine, and surgical drain or wound exudate), and antimicrobial susceptibility testing.

Patients were considered to have a medical device only when they were admitted or discharged with such devices in place (such as double-J stents, testicular prosthesis, urethral slings, or urinary catheters).

Prolonged antibiotic prophylaxis was defined as antibiotic coverage for more than 24 hours after surgery. Standard antibiotic coverage included prophylaxis initiated within one hour before surgery and up to 24 hours postoperatively.

Postoperative infection was defined as any infection occurring up to 30 days after a surgical procedure in a hospitalized patient, according to the ECDC protocol for surgical site infection and prevention.[10] Infections distant to the surgical site (e.g., catheter-associated urinary tract infection or pneumonia after a nephrectomy) were also considered. No distinction between type of infection was made for the analysis.

Drug-resistant organism (DRO) was defined as a microorganism resistant to at least one agent in one or more classes of antimicrobial categories tested. Culture results labelled as "contaminated" were considered negative. All microorganisms were considered in cases of positive cultures with more than one species.

Procedures were grouped as to compare differences at baseline between both periods. Based on baseline risk of infection[11] and surgery type, they were classified as: endoscopic intra-renal surgery (percutaneous nephrolithotomy and retrograde endoscopic intra renal surgery); ureter and lower urinary tract endoscopic surgery (transurethral bladder or prostate resection, endoscopic prostatic enucleation, ureter stenosis balloon dilation, ureter stenting, endopyelotomy, and semi-rigid urethroscopy); kidney and ureter surgery (partial and radical nephrectomy, simple nephrectomy, nephroureterectomy, pyeloplasty, renal cyst marsupialization, ureter reimplantation, and adrenalectomy); prostate surgery (simple and radical prostatectomy); radical cystectomy; genital and reconstructive surgery (circumcision, hydrocelectomy, vasectomy, simple and radical orchiectomy, radical penectomy, urethroplasty, vesico-vaginal fistula correction, urethral slings, surgery for Peyronie's disease, and sacral neuromodulation).

### Outcomes

The main outcomes were the number of postoperative infections during the pandemic and the number of drug-resistant isolates. We hypothesized that during the pandemic, the number of infections would be lower, and that a lower number of DROs would be isolated.

### Statistical analysis

Based on local and European data,[12] we estimated a postoperative infection rate of 10%. We postulated a relative reduction of 50% of postoperative infection during the pandemic. Based on these estimates, and for an alfa of 5% and power of 80%, sample size was calculated as 684 patients.

Data was analysed using IBM SPSS Statistics v.26®. Chi-squared test was used to compare categorial variables between periods. Mann-Whitney U test was used to compare continuous variables, and Fisher's exact test was used to compare culture isolates between both periods. Univariable regression analysis included variables of interest. A stepwise multivariable logistic regression model was developed, with $p<0.2$ for the main outcomes.[13,14] The model was adjusted for age, sex, ASA score, hospital (level of care), antibiotic prophylaxis, period of observation (pre-, during pandemic), presence of medical devices, and preoperative urine cultures.

Complete case analysis was performed. Odds ratios (OR) were reported with 95% confidence intervals (CI). Statistical significance was considered at an alpha <0.05.

## Results

Demographic data and the main results comparing the pre-pandemic and pandemic periods are summarized in Table 1. Final analysis included a total of 698 patients and no patient undergoing elective surgery was excluded. Missing data for variables of interest included information regarding antibiotic prophylaxis for 24 patients (14 during the pre-pandemic period), and one for ASA score. Overall, no significant differences were seen between both periods concerning the type of procedures. The number of radical cystectomies were considerably higher during the pandemic but the difference was not statistically significant (p=0.07).

The number of patients who did not receive antibiotic prophylaxis was greater during the pandemic (4.6% vs. 1.2%, p=0.02). Regarding the type of antibiotic used, 86.6%, 5.3%, 4.8%, and 3.3% received cefoxitin, cefazolin, ciprofloxacin, or other antibiotic before the pandemic, respectively. During the pandemic, antibiotics used remained largely unchanged (86.1%, 6.5%, 3%, and 4.3% for cefoxitin, cefazolin, ciprofloxacin, or other antibiotic, respectively, p=0.586).

The postoperative infection rate during the pre-pandemic period was 14.1% compared to 12.1% during the pandemic

**Table 1. Demographics and characteristics of patients submitted to elective urological surgery**

| | Pre-pandemic period (n=425) | Pandemic period (n=273) | p |
|---|---|---|---|
| Age, median (IQR) | 65 (55–74) | 65 (54–72) | 0.361 |
| Sex, male (%) | 319 (75.1) | 203 (74.4) | 0.858 |
| Hospital stay, median (IQR), days | 3 (2–5) | 3 (2–6) | 0.806 |
| ASA (%) | | | |
| I | 29 (6.8) | 13 (4.8) | 0.125 |
| II | 273 (64.2) | 168 (61.5) | |
| III | 113 (26.6) | 90 (33) | |
| IV | 9 (2.1) | 2 (0.7) | |
| Missing | 1 | 0 | |
| Antibiotic prophylaxis (%) | | | |
| None | 5 (1.2) | 12 (4.6) | 0.024 |
| Standard | 225 (54.7) | 139 (53.5) | |
| Prolonged | 181 (44) | 109 (41.9) | |
| Missing | 14 | 13 | |
| Perioperative devices (%) | 171 (40.2) | 127 (46.7) | 0.1 |
| Preoperative positive urine culture (%) | 33 (24.6) | 28 (27.5) | 0.654 |
| Postoperative infection (%) | 60 (14.1) | 33 (12.1) | 0.494 |
| Positive cultures | 25/60 (47.2) | 22/33 (62.9) | 0.192 |
| Drug-resistance species | 24/25 (92.3) | 11/22 (52.4) | 0.003 |
| Endoscopic intra-renal surgery | 54 (12.7) | 33 (12.1) | 0.816 |
| Ureter and lower urinary tract endoscopic surgery | 182 (42.8) | 111 (40.7) | 0.393 |
| Kidney and ureter surgery | 51 (12) | 33 (12.1) | 0.972 |
| Prostate surgery | 74 (17.4) | 35 (12.8) | 0.110 |
| Radical cystectomy | 9 (2.1) | 13 (4.8) | 0.074 |
| Genital surgery | 55 (12.9) | 48 (17.6) | 0.101 |

ASA: American Society of Anesthesiologists; IQR: interquartile range.

(p=0.494). No statistically significant difference was observed when analysis was repeated after excluding cases of infection without positive cultures (p=0.356). Only 47.2% and 62.9% of cultures were positive in the pre-pandemic and pandemic period, respectively (p=0.192). Patterns of drug-resistant infections were different between groups, with 92.3% of isolates being categorized as multidrug-resistant in the pre-pandemic period compared to 52.4% during the pandemic (p=0.002). The pathogens isolated in both periods are presented in Figure 1. Differences between isolated microorganisms were not statistically significant when tested with Fisher's exact test (p=0.776).

ASA score was associated with an increase odd of postoperative infection (OR 2.09, 95% CI 1.45–3.01, p<0.001) and DRO isolates (OR 4.22, 95% CI 1.1–15.89, p=0.03) on univariable analysis (Tables 2, 3). On the same analysis, the pandemic period was associated with a lower risk of DRO (OR 0.09, 95% CI 0.02–0.49, p=0.005) but not with a risk of postoperative infection (p=0.53).

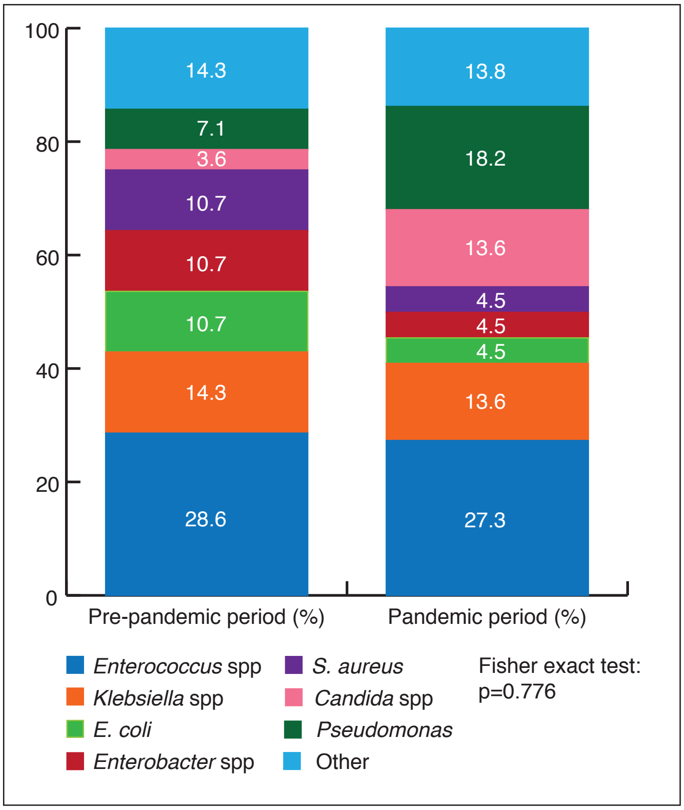


**Figure 1.** Microorganisms isolated in patients with healthcare-associated infections in urology wards according to study period.

The stepwise multivariable logistic regression models predicting the number of infections and the isolate's drug resistance pattern are presented in Tables 4 and 5. The model including the pandemic period and the ASA score was the one best predicting the outcome of DRO isolates, with an OR of 0.1 (95% CI 0.07–0.57, p=0.010). Although not statistically significant, a trend towards an increase in the number of postoperative infections was observed for the level of care, with an OR of 1.57 (95% CI 0.97–2.54, p=0.069) for the university teaching hospital.

**Table 2. Univariable regression analysis for risk of postoperative infection**

| | OR (95% CI) | p |
|---|---|---|
| Pandemic period | 0.87 (0.55–1.36) | 0.53 |
| Medical devices | 1.80 (1.16–2.79) | 0.008 |
| Male sex | 1.20 (0.05–1.25) | 0.089 |
| Preoperative urine culture (positive) | 1.96 (0.95–4.02) | 0.068 |
| Age | 1.01 (0.71–2.01) | 0.491 |
| ASA score | 2.09 (1.45–3.01) | <0.001 |
| Level of care (tertiary hospital) | 1.59 (0.99–2.54) | 0.055 |
| Antibiotic prophylaxis (standard or prolonged) | 2.54 (0.33–19.45) | 0.37 |

ASA: American Society of Anesthesiologists; CI: confidence interval; OR: odds ratio.

**Table 3. Univariable regression analysis for risk of drug-resistant organism**

| | OR (95% CI) | p |
|---|---|---|
| Pandemic period | 0.09 (0.02–0.49) | 0.005 |
| Medical devices | 0.24 (0.05–1.25) | 0.089 |
| Male sex | 1.33 (0.28–6.26) | 0.716 |
| Preoperative urine culture (positive) | 0.86 (0.14–5.2) | 0.867 |
| Age | 1.01 (0.98–1.06) | 0.317 |
| ASA score | 4.22 (1.1–15.89) | 0.03 |
| Level of care (tertiary hospital) | 0.72 (0.16–3.2) | 0.675 |
| Antibiotic prophylaxis (standard or prolonged) | * | * |

*Univariable analysis was not possible, as only one patient with no antibiotic prophylaxis had a non-drug-resistant organism (DRO) infection, and none had any DRO infection (p=1). ASA: American Society of Anesthesiologists; CI: confidence interval; OR: odds ratio.

**Table 4. Multivariate regression analysis for risks of postoperative infection**

| | OR (95% CI) | p |
|---|---|---|
| Hospital (level of care) | 1.57 (0.97–2.54) | 0.069 |
| Pandemic period | 0.84 (0.53–1.34) | 0.469 |
| ASA score | | |
| II | 1.03 (0.49–5.62) | 0.418 |
| III | 3.72 (1.08–12.84) | 0.037 |
| IV | 14.81 (2.70–81.11) | 0.002 |
| Presence of medical devices | 2.17 (1.37–3.43) | 0.001 |

ASA: American Society of Anesthesiologists; CI: confidence interval; OR: odds ratio.

## Discussion

To the best of our knowledge, this is the first paper addressing the differences in postoperative infection patterns during the COVID-19 pandemic on a surgical ward. We were not able to document a decrease in the number of postoperative infections during the COVID-19 pandemic, but our results show that the number of drug-resistant isolates were lower in patients with a nosocomial infection during this period. According to our results, we believe that hospital preventive measures to limit the spread of the virus contributed in some form to this outcome. Few studies have addressed this issue outside surgical specialties, with conflicting results. Some have documented an increase in colonization or infection with DROs in COVID-19 patients, although analysis was limited to intensive care units during peak incidence periods and when protective equipment and healthcare professionals were sparse.[15,16] Others have documented fewer *Clostridium difficile* infections and low rates of multidrug-resistant superinfections in COVID-19 patients.[17,18]

Infection prevention include measures such as hand hygiene and room disinfection, antimicrobial stewardship programs, and patient and staff cohorting in cases of DRO infection. Patient cohorting has been referred to as the most effective measure in cases of multidrug-resistant infection outbreak.[19] Compliance with infection prevention and control measures has been shown to be heterogenous in different European countries, and several areas of control have been noted as being critical, namely the number of clinical and infection control staff and educational programs.[20]

The reduced number of elective surgeries during the pandemic could have translated into an increase of unoccupied hospital beds and easier patient cohorting in cases of DROs bacteria colonization or infection. Yet, this was not the case, as many beds were allocated to COVID-19 or non-surgical patients, even as hospital capacity increased.[21] We argue that the heightened perception by healthcare professionals about the importance of nosocomial infections and their role in preventing them brought by the COVID-19 pandemic led to increased adherence to preventive strategies, driving the lower DRO infection number in our sample. Furthermore, increased compliance with best practices for hand hygiene, not only by healthcare staff but also by patients, could have contributed to our findings, as previous studies have demonstrated high rates of visitor and patient hand contamination by DRO species during hospital admission and stay.[22-24] Further studies are needed to confirm our hypothesis.

Interestingly, the number of positive cultures was higher during the pandemic in our sample, and this could be the result of increased hand hygiene and adherence to best practice on blood and urine collection, diminishing sample contamination (which were judged as negative in our analysis). However, such differences between periods were not statistically significant. Additionally, we observed a non-statistically significant increase in the odd of postoperative infections in the university teaching hospital on multivariable regression analysis (OR 1.57, 95% CI 0.97–2.54, p=0.069). Nosocomial infections have been showed to increase according to the level of care and hospital size but as concluded by Sax et al, this seems to be partly associated with an unfavorable case mix.[25]

Antimicrobial resistance is known to change over time and varies according to region, which could explain our results, independent from the COVID-19 pandemic. However, the annual epidemiological report for 2018 and 2019 from the ECDC addressing antimicrobial resistance in the European Union highlights that more than half of the *E. coli* and *Klebsiella pneumoniae* isolates were resistant to at least one antimicrobial group in Portugal, and combined resistance to several antimicrobial groups was frequent. In

**Table 5. Stepwise multivariate regression analysis for risks of drug-resistant organism isolates**

| | OR (95% CI) | p |
|---|---|---|
| Period | 0.1 (0.07–0.57) | 0.010 |
| ASA score[a] | | |
| III | 4.28 (0.88–20.86) | 0.072 |

[a]ASA score of 4 was excluded as all patients (n=3) had drug-resistant organism isolates. ASA: American Society of Anesthesiologists; CI: confidence interval; OR: odds ratio.

addition, for most Gram-negative species, changes in resistance patterns between 2015 and 2019 were moderate and remained at high levels. As for Gram-positive bacteria, such as *Enterococcus* species (the most prevalent in our study), a significant decrease in high-level gentamicin resistance for *E. faecalis* was noted in both periods (31.9% vs. 26.6%), although this was accompanied by an increase in vancomycin resistance in *E. faecium* isolates in the EU, from 10.5% in 2015 to 18.3% in 2019. Notably, for vancomycin-resistant *E. faecium*, no distinct geographical pattern could be seen, with high levels throughout Europe.[26]

Similarly, according to the Canadian antimicrobial resistance surveillance system, the rate of healthcare-associated vancomycin-resistant *Enterococcus* bloodstream infection more than doubled between 2014 and 2018 (from 0.12 to 0.31 cases per 10 000 patient-days).[27] Additionally, invasive *E. coli* resistance to third-generation cephalosporins is comparable between Portugal and Canada (10–25%), as reported in both surveillance systems. Our results contradict the increased trend of DRO infection.

If further studies confirm our results, another factor to consider is the inappropriate use of antibiotics in the community, which was showed to be lower in 2020 and could have a major impact on the rate of DROs. Data from INFARMED, the Portuguese drug authority, confirms a reduction of 20.7% ambulatory antibiotic use between January and September 2020 compared to the homologous period in the previous year.[28] Furthermore, antibiotic prophylaxis during surgery was lower in our sample (no antibiotic prophylaxis 1.2% vs. 4.6% in pre-pandemic and pandemic periods, respectively); however, the duration of antibiotic prophylaxis was statistically excluded by our stepwise multivariable regression analysis model.

As noted by Monnet and Harbath in their recent editorial, the COVID-19 pandemic reminds us that compliance with infection preventive measures is critical to ensure the safety of hospitalized patients.[29] The current pandemic has brought dramatic changes to healthcare, but some silver-linings should be emphasized and some old lessons relearned. HAIs and multidrug-resistance microorganism represent a public health crisis that will endure long after the current pandemic, and healthcare institutions, professionals, and patients should do their part to prevent them.

## Limitations

Several limitations to our study can be addressed, mainly related to the retrospective design, which makes information bias unavoidable. ECDC protocol was used to define surgical site infection and although the protocol has some objective definitions of infection, it also considers those diagnosed by the attending physician or surgeon. This fact introduces some subjectivity in everyday clinical practice that is difficult to overcome, such as, for example, when a patient submitted to a partial nephrectomy develops fever with increased analytical inflammatory markers and negative blood and urine cultures. This clinical scenario could be caused either by infection or be secondary to the surgical trauma or renal ischemia. Naturally, real infection rates could be either over or underestimated.

Our definition of drug resistance limits comparison to other reports and represents a potential bias. Although the definition of multidrug-resistant organisms is not consensual in the literature, efforts have been made to standardize it. The most accepted international terminology defines multidrug-resistance as non-susceptibility to at least one agent in three or more antimicrobial categories.[30] We broadened our definition to include resistance to at least one agent in one or more classes, and hence used the terminology "drug-resistant organisms" to avoid confusion. We have used such a definition because we did not have access to the full antibiogram panel. Nonetheless, we do not believe this had a major impact on our conclusions. Also, contaminated samples were grouped with negative cultures in order to improve statistical power. This categorization of data represents a potential bias.

Patients admitted to elective surgery during the pandemic might not be comparable to those admitted before the public healthcare crisis, as resources were concentrated on more serious cases. Multiple endogenous and exogenous risk factors for surgical site infection have been identified, and the former (related to patient's comorbidities), in addition to the type of procedure, might be the main predictors of surgical infections. Both endogenous factors (represented by the ASA score) and type of procedure remained mostly unchanged during the studied periods, explaining, in part, the similar rates of postoperative infections. ASA score is nonetheless an oversimplification of patient's comorbidities and we have excluded ambulatory and urgent surgery, limiting our analysis and representing a potential selection bias. However, exogenous risk factors — more dependent on healthcare staff and infrastructure —changed dramatically during the pandemic and might have a more dominant role on the dissemination of DROs.

Our results were unable to confirm a lower number of postoperative infections during the pandemic. Sample size calculation was based on a predetermined relative reduction of 50% on infection rate between periods. One might argue that we have overestimated the potential difference in the infection rate. However, nosocomial infection rate in Portugal is one of the highest in Europe, doubling those of similar healthcare systems,[12,31] and a recent systematic review reported that 33–55% of HAIs might be preventable.[32] Nonetheless, this implies that our study was underpowered to detect a smaller effect size. Additionally, we did not discriminate between different types of infection and this limitation could also justify the negative results in terms of the number of postoperative infections, as some types are more dependent on healthcare factors than others (e.g., *Clostridium difficile* infection).

## Conclusions

DRO isolates were lower during the pandemic in urology wards. Reinforced infection preventive measures to limit the spread of COVID-19, such as increased hand hygiene, room disinfection, and reduced family visits to inpatients, could have been responsible for the results. No statistically significant difference was found between the number of postoperative infections in our sample. Further reports, such as those from the ECDC and CDC, are needed to confirm our results. Such studies should try to distinguish different types of infections, as they are not homogenously influenced by infection preventive measures applied during the COVID-19 pandemic. Compliance rate with infection preventive measures should remain at high levels after the pandemic.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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