The Incidence of Cancer Associated with Total Hip And Knee Arthroplasty – A Meta - Analysis

Background: Polymethylmethacrylate, polyethylene and metal ions such as cobalt and chromium used in prosthetic alloys have been documented to produce cancer in animal studies. This raises the concern that orthopaedic implants used in humans may cause cancer. There have been 25 well-documented case studies in the English language of carcinoma associated with total hip or knee replacement. Metal-on-metal hip joints may have an increased risk of cancer development compared to metal-on-polyethylene joints because of an increased exposure to metal particles and ions. These concerns have caused researchers to study the relative risk of cancer after total hip and knee replacement versus the incidence in the general population. Epidemiological studies have also suggested a specific increase in hematopoietic cancers. The goal of this meta-analysis is to combine patient data from epidemiological studies to determine a relative risk of cancer development after total hip or total knee arthroplasty and the risk in association with metal-on-metal versus metal-on-polyethylene bearings in total hip replacement.

Methods: A literature search of the English language via MEDLINE from January 1966 to July 1999 was performed. Inclusion required that the studies compare the incidence of cancer in total hip or total knee replacement to a control population and that a standard incidence ratio (SIR) and relevant data be reported. The data retrieved included location of study, study design, sample size, type of implant, date of surgery, follow-up time, cases observed, cases expected, SIR for all cancers, and SIR for hematopoietic cancer. Data was further segregated into metal-on-metal and metal-on-polyethylene hip prostheses if possible. Analysis included the mean follow-up period for the studies and the relative risk for all cancers and hematopoietic cancers associated with a) total hip replacement, b) total knee replacement, c) metal-on-metal total hip replacement and d) metal-on-polyethylene total hip replacement. The relative risk was calculated by dividing the sum of the cancer cases observed by the sum of those expected. The 95% confidence interval for the relative risk was calculated by using a general linear model of random effects.

Results: Eight epidemiological studies involving 110,792 total hip and 20,356 total knee replacements were included in the analysis. The mean follow-up period for studies that provided follow-up data was 7.5 years and the range was 6 months to 17 years. The relative risk of cancer development after total hip arthroplasty was 0.96 (95% CI 0.95-0.98) and after total knee arthroplasty was 0.89 (95% CI 0.85-0.94) (Figure 1). The risk of hematopoietic cancer development was 1.01 (95% CI 0.94-1.08) after total hip replacement and 1.03 (95% CI 0.84-1.26) after total knee replacement (Figure 2). Metal-on-metal total hip arthroplasties were associated with a cancer risk of 0.95 (95% CI 0.79-1.13) and a hematopoietic cancer risk of 1.59 (95% CI 0.82-2.77). Metal-on-polyethylene total hip arthroplasties were found to have a cancer risk of 0.90 (95% CI 0.87-0.94) and a hematopoietic cancer risk of 0.93 (95% CI 0.69-1.22).

Conclusions: The aggregate data of these eight epidemiological studies do not support a causal link between total hip or knee arthroplasty and cancer. The widths of the confidence intervals simply do not provide a reasonable level of certainty. Further, the substantial number of cancers occurring within the first 2 years after joint replacement (34% of all cancers and 36% of hematopoietic cancers) in three of the studies suggests an associative rather than causal relationship (Figure 3). Inclusion of these cases likely overestimates the risk between hip and knee replacement and cancer development. Although the risk of developing hematopoietic cancer after metal-on-metal hip replacement appears elevated, the data comes from a single study that examined only 579 patients of which approximately 30% of the person years at risk were from patients that were less than 5 years post-surgery. The lack of long-term follow-up (over 10 years) is a deficit of the epidemiological studies. Similarly, in the four studies that related the number of cancers to latency, over 30% of all cancers and 35% of hematopoietic cancers developed less than 5 years after surgery (Figure 3). This again suggests an associative rather than causative link. Comorbidity issues, such as increased cancer risk for patients with rheumatoid arthritis, Paget’s disease, and bone infarcts, may also be the cause of any apparent increase in risk. Future studies should focus on larger sample populations, controlling for comorbidities, and increased follow-up time.