Total Joint Arthroplasty in Patients With a History of Cancer

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Abstract

In this review, we describe the pertinent issues that reconstructive surgeons face when treating patients with cancer. These issues include the various cancer management options and their influence on total joint arthroplasty outcomes, as well as prosthesis types and fixation types. We also present a strategy for reducing morbidity and complications during the perioperative period.

According to *Cancer Facts & Figures 2009,* published by the American Cancer Society,[1] an estimated 1.4 million new cases of cancer were diagnosed in 2008. That number excludes carcinoma in situ, save the bladder, and all basal and squamous cell cancers of the skin. Furthermore, 77% of all cancers are diagnosed in patients 55 years old or older. Patients with cancer are also surviving longer. The 5-year survival rate for all cancers increased from 50% in 1975-1977 to 66% in 1996-2004; the result was that 11.1 million Americans had a cancer notation in their medical charts in 2005. Longer survival is directly related to modern medical advances, which lead to improved survivorship of patients with cancer and a healthier, more active lifestyle.

Kurtz and colleagues[2] projected total joint arthroplasty (TJA) demands through 2030 and they estimated that by 2030, the annual demand for primary total hip arthroplasties (THAs) will have increased by 174%, to approximately 572,000 procedures, and that the number of primary total knee arthroplasties will have increased by 673%, to 3.48 million procedures. These numbers, combined with the improved survival rates of patients with cancer, make it a surety that orthopedic surgeons will be treating more patients with a history of cancer.

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It is therefore imperative that orthopedic surgeons familiarize themselves with the needs and special care requirements of this subpopulation.

In this review, we describe the pertinent issues that reconstructive surgeons face when treating patients with cancer. These issues include the various cancer management options and their influence on TJA outcomes, as well as prosthesis types and fixation types. We also present a strategy for reducing morbidity and complications during the perioperative period.

Patients With Cancer

TJA surgeons should be prepared to treat patients from 4 distinct cancer groups. The first group consists of patients with primary cancer of the musculoskeletal system. This group represents a minority of patients with cancer and encompasses both benign and malignant tumors. Malignant tumors, such as osteosarcoma and Ewing sarcoma, are more common in young patients, decreasing the likelihood that they will present de novo in adults undergoing reconstruction.[3] Chondrosarcoma is the most common malignant bone cancer in adults. Orthopedic surgeons must be able to identify such cases and properly refer them to an orthopedic oncologist, who has expertise in both management of primary bone cancer and advanced prosthetic reconstruction. These patients require proper workup, including both local and systemic staging as well as treatment under the supervision of a multidisciplinary team that includes pathologists, radiologists, chemo-oncologists, radio-oncologists, and, at times, microvascular surgeons. This cancer group is not the focus of our review.

The second group consists of patients with metastatic bone cancer, particularly that from high-prevalence primary cancer, such as breast, lung, thyroid, prostate, or kidney cancer.[4] This group and the third group, which consists of patients with hematopoietic cancer of the bone, are commonly encountered by orthopedic surgeons. These patients are likely to present with either bone pain or a fracture of pathologically weakened bone. Management can be complex, but several guidelines—such as the criteria of Mirels, used to manage the impending pathologic fracture of long bones—have been developed for the care of these patients.[5-7] As these 2 cancer groups also must be referred to a musculoskeletal oncologist, they are also not the focus of this review.

The fourth and final group consists of patients who have a previous history of cancer and are undergoing elective joint arthroplasty. Three issues arise in treating this group. First, orthopedic surgeons must consider cancer type and the different treatment modalities used. Second, and equally important, is prosthesis selection, particularly with respect to fixation mode. The third and primary issue involves which strategy to use to reduce the incidence of complications.

Cancer Types and Previous Treatment Modalities

Prostate cancer and female breast cancer, followed by lung, colon, kidney, and thyroid cancers, are the cancers with the highest incidence in the general population.[1] In both sexes, lung cancer is responsible for the most deaths. The most common site of cancer metastasis is bone. Cancers of the breast and prostate, along with thyroid, kidney, lung, and gastrointestinal cancers, have a strong predisposition to metastasize to bone.[4,7]

Treatment for patients with cancer potentially includes chemotherapy, radiotherapy, immunotherapy, and surgery. The effects of chemotherapy depend on the agent used and may involve all of a patient's systems. Some of the most common side effects are fatigue; malnutrition and weight loss, immunosuppression, anemia, and hemorrhage; heart, lung, liver, and kidney damage; and osteonecrosis.[8] Chemotherapy—induced osteonecrosis is usually associated with concomitant steroid treatment.[9] Methyltrexate, for example, depresses cancellous and longitudinal bone growth, and thus, is associated with decreased bone formation, volume, and osteoblast activity and increased osteoclast activity.[10-12]

Radiotherapy has acute and long-term effects, which the arthroplasty surgeon should access for in the setting of elective TJA. Acute effects occur immediately after treatment—they result from the damage caused to proliferating cells—and usually last for weeks. These effects may include generalized symptoms, such as fatigue and lethargy, and local symptoms affecting the skin (erythema, dryness, pruritis, moist desquamation), the gastrointestinal system (diarrhea, constipation, nausea, vomiting, radiation hepatitis, esophagitis), the respiratory system (radiation pneumonitis), the urinary system (frequency, urgency, dysuria), the hematopoietic system (cytopenia), and the neurologic system (paresthesia). Some of these may become long-term effects, which should be considered during TJA workup; bone mineral density (BMD) deficiencies, in particular, should be assessed.[13,14] These long-term effects usually become apparent months to years after treatment. Although the changes are progressive, resulting from vascular damage and the accumulation of cell dropout from organ population, surgeons must be cognizant of the possibility of secondary malignancy (postirradiation sarcoma). Secondary malignancy accounted for 16% of the cancers reported in 2003 to the Surveillance, Epidemiology, and End Results program of the National Cancer Institute. The risk for developing a secondary cancer is more than 3 times higher in patients with a history of Hodgkin disease than in the general population and is more than 20% within the first 20 years after treatment.[8,15]

The musculoskeletal system is not spared. The effects of radiation on bone have been studied extensively and found to cause osteonecrosis.[16-18] The exact mechanism is poorly understood, but theories variously point to direct damage to the cellular constituents of bone (osteoblasts) impeding the ability of bone to repair itself, collagen damage, and coarsening of apatite crystals.[18-20] These changes lead to empty lacunae on histologic specimens along with demineralization and a disorganized trabecular pattern. The radiographic characteristics of irradiated bone are nonspecific, with areas of lysis and sclerosis resembling the typical appearance of pagetoid bone. Weakening of the structural integrity of bone is responsible for the atraumatic fractures often encountered in irradiated bone.[18] Krishnamoorthy and colleagues[14] found that targeted irradiation had systemic effects, as children who had undergone localized irradiation treatment had decreased total body BMD. In another study, Mithal and colleagues[21] found that survivors of childhood medulloblastoma managed with radiation and chemotherapy had decreased BMD in the lumbar spine and femoral neck in adulthood. This finding suggests that irradiation has lasting effects on BMD, even in body areas not subjected to irradiation.

Immunotherapy has been demonstrated to result in epithelial damage, musculoskeletal pain, nausea and vomiting, and immunosuppression. The immunosuppression caused by some medications used in immunotherapy can lead to serious viral and fungal infections, which can be severe enough to be fatal in their own right.[22] Another worrisome effect of this treatment modality is the not always present but demonstrated connection with heart failure, as some of these medications can be cardiotoxic.[23]

Managing the side effects of these treatment modalities is pivotal to successful cancer management and to successful elective joint surgery. The side effects of chemotherapy are most often systemic. They are usually managed by administering other medications or, if possible, changing to an alternative chemotherapeutic agent. A preventive approach should be taken when managing the side effects of radiotherapy. Newer radiation-focusing techniques, such as intensity-modulated radiation therapy, reduce the inadvertent irradiation of tissue adjacent to cancerous masses. This technique allows the radiation to be aimed from several angles and the level of radiation delivered from each angle is reduced so that only the cancerous tissue receives the full dose. In the setting of adjuvant radiotherapy for primary bone cancer, preoperative irradiation leads to more wound complications. Although postoperative irradiation typically requires higher doses of radiation over a larger area, it is associated with fewer wound issues.[24] In elective TJA, surgeons should not operate through recently irradiated skin. We recommend waiting at least 6 months, if possible, to allow for acute skin symptoms to dissipate.

Prosthesis Selection and Fixation Types

To determine whether adjuvant perioperative radiotherapy affects implant survival, Jeys and colleagues[25] performed a multivariate analysis of 661 patients who had undergone endoprosthetic management for primary bone tumor. They did not find a significant difference in 10-year survival between patients who received radiation at time of reconstructive surgery (78%) and patients who underwent reconstruction alone (82%).

In the arthroplasty literature, information on prosthesis selection and fixation type is scarce, leaving little guidance for surgeons. Jacobs and colleagues[26] were the first to study acetabular bone in-growth in cementless THA in patients who had previously undergone radiation to the pelvis to treat different cancers. Retrospective chart review revealed a series of 11 patients and 12 hips. All patients were implanted with a cementless cup of hemispherical design coated with an in-growth surface of titanium fiber. Three patients died within the first year after surgery, leaving 9 hips for analysis. Preoperative diagnoses for these 9 hips were osteonecrosis of the femoral head secondary to radiation (5 hips) and osteoarthritis (4 hips). Mean follow-up was 37 months and revealed migration of 3 acetabular components (2 were revised) as well as progressive radiolucency in a fourth (no clinical symptoms). Jacobs and colleagues[26] advised against using cementless acetabular fixation in the irradiated pelvis and proposed that cemented acetabular fixation better suits these patients.

Massin and Duparc[27] retrospectively examined the cases of 56 patients (71 THAs) who had undergone pelvis irradiation. Most of the cancers were uterine cancers; there were some metastases to the pelvis. Dose and frequency of radiation varied. The 49 hips in the first cohort underwent cemented fixation of conventional polyethylene into irradiated bone; the procedures were performed between 1970 and 1982. The large number of early postoperative failures in this cohort prompted the surgeons to use a different fixation method (reinforcement ring) in the next cohort, 22 hips; these procedures were performed between 1983 and 1990. Mean follow-up was 69 months for the first cohort and 40 months for the second cohort. Radiographic analysis showed that 52% of the cemented polyethylene cups (first cohort) were loose and that loosening occurred predominantly during the first 4 postoperative years; 73% of these loose cups were revised. Only 19% of the reinforcement rings (second cohort) showed radiographic signs of loosening. Massin and Duparc[27] postulated that the high rate of acetabular loosening with the cemented component resulted from the mechanical insufficiency of the irradiated bone and that use of the reinforcement ring negated the effect of weakened bone by increasing the area to which the force of weight-bearing is transmitted. Furthermore, using long cancellous screws with the ring may allow for stronger fixation, as the screws obtain purchase in healthy bone. For the attainment of proper fixation, the authors recommended routine use of antiprotrusio rings in THAs for patients with an irradiated pelvis.

In a more recent study of prognostic factors related to implant failure, Cho and colleagues[28] reviewed the cases of 12 female patients (18 hips) who had undergone THA in a pelvis irradiated for cervical cancer. Of the 18 hips, 14 were implanted with a cementless hemispherical cup; the other 4 received a reinforcement ring. Nine (2 cemented, 7 cementless) of the 18 acetabular implants failed at a mean follow-up of 58 months, resulting in a 50% survival rate for both cemented and uncemented acetabular components, seemingly giving equal credence to these fixation methods. Multivariate analysis revealed that long latency (time from radiation to symptom onset) was the most significant risk for acetabular failure. Young age became only marginally significant after adjustment for other factors, whereas total radiation dose, type of acetabular implant, and infection were found to be predictors of outcome.

In 2007, Kim and colleagues[29] reported on the survivorship of 66 uncemented total hips in 58 patients with a pelvis previously irradiated for prostate cancer. By a mean follow-up of 4.7 years, 7 patients had died. The remaining 58 hips were functioning well and showed no signs of aseptic loosening. Four complications were reported: 3 draining wounds that did not require intervention and 1 deep infection that required 2-stage exchange arthroplasty. There were 3 mechanical failures: 1 single-event dislocation (managed nonoperatively) and 2 femoral revisions (1 for subsidence caused by an undersized femoral component, 1 for a periprosthetic fracture).

Given the findings of these studies, we favor uncemented fixation, which at midterm follow-up has results superior to those of cemented fixation.[27-29] In addition, in healthy patients, cement fixation has correlated with increased risk for fat embolization and pulmonary insult, as well as increased operative time and, thus, increased blood loss.[30]

Strategies to Prevent Complications

Assessment of a TJA candidate with a history of cancer should start with a thorough review of the patient's cancer history with an emphasis on treatment modalities, dosages, and timing of treatments. The patient's medication profile should also be examined for potential medication interactions. A surgeon with doubts about an aspect of management should consult an oncologist. All antibiotics and nonsteroidal anti-inflammatory drugs with nephrotoxic effects should be used cautiously, and steroids may have to be avoided entirely because of their effect on BMD when they are combined with chemotherapy.[9,31]

The patient should then be examined for systemic manifestation of the type of cancer in his or her history, and should be given the routine physical examination for TJA patients. Particular attention should be paid to any previous surgical incisions and to skin and soft-tissue quality, especially after irradiation therapy. In addition, it is prudent to obtain a detailed neurovascular examination, lest any deficiencies be missed.

Routine preoperative laboratory testing for this patient subset should be conducted in such a way that the results can be assessed for potential ongoing side effects of previous cancer or treatment. Particular attention should be paid to the patient's immunosuppression, coagulation profile, hepatic and renal function, and nutrition profile (lymphocytes, albumin, transferrin). A cardiac workup (Doppler ultrasound, stress test, etc) is recommended, particularly in patients with possible cardiac deficiencies or previous treatment with potentially cardiotoxic chemotherapy medications (doxorubicin). Some patients may also need electromyography to exclude neuropathy, and positron emission topography to rule out metastases. A bone scan for identifying any abnormalities of the bone (presence of metastatic cancer) may at times also be warranted, as may dual-energy x-ray absorptiometry for measuring BMD. Patients who have undergone adjuvant therapy for cancer should have BMD testing done and patients with T scores below –2.0 should be instructed to seek treatment from their primary physician. It is advisable to increase this cutoff to a T score of –1.5 if certain risk factors, such as long-term glucocorticosteroid or anticoagulation therapy, appear in the history.[32] Patients with low BMD are usually treated with bisphosphonates, which theoretically may cause issues surrounding component fixation because of their effects on osteoclast and, subsequently, bone turnover rates. However, bone turnover rates have been contradicted in animal model studies, as use of bisphosphonates at time of implantation has been shown to increase component fixation, though, to our knowledge, no studies have addressed fixation of components implanted after bisphosphonate treatment has begun.[33-35]

The easiest and most effective way to reduce complications is to make sure that the patient is in optimal health before the surgery is scheduled. Surgeons should not hesitate to delay elective joint arthroplasty in the event that the patient's condition is yet to be optimized. Although we recommend scheduling surgery no earlier than 6 months after cessation of adjacent therapy as a means of dramatically reducing complications, Tran and colleagues[36] found that complications of flap breast reconstruction in patients who received postmastectomy radiation therapy were significantly decreased in patients who underwent reconstruction only after adequately recuperating—in this case, for a full year after completion of radiation therapy. In addition, surgery should be avoided in the presence of poor epidermal health, specifically erythematous swollen skin that continues to exhibit postirradiation signs, or the presence of soft-tissue ulcers in the surgical area. Usual practice is to delay surgery in the presence of low hemoglobin level (<10 g/dL), low platelet count (<90,000 mcL), or malnourishment (albumin, <3 g/dL). Surgeons should routinely administer antibiotics (cefazolin or vancomycin) and make every effort to perform the procedure in expedited fashion to decrease the risk for infection, though not so quickly that special attention is not paid to soft-tissue handling.

Conclusion

With cancer treatments improving and life expectancy increasing, there will also be an increase in the number of patients with a history of cancer who are seen by reconstructive surgeons. Surgeons should not hesitate to offer these patients joint replacement surgery, as long as patients consent to the recommendations outlined here that will minimize the potential risks and allow patients to obtain the benefits of total joint arthroplasty.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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