

NIH Consensus Statement on Total Knee Replacement



NIH Consensus and State-of-the-Science Statements

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This statement is an independent report of the consensus panel and is not a policy statement of the NIH or the Federal Government. The statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge of the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.

Reference Information

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The Evidence Report prepared for this conference by the Agency for Healthcare Research and Quality is available on the Web via <http://www.ahrq.gov/clinic/epcix.htm>. Printed copies may be ordered from the AHRQ Publications Clearinghouse by calling 1-800-358-9295. Requestors should ask for AHRQ Publication No. 04-E006-1. An extensive bibliography by the National Library of Medicine is available on the Web at <http://www.nlm.nih.gov/pubs/cbm/tkr.htm>.

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Disclosure Statement

All of the panelists who participated in this conference and contributed to the writing of this statement were identified as having no financial or scientific conflict of interest, and all signed forms attesting to this fact. Unlike the expert speakers who present scientific data at the conference, the individuals invited to participate on NIH Consensus and State-of-the-Science panels are reviewed prior to selection to assure that they are not proponents of an advocacy position with regard to the topic and are not identified with research that could be used to answer the conference questions.

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Abstract

Objective

To provide health care providers, patients, and the general public with a responsible assessment of currently available data regarding total knee replacement.

Participants

A non-DHHS, nonadvocate 11-member panel representing the fields of orthopaedics, rheumatology, internal medicine, nursing, physical therapy, rehabilitation, biostatistics, epidemiology, and health services research, as well as a TKR patient. In addition, 21 experts in related fields presented data to the panel and to the conference audience.

Evidence

Presentations by experts; a systematic review of the medical literature provided by the Agency for Healthcare Research and Quality; and an extensive bibliography of total knee replacement research papers, prepared by the National Library of Medicine. Scientific evidence was given precedence over clinical anecdotal experience.

Conference Process

Answering pre-determined questions, the panel drafted its statement based on scientific evidence presented in open forum and on the published scientific literature. The draft statement was read in its entirety on the final day of the conference and circulated to the audience for comment. The panel then met in executive session to consider the comments received, and released a revised statement later that day at <http://consensus.nih.gov>. This statement is an independent report of the panel and is not a policy statement of the NIH or the Federal Government.

Conclusions

The success of primary TKR in most patients is strongly supported by more than 20 years of followup data. There appears to be rapid and substantial improvement in the patient's pain, functional status, and overall health-related quality of life in about 90 percent of patients; about 85 percent of patients are satisfied with the results of surgery.

Short-term outcomes, as documented by functional outcome scales, are generally substantially improved after TKR. Functional outcome is improved after TKR for people across the spectrum of disability status. Technical factors in performing surgery may influence both the short- and long-term success rate. There is consensus regarding the following perioperative interventions that improve TKR outcomes: systemic antibiotic prophylaxis, aggressive postoperative pain management, perioperative risk assessment and management of medical conditions, and preoperative education.

Revision TKR is done to alleviate pain and improve function. Contraindications for revision TKR include persistent infection, poor bone quality, highly limited quadriceps or extensor function, poor skin coverage, and poor vascular status. Results are not as good as with primary TKR; outcomes are better for aseptic loosening than for infections. Failed revisions require a salvage procedure (resection of arthroplasty, arthrodesis, or amputation), with inferior results compared with revision TKR.

Factors related to a surgeon's case volume, technique, and choice of prosthesis may have important influences on surgical outcomes. One of the clearest associations with better outcomes appears to be the procedure volume of the individual surgeon and the hospital.

Technical factors in performing surgery may influence both the short- and long-term success rate. Proper alignment of the prosthesis appears to be critical. Many design features, such as use of mobile bearings or designs sparing cruciate ligaments, have theoretical advantages, but durability and success rates appear roughly similar with most commonly used designs.

There is clear evidence of racial/ethnic and gender disparities in the provision of TKR in the United States. The limited role of economic and other access factors in these racial or ethnic disparities can be demonstrated by significant differences in the rate of procedures in the VA system, where cost and access are assumed equivalent across race or ethnic groups.

Introduction

Based on existing research evidence, total knee replacement (TKR) is a safe and cost-effective treatment for alleviating pain and restoring physical function in patients who do not respond to nonsurgical therapies. There are few contraindications to this surgery as it is currently used. Overall, TKR has been shown to be a very successful, relatively low-risk therapy despite variations in patient health status and characteristics, type of prosthesis implanted, orthopaedic surgeons, and surgical facilities. Improvements can be made in overall success of TKR by addressing each of these areas of variation through further research. Each year, approximately 300,000 TKR surgeries are performed in the United States for end-stage arthritis of the knee joint. As the number of TKR surgeries performed each year increases and the indications for TKR extend to younger as well as older patients, a review of available scientific information is necessary to enhance clinical decision-making and stimulate further research.

First used in the late 1950s, early TKR implants poorly mimicked the natural motion of the knee and resulted in high failure and complication rates. Advances in TKR technology in the past 10 years have enhanced the design and fit of knee implants, resulting in improved short- and long-term outcomes.

Despite the increased success of TKR, questions remain concerning which materials and implant designs are most effective for specific patient populations and which surgical approach is optimal for a successful outcome. Physical, social, and psychological issues may influence the success of TKR, and understanding patient differences could facilitate the decisionmaking process before, during, and after surgery, thereby achieving the greatest benefit from TKR. Particular attention also must be given to the treatment and timing options related to the revision of failed TKR surgery.

To address these questions, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Institutes of Health (NIH) Office of Medical Applications of Research (OMAR) convened a consensus development conference to explore and assess the current scientific knowledge regarding TKR. Specifically, the conference addressed the following key questions:

- What are the current indications and outcomes for primary TKR?
- How do specific characteristics of the patient, material and design of the prosthesis, and surgical factors affect the short- and long-term outcomes of primary TKR?
- Are there important perioperative interventions that influence outcomes?
- What are the indications, approaches, and outcomes for revision TKR?
- What factors explain disparities in the utilization of TKR in different populations?
- What are the directions for future research?

During the first 1 1/2 days of the conference, experts presented the latest TKR research findings to an independent panel. Included among the experts presenting data were the principal investigators of a systematic literature review prepared by the Minnesota Evidence-based Practice Center under contract with the Agency for Healthcare Research and Quality (AHRQ). After each set of presentations, a discussion period was held to allow conference attendees to ask questions of the speakers and make comments. The panel then met in executive session to weigh all of the scientific evidence and prepare its consensus statement answering the above questions. On the final day of the conference, the panel chairperson read the draft statement to the conference audience and invited comments and questions.

That afternoon, a press conference was held to allow the panel to respond to questions from the media.

In addition to its primary sponsors, the conference was cosponsored by the following: the National Institute of Child Health and Human Development (NICHD), the U.S. Food and Drug Administration (FDA), the National Institute of Standards and Technology (NIST), and the Office of Research on Women's Health (ORWH), NIH.

What are the current indications and outcomes for primary TKR?

Primary TKR is most commonly performed for knee joint failure caused by osteoarthritis (OA); other indications include rheumatoid arthritis (RA), juvenile RA, osteonecrosis, and other types of inflammatory arthritis. The aims of TKR are relief of pain and improvement in function. Candidates for elective TKR should have radiographic evidence of joint damage, moderate to severe persistent pain that is not adequately relieved by an extended course of nonsurgical management, and clinically significant functional limitation resulting in diminished quality of life. In patients with RA and other inflammatory arthropathies, additional disease-specific therapies may be needed to achieve control of disease activity before proceeding with the surgical procedure.

TKR is an elective procedure, and the risks and outcomes vary. Therefore, it is essential that patients be informed of the likely consequences of the surgery in terms that are specific to them. Every patient's goals and expectations (i.e., hopes and fears) should be ascertained before TKR to determine whether their goals are attainable and their expectations are realistic. Any discrepancies between the patient's expectations and the likely surgical outcome should be discussed in detail before surgery.

In the past, patients between 60 and 75 years of age were considered to be the best candidates for TKR. Over the past two decades, however, the age range has been broadened to include, on the one hand, more elderly patients (e.g., octogenarians and beyond), many of whom have a higher number of comorbid conditions, and, on the other hand, younger patients, whose implants may be exposed to greater mechanical stresses (because of higher levels of physical activity) over an extended time period. In patients younger than age 55, alternative surgical procedures, such as osteotomy and unicompartmental knee replacement, deserve consideration. Advanced age alone is not a contraindication for TKR; however,

perioperative complications are higher in patients who are older at surgery as well as in those with more comorbid conditions.

There are few absolute contraindications for TKR other than active local or systemic infection and other medical conditions that substantially increase the risk of serious perioperative complications or death. Obesity is not a contraindication to TKR; however, there may be an increased risk of delayed wound healing and perioperative infection in obese patients. Severe peripheral vascular disease and some neurologic impairments are both relative contraindications to TKR.

The success of primary TKR in most patients is strongly supported by more than 20 years of followup data. Perioperative mortality approximates 0.5 percent. There appears to be rapid and substantial improvement in the patient's pain, functional status, and overall health-related quality of life in about 90 percent of patients, and 85 percent of patients are satisfied with the results of surgery. Data suggest that these improvements in patient-reported outcomes persist in both the short- and long-term studies. Factors associated with the lack of improvement following surgery in the remaining patients are not well known.

Complications following TKR include wound-healing problems; wound and deep-tissue infection; deep-vein thrombosis and pulmonary embolism; pneumonia; myocardial infarction; patellar fracture and/or extensor mechanism disruption; joint instability, stiffness, and/or malalignment; and nerve and vascular injuries. Factors associated with wound and deep-tissue infection include a diagnosis of RA, diabetes mellitus, obesity, and use of glucocorticoids. One of the most important factors leading to successful TKR is proper surgical technique; the rate of complications in some studies that utilized national administrative databases was inversely related to both surgeons' and hospitals' volume of operations per year.

Rates of prosthesis failure requiring revision increase with duration of followup after surgery from about 10 percent at 10 years to about 20 percent at 20 years (~1 percent per year). Prosthesis failure rates vary substantially across studies; factors associated with shortened time to prosthesis failure include age younger than 55 years, male gender, diagnosis of OA, obesity, and presence of comorbid conditions. It is hypothesized that the higher rate of prosthesis failure observed in young obese men with OA is related to higher levels of physical activity after TKR in this population.

Thus, although the clinical conditions and circumstances leading to TKR are broadly defined, several issues regarding indications remain unresolved. Evidence-based indications from results obtained with standardized instruments that measure pain, physical function, and quality of life as perceived by the patient must be used to guide clinical decision-making and choice of surgery. Instruments such as the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the New Zealand Priority Criteria for Major Joint Replacement, the Knee Society Score (KSS), or the Hospital for Special Surgery (HSS) scale should be examined in this regard.

How do specific characteristics of the patient, material and design of the prosthesis, and surgical factors affect the short- and long-term outcomes of primary TKR?

In short- (1–5 years) and long-term (5–10 years or longer) outcome studies, outcomes typically include either self-reported measures of pain, function (Short-Form 36 [SF-36] or WOMAC), or physician-reported measures (KSS, HSS scales). Failure of the prosthesis is included in more long-term studies.

Short-term outcomes, as documented by functional outcome scales, are generally substantially improved after TKR. Age, gender, and obesity do not appear to be strongly associated with outcome, though lower body mass index was associated with greater satisfaction and better functional outcome in a large study of Canadian women. People with RA appear to have greater improvements from baseline compared with people with OA, but this may reflect the generally worse preoperative scores in those with RA. Functional outcome is improved after TKR for people across the spectrum of disability status. However, relatively lower functioning people, as measured by preoperative WOMAC scores, improve by a greater percentage than those who are higher functioning. Nonetheless, those with low baseline function do not achieve as high an absolute level of function as those with better baseline status.

In general, prostheses are durable, but failure does occur. Because the most common treatment for prosthesis failure is revision of the TKR, the incidence of revision is commonly used as a measure of prosthesis failure.

The role of gender on failure rate is variable depending on the study. Data based on two large studies (Sweden and Canada) demonstrate that gender has no influence on revision rates among patients with OA. However, an American study demonstrated that men had an overall greater risk of failure than women. Among patients with RA, the risk of failure was greater in men than in women. In addition, younger men who are obese appear to be at substantially higher risk of revision than other patients, especially compared with older, nonobese women.

Factors related to a surgeon's experience, technique, and choice of prosthesis may have important influences on surgical outcomes. One of the clearest associations with better outcomes appears to be the procedure volume of the individual surgeon and the procedure volume of the hospital. Medicare data indicate that the highest complication rate is observed among surgeons who perform 12 or fewer operations per year, and complication rates decrease as the number of operations performed each year increases. Similarly, complication rates are highest in hospitals that perform less than 25 operations per year, and rates fall with increases in numbers of operations performed.

Technical factors in performing surgery may influence both short- and long-term success rates. Proper alignment of the prosthesis appears to be critical in minimizing long-term wear, risk of osteolysis, and loosening of the prosthesis. Computer navigation may eventually reduce the risk of substantial malalignment and improve soft tissue balance and patellar tracking. However, the technology is expensive, increasing operating room time, and the benefits remain unclear.

Prosthesis design has evolved over time, with improvement in success rates. A number of knee prosthesis designs are on the market today, however, and their

relative merits are generally unclear. Many design features, such as use of mobile bearings or designs that spare cruciate ligaments, have theoretical advantages, but durability and success rates appear roughly similar with most commonly used designs.

The polyethylene components of modern prosthetic designs appear to be quite durable. In the past, certain sterilization techniques — especially gamma irradiation in air — appear to have had adverse effects on polyethylene structure and durability. Storage in air with oxygen exposure, therefore, may have had similar adverse effects. Modern sterilization and storage techniques may largely solve this problem, but surgeons may need to be cautious with polyethylene components that have been stored for several years.

Patients would benefit from being provided with an information card about prosthesis design and date of manufacture. External labeling on prosthesis packaging, including date of manufacture and sterilization, would be useful to surgeons.

Are there important perioperative interventions that influence outcomes?

Several medical and rehabilitative strategies for TKR patients are used to optimize surgical outcomes of reduced pain and improved function, and to minimize complications such as deep-wound infections, thromboembolic disease, postoperative anemia, and pulmonary infections. Despite the widespread use of TKR, there is a notable lack of consensus regarding which medical and rehabilitative perioperative practices should be employed, mostly because of the lack of well-designed studies testing the efficacy and effectiveness of such practices.

The use of perioperative antibiotics and other operating room procedures reduces deep wound infections after knee surgery to less than 1 percent. Although data also support the use of antibiotic impregnated bone cement as an additional means of reducing the deep-wound infection rate, concern regarding the availability, cost, and genesis of antibiotic resistant strains of bacteria has tempered the enthusiasm for this strategy. Some data also support the use of ultraclean-air operating rooms and whole-body exhaust-ventilated suits worn by the operating room team to reduce infection rates. However, these operating room procedures have not been universally adopted primarily because of the uncertainty of their impact.

The American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy classifies TKR as a high-risk procedure for venous thromboembolism and recommends prophylaxis with (1) low-molecular-weight heparin, (2) oral anticoagulants, (3) adjusted-dose heparin, or (4) intermittent pneumatic compression/elastic stockings plus low-dose unfractionated heparin or low-molecular-weight heparin. This recommendation is based primarily on the reduction of the occurrence of deep venous thrombosis (DVT) detected by venography following TKR. However, the vast majority of DVTs following TKR are asymptomatic,

and the available data indicate that DVT prophylaxis does not alter the occurrence of symptomatic DVTs or pulmonary embolism (PE), although no individual study was large enough to statistically assess effects on the occurrence of PE. In addition, changes in postoperative management that would be expected to reduce the incidence of DVT and PE, including early mobilization, have occurred since these studies were performed. Recent data demonstrate that detection and treatment of asymptomatic DVTs do not alter the occurrence of symptomatic DVTs or pulmonary embolism after TKR. Data from a large observational study of TKR published after the most recent ACCP consensus conference show that use of warfarin does not protect against pulmonary embolism or symptomatic DVTs compared with no anticoagulation. Furthermore, bleeding complications, including catastrophic gastrointestinal and wound hematoma, which could necessitate return to the operating room, are risks of anticoagulation that must be considered.

The use of rehabilitation services is perhaps the most understudied aspect of the perioperative management of TKR patients. Although there are several theoretical reasons why the treatment of preoperative and postoperative physical impairments such as muscle weakness and atrophy, joint contractures, abnormal joint mechanics, and gait patterns should lead to improved short- and long-term outcomes of surgery, there is no evidence supporting the generalized use of any specific preoperative or postoperative rehabilitation intervention. Similarly, the site of postacute care of TKR patients (home versus acute rehabilitation unit versus skilled nursing facility) is currently determined by local practice patterns and insurance reimbursement policies and not by available data. Finally, no evidence-based guidelines exist for promoting or limiting post-TKR physical activity.

Other practices for which there is no consensus either in the field or in the literature include the prevention and/or treatment of postoperative anemia (e.g., autologous blood transfusion, the use of erythropoietin, and various intra-operative techniques) and the method of postoperative analgesia (epidural analgesia versus intravenous narcotics, the use of cyclooxygenase-2 selective inhibitors). There is consensus that pain should be managed aggressively.

There is general consensus that preoperative cardiac risk assessment should be performed and cardiopulmonary function should be optimized before TKR. Smoking cessation can reduce the risk of cardiac ischemia and postoperative pneumonia and should be recommended for all smokers preoperatively although it may need to be initiated at least 2 months before surgery for optimal effect. Among patients older than age 70, preoperative assessment of mental status with a standardized instrument such as the Mini Mental Status Exam (MMSE) can help to identify patients at high risk for delirium. Postoperatively, incentive spirometry should be used to reduce the incidence of pneumonia. Preoperative patient education about what will happen during surgery and the postoperative period has been shown to improve patient outcomes, including reduced use of pain medications, reduced anxiety, and improved patient satisfaction.

What are the indications, approaches, and outcomes for revision TKR?

As the cumulative incidence of primary TKR increases, as indications extend to older and younger individuals, and as the population ages, the absolute number of revision knee replacements will increase even if the rate of failures in primary procedures continues to decrease. Revision surgery is complex and costly, requires technical expertise, and should be performed in high-quality hospitals by skilled health care teams. Consequently, the surgeon's experience, hospital characteristics, and related health care costs with revision should be examined carefully.

As with primary TKR, revisions for failed TKR are done to alleviate pain and improve function. The goals of TKR revision are restoration of mechanical and rotational alignment, restoration of joint line and space, and achievement of stable implant fixation.

It remains very important to refine the indications for revision and to do so on the basis of the best available outcome data. The decision to revise, as is true of decisions regarding primary procedures, must consider circumstances such as the presence of disabling pain, stiffness, and functional limitation unrelieved by appropriate nonsurgical management and lifestyle changes. Evidence of progressive and substantial bone loss alone is sufficient reason to consider revision in advance of catastrophic prosthesis failure. Fracture or dislocation of the patella, instability of the components or aseptic loosening, infection, and periprosthetic fractures are common reasons for total knee revision.

The results of TKR revision are not as good as those of primary TKR, the former being approximately 70 percent in the good-to-excellent range whereas the latter is approximately 90 percent. Outcomes are better for patients who undergo revision for aseptic loosening

as opposed to infection. The proportion of patients with good-to-excellent outcomes declines with each successive revision.

It is critical to identify the cause of the original prosthesis failure to improve the outcome following revision surgery. Early loosening may result from poor surgical technique of the original TKR, infection, mechanical overload, or osteolysis. Osteolysis appears to result from an inflammatory reaction to particulate debris generated from the prosthesis. Efforts to minimize osteolysis include a search for more durable and wear-resistant materials. Research in management of osteolysis includes nonsurgical treatment, such as use of bisphosphonates and cytokine inhibitors. Periodic radiographic monitoring, as part of standard, long-term orthopaedic followup care, may allow appropriate management before prosthesis failure.

A number of options must be considered in planning a revision operation. Current revision implants have been available only for the past decade and appear to improve results, although more long-term data are needed. Although the literature on revision TKR is limited, outcomes of revision for failed primary TKR show good results at 5 years, but long-term results are less certain. Revision for infection is a challenging problem, with the most successful functional results being obtained in a two-stage revision.

Salvage procedures for failed revision TKR include the following: (1) resection arthroplasty (usually reserved for nonambulatory patients with persistent infections), (2) arthrodesis, and (3) above-the-knee amputation. A salvage procedure is eventually required in less than 10 percent of revised TKRs. The primary indication for a salvage procedure is an infected revised TKR. The limited data available indicate that pain relief and improved function following any of these salvage procedures are limited and far inferior to revision TKR.

What factors explain disparities in the utilization of TKR in different populations?

There is clear evidence of racial/ethnic and gender disparities in the provision of TKR in the United States. Although the absolute rates of TKR for men and women are similar, they do not reflect the greater burden of arthritis suffered by women. A Canadian study, after adjusting for age, self-reports of arthritis, and willingness to accept surgery, found that women were significantly less likely to undergo knee replacements. Furthermore, at the time of surgery, women have worse pain and functional limitation than men.

A recent study of Medicare administrative data from 1998 through 2000 revealed annual procedure rates per 1,000 of 4.8 for white males, 3.5 for Hispanic males, and 1.9 for African American males. The corresponding rates were 5.9 for white women, 5.4 for Hispanic women, and 4.8 for African American women. These disparities are not new — Medicare data from 1980 through 1988 demonstrated a range of white-to-African American ratio for TKR from 3.0 to 5.1 for men and a range of ratio from 1.5 to 2.0 for women.

Racial or ethnic differences in the provision of care are not limited to joint replacements. Elderly whites are more likely than African Americans to receive care from a physician. Medicare data from 1993 showed significant racial or ethnic differences in the provision of angioplasties, coronary artery bypass grafts, and screening mammography. Other studies have demonstrated that African Americans are significantly less likely to undergo carotid endarterectomies, lumbar disc procedures, repair of abdominal aortic aneurysms, and kidney transplants.

Patients with Medigap insurance are more likely to have knee replacements than those with Medicare alone. A Maryland study found that population rates for discretionary orthopaedic, vascular, and laryngologic surgery increased with community income levels.

A number of factors may be critical in explaining these disparities, including issues related to equity and access, physician recommendations, patient perceptions and preferences, and interactions between health care providers and patients.

The limited role of economic and other access factors in these racial or ethnic disparities can be demonstrated by persistence of significance differences in the rate of procedures in the Veterans Administration (VA) system, where cost and access are presumed equivalent across race or ethnic groups. VA studies have found that white veterans are more likely than African American veterans to undergo cardiac catheterization, cardiac angioplasty, and coronary artery bypass grafts. Furthermore, African American veterans were 1.5 times more likely than whites to undergo lower extremity amputation versus lower extremity revascularization. Hispanic veterans were 1.4 times more likely than whites to undergo amputation.

To receive a knee replacement, the patient must either first seek care from a health care provider and be referred to an orthopaedic surgeon, or be self-referred directly to an orthopaedic surgeon. The orthopaedic surgeon must then offer TKR, and the patient must accept the recommendation of the surgeon. Disparities can result from inequities at any of these steps.

Patients' acceptance of physician recommendations varies greatly. Among persons with a potential need for TKR, only 12.7 percent of women and 8.8 percent of men were "definitely willing" to have the procedure. In a Cleveland VA study, African American veterans were more likely to perceive various traditional and complementary care modalities as efficacious and less likely to perceive joint replacement surgery as efficacious. African American patients in the same cohort were less likely than white patients to have had family or friends who had joint replacement, or to report a good understanding of joint replacement as a form of treatment.

The interaction between the patient and physician has a good deal to do with final recommendations and the patient's acceptance of those recommendations. There is support for the hypothesis that provider beliefs about patients and provider behavior during encounters are independently influenced by patient race or ethnicity. African American patients who visit physicians of the same race or ethnicity rate their visits as more satisfying and participatory than do patients who see physicians of other races or ethnicities. This argues for encouraging minority students to enter medical careers.

In summary, there are racial/ethnic and gender disparities in the provision of TKR. These disparities are not different from disparities in a number of other procedures. Physicians' beliefs about their patients, the limited familiarity with these procedures in minority communities, patient mistrust of the health care system, and personal beliefs about the most effective treatment of joint problems may all play a role in racial or ethnic disparities. In the final analysis, however, the full explanation for these differences is not known.

What are the directions for future research?

The panel proposes a research agenda that reflects different perspectives of knee-related disability and TKR surgery: (1) the societal perspective, (2) the provider and health care system perspective, and (3) the individual patient perspective. These perspectives are derived from a model of disease and disability in Enabling America (Institute of Medicine, 1997), in which disability (i.e., the alteration of the ability to perform expected social roles) is the end result of a process that begins with pathology and progresses to impairment and functional limitation. In the context of this panel's deliberations, pathology of the knee results in pain and functional limitation of the joint that is severe enough to affect the person's life. The full spectrum of research and research methods, including basic, applied, and clinical science and epidemiologic and health services research, should be used to study all aspects of knee disability and therapies for it. Potentially fruitful areas of basic and applied research include studies on the cellular and molecular biology of aseptic loosening and osteolysis, the relationship of knee kinematics to TKR function and durability, the relationship between the properties of the knee component materials and wear, and the development of surrogate markers for implant performance and survivorship.

Societal Need and Burden Perspective

Much of the research related to TKR has focused on factors that directly affect outcomes of the surgical procedure rather than societal-level factors. Relatively little population-based research exists on the prevalence of severe pain and disability related to pathology of the knee. The burden on society of this disability and the cost of its treatment have not been adequately assessed. In addition, the cost-effectiveness of various prevention and treatment modalities for the problem has not been well established.

Most of the existing research in this area has been limited to persons 65 years of age and older because the majority of the available data are derived from the Medicare system. However, some people begin to experience severe pain and disability in the knee in their 40s, and population data comparable to Medicare data are not available for this younger age group. Of critical importance to the consideration of knee-related disability and TKR surgery is the determination of the potential need for this procedure in the total population. To establish this need, research must systematically sample the community at large to avoid the biases inherent in studying only those persons with adequate access to the medical care system. The suggested design for this study is a prospective, longitudinal, population-based cohort to delineate how knee disability develops and how persons with this problem do or do not access effective treatments, including but not limited to TKR surgery. The design of such a cohort must ensure adequate representation of groups in the population who are currently underserved; then it can be used to identify the extent of disparities in the use of TKR surgery or other treatments for knee disability. The variables to be measured in such a cohort study must be broad enough to capture the disabling process. An additional goal of the cohort study would be to compare outcomes of surgically and nonsurgically treated patients in order to provide more accurate estimates of effect sizes for the studies of outcomes outlined in the following section.

Provider and Health Care System Perspective

This realm of research concerns the surgeon, surgery/prosthesis, perioperative care, and postoperative rehabilitation, and focuses on the surgical outcomes of TKR. We recommend broadening the scope of this ongoing research to include all variables related to the surgeon; surgical technique, including type of prosthesis and implantation technique; selection and perioperative care

of patients; quality and characteristics of the institution, such as infection control methods and surgical volume; preoperative and postoperative interventions, including rehabilitation therapy; and continuity of care, including the pre- and postoperative plan for longer term followup and all types of physical activity. Outcomes should be assessed in all patients who receive knee surgery, as opposed to a convenience sample of those who return to the surgeon, with sufficient followup over the life of the prosthesis. We suggest that a national, research-quality multicenter registry be established to serve as a national resource of data related to the short- and long-term sequelae of knee surgery, including functional outcomes. The registry should be of sufficient size to permit multivariable analyses of risk factors for poor outcomes, with aggressive followup of all patients and their health outcomes.

In addition to the use of comprehensive research registries to observe long-term outcomes, we advocate randomized controlled trials to evaluate select aspects of the knee replacement surgery. For example, a randomized, placebo-controlled trial of prophylactic anticoagulation that assesses the outcomes of PE, bleeding, wound complications, and death seems warranted. Given the lack of evidence about rehabilitative interventions and the resources utilized by these interventions, we recommend that rehabilitation in various sites be studied for its efficacy and effectiveness.

Individual Patient Perspective

This realm of research will evaluate the personal factors that affect the decision to proceed to surgery as well as those factors that affect surgical outcomes.

With respect to the decision to proceed to surgery, there is strong evidence of disparities between genders and among racial or ethnic groups in (1) knowledge of the surgery, given similar levels of medical need, (2) willingness to have surgery, given the same level of knowledge, and

(3) actual surgical rates, taking need and willingness into account. We do not know the extent to which these disparities are the result of subjective differences across groups in perception of pain or disability and orientation to surgery (e.g., risk aversion or cultural affinity with the health care providers who might refer to surgery, or both), objective differences in access to care as a result of the potential financial burden and extent and kind of health insurance, or discrimination on the part of health care providers.

Once individuals have TKR, we know little about the patient-level factors affecting outcomes, including medical and sociodemographic characteristics, participation in rehabilitation services, the extent of social support, and the level of patients' physical activity.

Patients may report outcomes more critically when asked explicitly in qualitative studies compared with outcomes as expressed in standardized quantitative measures, indicating that extant outcome measures may not capture some of the difficulties patients experience after surgery.

Conclusions

Primary TKR is most commonly performed for knee joint failure caused by OA; other indications include RA, juvenile RA, osteonecrosis, and other types of inflammatory arthritis. The aims of TKR are relief of pain and improvement in function. Candidates for elective TKR should have radiographic evidence of joint damage, moderate-to-severe persistent pain not adequately relieved by an extended course of nonsurgical management, and clinically significant functional limitation resulting in diminished quality of life.

The success of primary TKR in most patients is strongly supported by more than 20 years of followup data. There appears to be rapid and substantial improvement in the patient's pain, functional status, and overall health-related quality of life in about 90 percent of patients; about 85 percent of patients are satisfied with the results of surgery.

Short-term outcomes, as documented by functional outcome scales, are generally substantially improved after TKR. Functional outcome is improved after TKR for people across the spectrum of disability status. In general, prostheses are durable, but failure does occur.

Age younger than 55 at the time of TKR, male gender, diagnosis of OA, obesity, and presence of comorbid conditions are risk factors for revision.

Factors related to a surgeon's case volume, technique, and choice of prosthesis may have important influences on surgical outcomes. One of the clearest associations with better outcomes appears to be the procedure volume of the individual surgeon and the hospital.

Technical factors in performing surgery may influence both the short- and long-term success rate. Proper alignment of the prosthesis appears to be critical. Many design features, such as use of mobile bearings or designs sparing cruciate ligaments, have theoretical advantages, but durability and success rates appear roughly similar with most commonly used designs.

There is consensus regarding the following perioperative interventions that improve TKR outcomes: systemic antibiotic prophylaxis, aggressive postoperative pain management, perioperative risk assessment and management of medical conditions, and preoperative education.

The effectiveness of anticoagulation for the prevention of pulmonary emboli is unclear. There are insufficient data to support specific perioperative rehabilitation strategies, methods to reduce postoperative anemia, postoperative physical activity recommendations, and the site of post-acute care.

Revision TKR is done to alleviate pain and improve function. Fracture or dislocation of the patella, instability of the components or aseptic loosening, infection, and periprosthetic fractures are common reasons for total knee revision. A painful knee without an identifiable cause is a controversial indication. Contraindications for revision TKR include persistent infection, poor bone quality, highly limited quadriceps or extensor function, poor skin coverage, and poor vascular status. Results are not as good as with primary TKR; outcomes are better for aseptic loosening than for infections. When infection is involved, successful results occur with a two-stage revision. Failed revisions require a salvage procedure (resection of arthroplasty, arthrodesis, or amputation), with inferior results compared with revision TKR.

There is clear evidence of racial/ethnic and gender disparities in the provision of TKR in the United States. Racial or ethnic differences in the provision of care are not limited to joint replacements. The limited role of economic and other access factors in these racial or ethnic disparities can be demonstrated by significant differences in the rate of procedures in the VA system, where cost and access are assumed equivalent across race or ethnic groups.

Patients' acceptance of physician recommendations varies greatly. Among persons with a potential need for TKR, only 12.7 percent of women and 8.8 percent of men were "definitely willing" to have the procedure. The interaction between the patient and physician affects the final

recommendations and the patient's acceptance of those recommendations. Physicians' beliefs about their patients, the limited familiarity with these procedures in minority communities, patients' mistrust of the health care system, and personal beliefs about the most effective treatment of joint problems may all have a role in these racial or ethnic disparities.

The goal of new population-based observational research is to discover the need for services among persons with knee disability and the extent to which this need is currently being met by resources available within the family and in the community at large (including the health care system).

Research into the impact of providers and the health care system should be broadened to include all TKR variables related to the surgeon, such as training and experience; surgical technique, including type of prosthesis and implantation technique; selection and perioperative care of patients; quality and characteristics of the institution, such as infection control methods and surgical volume; preoperative and postoperative modalities, including rehabilitation therapy; and continuity of care, including the pre- and postoperative plan for longer term followup and physical activity. In addition to broadening the scope of variables studied, the outcomes assessment must include all persons who receive knee surgery, as opposed to a convenience sample of those who return to the surgeon, and the followup must be sufficiently long to encompass the expected life of the prostheses.

Research should identify the extent to which disparities in the use of TKR are the result of subjective differences across groups in perception of pain or disability and orientation to surgery (risk aversion or cultural affinity with the health care providers who might refer to surgery, or both); objective differences in access to care as a result of the potential financial burden and extent and kind of health insurance; or discrimination on the part of health care providers. Research also should identify the patient-level factors affecting outcomes after surgery, including medical and sociodemographic characteristics, participation in rehabilitation services, the extent of social support, and the level of a patient's physical activity after the surgery.

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