Symposium integrating evidence-based medicine into clinical practice

Rick W. Wright  
*Washington University School of Medicine in St. Louis*

John E. Kuhn  
*Vanderbilt University Medical School*

Annunziato Amendola  
*University of Iowa Hospitals and Clinics*

Morgan H. Jones  
*Cleveland Clinic Foundation*

Kurt P. Spindler  
*Vanderbilt University Medical School*

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Evidence-based medicine represents the combination of the best available clinical research evidence with clinical experience and expertise and the needs and expectations of patients. Evidence-based medicine as a concept has been available for years, but it has become increasingly important over the last decade. Some evidence has suggested that it began as early as the ancient Chinese medicine practices, while other evidence has indicated its origins were in postrevolutionary France with the systematic patient observations of Pierre Louis. Gordon Guyatt led a group at McMaster University in the early 1990s that introduced many of the current concepts of evidence-based medicine. This led to a major increase in interest in the area. One paper had been published in the literature in 1992, but by 1998 over a thousand manuscripts had been published in the field.

Evidence-based medicine utilizes the best available research evidence. In the hierarchy of medical evidence, systematic reviews including meta-analyses represent the highest form of evidence if inclusion is limited to Level-I or II studies (Table I). Systematic reviews of Level-III or IV observational studies can be performed, but they represent Level-III or IV evidence. Frequently, in orthopaedics, systematic reviews or meta-analyses may not be available and clinicians may need to rely upon randomized controlled trials, cohorts, case-control studies, case series, or, in some areas, expert opinion. Orthopaedists may not yet recognize this hierarchy. During the 2005 Annual Meeting of the American Orthopaedic Association (AOA), the audience was asked the question: “Findings from which type of study design are most likely to influence your clinical practice?” The responses indicated that a randomized controlled study design was used by 49%; a systematic review and/or meta-analysis of Level-I studies,
by 44%; expert opinion, by 5%; and case series, by 3%.

At a symposium at the 2005 Annual Meeting of the AOA, a series of eleven systematic reviews was presented. The series involved more than fifty randomized controlled trials performed to determine the best available evidence in the literature to address a series of clinical questions on the treatment of injuries in sports medicine involving the shoulder, knee, foot, and ankle. The symposium demonstrated the ability to use the highest form of evidence available in a practical manner to assist in clinical decision-making. In the present review of that symposium, we use selected examples of systematic reviews of major clinical questions to reveal the strength of evidence-based medicine in routine clinical practice. Areas that can be clarified through the use of systematic reviews include challenging previously held dogma, assessing the efficacy of new technology compared with previous methods, and improving decision making in the face of studies with a limited or low level of evidence.

The steps of performing a systematic review are reasonably straightforward and can be performed by most researchers (Table II). The systematic reviews in this symposium were developed with use of these methods. Each clinical question was assessed with a rigorous review of the literature, including a search of MEDLINE, EMBASE, and the Cochrane Controlled Trials Register. The bibliographies of the appropriate manuscripts identified by this search were also reviewed for additional relevant studies. To ensure that no recently published articles were missed, a hand search of journals published in the previous six months was performed and included a search of The Journal of Bone and Joint Surgery (American and British Volumes), Clinical Orthopaedics and Related Research, and appropriate subspecialty journals in the areas of sports medicine, shoulder, knee, and foot and ankle. The search was limited to English-language journals. Studies identified by this search were reviewed with use of a standardized worksheet as a method of quality appraisal. Biases were identified, and the study was included or excluded on the basis of the specific evidence available with each question that is outlined throughout the present article.

**The Shoulder**

There are a number of questions in the current treatment of shoulder disorders that can be addressed with use of an evidence-based medicine approach. The shoulder represents a clinical area where systematic reviews can assess the efficacy of recently introduced technology or methods and can help the clinician to determine whether the data supports changing his or her practice. The example presented is a systematic review regarding the success of arthroscopic compared with open shoulder stabilization procedures.

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**TABLE I Medical Evidence Hierarchy**

| Meta-analysis and/or systematic review (if performed on Level-I or II studies) |
| Randomized clinical trials |
| Clinical trials |
| Cohort studies |
| Case-control studies |
| Case series |
| Case reports |
| Expert opinion |

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**TABLE II Steps in Performing a Systematic Review**

1. Research question
   - Research protocol
   - Literature search
   - Data extraction
   - Quality assessment
   - Data analysis and results
   - Interpret results
tors, for their patient population, the evidence suggests that the recurrence rates are not significantly different and the statistical power of their studies allowed for stronger conclusions, the trial do not show a difference) and the evidence available was Level IV, or case series. Studies were excluded unless they collected data on consecutive patients and included only athletically active patients. In addition, only studies dealing with isolated syndesmosis sprains without radiographic evidence of widening of the mortise or an associated ankle fracture were included for review. Six studies met the criteria for review (see Appendix)\textsuperscript{20}. All studies were case series that were Level-IV evidence. All of the series reported included professional or college athletes. The diagnosis in all studies was clinical. Radiographs were made,
but the diagnosis was not based on the findings of radiographs or magnetic resonance imaging. There was a large variation in the time lost from sports and return to play, with a range of 6.3 practices and 1.4 games for professional football players, forty-five days for professional hockey players, and fifty-two days for army cadets involved in a variety of sports.

Homogeneous outcome measures were not used in these studies. In addition, functional outcome was not reported in every study. In four of the six studies, a functional outcome measure was used and most of the patients returned to good or excellent function once they had recovered from the injury. In terms of surgery, one of fourteen patients in the study by Hopkinson et al. and one of fifteen patients in the study by Hopkinson et al. were managed operatively14-16. In general, surgery was not required and conservative treatment was employed. A number of nonoperative modalities were used, and they included removal from activity, immobilization, ice, and anti-inflammatory medication. Once the patients became pain-free and were able to function, they were allowed to return to sports as tolerated.

 Syndesmotic, or high ankle, sprains continue to be a common injury that results in substantial time lost from sports. The lower level of evidence (a Level-IV case series) in this systematic review does not give solid or high-level scientific evidence for the best treatment and management. The conclusion to be made from this type of evidence is that the diagnosis does not allow accurate assessment of the severity of the injury and, thus, the ability to predict the time lost from sports. This can be an injury with a considerable period of time lost from sports, but there are also some instances with very few days lost. This suggests that current diagnostic methods are not prognostic.

 Therefore, an evidence-based medicine review was conducted to determine whether there is evidence to address this specific question. The result is a systematic review of ten Level-I randomized controlled trials on the choice of autograft (hamstring graft or bone-patellar tendon-bone graft).

**Does the Choice of a Hamstring or Bone-Patellar Tendon-Bone Graft Offer an Advantage for Patients?** How to Use Evidence-Based Medicine to Challenge or Confirm Commonly Held Beliefs

In The American Journal of Sports Medicine in 2004, a systematic review was published on the choice of autograft for anterior cruciate ligament reconstruction17. That article contained nine Level-I randomized controlled trials designed to compare autograft types (hamstring grafts and bone-patellar tendon-bone grafts)17-19. The objectives were to identify reproducible, clinically important differences in objective measures (stability, range of motion, and strength) and subjective measures (questionnaire results) to determine whether the choice of autograft is an important variable in the outcome after anterior cruciate ligament reconstruction. The results were presented in tabular form, and the absolute differences between outcome measures for the different grafts were evaluated and presented such that the reader could interpret the reproducibility and clinical importance of the results. The goal was to provide orthopaedic surgeons with the data on which to base their decisions on the highest level of evidence for their practice. The presentation of a systematic review in tabular form was deemed to be complementary to, not a substitute for, formal statistical combining of data as in a meta-analysis. This review builds on these nine randomized controlled trials and adds a tenth trial by Laxdal et al., which appeared in January 2005 in Arthroscopy20. Thus, this systematic review on autograft choice contains ten randomized controlled trials, all with Level-I evidence.

The studies were identified with a
rigorous review of the literature. A search of MEDLINE, EMBASE, and the Cochrane Controlled Trials Register was performed with use of the terms “ACL,” “anterior cruciate ligament,” “reconstruction,” “autograft,” “clinical trial,” and “randomized controlled trial” in combinations (connected with the Boolean operators “and” and “or”). The bibliographies of the appropriate manuscripts identified by this search were also reviewed for additional relevant studies. To ensure that no recently published articles were missed, a hand search of journals published in the previous six months was performed and included a search of The Journal of Bone and Joint Surgery (American and British Volumes), Clinical Orthopaedics and Related Research, The American Journal of Sports Medicine, Arthroscopy, and The Journal of Knee Surgery. The search was limited to English-language journals. Exclusion criteria included inadequate or lack of randomization (alternating sequence or consecutive series), or series using allografts.

These studies were conducted in five countries by a total of twenty-seven surgeons and consisted of a sample size with follow-up of 890 (91%) of a possible 974 patients. Eight of the studies used an endoscopic arthroscopic approach to bone-patellar tendon-bone grafts, and two of the studies used a rear-entry approach. With regard to the hamstring constructs, a similar distribution of endoscopic and rear-entry approach was compared. In all studies, the fixation points, whether interference screws, EndoButtons (Smith and Nephew, Andover, Massachusetts), screw and post, or staple, were thought to be satisfactory, thus eliminating differences in fixation technique between grafts. The hamstring studies were either three or four-graft constructs in seven of the ten studies. When the demographic data or rehabilitation protocols were evaluated, no differences were found between groups.

Instrumented laxity at the time of the final follow-up was usually the primary outcome measure to determine the results between the autograft groups. The results of the ten studies, including the method of measuring instrumented laxity, the force, the percentage with force of <3 mm, the actual millimeters of force, degree of variation, and p value are reported in a table in the Appendix. Seven of the ten studies demonstrated no significant difference between grafts with respect to instrumented laxity at the time of final follow-up. Three of the ten studies demonstrated a significant difference (p = 0.05 in two studies, and p = 0.004 in one), with the patellar tendon group being more stable in each study. However, the differences between the bone-patellar tendon-bone and hamstring grafts were 1 mm in two studies and 3.3 mm in another study. It should be noted that, in two of the three studies, a two-strand hamstring construct was used and not the typical three or four-bundle construct used most commonly today. It should also be noted that the follow-up periods reported by the authors were, in the majority, two years and up to three years in some studies.

Isokinetic strength at the time of final follow-up was also measured in seven studies. No differences were reported in quadriceps strength and in strength between the grafts. However, in three of the seven studies, there was a weakness in knee flexion with the hamstring graft. This weakness ranged between 7% and 11%, and averaged between those values.

Patellofemoral pain at the time of final follow-up should be divided into anterior knee pain and kneeling pain. All studies measured some component of patellofemoral pain, but their scales were not consistent. In eight of the ten studies, there was no significant difference in anterior knee pain between the groups. However, two of the studies demonstrated a significant difference, with less pain in the hamstring group (p = 0.007 and p = 0.05). The results of kneeling pain, defined as a knee walking test in two studies, as a visual analog scale score in two others, and as measured by a subjective scale in one, consistently showed that the patients with bone-patellar tendon-bone grafts had more kneeling pain than did those with hamstring tendon constructs. These two topics were thought to be the most important with regard to the graft decision, as shown by the results of the survey at the 2005 Annual Meeting of the AOA, in which kneeling pain and patellofemoral pain were thought by 31% and 32% of the responders, respectively, to be the most critical reproducible factors. Instrumented laxity and isokinetic strength at the time of final follow-up were thought to be the most critical factors by 19% and 18% of the responders, respectively.

Activity level and functional assessment were also obtained postoperatively in nearly every study. When activity levels were compared, by nonvalidated means in the majority of the studies, nine of the ten studies showed that there was no difference between groups. However, O’Neill demonstrated a significantly higher return to activity in the bone-patellar tendon-bone graft group compared with the hamstring construct group (p < 0.02), whereas a comparison with the preinjury activity level demonstrated a difference of only six percentage points. Furthermore, in a comparison of various clinical outcome assessments, in every case, no significant difference was observed between the autograft groups.

The present large, prospective cohort of ten randomized trials demonstrated that the failure rate of the anterior cruciate ligament reconstruction graft was 3.6% (95% confidence interval, 2.3% to 5.3%). No significant differences were found with regard to increased failure of the hamstring graft compared with the bone-patellar tendon-bone graft in any individual study, and, when the data of all of the studies were combined, no difference was found in the overall prevalence of failure of the bone-patellar tendon-bone graft compared with that of the hamstring graft. The rate of deep intra-articular infection ranged from 0% to 2.9%. When the data in the studies that noted infection were averaged, the frequency of infection was 1.0% (seven of 733 knees).
In conclusion, this systematic review did not find consistent reproducible differences between autograft patellar tendon and hamstring grafts that would separate or recommend a particular graft choice. How these graft choices may affect patient-centered outcomes or longer-term (i.e., five to ten-year) follow-up is unknown. However, the data and reviews suggest that the choice of autograft may not be the primary determinant of successful results in the short term after anterior cruciate ligament reconstruction. We hypothesize, given the excellent success rates of both surgical techniques and graft choices, that injury to and treatment of the meniscus and articular cartilage may have a more profound influence on anterior cruciate ligament reconstruction results and patient-centered outcomes than the specific graft selected.

**Overview**

As demonstrated by this symposium, the application of evidence-based medicine principles, highlighted by systematic reviews of the literature to determine the best available evidence, provides readers with guidance in patient-care decisions. Sometimes with systematic reviews, the available evidence is excellent. However, systematic reviews more frequently can use only Level-III or IV studies on which to base decisions and, thus, should lead to further studies in these areas.

We believe that, in the future, these principles should be applied to narrative reviews and current concept articles. In contrast to a current concepts narrative review, a systematic review answers a clinically relevant question in a scientific manner on the basis of evidence-based medicine principles. Thus, unlike the studies in a current concepts review that are self-selected by the authors, a systematic review includes or excludes studies on the basis of a transparent, defined set of criteria. This practice will elevate the level of evidence presented for review purposes in the orthopaedic literature.

**Appendix**

| Tables listing the specific studies evaluated in these analyses are available with the electronic versions of this article, on our website at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). |

Rick W. Wright, MD
Department of Orthopaedic Surgery, Washington University School of Medicine at Barnes Jewish Hospital, One Barnes-Jewish Plaza, Suite 11300, St. Louis, MO 63110

John E. Kuhn, MD
Kurt P. Spindler, MD
Department of Orthopaedic Surgery and Rehabilitation, Vanderbilt University Medical School, 1215 21st Avenue South, Suite 4200 MCE, South Tower, Nashville, TN 37232

Annunzio Amendola, MD
Department of Orthopaedic Surgery and Rehabilitation, University of Iowa Hospitals and Clinics, 01018 John Pappajohn Pavilion, 200 Hawkins Drive, Iowa City, IA 52242-1088

Morgan H. Jones, MD
Department of Orthopaedic Surgery, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195
doi:10.2106/JBJS.E.00934

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