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GERIATRIC ANESTHESIA

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An aging population carries profound implications for the practice of anesthesiology. Geriatric issues impact every aspect of anesthesiology. First, the preoperative evaluation of the geriatric patient is typically more complex than that of the younger patient because of the heterogeneity of this patient group and the greater number and complexity of comorbid conditions that usually accumulate with age. Perioperative functional status can be difficult to predict because many elderly patients have reduced preoperative function as a consequence of deconditioning, age-related disease, or cognitive impairment. This makes it difficult to adequately assess the patient's ability to respond to the specific stresses associated with surgery. A common example is trying to determine cardiopulmonary reserve in a patient very limited by osteoarthritis. Physiologic heterogeneity and decreased functional reserve are also manifested perioperatively. Normal aging results in changes in cardiac, respiratory, and renal physiology, and the response of the elderly patient to surgical stress is often unpredictable. The pharmacokinetics and pharmacodynamics of elderly and younger patients also differ; moreover, the elderly patient's use of multiple medications may alter homeostatic mechanisms.

This review of research on anesthesia for elderly patients first summarizes the normal physiologic changes that occur with aging, an overview that is essential to frame the discussion of research in the three sections that follow, on preoperative assessment, intraoperative management, and postoperative management of the older surgical patient. Postoperative respiratory complications and delirium are emphasized, and issues of acute and chronic pain management for elderly surgical patients are also highlighted. The goal throughout is to identify needed research in geriatric anesthesiology.

METHODS

The literature search was conducted on the National Library of Medicine's PubMed database. The time period covered was from 1980 to April 2001. The search strategy combined various terms for anesthesia, sedation, analgesics, and opiates with terms for surgical procedures (general or specific commonly performed operations), the terms *elective* and *emergency*, and various terms for the many elements of surgical care: preoperative assessment and management, intraoperative care, perioperative care, postoperative care, complications, and outcomes. Additional requirements were either that the publication be a review, clinical trial, randomized controlled trial, or meta-analysis, or that terms for risk or age factors be present as title words or MeSH headings. Terms denoting age were *age factors, age, aging , elderly, geriatric, gerontologic, older,* or *octogenarian, nonagenarian*, or *centenarian.* Finally, the term *aspirin* was excluded, as it had generated a large number of irrelevant titles in early iterations of this search.

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AGE-RELATED PHYSIOLOGIC CHANGES AND PERIOPERATIVE CARE

The physiology of aging bears on preoperative assessment, intraoperative and postoperative management, and the types and likelihood of major adverse events. Age-related changes in cardiac, respiratory, neurologic, and renal function as well as in pharmacokinetics have been well defined. The most important generalization from physiologic studies of aging is that the basal function of the various organ systems is relatively uncompromised by the aging process. However, functional reserve, and specifically the ability to compensate for physiologic stress, is greatly reduced (see Figure 2.1). This fact has profound implications for the preoperative assessment and the perioperative care of geriatric patients.

To receive a copy of Figure 2.1, please contact Rachael Edberg at redberg@americangeriatrics.org

CARDIOVASCULAR CHANGES

Numerous changes in cardiovascular function with aging have implications for anesthetic care. With aging, the progressive decrease in the elasticity of the arterial vasculature leads to an increase in systolic blood pressure. Diastolic blood pressure increases through middle age and typically declines after age 60. [1] The cross-sectional area of the peripheral vascular bed also decreases, resulting in a higher peripheral vascular resistance. [2] A decrease in the peripheral vasodilatory response to β-adrenergic stimulation may also contribute to the hypertension of aging. [3]

Progressive ventricular hypertrophy develops in response to increased afterload, resulting in both cellular hypertrophy and deposition of fibrotic tissue. Ventricular hypertrophy increases both wall stress and myocardial oxygen demand and makes the ventricle more prone to ischemia.

Although intrinsic contractility and resting cardiac output are unaltered with aging, the practical effect of ventricular hypertrophy and stiffening is that they limit the ability of the heart to adjust stroke volume. [4] Ventricular hypertrophy impairs the passive filling phase of diastole, making ventricular preload more dependent on the contribution of atrial contraction. At the same time, fatty infiltration and fibrosis of the heart increases the incidence of sinus, atrioventricular, and ventricular conduction defects. [5,6] Myocardial responsiveness to catecholamines also decreases with age; maximal heart rate response is correspondingly decreased. [4,7,8] The reduction in ventricular compliance and the attenuated response to catecholamines compromise the heart's ability to buffer increases in circulatory volume, which results in a predisposition to congestive heart failure. Similarly, even modest decreases in circulatory volume produce hypotension.

From the standpoint of perioperative hemodynamic stability, age-related changes in the autonomic control of heart rate, cardiac output, peripheral vascular resistance, and the baroreceptor response [9–13] are as important as the chronic changes in the myocardium and vasculature. It is evident that age-related changes in the cardiovascular system involve alterations in both mechanics and control mechanisms.

PULMONARY CHANGES

The pulmonary system also undergoes age-related changes in both mechanics and control mechanisms independently of comorbid disease processes. Functionally, there are remarkable parallels with changes in the heart. With aging, the thorax becomes stiffer. [14,15] This may not be evident in the sedentary patient, but reduced chest wall compliance increases the work of breathing and reduces maximal minute ventilation. [14–16] Loss of thoracic skeletal muscle mass aggravates this process. [17] Because of a decrease in elastic lung recoil, the closing volume increases such that by age 65 it exceeds functional residual capacity. [18] Inspiratory and expiratory functional reserve decrease with aging, and the normal matching of ventilation and perfusion decreases. [19,20] The latter process increases the alveolar–arterial O_2 gradient and decreases the resting Pao_2. [18,21] The respiratory response to hypoxia also diminishes in the aged patient. [22] (See Figure 2.2.) In addition, ciliary function is decreased and cough is reduced. [15] Finally, pharyngeal sensation and the motor function required for swallowing are diminished. [23,24]

These changes have important implications in the perioperative period. First, it is difficult to predict from a preoperative interview how an inactive, elderly patient will respond

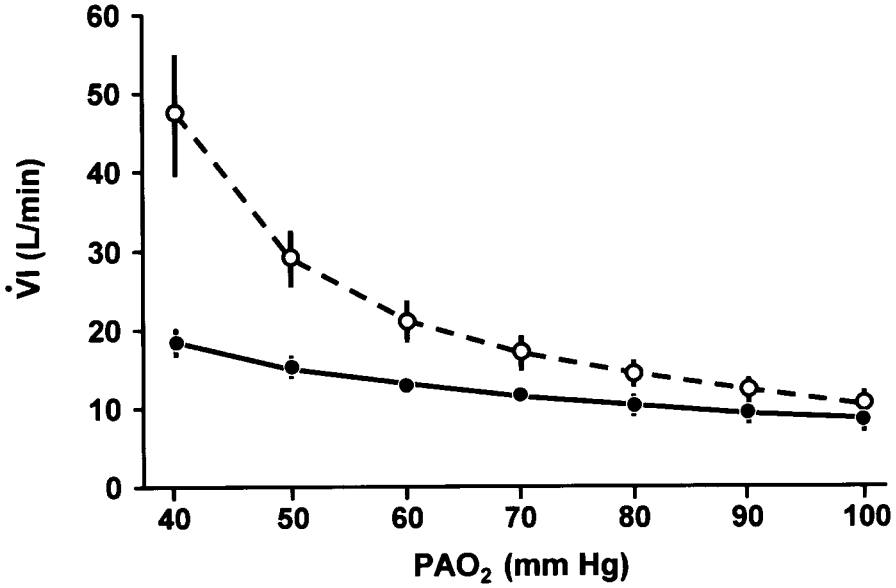

Figure 2.2—Ventilatory response (V_I) to isocapnic progressive hypoxia in eight young normal men (*broken line*) and eight elderly normal men aged 64 to 73 (*solid line*). Values are means ± SEM. BTPS = body temperature, ambient pressure, saturated with water vapor. (Reprinted with permission from Kronenberg RS, Drage CW. Attenuation of the ventilatory and heart rate responses to hypoxia and hypercapnia with aging in normal men. *J. Clin Invest* 1973;52:1812–1819, figure 1.)

to the perioperative respiratory challenges. Anesthetics, postoperative pain, the supine position, narcotics, as well as thoracic and upper abdominal operations impair pulmonary function and further depress respiratory drive. [15,25,26] Although blood gas analysis or spirometric tests may offer some value prior to thoracic operations, the alterations in pulmonary function following surgery are complex and typically not predictable from preoperative pulmonary function testing. [14,20,27] Other implications of age-related changes in pulmonary mechanics and respiratory control are that postoperative hypoxia is likely to occur [28,29] and that the risk of aspiration is significantly increased in the elderly patient. [24,30]

NEUROLOGIC CHANGES

Pulmonary and cardiac complications, respectively, account for most morbidity and mortality in older surgical patients. However, neurologic morbidity affects a large number of patients, and age-related degenerative changes in the central and peripheral nervous systems contribute to a variety of other morbidities. In themselves, neurologic complications have a dramatic impact on length of stay and discharge disposition, translating directly into altered functional status and quality of life.

Independently of any comorbid process, both the central and peripheral nervous systems are affected by aging. [31] There is a loss of cortical gray matter beginning in middle age,

resulting in cerebral atrophy, [32] although how much of this is attributable to aging itself or to degenerative diseases is a subject of ongoing investigation. [33] At the level of the neuron, the complexity of neuronal connections decreases, the synthesis of neurotransmitters decreases, and the enzymes responsible for their postsynaptic degradation increase. [32,34,35] While cerebral metabolism, blood flow, and autoregulation generally remain intact, [32] neuronal loss and the deficiency of neurotransmitters limit the ability of the older brain to integrate multiple neural inputs. This has been described as a loss of "fluid" intelligence. Neuronal loss and demyelinization also occur in the spinal cord. [36] Functionally, spinal cord reflexes change and proprioception is reduced. There are also important decreases in hypoxic and hypercarbic drive. [22,37] Declines in visual and auditory function further complicate the ability of the nervous system to acquire and process information. This combination of changes can limit the ability of the older patient to understand and process information in the perioperative period. These changes are probably important contributors to postoperative delirium, drug toxicity, and falls.

Aging is also associated with neuronal loss in the autonomic nervous system. Both sympathetic and parasympathetic ganglia lose neurons, and fibrosis of peripheral sympathetic neurons occurs. This peripheral neuronal adrenergic loss is associated with impairment of cardiovascular reflexes. At the same time, decreases in adrenoceptor responsiveness result in increased adrenomedullary output and plasma catecholamine concentrations. [11,13,36]

Skeletal muscle innervation decreases, translating into loss of motor units and a decrease in strength, coordination, and fine motor control. [38] Joint position and vibration sense may be compromised, and the literature suggests some diminution in the processing of painful stimuli. [39–42] However, this effect, if it exists, appears to be modest at best, and not affecting all nerve types equally. [42–45] Furthermore, given huge inter-patient variability in nervous system function and in the experience of pain, alterations in subtypes of pain perception do not translate into a decreased need for analgesia in the elderly patient. [44–48]

RENAL CHANGES

Aging is accompanied by a progressive decrease in renal blood flow and loss of renal parenchyma. [49,50] By age 80, half of all older persons may have reduced renal blood flow. This is accompanied by renal cortical atrophy, resulting in a 30% decrease in nephrons by the end of middle age. [49,51] Furthermore, aging is associated with sclerosis of remaining nephrons so that some of those remaining are dysfunctional. [50,52] Together, these processes result in a progressive decrease in glomerular capillary surface area and glomerular filtration rate. [50,52–54] However, because of loss of muscle mass, aging is not associated with an increase in serum creatinine. This physiologic, and often occult, aspect of senescence has practical implications in the perioperative period.

The old kidney has difficulty in maintaining circulating blood volume and sodium homeostasis in the perioperative period. [11,53–55] Sodium conservation and excretion are both impaired by aging. Fluid homeostasis is further complicated by alterations in thirst mechanisms and antidiuretic hormone release that frequently result in dehydration. [53–56] In the perioperative period, metabolic acidosis is also relatively common, particularly in elderly patients who are less efficient in the renal excretion of acid. [57]

Reductions in basal renal blood flow render the elderly kidney particularly susceptible to the deleterious effects of low cardiac output, hypotension, hypovolemia, and hemor-

rhage. Anesthetics, surgical stress, pain, sympathetic stimulation, and renal vasoconstrictive drugs may all compound subclinical renal insufficiency. The likelihood of acute renal insufficiency is especially great in intra-abdominal operations and following aortic surgery and is increased further by many drugs used in the perioperative period. Finally, age-related decreases in glomerular filtration rate reduce the clearance of a number of drugs given in the perioperative period.

PHARMACOKINETIC AND PHARMACODYNAMIC CHANGES

Aging is associated with multiple physiologic changes that may affect drug pharmacokinetics. [58] Decreased lean body mass and total body water and an increased proportion of body fat alter the volume of distribution of drugs, their redistribution among body compartments, and subsequently their rates of clearance and elimination. [59–61] The effect of changes in body composition on drug distribution and action varies, depending on the lipid or aqueous solubility of the drug. Water-soluble drugs can have higher serum concentration and lower redistribution, whereas fat-soluble drugs tend to undergo wider distribution and accumulation, followed by delayed release.

Although age-related changes in the proportions of different plasma proteins make predictions about pharmacokinetics complex in the elderly person, for many drugs, decreased protein binding and increased free fraction have the potential to increase the pharmacologic effect of drugs administered in the perioperative period. [58] Furthermore, potential alterations in cardiac output and renal or hepatic clearance may change effective plasma concentrations and duration of action. [62] Neuronal loss and decreased levels of neurotransmitters in the central nervous system may increase sensitivity to anesthetic agents. The changes in pharmacokinetics that occur with aging make it difficult to identify an independent effect of aging on pharmacodynamics. [59,60] However, age-related changes in the central nervous system appear to increase the older person's sensitivity to a variety of anesthetic agents. [63–65] (See Figure 2.3.)

It has been known for decades that pharmacokinetic changes, particularly decreased metabolism, plus drug interactions coupled with polypharmacy conspire to make the elderly person prone to adverse drug effects. [66–68] There is an almost linear increase in adverse drug reactions with age, from below 10% at age 25 to above 20% at age 80. [69,70] The likelihood of adverse drug reactions increases with the number of drugs administered. [66,67] As many elderly patients come to surgery on multiple medications, the addition of several, even short-acting drugs in the perioperative period makes adverse reactions likely. [68]

IMPLICATIONS FOR ELDERLY SURGICAL PATIENTS

What is clear from a review of normal changes in physiologic function with aging is that even the fit elderly patient's ability to compensate for perioperative stress is compromised. The cardiac, pulmonary, neurologic, and neuroendocrine changes that occur with aging make hypotension, low cardiac output, hypoxia, hypercarbia, and disordered fluid regulation more likely in the perioperative period. Furthermore, because baseline cardiac, pulmonary, renal, and neurologic function is typically adequate in the absence of acute challenges, it can be very difficult to predict the effect of perioperative stress on the older patient.

To receive a copy of Figure 2.3, please contact Rachael Edberg at redberg@americangeriatrics.org

PREOPERATIVE ASSESSMENT OF THE ELDERLY PATIENT

The preoperative assessment of the elderly surgical patient is determined by the underlying health of the patient and influenced by the urgency of the procedure. That said, preoperative evaluation could serve several purposes in most patients. Historically, it has served two primary functions: One is to alert the surgical care providers to physiologic conditions that may alter perioperative management, and the other is to determine if medical intervention is indicated before proceeding. Two more contemporary uses of the preoperative assessment are to provide an index of risk and therefore contribute to decisions about the most appropriate intervention, and to provide baseline data on which the success of a surgical intervention might be judged.

Physiologic studies of aging and clinical experience with the elderly population yield three important conclusions that bear on preoperative assessment. First, the geriatric population is tremendously heterogeneous. This concept was superbly expressed by Muravchick, who noted that humans are never so similar as at birth, and never so dissimilar as in old age. [71] The second conclusion is that basal function in most elderly patients is sufficient to meet daily needs, but that under conditions of physiologic stress, impairment in functional reserve becomes evident. Third, it is evident that most older surgical patients have significant comorbidities. Up to 80% of elderly surgical patients have at least one comorbid condition, and one third have three or more pre-existing conditions. [72,73]

In spite of these limitations, even extreme age is not a contraindication to surgery. Acceptable outcomes are reported for operations even in very old patients. [74–78] What is less clear is how to identify which patients will do well and which will do poorly. Even though this has been the subject of considerable research, no area of perioperative anesthetic care and management requires more investigation. The preoperative assessment of the individual patient is composed of four interrelated functions:

- risk assessment that is based on a stratification of risk derived from population-based studies,
- the history and physical examination to determine health and functional status,
- preoperative testing, and
- in some cases, preoperative optimization.

Each of these functions requires development and better definition for the geriatric surgical population.

RISK ASSESSMENT

Because age itself adds very little additional risk in the absence of comorbid disease, [79] most risk-factor identification and risk-predictive indices have been disease oriented. [80–84] Typically, these investigations have studied a broad age range of patients and in multivariate analyses identified the relative contribution of age and comorbid conditions to surgical morbidity and mortality. [81,82,85–88] Others have looked at the predictive value of the number of comorbid diseases independently of the operative condition or have evaluated the impact of ASA (American Society of Anesthesiologists) status, specific surgical factors, and intra-operative management. [82,88–93]

The applicability of many existing risk indices to the geriatric population is unclear. Because of the prevalence of comorbid conditions, it becomes hard to stratify the older patient population into smaller subsets of more clearly defined risk. The scarcity of population studies of perioperative risk and outcomes specifically in geriatric populations can make choosing the most suitable course of care and providing good information more difficult. Furthermore, elderly patients have some unique risks. In addition to death, myocardial infarction, or congestive heart failure, older patients are particularly more prone than their younger counterparts to postoperative delirium, aspiration, urosepsis, adverse drug interactions, pressure ulcers, malnutrition, falls, and failure to return to ambulation or to home. Therefore, preoperative assessment tools and the variables evaluated in outcomes trials require expansion for application to the geriatric surgical population.

Population studies need to examine not only mortality and major cardiopulmonary morbidity but also outcomes specific to the geriatric population. Once completed, epidemiologic studies that better stratify older patients would help define the preoperative assessment appropriate to older patients.

FUNCTIONAL ASSESSMENT

The efficacy of preoperative functional evaluation in elderly surgical patients requires investigation. This is important for several reasons. The evaluation of the "resting" patient does not indicate how the patient will respond to the cardiac, pulmonary, and metabolic demands of the perioperative period. This approach is emphasized in the guidelines of the American College of Cardiology and the American Heart Association for preoperative cardiac evaluation, in which the patient's activity level, expressed in metabolic units, is a primary determinant of the need for subsequent evaluation. [80] However, this concept must be expanded because the geriatric population has a unique need for functional evaluation in more areas than just cardiopulmonary capacity. Because of patient heterogeneity, functional assessments may be indicated to better characterize patient differences, whether it is for activities of daily living (ADLs), instrumental activities of daily living (IADLs), cognitive and emotional status, or urologic function. [94,95] Scales like the Medical Outcomes Study Short Form–36 (SF-36) [96] have multiple domains that are particularly useful in assessing older patients. Although these metrics have been applied successfully in orthopedic and thoracic surgery [97–99] and can have predictive value for longer term outcomes, [100–104] multidimensional assessment and perioperative functional assessment are largely absent from the surgical literature. [98,105,106]

An example of their application is provided in the study of hip fracture patients by Keene and Anderson, who scored patients preoperatively on the basis of physical condition, ambulation, ADLs, preoperative living situation, and pre-existing disabilities. [102] The scoring system was then used to predict which patients would be discharged to nursing homes following surgery. The actual outcome following surgery was observed for 1 year and compared with the models' predictions (see Table 2.1). Though the study is small, it serves as an example of the type of research needed in geriatric surgery.

Table 2.1—Predicted and Actual Outcomes 1 Year After Hip Fracture Surgery in 39 Elderly Patients

Patients (N)	Residence Before Fracture	Predicted Nursing Home Placement	Actual Nursing Home Placement	Functional Rating* (avg)
10	Home	Temporary	Temporary	72
8	Home	Temporary	Permanent	52
6	Home	Permanent	Permanent	51
15	Nursing Home	Permanent	Permanent	30

* Functional rating was the composite score of five scales: physical condition (maximum 35 points), ambulation (maximum 30 points), activities of daily living (maximum 25 points), prefracture living situation (maximum 10 points), and prefracture disabilities (maximum points 0, maximum deduction for disabilities −40).

SOURCE: Keene JS, Anderson CA. Hip fractures in the elderly: discharge predictions with a functional rating scale. *JAMA* 1982;248:564–567, table 1. Modified with permission.

With regard to preoperative functional assessment, cognitive and psychologic evaluation of the elderly surgical patient deserve special comment. Although frank delirium or dementia at admission clearly predicts poorer acute and long-term outcome, [107,108] subtle forms of cognitive impairment are infrequently diagnosed prior to surgery even though they are more common in elderly patients. In the absence of careful screening, preoperative cognitive deficits may not become evident until the postoperative period. Subtle forms of cognitive impairment can predict subsequent delirium in hospitalized medical patients [109] and worsened cognitive outcome in cardiac, orthopedic, and gastrointestinal surgery patients. [110–114] Preoperative mental status examination [115,116] should be considered for all geriatric surgical patients. Preoperative depression and alcohol abuse are also relatively common and can affect postoperative outcomes in similar ways; [107,117–119] a variety of assessment tools for depression are available. [120,121] The impact of screening for mental status, depression, and alcohol abuse on perioperative management of elderly patients is a huge potential area of investigation.

Preoperative functional assessment is important because the goal should be to return the patient to at least his or her preoperative activity level. The success of surgery must be questioned if the procedure is technically adequate but the patient suffers loss of independence. Multidimensional assessment may help redefine standards for success of surgery and thus reset therapeutic priorities. [97,98,122–124] Application of this type of assessment is exemplified by the work of Mangione et al, who longitudinally measured quality-of-life indicators in patients undergoing hip, thoracic, and aortic surgery. [98] A variety of metrics, including the SF-36, were used to measure physical, psychologic, and social functions and health perceptions preoperatively as well as 1, 6 and 12 months after surgery. (See Figure 2.4 for examples.) Major morbidity and mortality aside, these types of measures address what is fundamentally most important in the medical management of older patients: whether the surgical intervention improves functional status and well-being. These measures are of particular importance to the elderly patient because, unlike the younger patient, the older one is at far greater risk for long-term functional compromise following the stress of surgery.

PREOPERATIVE TESTING

The third dimension of the preoperative evaluation of the elderly surgical patient is preoperative testing. Work in this area has been done for large populations of mixed-age groups. However, it is not clear whether selected preoperative screening tests have a different yield in the elderly age group or, more likely, if specific testing is indicated for elderly patient populations undergoing certain types of surgical procedures.

In the general population there is agreement that most routine tests are not indicated. [125–128] In an evaluation of preoperative screening in 1010 persons undergoing cholecystectomy, abnormal results were found in only 4.5% of tests. [125] In another investigation of 3131 patients aged 0 to 98 years who underwent 38,286 tests, unexpected abnormal results were found in 15% of patients. [126] However, only 3% had a change in their anesthetic or surgical plan that was based on those results. Unfortunately, in neither report was age-specific data provided, so it is unclear if the results can be applied to an elderly surgical population.

Smaller studies of elderly populations suggest that there is a higher yield for specific tests. Seymour et al examined the value of routine chest x-ray (CXR) in 223 patients aged

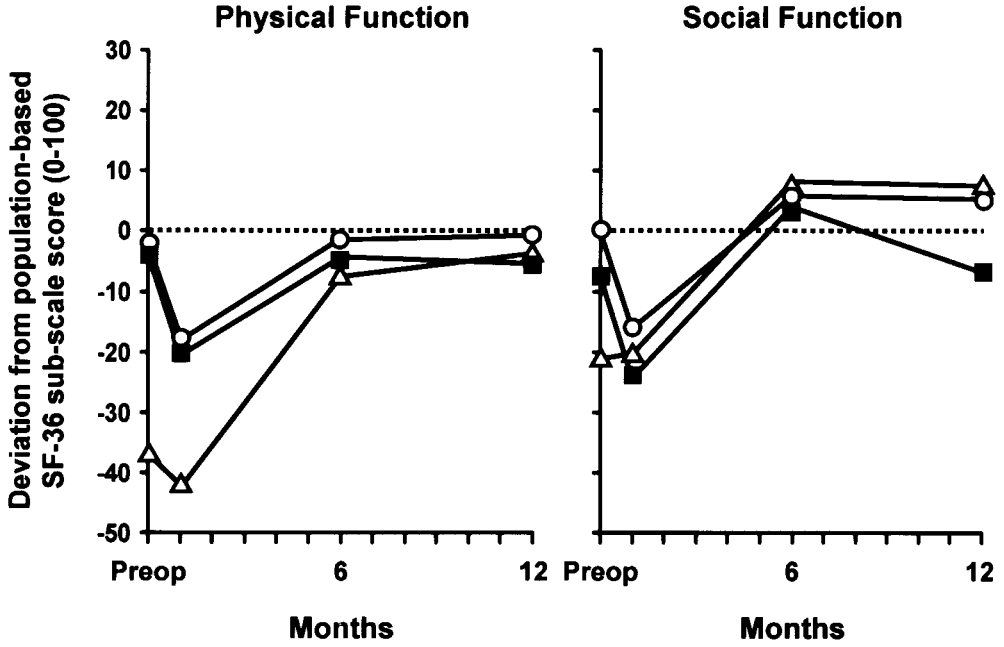

Figure 2.4—Deviation from age- and gender-adjusted population-based SF-36 subgroup scores by surgical procedure. Triangles indicate thoracic surgery for lung cancer; filled squares, total hip arthroplasty; open circles, abdominal aortic aneurysm; dotted line, age- and gender-adjusted population-based value. (Modified with permission from Mangione CM, Goldman L, Orav EJ, et al. Health-related quality of life after elective surgery: measurement of longitudinal changes. *J Gen Intern Med* 1997;12:686–697, figure 2.)

65 years and older undergoing general surgery. [129] Of these, 40% had an abnormality regarded as clinically significant, although in only 5% of the patients did the CXR affect the course of treatment. Seymour et al also examined the value of an electrocardiogram (ECG) in routine screening in 222 patients aged 65 years and older, finding that only 21% of patients had a normal ECG and that 53% had a major abnormality. [130] They reported that although only 1% of patients had abnormalities that delayed surgery, 30% developed new ECG abnormalities postoperatively. The authors concluded that the screening ECG has little or no value for predicting cardiac complications but recommended preoperative ECG for all elderly patients to provide a basis for comparison and as a means of detecting patients for whom surgery should be deferred.

In a small study of acutely ill elderly (mean age 81 years) medical patients (50 admissions), Sewell et al examined the value of full blood cell count, sedimentation rate, urinalysis, electrolyte, liver, thyroid tests, and CXR. [131] Six of 28 patients had abnormalities on CXR (21%), although management was influenced only in one. The most important finding in the screening battery was the frequency of unknown urinary tract infections (16 of 50 patients, 32%). A different retrospective analysis of 86 patients undergoing hip arthroplasty studied the impact of 24 laboratory tests on postoperative course. [132] In four patients (4.6%) care was altered, three of whom had urinary tract infections. A cost-benefit

analysis justified routine urinary analysis to reduce hip infections in elderly patients undergoing total hip arthroplasty.

Assessment of nutritional status can also be useful in subpopulations of surgical patients. A 44-center Veterans Administration study found that serum albumin concentration was a better predictor of surgical outcomes than were many other patient characteristics. [133,134] Though it can be difficult to separate the role of the disease process resulting in protein-calorie malnutrition from the effect of the malnutrition itself, [135] a study of elderly hospitalized nonsurgical patients found that adverse outcomes could be attributed to malnutrition independently of greater acuity of illness or comorbidity. [136] Because of wide confidence limits, laboratory assessment of nutritional status may make its application to individual patients less useful than to populations. [135] It may prove useful to combine laboratory tests with anthropomorphic measurements, such as body mass index, limb circumferences, and weight loss. [137–140] The latter assessments are simple and inexpensive, but their clinical yield has not been determined. Nutritional assessment may have implications for preoperative management and the timing of surgery as well as for risk stratification in certain types of surgery, but nutritional evaluation has not been adequately studied in elderly surgical patients.

A recent study on preoperative testing in 18,000 patients undergoing cataract procedures also deserves comment. Patients were randomly assigned to undergo or not undergo routine testing (ECG, complete blood cell count, electrolytes, blood urea nitrogen, creatinine, and glucose). [141] The analysis was stratified by age and showed no benefit to routine testing for any group of patients. Similar conclusions were drawn in a study of 544 elderly noncardiac surgical patients by Dzankic et al. [142]

From these investigations and a body of work in younger subjects, three themes become evident. First, routine screening in a general population of elderly patients does not add significantly to information obtained in the clinical history. Second, in a general population, the positive predictive value of abnormal findings on routine screening is limited. Third, positive results on screening tests have relatively little impact on the course of patient care. In spite of those observations, further research is required.

Even though the yield for routine screening is very low, it can be clinically valuable and cost-effective to develop guidelines for preoperative testing that are based on the type of surgery. It is evident that different types of surgery impose different types and degrees of physiologic stress. The results of the cataract trial will not be applicable to patients undergoing vascular surgery. Preoperative tests such as echocardiography and thallium scanning can have predictive value and potentially alter the course of care and outcomes if applied to specific populations at higher risk. [80,143,144] Similarly, nutritional assessment [134,145] might be very useful prior to abdominal or major orthopedic surgery but would have a much lower impact for carotid endarterectomy. Screening for urinary tract infection prior to orthopedic surgery or pulmonary function testing prior to thoracic surgery are other examples. Because it is the interaction of the patient and the surgical stress that determines outcome, specific testing might be equally indicated in a very physiologically challenged older patient undergoing minimally stressful surgery (hernia repair), and in the mildly compromised older patient undergoing surgery that imposes severe physiologic stress (eg, aortic aneurysm surgery). Future studies of older patients will need to stratify patients according to the severity of their pre-existing risk factors (low, intermediate, or high) and

specifically examine the interaction of these factors with the specific surgical challenges most common in the elderly age group.

PREOPERATIVE OPTIMIZATION

The fourth dimension of preoperative evaluation determines whether medical intervention is indicated before proceeding with surgery. To some extent, this dimension has been lost with the foreshortening of the preoperative period, the "AM admit," and a progressive elimination of preoperative testing.

If we are going to define research agendas for the care of elderly surgery patients, preoperative optimization of medical status must be revisited. This is an area where relatively little work has been done. Again, in specific populations undergoing high-risk surgery, the value of preoperative optimization, particularly of cardiac and pulmonary status, can be demonstrated. Examples where the data are compelling include intervention for coronary disease before vascular surgery; pulmonary toilet, antibiotics, and corticosteroid therapy for some types of thoracic surgery; and preoperative β-blockade. [143,144,146–150] Nevertheless, many areas have not been evaluated, particularly in the elderly population. Improving nutritional status before major elective surgery, preoperative hydration, and optimization of renal function in those with chronic or acute insufficiency could have broad impact. Preoperative management of antibiotic therapy, anticoagulation, antiplatelet therapy, and anemia are other obvious areas to examine. There are also suggestions that preoperative education, psychologic support, and physical therapy might facilitate pain management and rehabilitation following some types of surgery, [151,152] but these have not been adequately assessed.

In today's environment it will be difficult to conduct studies on preoperative optimization. It will be difficult to justify randomizing a patient to a control group when he or she is clearly malnourished and surgery can be delayed. Moreover, intervention and delay will add costs. However, limited studies in orthopedic and cardiac surgical patients suggest that appropriately applied preoperative care can be cost-effective in shortening hospital stays or improving functional status following discharge. [152,153] Preoperative optimization will not be practical or necessary in many instances; however, much geriatric surgery is elective, so these studies can be conducted and, if positive, could affect large numbers of patients.

THE PREOPERATIVE RESEARCH AGENDA

The most pressing need for preoperative assessment is to develop better tools to predict which patients will do well and which will do poorly (see also Key Research Questions in Geriatric Anesthesia, end of chapter).

Anes 1 (Level B): **Prospective epidemiologic studies are needed to describe the relative frequency of various outcomes characteristic of older surgical patients for the most common types of surgery.**

Anes 2 (Level B): **Once better understanding of characteristic outcomes of specific types of surgery for older patients is attained, patient- and surgery-specific risk factors for geriatric complications should be identified by multivariate analysis that would stratify surgical risk as low, intermediate, or high, depending on type of surgery.**

Anes 3 (Level B): **The positive predictive value of preoperative assessment instruments should be determined in prospective nonrandomized or prospective cohort trials.**

Anes 4 (Level A): **Following evaluation of preoperative assessment instruments (Anes 3), prospective randomized trials should be performed to determine whether the application of these metrics could improve outcomes for elderly surgical patients by altering perioperative intervention, surgical timing, the type or extent of surgery, or postoperative management.**

Anes 5 (Level B): **Prospective cohort studies are needed to determine whether assessment of the older surgical patient's preoperative functional status affects surgical decision making or perioperative care.**

Anes 6 (Level A): **Depending on findings of prospective cohort studies (Anes 5), randomized trials should be performed to determine whether preoperative functional status assessment of elderly patients changes decisions about type or timing of surgery, or pre- or postoperative care strategies and outcomes.**

Anes 7 (Level B): **Cross-sectional or prospective cohort studies are needed to determine by multivariate analysis whether there is an association between pre-existing cognitive impairment, depression, or alcohol abuse and adverse outcomes in geriatric patients.**

Anes 8 (Level A): **For any association that is established by cross-sectional cohort studies between cognitive impairment, depression, or alcohol abuse and adverse outcomes in elderly surgical patients (Anes 7), prospective randomized trials should be performed to determine the effect of pre- or postoperative interventions on these adverse outcomes.**

INTRAOPERATIVE MANAGEMENT

Anesthetic care is episodic, so most of the criteria to judge the success of anesthetic interventions are short-term. Studies of anesthetic drugs and techniques typically address hemodynamic stability, time to awakening, extubation time, postoperative nausea and vomiting, recovery room time, and length of stay. Awareness of the physiologic and pharmacokinetic changes characteristic of the elderly patient have led investigators to examine the effects of a host of anesthetic agents and adjuncts in this population. The effects on elderly patients of intravenous induction agents, narcotics, benzodiazepines, volatile anesthetics, neuromuscular blocking agents, and various types of local anesthetics have all been evaluated. Studies have included the use of these agents for inpatient surgical procedures, outpatient procedures, premedication, sedation, and their administration by bolus and infusion techniques. Because there is a theoretical advantage to shortening recovery time in patients for whom awakening, ambulation, and discharge might otherwise be delayed (ie, elderly patients), much of the more recent work focusing on elderly patients has been devoted to the ultra–short-acting agents.

Some of these studies have identified age-related alterations in the pharmacokinetics, induction, awakening, or recovery room stay. However, perspective is needed. Even though a drug may shorten extubation time by 10 minutes, recovery room time by 45 minutes, or total hospitalization for an outpatient procedure by 90 minutes, the clinical impact of these changes on patient outcomes is probably minimal. There is a role for this type of research in geriatric anesthesia, but in an era of limited time and research dollars, research efforts should probably be directed elsewhere.

REGIONAL VERSUS GENERAL ANESTHESIA

Most general anesthetic agents depress cardiovascular and pulmonary function as well as alter consciousness, which is why it is often advocated that regional anesthesia be used for geriatric patients whenever possible. A major area of research has been to compare the risks and benefits of regional versus general anesthesia in elderly surgical patients. Elderly patients undergoing orthopedic procedures have been the focus of such research. These comparative studies have examined intraoperative cardiovascular stability; cardiac, pulmonary, and thrombotic complications; pain control; and cognitive outcomes. This subject was reviewed recently by Roy. [154]

A few early studies reported that regional anesthesia for hip surgery was associated with better outcomes. Reduced mortality, higher postoperative Pao_2, and fewer mental changes have been reported in patients receiving regional anesthesia. [155,156] However, these studies were very small, and their assessment of cognitive function would not meet current standards for reliability or validity. [157]

Subsequent investigations of elderly patients undergoing hip surgery found that intraoperative hypotension is more common with regional anesthesia, and although the incidence of deep-vein thrombosis (DVT) and blood loss were typically lower with regional techniques, no difference in major morbidity or mortality could be identified. [85,158–163] Because most of these studies are underpowered for rare events, meta-analysis has been used to help address statistical limitations.

The respective benefits of regional and general anesthesia were addressed in a 1992 meta-analysis. [164] Sorenson and Pace examined 13 randomized controlled trials conducted between 1966 and 1991 that reported follow-up to at least 1 month. Meta-analysis endpoints were mortality, DVT, and blood loss. Other complications or adverse events were not evaluated because of inconsistencies in definitions or "the absence of systematic and unbiased application of diagnostic tests to record these events." Sorenson and Pace were unable to identify any statistically significant difference in mortality or blood loss by anesthetic technique, although the study found a clearly reduced incidence of DVT in regional anesthesia groups. Most of the data in the study were recently reanalyzed in another meta-analysis, along with some additional trials. [165] Like Sorenson and Pace's, the analysis by Urwin et al identified reduced DVT and 1-month mortality in 2162 hip-fracture patients receiving regional anesthesia, although no other outcome measure reached statistical significance. [165] (See Figure 2.5.) The reduction in mortality, when that information was available, was not evident at 3, 6, or 12 months. Subsequent large, single-center observational studies involving 741, [166] 1333, [167] and 9425 [168] patients have also not identified meaningful differences in cardiopulmonary morbidity or mortality between regional and general anesthesia in hip-surgery patients.

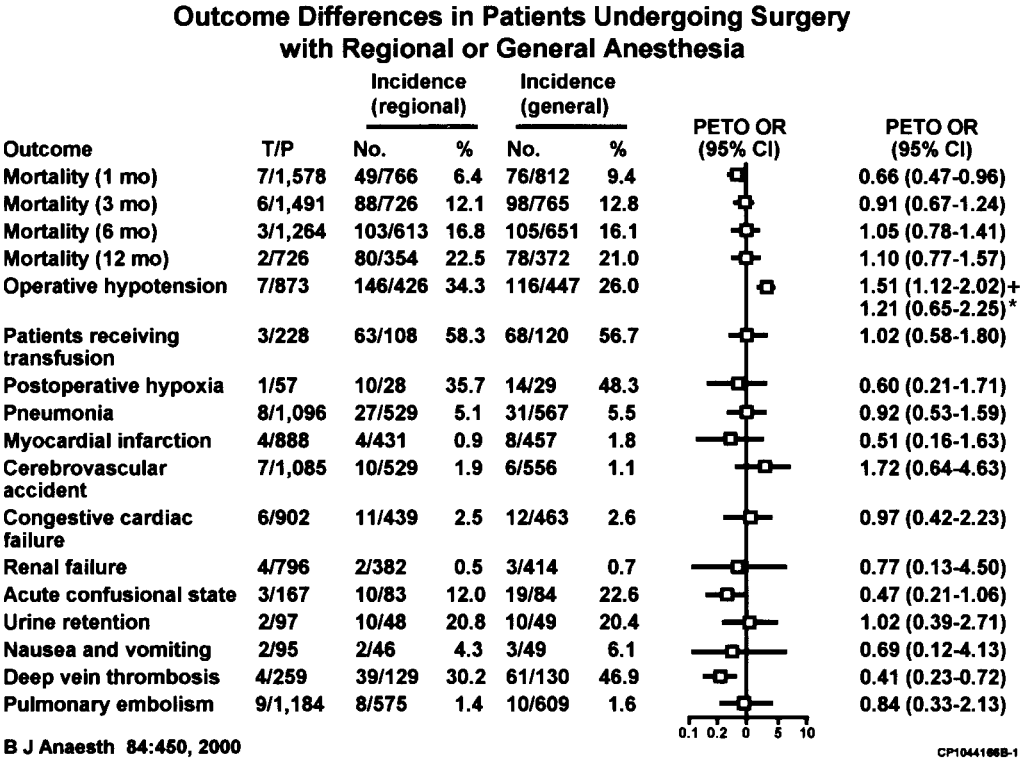

Figure 2.5—Comparison of outcome between regional and general anesthesia for dichotomous variables. All results were derived by the use of fixed-effects analysis except for those marked *, which were derived by the use of random-effects analysis. Statistically significant results are indicated by +. Results to the left of the vertical line indicate an advantage for regional anesthesia over general anesthesia. Results show the incidence of each outcome measure. T = number of trials; P = number of patients; OR = odds ratio; CI = confidence intervals. (Reprinted with permission from Urwin SC, Parker MJ, Griffiths R. General versus regional anesthesia for hip fracture surgery: a meta-analysis of randomized trials. *Br J Anaesth* 2000;84:450–455, table 2.)

Another meta-analysis was conducted by Rodgers et al. [169] The authors examined the effects of regional anesthesia in 141 randomized trials involving 9559 patients. As in the report by Urwin et al, these researchers found a reduction in 30-day mortality and DVT in the regional group; the effect on mortality was not evident beyond 1 month. They also describe reductions in pulmonary embolism, transfusion, respiratory depression, myocardial infarction, and renal failure. Although the results are enticing, the reporting of many outcomes was incomplete across studies, so the analysis was based on smaller subsets of patients. Additionally, studies were not rated for quality, and data were used that were not reported in the published trial. Studies for general, obstetrical and gynecologic, urologic, orthopedic, and "other" surgeries were combined, and no information about age is provided. Finally, it is impossible to base practice on the results of this meta-analysis because all of the following groups of patients were combined in the regional anesthesia group: those receiving spinal anesthesia alone, those receiving epidural anesthesia alone, those receiving general anesthesia followed by postoperative regional anesthesia, those

receiving general anesthesia combined with intraoperative spinal anesthesia, and those receiving general anesthesia combined with intraoperative epidural anesthesia. Additionally, in 22 studies where general anesthesia was combined with regional anesthesia, the general anesthesia in the regional group differed from that in the general anesthesia alone group. From this, it is difficult to determine if the effects described in the meta-analysis are real and, if so, what their origin is, or which patients they would apply to. It is certainly not possible to recommend any practice on the basis of the results.

In addition to the more typical outcomes measures, several of the studies of orthopedic surgery patients have examined the effect of anesthetic technique on cognitive or functional outcome, often following patients for 3 months or longer. Each of the prospective studies is small, and only the study by Hole et al [156] showed regional anesthesia to be associated with better cognitive outcome in elderly patients undergoing hip or knee surgery. The bulk of investigations could identify no difference. [117,157,170–172]

Even though not all the studies are in agreement, [173,174] similar conclusions must be drawn for patients undergoing regional or general anesthesia for transurethral prostatectomy and peripheral vascular surgery. [172,175–178] In carotid surgery there is a suggestion of a better outcome with a regional technique; however, most investigations are retrospective or nonrandomized, so the effect of patient selection cannot be eliminated. [179–182] Additionally, in the multicenter North American Symptomatic Carotid Endarterectomy Trial, an independent effect of anesthetic technique (or intraoperative monitoring) on carotid surgical outcome could not be found. [183]

The difficulty in identifying clear and meaningful differences between regional and general anesthesia has tremendous implications for the conduct of research in geriatric anesthesia. Probably the most substantive difference in the choice of anesthetic is whether the patient undergoes a regional or a general anesthetic. The pharmacologic difference with that choice is far greater than the difference between different induction agents, narcotics, local anesthetics, or muscle relaxants, or between different doses of those medications. If little or no difference in outcome can be identified for elderly patients undergoing major procedures with general or regional anesthesia, then the yield for similar outcome studies on differing anesthetic agents is likely to be low.

PHYSIOLOGIC MANAGEMENT

In addition to establishing a surgical plane of anesthesia, the anesthesiologist maintains physiologic stability. Although numerous studies have examined the relationship between intraoperative physiologic management and outcome, outside of relatively rare catastrophic events, such as loss of the airway or uncontrolled hemorrhage, it appears that physiologic management plays a modulatory rather than a primary role in outcomes. The best example is in cardiac surgery, where the acute changes in blood pressure, hematocrit, and temperature typically exceed those seen with any other type of surgery. Additionally, most of the patients are older. In spite of that, it has been difficult to demonstrate a direct relationship between physiologic management and outcome. [184–186] Rather, it appears that technical issues during surgery and the comorbidities that the patient brings to the operating room primarily determine outcome. [187,188]

There is a role for specific studies of physiologic or pharmacologic management in elderly surgical patients, but those investigations are likely to have a smaller yield than

risk stratification based on population studies and tailoring the surgical procedure to the patient on the basis of preoperative assessment.

It is important to note that these conclusions are not an indictment of anesthetic practice or the role of the anesthesiologist in the operating room. Just the opposite is true. Over the past three decades, anesthesiology has made tremendous strides in patient safety, monitoring, drugs, and education that have made the intraoperative period extraordinarily safe. Those advances will continue to expand what is possible surgically. At the same time, it is because the advances in intraoperative care have been so great that the greatest needs for research lie in the preoperative assessment and the postoperative management of patients.

There are also broad areas related to intraoperative management (rather than the specifics of anesthetic choice) where research focused on the elderly patient would be productive. It is clear that anesthetics and alterations in autonomic function make it more difficult for older patients to maintain their body temperature, and postoperative hypothermia increases the risk of adverse outcomes. [189–193] Studies of temperature control in older patients could be expanded. The appropriate place for prophylactic β-blockade, antiplatelet agents, and H_2 blockers in elderly surgical patients needs to be examined. Given that the immune response may be attenuated in elderly persons and that infectious complications are very common, the appropriate dosage and scheduling for perioperative antibiotics may be a useful area of research. Furthermore, elderly patients receive most of blood given in the perioperative period, so investigation of the immunosuppressive effects of homologous blood transfusion would be instructive. Elderly patients are also at increased risk for musculoskeletal and nerve injury, as well as thrombotic complications. Therefore, documenting the relationship between patient positioning, nerve and skin injury, and thrombotic complications is indicated. Similarly, the appropriateness of nothing-by-mouth (NPO) status, its relationship to hypovolemia, and aspiration risk in the elderly patient would be an area of research with a large potential impact on practice and patient satisfaction.

The fact that anesthetic choice or physiologic management has little independent effect on outcome is not surprising. Very large studies of perioperative morbidity and mortality have found that, apart from catastrophic events, the anesthetic episode per se appears to have little or no impact on 30-day outcomes. [89,92,194] Although certain pathophysiologic processes may be initiated during the intraoperative period, with few exceptions, major morbidity and mortality in the operating room are rare.

THE INTRAOPERATIVE RESEARCH AGENDA

Anes 9 (Level B): **Cross-sectional or retrospective case-control studies are needed to identify the incidence of adverse cardiac or thrombotic-embolic complications in elderly patients undergoing surgery with and without preoperative β-blockade, antithrombotic or antiplatelet therapy, or with a hematocrit above a target value. These studies should be in surgeries identified as having an intermediate or high risk for related complications.**

Anes 10 (Level A): **For any association in elderly patients of cardiac thrombotic-embolic complications with a specific preoperative therapy or hematocrit level, prospective cohort or randomized**

studies are needed to determine if pre- or intraoperative therapies would reduce the complications.

Anes 11 (Level D): **Prospective nonrandomized investigation of the effect of perioperative temperature management on surgical morbidity in the geriatric population is needed. These investigations should be conducted under conditions where either the surgery is physiologically very challenging or the older patient carries a high burden of comorbidity. Cardiac, respiratory, bleeding, and renal outcomes would be the primary focus of these investigations.**

Anes 12 (Level D): **Retrospective or cross-sectional research studies should be conducted to identify any relationship between the use or timing of perioperative antibiotic therapy and postoperative pneumonia or wound infection. Differences, if any, between younger and older patients undergoing the same type of surgery should also be examined.**

Anes 13 (Level C): **Depending on the findings in Anes 12, prospective randomized studies should be used to determine whether preoperative or postoperative antibiotic therapies reduce complications related to infections in elderly surgical patients.**

Anes 14 (Level D): **Multicenter case-control or prospective cohort studies should be performed to determine whether receiving or not receiving blood in the perioperative period affects the incidence of perioperative infection and immunosuppression in elderly patients. Multivariate analysis would be required to separate the effect of homologous blood transfusion from the comorbid conditions making transfusion more likely.**

Anes 15 (Level C): **If perioperative infection and immunosuppression in older surgical patients are shown to be associated with receiving blood in the preoperative period (Anes 14), alternative strategies such as delaying surgery or erythropoietin therapy should then be compared with blood transfusion in prospective cohort studies, because a randomized trial could not be justified.**

Anes 16 (Level D): **Cohort or case-control studies are needed to determine the relationship in older surgical patients between perioperative termination of anticoagulation and thromboembolic or bleeding risk.**

Anes 17 (Level C): **The effect of timing of termination and resumption as well as the temporizing use of antiplatelet agents in older surgical patients should be compared in case-control or prospective cohort studies.**

Anes 18 (Level B): **In prospective cohort studies the incidence of perioperative hypotension, aspiration, and renal insufficiency should be compared in elderly patients undergoing standard nothing-by-mouth orders before surgery and in elderly patients**

who would be allowed clear liquids closer to the time of surgery. This study would need to be conducted in:

- **patients undergoing specific types of procedures where liberalization of fluid intake is not contraindicated for surgical reasons,**
- **patients undergoing procedures that place them at greater risk for developing hypovolemia (bowel prep), and**
- **instances where preoperative hypovolemia may contribute to complications (angiographic procedures).**

POSTOPERATIVE MANAGEMENT

Most surgical morbidity and mortality occurs in the postoperative period. Pedersen et al examined perioperative mortality in 7306 adult patients undergoing lower-risk surgery (no cardiac, thoracic, or neurosurgical procedures) and found that mortality during anesthesia was 0.05% (1:1800). [85] In the first 24 hours the mortality was twice as high, 0.1%, and it rose fivefold over the next 6 days to 0.56%. Morbidity, including myocardial ischemia and infarction, stroke, renal insufficiency, pneumonia, and delirium, is also most common postoperatively. [183,195,196]

POSTOPERATIVE RESPIRATORY INSUFFICIENCY

The most common morbidity following noncardiac surgery is respiratory. A Veterans Administration study of 84,000 patients (97% male, mean age of 60) found that 17% of patients experienced complications, with pneumonia in 3.6%, ventilatory failure in 3.2%, and unplanned intubation in 2.4%. [88] In a study of 288 general surgical patients aged 65 and over, Seymour and Vaz reported that 17% of patients had atelectasis, 12% had acute bronchitis, and 10% developed pneumonia. [197]

For many reasons, postoperative hypoxia may occur in 20% to 60% of elderly surgical patients. [28,29] As highlighted previously, elderly patients have an increased alveolar-arterial gradient, reduced respiratory muscle strength, and hypoxic and hypercarbic drives at baseline. [14,20,27] Additionally, there is a progressive loss of airway reflexes with age, and apnea and periodic breathing following administration of narcotics are more common. [18,25,198] Postoperative pain, atelectasis, and fluid shifts further increase the likelihood of respiratory complications, as do reductions in cardiac output, hemoglobin concentration, and shivering. [19,191] The supine position during recovery increases the transpulmonary shunt and makes hypoxia more likely. [18] Finally, orthopedic and upper abdominal surgeries, which are common in elderly persons, have an independent effect in increasing postoperative hypoxia and respiratory complications. [26,197,199]

In spite of the frequency of postoperative hypoxia and hypercarbia in elderly surgical patients, clear guidelines for oxygen therapy, pulse oximetry, and capnography in older patients have been poorly defined. [200,201] This issue is of pressing importance, as "day surgery" has increased and continued efforts are made to abbreviate the time to discharge. Further, more and more patients, most of them elderly, undergo conscious sedation outside the operating room environment. Even though the study by Bailey et al is more than 10

years old, its implications are unchanged. [202] In a study of hypoxemia and apnea after sedation with fentanyl and midazolam, they describe deaths associated with the use of these drugs. Of 86 reported U.S. deaths, "All but three . . . occurred outside the operating room . . . where patients are typically unattended by anesthesia personnel." Determination of the requirements for oxygen therapy, pulse oximetry, and capnography in elderly patients undergoing inpatient and outpatient surgery, including procedures with conscious sedation, is indicated.

The risk of postoperative aspiration for the elderly surgical patient also requires attention. Because of alterations in pharyngeal function, diminished cough, and an increased incidence of gastroesophageal reflux, elderly patients are at increased risk of aspiration. [23,24] This risk is accentuated by the effect of anesthesia, sedatives, and narcotics as well as by endotracheal intubation, nasogastric tube placement, and upper abdominal or neck surgery. [30,203,204] Even though the incidence of aspiration in the operative period is low and is uncommonly associated with clinically important pneumonitis or pneumonia, [205] the risk for aspiration extends well beyond the acute operative period.

It is likely that instrumentation of the pharynx, whether from an endotracheal tube, [30] nasogastric tube, [204] or a transesophageal echocardiography probe, [203] alters sensation, motor function, and the protective reflexes preventing aspiration. For patients with prolonged endotracheal intubation ($>$ 24 hours), this effect is persistent for at least 48 hours following extubation. [30] Nasogastric tubes may also contribute to aspiration by increasing the incompetence of the gastroesophageal junction. Pharyngeal dysfunction and aspiration may be related to a greater acuity of illness, but sufficient evidence suggests pharyngeal trespass itself has independent effects.

Given perioperative risk factors, the frequency of aspiration in the elderly population, and the incidence of postoperative respiratory morbidity, insufficient research has been directed to this issue in elderly surgical patients. Pharmacologic interventions to reduce gastric volume or increase pH have received attention in the anesthesia literature, but the investigation by Warner et al of aspiration occurring within 2 hours of surgery [205] implies that research on aspiration and postoperative pneumonia must look beyond the immediate operative period. [206] Additional important research will focus on establishing the appropriate use of nasogastric tubes, the restoration of pharyngeal and tracheal reflexes and gastrointestinal motility, and the advancement of feeding following surgery in the elderly patient. General studies as well as surgery-specific studies are needed.

ACUTE PAIN MANAGEMENT

The same questions that dominate research in pain management in the general population apply to the elderly age group. However, in many ways the questions for elderly persons are more pressing because they might receive the most potential harm as well as the greatest potential benefit from improved treatment of postoperative pain. Because of ischemic heart disease, diminished pulmonary capacity, altered drug clearance, or increased drug sensitivity, the elderly patient is probably more vulnerable to the physiologic consequences of inadequate analgesia, as well as to the side effects of analgesic use. Additionally, there is evidence in the literature indicating that in certain circumstances the older person's pain may be less adequately treated. [48]

PAIN AND ADVERSE OUTCOMES

The perioperative period results in stress and inflammatory responses that peak postoperatively when cardiopulmonary and neurologic complications occur. Therefore, efforts have been made to link the adequacy of analgesia with the magnitude of the stress response. In particular, it has been proposed that inadequate postoperative analgesia may be associated with myocardial ischemia and pulmonary failure. Researchers have examined the effect of the intraoperative anesthetic [207–210] and postoperative epidural analgesia on plasma levels of cortisol, epinephrine, norepinephrine, leucocyte counts, and acute phase proteins and have tried to relate these to cardiopulmonary outcomes. [173,207,211–215] Both negative and positive conclusions have been reached.

When this subject was reviewed by Liu, Carpenter, and Neal, [216] they concluded that intensive analgesia using regional techniques has a limited impact on cardiopulmonary outcomes or the stress response in a general population of surgical patients. They also concluded that pain and the stress response are not directly coupled because the neuroendocrine response is still demonstrated (although blunted) in the presence of intense surgical analgesia with local anesthetics or opioids. However, studies in the groups with highest risk suggest a possible improvement in outcome with intense analgesia that uses regional techniques. [173,217] Intensive pain management strategies may be indicated in high-risk elderly patients or in low-risk elderly patients undergoing high-risk surgery. Defining the circumstances under which epidural analgesia or any other pain management strategy can improve outcomes is an important area for future research.

In addition to the stress response typically associated with the sympathetic-adrenal axis, most types of surgery initiate a significant catabolic state. An inhibitory effect of analgesia on protein wasting has been suggested, [218–220] but a more pressing area for research is to understand postsurgical catabolism in elderly patients. The relationship between preoperative nutritional status and postoperative catabolism must be better understood. Experience with some critically ill patients suggests that catabolism may become dissociated from the initial surgical stress. Because elderly patients have decreased nutritional and metabolic reserve, they are most challenged by the postoperative catabolic state. Basic investigation into postoperative catabolism in the elderly person is important, as are investigations of interventions that might attenuate catabolism or facilitate the transition back to an anabolism.

The adequacy of postoperative analgesia does not appear to be an independent determinant of outcomes in the general population of surgical patients; however, a variety of other issues related to postoperative analgesia require attention. The relative benefit of patient-controlled analgesia (PCA) [221] versus an as-needed or scheduled analgesic administration is of special importance for the elderly surgical patient. Because of the physiologic and psychologic heterogeneity in the geriatric population, it is unlikely that fixed formulae for age-appropriate drug dosing can be identified. Thus, the administration of narcotics on a set schedule in the elderly person is fraught with the potential for both over- and underdosing. These considerations potentially make PCA analgesia an ideal choice. Nevertheless, the issue is complicated. The side-effect profile for PCA analgesics in elderly patients has not been established. [222,223] It has also been suggested that many elderly patients may struggle with the technology. Similarly, the application of PCA for patients with altered mental status is troubling. Outcomes with PCA in the elderly patient must be

compared with fixed and as-needed dosing techniques, as well as with postoperative pain control by regional blockade.

The same is true regarding route of administration for analgesic agents. Is there a clear advantage or disadvantage to the use of the intravenous, epidural, or intrathecal routes for analgesic administration in the elderly patient? The elderly person is unusually susceptible to drug interactions and has an increased incidence of respiratory depression, urinary retention, ileus, constipation, and postoperative falls. These are influenced by choices in postoperative analgesia and may differ by route of administration. [222–225] Investigations of analgesic strategies for elderly surgical patients will need to determine not only the quality of analgesia but also the risks and benefits specific to that population. Additionally, because narcotics are commonly associated with side effects in the elderly population, the use of analgesic adjuncts in postoperative pain management requires further investigation. Drugs like ketorolac, clonidine, dexmedetomidine, and COX-2 inhibitors have the potential to achieve adequate analgesia with lower doses of opioids, potentially reducing side effects. [226–230]

A final reason why studies of acute pain management in the elderly person are required is that acute pain management may bear on rehabilitation and subsequently on functional status on discharge. [231] This has been shown with analgesic programs for continuous passive motion machines used following knee replacement. [231–233] Research is required following other types of surgical procedures to determine whether facilitating rehabilitation by effectively managing acute pain can improve other functional outcomes.

Another opportunity for research in the postoperative care of hospitalized elderly patients is related to polypharmacy and adverse drug events. Elderly patients tend to accumulate drug prescriptions over time, and there is a clear relationship between the number of drugs taken and the incidence of adverse drug-related events. [66–70] This problem will be compounded during the surgical period when even more medications are added.

A study by Cullen et al prospectively compared adverse drug events among surgical and medical hospitalized patients in intensive care (ICU) and in general units. [234] The researchers found that the rate of preventable and potential adverse drug events is related to the number of drugs administered rather than to the type of care delivered (ICU or non-ICU, surgical or medical). The earlier report of the same data on 4031 adult hospital admissions identified, among other things, the incidence of adverse drug events, their preventability, and the classes of drugs that caused most events. Those results have particular bearing on the perioperative care of the elderly person. [68]

In the investigation by Bates et al, analgesics were found to be the class of drug that is associated with the highest number of adverse drug events. [68] Antibiotics were found to cause the second greatest number of adverse reactions. Analgesics are also the leading class of drug associated with preventable adverse drug events, followed by sedatives and then antibiotics (see Table 2.2). In the 20 preventable adverse events related to analgesics, 40% were found to be caused by overmedication.

There is a pressing need for research in pain management of the elderly surgical patient. There is also a compelling need for research into the prevention of adverse drug events in elderly hospitalized patients. The intersection of pain management and preventable adverse events associated with analgesics and sedatives places anesthesiologists squarely in a leadership role for research into appropriate analgesic and sedative strategies for the elderly age group.

Table 2.2—Adverse Drug Events and Preventability by Drug Class

Drug Class	Adverse Drug Events *N (%)* *N* = 247	Preventable Adverse Drug Events *N (%)* *N* = 70
Analgesics	73 (30)	20 (29)
Antibiotics	59 (24)	6 (9)
Sedatives	20 (8)	7 (10)
Antineoplastics	18 (7)	3 (4)
Cardiovascular	9 (4)	3 (4)
Anticoagulants	8 (3)	3 (4)
Antipsychotics	6 (2)	5 (7)
Diabetes	5 (2)	4 (6)
Electrolytes	3 (1)	3 (4)
Other	46 (19)	16 (23)

SOURCE: Bates DW, Cullen DJ, Laird N, et al. Incidence of adverse drug events and potential adverse drug events: implications for prevention. ADE Prevention Study Group. *JAMA* 1995;274:29–34. Used with permission.

In patients who are hospitalized, there is also a window of opportunity to review patient medications, in particular to examine redundancy in therapeutic profile and to look for combinations that may make complications like respiratory depression, aspiration, confusion, postural hypotension, urinary retention, and falls more likely. The development of pharmacy and electronic drug databases for this work would be appropriate; hospitals are more likely than community practitioners to have the resources to support such database development. It would not be practical or appropriate to modify most patients' chronic drug regimens in the postoperative period, but surgical hospitalization nonetheless provides an opportunity for a thorough drug review and recommendations to reduce iatrogenic complications in elderly patients.

DELIRIUM AND COGNITIVE DECLINE

Postoperative delirium or cognitive decline affect 5% to 50% of elderly patients; both disorders have similar predisposing factors, but the syndromes are not equivalent. [111,196,235–237] Disordered thinking and confusion that waxes and wanes characterize postoperative delirium. The onset is typically on the first to third postoperative day, may be sustained for more than a week, and is associated with other medical complications, prolonged hospitalization, and decreased functional status on discharge. [114,121,196,236,238–240] To date, much of the research has centered on the impact of regional versus general anesthesia in orthopedic surgery. [117,118,157,170–172,241] Cognitive dysfunction, a deterioration of such capacities as memory, central processing time, and acquisition of new information, has been well described in both cardiac and noncardiac surgical patients. [242–245]

In anesthesia, the effect of differing anesthetics on postoperative delirium has been studied, [118,157,172,246–249] and a leading hypothesis has been that offending agents aggravate an age-associated central cholinergic insufficiency. [117,250,251] However, from review

of the literature it becomes evident that delirium is a syndrome that can be triggered by many different perioperative events, so no single cause is identifiable and no single intervention is likely to be successful.

In addition to being linked to narcotics, sedatives, and anticholinergics, delirium has been associated with urinary tract infection, pneumonia, hypoxia or hypercarbia, fever, blood loss, and electrolyte disturbances. [196,235,236,252–254] Chronic patient factors such as pre-existing frank or subclinical dementia, other organic brain disease, and vision and hearing loss are also predictors of postoperative delirium and cognitive decline. [103,111,114,196,235,255,256] Finally, in the elderly patient it has been suggested that pain, sleep deprivation, sensory deprivation, and an unfamiliar environment may contribute to delirium. [113,196,235,257,258]

Most of the research in the anesthesia literature has focused on the effect of anesthetic and analgesic agents, but the literature in medical patients suggests that the yield for those studies will be low. Studies of the type conducted by Inouye might serve as a model for research in anesthesia. [104,109,254–256,259–261] Inouye describes a multifactorial model for delirium involving the interrelationship between a vulnerable patient and acute insults. [254,259] In a study of elderly medical patients, multivariate modeling identified four risk factors for developing hospitalization delirium: vision impairment, severe illness, pre-existing cognitive impairment, and a blood urea nitrogen–creatinine ratio ≥ 18. [259,262] Patients were then divided into low-, intermediate-, and high-risk groups, depending on the number of risk factors. In a subsequent validation cohort, the rates of delirium in the low-, intermediate-, and high-risk groups were 3%, 16%, and 32%, respectively. [259] In those patients the rate of death or nursing-home placement was 3%, 14%, and 26%, respectively, an eightfold increase from the lowest to highest risk group. [262]

Precipitating factors for delirium in hospitalized medical patients have also been described by Inouye and Charpentier [254] Twenty-five factors occurring at least 24 hours before the onset of delirium were considered. Of those, a multivariate model identified five as predictive: use of physical restraints, malnutrition, more than three medications added, use of a bladder catheter, and any iatrogenic event (eg, volume overload, urinary tract infection, pressure ulcer). Even though the precipitating factors were independent of each other, the authors note that "baseline and precipitating factors are highly interrelated and contribute to delirium in a cumulative fashion."

In a subsequent publication, Inouye et al [260] determined the effect of interventions that were based on their predictive model. Four hundred and twenty-six elderly medical patients in an intervention group were matched to an equal number in a usual care group. In the intervention group, six risk factors for delirium were targeted for intervention: cognitive impairment, sleep deprivation, immobility, visual and hearing impairment, and dehydration. The group receiving intervention by an interdisciplinary team had a 9.9% incidence of delirium versus 15% in the usual care group (a 34% difference). Subdivision of patients into intermediate- or high-risk groups demonstrated that intervention reduced delirium diagnosed by the Confusion Assessment Method (CAM) [263] in intermediate-risk patients, but the tendency to reduce delirium in the high-risk group was not found to be statistically significant.

These studies indicate that presence and severity of cognitive deficit is a strong predictor of the likelihood of delirium during the hospitalization. [259] The same effect has been identified in surgical patients. [111–114] This brings us back to the recurring theme: Subclini-

cal decrements in functional status may become evident during the perioperative period. These findings are extended by the observation that postoperative delirium or cognitive decline may be a harbinger of a potentially permanent decrease in mental status. [242,264]

Together, the data on the predictive value of preoperative cognitive status [259] and the effect of that assessment on the success of intervention [260] provide a compelling rationale to conduct a simple, short mental status examination as part of the preoperative interview. Short functional scales have been designed that might be applicable in the preoperative interview. [116,265,266] The practicality of using such metrics in elderly surgical patients must be established. Following that, the incidence of preoperative cognitive impairment, and its severity, could be identified in populations of elderly patients undergoing different types of procedures. Research into the effectiveness of differing prevention strategies could follow. Those investigations could also examine whether reductions in delirium translate into reduced medical complications or improved functional status on discharge.

For further discussion of the problems of delirium and cognitive decline in the older surgical patient, see Chapter 13, Cross-Cutting Issues.

THE POSTOPERATIVE RESEARCH AGENDA

Anes 19 (Level B): **Prospective studies that better identify patient and procedural risk factors for respiratory failure, aspiration, and pneumonia in elderly surgical patients are needed.**

Anes 20 (Level A): **Randomized trials are needed to determine if respiratory monitoring or O_2 therapy can reduce the incidence of respiratory failure in elderly surgical patients.**

Anes 21 (Level A): **Randomized studies of prophylactic antibiotics, changes in pharyngeal instrumentation, or the way feeding is advanced are needed to determine whether practice changes reduce aspiration and postoperative pneumonia in elderly surgical patients. (See also Key Research Questions in Geriatric Anesthesia, end of chapter.)**

Anes 22 (Level B): **Cross-sectional studies capable of identifying any relationship in elderly surgical patients between intensive nutritional support in high-risk surgery and functional status on discharge (eg, chronic respiratory failure, ambulation, independent living) are needed.**

Anes 23 (Level A): **Data from studies of associations between nutritional support and postoperative functional status after high-risk surgery in elderly patients (Anes 22) should be used to design prospective cohort or randomized controlled trials comparing feeding strategies in elderly patients at risk for malnutrition and muscle wasting following major surgery.**

Anes 24 (Level C): **Randomized trials of interventions that might attenuate postoperative catabolism or facilitate the transition to anabolism in the elderly patient are needed.**

Anes 25 (Level D): **Large cross-sectional studies describing analgesic practice and its complications in the elderly surgical patient are needed.**

Anes 26 (Level B): **Depending in part on findings of large, descriptive studies of analgesia in elderly patients (Anes 25), prospective cohort studies are needed to determine the effect of analgesic modes (patient-controlled versus as-needed versus scheduled dosing), route of administration, the role of nonopioid adjunctive drugs, and nonpharmacologic interventions. These investigations must define a balance between adequate analgesia and reduction of the incidence of adverse drug events in the elderly patient.**

Anes 27 (Level A): **Prospective randomized controlled trials comparing outcomes with analgesic programs specific to types of surgery are needed to determine whether analgesic regimes designed for the elderly patient reduce in-hospital morbidity or improve functional status on discharge. (See also Key Research Questions in Geriatric Anesthesia, end of chapter.)**

Anes 28 (Level D): **Improved tools for the assessment of pain in the cognitively impaired elderly patient should be developed.**

Anes 29 (Level C): **Improved tools for assessing pain in cognitively impaired elderly patients (Anes 28) should be used to determine the adequacy of pain management strategies in this group of patients.**

Anes 30 (Level D): **A retrospective review is needed to determine the incidence of polypharmacy with combinations of drugs that might contribute to complications (hypotension, bradycardia, falls, confusion, bleeding diathesis, constipation, and urinary retention) in geriatric surgical patients.**

Anes 31 (Level A): **The effect on outcomes for elderly surgical patients of simplifying drug regimens in hospital or of communicating that information to primary care physicians should be examined in a randomized controlled trial.**

Anes 32 (Level B): **Cross-sectional studies, with multivariate analysis, are needed to determine whether the risk factors for delirium in elderly surgical patients are the same as those for elderly medical patients.**

Anes 33 (Level B): **Studies are needed on the utility of the Confusion Assessment Method (CAM) for serial testing of elderly patients before and after surgery to facilitate the diagnosis of postoperative delirium. The CAM should be compared with other tests of cognitive function and with the clinical diagnosis for delirium. At the same time, since dementia is the leading predisposing factor for delirium, the utility of short mental status tests to make the preoperative diagnosis of early dementia should be tested, using a full psychiatric examination as the gold standard.**

Anes 34 (Level A): **Prospective controlled (nonrandomized; ie, by ward or unit) trials in patients at moderate to high risk for delirium should be performed to determine the effect of preoperative or postoperative interventions on the incidence of delirium.**

CHRONIC PAIN

A significant proportion of the geriatric population suffers from chronic pain conditions. [46,47] Much of this is related to osteoarthritis; other neuropathic pain disorders that afflict older patients include postherpetic neuralgia (PHN), diabetic neuropathies, and causalgias. [267] Care of these patients is complex, and for many of these painful conditions, therapy is inadequate.

A number of factors limit success in treating chronic pain in elderly persons. First, unlike acute postoperative pain, chronic pain is caused by conditions that typically are not reversible. Second, pain conditions in the elderly person may have a central nervous system component. Third, effective treatment of chronic pain is hampered by the side effects of medications and complications from polypharmacy. Fourth, depression and behavioral changes commonly complicate therapy. [268] Fifth, assessment of pain in older patients can be difficult, [46] and, finally, chronic pain in the elderly person is often associated with unrelated comorbid conditions that may alter treatment plans. [43,269] In spite of these limitations, geriatric patients benefit, as do younger patients, from chronic pain therapy. [43,270,271]

As described by the American Geriatric Society Panel on Persistent Pain in Older Persons, most pain syndromes can be classified into one of four types: nociceptive, neuropathic, mixed or unspecified, and psychogenic. [47] The usefulness of different classes of analgesic agents in these types of syndromes is reasonably well described. Nociceptive pain includes the pain typically associated with arthropathies, myalgias, and ischemic disorders; the mainstays of analgesia are initially acetaminophen and nonsteroidal anti-inflammatory drugs, followed later by narcotics. [46,47,267] In contrast, narcotics are thought to have a lesser place in the treatment of neuropathies such as diabetic neuropathy, PHN, and complex regional pain syndromes. [267,272,273] Instead, the primary pharmacologic therapies are tricyclic antidepressants and anticonvulsant agents. [46,267,274–276] Antiarrhythmic drugs are second-tier agents for neuropathic conditions. Treatment of mixed or unspecified pain syndromes is challenging, as the mechanisms are unknown and treatment may require trials of differing analgesic approaches. [47] For patients whose pain has been classified as psychogenic, psychiatric intervention rather than analgesic agents is indicated. [47]

In addition to familiar analgesics and adjuncts, there is a need for a multidimensional approach to chronic pain in elderly persons. Neuraxial opioids, local anesthetics, and corticosteroids have a role for some patients, as do peripheral or central neuromodulatory techniques and a host of physical, physiatric, and cognitive-behavioral strategies. [43,46,47]

Defining research priorities for anesthesiologists in such a broad and complex area is difficult. The first priority is that chronic pain trials must have sufficient control groups and statistical power. As pointed out by Stanton-Hicks et al regarding neuropathic pain conditions, studies are typically small and anecdotal with few experimental findings, and "without adequate predictors for the choice of therapy, current practice is chaotic, and continues to use the trial-and-error approach." [275]

After design issues are addressed, probably the most basic research recommendation for any of these types of pain conditions is that outcomes should emphasize functional status [271,277] rather than a change in a pain score per se. This is superbly outlined in the consensus report on complex regional pain syndromes. [275] Though quantifying pain is relevant, ultimately the determination of which interventions facilitate rehabilitation, maintain or increase mobility, and support ADLs is a priority. [271,277]

The second broad area requiring further investigation relates to prevention. One of the best examples is in PHN. The rash of acute herpes zoster is very common in elderly persons; a lesser but significant percentage of those affected develop the chronic debilitating pain condition of PHN. [278] Because zoster is chronic and recurring, the percentage of the population affected with PHN increases with age. [278] Although PHN may develop in less than 5% of younger patients with zoster, it may develop in half of patients aged 60 and over. [279] Once established, PHN is difficult to treat. Further research is indicated to determine whether antiviral, analgesic, or anti-inflammatory therapies during acute zoster can prevent the development of chronic PHN. [280–283] A better understanding of precipitating events for other chronic pain conditions, as in PHN, [284] might allow the introduction of preventive measures.

In addition to directing research efforts toward functional effects and trying to define opportunities for prevention of chronic pain conditions, for any strategy it is important to examine the risk-benefit ratio, emphasizing adverse outcomes that are more likely to occur in a geriatric population. As in acute pain management, the effect of chronic therapy on the incidence of complications like confusion, postural hypotension, falls, urinary retention, and constipation must be reported.

Finally, cognitive impairment is a continuum and in milder forms is very common. There is a two-way relationship between pain and cognitive impairment: pain may impair cognition and cognitive impairment can interfere with the communication of pain. [46,285] Therefore, a further area of investigation relevant to the care of patients with chronic pain is its assessment in the cognitively impaired.

THE RESEARCH AGENDA IN CHRONIC PAIN

Anes 35 (Level B): **The first priority in chronic pain trials is large cross-sectional studies that are powered to identify any relationship between pain intervention and functional outcomes.**

Anes 36 (Level A): **With the establishment of any relationship between intervention for chronic pain and functional outcomes in elderly patients (Anes 35), it must be determined prospectively if specific chronic pain therapies can improve functional outcomes in treatment groups relative to a historical or concurrent, nonrandomized control.**

Anes 37 (Level C): **Given the high incidence rate of herpes zoster in the geriatric population, further prospective studies are needed to determine if antiviral, analgesic, or anti-inflammatory therapies during acute zoster can reduce, relative to standard care, the development of chronic post-herpetic neuralgia.**

Anes 38 (Level D): **Cross-sectional studies documenting the association of chronic pain therapy with the incidence of complications like confusion, postural hypotension, falls, urinary retention, and constipation in the elderly population are needed.**

Anes 39 (Level D): **Cross-sectional studies that describe pain management in cognitively impaired patients, relative to a nonimpaired population, are needed.**

Anes 40 (Level D): **Pain assessment tools for chronic pain in the cognitively impaired elderly patient must be compared prospectively with standard assessment methods.**

Anes 41 (Level C): **Prospective trials comparing different analgesic strategies with regard to clinical and functional outcomes are needed.**

SUMMARY

The perioperative care of the geriatric patient is complex. Older patients are at increased risk for a host of complications, and it is probably easier to precipitate these complications than to directly prevent them. This precarious state is a function of decreased functional reserve, variable response to stress, and the number of comorbidities in older patients

Nevertheless, we have learned a great deal that can guide future research. Rather than continuing to focus attention on the choice of anesthetic technique or on short-term outcomes, such as time to extubation or recovery room stay, we should focus attention on better risk stratification of elderly patients in order to better serve the goal of improving patient outcomes. If identified risk factors are amenable to therapy, it should be determined whether improvement in patient status leads to improved outcome. An essential element of both types of investigations will be a focus on preoperative functional status and outcomes appropriate to the geriatric population, rather than just major cardiopulmonary morbidity and mortality.

Outcome is determined by the interaction of patient factors and the challenges introduced by surgery. Surgical impact varies widely by type, so the development of comprehensive care strategies for specific types of surgery common in the elderly age group is indicated. Such an approach is more likely to generate positive results and practical guidelines than pooling elderly patients undergoing differing types of surgery. Developing comprehensive clinical pathways specific to the care of the elderly patient undergoing specific types of surgeries is indicated because these would bring together preoperative, intraoperative, and postoperative management. This approach could improve outcomes and would serve as a foundation for assessing alternative strategies. These might have particular value in postoperative care, particularly with regard to the prevention of delirium, respiratory monitoring, and pain management. In these investigations the anesthesiologist has a unique role, as the clinician responsible for preoperative assessment as well as intraoperative and postoperative management for every elderly patient undergoing every type of surgery.

KEY RESEARCH QUESTIONS IN GERIATRIC ANESTHESIA

Anes KQ1: **What preoperative assessments are useful in developing patient management plans for surgeries common in the elderly population?**

Hypothesis-generating: Large observational studies are needed to identify preoperative risk factors for adverse geriatric outcomes following common surgeries. These will identify both patient- and surgery-dependent factors. Assessment tools for mental status, nutrition, hydration, thrombotic risk, and ADLs must be applied or developed when necessary. It then should be determined which risk factors are potentially modifiable.

Hypothesis-testing: Randomized controlled trials are needed to determine if preoperative or postoperative intervention against modifiable risk factors will decrease perioperative geriatric complications. The adverse effects of such interventions, such as delay of surgery or postoperative bleeding, must be examined along with the potential benefits of interventions.

Examples of interventions that could reasonably be attempted include intensive nourishment for malnutrition and precise management of hydration, multifactorial interventions to prevent postoperative delirium, pre- or postoperative rehabilitation programs to maintain or improve functional status (ADLs, exercise capacity), and antiplatelet therapy for thrombotic and embolic complications.

Anes KQ2: **Can proper choice of postoperative analgesic techniques reduce postoperative morbidity or improve functional status at discharge?**

Hypothesis-generating: Large prospective studies describing analgesic practice and its complications in the elderly patient are needed. The efficacy and complications of regional analgesic techniques, nonopioid adjunctive drugs, and physiatric interventions must be investigated. These investigations must emphasize the type and incidence of adverse drug events in the elderly population.

Hypothesis-testing: Prospective randomized trials are needed to determine if perioperative intensive analgesic techniques (including traditional narcotic, regional, nonopioid adjunctive drugs and physiatric interventions) designed for the elderly patient reduce in-hospital morbidity or improve functional status on discharge.

Anes KQ3: **How can postoperative pulmonary complications in the elderly patient be reduced?**

Hypothesis-generating: Cross-sectional or cohort studies that better identify high-risk procedures or perioperative periods of vulnerability for postoperative hypoxia, respiratory failure, and pneumonia in the elderly surgical patient are needed. These investigations should identify both patient and procedure risk factors, as well as their interaction, for these complications.

Hypothesis-testing: Randomized trials are needed to determine if respiratory monitoring, prophylactic antibiotics, changes in pharyngeal instrumentation, or the way feeding is advanced will reduce respiratory failure, aspiration, and postoperative pneumonia among elderly patients.

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