

OBJECTIVES

1) Discuss preoperative preparation of the older patient for elective surgery; 2) Apply the results of recent evidence-based studies and meta-analyses to perioperative management, including the choice of neuromuscular blocking agents, regional versus general anesthesia, transfusion triggers, and inspired oxygen concentrations; 3) Discuss moderate and deep sedation; 4) Discuss postoperative issues, including analgesia, myocardial ischemia, and delirium; and 5) Present two anesthetic techniques that work well in older patients.

CASE PRESENTATION

INTRODUCTION

According to the Guinness Book of Records the oldest authenticated age for a woman is 112 years 164 days; for a man, 120 years 237 days. The oldest patient to undergo major surgery is a British woman who had her fractured right femoral shaft repaired when she was 113 yrs old. Pre-fall her medical history was significant for ankle edema and intermittent confusion. She initially received conservative care (rehydration, blood transfusion, traction, and analgesia) for 7 days, but the inability to alleviate pain led to the decision to operate on day 8. She experienced atrial fibrillation during induction with etomidate (8 mg), fentanyl (75 mg), and atracurium (35 mg) that responded to digoxin (250 mg). Anesthesia was maintained with isoflurane, nitrous oxide, and morphine (8 mg). The systolic pressure, monitored non-invasively, was maintained greater than 100 mm Hg. A CVP was placed but no arterial line or pulmonary artery catheter. She was extubated in the ICU 5 h after surgery, spent the night in intensive care, experienced two episodes of pulmonary edema that responded to diuretics while on the orthopedic ward, was discharged on postoperative day 23 wheelchair bound and confused but lived to celebrate her 114th birthday (1).

People are living longer and as they age they are more likely to require surgery. The life expectancy at birth in the United States in 1997 was 79.9 and 74.7 years for Caucasian and African-American women, respectively, and 74.3 and 67.2 years for the men. The annual rate of anesthetic administrations per 100 people in 1996 in France increased from 8.9 and 13.2 for men and women age 35 to 44 years of age, respectively, to 30.2 and 23.6 for men and women 75 to 84 years of age (2). Mortality and morbidity increase with advancing age with steep increases after age 75 years (3).

This presentation will present current information regarding: 1) preoperative testing; 2) beta-adrenergic blockade and perioperative myocardial infarction; 3) preoxygenation; 4) propofol-opioid-rocuronium inductions; 5) shorter versus longer-acting neuromuscular blocking agents; 6) brain versus end-tidal anesthetic concentrations during emergence; 7) regional versus general anesthesia; 8) sedation during spinal or epidural anesthesia; 9) minimum diastolic pressure; 10) transfusion trigger; 11) postoperative analgesia; and 12) postoperative delirium. The importance of timely antibiotic administration and maintaining normothermia (4) is assumed to be appreciated, accepted, and practiced.

PREOPERATIVE TESTING

For low risk surgery the overall perioperative complication rate is around 3 percent and “tests should be ordered only when the history or a finding on physical examination would have indicated the need for the test even if surgery had not been planned (5).” In a Medicare general and orthopedic surgery population (N = 194,430), 41 percent of patients experienced a complication (anesthesia, medical, or surgical) during their hospitalization (6). For intermediate risk surgery preoperative testing depends on the functional state of the patient (7). No noninvasive or invasive cardiac testing is indicated for patients with moderate

functional capacity (capable of 4 - 7 MET's) and intermediate clinical predictors (mild stable angina, prior MI, compensated CHF, prior CHF, diabetes mellitus) or for patients with poor functional capacity (1 - 4 MET's) with minor clinical predictors (advanced age, abnormal ECG, non-sinus rhythm, stroke history, poorly controlled blood pressure).

beta-ADRENERGIC BLOCKADE & PERIOPERATIVE MYOCARDIAL INFARCTION

Adding beta-blockers to patients not already receiving them reduces the risk of perioperative myocardial ischemia and infarction in high-risk (3 or greater cardiac risk index criteria) and intermediate-risk patients (any two minor criteria or 1-2 cardiac risk index criteria) (8). The target for the therapy is usually a heart rate between 55 and 65 beats per minute and systolic blood pressure greater than 100 mm Hg. The minor clinical criteria are 65 years of age or older, hypertension, current smoker, elevated serum cholesterol, and non-insulin dependent diabetes mellitus. Most elderly patients have at least 2 minor criteria. The cardiac risk index criteria include high risk surgery (intraperitoneal, intrathoracic, and suprainguinal vascular), ischemic heart disease, cerebrovascular disease, insulin-dependent diabetes mellitus, and chronic renal insufficiency (baseline creatinine at least 2.0 mg/dL).

Data suggest withholding beta-blockers in patients taking them chronically increases the risk of perioperative ischemia. The data is unclear in the following situations: 1) increasing dose of beta-blockers in patients who take beta-blockers chronically and already are at targeted heart rate, 2) aortic stenosis, 3) patients with CHF, 4) during regional anesthesia, 5) non-selective versus beta-1 selective, and 6) low risk patients.

Although many anesthesiologists administer esmolol as a bolus so that long-acting beta-blockade is not established as it would be with atenolol, metoprolol, or labetalol, no study has been performed to demonstrate that this practice is comparable. Data from Raby (9) may loosely be interpreted as supportive if heart rate is kept 20 percent below the ischemic threshold determined preoperatively for each patient from Holter monitoring (10).

Most perioperative myocardial infarctions occur on the day of surgery (11,12). Zaugg observed a trend toward lower intraoperative cardiac troponin I release in the atenolol groups, but the groups were not large enough for the differences to achieve statistical significance. They demonstrated that patients receiving atenolol showed improved hemodynamic stability during emergence and in the postoperative period. Interestingly the beta-blockade did not reduce the neuroendocrine stress response to surgery but did appear to reduce postoperative analgesic requirements and allow for faster recovery from anesthesia (13).

PREOXYGENATION

Although four deep breaths of 100 percent oxygen within 30 seconds is an acceptable technique to preoxygenate healthy younger patients, it is not as satisfactory in elderly patients. Maximal preoxygenation is needed in elderly patients for at least three reasons. First, desaturation occurs faster in older patients than in younger adults for any given oxygenation technique. Second, the time to peak relaxation from succinylcholine or non-depolarizing neuromuscular blocking agents is delayed with increasing age during a rapid sequence induction (14). Third, the elderly are more likely to suffer a cardiac event from desaturation. Maximal preoxygenation, as described Benumof, is achieved not only when the alveolar and arterial compartments are filled with oxygen but also the tissue and venous compartments (15). Practically, the longest time before desaturation is more important than the highest

PaO₂. A technique that seems to provide maximal oxygenation in the shortest period of time requires eight deep breaths of 100 percent oxygen within 60 seconds with an oxygen flow of 10 L/min (16).

PROPOFOL, OPIOID, ROCURONIUM INDUCTIONS

When anesthesia is induced with propofol 2 mg/kg (1 mg/kg if over 65 yrs of age) bolus intravenously (13-24 s) to healthy volunteers ranging in age from 25 to 81 years, two interesting observations were made (17): 1) the time to loss of consciousness was essentially independent of age and equal to approximately 40 s; and 2) the time to return of consciousness increased from 6 min at age 30 years to 10 min at age 75 years.

When target-controlled infusions of propofol were used to attain and maintain selected plasma concentrations in patients ranging in age from 20 to 84 years, two observations were made (18): 1) the half-times for the plasma-effect-site equilibration for the EEG Bispectral Index were independent of age; and 2) the half-times for the nadir in systolic blood pressure increased with age from 5.7 min in patients 20-29 years to 10.2 min in patients 70-85 years, i.e., considerably longer than their loss of consciousness times.

When the hemodynamic effects of propofol inductions (0.5 mg/kg plus 10 mg/s until loss of verbal contact) were studied in patients over the age of 65 years who had received glycopyrrolate and either remifentanyl (0.5 ug/kg bolus and 0.1 ug/kg/min infusion) or alfentanil (10 ug/kg), the following observations were made (19): 1) a total propofol dose of approximately 1 mg/kg was sufficient; and 2) systolic blood pressure below 100 mm Hg measured non-invasively was observed at 3 min in 50% and below 80 mm Hg in 8%.

Remifentanyl simulations based on an EEG model suggest that age is an important variable in calculating bolus doses (elderly one-half that of young) and infusion rates (elderly one-third of young) (20,21). For propofol at any given infusion rate the resulting plasma concentrations are higher in older patients than in younger ones. To achieve the same target level, the infusion rates must be lower older patients. When the propofol infusion is discontinued, the plasma concentrations of propofol fall faster in older patients than in younger ones (22,23). The lowest dose of propofol required to achieve loss of consciousness with the least hemodynamic effect requires infusion over 2 minutes (24,25). Faster injection increases peak arterial concentration, but the arterial peak is too transient to permit maximum loading of the brain because of the relatively long blood:brain equilibration time for propofol (compared to thiopental). For injections slower than 2 minutes drug lost to redistribution limit the brain concentrations to less than those seen with 2-minute injections. Hemodynamic side effects correlate better with arterial concentrations than with brain concentrations. Time to loss of consciousness does not seem to shorten with higher dose, but the duration of hypotension lengthens.

When propofol induction 0.6 mg/kg in elderly ambulatory patients receiving 50 percent nitrous oxide was compared with "single breath" 8 percent sevoflurane in 50 percent nitrous oxide or relatively rapid incremental sevoflurane in 50 percent nitrous oxide, mean arterial pressure fell by 30 percent in the propofol group and 20 percent in the sevoflurane groups and the heart rate was approximately 10 beats per minute faster in the sevoflurane group. The onset times for propofol and 8 percent sevoflurane were the same but incremental sevoflurane was about 30 s slower (26).

I draw the following conclusions from these studies: 1) elderly require less propofol for induction; 2) concurrent administration of midazolam, ketamine, and/or opioids with propofol synergistically increase

anesthetic depth so that dose reductions for propofol are indicated; 3) even with reduced dose of propofol, hypotension frequently occurs; 4) the nadir for hypotension occurs minutes after loss of consciousness from propofol (The stimulus of intubation tends to offset this hypotension if no other drugs are given. But with LMAs, hypotension can be a problem because their insertion produces less stimulation than insertion of an endotracheal tube.); 5) the peak effects of midazolam administered preinduction occur at 5 min , fentanyl 6-8 min, and propofol 10 min so that severe hypotension can occur after intubation and before surgical stimulus unless doses are adjusted downward, e.g., 1.0-1.5 mg/kg without opioids, 0.5-1.0 mg/kg with opioids, especially if small doses of midazolam and/or ketamine are given; 6) less hypotension is seen with mask sevoflurane inductions than intravenous propofol inductions.

SHORTER VERSUS LONGER ACTING NEUROMUSCULAR BLOCKING AGENTS

Evidence is accumulating that long-acting neuromuscular blocking agents are associated with longer PACU stays (27) and an increased incidence of postoperative pulmonary complications, such as atelectasis and pneumonia (28). The likelihood of postoperative pulmonary complications with long acting muscle relaxants increased with advanced age, with increased duration of surgery, with decreased body temperature, and with the increased density of neuromuscular blockade that is required for laparotomies compared with orthopedic procedures. There is also evidence to suggest that a sizable percentage of patients who satisfy rigorous extubation criteria in the operating room after reversal of their neuromuscular blockade deteriorate in the PACU (28,29). I recommend that short-to-intermediate acting muscle relaxants be used in all elderly patients for whom extubation is planned at the end of the surgical procedure. During fast-track recovery of the cardiac surgical patient, longer weaning times and more patient complaints of weakness after extubation are seen in the pancuronium group than in the rocuronium one (30).

BRAIN VERSUS END-TIDAL ANESTHETIC CONCENTRATION DURING EMERGENCE

End-tidal gas monitoring significantly underestimates brain concentration of inhaled agents during emergence (31). This hysteresis effect is more dramatic with a more soluble agent, such as isoflurane, than with a less soluble agent, such as desflurane. Failure to take this effect into account leads to prolonged emergence times. Patients are amnesic for a variable period of time in the recovery room after inhalational anesthesia with isoflurane and sevoflurane. The rate at which the brain concentration ratio approaches zero is indicated in the table below and compared with the rate at which the alveolar concentration ratio decreases. Because of this hysteresis effect MACawake determined when the vaporizer is immediately turned off is lower than MACawake determined when the vaporizer is turned down in small stepwise decrements every 10 to 15 minutes before off is reached, e.g., 0.34 MAC versus 0.22 MAC for isoflurane and sevoflurane (32). The most common reason clinically why anesthesiologists are reluctant to turn down the anesthetic agent toward the end of surgery is that the older patient tends to become hypertensive and this hypertension is interpreted as light anesthesia. Emergence is then prolonged with inhaled agents other than desflurane. The administration of beta-blockers, such as labetalol or metoprolol, as inhalational agents are being withdrawn helps avoid this problem and promotes hemodynamic stability during emergence, extubation, and recovery.

Comparison of cerebral and alveolar elimination for isoflurane [Modified from (31)]

Concentration Ratio

Time (min)	Cerebral	Alveolar
0-6	0.686	0.242
6-12	0.337	0.102
12-18	0.236	0.072
18-24	0.136	0.056
24-30	0.101	0.047
90-120	0.048	0.017

REGIONAL VERSUS GENERAL ANESTHESIA

Regional anesthesia and analgesia completely blocks the stress response associated with surgery, if normothermia and nutrition are maintained perioperatively. Carli compared two anesthetic techniques in patients who were undergoing elective colorectal surgery - combined epidural-general anesthesia with postoperative epidural analgesia and general anesthesia and parenteral analgesia (33). They used an increase in muscle protein degradation and a decrease in muscle protein synthesis as their markers for surgical stress. Their patients were continuously nourished and kept normothermic for 48 hours. In the continuous epidural anesthesia and analgesia group, there was no change in the rates of muscle protein degradation and synthesis in the perioperative period. In the general anesthesia with traditional analgesia group, the typical changes in protein metabolism were observed.

Regional anesthesia also prevents central sensitization, or spinal cord “wind-up,” and in doing so may provide preemptive analgesia, i.e., analgesic requirements are diminished postoperatively if regional anesthesia is established before surgical incision is made. Both Shir and Gottschalk have demonstrated this phenomenon in patients undergoing radical prostatectomy (34,35). Shir divided patients into 3 groups, epidural-only anesthesia, combined epidural-general anesthesia, and general anesthesia. The epidural-only group received significantly more local anesthesia via the epidural than the combined epidural-general group. In all patients postoperative analgesia was provided with epidural patient-controlled analgesia (PCA). The epidural PCA demand was significantly less in the epidural-only group compared with both general anesthesia groups. Gottschalk divided his patients into 3 intraoperative groups, epidural local anesthetic, epidural opioid, and no epidural medication. All patients received a general anesthetic and all patients received epidural PCA for postoperative analgesia. Significantly less epidural PCA was required in the epidural local anesthetic group versus the control group than in the epidural fentanyl group versus control group. Overall the preemptive analgesia groups experienced 33 percent less pain while hospitalized. At nine and one-half weeks 86 percent of the preemptive analgesia groups were pain-free and more active as compared with 47 percent in the control group. If less pain medication is required, then side effects of opioid medications may be reduced, such as respiratory depression, ileus, and urinary retention.

Despite these theoretical advantages for regional anesthesia, tightly controlled studies comparing regional and general anesthesia using mortality and morbidity as endpoints do not reflect this (36). But in studies designed to reflect typical clinical practice, regional anesthesia wins out (37,38). This may be as much a criticism of typical clinical practice as it is a plus for regional anesthesia. Certainly in studies comparing regional and general anesthesia, more effort and interventions tend to be required to produce equivalent outcomes.

SEDATION DURING SPINAL AND EPIDURAL ANESTHESIA

Spinal anesthesia without sedation produces an EEG effect associated with sedation (39). T2 epidural anesthesia reduces MAC and MACawake by as much as 50 percent (40,41). Lower levels of inhalational agents during combined epidural-general anesthesia are required for endotracheal tube tolerance and to prevent intraoperative awareness as compared to general anesthesia without a functioning epidural. Emergence is prolonged if the same alveolar concentration of inhalational agent is maintained during combined epidural-general anesthesia as during general anesthesia without an epidural.

The ED50 for loss of consciousness for intravenous midazolam was 75 percent less during T8 spinal bupivacaine anesthesia (42) and 80 percent less during T8 epidural bupivacaine anesthesia when compared to monitored anesthesia care (43). When midazolam is administered at a rate of 1 mg every 30 seconds to healthy women about to undergo gynecologic procedures, the women in the spinal group required only 7.6 mg to achieve loss of consciousness versus 14.7 mg in the monitored anesthesia care group (44). If morphine were added to the spinal and propofol substituted for midazolam and infused at a rate of 20 mg per kg per hour, loss of consciousness was achieved sooner (4.7 vs 6.0 min) in the spinal group (45). In a relevant rat study, spinal bupivacaine reduced the dose of intraperitoneal thiopental associated with blocking the corneal reflex by one-third. The brain concentration of thiopental in the bupivacaine spinal group associated with an absent corneal reflex was also one-third the concentration in the saline spinal group (46). Thus both spinal and epidural anesthesia dramatically reduce sedative requirements for midazolam and propofol.

This question has also been indirectly addressed in several other studies. The BIS50 is the BIS index below which 50 percent of patients experience loss of consciousness. When the BIS50 for midazolam was determined in healthy volunteers in one study of monitored anesthesia care (47) and compared to the BIS50 determined during spinal or epidural anesthesia (48), it was higher in the regional anesthesia study (79 vs. 70). Thus the BIS50 for loss of consciousness is not a constant. Regional anesthesia attenuates sensory input to the brain and shifts the BIS50 to a higher index. A higher BIS50 and a lower midazolam dose are associated with loss of consciousness during spinal or epidural anesthesia than during monitored anesthesia care. Similarly, 0.5 mg of midazolam was predictably associated with apnea in elderly patients during spinal anesthesia in one study (49) but in another produced only mild sedation in 16 of 29 patients (and no apparent sedation in 13/29) at 7 minutes during monitored anesthesia care (50). However, at 15 minutes during monitored anesthesia care, 3/29 became moderately sedated and 1/29 deeply sedated after 0.5 mg.

Spinal or epidural anesthesia reduces sedative requirements, presumably by decreasing afferent input to the brain. This observation may be the new mechanism Keats (51) was looking for to explain the cardiac arrests during spinal anesthesia reported in the closed claims study (52), especially in view of the effects of sedatives and opioids on hypoxic control of cardiorespiratory responses.

DIASTOLIC PRESSURE

Evidence is accumulating that maintaining diastolic pressure within ten percent of baseline and certainly above 60 mm Hg is important in elderly patients. 10% baseline (53-55).

TRANSFUSION TRIGGER

The transfusion trigger in elderly patients is a hematocrit below 30 percent (56)

POSTOPERATIVE ANALGESIA

There was no difference in the incidence of adverse events in patients over 70 years of age versus under 70 from intravenous morphine 2 mg q 5 min to achieve postoperative analgesia (57). Patient-controlled analgesia is effective in elderly surgical patients (58).

POSTOPERATIVE DELIRIUM

Postoperative delirium is a common problem in elderly patients that can be reduced by protocol-driven postoperative treatment (59). Long-term postoperative cognitive dysfunction remains a significant problem in the elderly (60).

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