

Outcomes Research in Regional Anesthesia and Analgesia

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Outcomes research evaluates the effectiveness of health care interventions in many aspects of patient care (clinical outcomes, functional health status, patient satisfaction, and economic measurements) and reflects national trends in determining the appropriateness, value, and quality of health care in the United States (1). Outcomes research incorporates diverse types of data and data analysis. Although outcomes measurements include a wide variety of patient-related assessments, anesthesiologists have traditionally focused on clinically related patient outcomes.

The benefit of regional anesthesia on patient-related outcomes is controversial. Many questions involving study design, data analysis and sample size contribute to the uncertainty of the benefits of regional anesthesia-analgesia on patient outcomes. Like those from other subspecialties in anesthesiology, investigators evaluating the efficacy of regional anesthesia have emphasized traditional, clinically oriented, patient-related outcomes. Little has been done to determine the consequences of regional anesthesia and postoperative analgesia on "nontraditional" patient outcomes, such as health-related quality-of-life (HRQL) measurements, patient satisfaction, and economic assessments. This article provides an overview of outcomes research, the current status of outcomes research in regional anesthesia, and future directions for determining the benefits of regional anesthesia and postoperative analgesia.

Outcomes Research: An Overview

Substantial increases in health care costs have contributed to the development of outcomes research in the United States. Health care costs constitute a significant percentage of the gross national product (GNP) and have increased at a rate much greater than that of inflation or overall growth in GNP. Despite the high

percentage of GNP spent on health care, the United States lags behind many other industrial nations in major indexes of health, such as life expectancy and infant mortality (1). These factors, along with the presence of significant geographical variations in clinical practice without differences in clinical outcomes, have resulted in political and economic pressures to reevaluate the appropriateness, value, and quality of health care in the United States (1).

What Are "Outcomes"?

Although "outcomes research" has become a popular topic for investigators, true outcomes research incorporates a wide variety of patient-related measurements, including those other than the more familiar clinically related assessments. In general, outcomes research involves an assessment of the effectiveness of a health care intervention on various aspects of patient benefits and includes not only clinical outcomes but also functional health status, patient satisfaction, and economic measurements (see Table 1) (1). Functional health status of a patient may be assessed by using validated instruments to measure quality-of-life, physical, psychologic, and social variables. There are few validated instruments to measure patient satisfaction with various aspects of anesthetic care, and patient satisfaction surveys must be carefully constructed and validated to ensure that specific health care interests are addressed (2). Economic measurements have become more prevalent in the anesthesia literature; however, there are a variety of economic analyses, each which may result in a different conclusion depending on the type and perspective (societal, patient, payer, provider) of analysis (3).

Types of Data and Data Analysis

Many types of data and data analysis may be used in outcomes research. Although a detailed discussion of all types of data and data analysis is beyond the scope of this article, a brief description of those most relevant to the evaluation of the benefits of regional anesthesia on patient outcomes will be discussed to facilitate interpretation of results and conclusions derived from outcomes research studies (see Table 2).

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Table 1. Types of Patient-Related Outcomes in Regional Anesthesia

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- A. Clinically oriented or "traditional" outcomes
 - 1. Mortality
 - 2. Major morbidity
 - Cardiovascular, coagulation, cognitive, gastrointestinal, immune, pulmonary, stress response
 - B. "Nontraditional" outcomes
 - 1. Health-related quality-of-life measurements
 - 2. Patient satisfaction
 - 3. Economic outcomes
 - a. Types of costs and benefits: direct and indirect, medical and nonmedical
 - b. Type of analysis: cost-effectiveness, cost-benefit, cost-utility
 - c. Perspective for analysis: patient, payer, provider, societal
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Adapted from Reference 3.

Prospective Data: Randomized, Controlled Trial. The randomized controlled trial (RCT) is considered by many to be the "gold standard" in evaluating the effect of an intervention on patient outcomes. Randomization minimizes the possibility that confounding factors may interfere with analysis of any potential association between risk factors and outcomes (4). By standardizing inclusion-exclusion criteria and treatment protocols, prospectively defining outcomes and using a placebo or accepted alternative treatment, a RCT maximizes the likelihood that outcomes obtained are the result of the intervention applied.

Despite the strength of the RCT, it has several disadvantages, some of which are relevant when determining the effect and efficacy of regional anesthesia and analgesia on patient outcomes. Significant drawbacks to RCTs include the cost, time, and need for extremely large sample sizes when evaluating rare outcomes. For example, a sample size of 24,000 patients would be needed to determine if regional anesthesia would have a beneficial effect in decreasing the incidence of overall mortality by 50% (power of 80%) when compared with that from general anesthesia (5). Execution of such a study at one center would be extremely time consuming and expensive. Although multicenter trials are possible, protocol deviation and institutional differences may affect the study results. Furthermore, increasing sample size through multicenter trials may not necessarily improve statistical power (6). Other disadvantages of RCTs include ethical concerns and less external validity (applicability of the findings to a more heterogeneous population). In addition, RCTs examining regional versus general anesthesia are necessarily unblinded (with exception of the Perioperative Ischemic Randomized Anesthesia Trial or PIRAT 2), allowing for the introduction of bias.

Meta-analysis. Despite the increasingly common use of meta-analysis to combine and evaluate data from

various sources, meta-analysis is relatively controversial. The effect of an intervention, such as regional anesthesia, on patient outcomes may be difficult to determine as a result of the need for extremely large sample sizes. Studies in these areas are, for the most part, underpowered and may yield conflicting results. Meta-analysis, which involves strict criteria for the inclusion of studies for analysis and statistical methods specific for this type of analysis, attempts to integrate and synthesize the results from several smaller trials.

There are several disadvantages of meta-analysis, one of the most significant of which is the creation of results and conclusions based on nonoriginal data from studies that may vary in study design, subject population, and outcomes criteria. Although some may argue that the heterogeneity of data reflects random error, small differences in one of several factors may affect whether a trial is acceptable to include for analysis, thus potentially altering the final results and conclusions of the meta-analysis (7). Meta-analysis may also contain publication biases (exclusion of non-English languages trials and unpublished data) (8). Although meta-analysis may be a useful tool to synthesize data from a variety of sources, the analysis and conclusions from a meta-analysis must be carefully worded (and read) in an attempt to prevent oversimplifying a complex issue (7). Finally, conclusions from meta-analysis may not correlate with that from subsequent large-scale RCTs (7).

Retrospective Data: Databases. With the availability of large administrative or insurance claims databases, there have been an increasing number of studies analyzing database information in outcomes research. Database analysis and data acquisition generally cost less and require less time when compared with equally large RCTs. Databases contain information from regional and national populations, which may facilitate assessment of small frequency outcomes. In addition, information from databases reflects typical clinical practice.

However, databases are retrospective in nature, may contain missing data points, and may not accurately measure the outcomes of interest. In addition, the informational content reflects the purpose of the database (mostly billing and claims) which, despite the presence of demographic and diagnosis codes, may not necessarily be useful in outcomes research. Incomplete coding may also hinder data analysis and result from limitations in the number of available diagnostic or procedural coding slots (9). Thus, there may not be enough information available to answer the hypothesis posed. Finally, large databases may be "massaged" to obtain "significant" associations between risk factors and outcomes (10).

Although databases may provide an alternative form for outcomes research, especially in situations in which appropriately large RCTs would unlikely be

Table 2. Randomized, Controlled Trials Versus Databases for Research in Regional Anesthesia

Advantages	Disadvantages
Randomized-Controlled Trials Considered by many to be the "gold standard" Randomization minimizes effect of confounding factors Prospective definitions of outcomes Results likely caused by the effect of the intervention applied	Large sample sizes needed with rare outcomes Increases in cost and time with data collection Limited applicability to the general population Ethical concerns with randomization
Databases Lower costs and time with data acquisition Data reflects regional and national populations Reflects typical clinical practice Facilitates assessment of rare outcomes	Retrospective data Created for billing and claims purposes Databases may be manipulated Does not provide cause-and-effect relationships

performed, it is important to remember that database analysis can only propose associations and not causation. The current format of many databases limits the type of questions that may be answered.

Current Status of Outcomes Research in Regional Anesthesia

Despite some convincing data on specific organ systems (coagulation, pulmonary, gastrointestinal), the overall benefits of regional anesthesia on patient-related outcomes is still controversial. Available studies are frequently beset by methodological issues, including study design and sample size, which contribute to the uncertainty of the effectiveness and efficacy of regional anesthesia on patient outcomes. Studies, for the most part, have only measured "traditional," clinically oriented, patient-related outcomes (see Table 3).

Overview of Current Studies: Methodological Concerns

There are many methodological concerns in evaluation of the efficacy and effectiveness of regional anesthesia and analgesia on (clinically oriented) patient outcomes. One major criticism of available studies is inadequate sample sizes reflecting the small incidence of outcome events, thus affecting the ability of investigators to detect clinically significant differences. For example, approximately 3000 patients would be needed to determine if an intervention (regional anesthesia) could decrease the incidence of a surrogate endpoint (myocardial ischemia) from 30% to 20% (11). Enrollment of smaller-risk subjects or those undergoing less invasive surgery would increase sample sizes even further because of the consequent smaller incidence of the outcome event studied (12-14).

One of the difficulties in measuring some anesthesia-related clinical outcomes is the rarity in which these events occur (e.g., death, myocardial infarction). Because of the infrequency of such an event, it may be difficult (and expensive as a result of the

Table 3. Methodological Issues with Available Studies in Regional Anesthesia

Inadequate sample sizes Use of surrogate endpoints Lack of incorporation of appropriate postoperative analgesic regimens Inadequate assessments of pain Limited ability to apply results of randomized, controlled trial to a more generalized population

large sample size) to properly evaluate the effectiveness of an intervention on outcomes. Use of a surrogate endpoint, a related but more frequently or easily measured event, may facilitate determination of outcomes with a smaller sample size and decreased cost. Despite some controversy, anesthesiologists have commonly used surrogate endpoints, such as myocardial ischemia, hospital charges, and postoperative nausea and vomiting (15,16).

Conclusions from a trial using surrogate endpoints may be valid if there is a positive relationship between the surrogate (e.g., myocardial ischemia) and true outcomes (e.g., myocardial infarction); however, it is rare that these relationships are established and validated. Occasionally, the relationship between surrogate endpoints and true outcomes have been invalidated with subsequent analysis (17). Strict validation of the relationship between a surrogate endpoint and true outcome may require a trial using a large sample size similar to that using true outcomes (18,19). Thus, surrogate endpoints may not be a reliable predictor of patient-related outcomes.

Although most studies focus on the efficacy of intraoperative regional versus general anesthesia on clinically oriented patient outcomes, few trials have properly incorporated postoperative analgesic regimens into the study design. To properly determine the effects of postoperative regional analgesia on patient outcomes, an appropriate postoperative regional analgesic regimen (most likely using local anesthetics) should be administered for an adequate duration to provide maximal physiologic benefits as the incidence of some outcomes peak in the postoperative period

possibly after discontinuation of regional analgesia (5,14,20). An example of an appropriately designed trial to investigate the effect of postoperative regional analgesia on outcomes is the PIRAT 2 study in which patients undergoing aortic cross-clamp procedures were randomized to one of four groups: intraoperative general anesthesia with postoperative epidural local analgesia or IV opioids, or intraoperative regional-general anesthesia with postoperative epidural local analgesia or IV opioids (21). In general, there are few trials in this area; consequently, it is difficult to determine the effect of postoperative regional analgesia *per se* on outcomes.

In addition, many studies do not measure pain both at rest and with activity. Although regional anesthesia-analgesia provides superior postoperative analgesia, static (at rest) pain control alone cannot improve clinically oriented outcomes despite the physiologic benefits of regional analgesia with local anesthetics. Only dynamic (with activity) pain control will potentially allow patients to participate in postoperative physiotherapy (e.g., deep breathing, ambulation), which may facilitate recovery and improvement in outcomes (22).

Finally, even if a properly conducted RCT could be conducted with adequate sample sizes, it may not be appropriate to generalize results from such a structured protocol to typical clinical care in the "real world," and at best, application of any conclusions from such a trial to the clinical setting would need to be made with caution (23). In general, RCTs (e.g., PIRAT 1 and 2) comparing the efficacy of regional versus general anesthesia on patient outcomes skew delivery of normal clinical care by setting management guidelines and limits on physiologic variables, such as blood pressure and heart rate. Thus, the results of regional versus general anesthesia RCTs may be difficult to generalize, as such tight control is not likely to occur in the typical clinical setting (23). However, this does not imply that the results from such RCTs would be useless. For example, detailed examination of the PIRAT 1 reveals that patients randomized to receive general anesthesia required more interventions to maintain study variables (24). As a result, regional anesthesia-analgesia may provide benefits in a less structured setting, especially in the presence of postoperative pain management protocols that may include regional analgesic techniques (23).

Designing, funding, and executing a prospective, randomized trial investigating the efficacy of regional anesthesia to that of general anesthesia on patient outcomes is a difficult proposition at best, especially in the current academic environment. Multicenter trials may be possible; however, inherent problems with data collection and analysis from multiple centers and the difficulty of enrolling patients in randomized trials

with widely differing treatments may prevent completion of these trials (6,25,26). Current studies investigating this issue have methodological concerns, including inconsistent definitions for, and thus incidence of, outcomes, which may affect interpretation of data and result in potentially erroneous conclusions.

Current Outcomes Data

Clinical-Orientated Outcomes. Overall Mortality. Although many small trials comparing the efficacy of regional to general anesthesia on a variety of outcomes have been conducted, the global benefits of regional anesthesia-analgesia are controversial. However, there have been some preliminary data that attempt to address this issue. A group of investigators have performed an overview of all randomized trials comparing intraoperative regional or general anesthesia, regardless of the original outcomes of interest. Studies before January 1, 1997, were eligible, and the original study authors were contacted to confirm published data and provide additional unpublished details (27).

One hundred forty-two trials with 9553 subjects were identified and analyzed on an intention-to-treat basis. When compared with general anesthesia, regional anesthesia reduced overall mortality by approximately 30% (27). The use of regional anesthesia was associated with one fewer death per 100 patients within 30 days of randomization with more than 75% of deaths caused by pulmonary embolism, cardiac events, stroke, or infection (27). Although there was limited power to analyze certain subgroups and limitations to meta-analysis in general (see Types of Data and Data Analysis), regional anesthesia decreased the odds of deep venous thrombosis (DVT) by 44%, pulmonary embolism (PE) by 55%, transfusion by 50%, pneumonia by 39%, respiratory depression by 59%, myocardial infarction by 33%, and renal failure by 43% (27). Thus, it appears that use of intraoperative regional anesthesia globally decreases postoperative complications in a wide variety of surgical patients. Although not discussed in detail here, there are many analgesic and physiologic benefits of regional anesthesia that may explain and corroborate these findings (12).

Coagulation. A hypercoagulable state occurs after surgery under general anesthesia and may be attenuated with use of regional anesthesia. Although the etiology of this hypercoagulable state is uncertain, possible mechanisms include potentiation by the stress response, endothelial damage with tissue factor activation, and synergism with inflammation (21). Postoperative hypercoagulability may lead to vasoocclusive and thromboembolic events, such as DVT, PE, and vascular graft failure, and may contribute to more

than 200,000 deaths annually in the United States (12,28,29).

Compared with general anesthesia, use of regional anesthesia is associated with a significant decrease in hypercoagulable-related events, especially after orthopedic and vascular surgery. Regional anesthesia clearly decreases incidence of DVT after orthopedic surgery, as documented by several randomized trials (30–36). A meta-analysis of 13 randomized trials comparing regional versus general anesthesia for repair of femoral neck fractures also confirmed that patients receiving general anesthesia had a 33% increased incidence of DVT (37). Continuation of postoperative regional analgesia with local anesthetics may also contribute to a decreased incidence of DVT (32). Although many of these trials have not concurrently used systemic DVT prophylaxis or have failed to specify presence of prophylaxis, retrospective data suggest that regional anesthesia will still provide a benefit in diminishing the incidence of DVT regardless of presence or absence of prophylaxis (38).

Use of regional anesthesia is associated with a significant decrease in graft thrombosis after vascular surgery. Randomized trials have shown that the use of epidural anesthesia alone or in combination with general anesthesia decreases the incidence of graft occlusion or failure through attenuation of perioperative hypercoagulability (13,39,40). In addition, a randomized trial has shown a significantly decreased incidence of DVT in patients undergoing open prostatectomy under regional anesthesia (41). Finally, in an analysis of 18 randomized trials (27), regional anesthesia decreased the odds of DVT by 44% and PE by 55%.

Gastrointestinal. Transient postoperative ileus is common after abdominal surgery under general anesthesia and may be caused by several factors, including an increase sympathetic efferent outflow from pain or stress response, postoperative use of opioids for analgesia, and spinal reflex inhibition of gastrointestinal motility (42). Use of regional anesthesia-analgesia facilitates recovery of postoperative gastrointestinal function and is associated with an earlier fulfillment of discharge criteria (42).

Several randomized trials have demonstrated that, when compared with systemic opioid analgesia after general anesthesia, the use of thoracic epidural analgesia with a local anesthetic-based regimen is associated with significantly earlier return of gastrointestinal function after abdominal surgery (42–48). Two randomized trials revealed no differences between regional analgesia and systemic analgesia in return of bowel function after abdominal surgery; however, the duration of postoperative regional local anesthesia-based analgesia may have been too brief (≤ 24 hours) to provide significant physiologic benefits (14,49).

Four randomized trials have shown that, when compared with epidural opioids for postoperative analgesia, the use of epidural local anesthetics is associated with earlier return of gastrointestinal motility after abdominal surgery (42,46,50,51). It is unclear whether the use of neuraxial opioids will provide earlier return of gastrointestinal function when compared with that with systemic opioids, as the randomized trials comparing the effects of neuraxial to that of systemic opioids provide conflicting results (14,42,52).

Pulmonary. There is a significant decrease in respiratory function after upper abdominal and thoracic surgery under general anesthesia as a result of inadequate analgesia, increase in upper abdominal and intercostal muscle tone, and spinal reflex inhibition of diaphragmatic function (12). Many individual trials with different study designs and analgesic regimens have been conducted to determine the effect of the analgesic regimen on a variety of pulmonary outcomes. It is difficult to draw any definitive conclusions from individual trials, as many are underpowered, use surrogate endpoints, and yield conflicting results.

A meta-analysis of 48 RCTs investigating the effect of seven postoperative analgesic therapies on postoperative pulmonary function was conducted (17). Compared with systemic opioids, postoperative epidural analgesia with local anesthetics significantly decreased incidence of pulmonary morbidity, despite there being no differences in surrogate measures of pulmonary function (forced expiratory volume in 1 s, forced vital capacity, peak expiratory flow rate) between groups. Compared with systemic opioids, epidural opioids decreased the incidence of atelectasis but did not significantly diminish the incidence of pulmonary complications. There were no significant differences in analgesia or pulmonary function between lumbar or thoracic administration of opioids. The use of intercostal blocks, wound infiltration, or intrapleural analgesia was not associated with any significant improvement in pulmonary function or complications (17).

Other (Cardiovascular, Stress Response, and Immune and Cognitive Function). The benefits of regional anesthesia-analgesia on outcomes with regard to other organ systems, such as the stress response, immune function, cognitive function, and cardiovascular system, are not certain. The neuroendocrine stress response after surgery under general anesthesia has been well documented and may be attenuated or even completely inhibited by the use of regional anesthesia. The stress response results in a hypermetabolic, catabolic state and may affect cardiovascular, immune, and coagulation function. Despite the many potentially detrimental effects on various organ systems, the association between the neuroendocrine stress response *per se* and patient outcomes is inconclusive. Thus, without establishing this relationship,

any direct or indirect effect of regional anesthesia-analgesia on patient outcomes through attenuation of the stress response cannot be determined.

Postoperative immune function is diminished after surgery under general anesthesia and may adversely affect patient outcomes by contributing to the development of infections, increasing cost of care, and enhancing the possibility tumor growth and metastases (53,54). Although the etiology is not clear, stress response potentiation and perioperative administration of medications (opioids, anesthetics) may contribute to perioperative immunodepression. Regional anesthesia may preserve perioperative immune function either through attenuating immunodepression (via the stress response) or decreasing intraoperative blood loss, with a subsequent decrease in the need for perioperative opioid administration or blood product transfusions, which has been associated with immunosuppression (55-58). Although the effect of regional anesthesia-analgesia on patient outcomes through preservation of immune function is not clear, two randomized trials have noted a decrease in the incidence of postoperative infectious complications in subjects receiving epidural analgesia (40,59). Furthermore, analysis of data from 14 randomized trials revealed that regional anesthesia was associated with a decreased risk of developing pneumonia or other infections (27).

The effect of regional versus general anesthesia on cognitive function has been examined in several randomized trials (60-67). Only one demonstrated any advantage of regional anesthesia on postoperative cognitive function as measured by investigator interviews (59). Although most trials have shown no advantage of intraoperative regional anesthesia in the preservation of postoperative cognitive function, the effect of postoperative regional analgesia on cognitive function has not been carefully examined. There are many independent predictors for the development of postoperative delirium, including higher levels of postoperative pain (63,68-71). Because regional analgesic techniques are associated with superior analgesia when compared with systemic analgesic techniques, regional analgesia may provide some advantages with regard to postoperative cognitive function.

Cardiac events, such as myocardial ischemia and infarction, congestive heart failure, ventricular arrhythmias, and sudden death, occur primarily in the postoperative period (72). Although regional anesthesia-analgesia may provide many cardiovascular benefits by diminishing the stress response, attenuating postoperative hypercoagulability, and providing a favorable redistribution of coronary blood flow, there are no definitive conclusions concerning the effect of regional anesthesia-analgesia on outcomes (12). Several randomized trials have not demonstrated any advantages of regional

anesthesia-analgesia on patient outcomes (5,73,74); however, one study did show an increase in myocardial ischemia on discontinuation of postoperative epidural analgesia (74). Although, analysis of 30 randomized trials revealed that there were approximately one-third fewer myocardial infarctions in those receiving regional anesthesia (27).

Nontraditional Outcome Measurements. Economic Outcomes and Analysis. The effect of regional anesthesia-analgesia on economic outcomes has not been adequately examined. In general, comprehensive economic evaluation of any intervention on outcomes is difficult at best (75). Proper economic evaluation of the effects of regional anesthesia requires consideration of many issues, including types of economic measurements (e.g., "cost") and analysis and the economic impact of any beneficial clinical outcomes provided by regional anesthesia-analgesia. Inappropriate measurements or analysis of economic data may result in erroneous conclusions regarding the economic impact of regional anesthesia-analgesia.

Examining economic data can be complicated, because there are several types of economic analysis, including type of analysis (cost-effectiveness, cost-benefit, cost-utility), types of costs and benefits (direct and indirect, medical and nonmedical), and perspective for analysis (patient, provider, payer, societal) (3). RCTs, which may be appropriate for addressing clinical hypothesis, may not be suitable for answering economic questions, as many RCTs include contemporaneous economic evaluation without appropriate or proper sample size calculations, descriptive statistics (including confidence intervals), or formal methods of statistical inference (76,77). Often, cost data are highly skewed, and the use of standard statistical methods may result in misleading results (76). The use of nonparametric analysis, such as "bootstrapping," requires no assumptions with regard to the shape of the sampling distribution and is especially useful when working with ratios (e.g., cost-effectiveness or cost-utility analysis) where the numerator and denominator may have different distributions (77,78).

The "cost" of a specific service incorporates the total resources used to provide that service (3). Clinicians commonly equate cost with what are considered direct hospital costs, or typical operational expenditures (e.g., equipment and medications) associated with routine clinical care. Although direct hospital costs are an important component of total cost, this concept of cost is not complete, as the total cost of a service should also include direct nonhospital or medical costs and assessment of indirect costs, which may include lost income, lost opportunities, decreased productivity, and indirect morbidity and mortality (3). Because unsubstantiated and unreliable statements regarding "costs" and economic analysis of interventions occur frequently in the literature, comprehensive

economic data and appropriate evaluation of an intervention (such as regional anesthesia) for subsequent studies is important as clinical guidelines or health policy may be based on these data (79–82).

To date, there has been no comprehensive examination of costs (direct or indirect) associated with use of regional anesthesia and analgesia. Although direct costs associated with regional analgesia may intuitively seem greater than that of systemic analgesics, regional anesthesia-analgesia may provide economic benefits through indirect costs, such as decreasing indirect costs, patient morbidity and mortality, or length of stay. For example, preliminary data from a meta-analysis of 142 randomized trials revealed that mortality was decreased by approximately 30% in patients receiving regional anesthesia when compared with those receiving general anesthesia (27). Regional anesthesia also decreased patient morbidity by decreasing risk of development of DVT, PE, transfusion, pneumonia, respiratory depression, myocardial infarction, and renal failure (27). Other randomized trials and meta-analysis also demonstrated a decrease in pulmonary complications and vascular graft failure (13,17,39).

Regional anesthesia-analgesia may also provide economic benefits by decreasing length of stay through control of postoperative pain or physiologic benefits of a local anesthetic-based regional analgesic technique. Although postoperative pain *per se* is not an independent predictor of inpatient length of stay, inadequate control of postoperative pain is one of the leading reasons for readmission after ambulatory surgery (83). Randomized trials reveal that the physiologic benefits of thoracic epidural analgesia with local anesthetics facilitate fulfillment of discharge criteria significantly sooner than those receiving systemic opioids in patients undergoing colectomies (42,84). Thus, regional anesthesia-analgesia may significantly improve clinically oriented outcomes and decrease length of stay which may, in turn, confer beneficial economic outcomes.

HRQL Measurements. Although commonly used in other specialties, HRQL measurements have not been widely used to assess the effects of regional anesthesia-analgesia. HRQL generally consists of validated instruments that assess physical, psychologic, and social variables. Data obtained from these instruments may be statistically analyzed. Although there are many validated instruments available for measuring HRQL, some studies may not incorporate those which are appropriate or standardized, which may cast some doubt as to the validity of their results.

There are several reasons why HRQL measurements may not have been prevalent in the anesthesiology literature. Health care providers, like anesthesiologists, who interact with patients on a more acute basis are generally more familiar with “traditional”

outcomes measurements (e.g., mortality and morbidity). The application of HRQL measurements to daily clinical situations may be difficult to conceptualize, as there has been little research on models describing the relationships between clinical variables and HRQL measurements and the effect of clinical interventions on HRQL (85). Finally, HRQL measurements have not been applied in an acute setting, such as in the postoperative period, and have been generally used over a longer time frame (more than one month). Thus, widespread use of HRQL measurements is hindered by lack of information with regard to their value and benefits in an acute clinical setting and perception of measurements as being “soft” or “unscientific” (86).

The effects of regional anesthesia-analgesia on HRQL measurements have not been extensively examined. Preliminary data suggest that regional anesthesia-analgesia as part of a multimodal approach to postoperative rehabilitation will facilitate earlier recovery of HRQL measurements assessed at three and six weeks after colorectal surgery (87). It is unclear whether using previously validated HRQL instruments to assess patient recovery in the immediate postoperative period (within one week after surgery) is appropriate. The nonspecific nature of some HRQL measurements and the possibility that the expected postsurgical decrease in general functional status may overwhelm any observable HRQL differences between postoperative analgesic treatments and may discourage the use of current validated HRQL measurements in the immediate postoperative setting (88,89). However, regional analgesia generally provides superior postoperative analgesia, and higher levels of postoperative pain may affect HRQL measurements by interfering with activity and sleep (90). The quality of analgesia is an important outcome *per se* and may directly improve physical and functional domains of HRQL. Thus, several issues need to be addressed before HRQL measurements can be meaningfully applied in the acute setting, and until that time, no definitive conclusions can be formed on the effect of regional anesthesia-analgesia on HRQL measurements.

“Patient satisfaction” is an important measure of outcome and has become more significant as health care organizations use it as a measure of “quality” or as a part of marketing services. Measuring patient satisfaction may seem intuitively simple; however, poor survey design and use of unstandardized ratings may lead to erroneous conclusions. Many surveys of “satisfaction” lack refinement and cannot distinguish between satisfaction with the item of interest or with their overall surgical or hospital care (2). Because patient satisfaction reflects complicated psychological factors, its accurate assessment requires a psychometric methodology that can produce valid and reliable multidimensional instruments capable of capturing its true dimensions (2).

Most studies investigating patient satisfaction and regional anesthesia-analgesia have not used validated instruments for measuring satisfaction. Patient satisfaction of regional anesthesia has been examined (91-93), but the effect of regional anesthesia-analgesia on patient satisfaction has not been fully evaluated. Although there are many factors that may influence patient satisfaction, increased ratings of postoperative pain are associated with decreased levels of patient satisfaction (90,94). By providing superior postoperative analgesia, regional analgesia may potentially favorably affect patient satisfaction; however, it may be difficult to differentiate between satisfaction with pain control *per se* and other aspects of medical care (95).

Outcomes Research in Regional Anesthesia and Analgesia: Future Directions. The future of outcomes research in regional anesthesia-analgesia lies in the evaluation of the effect of regional anesthesia-analgesia on economic and "nontraditional" (HRQL and patient satisfaction) outcomes. Establishment of any potential economic or other patient-related benefits of regional anesthesia-analgesia is especially important in light of decreasing reimbursement for postoperative pain services. Another potential area for research is the evaluation of the contribution of postoperative regional analgesia *per se* to patient outcomes. Finally, adoption of an evidence-based approach to decision-making may facilitate the use of regional anesthetic techniques in the perioperative period. A paradigm for future investigation of the effect of regional anesthesia-analgesia on patient outcomes is illustrated in Figure 1.

Movement Toward "Nontraditional" Outcomes. Despite the overwhelming use of clinically oriented measurements, we are beginning to see increasing use of validated HRQL and patient satisfaction instruments to evaluate the efficacy of regional anesthesia-analgesia on patient outcomes. Validation and clinical incorporation of HRQL measurements in the acute perioperative setting may reveal advantages of regional anesthesia-analgesia, especially in the postoperative setting where regional analgesia may improve HRQL and patient satisfaction. Although there are several methodological issues that may hinder widespread use of these measurements in the acute postoperative setting, adoption of HRQL and patient satisfaction assessments in clinical trials may add another dimension to the efficacy of regional anesthesia-analgesia on patient outcomes.

Economic Evaluation of Regional Anesthesia and Analgesia. Although anesthesia providers may influence up to 5% of total health care costs in the United States (96), there is currently a lack of information regarding the effect of regional anesthesia-analgesia on economic outcomes. The relationship between the use of regional anesthesia and postoperative regional analgesia and potential beneficial economic outcomes, in part through improvements in clinically oriented

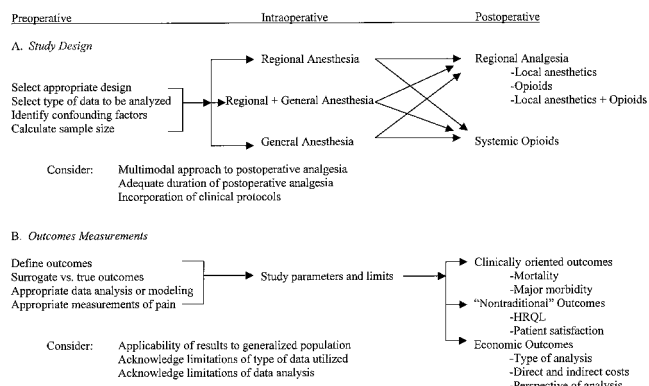


Figure 1. Paradigm for the investigation of regional anesthesia and postoperative regional analgesia on patient outcomes.

outcomes, and possibly decreases in length of stay, should be established. It is important that appropriate economic data presentation and analysis be incorporated into future studies, because administrators, policy-makers, and managed-care insurers may base clinical or economic policy decisions on these data.

Differentiating the Contribution of Postoperative Analgesia to Outcomes. The focus of current trials has been to elucidate potential benefits of intraoperative regional anesthesia on clinically oriented patient outcomes. Despite some data suggesting improvement in outcomes (97), the role of postoperative regional analgesia *per se* on traditional and nontraditional patient outcomes has not been extensively investigated, even though many clinically oriented outcomes, such as myocardial ischemia or infarction and PE, may peak in the postoperative period. Part of the difficulty in teasing out the contribution of postoperative regional analgesia on patient-related outcomes lies in the fact that many postoperative processes begin in the intraoperative period (e.g., DVT) and continue into the postoperative period. Further research is needed on the effect of postoperative regional analgesia *per se* on various outcomes including HRQL, patient satisfaction, length of stay and other clinically related outcomes. In addition, the role of regional analgesia as an important component of a multimodal approach to promote postoperative patient recovery by facilitating early ambulation and enteral nutrition and diminishing complications needs to be further elucidated (22).

Evidence-Based Approach to Decision-Making. Evidence-based medicine (EBM) refers to the integration of the best available evidence from research and application to clinical policy and practice. The relatively recent trend in using EBM in an attempt to provide the best care for an individual patient has been facilitated by easier access to research evidence (e.g., MEDLINE via the Internet). Despite some drawbacks (98-100), EBM may soon become a reality in daily clinical practice. In addition, EBM may play a significant role in the development of clinical practice guidelines. It is imperative

that investigators continue to properly investigate the efficacy of regional anesthesia-analgesia on various outcomes as practitioners and policy-makers critically examine at the benefits of regional anesthesia-analgesia in clinical practice.

Conclusions

Outcomes research in regional anesthesia-analgesia has traditionally focused on clinically oriented outcomes. There is significant data to demonstrate the benefits of regional anesthesia-analgesia on overall mortality and certain organ systems (coagulation, pulmonary, gastrointestinal). The efficacy of regional anesthesia-analgesia on nonclinical outcomes, such as economic, patient satisfaction, and HRQL assessments, is not clear at this time. A trend toward more global assessments of patient-related outcomes and differentiating the contribution of postoperative regional analgesia *per se* will provide new opportunities in regional anesthesia-analgesia outcomes research as we begin the next millennium.

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