Trends in bacterial resistance among perioperative infections in patients with primary ovarian cancer: A retrospective 20-year study at an affiliated hospital in South China

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Abstract

Background: We aimed to analyze the epidemiological and drug-resistance trends among bacterial cultures from perioperative infections in patients with primary ovarian cancer.

Methods: Medical and bacteriological records for patients with ovarian cancer patients who developed perioperative infections after primary cytoreductive surgery from 1999 to 2018 were reviewed retrospectively.

Results: The incidence of perioperative infections and the culture-positive percentage among patients in the first 10 years were 20.2% and 29.3%, respectively, and the equivalent rates in the second 10 years were 18.0% and 33.5%. The most commonly isolated pathogens in both year-groups were *Escherichia coli* and *Enterococcus* spp., but the respective percentages differed between the groups. Some strains of *Staphylococcus aureus* and *Enterococcus* spp. in the second 10-year group were resistant to linezolid and vancomycin, and ciprofloxacin resistance among Gram-negative bacteria isolates also increased in this group. However, resistance of Gram-negative bacteria to imipenem and meropenem was low among in both groups.

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Conclusion: The pathogen distribution in perioperative infections in patients with primary ovarian cancer undergoing cytoreductive changed slightly from 1999 to 2018, and the antibiotic resistance of the main isolated pathogens increased. These results indicate the importance of periodic bacterial surveillance of surgical infections in these patients.

Keywords
Perioperative gynecologic infection, ovarian cancer, antibiotic resistance, pathogen distribution, cytoreductive surgery, bacterial infection

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Background
Ovarian cancer remains a common gynecologic malignancy, with the third-highest incidence among malignant female gynecologic tumors, after cervical and endometrial cancer.1,2 Ovarian cancer is also the fifth-leading cause of cancer-related deaths among women,3 with an increasing incidence year by year.4 However, the symptoms of early-stage ovarian cancer are less obvious, and most patients are therefore initially diagnosed at an advanced-stage.3,5 Although primary or secondary cytoreductive surgery remains an important treatment for ovarian cancer,6 residual cancer foci after cytoreductive surgery may affect the survival outcome,7,8 and relatively radical and extensive excision are usually carried out to obtain maximal cytoreduction and improve survival outcomes.9,10 However, the use of radical and extensive surgery is directly related to postoperative complications, including perioperative infection.9,11

Perioperative infection is one of the most common complications in patients with ovarian cancer, and is associated with not only surgical morbidity and mortality, but also with high health care-related costs.12,13 Perioperative infection was the third-leading cause of death within 30 days after primary cytoreductive surgery among patients with advanced-stage ovarian cancer.14 Perioperative infections can also delay the onset of postoperative chemotherapy.15 Perioperative infections after cytoreductive surgery therefore represent a crucial problem that requires further study. The urinary tract and surgical wound are common sites of infection after primary or secondary cytoreductive surgery in patients with ovarian cancer.16 Regarding the causative organisms, Escherichia coli and Enterococcus spp. have been reported to be the most common and important isolated pathogens,3 while the pathogen distribution and antibiotic resistance profiles of the main pathogens have gradually changed.3 However, the morbidity and mortality of perioperative infections in patients with ovarian cancer remain unclear.17 There have been no large, long-term studies of the species distribution and antibiotic resistance of perioperative bacterial infections in patients with primary ovarian cancer in mainland China. The present study therefore aimed to analyze the trends in bacterial epidemiology and antibiotic resistance in bacterial cultures isolated from perioperative infections in patients with primary ovarian cancer at an affiliated hospital in South China over a 20-year period.
Materials and methods

We retrospectively extracted and reviewed the records of patients with primary ovarian cancer admitted to a university teaching hospital (The Second Xiangya Hospital of Central South University, Changsha, Hunan) with perioperative infection from 1 January 1999 to 31 December 2018. Perioperative infection after surgery for primary ovarian cancer, advanced stage ovarian cancer, tumor grade, and culture-positive percentage were defined as reported previously.3,18,19 The inclusion criterion was patients with primary ovarian cancer who underwent cytoreductive surgery. The exclusion criteria were: (i) patients with metastatic ovarian carcinoma; (ii) patients with synchronous cancer types; (iii) patients with low-grade malignant ovarian tumor; and (iv) patients with incomplete information. Information from the patient’s medical records was extracted and reviewed, including clinical demographics, results of pathological examinations, clinical and surgical details, and details of inpatient treatment. We also retrospectively extracted the results of microbiology tests and antimicrobial sensitivity assays to evaluate perioperative infections. All samples were analyzed using standard microbiological methods and all antimicrobial susceptibility tests were carried out in our hospital using a unified protocol.20,21 To avoid duplicate counts, we extracted and recorded similar bacteria isolated from different specimens from the same patient or similar bacteria isolated at different times as one isolate.20,22

This study was approved by the ethics committee of The Second Xiangya Hospital Committee for clinical research (No. 2010-S233), and informed consent was obtained from the participating patients and/or their parents/guardians for publication of their individual clinical details.

Results

Demographics of perioperative infection

The demographic data of the enrolled patients with primary ovarian cancer are reported in Table 1 and Table 2. During the 20-year period, a total of 854 patients with ovarian cancer were treated with primary cytoreductive surgery in our hospital, including 322 patients from 1999 to 2008 and 532 from 2009 to 2018. Among these patients, 161 (161/854) patients developed a perioperative infection within 6 weeks after surgery, including 65 (65/322) patients in the first 10-year group and 96 (96/532) in the second 10-year group. There were no significant differences in any characteristics between the two groups.

Causative organisms and bacterial resistance

Totals of 522 and 674 samples of bacterial cultures were analyzed for the first and second 10-year groups, respectively.
The positivity rate of the bacterial cultures was higher in the second group (226/674) compared with the first group (153/522), but the difference was not significant. The top three most common sites of perioperative infections in both groups were the urinary tract, surgical wound, and blood (Table 2). Regarding the distribution of all causative organisms, the percentage of Gram-negative bacteria was higher than that of Gram-positive bacteria and fungi at all sites and in both groups. Among top five most common species, *Enterococcus* spp. were responsible for 22.9% of infections in the first 10-year group, followed by *E. coli* (20.9%), *Klebsiella pneumoniae* (13.1%), *Acinetobacter baumannii* (12.4%), and *Staphylococcus aureus* (11.8%), while *E. coli* was responsible for 27.4%, followed by *S. aureus* (15.0%), *K. pneumoniae* (14.2%), *A. baumannii* (13.3%), and *Enterococcus* spp. (10.2%) in the second 10-year group (Figure 1). Among urinary tract infections, the most commonly isolated pathogens were *Enterococcus* spp. (21.7%) and *E. coli* (20.7%) in the first group, compared with *E. coli* (23.8%) and *S. aureus* (15.6%) in the second group. *E. coli* was the most common organism isolated from surgical wound infections in both groups (Table 2).

Gentamicin resistance remained high among the common causative organisms. One strain of *S. aureus* and one strain of *Enterococcus* spp. were resistant to vancomycin, and two strains of *Enterococcus* spp. were resistant to linezolid in the second 10-year group. Ciprofloxacin and erythromycin resistance were decreased in *S. aureus* in the second 10-year group (Table 3), and penicillin had no effect on most *S. aureus*. However, levofloxacin and ciprofloxacin resistance increased in *Enterococcus* spp. in the second 10-year group. Regarding *E. coli*, resistance to cefazolin, cefuroxime, and cefoxitin were high in both groups, and

### Table 1. Clinical demographics of patients with ovarian cancer.

| Characteristic          | 1999–2008 (n, %)       | 2009–2018 (n, %)       |
|-------------------------|------------------------|------------------------|
| Number of patients      | 322                    | 532                    |
| Age, years\(^a\)        | 52 ± 5.7 (28–74)       | 54 ± 6.6 (34–78)       |
| BMI, kg/m\(^2\)         | 25.8 ± 4.3             | 26.3 ± 4.6             |
| FIGO stage              |                        |                        |
| I                       | 18 (5.6%)              | 28 (5.3%)              |
| II                      | 21 (6.5%)              | 37 (7.0%)              |
| III                     | 254 (78.9%)            | 415 (78.0%)            |
| IV                      | 29 (9.0%)              | 52 (10.0%)             |
| Histology               |                        |                        |
| Serous                  | 251 (78.0%)            | 427 (80.3%)            |
| Mucinous                | 45 (14.0%)             | 73 (13.7%)             |
| Endometrioid            | 15 (4.7%)              | 25 (4.7%)              |
| Other                   | 11 (3.4%)              | 7 (1.3%)               |
| Grade                   |                        |                        |
| Low-grade tumor         | 54 (16.8%)             | 90 (17.0%)             |
| Middle-grade tumor      | 112 (34.8%)            | 186 (35.0%)            |
| High-grade tumor        | 156 (48.4%)            | 256 (48.1%)            |
| Optimal surgery         | 168 (52.2%)            | 288 (54.1%)            |
| Bowel resection         | 90 (28.0%)             | 137 (25.8%)            |

\(^a\)Values given as mean ± standard deviation (range); \(^b\)values given as mean ± standard deviation. BMI, body mass index.
one strain of *E. coli* in the second group was resistant to imipenem. The resistance of *K. pneumonia* to piperacillin was nearly 100% in the second 10-year group. Resistance of Gram-negative bacteria to imipenem and meropenem was low in both groups, but resistance of Gram-negative bacterial isolates to ciprofloxacin resistance increased in the second 10-year group (Table 4).

**Discussion**

Ovarian cancer is the third-most prevalent gynecologic malignant tumor,\textsuperscript{1,2} and the fifth-leading cause of cancer-related deaths among women,\textsuperscript{3} and thus presents a serious threat to women’s health and quality of life. Although treatments for ovarian cancer have become more effective in recent
years, the best results occur in patients treated in the early stages of the disease; however, most patients with ovarian cancer are initially diagnosed at an advanced stage. Current therapeutic modalities for ovarian cancer comprise surgery and chemotherapy. Primary cytoreductive surgery aims to eradicate cancer cells as thoroughly as possible, but aggressive cytoreductive surgery has been associated with perioperative infections, including surgical site, urinary tract, and other site infections. Many factors contribute to the development of perioperative infections in patients with ovarian cancer after cytoreductive surgery, including the microorganism, the environment, and host defense mechanisms, while ovarian cancer patients frequently undergo extensive, prolonged, and highly invasive surgery, experience significant blood loss, have received preoperative chemoradiotherapy, and have primary or secondary hypoimmunity. In the present study, the rate of perioperative infections in patients with ovarian cancer after primary cytoreductive surgery was higher (18.9%) than previously reported, suggesting the need to take preventive preoperative and perioperative actions to reduce the rate of perioperative infections in these patients in our hospital.

Perioperative infections were common in women with ovarian cancer after primary cytoreductive surgery in the present study. The urinary tract and surgical wound were the most common infection sites in both groups, but the percentage of urinary tract infections was higher in the second 10-year group (65.0%) compared with the first 10-year group (60.1%). Numerous factors increase the risk of perioperative urinary tract infections during ovarian cancer surgery, including anatomical features, ascending infection from the lower genital tract, invasive instrumentation such as cystoscopy and catheterization, surgical intervention, chemoradiotherapy, and dysbiosis of vaginal microbiota.

The distribution of the causative organisms changed slightly between the two decades in the current study. Some previous studies found that the most common isolated pathogens were *Pseudomonas aeruginosa* followed by *Enterococcus* and *E. coli*, while other studies reported that *E. coli* was the main causative organism, followed by *Enterococcus*. Furthermore, a shift in the vaginal flora may have affected the distribution of causative organisms in perioperative infections. Many factors may alter the host microbial flora leading to pathogenic bacterial colonization, including...
surgery, antimicrobial therapy, chemoradiotherapy, hospital equipment, and patient to patient transmission.\textsuperscript{17} Similarly, use of foreign bodies such as contraceptive devices, frequent use of vaginal tampons, previous ectopic pregnancies, prenatal infections, and a history of sepsis history are also possible factors. In the present study, although \textit{E. coli} and \textit{Enterococcus} spp. were the most commonly isolated pathogens in both 10-year groups, their respective percentages changed between the first and second group. The use of aseptic techniques, surgical skill, and periodic surveillance of the causative microbial pathogens are all required to help prevent perioperative infections in patients with ovarian cancer.

| Table 3. Resistance rates (%) of Gram-positive bacteria to antimicrobial agents. |
|---------------------------------|-----------------|-----------------|-----------------|
| Antimicrobial agent             | \textit{Staphylococcus aureus} |                      | \textit{Enterococcus} spp. |                      |
|                                 | 1999–2008 (n = 18) | 2009–2018 (n = 34) | 1999–2008 (n = 35) | 2009–2018 (n = 23) |
| Vancomycin                      | 0.0              | 2.9              | 0.0              | 4.3                |
| Linezolid                       | 0.0              | 0.0              | 0.0              | 8.7                |
| Teicoplanin                     | 0.0              | 0.0              | 0.0              | 0.0                |
| Rifampin                        | 11.1             | 14.7             | 28.6             | 34.8               |
| Levofoxacin                     | 44.4             | 47.1             | 42.9             | 56.5               |
| Ciprofloxacin                   | 38.9             | 35.3             | 45.7             | 52.2               |
| Gentamicin                      | 38.9             | 41.2             | 62.9             | 73.9               |
| Clindamycin                     | 33.3             | 38.2             | 65.7             | 91.3               |
| Erythromycin                    | 88.9             | 94.1             | 77.1             | 87.0               |
| Penicillin G                    | 83.3             | 100.0            | 62.9             | 82.6               |

| Table 4. Resistance rates (%) of Gram-negative bacteria to antimicrobial agents. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Antimicrobial agent             | \textit{Escherichia coli} | \textit{Klebsiella pneumoniae} | \textit{Acinetobacter baumannii} |
|                                 | 1999–2008 (n = 32) | 2009–2018 (n = 62) | 1999–2008 (n = 20) | 2009–2018 (n = 32) | 1999–2008 (n = 19) | 2009–2018 (n = 30) |
| Amikacin                        | 18.8             | 21.0             | 0.0             | 6.3             | 68.4             | 76.7             |
| Gentamicin                      | 62.5             | 66.7             | 30.0            | 34.4            | 42.1             | 53.3             |
| Piperacillin                     | 75.0             | 80.6             | 95.0            | 100.0           | 36.8             | 43.3             |
| Piperacillin/tazobactam         | 6.3              | 16.1             | 35.0            | 40.6            | 15.8             | 30.0             |
| Cefazolin                       | 78.1             | 77.4             | 55.0            | 46.9            | 57.9             | 43.3             |
| Cefuroxime                      | 84.3             | 66.1             | 60.0            | 53.1            | 47.4             | 53.3             |
| Cefotaxime                      | 40.6             | 30.6             | 25.0            | 31.3            | 5.3              | 6.7              |
| Cefazidime                      | 46.8             | 35.5             | 20.0            | 18.8            | 0.0              | 10.0             |
| Cefepime                        | 34.4             | 29.0             | 25.0            | 28.1            | 5.3              | 10.0             |
| Cefoxitin                       | 87.5             | 74.2             | 40.0            | 46.9            | 63.2             | 66.7             |
| Imipenem                        | 0.0              | 1.6              | 0.0             | 0.0             | 0.0              | 0.0              |
| Meropenem                       | 0.0              | 0.0              | 0.0             | 0.0             | 0.0              | 0.0              |
| Ciprofloxacin                   | 43.8             | 45.2             | 15.0            | 18.75           | 42.1             | 43.3             |
After the introduction of antibiotics into clinical practice, they were widely used as preoperative prophylaxis to prevent perioperative infections. The choice of prophylactic antibiotic should take into consideration numerous factors, including the common pathogenic bacteria and their drug resistance, the pharmacokinetics and pharmacodynamics of the drug, and its cost effectiveness and toxicity. Rapid and accurate identification of causative organisms is thus an cornerstone of antimicrobial therapy. E. coli and Enterococcus were reported to be sensitive to nitrofurantoin, norfloxacin, gentamicin, amikacin, and cotrimoxazole in 1995; by 2012, pathogens responsible for urinary tract infections showed high levels of resistance to ciprofloxacin, ampicillin/sulbactam, cefazolin, and levofloxacin, and some strains of E. coli were resistant to imipenem and piperacillin/tazabactam. In the present study, we detected vancomycin-resistant S. aureus and Enterococcus spp., linezolid-resistant Enterococcus spp., and imipenem-resistant E. coli in the second 10-year group. Treatment options for infections caused by multidrug-resistant pathogenic bacteria are thus limited, and inappropriate empirical antibiotic therapy may have poor outcomes. Periodic surveillance of drug resistance can guide the use of empirical clinical medications and the appropriate employment of antibiotics.

Penicillin has not been considered as an appropriate empiric antibiotic therapy for S. aureus in most countries since 1980, and the overuse of penicillin meant that penicillin resistance among S. aureus isolates in the current study was nearly 100%. Furthermore, the wide use of macro-lides in patients allergic to penicillin and cephalosporins, especially oral azithromycin and roxithromycin, has increased the incidence of erythromycin-resistant S. aureus and Enterococcus spp., according to a Spanish study. Meanwhile, gentamicin is no longer considered as an appropriate empiric antibiotic therapy for Gram-negative bacteria. During the 20-year period of this study, the incidence of resistance to second generation cephalosporins among Gram-negative bacterial isolates was high level, but the causative isolates showed high sensitivity to third or fourth generation cephalosporins such as cefotaxime, ceftazidime, and cefepime, and Gram-negative bacteria showed low resistance to imipenem and meropenem. We therefore recommend the use of third or fourth generation cephalosporins as the first-line treatment for perioperative infections in women with ovarian cancer, while carbapenems should be reserved for severe infections caused by Gram-negative bacteria.

Perioperative infections in women with ovarian cancer are associated with increasing health-care-related costs, reduced quality of life, and significant strains on inpatient care. We should therefore adopt suitable prevention strategies to decrease the incidence of perioperative infections. Drug resistance is an increasing problem, especially in patients with malignant gynecologic tumors. Previous studies have suggested that numerous factors may contribute to the emergence of resistance, including inappropriate antibiotic selection, long-term incorrect antibiotic usage, and the duration of prophylactic antibiotic use. To reduce the rates of infection and bacterial resistance, it is therefore necessary to first take preventive measures against perioperative infections, followed by the use of narrow-spectrum antibiotics whenever possible, discontinue or change the antibiotics based on the results of bacterial cultures, and finally take heed of dynamic antibiotic resistance surveillance research.

We acknowledge some limitations of this study. First, the study had a retrospective design, which is associated with potential bias; however, the sample size was relatively
large. Second, we did not record or analyze operation duration, the interval between the operation and infection, or the change in prophylactic antibiotics during the course of the ovarian cancer. Finally, this was a single-center study, and there is thus a clear need for larger, multicenter studies in the future.

Conclusions

Based on the results of this study, we concluded that the incidence of perioperative infections after cytoreductive surgery in women with primary ovarian cancer remains high. During the 20-year study period, the pathogen distribution changed slightly and antibiotic resistance of the major pathogens increased gradually. Periodic bacterial surveillance and various preventive actions during the preoperative and perioperative periods play important roles in the prevention and treatment of perioperative infections in women with ovarian cancer.

Availability of data and materials

All the data used and/or analysis during this study are included in this published article and its supplementary information files.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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References

1. Pujade-Lauraine E, Hilpert F, Weber B, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: the AURELIA open-label randomized phase III trial. J Clin Oncol 2014; 32: 1302–1308.
2. Castera L, Krieger S, Rousselin A, et al. Next-generation sequencing for the diagnosis of hereditary breast and ovarian cancer using genomic capture targeting multiple candidate genes. Eur J Hum Genet 2014; 22: 1305–1313.
3. Matsuo K, Prather CP, Ahn EH, et al. Significance of perioperative infection in survival of patients with ovarian cancer. Int J Gynecol Cancer 2012; 22: 245–253.
4. Ledermann J, Harter P, Gourley C, et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncol 2014; 15: 852–861.
5. He C, Lu K, Liu D, et al. Nanoscale metal-organic frameworks for the co-delivery of cisplatin and pooled siRNAs to enhance therapeutic efficacy in drug-resistant ovarian cancer cells. J Am Chem Soc 2014; 136: 5181–5184.
6. Hennessy BT, Coleman RL and Markman M. Ovarian cancer. Lancet 2009; 374: 1371–1382.
7. Bristow RE, Tomacruz RS, Armstrong DK, et al. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. J Clin Oncol 2002; 20: 1248–1259.
8. Bartels HC, Rogers AC, McSharry V, et al. A meta-analysis of morbidity and mortality in primary cytoreductive surgery compared to neoadjuvant chemotherapy in advanced ovarian malignancy. Gynecol Oncol 2019; 154: 622–630.
9. Chi DS, Eisenhauer EL, Zivanovic O, et al. Improved progression-free and overall
survival in advanced ovarian cancer as a result of a change in surgical paradigm. 

Gynecol Oncol 2009; 114: 26–31.

10. Bartels HC, Rogers AC, Postle J, et al. Morbidity and mortality in women with advanced ovarian cancer who underwent primary cytoreductive surgery compared to cytoreductive surgery for recurrent disease: a meta-analysis. Pleura Peritoneum 2019; 4: 20190014.

11. Leitao MM Jr and Chi DS. Surgical management of recurrent ovarian cancer. Semin Oncol 2009; 36: 106–111.

12. Oza AM, Cook AD, Pfisterer J, et al. Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. Lancet Oncol 2015; 16: 928–936.

13. Rini BI, Bellmunt J, Clancy J, et al. Randomized phase III trial of temsirolimus and bevacizumab versus interferon alfa and bevacizumab in metastatic renal cell carcinoma: INTORACT trial. J Clin Oncol 2014; 32: 752–759.

14. Gerestein CG, Damhuis RA, Burger CW, et al. Postoperative mortality after primary cytoreductive surgery for advanced stage epithelial ovarian cancer: a systematic review. Gynecol Oncol 2009; 114: 523–527.

15. Vizzielli G, Costantini B, Tortorella L, et al. A laparoscopic risk-adjusted model to predict major complications after primary debulking surgery in ovarian cancer: a single-institution assessment. Gynecol Oncol 2016; 142: 19–24.

16. Lippitt MH, Fairbairn MG, Matsuno R, et al. Outcomes associated with a five-point surgical site infection prevention bundle in women undergoing surgery for ovarian cancer. Obstet Gynecol 2017; 130: 756–764.

17. Adam RA and Adam YG. Infectious diseases in gynecologic oncology: an overview. Obstet Gynecol Clin North Am 2001; 28: 847–868.

18. Elg SA, Carson LF, Brooker DC, et al. Infectious morbidity after radical vulvectomy. Infect Dis Obstet Gynecol 1994; 2: 130–135.

19. Johnson MP, Kim SJ, Langstraat CL, et al. Using bundled interventions to reduce surgical site infection after major gynecologic cancer surgery. Obstet Gynecol 2016; 127: 1135–1144.

20. Zhang X, Lu Q, Liu T, et al. Bacterial resistance trends among intraoperative bone culture of chronic osteomyelitis in an affiliated hospital of South China for twelve years. BMC Infect Dis 2019; 19: 823.

21. Iyer RN, Jangam RR, Jacinth A, et al. Prevalence and trends in the antimicrobial susceptibility pattern of Salmonella enterica serovars Typhi and Paratyphi A among children in a pediatric tertiary care hospital in South India over a period of ten years: a retrospective study. Eur J Clin Microbiol Infect Dis 2017; 36: 2399–2404.

22. Hu FP, Guo Y, Zhu DM, et al. Resistance trends among clinical isolates in China reported from CHINET surveillance of bacterial resistance, 2005-2014. Clin Microbiol Infect 2016; 22: S9–S14.

23. Narod S. Can advanced-stage ovarian cancer be cured? Nat Rev Clin Oncol 2016; 13: 255–261.

24. Szymankiewicz M, Dziobek K, Sznejdorwska M, et al. An analysis of the influence of infection on overall survival rates, following modified posterior pelvic exenteration for advanced ovarian cancer. Ginekol Pol 2018; 89: 618–626.

25. Prasad KN, Pradhan S and Datta NR. Urinary tract infection in patients of gynecological malignancies undergoing external pelvic radiotherapy. Gynecol Oncol 1995; 57: 380–382.

26. Sathiananthamoorthy S, Malone-Lee J, Gill K, et al. Reassessment of routine midstream culture in diagnosis of urinary tract infection. J Clin Microbiol 2019; 57: e01452-18.

27. Conde-Ferraez L, Suarez Allen RE, Carrillo Martinez JR, et al. Factors associated with cervical cancer screening amongst women of reproductive age from Yucatan, Mexico. Asian Pac J Cancer Prev 2012; 13: 4719–4724.

28. Ohm MJ and Galask RP. The effect of antibiotic prophylaxis on patients undergoing total abdominal hysterectomy. II. Alterations of microbial flora. Am J Obstet Gynecol 1976; 125: 448–454.
29. Ayeleke RO, Mourad S, Marjoribanks J, et al. Antibiotic prophylaxis for elective hysterectomy. *Cochrane Database Syst Rev* 2017; 6: Cd004637.

30. Lopes LF, Macedo CR, Aguiar Sdos S, et al. Lowered cisplatin dose and no bleomycin in the treatment of pediatric germ cell tumors: results of the GCT-99p from the Brazilian Germ Cell Pediatric Oncology Cooperative Group. *J Clin Oncol* 2016; 34: 603–610.

31. Yu F, Liu H, Li KH, et al. Causative organisms and their antibiotic resistance patterns for childhood septic arthritis in China between 1989 and 2008. *Orthopedics* 2011; 34: 179.

32. Granizo JJ, Aguilar L, Casal J, et al. *Streptococcus pyogenes* resistance to erythromycin in relation to macrolide consumption in Spain (1986-1997). *J Antimicrob Chemother* 2000; 46: 959–964.

33. Hamed SM, Aboshanab KMA, El-Mahallawy HA, et al. Plasmid-mediated quinolone resistance in Gram-negative pathogens isolated from cancer patients in Egypt. *Microb Drug Resist* 2018; 24: 1316–1325.

34. Thomas ED, Nugent EK, MacAllister MC, et al. Effectiveness of cyanoacrylate microbial sealant in the reduction of surgical site infection in gynecologic oncology procedures: a phase III single institution prospective randomized trial. *Gynecol Oncol* 2017; 144: 193–199.

35. Anderson DJ, Podgorny K, Berrios-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014; 35: 605–627.

36. Harbarth S, Samore MH, Lichtenberg D, et al. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 2000; 101: 2916–2921.

37. Postier RG. Antibiotic-resistant organism infection. *Am Surg* 2000; 66: 112–116.