

Review Article

Twenty-year perspective of randomized controlled trials for surgery of chronic nonspecific low back pain: citation bias and tangential knowledge

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Abstract

BACKGROUND CONTEXT: After decades of clinical research, the role of surgery for chronic nonspecific low back pain (CNLBP) remains equivocal. Despite significant intellectual, human, and economic investments into randomized controlled trials (RCTs) in the past two decades, the role of surgery in the treatment for CNLBP has not been clarified.

PURPOSE: To delineate the historical research agenda of surgical RCTs for CNLBP performed between 1993 and 2012 investigating whether conclusions from earlier published trials influenced the choice of research questions of subsequent RCTs on elucidating the role of surgery in the management of CNLBP.

STUDY DESIGN: Literature review.

METHODS: We searched the literature for all RCTs involving surgery for CNLBP. We reviewed relevant studies to identify the study question, comparator arms, and sample size. Randomized controlled trials were classified as “indication” trials if they evaluated the effectiveness of surgical therapy versus nonoperative care or as “technical” if they compared different surgical techniques, adjuncts, or procedures. We used citation analysis to determine the impact of trials on subsequent research in the field.

RESULTS: Altogether 33 technical RCTs (3,790 patients) and 6 indication RCTs (981 patients) have been performed. Since 2007, despite the unclear benefits of surgery reported by the first four indication trials published in 2001 to 2006, technical trials have continued to predominate (16 vs. 2). Of the technical trials, types of instrumentation (13 trials, 1,332 patients), bone graft materials and substitutes (11 trials, 833 patients), and disc arthroplasty versus fusion (5 trials, 1,337 patients) were the most common comparisons made. Surgeon authors have predominantly cited one of the indication trials that reported more favorable results for surgery, despite a lack of superior methodology or sample size. Trials evaluating bone morphogenic protein, instrumentation, and disc arthroplasty were all cited more frequently than the largest trial of surgical versus nonsurgical therapy.

CONCLUSIONS: The research agenda of RCTs for surgery of CNLBP has not changed substantially in the last 20 years. Technical trials evaluating nuances of surgical techniques significantly predominate. Despite the publication of four RCTs reporting equivocal benefits of surgery for CNLBP between 2001 and 2006, there was no change in the research agenda of subsequent RCTs, and technical trials continued to outnumber indication trials. Rather than clarifying what, if any, indications for surgery exist, investigators in the field continue to analyze variations in surgical technique, which will probably have relatively little impact on patient outcomes. As a result, clinicians unfortunately have little evidence to advise patients regarding surgical intervention for CNLBP. © 2013 Elsevier Inc. All rights reserved.

Keywords: Lumbar fusion; Chronic nonspecific low back pain; Evidence-based medicine; Clinical trials; Citation bias

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Introduction

The validity and benefit of clinical research depend on addressing questions that need to be answered. Generation of evidence depends on investigators' decisions about patient population, outcomes, and comparator arms. Ideally, such decisions are made rationally, after systematic review of evidence from previous experimentation [1,2], although there are numerous examples to suggest that such analysis is not undertaken, and potentially unnecessary trials are performed [3,4]. Trial funding sources may lead to systematic avoidance of potentially valuable head-to-head comparisons of proven therapies [5–7]. Conversely, much of medicine relies on historical tradition, rather than rigorous experimentation, and randomized controlled trial (RCT) evidence of treatment effectiveness, even for the most frequently performed interventions, is often still lacking. Such accepted, but unproven, medical practices are frequently reversed when subjected to rigorous testing [8]; therefore, evaluation of such popular practices is desirable from a societal perspective. It has been suggested that the reluctance of practitioners to test the fundamental effectiveness of their specialty's treatments might limit the generation of evidence on such topics [9] and lead to the generation of “tangential” evidence [10].

Chronic nonspecific low back pain (CNLBP) has been defined as “LBP persisting for at least 12 weeks, not attributable to a recognizable, known specific pathology (eg, infection, tumor, osteoporosis, fracture, structural deformity, inflammatory disorder [eg, ankylosing spondylitis], radicular syndrome, or cauda equina syndrome)” [11]. The frequency and cost of diagnostic imaging and medical and surgical therapies for this condition have risen dramatically in recent decades, without a commensurate improvement in population measures of outcome [12,13].

Surgical interventions, including fusion and disc arthroplasty, have been applied with the belief that abnormal intersegmental movement or degenerative pathology may be the cause of CNLBP. However, diagnostic criteria are variable [14], and lumbar degenerative changes are prevalent in the asymptomatic population [15], making the validity of this pathophysiologic concept uncertain. Rates of lumbar fusion vary dramatically within the United States and among countries, underscoring the uncertain indications for surgery in current clinical practice [16,17]. Four RCTs published between 2001 and 2006 compared lumbar fusion with nonoperative care [18–21]. Based on these results, recent systematic reviews and clinical guidelines have indicated a limited role for lumbar fusion in the treatment for CNLBP [11,22,23].

The tenets of evidence-based medical practice would predict that these results would temper enthusiasm for and reduce performance of surgery for CNLBP. On the contrary, lumbar fusion has been one of the most rapidly growing, commonly performed, and costly surgical procedures in the United States, despite the absence of new indications [24,25]. In light of this apparent lack of influence of

previous trials on clinical practice, we sought to determine the effects of these trials on the subsequent research agenda on this topic.

Methods

We searched for trials published in English indexed in PubMed and Web of Science (last search September 2012) with the search strategy “lumbar fusion” OR “back pain surgery” OR “lumbar instrument*” OR “disc degen*.” We also searched “clinicaltrials.gov” and other databases to identify unpublished or ongoing clinical trials. We included RCTs that involved patients with CNLBP and included a surgical intervention as a comparator arm. We manually reviewed each article and excluded trials limited to patients with spondylolisthesis or scoliosis. We also checked the citation lists of systemic reviews and meta-analyses on the same topics to make sure that all relevant trials were included.

For each article, we recorded information on the authors, year, journal, comparator arms, and sample size of the trial. As a measure of recent relevance, we recorded the number of times that publications from 2010 to 2011 (the most recent two complete years before investigation) cited the trials or their follow-up publications. We categorized trials comparing surgical versus nonsurgical therapies as “indication” trials and those comparing different surgical techniques, approaches, or adjuncts as “technical” trials.

Because the first four indication trials published in 2001 to 2006 [18–21] reported uncertain benefits of surgery, we analyzed the number of indication and technical trials published after 2006 to see what influence these trials had on subsequent clinical research. We also used Web of Knowledge to analyze citation frequency as a measure of the relative impact of the indication trials in particular. Given the different years of publication, and thus the amount of time available to accrue citations, we analyzed citations made after January 2007, by which time these indication trials had been published. We categorized the affiliation of citing authors: if the primary or senior author of the citing publication had primary affiliation with a neurosurgery or orthopedic surgery department, we considered the publication to have a “surgeon author.” We also analyzed how subsequent CNLBP surgical trials—published since January 2007—cited these initial four indication trials. Two investigators performed all data extraction separately (NSA and JPF), which was then checked by another investigator (VB). The study had no outside funding.

Results

Altogether 39 RCTs were published involving surgery for CNLBP [18–21,26–60] (Table). From these 39 RCTs, 6 trials compared operative versus nonoperative treatments for CNLBP (indication trials) and 33 RCTs compared

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