Perioperative Management of Elderly Patients

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KEYWORDS

• Elderly • Geriatric • Perioperative management • Surgery • Frailty
• Preoperative care • Postoperative care

KEY POINTS

- The older population is rapidly growing and living longer, and this growth is expected to drastically increase surgical demand for both elective and emergent cases.
- The elderly population undergoes significant changes of numerous organ systems as a result of the aging process; their tenuous homeostasis can be drastically unraveled by minor changes in the perioperative period.
- The perioperative management of the elderly population is complex and requires a multidisciplinary team focusing on education, frequent assessment, functional status, and quality-of-life outcomes as well as traditional outcome measures.
- There remains a paucity of best-practice guidelines and randomized control trials focusing on the elderly; there are growing data investigating frailty indices as predictors of outcomes in perioperative elderly patients.

INTRODUCTION

Because of longer life expectancies and the aging baby boomer generation, the growth of the aging American population at this time is unprecedented.[1–3] One out of every 7 Americans is older than 65 years, and there has been a 21% increase in this age group over the past 10 years.[1] With a life expectancy of about 20 years, the older population (65+ years) is becoming older. Since 1900, the 65- to 74-year age group is 10 times larger; the 75- to 84-year group is 17 times larger; and the group aged 85 years and older is 48 times larger.[1] The centenarian population has had a 93% increase since 1980, a larger percentage increase than the total population.[1]

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Moreover, the older population has the highest incidence rate for 60% of operations compared with other age groups.[4] It is predicted that the amount of procedure-based work in general surgery will grow by 31% by 2020 because of the growing older patient population.[4] These patients often are not the healthiest, with multiple comorbidities, malnutrition, frailty, and little reserve. As the elderly become our primary surgical population, we will need to understand the differences in their physiology as we are challenged with their perioperative care.

ASSESSMENT OF OPERATIVE RISK

Geriatric patients now compose a significant number of patients undergoing surgical intervention in the United States,[5] and many of these patients undergo operative procedures in the last year of their life.[6] The geriatric surgical population with its unique physiology and response to surgical insult poses challenges in perioperative assessment. It is now well established that frailty is a strong predictor of perioperative complication and mortality in surgical patients. Frailty is a recognized geriatric syndrome with no agreed on or recognized definition unfortunately.[7–9] For the sake of surgical understanding, the most important definition would be an inability to tolerate physiologic insult. What is better known, however, is that frailty can be defined by specific indicators, including cognitive, functional, social, and nutritional function. Varying measures of these functional areas are now recognized as strong predictors of perioperative outcomes.[10,11]

As frailty is now recognized as a strong predictor of postoperative outcomes in multiple specialties, it is imperative to recognize frailty in geriatric surgical patients. Therefore, one must be able to assess frailty before operations and be familiar with the tools to assess frailty. A stepwise approach to assessing frailty will be the accepted approach in the future. This approach will consist of a screening tool to identify those patients who are potentially frail based on a bedside screen of frailty characteristics. If patients have findings consistent with frailty, a more formal assessment in the form of the comprehensive geriatric assessment would be in order to provide for a more detailed workup and provide for shared decision making, surgical buy-in, discussion about increased morbidity and mortality compared with younger patients, and ultimately bring the surgical team together to increase communication in high-risk patients. The comprehensive geriatric assessment is a multidisciplinary process that serves to identify limitations in frail patients in an effort to develop a coordinated treatment plan to optimize their management.[10,12] The assessment accounts for functional independence—caring for themselves in their environment, which is usually the most important factor to geriatric patients—maintaining quality of life. This multidisciplinary assessment results in patients less likely to require nursing home admission as demonstrated in a randomized controlled trial.[13] Fried and colleagues[9] describe a phenotype (Fried-Hopkins frailty index):

- Shrinking
- Weakness
- Poor endurance and energy
- Slowness
- Low physical activity level

When combined with other standard prediction models (American Society of Anesthesiologists, Lee, and Eagle scores), the Fried phenotype improved the predictive power of the usual models[11]; when used alone for elective operations, it showed an increased risk of complications, length of stay, and discharge to facility.[11] Other

assessment tools to date include the Rockwood-Robinson frailty index[7,14] and assessments of gait speed,[15] grip strength,[16] and initiation of movement.[17] These specific tools help clinicians to recognize additional risk factors compared with younger, nonfrail surgical patients. It is imperative that risk factors be defined preoperatively using an appropriate geriatric risk assessment to allow for a candid and a more accurate discussion with elderly patients regarding their risk of surgical intervention and outcomes.

Another related but distinct concept to be aware of in geriatric patients is that of sarcopenia. Sarcopenia is distinctly different from frailty with areas of overlap in the relationship primarily with regard to nutrition with markedly decreased muscle mass compared with age-matched controls. This decreased muscle mass similar to frailty is correlated with markedly increased risks of mortality and complications.[18,19] Sarcopenia, in contrast to frailty, has more defined measurement tools consisting of hand grip strength and psoas or total abdominal muscle area as measured by computed tomography scan. Similar to frailty, sarcopenia seems reasonable to assess, specifically in specialties whereby frail patients are not routinely considered for major surgical intervention (transplant, cardiac surgery). Cachexia is a metabolic syndrome associated with underlying illness leading to muscle loss. An upregulation of interleukin 1 (IL-1), IL-6, and tumor necrosis factor–alpha is observed leading to lipolysis, muscle breakdown, and anorexia.[20,21] Sarcopenia, present in half of patients older than 80 years,[22] not only involves the loss of muscle mass but also the loss of strength and functionality.[23,24]

PHARMACOKINETICS

The normal aging process results in changes in body composition and essentially all tissues. These changes significantly influence the pharmacologic effects and dosing of analgesic and anesthetic medications.

As the body ages, there is a shift in body mass from muscle to adipose tissue. This progressive adiposity is also associated with a loss of lean body mass and a decrease in total body water, making appropriate dosing of medications challenging. The expansion of adipose tissue increases the reservoir of lipid-soluble agents, contributing to the protracted clearance and increased duration of action for benzodiazepines, volatile agents, narcotics, and sedative-hyponotics.[25] In addition, the decrease in total body water decreases the volume of distribution for water-soluble medications, resulting in higher average and peak plasma concentrations.[26] This condition ultimately results in an exaggerated drug effect. For example, the initial volume of distribution for thiopental in patients aged 20 to 40 years is 15 to 30 L; however, this decreases to 3 to 7 L in patients aged 60 to 90 years.[27] The end result is that the dosing of many anesthetic drugs needs to be reduced. Complicating matters further, geriatric patients frequently suffer from malnutrition. Medications such as propofol and diazepam are highly bound to albumin. Low albumin levels can result in increased levels of free drug and subsequent increased sensitivity to these drugs.[28]

In addition to changes in body composition, age-related changes to the anatomy and physiology of various organs also influence the use of various medications. The kidneys lose approximately 10% of parenchymal thickness per decade of life.[29] Between 20 and 90 years of age, a 50% decrease in renal blood flow contributes to a 30% to 50% decrease in glomerular filtration rate.[26,29] Simultaneously, there is a decrease in hepatic mass by 20% to 40% and a decline in hepatic blood flow with advancing age.[30] This age-related impairment in renal and hepatic function affects the metabolism and excretion of multiple analgesic, sedative, and anesthetic agents.

The loss of neurons and decline in cognitive function in the elderly may increase the sensitivity to certain medications. These neuronal changes result in increased sedation and cardiorespiratory depression at lower blood concentration levels.[31] In contradistinction, the elderly may also have a higher threshold for pain perception.[32] Another consideration in the elderly is delayed drug absorption from the gastrointestinal tract, which leads to an inconsistent dose response relationship.[28]

It has been estimated that 40% of elderly patients take 5 or more different medications per week, and up to 19% use 10 or more medications per week.[33] This polypharmacy and drug-drug interactions are additive to the age-related changes in body composition and organ function rendering pharmacologic management in the elderly very challenging.

ANALGESIA IN THE ELDERLY

Narcotics are the mainstay of pain control. As a result of age-related increases in adipose tissue, narcotics and other lipophilic medications have a relatively larger reservoir and should be anticipated to have a prolonged or inconsistent effect. Elderly patients have been shown to have a 2-fold higher sensitivity to ventilatory depressive effects of opiates compared with younger patients.[34] Therefore, in the elderly, it is recommended to use a balanced (or multimodal) analgesic approach, which can minimize the adverse effects of opioids. Using a combination of local anesthetics, acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), steroids, and nontraditional analgesic agents is safe and efficacious in this age group. White and colleagues[28] have compressively reviewed the use of this strategy in the elderly.

Local Anesthetics

The preemptive, adjunctive use of a subcutaneous or intra-articular local anesthetic has been demonstrated to reduce narcotic use.[35,36] The utility of adding epinephrine to prolong the duration is well known. However, the addition of clonidine, ketorolac, methylprednisolone, or dexamethasone also prolongs the duration of the local analgesic effect.[28,37–39]

Acetaminophen

Despite reduced hepatic function, acetaminophen has been shown to be safe in the elderly and does not require dosage adjustment compared with younger patients.[40,41]

Nonsteroidal Antiinflammatory Drugs

The effectiveness of NSAIDs for prevention of postoperative pain and reducing narcotic requirement is well known. However, the complications of these agents, such as platelet dysfunction, gastrointestinal bleeding, and kidney injury deserve special attention in the elderly.

Steroids

In addition to combining steroids with local anesthetics, steroids alone or as part of a multimodal regimen also have a beneficial effect on pain control.[42–44] Although there were no increased bleeding complications with this strategy, there may be an additional benefit of decreasing postoperative nausea and vomiting.[44–46]

Nontraditional Analgesic Drugs

Several nontraditional agents have been shown to improve pain management in the postoperative period. Ketamine (in a single dose, as an infusion during surgery, or

as part of a multimodal approach) has been demonstrated to reduce postoperative pain and narcotic consumption and decrease the development of chronic pain.[47,48] The efficacy of adding gabapentin to a multimodal strategy for pain control may be useful, but the associated sedation and dizziness may limit its use in the elderly.[49,50] Alpha-2-agonists (ie, dexmedetomidine) have long been known to have an anesthetic-sparing effect but are now being used in the perioperative period where they have decreased fentanyl use, improved postanesthesia care unit length of stay, and decreased postoperative emesis.[51,52] Although not frequently considered to augment pain control, esmolol infusions have also been demonstrated to decrease opioid usage in the postoperative period.[53,54]

ANESTHESIA CONSIDERATIONS IN THE ELDERLY

Peripheral Nerve Blocks

Properly done, this approach is an excellent anesthetic in the elderly because it is site specific with few side effects. The use of peripheral nerve block offers better postoperative pain control, decreased opioid requirement, and increased patient satisfaction.[28] One potential downside of this approach is a documented higher risk of permanent nerve damage in elderly patients.[55]

General Anesthesia

Although fragile patients with multiple comorbidities may be best served by local or regional anesthesia, this is not true for most elderly patients. In a study of 800,000 patients, Arbous and colleagues[56] found that advanced age was not an independent risk factor for serious morbidity or mortality in patients undergoing general anesthesia. However, anesthetic management needs to be individualized for elderly patients. For example, when using propofol in the elderly, a lower induction dose is needed[57]; the slower blood-brain circulation results in a slower onset and delayed maximal cardiopulmonary depressive effect.[58] As a result of less compliant vasculature, the elderly are also more prone to develop hypotension with this agent.[28] The use of inhalational anesthetics also needs to be adjusted in the elderly. For every decade after 30 years of age, there is a 7% increase in the potency of inhalational agents.[59] In particular, desflurane offers more rapid recovery than other agents in this age group.[28,60]

Spinal and Epidural Anesthesia

The use of spinal or epidural techniques may be appropriate in the elderly; but the side effects of hypotension, dizziness, and delayed ambulation may especially have negative impacts in the elderly.[55] Additionally, given that prostatic hypertrophy is nearly universal in elderly men, this approach may be problematic.

POSTOPERATIVE COGNITIVE IMPAIRMENT IN THE ELDERLY

The importance of postoperative central nervous system dysfunction after surgery in the elderly is coming into greater focus. The basic science mechanisms underlying this are complex and beyond the scope of this publication. However, the work by Hussain and colleagues[61] provides an excellent overview of the topic. Two cognitive syndromes have been described in elderly postoperative patients: postoperative delirium (POD) and postoperative cognitive dysfunction, which differ with respect to onset, manifestations, and permanency.

Postoperative Delirium

POD occurs shortly after surgery and is an acute change in cognitive status characterized by fluctuating attention and consciousness as well as abnormalities in memory and perception.[62,63] It is estimated that the incidence of POD in older adults occurs between 36.8% and 73.5%.[62,64] Although common, this well-recognized clinical entity is associated with a prolonged hospital stay, delayed functional recovery, and increased morbidity and mortality.[65]

Pathophysiology

In general the pathophysiology of delirium is caused by an absolute or relative lack of the neurotransmitter acetylcholine or an excess of dopamine.[66,67] There are, however, multiple other contributing factors in play, including hypoglycemia; hypoxia; cytokines associated with the stress response; medications, such as penicillin, vasoactive agents, and tranquilizers; as well as histamine (type 2) blockers.[68] Dehydration and hypoperfusion are frequent causes of delirium in the elderly.[69] Delirium may also be the only finding in the elderly suffering from a postoperative infection.

The relative contributions of the surgical procedure and the type of anesthetic used yield interesting results. The inflammatory response and the resultant cognitive deficits are caused more by the operation than the use of a general anesthetic.[61] Likewise, the use of a general anesthetic did not confer a higher risk of POD compared with regional anesthesia in a meta-analysis.[70]

Risk Factors

Although preexisting psychiatric diseases, withdrawal from alcohol, nutritional deficiencies, and anticholinergic medications predispose the elderly to delirium, many of these are interrelated; it is difficult to identify the specific culprit.[65] Inouye and colleagues[71] have identified 5 independent risk factors in the elderly: baseline dementia, vision impairment, physical restraints, functional impairment, and several comorbidities.

Diagnosis

Delirium is chiefly characterized by acute onset, disorientation, disorganized thought and speech, disrupted sleep-wake cycle, memory disturbance, clouded consciousness, and hallucinations and elusions that last for days to weeks.[72] Several bedside cognitive function tests, such as the Mini-Mental Status Examination, the Abbreviated Mental Test, and the Confusion Assessment Method are easy to perform and are useful in confirming the diagnosis and following the level of improvement or decline.[65]

Prevention and Treatment

To reduce dopamine levels in order to prevent delirium, it would be reasonable to give haloperidol preoperatively. The prophylactic use of haloperidol demonstrated a reduction in the duration and severity of delirium but unfortunately not the incidence.[73] Rapid correction of dehydration and infectious cause will be beneficial in preventing delirium from developing. Continuation of eyeglasses and hearing aids should also be of utmost importance.

Once delirium has developed, the best acute treatment is haloperidol. This drug can be dosed starting at 0.5 mg and repeated every 15 to 30 minutes to a maximum dosage of 20 mg every 24 hours. If this is not effective, the addition of low-dose lorazepam, 0.5 mg up to 6 mg per 24 hours, can be used.[68] In addition to medication, frequent reorientation, normalization of the sleep-wake cycle, and increased daytime activities may also be beneficial.

Postoperative Cognitive Dysfunction

Unlike POD, postoperative cognitive dysfunction (POCD) occurs days to weeks after surgery and is characterized by impairment of memory, concentration, and social integration. Also unlike POD, POCD is milder but may remain a permanent disorder.[65] As a result, the implications of POCD have significant socioeconomic implications because of the increased need for long-term care.[65] Following noncardiac surgery, 25% of patients were demonstrated to have POCD. Although this improved to 10% at 3 months postoperatively, this is still a significant percentage far out from an operation.[74] Like POD, POCD is also associated with an increased mortality.[75]

Pathophysiology

Little is understood about the pathophysiologic mechanisms that cause POCD.

Risk Factors

The specific risk factors for the development of POCD are still under investigation. It is likely that there are multiple contributing factors. Unlike POD, there is an increased risk associated with general anesthesia[70] and inhalational anesthetics but no difference between desflurane versus servoflurane.[76] Similar to POD, patients with multiple medical problems and poor functional status are at an increased risk.[65]

Diagnosis

Diagnosis of POCD remains difficult because of the lack of uniform criteria and unreliable neuropsychological tests capable of detecting mild functional impairment.[65] POCD also shares several features of Alzheimer disease that further confounds the diagnosis.[61] Of note, POCD is not recognized in the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition).

Treatment

Unfortunately, there is no evidence that once POCD is diagnosed it can be successfully treated.[65]

PULMONARY

Pulmonary function is most notably affected by anatomic changes in the elderly. Kyphosis, vertebral compression, calcification of the costal cartilage, and contracture of the intercostal muscles lead to decreased chest wall compliance.[77] Loss of intercostal muscle strength alone can decrease maximum inspiratory and expiratory force by as much as 50%.[77,78] The loss of the elasticity of the lung parenchyma collapses small airways, leading to increased alveolar compliance with uneven ventilation and air trapping.[77,78] This perfusion mismatch results in a 0.3- to 0.4-mm Hg decrease per year in arterial oxygen tension.[78] Although total lung capacity remains unchanged, there is a mild increase in functional residual capacity (FRC; 1%–3% per decade) and an increase in residual volume (5%–10% per decade).[77,78] Thus, vital capacity decreases 20 to 30 mL per year.[77] Mucociliary clearance decreases, whereas swallowing dysfunction, loss of cough reflex, and oropharyngeal colonization contribute to aspiration.[79] Additionally, the neurologic autonomic response to hypoxia and hypercapnia is decreased by 40% and 50%, respectively.[79]

Just before extubation and in the immediate postoperative period, respiratory drive may be decreased because of the incomplete elimination of inhalational anesthetics, opioids, and benzodiazepines.[80] These medication side effects may be more prominent in the elderly because of altered pharmacokinetics and pharmacodynamics.[77]

Aggressive pulmonary toilet using incentive spirometry, early mobilization, and upright positioning, which increases FRC, are absolutes for elderly patients to prevent atelectasis.[77,80] Voluntary movement of the chest wall muscles may be limited by pain or physically disrupted with an incision.[77] Thoracic and abdominal operations are associated with higher rates of pulmonary complications,[79] and it is postulated that manipulation in these cavities results in afferent nerve inhibition of respiratory muscle function.[77]

Noninvasive ventilation has not been studied in elderly surgical patients; but in other patient populations, it has reduced intubation rates. Although noninvasive ventilation may initially be attempted in the elderly struggling after extubation, the failure rate is still about 30%.[79] A study of 330,000 patients demonstrates an exponential increase in the incident of acute respiratory failure each decade until 85 years of age.[81] Unfortunately, we as providers are inaccurate in identifying respiratory failure, attributing confusion, agitation, delirium, and altered level of consciousness to dementia and previous stroke rather than hypoxia and hypercarbia.[82] Our patients' self-perception of dyspnea and bronchoconstriction also decreases with age.[83]

Mechanical ventilation should not be withheld because of age alone.[84,85] After adjusting for severity of illness, Ely and colleagues[84] demonstrated that the 75-years-of-age-and-older cohort had an equivalent number of ventilator days, intensive care unit and hospital length of stay, and mortality rate compared with their younger counterparts. Theoretically we would expect the aforementioned physiologic changes with age to affect ventilator weaning.[86] Readiness to extubate may be as difficult to assess as need for intubation. Usual tools such as frequency-tidal volume ratio, negative inspiratory force, and minute ventilation are not predictive of extubation failure in the elderly.[84,87] For those intubated greater than 7 days, one prospective study of critically ill medical patients found that a rapid shallow breathing index less than 130 may improve the accuracy in predicting successful extubation.[88] Once an elderly patient has been on the ventilator for greater than 6 hours per day for more than 21 days, long-term ventilator dependence increases proportionately in those aged 70 years and older.[89]

Age is not an independent risk factor for perioperative pulmonary complications; comorbidities, especially chronic obstructive pulmonary disease (COPD), have a greater risk association with perioperative pulmonary complications.[90] COPD is the single most important predictor of perioperative pulmonary complications in the elderly with a 3- to 4-fold increased risk.[90]

CARDIOVASCULAR

The most common cause of death in perioperative elderly patients is cardiac.[91] In the elderly, it is difficult to decipher if complications arise because of cardiac disease versus the physiologic changes that accompany the normal aging process.

Specific anatomic changes are noted in the heart as aging occurs. The overall weight of the heart increases in women, the ventricular septum thickens proportionally more than the left ventricle wall, and the left atria dilates.[91–95] The diameter of the aortic root increases[94]; although the valves may become sclerosed and calcified, this has a minor impact on their function.[96] In fact, all 4 valves may become dilated,[97] explaining the multi-valvular regurgitation in healthy older adults. The actual shape changes from elliptical to spheroid.[95] The epicardium's fat content, especially overlying the right ventricle, increases.[91] On a cellular level, the actual number of myocytes decreases, whereas the size of those remaining increases.[98] There is an increase in intracellular lipofuscin, the degenerative pigment, amyloid, collagen, and elastin.[91,99,100] Within the conduction system, 90% of the sinus node cells are replaced by fat and connective

tissue, and the tracts become fibrosed.[101] These changes also affect the cardiac vasculature, resulting in dilation, intimal thickening, and calcification independent of atherosclerosis.[91,93,100] The vessels become less compliant and reactive to nitric oxide and the renin-angiotensin system, resulting in increased systolic blood pressure and pulse pressure, turbulent flow, and elevated pulse wave velocities.[91,93,100] In fact, Roman and colleagues[102] demonstrated that the pulse pressure is a better predictor of cardiovascular events than systolic or diastolic blood pressure. Overall, these structural changes result in a stiff heart with decrease contractility and compliance and at risk for sick sinus syndrome, arrhythmias, and bundle branch blocks.

The impact of these structural changes on the function of the heart is difficult to assess with age, frailty, metabolic changes, overall cardiac health, and atherosclerotic disease complicating the picture. Generally, function is divided into systolic and diastolic function. Systolic function is usually preserved as the heart ages.[91,93,100] In diastole, the heart is slower to relax, so it fills slower and later in the phase.[93] However, as flow demand is increased, the aged heart is less responsive to catecholamines. Maximum heart rate is decreased. End diastolic volume and stroke volume increase. There is no change in end systolic volume. Peak ejection fraction and cardiac output decrease; overall, the size of the left ventricle increases, leading to decreased or nil reserve with greater risk for cardiac failure.[91,93,100]

Fifty percent of the elderly have abnormal resting electrocardiograms frequently caused by the aforementioned anatomic changes.[103] Echocardiograms are excellent in assessing chamber size and function, but can be difficult in the elderly because of chest wall deformities.[103] Likewise, exercise stress tests are limited by the physical ability of older patients. The sensitivity and specificity of dobutamine stress echocardiography to detect myocardia ischemia have not been studied in the elderly,[103] but myocardial perfusion scintigraphy using dipyridamole (Persantine) is well tolerated, with sensitivity, specificity, and safety equivalent to those less than 65 years old.[104]

Myocardial infarction mortality is increased in the elderly: 17.8% in those 75 years and older versus 2.0% in those less than 55 years.[105] In the perioperative period, it is important to remember that only one-third of those older than 85 years will present with classic chest pain.[103] Older patients may present with vague, nonspecific, nonclassic signs and symptoms caused by comorbidities and altered pain sensitivity,[103] such as

- Shortness of breath
- Heart failure
- Pulmonary edema
- Nausea
- Emesis
- Syncope
- Confusion
- Delirium
- Agitation
- Stroke

When assessing perioperative elderly surgical patients in failure, precipitants include anemia, infection, thyroid dysfunction, atrial fibrillation, dietary, and medications. A quick review of the overall picture can be insightful. First, determine if the failure is systolic or diastolic. Systolic failure presents with an insidious onset in patients with hypertension, history of myocardial infarction, diabetes, and chronic valvular insufficiency. They present with progressive shortness of breath, displaced point of maximal impulse (PMI), cardiomegaly, q waves on electrocardiogram, and decreased

left ventricular ejection fraction on echocardiogram.[106] Although diastolic failure occurs in patients with similar histories, they have acute pulmonary edema and congestion, an S4 gallop with PMI unchanged, a normal-sized heart with left ventricular hypertrophy on electrocardiogram, and a normal or even increased left ventricular ejection fraction on echocardiogram.[106] Treatment varies depending on the cause. Although venodilators like digitalis and diuretics are mainstays in systolic heart failure, they may exacerbate diastolic dysfunction that responds to medications that improve preload and ventricular relaxation like calcium channel blockers, angiotensin-converting enzyme inhibitors, and beta-adrenergic antagonists.[106] Unfortunately, the elderly are highly susceptible to the side effects of these medications, which include dehydration, electrolytes disturbances, and further conduction slowing resulting in bradyarrhythmias to name a few.[103] As a result, the elderly frequently need lower doses because of impaired excretion.

Arrhythmias are also frequently encountered in perioperative elderly surgical patients. They may present as syncope or as mental status changes, but significant arrhythmias may present without symptoms or with palpitations.[103] A syncopal episode with a cardiovascular cause carries a 24% 1-year mortality rate.[107] Single supraventricular premature beats are present in almost all individuals older than 80 years, are usually asymptomatic, and do not require treatment.[103] Atrial fibrillation is present in 10% of patients older than 80 years.[108] Unfortunately in the elderly, antiarrhythmic adverse drug reactions caused by altered metabolic function, drug elimination, and polypharmacy can potentiate conduction abnormalities and ventricular dysfunction.[103]

Given the elderly's tenuous nature and sometimes unpredictable response to cardiac medications, more frequent monitoring, follow-up, and closer surveillance to ensure compliance and recognize early signs and symptoms of toxicity and progressing disease are imperative. Truly a multidisciplinary approach is needed involving education, frequent assessment, and careful management. A team approach has proven to reduce readmissions, improve medication compliance, be more cost-effective, and ultimately improve the functional status of patients.[109,110] In fact, lack of emotional support is a strong independent predictor of fatal and nonfatal cardiovascular events following a hospitalization in elderly women.[111]

GASTROINTESTINAL AND NUTRITION

The gastrointestinal tract is one of the systems relatively unchanged functionally by aging.[112–115] Dysphagia is a common elderly problem leading to aspiration in the perioperative period. This problem may be caused by decreased senses (olfactory, taste), decreased tongue muscle mass and strength, medications and as a result of neurologic disorders and neurovascular disease.[116] Treatment is multidisciplinary involving nursing care, speech therapists, and medical and surgical specialists. There is an increased incidence of certain gastrointestinal disorders in the elderly. Gastroesophageal reflux disease (GERD) is present in about 30% of the elderly.[117,118] There are conflicting data about whether gastric acid secretion and gastric emptying decrease or remain normal in the elderly.[116] What is proven extensively through epidemiologic studies is that *Helicobacter pylori* and subsequently gastric ulcer incidence increases with age,[119] such that half of all adults are seropositive by 50 years of age. Gastritis and gastric atrophy are 2 of the most common gastrointestinal disorders in the elderly, placing them at risk for gastrointestinal bleeding. The stress in the perioperative period, along with the use of NSAIDs that deplete mucosal prostaglandins may incite bleeding and ulceration.[116] Particularly at risk are women,[120–122] those patients with a

prior history of peptic ulcer disease, and patients with increased age.[123,124] The treatment of GERD and peptic ulcer disease is the same in the elderly: antacids, H_2 receptor antagonists, proton pump inhibitors, sucralfate, misoprostol, and antibiotics for *H pylori* eradiation. Care must be taken as elderly are prone to side effects and medication interactions, altering absorption. Antacids may increase sodium and magnesium, affecting the kidneys and causing diarrhea, and alter absorption (antibiotics, quinidine)[125,126] as can proton pump inhibitors. Cimetidine may cause confusion with high doses or parenteral administration.[125,126] Sucralfate can cause constipation.[127,128] Misoprostol may cause diarrhea.[128]

If an elderly patient develops a gastrointestinal bleed, upper or lower, independent of cause, then mortality can range from 10% to 25%.[129,130] Bleeds are approached in the same manner in the elderly: assessment, resuscitation, identification of source, and treatment. Vascular ectasias of the colon are primarily a recurrent and subacute elderly disease (two-thirds of patients older than 70 years), but 15% present with severe hemorrhage.[116] Additionally, vascular disease in the elderly often involves the mesenteric vasculature. Despite significant collaterals, embolic disease, ischemic colitis, or severe disease (involving 2 main mesenteric trunks) complicating the perioperative period may be encountered because of arrhythmias or hypotension. Presentation may be subtle, such as a postoperative ileus, or as severe as shock caused by acute intestinal infarction or gastrointestinal bleed in ischemic colitis.[116]

The liver decreases in weight and number of hepatocytes with age,[116] impacting pharmacokinetics. Alcoholic cirrhosis may be encountered in elderly surgical patients without previous knowledge of its existence, impacting surgical and perioperative management.[116] More importantly, providers must be cognizant of acetaminophen toxicity, with multiple medications containing acetaminophen and attempts to avoid opioids. As a result of cardiovascular failure in the perioperative period, patients may develop hepatic ischemia or congestion. Although pancreatic function is not altered by age, the main duct increases in size 8% per decade.[131]

One of the most commonly encountered perioperative issues arising in the elderly is constipation. Although 60% to 70% of the functional elderly have a daily bowel movement, 15% to 30% take laxatives on a regular basis.[132,133] It is important to identify those at risk and ask daily about bowel function. Opioid use, immobility, decreased oral water intake, and dietary changes while hospitalized contribute to perioperative constipation. In patients naïve to over-the-counter constipation regimens, treatment involves laxatives (milk of magnesia, lactulose, sorbitol, anthraquinones, saline laxatives, combination preparations of polyethylene glycol 3350 and electrolytes [GoLYTELY]) and mild stimulants (senna and bisacodyl).[116] Mineral oil is discouraged in those with dysphagia because of the aspiration pneumonitis risk. The elderly should be assessed for impaction if there is no output or diarrhea and manually disimpacted on identification. Enemas may soften the stool in the rectal vault and reach fecal material above manual manipulation.

Finally, chronic vascular occlusion may contribute to abdominal angina, leading to weight loss and malnourishment. Additionally with age, the villi of the small intestine shorten and become clubbed, decreasing the surface area, which is also thought to contribute to malnutrition.[113,134,135] More than 70% of hospitalized elderly patients are malnourished or at an increased nutritional risk, which is associated with increased mortality.[136,137] The Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition has provided a consensus for the diagnosis of malnutrition including insufficient nutritional intake, weight, muscle mass and subcutaneous fat loss, fluid overload, and decreased handgrip strength.[138] They recommend regular and consistent weight measurements for hospitalized and high-risk patients.[138]

Unintentional weight loss and decreased appetite in older community-dwelling patients is associated with increased mortality.[139] Similar results are also observed in obese patients older than 70 years.[140] Although a variety of definitions of weight loss exist, it is considered clinically significant if there is a 5% decrease in weight over 1 month's time period (>5% considered severe), 7.5% decrease in weight over 3 months' time period (>7.5% considered severe), or 10% decrease in weight over 6 months' time period (>10% severe).[141] There are several nutrition screening tools available for malnutrition and nutritional risk in older patients. The Mini Nutritional Assessment and the Malnutrition Screening Tool have the highest sensitivity and specificity.[142] Although these are formal tools, data suggest even a simple question such as presence of a good appetite can be predictive of outcomes.

Involuntary weight loss is multifactorial but ultimately is attributed to inadequate intake. Inadequate oral intake is similarly multifactorial because of social, psychiatric, and medical factors.[143,144] Malignancy and depression are identified as the most frequent causes of malnutrition in elderly patients.[145,146] Dysphagia, reportedly present in up to 10% of older patients, is also a contributing factor.[147] Nutritional supplementation is often used in elderly patients; however, data suggest morbidity and mortality was noted to improve only in malnourished hospitalized patients older than 75 years.[148] Results of appetite stimulants, such as megestrol, dronabinol, and mirtazapine, are mixed and not definitive for clinically significant and sustained weight gain. This subject is an obvious area ripe for research in the future to determine the impact of intensive preoperative or targeted nutritional supplementation.

RENAL

Total body water is reduced by 10% to 15% in older patients.[149] In contrast, they have a reduced glomerular filtration rate and reduced ability to concentrate urine, which predisposes them to fluid retention and volume overload.[150] Elderly patients are susceptible to acute kidney injury or acute on chronic kidney injury and electrolyte abnormalities. However, the older patient population is unique in that they are at an increased risk of electrolyte disturbances without underlying renal dysfunction, dehydration, and polypharmacy simply as a result of physiologic aging.[151,152] These disturbances result in increased morbidity and mortality and readmission rates in surgical patients particularly.[149,153–155] This condition is further exacerbated by age-related physiologic changes, including renal senescence defined as irreversible functional and structural changes associated with the kidneys of aging patients.[152]

Dehydration with a loss as little as 2% of total body water can result in a significant impairment of physical and cognitive performance.[156] Elderly patients are also more susceptible to water retention and associated electrolyte abnormalities that are exacerbated in the perioperative period, a time of increased physiologic stress.[157] Positive fluid balance is an independent risk factor for mortality in critically ill patients with acute kidney injury.[158,159]

Glomerular sclerosis leads to a decrease in glomerular mass in the elderly.[160,161] Creatinine clearance is also reduced.[150] Tubular dysfunction impairs the ability to concentrate urine, leading to electrolyte disturbances.[150] Furthermore, ischemia has also been noted to contribute to nephron loss.[162–164] Hormonal alterations have been noted to similarly affect fluid and electrolyte balance, particularly reduced levels of renin and aldosterone caused by increased atrial natriuretic peptide secondary to hypertension and increased right atrial filling at baseline.[165] There is also a decreased tubular response to hormones predisposing patients again to fluid and electrolyte abnormalities.[164]

Thirst response is blunted in older patients, resulting in a persistent hyperosmolar state that is further heightened by a reduction in the ability of the kidney to concentrate urine. Dysnatremia in older patients is of particular concern, and age is noted to be an independent risk factor.[166] It has been shown reproducibly that particularly hypernatremia is a risk factor for increased mortality.[167–169] Hyponatremia, which is more common, is noted to be a risk factor for bone fracture.[170–172] Hyperkalemia is a concern as tubular dysfunction impairs the secretion of potassium.[173–175] Hyperkalemia is further exacerbated by a decreased response to aldosterone and renin.[176] Furthermore, polypharmacy and physiologic stress increase the risk of abrupt alterations in potassium balance. Patients on angiotensin-converting enzyme inhibitors, diuretics, and NSAIDs are particularly susceptible.[177,178]

Physiologic changes in the perioperative period include systemic neurologic, hormonal, immune, and hematologic responses. Cognitive decline is a risk factor for dehydration.[179] Increased secretion of antidiuretic hormone, renin, and aldosterone during stress results in fluid retention. Older patients are increasingly susceptible given their underlying age-related physiologic changes at baseline.[157] Salt and water retention has been associated with increased risk of infection, cardiopulmonary complications, and impaired gastrointestinal function as well as a prolonged hospital stay.[180–185] Other studies report improved perioperative outcomes with zero fluid balance in the perioperative period.[186–189] Positive fluid balance was noted to be an independent factor for immediate perioperative mortality.[159] More recent data suggest that surgical patients are often noted to have a hyperchloremic acidosis secondary to the use of normal saline.[190,191] Data suggest that chloride-restricted intravenous fluid resuscitation in the perioperative period reduces the incidence of acute kidney injury, improves gastrointestinal blood flow, decreases salt and water retention, and overall decreases the risk of morbidity and mortality, particularly important as this age group is increasingly susceptible to these physiologic changes.[192–194] Additionally, studies report in older adults and high-risk patients small boluses of colloid to optimize stroke volume result in improved outcomes and decreased morbidity and mortality.[195–200]

Knowledge of age-related physiologic changes, particularly renal senescence and hormonal alterations that directly affect the fluid and electrolyte balance in older patients, is key in the perioperative period as even the slightest change in this delicate balance in this patient population can have significant effects on morbidity and mortality. Age-related changes in fluid and electrolyte homeostasis greatly affects the ability of these patients to adapt to situations that exacerbate this homeostasis, like surgical intervention and hospitalization.

OUTCOMES

When reviewing guidelines pertaining to the elderly in perioperative period, there is a paucity. Many guidelines are based on multiple randomized controlled trials that generally exclude the elderly. Furthermore, they are unable to account for the multiple comorbidities the elderly have and the statistical impact the morbidities have on outcomes.[201]

Selective use of routine studies guided by the patients' history (complete blood count, basic blood chemistries, chest radiograph, and electrocardiogram) is supported by the American Society of Anesthesiologists and Cochrane review.[202–204] Several cardiovascular risk indices, the American Heart Association, The New England Vascular Surgery Group, and others, attempt to risk stratify the elderly's cardiovascular risk. While looking at quantitative traditional outcomes, they fail to account for things the elderly cherish the most: independence, functional capacity, and quality

of life. The American Diabetes Association leads the way in recognizing the limitations of its guidelines with respect to the elderly, strongly recommending individualized treatment.[205] The American College of Surgeons in collaboration with the American Geriatrics Society has created best-practice guidelines to help surgeons identify high-risk patients, prevent complications, and achieve best outcomes in elderly surgical patients[17]; unfortunately, these are labor intensive, require extensive financial resources, and are not usually feasible in the emergent setting.

Overall surgical mortality in the elderly has been on the decline even in the most complex, risky operations.[206] Furthermore, even in those patients older than 90 years, long-term survival does not seem to be affected by surgical intervention.[207] The death rate for elective operations ranges from 0% to 5.4%, with 7.0% to 20.0% suffering a nonfatal complication[208–210]; these statistics hold true with age-matched cohorts.[211,212] Unfortunately, many operations are of the emergent nature in the elderly when they do not fair as well. The percentage of emergent operations increases with age: 14.5% aged 65 to 74 years, 27.9% aged 75 years and older,[209] 69.0% aged 90 years and older.[210] Usually the emergent cases are related to infection, intestinal obstruction, incarcerated hernias, and hemorrhage.[210,213] Because of the emergent nature, morbidity rates range from 30% to 68% and mortality 13.6% to 31.0%.[209,210,213] In fact, Rigberg and colleagues[210] found that all postoperative deaths in patients older than 90 years were emergent operations. With regard to oncologic operations, Dekker and colleagues[214] demonstrated that elderly patients who survive the first year following resection of their colorectal cancer have the same cancer survival rate as younger patients. Long-term survival is related to early morbidity and mortality.

As previously mentioned outcomes in elderly patients are not just about morbidity and mortality; independence, functional capacity, and quality of life play a major role. Postoperative cognitive dysfunction impairs nearly 13% of the elderly 3 months after an operation, double the rate of other age groups.[215] In a cohort of elderly patients aged 75 years and older independent at admission, 75% were not independent at discharge, 15% of whom were discharged to a nursing home[216]; they do not leave the nursing homes, 33% of those sent to a nursing home after a hip fracture remain there a year later.[217] Kemper found that of those who enter nursing homes, 55% will spend at least 1 year of total lifetime and 21% will spend 5 years or more.[218] Many die, are sent to other hospitals, rehabilitation facilities, and other long-term care facilities. In fact, only 12% ever return home.[219]

SUMMARY

The older population continues to grow at an unprecedented rate and is living longer. Thus, surgeons are encountering older patients more frequently and can expect an increase in surgical demand because of this rapidly growing population. This article highlights some of the anatomic and physiologic changes that are a result of aging. These changes can sometimes drastically alter the perioperative care of the elderly, leaving the surgeon to face challenging, complex treatment decisions and ethical questions. Clearly, the management of the older patient population requires meticulous management with a multidisciplinary approach.

REFERENCES

1. U.S. Department of Health and Human Services Administration on Aging. Available at: http://www.aoa.gov/Aging_Statistics/Profile/2013/2.aspx. Accessed November 17, 2014.

2. Centers for Disease Control and Prevention. The state of aging and health in America 2013. Atlanta (GA): Centers for Disease Control and Prevention, US Dept of Health and Human Services; 2013. Available at: http://www.cdc.gov/features/agingandhealth/state_of_aging_and_health_in_america_2013.pdf.
3. U.S. Department of Health and Human Services Administration on Aging. Available at: http://www.aoa.acl.gov/Aging_Statistics/Profile/2013/3.aspx. Accessed November 17, 2014.
4. Etzioni DA, Liu JH, Maggard MA, et al. The aging population and its impact on the surgery workforce. Ann Surg 2003;238:170–7.
5. Neuman MD, Bosk CL. The redefinition of aging in American surgery. Milbank Q 2013;91:288–315.
6. Kwok AC, Semel ME, Lipsitz SR, et al. The intensity and variation of surgical care at the end of life: a retrospective cohort study. Lancet 2011;378:1408–13.
7. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. Clin Geriatr Med 2011;27:17–26.
8. Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 2004;59:255–63.
9. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56(3):M146–56.
10. Stuck AE, Siu AL, Wieland GD, et al. Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet 1993;342(8878):1032–6.
11. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg 2010;210:901–8.
12. Devons CA. Comprehensive geriatric assessment: making the most of the aging years. Curr Opin Clin Nutr Metab Care 2002;5:19–24.
13. Rubenstein LZ, Josephson KR, Wieland GD, et al. Effectiveness of a geriatric evaluation unit: a randomized trial. N Engl J Med 1984;311:1664–70.
14. Robinson TN, Wu DS, Pointer L, et al. Simple frailty score predicts postoperative complications across surgical specialties. Am J Surg 2013;206:544–50.
15. Afilalo J, Eisenberg MJ, Morin JF, et al. Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. J Am Coll Cardiol 2010;56:1668–76.
16. Chung CJ, Wu C, Jones M, et al. Reduced handgrip strength as a marker of frailty predicts clinical outcomes in patients with heart failure undergoing ventricular assist device placement. J Card Fail 2014;20:310–5.
17. Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. J Am Coll Surg 2012;215:453–66.
18. Malafarina V, Uriz-Otano F, Iniesta R, et al. Sarcopenia in the elderly: diagnosis, physiopathology and treatment. Maturitas 2012;71:109–14.
19. Pahor M, Kritchevsky S. Research hypotheses on muscle wasting, aging, loss of function and disability. J Nutr Health Aging 1998;2:97–100.
20. Evans WJ, Morley JE, Argiles J, et al. Cachexia: a new definition. Clin Nutr 2008;27:793–9.
21. Martinez M, Arnalich F, Hernanz A. Alterations of anorectic cytokine levels from plasma and cerebrospinal fluid in idiopathic senile anorexia. Mech Ageing Dev 1993;72:145–53.

22. Lindle RS, Metter EJ, Lynch NA, et al. Age and gender comparisons of muscle strength in 654 women and men aged 20–93 yr. J Appl Physiol (1985) 1997;83:1581–7.
23. Roubenoff R. Origins and clinical relevance of sarcopenia. Can J Appl Physiol 2001;26:78–89.
24. Janssen I. The epidemiology of sarcopenia. Clin Geriatr Med 2011;27:355–63.
25. Vuky J. Pharmacodynamics in the elderly. Best Pract Res Clin Anaesthesiol 2003;17:207–18.
26. Aymanns C, Keller F, Maus S, et al. Review on pharmacokinetics and pharmacodynamics and the aging kidney. Clin J Am Soc Nephrol 2010;5:314–27.
27. Homer TD, Stanski DR. The effect of increasing age on thiopental disposition and anesthetic requirement. Anesthesiology 1985;62:714–24.
28. White PF, White LM, Monk T, et al. Perioperative care for older outpatient undergoing ambulatory surgery. Anesth Analg 2012;114:1190–215.
29. Gourtsoyiannis N, Prassopoulos P, Cavouras D, et al. The thickness of renal parenchyma decreases with age: a CT study of 360 patients. Am J Roentgenol 1990;155:541–4.
30. Schmucker DL. Age-related changes in liver structure and function: implications for disease? Exp Gerontol 2005;40:650–9.
31. Tang J, Eckenhoff MF, Eckenhoff RG. Anesthesia and the old brain. Anesth Analg 2010;110:421–6.
32. Gibson SJ, Helme RD. Age-related differences in pain perception and report. Clin Geriatr Med 2001;17:433–56.
33. Barnett SR. Polypharmacy and perioperative medications in the elderly. Anesthesiol Clin 2009;27:377–89.
34. Minto CF, Schider TW, Egan TD, et al. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil: I model development. Anesthesiology 1997;80:143–8.
35. Ong CK, Lirk P, Seymour RA, et al. The efficacy of preemptive analgesia for acute post-operative pain management: a meta-analysis. Anesth Analg 2005;100:757–73.
36. Moinche S, Mikkelsen S, Wetterslev J, et al. A systematic review of intra-articular local anesthesia for post-operative pain relief after arthroscopic knee surgery. Reg Anesth Pain Med 1999;24:430–7.
37. Popping DM, Elia N, Marret E, et al. Clonidine as an adjuvant to local anesthetics, for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology 2009;111:406–15.
38. Essving P, Axelsson K, Kjellberg J, et al. Reduced hospital stay, morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. Acta Orthop 2010;81:354–60.
39. Vieira P, Pulai I, Tsao GC, et al. Dexamethasone with bupivacaine increases duration of analgesia with ultrasound guided brachial plexus blockade. Eur J Anaesthesiol 2010;27:285–8.
40. Toms L, McQuay HJ, Derry S, et al. Single dose oral paracetamol (acetaminophen) for postoperative pain in adults. Cochrane Database Syst Rev 2008;(4):CD004602.
41. Miners JO, Penhall R, Robson RA, et al. Comparison of paracetamol metabolism in young adult and elderly males. Eur J Clin Pharmacol 1988;35:157–60.
42. Bisgaard T, Klarskov B, Kehlet H, et al. Preoperative dexamethasone improves surgical outcomes after laparoscopic cholecystectomy: a randomized double-blind placebo-controlled trial. Ann Surg 2003;238:651–60.

43. Hval K, Thagaard K, Schlichting E, et al. The prolonged postoperative analgesic effect when dexamethasone is added to a nonsteroidal anti-inflammatory drug (rofecoxib) before breast surgery. Anesth Analg 2007;105:481–6.
44. Rommundstad L, Brevik H, Roald H, et al. Methylprednisolone reduces pain, emesis, and fatigue after breast augmentation surgery: a single dose, randomized, parallel-group study with methylprednisolone 125 mg, parecoxib 40 mg, and placebo. Anesth Analg 2006;102:419–25.
45. Whitlock RP, Chan S, Devereaux PJ, et al. Clinical benefit of steroid use in patients undergoing cardiopulmonary bypass: a meta-analysis of randomized trials. Eur Heart J 2008;29:2592–600.
46. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2000;90:186–94.
47. Loftus RW, Yeager MP, Clark JA, et al. Intraoperative ketamine reduces perioperative opiate consumption in opiate-dependent patients with chronic back pain undergoing back surgery. Anesthesiology 2010;113:639–46.
48. Remerand F, Le Tendre C, Baud A, et al. The early and delayed analgesic effects of ketamine after total hip arthroplasty: a prospective, randomized, controlled, double-blind study. Anesth Analg 2009;109:1963–71.
49. Gilron I, Orr E, Tu D, et al. A randomized double-blind, controlled trial of perioperative administration of gabapentin, meloxicam and their combination for spontaneous and movement-evoked pain after ambulatory laparoscopic cholecystectomy. Anesth Analg 2009;108:623–30.
50. Turan A, White PF, Karamanlioglu D, et al. Gabapentin-an alternative to COX-2 inhibitors for perioperative pain management. Anesth Analg 2006; 102:175–81.
51. Erola O, Kortila K, Aho M, et al. Comparison of intramuscular dexmedetomidine and midazolam premedication for elective abdominal hysterectomy. Anesth Analg 1994;79:646–53.
52. Tufanogullari B, White PF, Peixoto MP, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery room outcome variables. Anesth Analg 2008;106:1741–8.
53. Coloma M, Chiu JW, White PF, et al. The use of esmolol as an alternative to remifentanil during desflurane anesthesia for fast-track outpatient gynecologic laparoscopic surgery. Anesth Analg 2001;92:352–7.
54. Lee SJ, Lee JN. The effect of perioperative esmolol infusion on postoperative nausea, vomiting and pain after laparoscopic appendectomy. Korean J Anesthesiol 2010;59:179–84.
55. Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France: the SOS regional anesthesia hotline service. Anesthesiology 2002;97:1274–80.
56. Arbous MS, Meursing AE, van Kleef JW, et al. Impact of anesthesia management characteristics on severe morbidity and mortality. Anesthesiology 2005; 102:257–68.
57. Schnider TW, Minto CF, Shafer SL, et al. The influence of age on propofol pharmacodynamics. Anesthesiology 1999;90:1502–16.
58. Kazama T, Ikeda K, Morita K, et al. Comparison of the effect-site k(eO)s of propofol for blood pressure and EEG bispectral index in elderly and younger patients. Anesthesiology 1999;90:1517–27.
59. Eger EL. Age, minimal alveolar anesthetic concentration and minimum alveolar anesthetic concentration-awake. Anesth Analg 2001;93:947–53.

60. Chen X, Zhao M, White PF, et al. The recovery of cognitive function after general anesthesia in elderly patients: a comparison of desflurane and sevoflurane. Anesth Analg 2001;93:1489–95.
61. Hussain M, Berger M, Eckenhoff RG, et al. General anesthetic and the risk of dementia in the elderly: current insight. Clin Interv Aging 2014;4:1619–28.
62. Dyer CB, Aston CM, Teasdale TA. Postoperative delirium: a review of 80 primary data-collection studies. Arch Intern Med 1995;155:461–5.
63. Practice guidelines for the treatment of patients with delirium. American Psychiatric Association. Am J Psychiatry 1999;156:1–20.
64. Kimball CP. The experience of open heart surgery. 3. Toward a definition and understanding of postcardiotomy delirium. Arch Gen Psychiatry 1972;27:57–63.
65. Bekker AY, Weeks EJ. Cognitive function after anaesthesia in the elderly. Best Pract Res Clin Anaesthesiol 2003;17:259–72.
66. Flacker JM, Cummings V, Mach JR Jr, et al. The association of serum anticholinergic activity with delirium in elderly medical patients. Am J Geriatr Psychiatry 1998;6:31–41.
67. Trzepacz PT. Is there a final common pathway in delirium? Focus on acetylcholine and dopamine. Semin Clin Neuropsychiatry 2000;5:132–48.
68. Hamrick I, Meyer F. Perioperative management of delirium and dementia in the geriatric surgical patient. Langenbecks Arch Surg 2013;298:947–55.
69. Inouye SK, Bogardus ST Jr, Charpentier PA, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med 1999;340:669–76.
70. Mason SE, Noel-Storr A, Ritchie CW. The impact of general and regional anesthesia on the incidence of post-operative cognitive dysfunction and post-operative delirium: a systematic review with meta-analysis. J Alzheimers Dis 2010;22:67–79.
71. Inouye SK, Zhang Y, Jones RN, et al. Risk factors for delirium at discharge: development and validation of a predictive model. Arch Intern Med 2007;167:1406–13.
72. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. IV-TR ed. Washington, DC: American Psychiatric Association; 2000.
73. Kalsvaart KJ, de Jonghe JF, Bogaards MJ, et al. Haloperidol prophylaxis for elderly hip fracture patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc 2005;53:1658–66.
74. Moller JT, Cluitmans P, Raqssmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet 1998;351:857–61.
75. Steinmetz J, Christensen KB, Lund T, et al. Long-term consequences of post-operative cognitive dysfunction. Anesthesiology 2009;110:548–55.
76. Rortgen D, Kloos J, Fries M, et al. Comparison of early cognitive function and recovery after desflurane or sevoflurane anaesthesia in the elderly: a double-blinded randomized controlled trial. Br J Anaesth 2010;104:167–74.
77. Rosenthal RA, Kavic SM. Assessment and management of the geriatric patient. Crit Care Med 2004;32:S92–105.
78. Sprung J, Gajic O, Warner DO. Review article: age related alteration in respiratory function – anesthestic considerations. Can J Anaesth 2006;53:1244–57.
79. Antonelli M, Conti G, Moro ML, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multicenter study. Intensive Care Med 2001;27:1718–28.
80. Warner DO. Preventing postoperative pulmonary complications. Anesthesiology 2000;92:1467–72.

81. Behrendt CE. Acute respiratory failure in the United States. Chest 2000;118: 1100–5.
82. Solh AA, Ramadan FH. Overview of respiratory failure in older adults. J Intensive Care Med 2006;21:345–51.
83. Connolly MJ, Crowley JJ, Charan NB, et al. Reduced subjective awareness of bronchoconstriction provoked by methacholine in elderly asthmatic and normal subjects as measured on a simple awareness scale. Thorax 1992;47:410–3.
84. Ely EW, Evans GW, Haponik EF. Mechanical ventilation in a cohort of elderly patients admitted to an intensive care unit. Ann Intern Med 1999;131:96–104.
85. Pesau B, Falger S, Berger E, et al. Influence of age on outcome of mechanically ventilated patients in an intensive care unit. Crit Care Med 1992;20:489–92.
86. Thompson LF. Failure to wean: exploring the influence of age-related pulmonary changes. Crit Care Nurs Clin North Am 1996;8:7–16.
87. Krieger BP, Ershowsky PF, Becker DA, et al. Evaluation of conventional criteria for predicting successful weaning from mechanical ventilator support in elderly patients. Crit Care Med 1989;17:858–61.
88. Krieger BP, Isber J, Breitenbucher A, et al. Serial measurements of the rapid-shallow-breathing index as a predictor of weaning outcome in elderly medical patients. Chest 1997;112:1029–34.
89. Kleinhenz ME, Lewis CY. Chronic ventilator dependence in elderly patients. Clin Geriatr Med 2000;16:735–56.
90. Smetana G. Preoperative pulmonary evaluation. N Engl J Med 1999;340: 937–44.
91. Rosenthal RA, Perkal MF. Physiologic considerations in the elderly surgical patient. In: Miller TA, editor. Modern surgical care: physiologic foundations and clinical applications. 2nd edition. New York: Informa; 2006. p. 1129–48.
92. Kitzman DW, Edwards WD. Age-related changes in the anatomy of the normal human heart. J Gerontol 1990;45:M33–9.
93. Strait JB, Lakatta EG. Aging-associated cardiovascular changes and their relationship to heart failure. Heart Fail Clin 2012;8:143–64.
94. Gerstenblith G, Frederiksen J, Yin FC, et al. Echocardiographic assessment of a normal adult aging population. Circulation 1977;56:273–8.
95. Hees PS, Fleg JL, Lakatta EG, et al. Left ventricular remodeling with age in normal men versus women: novel insights using three-dimensional magnetic resonance imaging. Am J Cardiol 2002;90:1231–6.
96. Sahasakul Y, Edwards WD, Naessens JM, et al. Age-related changes in aortic and mitral valve thickness: implications for two-dimensional echocardiography based on an autopsy study of 200 normal human hearts. Am J Cardiol 1988; 62:424–30.
97. Kitzman DW, Scholz DG, Hagen PT, et al. Age-related changes in normal human hearts during the first 10 decades of life. Part II (maturity): a quantitative anatomic study of 765 specimens from subjects 20 to 99 years old. Mayo Clin Proc 1988;63:137–46.
98. Olivetti G, Melissari M, Capasso JM, et al. Cardiomyopathy of the aging human heart. Myocyte loss and reactive cellular hypertrophy. Circ Res 1991;68:1560–8.
99. Lakatta EG, Mitchell JH, Pomerance A, et al. Human aging: changes in structure and function. J Am Coll Cardiol 1987;10:42A–7A.
100. Priebe HJ. The aged cardiovascular risk patient. Br J Anaesth 2000;85:763–78.
101. Davies MJ. Pathology of the conduction system. In: Caird FL, Dalle JL, Kennedy RD, editors. Cardiology in old age. New York: Plenum Press; 1976. p. 57–9.

102. Roman MJ, Devereux RB, Kizer JR, et al. High central pulse pressure is independently associated with adverse cardiovascular outcome the strong heart study. J Am Coll Cardiol 2009;54:1730–4.
103. Wenger NK. Cardiovascular disease. In: Cassell CK, Leipzig RM, Cohen HJ, et al, editors. Geriatric medicine. 4th edition. New York: Springer; 2003. p. 509–43.
104. Lam JY, Chaitman BR, Glaenzer M. Safety and diagnostic accuracy in dipyridamole-thallium imaging in the elderly. J Am Coll Cardiol 1988;11:585–9.
105. Weaver WD, Litwin PE, Marte JS, et al. Effect of age on use of thrombolytic therapy and mortality in acute myocardial infarction. J Am Coll Cardiol 1991;18:657–62.
106. Tresch DD, McGough MF. Heart failure with normal systolic function: a common disorder in older people. J Am Geriatr Soc 1995;43:1035–42.
107. Lipsitz LA, Wei JY, Rowe JQ. Syncope in an elderly, institutionalized population: prevalence, incidence, and associated risk. Q J Med 1985;55:45–54.
108. Ryder KM, Benjamin EJ. Epidemiology and significance of atrial fibrillation. Am J Cardiol 1999;84:131R–8R.
109. Rich MW, Beckham V, Wittenberg C, et al. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. N Engl J Med 1995;333:1190–5.
110. Rich MW, Gray DB, Beckham V, et al. Effect of a multidisciplinary intervention on medication compliance in elderly patients with congestive heart failure. Am J Med 1996;101:270–6.
111. Krumholz HM, Butler J, Miller J, et al. Prognostic importance of emotional support for elderly patients hospitalized with heart failure. Circulation 1998;97:958–64.
112. Shamburek RD, Farrar J. Disorders of the digestive system in the elderly. N Engl J Med 1990;322:438–43.
113. Holt PR. Gastrointestinal system: changes in morphology and cell proliferation. Aging 1991;3:392–4.
114. Russell RM. Change in gastrointestinal function attributed to aging. Am J Clin Nutr 1992;55:1203S–7S.
115. Blechman MB, Gelb AM. Aging and gastrointestinal physiology. Clin Geriatr Med 1999;15:429–38.
116. Wilson JAP. Gastroenterologic disorders. In: Cassell CK, Leipzig RM, Cohen HJ, et al, editors. Geriatric medicine. 4th edition. New York: Springer; 2003. p. 835–51.
117. Ellis FH. Current concepts. Esophageal hiatal hernia. N Engl J Med 1972;287:646–69.
118. Spechler SJ. Epidemiology and natural history of gastro-oesophageal reflux disease. Digestion 1992;51:24–9.
119. Perez-Perez GI, Dworkin BM, Chodos JE, et al. *Campylobacter pylori* antibodies in humans. Ann Intern Med 1988;109:11–7.
120. Allison MC, Torrance CJ, Russell RI. Non-steroidal anti-inflammatory drugs, gastroduodenal ulcers and their complications: prospective controlled autopsy study. N Engl J Med 1992;327:749–54.
121. Skander MP, Ryan FP. Non-steroidal anti-inflammatory drugs and pain-free peptic ulceration in the elderly. BMJ 1988;297:833–4.
122. Gabriel SE, Jaakkimainen L, Bombardier C. Risk for serious gastrointestinal complications related to use of NSAIDs: a meta-analysis. Ann Intern Med 1991;115:787–96.
123. Griffin MR, Piper JM, Daughtery MS, et al. Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. Ann Intern Med 1991;114:257–63.

124. Borum MA. Peptic-ulcer disease in the elderly. Clin Geriatr Med 1999;15:457–71.
125. Walt RP, Langman MJ. Antacids and ulcer healing. A review of the evidence. Drugs 1991;42:205–12.
126. Freston JW. Overview of medical therapy of peptic ulcer disease. Gastroenterol Clin North Am 1990;19:121–40.
127. Rees WD. Mechanisms of gastroduodenal protection by sucralfate. Am J Med 1991;91:58S–63S.
128. Scheiman JM. Pathogeneses of gastroduodenal injury due to nonsteroidal anti-inflammatory drugs: implications for prevention and therapy. Semin Arthritis Rheum 1992;21:201–10.
129. Reinus JF, Brandt LJ. Lower intestinal bleeding in the elderly. Clin Geriatr Med 1991;7:301–19.
130. Rosen AM. Gastrointestinal bleeding in the elderly. Clin Geriatr Med 1999;15:511–25.
131. Gullo L, Ventrucci M, Naldoni P, et al. Aging and exocrine pancreatic function. J Am Geriatr Soc 1986;34:790–2.
132. Wilson JA. Constipation in the elderly. Clin Geriatr Med 1999;15:499–510.
133. Whitehead WE, Drinkwater D, Cheskin LJ, et al. Constipation in the elderly living at home—definition, prevalence, and relationship to lifestyle and health status. J Am Geriatr Soc 1989;37:423–9.
134. Holt PR, Tierney AR, Kotler DP. Delayed enzyme expression: a defect of aging rat gut. Gastroenterology 1985;89:1026–34.
135. Holt PR. Gastrointestinal disorders in the elderly: the small intestine. Clin Gastroenterol 1985;14:689–723.
136. de Luis D, Lopez GA. Nutritional status of adult patients admitted to internal medicine departments in public hospitals in Castilla y Leon, Spain: a multicenter study. Eur J Intern Med 2006;17:556–60.
137. Wallace JI, Schwartz RS, LaCroix AZ, et al. Involuntary weight loss in older outpatients: incidence and clinical significance. J Am Geriatr Soc 1995;43:329–37.
138. White JV, Guenter P, Jensen G, et al. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). J Acad Nutr Diet 2012;112:730–8.
139. Wannamethee SG, Shaper AG, Lennon L. Reasons for intentional weight loss, unintentional weight loss, and mortality in older men. Arch Intern Med 2005;165:1035–40.
140. Allison DB, Gallagher D, Heo M, et al. Body mass index and all-cause mortality among people age 70 and over: the longitudinal study of aging. Int J Obes Relat Metab Disord 1997;21:424–31.
141. Health Care Financing Administration. Long term care facility resident assessment user's manual, minimum data set, version 2. Natick (MA): Elior Press; 1999.
142. Skipper A, Ferguson M, Thompson K, et al. Nutrition screening tools: an analysis of the evidence. JPEN J Parenter Enteral Nutr 2012;36:292–8.
143. de Castro JM, Brewer EM. The amount eaten in meals by humans is a power function of the number of people present. Physiol Behav 1992;51:121–5.
144. Locher JL, Robinson CO, Roth DL, et al. The effect of the presence of others on caloric intake in homebound older adults. J Gerontol A Biol Sci Med Sci 2005;60:1475–8.
145. Wilson MM, Vaswani S, Liu D, et al. Prevalence and causes of undernutrition in medical outpatients. Am J Med 1998;104:56–63.

146. Thompson MP, Morris LK. Unexplained weight loss in the ambulatory elderly. J Am Geriatr Soc 1991;39:497–500.
147. Achem SR, Devault KR. Dysphagia in aging. J Clin Gastroenterol 2005;39: 357–71.
148. Milne AC, Avenell A, Potter J. Meta-analysis: protein and energy supplementation in older people. Ann Intern Med 2006;144:37–48.
149. Allison SP, Lobo DN. Fluid and electrolytes in the elderly. Curr Opin Clin Nutr Metab Care 2004;7:27–33.
150. Lindeman RD, Tobin J, Shock NW. Longitudinal studies on the rate of decline in renal function with age. J Am Geriatr Soc 1985;33:278–85.
151. Schlanger LE, Bailey JL, Sands JM. Electrolytes in the aging. Adv Chronic Kidney Dis 2010;17:308–19.
152. Melk A. Senescence of renal cells: molecular basis and clinical implications. Nephrol Dial Transplant 2003;18:2474–8.
153. Hari M, Rosenzweig M. Incidence of preventable postoperative readmissions following pancreaticoduodenectomy: implications for patient education. Oncol Nurs Forum 2012;39:408–12.
154. Khan MA, Hossain FS, Dashti Z, et al. Causes and predictors of early readmission after surgery for a fracture of the hip. J Bone Joint Surg Br 2012; 94:690–7.
155. Messaris E, Sehgal R, Deiling S, et al. Dehydration is the most common indication for readmission after diverting ileostomy creation. Dis Colon Rectum 2012; 55:175–80.
156. Grandjean AC, Grandjean NR. Dehydration and cognitive performance. J Am Coll Nutr 2007;26:S549–54.
157. Desborough J. The stress response to trauma and surgery. Br J Anaesth 2000; 85:109–17.
158. Bagshaw SM, Brophy PD, Cruz D, et al. Fluid balance as a biomarker: impact of fluid overload on outcome in critically ill patients with acute kidney injury. Crit Care 2008;12:169.
159. Payen D, de Pont AC, Sakr Y, et al. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. Crit Care 2008;12:R74.
160. Nyengaard JR, Bendtsen TF. Glomerular number and size in relation to age, kidney weight, and body surface in normal man. Anat Rec 1992;232:194–201.
161. Epstein M. Aging and the kidney. J Am Soc Nephrol 1996;7:1106–22.
162. Messerli FH, Sundgaard-Riise K, Ventura HO, et al. Essential hypertension in the elderly: haemodynamics, intravascular volume, plasma renin activity, and circulating catecholamine levels. Lancet 1983;2:983–6.
163. Hollenberg NK, Adams DF, Solomon HS, et al. Senescence and the renal vasculature in normal man. Circ Res 1974;34:309–16.
164. Beck LH. The aging kidney. Defending a delicate balance of fluid and electrolytes. Geriatrics 2000;55:26–8, 31–2.
165. Lobo DN, Stanga Z, Aloysius MM, et al. Effect of volume loading with 1 liter intravenous infusions of 0.9% saline, 4% succinylated gelatine (Gelofusine) and 6% hydroxyethyl starch (Voluven) on blood volume and endocrine responses: a randomized, three-way crossover study in healthy volunteers. Crit Care Med 2010; 38:464–70.
166. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta 2003;337:169–72.
167. Alshayeb HM, Showkat A, Babar F, et al. Severe hypernatremia correction rate and mortality in hospitalized patients. Am J Med Sci 2011;341:356–60.

168. Snyder NA, Feigal DW, Arieff AI. Hypernatremia in elderly patients. A heterogeneous, morbid, and iatrogenic entity. Ann Intern Med 1987;107:309–19.
169. Herrod PJ, Awad S, Redfern A, et al. Hypo- and hypernatraemia in surgical patients: is there room for improvement? World J Surg 2010;34:495–9.
170. Gankam Kengne F, Andres C, Sattar L, et al. Mild hyponatremia and risk of fracture in the ambulatory elderly. QJM 2008;101:583–8.
171. Zilberberg MD, Exuzides A, Spalding J, et al. Epidemiology, clinical and economic outcomes of admission hyponatremia among hospitalized patients. Curr Med Res Opin 2008;24:1601–8.
172. Kinsella S, Moran S, Sullivan MO, et al. Hyponatremia independent of osteoporosis is associated with fracture occurrence. Clin J Am Soc Nephrol 2010;5:275–80.
173. Musso C, Liakopoulos V, De Miguel R, et al. Transtubular potassium concentration gradient: comparison between healthy old people and chronic renal failure patients. Int Urol Nephrol 2006;38:387–90.
174. Frassetto L, Sebastian A. Age and systemic acid-base equilibrium: analysis of published data. J Gerontol A Biol Sci Med Sci 1996;51:B91–9.
175. Berkemeyer S, Vormann J, Gunther AL, et al. Renal net acid excretion capacity is comparable in prepubescence, adolescence, and young adulthood but falls with aging. J Am Geriatr Soc 2008;56:1442–8.
176. Mulkerrin E, Epstein FH, Clark BA. Aldosterone responses to hyperkalemia in healthy elderly humans. J Am Soc Nephrol 1995;6:1459–62.
177. Gurwitz JH, Field TS, Harrold LR, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA 2003;289:1107–16.
178. Chapman MD, Hanrahan R, McEwen J, et al. Hyponatraemia and hypokalaemia due to indapamide. Med J Aust 2002;176:219–21.
179. Adan A. Cognitive performance and dehydration. J Am Coll Nutr 2012;31:71–8.
180. Arieff AI. Fatal postoperative pulmonary edema: pathogenesis and literature review. Chest 1999;115:1371–7.
181. Lobo DN, Macafee DA, Allison SP. How perioperative fluid balance influences postoperative outcomes. Best Pract Res Clin Anaesthesiol 2006;20:439–55.
182. Holte K, Sharrock NE, Kehlet H. Pathophysiology and clinical implications of perioperative fluid excess. Br J Anaesth 2002;89:622–32.
183. Michell AR. Diuresis and diarrhea: is the gut a misunderstood nephron? Perspect Biol Med 2000;43:399–405.
184. Lobo DN, Bostock KA, Neal KR, et al. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. Lancet 2002;359:1812–8.
185. Chowdhury AH, Lobo DN. Fluids and gastrointestinal function. Curr Opin Clin Nutr Metab Care 2011;14:469–76.
186. Brandstrup B, Tonnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. Ann Surg 2003;238:641–8.
187. McArdle GT, McAuley DF, McKinley A, et al. Preliminary results of a prospective randomized trial of restrictive versus standard fluid regime in elective open abdominal aortic aneurysm repair. Ann Surg 2009;250:28–34.
188. Neal JM, Wilcox RR, Allen HW, et al. Near-total esophagectomy: the influence of standardized multimodal management and intraoperative fluid restriction. Reg Anesth Pain Med 2003;28:328–34.
189. Varadhan KK, Lobo DN. A meta-analysis of randomized controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right. Proc Nutr Soc 2010;69:488–98.

190. Reid F, Lobo DN, Williams RN, et al. (Ab)normal saline and physiological Hartmann's solution: a randomized double-blind crossover study. Clin Sci (Lond) 2003;104:17–24.
191. Williams EL, Hildebrand KL, McCormick SA, et al. The effect of intravenous lactated Ringer's solution versus 0.9% sodium chloride solution on serum osmolality in human volunteers. Anesth Analg 1999;88:999–1003.
192. Yunos NN, Bellomo R, Hegarty C, et al. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. JAMA 2012;308:1566–72.
193. McCluskey SA, Karkouti K, Wijeysundera D, et al. Hyperchloremia after noncardiac surgery is independently associated with increased morbidity and mortality: a propensity-matched cohort study. Anesth Analg 2013;117:412–21.
194. Shaw AD, Bagshaw SM, Goldstein SL, et al. Major complications, mortality, and resource utilization after open abdominal surgery: 0.9% saline compared to plasma-lyte. Ann Surg 2012;255:821–9.
195. Sinclair S, James S, Singer M. Intraoperative intravascular volume optimization and length of hospital stay after repair of proximal femoral fracture: randomized controlled trial. BMJ 1997;315:909–12.
196. Venn R, Steele A, Richardson P, et al. Randomized controlled trial to investigate influence of the fluid challenge on duration of hospital stay and perioperative morbidity in patients with hip fractures. Br J Anaesth 2002;88:65–71.
197. Noblett SE, Snowden CP, Shenton BK, et al. Randomized clinical trial assessing the effect of Doppler-optimized fluid management on outcome after elective colorectal resection. Br J Surg 2006;93:1069–76.
198. Gan TJ, Soppitt A, Maroof M, et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. Anesthesiology 2002;97:820–6.
199. Mythen MG, Webb AR. Intraoperative gut mucosal hypoperfusion is associated with increased post-operative complications and cost. Intensive Care Med 1994;20:99–104.
200. Walsh SR, Tang T, Bass S, et al. Doppler-guided intra-operative fluid management during major abdominal surgery: systematic review and meta- analysis. Int J Clin Pract 2008;62:466–70.
201. Akhtar S. Guidelines and perioperative care of the elderly. Int Anesthesiol Clin 2014;52:64–76.
202. Committee on Standard and Practice Parameters, Apfelbaum JJ, Connis RT, et al. Practice advisory for preanesthesia evaluation: an updated report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Anesthesiology 2012;116:522–38.
203. Benarrock-Gampel J, Sheffied KM, Duncan CB, et al. Preoperative laboratory testing in patients undergoing elective, low-risk ambulatory surgery. Ann Surg 2012;256:518–28.
204. Keay K, Lindsley K, Tielsch J, et al. Routine preoperative medical testing for cataract surgery. Cochrane Database Syst Rev 2012;(3):CD007293.
205. American Diabetes Association. Standards of medical care in diabetes – 2013. Diabetes Care 2013;36:S11–66.
206. Thomas DR, Ritchie DS. Preoperative assessment of older adults. J Am Geriatr Soc 1995;43:211–5.
207. Hosking MP, Warner MA, Lobdell CM, et al. Outcomes of surgery in patients 90 years of age and older. JAMA 1989;261:1909–15.

208. Keller SM, Markovitz LJ, Wilder JR, et al. Emergency and elective surgery in patients over age 70. Am Surg 1987;53:636–40.
209. Barlow AP, Zarifa Z, Shillito RG, et al. Surgery in a geriatric population. Ann R Coll Surg Engl 1989;71:110–4.
210. Rigberg D, Cole M, Hiyama D, et al. Surgery in the nineties. Am Surg 2000;66:813–6.
211. Warner MA, Hosking MP, Lobdell CM, et al. Surgical procedures among those greater than or equal to 90 years of age. A population-based study in Olmsted County, Minnesota, 1975–85. Ann Surg 1988;207:380–6.
212. Edwards AE, Seymour DG, McCarthy JM, et al. A 5-year survival study of general surgical patients aged 65 years and over. Anaesthesia 1996;51:3–10.
213. Keller SM, Markovitz LJ, Wilder JR, et al. Emergency surgery in patients aged over 70 years. Mt Sinai J Med 1987;54:25–8.
214. Dekker JW, van den Broek CB, Bastiaannet E, et al. Importance of the first postoperative year in the prognosis of elderly colorectal cancer patients. Ann Surg Oncol 2011;18:1533–9.
215. Monk TG, Weldon BC, Garvan CW, et al. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology 2008;108:18–30.
216. Lamont CT, Sampson S, Matthias R, et al. The outcome of hospitalization for acute illness in the elderly. J Am Geriatr Soc 1983;31:282–8.
217. Fitzgerald JF, Moore PS, Dittus RS. The care of elderly patients with hip fracture. Changes since implementation of the prospective payment system. N Engl J Med 1988;319:1392–7.
218. Kemper P, Murtaugh CM. Lifetime use of nursing home care. N Engl J Med 1991;324:595–600.
219. Sloane PD, Pickasrd CG. Custodial nursing home care. Setting realistic goals. J Am Geriatr Soc 1985;33:864–8.