Research Article

Changes in Clinical Practice After Publication of the Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) Randomized Controlled Trial

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ABSTRACT

Background: The Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial was a multicenter randomized clinical trial comparing a 1-day with a 5-day postoperative intravenous antibiotic regimen after lower extremity bone tumor resection and endoprosthetic reconstruction. The trial found no difference in surgical site infections between groups, but a markedly increased risk for antibiotic-related complications in the 5-day group. The study was published in January 2022. The objective of this study was to assess the effect of these findings on the clinical practice of musculoskeletal oncologists.

Methods: We developed an anonymous survey exploring changes in clinical practice after the publication of the PARITY trial and electronically distributed the survey to practicing musculoskeletal oncologists through REDCap in March 2024. Data were analyzed descriptively, and changes in practice from before to after the publication of the PARITY study were analyzed through the Pearson chi-square test.

Results: We obtained 101 responses from surgeons across six continents. Nearly all respondents (94 of 101, 93%) were aware of the PARITY trial results. Forty respondents (40%) reported a meaningful change in clinical practice after PARITY, most frequently a reduction of antibiotic administration in >75% of patients. After PARITY, the proportion of respondents who reported limiting antibiotics to 24 hours increased from 25% to 51% ($P < 0.001$), and the proportion prescribing oral antibiotics after discharge from the hospital declined from 23% to 16% ($P < 0.001$). Among those who did not change their practice, personal experience/professional opinion was the most frequently cited reason. Adherence to institutional standards was cited as an additional barrier.

Conclusions: Many respondents reported meaningful change in their clinical practice after the publication of the PARITY trial, most notably

limiting perioperative antibiotics to 24 hours. The complexities influencing the personal decision to adopt a notable change in clinical practice in response to new evidence warrant additional study.

Level of Evidence: IV

Limb-sparing surgery has become the standard of care for patients undergoing oncologic resection of the femur or tibia, due in part to advancements in endoprosthetic reconstruction. However, infection of tumor endoprostheses is a devastating postoperative complication and is the most common mode of failure of these implants.[1] Potential contributors to this problem include the size of bone and soft-tissue defects, the compromised immune and nutritional status of patients with cancer, bacteremia due to indwelling central venous catheters, and neutropenia resulting from the cytotoxic chemotherapy that patients with cancer receive.[2] Infection rates as high as 25% have been reported in patients undergoing limb-preserving tumor resection and endoprosthetic reconstruction, and the largest systematic review of retrospective data in this population found a pooled infection rate of 10%.[3]

Although intravenous antibiotic prophylaxis for primary arthroplasty in patients with degenerative joint disease has been well-studied, and guidelines have been established regarding dose and duration (generally no longer than 24 hours postoperatively), no analogous guideline exists for tumor endoprostheses.[4] The above-cited systematic review highlighted both the heterogeneity in antibiotic prescribing practices for patients undergoing lower extremity tumor resection and endoprosthetic reconstruction and the need for such guidelines.[3] A 2012 survey of musculoskeletal oncologists reiterated this heterogeneity in practice: Prolonged administration was common, but a minority of respondents limited perioperative antibiotics to 24 hours after reconstruction with a tumor endoprosthesis.[5]

The Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) study was a multicenter randomized controlled clinical trial comparing the efficacy of a 1-day with a 5-day postoperative intravenous antibiotic regimen on the rate of surgical site infections after lower extremity tumor resection and endoprosthetic reconstruction.[6] The study was conducted across 48 clinical sites in 12 countries. Published in January 2022, the study found no notable difference in surgical site infections between groups, failing to confirm superiority of the prolonged antibiotic regimen in this context. However, the investigators did find a markedly increased risk for antibiotic-related complications in the patients receiving the 5-day regimen, most commonly *Clostridium difficile*–associated colitis.

Although the publication of the PARITY trial represented an effort toward providing high-quality evidence to help guide prophylactic antibiotic-prescribing practices for patients undergoing tumor resection and endoprosthetic reconstruction, it is important to determine whether new evidence has prompted changes in clinical practice. The objective of this study was to assess the effect of the PARITY trial findings on the clinical practice of musculoskeletal oncologists.

Methods

Survey Development

We developed a comprehensive survey assessing changes in clinical practice after the publication of the PARITY trial. We consulted the literature, including a previously published cross-sectional survey administered to practicing musculoskeletal oncologists before the PARITY trial, to help inform our question selection.[5] Questions were included to describe respondent demographic and clinical training and practice characteristics, including training location, practice environment, and clinical volume; awareness of (or participation in) the PARITY trial and its results; and routine perioperative prophylactic antibiotic-prescribing practices (including duration, choice of standard intravenous antibiotic, and prescription of oral antibiotics after hospital discharge) for patients undergoing lower extremity tumor resection and reconstruction, before and after the PARITY trial's publication. We then internally piloted the survey among a core group of practicing orthopaedic oncologists and iteratively assessed and revised the survey for face and content validity before distribution. The final survey consisted of 27 questions (most of which were multiple choice, with the option for the respondent to

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elaborate in free text) that were organized in three sections (entire survey available in Appendix 1, http://links.lww.com/JAAOS/B479).

The survey was designed to provide anonymous responses so that the participant's identity could not readily be ascertained. The survey and study protocol underwent review by the Memorial Sloan Kettering Cancer Center Institutional Review Board and was deemed exempt.

Survey Distribution

We began electronic distribution of the survey to practicing musculoskeletal oncologists through REDCap in March 2024. After initial distribution to the 393 members of the Musculoskeletal Tumor Society (MSTS) by blast e-mail, with a 2-week follow-up reminder, the participants of the Birmingham Orthopaedic Oncology Consensus Meeting[7] (BOOM) were contacted by social media channels, also with a 2-week reminder. The total number of BOOM participants contacted, many of whom were MSTS members, is unknown due to the open nature of social media. We closed the survey on April 15, 2024.

Data Analysis

We analyzed the survey data descriptively. We characterized and then compared practice patterns reported before and after publication of the PARITY trial. Categorical variables were analyzed through the Pearson chi-square test, and continuous variables were analyzed via the *t*-test, with significance defined as $P < 0.05$. All analyses were conducted in IBM SPSS Statistics, version 29.0 (IBM Corp).

Results

Respondent Demographics and Familiarity With the PARITY Trial Results

We obtained 101 responses from surgeons across six continents (Table 1). Slightly more than half (51%) had completed their training in North America, and 39% were currently practicing in North America. A plurality of respondents (28%) reported having been in practice for more than 20 years, and the vast majority practiced in academic medical centers that were either cancer-specific (38%) or not specific to oncology (54%). Most respondents (58%) reported that management of patients with bone or soft-tissue tumors accounted for 76% to 100% of their clinical practice, and a preponderance (42%) reported annually treating ≥25 patients undergoing lower extremity tumor resection and endoprosthetic reconstruction. Nearly all respondents (94 of 101; 93%) were aware of the PARITY trial results, and 43 (43%) had personally enrolled patients in the trial. Of the 97 respondents who answered the question regarding whether the PARITY trial data represented level 1 evidence,[8] 58 (60%) strongly agreed and 31 (32%) agreed.

Practice Patterns Before and After Publication of the PARITY Trial

Before publication of the PARITY trial results, 25% of respondents reported limiting postoperative antibiotics to 24 hours for patients undergoing lower extremity tumor resection and endoprosthetic reconstruction, and an identical proportion reported continuing standing intravenous antibiotics until removal of the surgical drain(s) (Table 2). Twenty-three percent of respondents routinely prescribed oral antibiotics after discharge from hospital regardless of drain status (Table 3). Nearly two-thirds of respondents (63%) selected a first-generation cephalosporin as their standard agent (Table 4).

After the publication of the PARITY trial, the percentage of respondents who reported limiting antibiotics to 24 hours for patients undergoing lower extremity tumor resection and endoprosthetic reconstruction doubled to 51%, and the percentage who continued standing intravenous antibiotics until removal of the surgical drain(s) decreased to 18%. The proportion of participants who reported currently prescribing oral antibiotics after discharge, regardless of drain status, declined by nearly a third, to 16%. Most respondents continued to select a first-generation cephalosporin as their standard agent (62%).

Comparative Changes in Clinical Practice

Forty respondents (40%) reported the PARITY results markedly changed their clinical practices. Among these respondents, 16 (40%) reported reducing antibiotic administration in more than 75% of patients undergoing endoprosthetic reconstruction after lower extremity tumor resection, 10 (25%) reported a reduction in 50% to 75% of these patients, and an additional 10 (25%) reported a reduction in "some patients." After PARITY, the proportion of respondents who limited antibiotics to 24 hours increased significantly, from 25% to 51% ($P < 0.001$). The proportion who reported prescribing oral antibiotics after discharge from hospital also changed significantly, declining from 23% to 16% ($P < 0.001$).

Barriers to Adoption of New Evidence

Among the 61 respondents who reported no change in clinical practice, reasons cited (multiple answers were

Table 1. Participant Demographics

Characteristic	N (%) or Mean ± SD
Current location (N = 100)	
North America	39 (39)
Europe	28 (28)
South America	18 (18)
Asia	10 (10)
Oceania	3 (3)
Africa	2 (2)
Mean age, yr	48 ± 7.5
Sex identity (N = 97)	
Male	87 (90)
Female	10 (10)
Specialized musculoskeletal oncology training (N = 94)	
Yes	90 (96)
No	4 (4)
Location of oncology training (N = 90)	
North America	46 (51)
Europe	28 (31)
South America	10 (11)
Asia	3 (3)
Oceania	2 (2)
Africa	1 (1)
Years in practice (N = 99)	
<5	6 (6)
5-10	21 (21)
11-15	27 (27)
16-20	17 (17)
>20	28 (28)
Primary practice environment (N = 99)	
Cancer-specific academic medical center	38 (38)
Academic medical center, not cancer-specific	54 (54)
Private medical center, not academically affiliated	3 (3)
Public medical center, not academically affiliated	4 (4)

allowed) included already limiting perioperative antibiotics to 24 hours (19 respondents), personal experience or professional opinion (20 respondents), insufficient data to change practice (15 respondents), and adherence to institutional standards (14 respondents). Sixty-two respondents in the full sample (61%) reported having an institutionally mandated or strongly recommended prophylactic antibiotic protocol for endoprosthetic reconstructions.

Discussion

Summary of Findings

The evidence provided by the PARITY trial markedly affected the prescribing practices of postoperative prophylactic antibiotics among the musculoskeletal oncologists surveyed in this study. Notably, 2 years after publication of the trial data, the proportion of respondents who limited intravenous antibiotics to 24 hours after lower extremity tumor resection and endoprosthetic reconstruction had doubled. Similarly, markedly fewer surgeons reported prescribing oral antibiotics for these patients after discharge from hospital. First-generation cephalosporin remained the antibiotic agent of choice after PARITY. Frequently cited barriers to adoption of clinical practices consistent with the PARITY findings included personal experience/professional opinion, insufficient data to change practice, and adherence to institutional standards.

Contextualizing Results

The problem of translating medical evidence into clinical practice has been characterized in other domains. After a series of randomized clinical trials established that immobilization using removable splints was as effective as using circumferential casts for pediatric patients with minimally or nondisplaced distal radius or fibula fractures, investigators surveyed practicing surgeons and found that only small minorities would use removable splints for these fracture types, despite the evidence.[9] Common barriers to splint use included concerns regarding patient compliance, perceived risk of potential complications, and potential medicolegal implications.[9] In the same vein, after multiple randomized trials established that prophylactic nasogastric decompression rendered no benefit in patients undergoing elective colon resection, investigators who distributed a summary of the evidence to general surgeons found that familiarization with the evidence was insufficient to result in a change in practice.[10]

Implications for Clinical Practice

The evidence from the PARITY trial filled a previously identified gap in clinical knowledge by demonstrating that prolonged intravenous postoperative antibiotic prophylaxis was no more effective than a short-term

Table 2. Reported Duration of Intravenous Antibiotic Administration After Lower Extremity Tumor Resection and Endoprosthetic Reconstruction, Before and After Publication of PARITY Data

Regimen	N (%)	
	Before Publication	After Publication
Preoperative/intraoperative IV antibiotics only	0 (0)	1 (1)
Perioperative antibiotics + IV antibiotics for up to 24 hr postoperatively	25 (25)	51 (51)
Perioperative antibiotics + IV antibiotics for 2 d postoperatively	7 (7)	9 (9)
Perioperative antibiotics + IV antibiotics for 3 d postoperatively	7 (7)	6 (6)
Perioperative antibiotics + IV antibiotics for 4-5 d postoperatively	17 (17)	7 (7)
Perioperative antibiotics + IV antibiotics for 6-7 d postoperatively	13 (13)	6 (6)
Perioperative antibiotics + IV antibiotics for >7 d postoperatively	1 (1)	0 (0)
Perioperative antibiotics + standing IV antibiotics until removal of drain(s)	25 (25)	18 (18)
Other	5 (5)	3 (3)

IV = intravenous

regimen in preventing surgical site infection in patients undergoing lower extremity tumor reconstruction and endoprosthetic reconstruction. Moreover, prolonged prophylaxis was associated with an increased rate of antibiotic-related complications, including *C difficile* infection.[3,5,6] Our study documented the effect of these findings on clinical practice, but perhaps more importantly identified barriers to adoption. The most frequently cited barriers were personal experience/professional opinion, insufficient data to change practice, and adherence to institutional standards. As such, the translation of PARITY evidence into clinical practice guidelines and institutional protocols may provide additional effect. Since awareness among our respondents of the trial's findings may not equate to awareness among those in position to amend institutional standards, presenting this evidence to key stakeholders on an institutional level may represent the next step toward increased adoption of evidence into practice.

Implications for Future Research

Along with tracking ongoing changes in surgeons' prescribing practices of perioperative antibiotics, future research should include study of the second-order effects of these changes. These may include items such as the duration and cost of hospitalizations after tumor surgery and the incidence of long-recognized adverse effects of intravenous antibiotic treatment, such as *C difficile* infection (and potential decrease in iatrogenic *C difficile* cases). Other, more recently identified areas of interest include the gut microbiome and the potential implications of its disruption, including changes in immune checkpoint inhibitor efficacy and the incidence of thromboembolism.[6,11,12] From a systems standpoint, the effect of the trial's results on institutional protocols

Table 3. Postdischarge Prescription of Oral Antibiotics After Lower Extremity Tumor Resection and Endoprosthetic Reconstruction, Before and After Publication of PARITY Data

Prescribed Oral Antibiotics After Discharge	N (%)	
	Before Publication	After Publication
Yes, in patients discharged with drain	11 (11)	11 (11)
Yes, regardless of drain status	23 (23)	16 (16)
No	67 (66)	74 (73)

Table 4. Preferred Intravenous Antibiotic Agent After Lower Extremity Tumor Resection and Endoprosthetic Reconstruction, Before and After Publication of PARITY Data

Antibiotic	Before Publication	After Publication
First-generation cephalosporin	64 (63%)	63 (63%)
Second-generation or third-generation cephalosporin	28 (28%)	31 (31%)
Vancomycin	19 (19%)	16 (16%)
Gentamycin	7 (7%)	2 (2%)
Piperacillin-tazobactam	2 (2%)	2 (2%)
Clindamycin	0 (0%)	1 (1%)
Other	5 (5%)	4 (4%)

Note: More than one option could be selected.

(and associated barriers to change) should be assessed. In addition, the factors and complexities that influence the personal decision to adopt a notable change in clinical practice in response to new evidence warrant additional study.

Limitations

Our study has several limitations. Owing to the distribution methods used, our response rate is unknown. Although unlikely, the anonymized nature of the survey prevents us from ensuring that the same individual did not provide responses from both the MSTS and the BOOM invitations for participation. Furthermore, selection and response biases may paint an inaccurate picture because the surgeons who received the survey and the subset who responded may not necessarily represent the whole of practicing musculoskeletal oncologists. Participants may have been more likely than their peers to be aware of the PARITY findings, or more likely to have changed their practice in response to the findings. However, the number of respondents and their international spread is encouraging because it suggests we achieved broad representation among practicing surgeons. An additional limitation is the self-reported nature of this investigation—although their responses were anonymized, participants may not have judged their past and current practice patterns with accuracy and objectivity, the way an unbiased third-party observer may have.

Conclusions

The PARITY trial has affected clinical practice because the proportion of survey respondents limiting perioperative antibiotics to ≤24 hours has increased markedly. However, adoption of the trial evidence into clinical practice was not universal, and the complexities influencing the personal decision to adopt changes in clinical practice warrant additional study.

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