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In Children and Elderly Patients, What are the Effects of General Anesthesia on Neurological Health Compared with Procedural Sedation?

Taylor G. Caldwell
Columbus State University, caldwell_taylor@columbusstate.edu

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by

Taylor Caldwell

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Thesis Advisor Sally Richter MSN RN Date 4/14/14
Mrs. Sally Richter

Committee Member Dr. Dell Miller Date 4/14/14
Dr. Dell Miller

Honors Committee Member Dr. Monica Frazier Date 4/14/14
Dr. Monica Frazier

Honors Program Director Dr. Cindy Ticknor Date 4/14/14
Dr. Cindy Ticknor

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Introduction

Anesthesia has been a necessity in the field of health care since it was discovered in the early to middle 1800s. Before anesthesia, many procedures and surgeries that are now considered an easy fix were life-threatening and patients often chose the inevitable death over the pain of surgery. The idea was stumbled upon when "laughing gas," nitrous oxide, was inhaled and credited in "produc[ing] a state of intoxication during which people became highly amused and insensitive to pain" (Palo Alto, 2013, para. 2). Anesthesia has come an unbelievably long way since the first surgery under anesthesia was performed by Dr. Crawford Long in Jefferson, Georgia in 1842 (Long, 1849). The industry boomed after World War II and recently in the past 20 years. As technology continues to advance, research on ways to prevent the common side effects of nausea and vomiting and the complications of respiratory collapse have been well controlled with the introduction of the laryngeal mask (Mayo Clinic, 2013). A recent concern for at risk populations, such as children and the elderly, has stirred a great deal of research on the effects anesthetics may have on the cognitive function and long term health of children and individuals over 65 years of age. This paper will summarize the most recent research conducted comparing the best practices for anesthesia in these two populations. It will compare general anesthesia to intravenous procedural sedation and their effects on the cognitive function and long term health and wellbeing of elderly and pediatric patients.

General Anesthesia versus Procedural Sedation

General anesthesia is a controlled and reversible state of unconsciousness with amnesia, muscle paralysis, sedative, and analgesic features. It can be administered via inhalation or intravenously with rapid onset. General anesthesia can be manipulated easily throughout surgery and can keep a patient unconscious for prolonged periods of time (Johns Hopkins, n. d.). Airway patency and respiration is easily controlled without manipulation of the patient's current position. Recent advances have decreased risks usually associated with general anesthesia such as nausea, vomiting, sore throat from intubation, and incisional pain. However, downfalls to general anesthesia include cost, patient compliance to a fasting regimen up to 6 hours before scheduled surgery, and continuous supervision by an anesthesiologist or certified registered nurse anesthetist in case of complications during procedure (Press, 2013).

The process of getting a patient under general anesthesia has three phases: premedication, induction, and maintenance (Press, 2013). The premedication phase eases or relaxes the patients as they transition from the preoperative unit to the operating room. One of the more commonly used agents to promote relaxation before a procedure is midazolam (Versed) which is a benzodiazepine. Midazolam, like other benzodiazepines, enhances the inhibitory activity of gamma-aminobutyric acid (GABA) causing calmness and respiratory depression with a duration of 30 to 60 minutes and a 3 hour half-life (Kee, Hayes, & McCuistion, 2012). Following premedication is induction. Induction medications for the second phase of general anesthesia are only administered once the mnemonic DAMMIS has been confirmed: Drugs, Airway equipment, Machine, Monitors, IV, and Suction (Press, 2013). As stated earlier, these drugs can either be inhaled or injected through an intravenous line. Propofol is the primary induction agent used with an action onset of 30 to 45 seconds and a half-life of 3 to 8 hours (Kee, Hayes, &

McCuistion, 2012). The most common side effects of propofol are nausea, vomiting, and involuntary muscle movements. After propofol administration, an opioid such as fentanyl is provided as an analgesic. Fentanyl and propofol work together to achieve a comfortable, unconscious state with stabilization of the heart rate and blood pressure that usually rises upon intubation and incision (Press, 2013). Other opioids may include morphine, meperidine, hydromorphone, sufentanil, and remifentanil. Securing the airway in general anesthesia is one of the most important steps due to respiratory depression caused by propofol. This can be achieved by manipulation of the jaw or by use of an artificial airway device such as a laryngeal mask or an endotracheal tube (Press, 2013). The third phase of general anesthesia is the maintenance phase and thus begins when the initial anesthesia begins to wear off. Traditionally, the amount of anesthesia needed to maintain the correct depth was a clinical decision but recent technology has developed new electroencephalogram machines, known as the bispectral index (BIS monitoring), that tell the providers the current anesthetic depth of the patient in real time (Press, 2013). Muscle relaxants, such as succinylcholine, may also be administered for maintenance if a patient experiences twitching or jerks of different muscle groups.

There is a difference between general anesthesia and procedural sedation. This difference is in the patient's level of consciousness. The goal of procedural sedation, according to Brown, Lovato, and Parker (2005), is to produce a level of consciousness that is adequate to allow surgical or therapeutic procedures in a way that reduces patient awareness, discomfort, and memory, while preserving spontaneous respiration. Procedural sedation often includes the use of a benzodiazepine and an opioid analgesic, such as midazolam and fentanyl as discussed previously. Although combining the opiate and benzodiazepine does cause an increased risk for

cardiac and respiratory complications, it is the preferred method for longer procedures under intravenous sedation because it ensures pain control and an adequate level of relaxation.

Lorazepam (Ativan) is a benzodiazepine that is often used for mild to moderate sedation but has a longer time of onset (15 to 20 minutes) than midazolam. It is often used in the intensive care units for long-term sedation due to its increased duration of 6 to 8 hours (Brown, Lovato, & Parker, 2005). For many procedures, sedation alone is not enough and an analgesic is necessary. Unlike general anesthesia, morphine is rarely used in procedural sedation due to its respiratory depressive effects. Therefore, fentanyl is the drug of choice for most anesthesia providers because of the ability it has to suppress the cough reflex and provide analgesics with minimal side effects. Fentanyl binds with receptors at many sites within the central nervous system thereby increasing the pain threshold and altering pain reception (Orlewicz, 2013). An alternative to fentanyl is ketamine. Ketamine is a drug that has been involved in many studies performed in the past few years and has been shown to have no affects on the pharyngeal-laryngeal reflexes. Because of this, it is often used in emergency situations when the last dietary consumption is unknown. It also allows for a patent airway and spontaneous respirations unless administered in doses above the recommended amount or too quickly. Common side effects in recent studies show confusion and agitation upon awakening known as emergence delirium in 10% to 20% of adults (Orlewicz, 2013). This phenomenon can be decreased if sedation is administered with a benzodiazepine such as midazolam and more research is being done on a ketamine-propofol mixture to be used for sedation. Etomidate is a nonbarbituate and is another alternative in achieving sufficient sedation levels. Etomidate has no pain-relieving properties but produces a hypnotic state for the client. Its cardiovascular effects are very minimal and adverse

reactions are rare (Brown, Lovato, & Parker, 2005). For a general overview of general anesthesia and the three types of procedural sedation see Table 1 for clarification.

General Anesthesia and the Elderly

As research unfolds about the possible causes of Alzheimer's disease and dementia, being "put under" is thought to have contributed to an increased risk for developing permanent memory loss or postoperative cognitive decline (POCD). Alzheimer's disease is characterized by specific lesions in the brain. Current research with rodents exposed to the general anesthetics in Table 1 has shown the same development of these lesions characteristic of Alzheimer's disease in their brains (Sprung et al., 2013). Previous human subject research on Alzheimer's has had many limitations as it has been unable to form generalizations for larger populations. Dr. Juraj Sprung et al. (2013) sought to develop a case-control study to test the relationship between dementia and anesthetic agents without the limitations and issues faced in previous works. Using the Rochester Epidemiology Project and the Mayo Clinic Alzheimer's Disease Patient Registry, he and his colleagues were able to access Olmstead County, Minnesota residents' medical records and all cases of dementia in Olmstead County from 1985 to 1994. With this information, Sprung (2013) and colleagues were able to find age- and sex-matched cohorts for his control group. The control groups were dementia-free residents of Rochester, Minnesota with no cognitive impairments (Sprung et al., 2013). The criterion for the experimental group was as follows: 45 years of age or older residents of Rochester, Minnesota, diagnosed with dementia between January 1, 1985 and December 31, 1994, while residing in Rochester, Minnesota at the time of onset and for 1 year preceding onset. Subjects meeting the criteria were evaluated by behavioral neurologists who used the Diagnostic and Statistical

Manual of Mental Disorders (Fourth Edition) to confirm and classify the type of dementia present in the individual (Sprung et al., 2013).

Due to the nature of this particular study, there were no interventions required and participation involved no risk or benefit for the selected participants. In order to review each participant's anesthetic history, the randomly selected participant's medical records were reviewed and exposures to general anesthesia from birth were recorded. The information recorded included the type of anesthesia administered and how it was maintained, the type of surgical procedure, and the amount of time under anesthesia. The researchers took into consideration the educational level of each individual as previous studies have related level of education to incidence of Alzheimer's diagnosis (Sprung et al., 2013). Nine hundred eight experimental group participants and 908 control group participants were selected for participation in this study (Sprung et al., 2013). Fifty six participants denied authorization for use of their medical records and three individuals in the experimental group were younger than age 45 at the time of dementia onset, giving a 96.6% completion rate (Sprung et al., 2013). For a comparison of demographic characteristics of the experimental and control groups, see Table 2. Clinically, the experimental group date of first medical entry age average was 31, while the control age average was 32; the median length of the medical record after age 45 was 34.3 years for the experimental group and 34.4 for the control group. Of those in the control group, 72 individuals developed dementia before 1994 so they were moved to the experimental group (Sprung et al., 2013).

An initial p value was set at $p \leq .05$ to determine if the results were statistically significant. An odds ratio (OR) was determined with each anesthetic agent and number of exposures that could cause dementia, and a 95% confidence interval (CI) to determine the

precision of the results (Sprung et al., 2013). A summary of these results are shown in Table 3. The association linking dementia to general anesthesia showed no statistical significance (OR 0.89, CI 95% between 0.73-1.10, p=.27) (Sprung et al., 2013). Sprung et al. (2013) stated that "no association was found when anesthetic was quantified as the number of procedures (ORs, 0.87, 0.86, and 1.0 for 1, 2-3, and ≥4 exposures, respectively, compared with no exposure as the reference; p =.51)" (p. 556). This is also true for when total cumulative time under anesthesia was assessed as an ongoing variable (OR, 1.00; 95% CI, 0.99-1.01 per 30-minute increase; p =.86) (Sprung et al., 2013). Those individuals that were moved from the control group to the experimental group did not have a significant effect on the results (Sprung et al. 2013). In the experimental and control groups, 93% of all procedures were induced with sodium thiopental and maintained with nitrous oxide (90%) (Sprung et al., 2013). A list of the specific agents and the corresponding odds ratios, confidence intervals, and p values can be seen in Table 4. With the given results, this study has shown that the correlation between dementia or postoperative cognitive decline and general anesthetic agents is not statistically significant (Sprung et al., 2013). Even when compared to only those cases with Alzheimer's disease, no statistical significance is present (OR 0.88, 95% CI between 0.71-1.1, p=.28) (Sprung et al., 2013).

Many of the factors that contributed to the dismissal of previous studies on the topic were improved upon but this study had a few negative features. Sprung et al. (2013) states that "several challenges in studying this area [include] lack of diagnostic criteria for POCD; separation of any independent effects of anesthesia from those of illness, surgical stress, and aging; the potential role of preexisting cognitive impairment" (p. 557). During the years of 1985 to 1994, most of the residents of Olmstead County were Caucasian, which detest the generalization of this study as it applies to the overall United States population (Sprung et al.,

2013). This evidence shows that general anesthesia does not have a statistically significant effect on elderly Caucasian populations.

General Anesthesia and Children

Learning disabilities can cause major setbacks in children by limiting their ability to listen, think, speak, read, write, spell, or do mathematical equations. Minimal studies have been done on children who are not seriously ill due to extensive research on critically-ill neonates and congenital heart disease repairs, causing a lack in the ability to be applied in many clinical settings. Dr. Robert Wilder and his colleagues (2009) set out to determine whether or not learning disabilities can result from exposure to anesthesia and surgery in the first few years of life. The basic psychological processes of being able to listen, think, speak, read, write, spell, and do mathematical equations are the core of Wilder's main study outcome and are applicable to a large variety of clinical settings.

The Mayo Clinic and Olmstead Medical Center Institutional Review Boards approved this population-based, birth cohort study within Rochester, Minnesota (Wilder et al., 2009). Criteria to be within this study included: born to mothers residing in Rochester between January 1, 1976 and December 31, 1982 within the Minnesota Independent School District No. 535, the Rochester public school system, still residing in Rochester by the age of five (any children who moved or died were excluded from this study), and had exposure to general anesthesia prior to their fourth birthday (Wilder et al., 2009). Dr. Wilder (2009) was able to determine that the number of children born between the set years that still resided in the area totaled at 5,718 and this study includes 5,357, therefore 93.6% of the available candidates completed this study. The children were identified by examining computerized birth certificate information made available to the researchers by the Minnesota Department of Health, Division of Vital Statistics (Wilder et

al., 2009). The Rochester Epidemiology Project allowed Wilder and his collaborator's access to the children's vital status and all recorded procedures at any Rochester medical facilities including outpatient clinics and emergency departments. This allowed for quick retrieval of history of all hospital visits, community and ambulatory medical and social services, and home visits as long as the parents were still living in the area (Wilder et al., 2009). Laboratory and psychological test results were also made available to Dr. Wilder by the Rochester Epidemiology Project. The Reading Center/Dyslexia Institute in Minnesota also allowed the researchers access to records having evaluation and outcomes of tutorial instruction, IQ and achievement tests, and socioeconomic information within their text (Wilder et al., 2009). A summary of these characteristics can be found in Table 5. All public and nonpublic schools (51 total) gave permission to Wilder and his colleagues to access educational records for the children involved in the study. Information was obtained during the 1995-1996 school year making the children between the ages of 13 and 19 (Wilder et al., 2009). The discrepancy nonregression method and the low achievement method were used in determining whether a learning disability was present regardless of comorbid conditions. And, in the multivariate analysis using the SAS statistical software (Version 9.1; SAS institute, Inc., Cary, NC), factors such as birth weight, gestational age at birth, and gender were used (Wilder et al., 2009). Those that had undergone general anesthesia before their fourth birthday totaled at 593; these individuals tended to have a lower birth weight, younger gestational age at birth, and were more likely to be male ($p<.0001$) (Wilder et al., 2009). Clinically, Wilder et al. discovered that APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) scores and peripartum complications were similar for each group (those exposed to general anesthesia and those that were not). Those that had been exposed had

a slightly higher occurrence of maternal postpartum hemorrhage and prolonged labor (Wilder et al., 2009).

The anesthetic characteristics were categorized by number of exposures to general anesthesia (none, 1, 2, and 3 or more) and cumulative duration of exposure (Wilder et al., 2009). A summary of these results can be seen in Table 6, the anesthetics used in Table 7, and types of surgeries performed in Table 8. Wilder and his colleagues (2009) deemed the results statistically significant at a p value of <.05 and a 95% confidence interval. The risk of developing a learning disability increased with the number of exposures (p<.001) but it did not increase for the 75.7% of children who only had a single exposure before age 4 (95% CI for 0.79 to 1.27) as seen in Table 9 (Wilder, 2009). By age 19, 20% of patients with no exposure were diagnosed with a learning disability (95% CI 18.8% to 21.3%), 20.4% of patients with single exposure (95% CI 16.3% to 24.3%), and 35.1% of those with multiple exposures (95% CI 26.2% to 42.9%) (Wilder et al., 2009). In addition to these analysis, Wilder et al. (2009) performed adjusted and unadjusted analysis for sex, birth weight, and gestational age at birth. Through the adjusted analysis, Wilder et al. found that a longer duration of cumulative exposure is statistically significant in causing a learning disability when view as a continuous exposure (p=.016) or categorical exposure (p=.027). A higher American Society of Anesthesiologists physical status (ASA PS) score was seen in those patients with multiple anesthetic exposures when compared with those with only a single exposure (Wilder et al., 2009); a visual of this can be seen in Figure 1. Many anesthesia providers would agree that a higher ASA PS score mean more severe comorbidities, therefore a higher likelihood of needing surgical interventions over a low ASA PS child (Wilder et al., 2009).

Although this research is detailed and can be applied to many clinical settings, it is still unknown whether or not anesthesia predetermines neurology deficits in humans. In the rodents, the stages of neurodevelopment are controversially different than those of humans and some scientists argue that the neurodevelopment peaks approximately 1 to 2 days before birth until 2 weeks after birth for rodents (Wilder et al., 2009). Because of this, Wilder and his cohorts repeated the study with a stricter age range of 2 years instead of 4 years of age and achieved similar results. The lack of the number of infants caused the researchers to not restrict the age range further. A few limitations in this study include Rochester being a mostly white, middle class community as discussed in the previous study involving the elderly (Wilder et al., 2009). Also, children that resided in Rochester may have stayed due to the quality of healthcare available to its residents, therefore over-representing those with higher medical needs. Due to a lack of research on ketamine, many children have not been exposed to the drug, further limiting generalization of the results to all anesthetic agents (Wilder et al., 2009). Overall, the research presented within this article shows that multiple exposures to general anesthesia prior to a child's fourth birthday increases the likelihood of a learning disability.

Procedural Sedation and the Elderly

Postoperative delirium is often a side effect of sedation in elderly clients (Barclay & Nghiem, 2012). This may lead to a postsurgical recovery in an assisted living facility as opposed to the patient's home or a longer stay in the hospital. Postoperative delirium occurs in about 10% to 37% of patients over the age of 65 and as much as 62% in patient's after a hip fracture repair (Sieber et al., 2010). Hip fractures in the elderly populations are usually the result of a fall and Ilse Truter (2011) states that for patients over the age of 65 being admitted to the hospital, their admission is due to a fall 80% of the time. The Johns Hopkins Medical Institute approved a

study conducted by Frederick Sieber and his colleagues to determine the effects of light versus deep sedation via intravenous propofol on postoperative delirium in hip fracture patients over the age of 65. The goal of this study was to determine which depth of sedation decreases the prevalence of postoperative confusion in the patients within this criterion. According to Sieber and his collaborators, of the many risks factors associated with postoperative delirium, anesthetic technique is one of the only modifiable risks. Sieber also notes that use of perioperative opioids such as morphine is a modifiable risk factor but is difficult to avoid in patients within this study due to the magnitude of the surgery the patients are undergoing. Nonmodifiable risks for these patients include age, preoperative dementia, comorbidities, ability to function and complete activities of daily living, and medications currently taken day-to-day (Sieber et al., 2010).

This randomized controlled trial was a double blind study conducted from April 2, 2005 through October 30, 2008 and had 114 patients. Sieber et al. (2010) selected individuals using a randomized block design with random length blocks to determine which would receive light sedation (a Bispectral index of ≥ 80) and which would receive deep sedation (a Bispectral index of approximately 50). The block factors that were incorporated into the randomization were based on age (65 to 80 years or >80 years) and cognition impairment (Mini-Mental State Examination score of 15 to 23 or 24 to 30) (Sieber et al., 2010). The patients in the light sedation and deep sedation groups were similar demographically as shown in Table 10. Clinical characteristics included admission to the Johns Hopkins Bayview Medical Center's multidisciplinary hip fracture service, over the age of 65, and having spinal anesthesia and propofol sedation during the hip fracture repair procedure (Sieber et al., 2010). The tools to determine the level of cognition and functionality included the Mini-Mental State Examination, Confusion Assessment Method, and the Diagnostic and Statistical Manual of Mental Disorders

(Third Edition Revised). As seen in Figure 2, 100% of the participants completed the study and no participant was moved from the light sedation group to the deep sedation group or vise versa. The surgical interventions for each group were similar. As the patient arrived for surgery spinal anesthesia was given with the patient's affected hip dependent lying in the lateral position. A propofol bolus or midazolam bolus was initially given with optional fentanyl. Once the sedative began, supplemental oxygen via non-rebreathing mask was provided and BIS monitoring was initiated. During the surgery, blood pressure, pulse oximetry, 5-lead electrocardiography, and end-tidal carbon dioxide measurements were recorded (Sieber et al., 2010). Intraoperative data between the two study groups can be seen in Table 11. Pain medication was standardized for both study groups, initially using intravenous hydromorphone then using a patient controlled infusion or nursing staff administration of morphine sulfate once in recovery on postoperative day 0 (Sieber et al., 2010). Once the ability to swallow returned (typically around postoperative day 1 or 2), oral analgesics, such as oxycodone and acetaminophen, were given by Sieber and his cohorts. The Cognitive Assessment Method and the Mini-Mental State Examination were used on the second postoperative day to determine if confusion was present and from the third postoperative until discharge, only the Cognitive Assessment Method was used (Sieber et al., 2010). All delirium assessments were done to the patients around 10 a.m. by a trained research nurse who was blinded to which study groups the patients belonged (Sieber et al., 2010).

The authors of this study set a p value of $<.05$. Sieber and colleagues determined that those patients undergoing deep sedation experienced a higher prevalence (40% for deep sedation compared to 19% of those lightly sedated) and longer average duration (1.4± 4.0 days for deep sedation compared with 0.5± 1.5 days for light sedation) of postoperative dementia than those undergoing light sedation (p=.02 and p=.01 respectively). However, the number of days

delirium occurred for those individuals who experienced delirium was not statistically significant between both groups (p=.77) (Sieber et al., 2010). Postoperative delirium was experienced in 14 of the 32 deep sedation patients and in 5 of the 35 light sedation patients that had minimal cognitive impairment (Mini-Mental State Examination score of ≥20) (p=.01). Postoperative delirium was experienced in 11 of the 28 deep sedation patients and in 3 of the 27 light sedation patients that had no cognitive impairment (Mini-Mental State Examination score of ≥24) (p=.03) (Sieber et al., 2010). For those with minimal or no cognitive impairment, as discussed previously, 1 out of every 3.5 patients would not experience postoperative delirium (Sieber et al., 2010). More of the results, including different variation factors can be seen in Table 12.

When determining which clients were eligible to be enrolled in this study, many contraindications were applied that could downgrade the generalization characteristics of the study. Those patients with the inability to receive spinal anesthesia, prior hip surgery, preoperative dementia, severe congestive heart failure (New York Heart Association class IV), severe chronic obstructive pulmonary disease (Global Initiative for Chronic Obstructive Lung Disease guidelines, stage 111 or higher), or a Mini-Mental State Examination score below 15 were not allowed to participate (Sieber et al., 2010). Another limiting factor to this study conducted by Sieber is that early postoperative delirium was not observed in the post anesthesia care unit or on the first postoperative day. Despite these downfalls, this study concludes that the prevalence of confusion after undergoing a hip fracture repair with spinal anesthesia and propofol sedation can be reduced by 50% with the use of light sedation over deep sedation (Sieber et al., 2010). Deep sedation requires much higher doses than light sedation but the study concludes that "despite this association, propofol dose was not predictive of postoperative delirium. This finding suggests that the intraoperative sedation itself, rather than the amount of

propofol administered, was what contributed to the greater prevalence of delirium in the deep sedation group" (Sieber, 2010, p. 23). For the elderly, the effects of deep sedation appears to be more risky in the chance of developing postoperative delirium and may even require longer recovery care than light sedation or general anesthesia.

Procedural Sedation and Children

When compared to adults, children more frequently require anesthetics for minor procedures such as suture removal, intravenous starts, catheter insertion, Magnetic Resonance Imaging (MRI), and Computed Tomography (CT) scans to ease their anxiety and make them feel more comfortable (Nemours, 2013). Nationwide discharge criteria has been established for those children that have undergone any type of sedation, but lack of health resources and health care professionals have limited the ability to monitor these patients for long periods of time (Malviya, Voepel-Lewis, Prochaska, & Tait, 2000). Return of the child to baseline vital signs, a level of consciousness close to the child's baseline, and the ability of the child to maintain a patent airway comprise the preexisting discharge criteria but the adverse events that occur after discharge in the clients' homes are highly underreported. This study followed up with 376 children who underwent an MRI or a CT scan that required sedation for 1 week after discharge to evaluate the child's recovery after discharge, determine incidence of adverse events and medical follow-up once the child had already been discharged following the procedure, and to evaluate parent satisfaction with their child's sedation experience (Malviya et al., 2000).

This study followed patients under the age of 18 from May 1998 until November 1998 that received sedation for an outpatient MRI or CT scan. Malviya and colleagues did not separate its subjects into groups due to the goal of patient evaluation after discharge home. Clinically, all patients received either a CT scan (n=100) or MRI (n=276) and sedation drugs

administered by pediatric nurses in accordance with the preexisting institutional guidelines (Malviya et al., 2000). Four hundred twenty-nine families were asked to be a part of this study but only 87.6% accepted the invitation due to refusal (7%) or inability to be reached for follow-up evaluation (5%) (Malviya et al., 2000). Three hundred thirty-six children received oral chloral hydrate, and 10% of those children also received intravenous midazolam to aid in achieving the right level of sedation while the remaining 40 children (11%) received midazolam as a sole agent (Malviya et al., 2000). The mean age of the participating children was 3.8 ± 3.4 years old with 53% male and 47% female (Malviya et al., 2000). Prior to discharge, Malviya and his colleagues gave the parents a survey to be completed at home within the next 24 hours regarding their child's behavior and recovery once discharged from the hospital. The survey consisted of the degree of the child's wakefulness, the presence of side effects, the time the child returned to baseline behavior, and whether medical follow-up was sought after discharge. The side effects reported included restlessness and hyperactivity, agitation, motor imbalance, respiratory difficulties, and gastrointestinal upset. At the end of the survey parents were asked to rate their overall satisfaction with the sedation experience using a 4-point scale (Malviya et al., 2000). Descriptive statistics was used to analyze data and reported in a mean ± standard deviation format when appropriate (Malviya et al., 2000).

The authors of this study set a p value of $<.05$ and considered this statistically significant. Inadequate sedation caused 28 procedures to be cancelled (MRI: 25 vs. CT: 3, $p= .05$) and those experiencing inadequate sedation tended to be older (4.8 ± 3.2 years) than those who received sufficient sedation (2.7 ± 3.4 years) achieving a p value of .03 (Malviya et al., 2000). The average time from the end of the procedure to discharge was 26 ± 15 minutes including three children receiving care from the post anesthesia care unit due to one allergic reaction to chloral

hydrate, one with asthma history experiencing oxygen desaturation to 85%, and one experiencing prolonged sedation (Malviya et al., 2000). Malviya et al. (2009) discovered no further adverse reactions occurred in these children that were held for longer periods of time. Motor imbalance and drowsiness were the two most common adverse reactions reported resulting in 53% of children sleeping on the way home and 31% sleeping for at least 6 hours after discharge. Of the patients receiving chloral hydrate, 31% experienced motor imbalance versus 18% receiving midazolam (Malviya et al., 2000). The motor imbalance percentage difference between those receiving chloral hydrate versus those receiving midazolam alone is statistically significant with a p value of .05 (Malviya et al., 2000). Agitation occurred in 18% of children but Malviya determined that the agent used was not statistically significant. Eighteen of the 53 children whose parents reported restless behaviors were restless for greater than 6 hours. This was significantly related to those with younger ages ($p< .05$) (Malviya et al., 2000). A summary of these statistics can be seen in Tables 13 and 14.

Satisfaction with the sedation experience was achieved by 84% of parents. Those that were dissatisfied, post-discharge agitation, failed sedation, or inadequate sedation are the causes (Malviya et al., 2000). These satisfactory numbers can be increased with thorough parent teaching about sedation medications, possible side effects, and how to acquire appropriate medical follow-up if needed prior to the procedure (Malviya et al., 2000). A decrease in adverse events can be reached by longer procedure to discharge times and use of midazolam over chloral hydrate if possible (Malviya et al., 2000). Malviya states that younger children are also more at risk (see Figure 3) for adverse events or delayed recovery times and teaching parents about these risks is important. Sedation methods to reduce the related adverse events were not closely

monitored in this study and future studies to promote the safety and efficacy of sedated children should focus on these (Malviya et al., 2000).

Conclusion

Since 1842, many studies have contributed to the advancement of anesthesia care and the agents used. Ketamine, one of the newest anesthetic agents, is the focus of many research topics now that have yet to be published. Management of postoperative nausea and vomiting has been improved by combining antinausea and antiemetic drugs with the anesthetics during the procedure. The beliefs surrounding general anesthesia and its causation of permanent memory loss in elderly adults have been laid to rest by Dr. Sprung and his colleagues (2013). His study on anesthesia and incident dementia proved that the link between any form of dementia and general anesthesia is not statistically significant (OR 0.89, CI 95% between 0.73-1.10, p=.27) (Sprung et al., 2013). However, Dr. Wilder and his co-researchers (2009) discovered that general anesthesia does have harmful long term neurological effects on children. The children who underwent two or more procedures with general anesthesia were at a greater risk for developing a learning disability when compared to those children under the age of 4 who had only a single exposure or none at all (p<.001). Also, the percentage was nearly 15% higher for those having multiple anesthetic exposures in developing a learning disability compared with those having one exposure or none at all (Wilder et al., 2009). Sedation effects on the cognitive, long term health of elderly patients are minimal. Postoperative delirium has the potential to increase recovery time, but with the use of light sedation over deep sedation techniques, this chance can be lessened by 21%. This study also concludes that postoperative delirium will be prevented in 1 out of every 4.7 patients over the age of 65 when using light sedative techniques (Sieber et al., 2010). Sedation effects in children are just as minimal as elderly when cognitive,

long term health is analyzed. Baseline activity level was most affected in children and was achieved in 24 hours by 89% of patients and 5% did not return to baseline until the second post-procedure day (Malviya et al., 2000). Also using midazolam alone instead of chloral hydrate can aid in decreasing the immediate side effects of light sedation in children (Malviya et al., 2000). After summarizing these four articles, it appears the intravenous procedural sedation is the most safe and efficient route when having to undergo anesthesia. Not all procedures can be done under intravenous sedation and thorough teaching about the risks of general anesthesia can give clients a clear idea of what to expect. Long term neurological health can be manipulated by many factors so relying on these studies alone is not recommended. As more research is developed, the world of anesthesia will continue to evolve as the entire medical field advances.

Table 1

Overview of General Anesthesia and Minimal, Moderate, and Deep Sedation

	General Anesthesia	Minimal Sedation	Moderate Sedation	Deep Sedation
Common Drugs Used	*Induction*: propofol, nitrous oxide, and sodium thiopental *Analgesics*: morphine, meperidine, hydromorphone, fentanyl, sufentanil, and remifentanil *Muscle Relaxant*: succinylcholine	*Sedatives*: midazolam, lorazepam, ketamine, nitrous oxide, chloral hydrate *Analgesic*: fentanyl	*Sedatives*: midazolam, lorazepam, etomidate, ketamine, dexmedetomidine, nitrous oxide *Analgesic*: fentanyl, morphine, meperidine	*Sedatives*: midazolam, etomidate, ketamine, propofol, nitrous oxide, *Analgesic*: fentanyl, morphine, meperidine
Common Side Effects upon Awakening	nausea, vomiting, sore throat from intubation, hypotension, decrease oxygen saturation, decreased respirations & cardiac output, burning on injection	Emergence delirium, nausea, vomiting	Emergence delirium, nausea, vomiting, respiratory depression	Emergence delirium, nausea, vomiting, respiratory depression, cardiovascular depression, burning on injection of propofol
Responsiveness	Unarousable with any stimulation including pain	Normal response to verbal cues	Purposeful response to verbal/tactile cues	Purposeful response after repeated or painful stimulation
Airway	Frequently use laryngeal mask, endotracheal tube, or head tilt, jaw thrust maneuver	Patent	Usually unaffected/Patent	Intervention may be required via bag-mask ventilation
Spontaneous Ventilation	Usually inadequate	Unaffected	Adequate	May be inadequate
Cardiovascular Effects	May be impaired	Unaffected	Usually unaffected	Usually maintained
Fasting Requirements	Nothing by mouth (NPO)	Heavy meal allowed	Light snacks allowed	Clear liquids but generally NPO

Note. Adapted from "Pharmacologic options for procedural sedation and analgesia," by M. S. Orlewicz, 2013, *Medscape*. Retrieved from http://emedicine.medscape.com/article/109695-overview#aw2aab6b4

Table 2

Demographic Characteristics[a]

Characteristic	Dementia due to all causes[b]		Dementia due to Alzheimer disease	
	Controls (N 877)	Cases (N 877)	Controls (N 732)	Cases (N 732)
Age at index date (y)				
Mean ± SD[c]	87.7 ± 8.0	87.7 ± 8.0	81.3 ± 7.9	81.3 ± 7.9
Sex				
Male	241 (27.5)	241 (27.5)	203 (27.7)	203 (27.7)
Female	636 (72.5)	636 (72.5)	529 (72.3)	529 (72.3)
White Race	868 (99.0)	870 (99.2)	723 (98.8)	726 (99.2)
Education (y)				
<12	298 (34.0)	291 (33.2)	240 (32.8)	228 (31.2)
12	225 (25.7)	214 (24.4)	187 (25.6)	184 (25.1)
>12	331 (37.7)	351 (40.0)	288 (39.3)	304 (41.5)
Unknown	23 (2.6)	21 (2.4)	17 (2.3)	16 (2.2)

Note. From "Anesthesia and incident dementia: A population-based, nested, case-control study" by J. Sprung et al., 2013, *Mayo Clinic Proceedings, 88*(6), 555.

[a] Data are presented as No. (percentage) expect where indicated otherwise. [b] Dementia due to all causes includes any etiology, including Alzheimer disease dementia. [c] Standard Deviation (SD)

Table 3

Association Between Exposure to Anesthesia and Subsequent Dementia[a]

Exposure	Controls	Cases	OR	95% CI	*P* value
Any anesthetic	636 (72.5)	615 (70.1)	0.89	0.73-1.10	.27
Anesthetic exposure					.51
0	241 (27.5)	262 (29.9)	1.00	Reference	
1	224 (25.5)	211 (24.1)	0.87	0.68-1.12	
2-3	282 (32.2)	263 (30.0)	0.86	0.67-1.10	
≥ 4	130 (14.8)	141 (16.1)	1.00	0.74-1.35	
Cumulative length of anesthesia (min)[b]	140 (0-305)	135 (0-307.5)	1.00	0.99-1.01	.86
Cumulative length of anesthesia (min)					.58
0	241 (27.5)	262 (29.9)	1.00	Reference	
1-120	163 (18.6)	159 (18.1)	0.90	0.69-1.19	
121-240	195 (22.2)	175 (20.0)	0.83	0.64-1.08	
≥ 241	278 (31.7)	281 (32.0)	0.93	0.73-1.19	
Duration of longest single exposure (min)	105 (0-165)	100 (0-170)	0.99	0.96-1.02	.49
Duration of longest single exposure (min)					.54
0	241 (27.5)	262 (29.9)	1.00	Reference	
1-120	268 (30.6)	249 (28.4)	0.86	0.67-1.10	
121-240	280 (31.9)	269 (30.7)	0.89	0.70-1.14	
≥241	88 (10.0)	97 (11.1)	1.02	0.72-1.44	

Note. Adapted from "Anesthesia and incident dementia: A population-based, nested, case-control study" by J. Sprung et al., 2013, *Mayo Clinic Proceedings, 88*(6), 557.

[a] Data are No. (percentage) or median (25th-75th percentile). This chart is for those with dementia (including Alzheimer dementia) (N=877). [b] Cumulative duration of anesthesia is the total time an individual was exposed to general anesthesia after age 45 years and before their index date. The odds ratio for total anesthesia duration reflects increased risk per 30 minutes of anesthesia. In all cases, odds ratios were obtained using conditional logistic regression taking into account the matched study design.

Table 4

Association Between Exposure to Individual Anesthetic Agents and Subsequent Dementia[a]

Anesthetic agent	No. (%) of controls (N 877)	No. (%) of cases (N 877)	Odds ratio	95% CI	*P* value
Inhalation agents					
Ether	149 (17)	152 (17)	0.94	0.71-1.26	.69
Methoxyflurane	36 (4)	42 (5)	1.08	0.67-1.74	.75
Cyclopropane	9 (1)	7 (1)	0.73	0.27-1.98	.54
Halothane	255 (29)	249 (28)	0.90	0.70-1.15	.40
Enflurane	276 (31)	292 (33)	0.97	0.77-1.23	.82
Isoflurane	223 (25)	191 (22)	0.78	0.60-1.02	.07
Nitrous oxide	616 (70)	607 (69)	0.91	0.74-1.12	.38
Intravenous drugs					
Benzodiazepines	186 (21)	174 (20)	0.86	0.65-1.13	.28
Sodium thiopental	612 (70)	596 (68)	0.90	0.73-1.10	.30
Ketamine	9 (1)	7 (1)	0.72	0.27-1.95	.52
Propofol	6 (1)	4 (<1)	0.62	0.18-2.22	.47
Intraoperative opioids	595 (68)	571 (65)	0.88	0.72-1.09	.24

Note. From "Anesthesia and incident dementia: A population-based, nested, case-control study" by J. Sprung et al., 2013, *Mayo Clinic Proceedings, 88*(6), 558.

[a]Odds ratios and corresponding 95% CIs are presented using no exposure to any general anesthesia as the reference group. In all cases, odds ratios were obtained using conditional logistic regression taking into account the matched study design. Among cases, 615 individuals underwent 1681 procedures under general anesthesia; in the control group, 636 individuals underwent 1638 procedures. Patients may be exposed to multiple inhalational and intravenous agents in the same procedure.

Table 5

Birth, Maternal, and Paternal Characteristics

	No Anesthesia (N=4,764)		Anesthesia (N=593)		
Characteristic	N[a]	Summary Statistics[b]	N[a]	Summary Statistics[b]	*P*
Sex	4,764		593		<.001
Male		2,357 (49.5)		207 (34.9)	
Female		2,407 (50.5)		386 (65.1)	
Birth Weight, g	4,755	3,476 ± 531	592	3,396 ± 655	<.001
<2500 g		185 (3.9)		43 (7.3)	
>2500 g		4,570 (96.1)		549 (92.7)	
Gestational age, weeks	4,467	40 ± 2.0	558	39.7 ± 2.6	.001
<32		25 (0.6)		17 (3.0)	
32 to <37		254 (5.7)		41 (7.3)	
>37		4,188 (93.7)		500 (89.6)	
APGAR score at 1 min	1,446	7.9 ± 1.4	201	8.0 ± 1.3	.2775
APGAR score at 5 min	1,447	9.1 ± 0.8	201	9.0 ± 8.0	.163
Number at birth	4,764		593		.237
Single		4,677 (98.2)		578 (97.5)	
Twins		87 (1.8)		15 (2.5)	
Induction of labor	4,739		590		.286
No		3,729 (78.7)		453 (76.8)	
Yes		1010 (21.3)		137 (23.2)	
Mother's education	4,356		536		.039
<12 years		294 (6.7)		21 (3.9)	
12 years		1,482 (34.0)		192 (35.8)	
>12 years		2,580 (59.2)		323 (60.3)	
Father's education	4,111		505		.127
<12 years		195 (4.7)		14 (2.8)	
12 years		1,250 (30.4)		160 (31.7)	
>12 years		2,666 (64.9)		331 (65.5)	
Mother's age, years	4,764	26.5 ± 4.7	593	26.8 ± 4.5	.182
Father's age, years	4,515	28.8 ± 5.4	568	29.0 ± 5.2	.369

Note. From "Early exposure to anesthesia and learning disabilities in a population-based birth cohort" by R. T. Wilder et al., 2009, *Anesthesiology, 110*(4), 13-14.
[a]Number with information available for the given characteristic. APGAR (Activity, Pulse, Grimace, Appearance, Respiration) scores. [b]Mean ± SD or N (%). [c]Data were available for 1980-1982 only.

Table 6

Patient and Anesthesia Characteristics (N=593)[a]

Characteristic	N (%)
ASA physical status[b]	
1	438 (73.9)
2	124 (20.9)
3	24 (4.0)
4	7 (1.2)
Age at first exposure, years	
<1	195 (32.9)
1	155 (26.1)
2	131 (22.1)
3	112 (18.9)
Anesthetic exposures (N)	
1	449 (75.7)
2	100 (16.9)
3-4	31 (5.2)
5-9	8 (1.3)
10 or more	5 (0.8)
Duration of anesthesia, minutes[c]	
Mean ± SD	125 ± 227
Median (IQR)	75 (45,120)

Note. ASA, American Society of Anesthesiologists; IQR, interquartile range. N, number; %, percentage; SD, standard deviation; From "Early exposure to anesthesia and learning disabilities in a population-based birth cohort" by R. T. Wilder et al., 2009, *Anesthesiology, 110*(4), 16.

[a]Data related to anesthesia characteristics were available for all patients. [b]For infants the underwent multiple anesthetics the highest ASA physical status is used. These 593 individuals underwent a total of 875 anesthetics (range from 1 to 25 per person). [c]Data presented correspond to the cumulative total duration of anesthesia for each individual (N=593). The median duration per anesthetic (N=875) was 70 minutes (range 10 to 560).

Table 7

Types of Anesthetics Used (N=875)[a]

Variable	N (%)
Inhalation agents	
Isoflurane	17 (1.9)
Halothane	769 (87.9)
Enflurane	14 (1.6)
Intravenous agents	
Sodium Thiopental	46 (5.3)
Etomidate	5 (0.6)
Ketamine	77 (8.8)
Other	32 (3.7)
Nitrous Oxide	793 (90.7)
Diazepam	12 (1.4)

Note. N, number; %, percentage; From "Early exposure to anesthesia and learning disabilities in a population-based birth cohort" by R. T. Wilder et al., 2009, *Anesthesiology, 110*(4), 18.

[a]A total of 875 anesthetics were performed on 593 patients; Data related to anesthesia were available for all procedures

Table 8

Surgeries Performed Under the Age of 4 (N=875)

		According to age at surgery			
	Overall	< 1 year	1 year	2 year	3 year
Type of Surgery, N (%)	N=875	N=251	N=246	N=205	N=173
Cardiac	15 (1.7)	8 (3.2)	6 (2.4)	0 (0.0)	1 (0.6)
Ear Nose and Throat	229 (26.2)	21 (8.4)	57 (23.2)	73 (35.6)	78 (45.1)
General	220 (25.1)	114 (45.4)	43 (17.5)	35 (17.1)	28 (16.2)
Neurosurgery	9 (1.0)	3 (1.2)	3 (1.2)	3 (1.5)	0 (0.0)
Ophthalmology	83 (9.5)	23 (9.2)	38 (15.4)	9 (4.4)	13 (7.5)
Oral Surgery	10 (1.1)	0 (0.0)	5 (2.0)	1 (0.5)	4 (2.3)
Orthopedics	115 (13.1)	25 (10.0)	43 (17.5)	30 (14.6)	17 (9.8)
Plastics	56 (6.4)	18 (7.2)	21 (8.5)	8 (3.9)	9 (5.2)
Urology	112 (12.8)	29 (11.6)	25 (10.2)	36 (17.6)	22 (12.7)
Other[a]	26 (3.0)	10 (4.0)	5 (2.0)	10 (4.9)	1 (0.6)

Note. N, number; From "Early exposure to anesthesia and learning disabilities in a population-based birth cohort" by R. T. Wilder et al., 2009, *Anesthesiology, 110*(4), 17.
[a]Indicates diagnostic procedures, catheterization, angiography, and examination under anesthesia.

Table 9

Effects of Anesthetic Exposures Before the Age of 4 on Risk for Developing Learning Disabilities

	Unadjusted			Adjusted[a]		
	Hazard Ratio	95% C.I.	*P*	Hazard Ratio	95% C.I.	*P*
Number of Exposures			<.001			<.001
0 (N=4,764)	Reference			Reference		
1 (N=449)	1.05	0.84 to 1.32		1.00	0.79 to 1.27	
2 (N=100)	1.78	1.22 to 2.59		1.59	1.06 to 2.37	
3 or more (N=44)	2.50	1.55 to 4.04		2.60	1.60 to 4.24	
Total duration of anesthesia exposure						
Continuous (per 30 min)	1.02	1.00 to 1.03	.011	1.02	1.00 to 1.03	.016
Categorical (30 min intervals)			.004			.027
No anesthesia (N=4,764)	Reference			Reference		
<30 min (N=95)	0.93	0.56 to 1.55		0.94	0.56 to 1.60	
31 to 60 minutes (N=135)	0.80	0.51 to 1.26		0.74	0.46 to 1.20	
61 to 90 minutes (N=135)	1.50	1.06 to 2.14		1.40	0.97 to 2.02	
91 to 120 minutes (N=87)	1.45	0.94 to 2.24		1.36	0.89 to 2.10	
>120 minutes (N=141)	1.65	1.19 to 2.29		1.56	1.11 to 2.19	
Any Exposure			.014			.067
No (N=4,764)	Reference			Reference		
Yes (N=593)	1.27	1.05 to 1.53		1.20	0.99 to 1.46	

Note. C.I., confidence interval; N, number; From "Early exposure to anesthesia and learning disabilities in a population-based birth cohort" by R. T. Wilder et al., 2009, *Anesthesiology, 110*(4), 19.

[a]Adjusting for sex, birth weight (<2500, >2500) and gestational age (<32 weeks, 32 to <37 weeks, >37 weeks). Due to missing covariant information, only 5,020 individuals were included in the adjusted analysis.

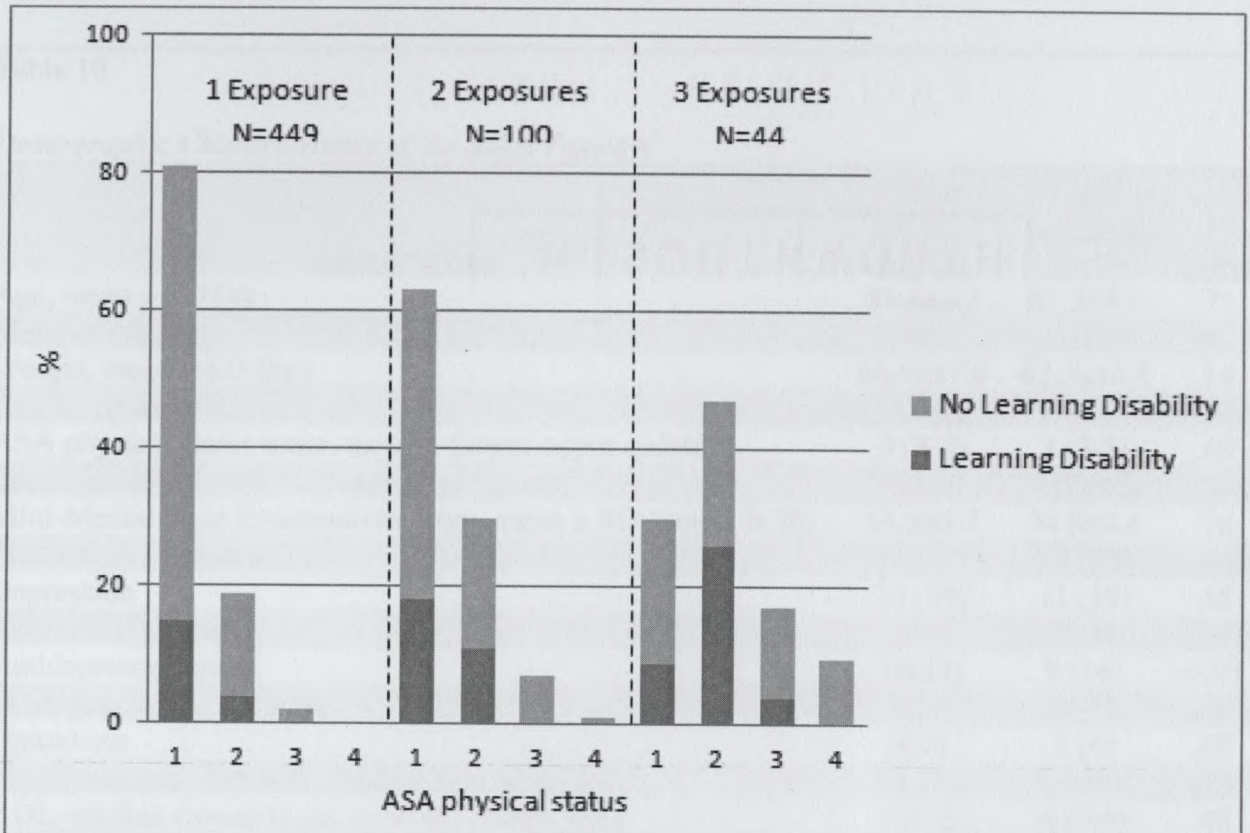

Figure 1. Distribution of American Society of Anesthesiologists (ASA) physical status across patients with 1, 2 and ≥3 anesthetic exposures. Shading is used to indicate the percentage diagnosed with a learning disability under the age of 19 versus not. For this presentation individuals who had incomplete follow-up are categorized based on information available through last follow-up prior to 19 years of age. Adapted from "Early exposure to anesthesia and learning disabilities in a population-based birth cohort" by R. T. Wilder et al., 2009, *Anesthesiology, 110*(4), 12. Copyright 2010 by PubMed Center.

Table 10

Demographic Characteristics of the Study Patients[a]

Characteristic	Deep sedation (n=57)	Light sedation (n=57)	*P* value
Age, mean ± SD (y)	81.8±6.7	81.2±7.6	.71
Male/female, No.	14/43	17/40	.67
Weight, mean ± SD (kg)	66.6±17.0	62.1±14.8	.14
Height, mean ± SD (cm)	164±10	164±11	.96
ASA physical status score, median (lower-upper quartile)	3 (3-3)	3 (3-3)	.69
Education level, median (lower-upper quartile)[b]	3 (2-4)	3 (2-3.5)	.89
Mini-Mental State Examination score, mean ± SD (range, 0-30)	24.5±5.3	24.8±4.6	.78
Preoperative dementia[c]	21 (37)	19 (33)	.85
Depression	14 (25)	11 (19)	.65
Benzodiazepine use	2(4)	3 (5)	>.99
Antidepressant use	10(18)	9 (16)	>.99
Other psychiatric drug use	8(14)	4 (7)	.36
Opioid use	4(7)	2 (4)	.68
No. of systemic illnesses, mean ± SD (range, 0-7)[d]	1.4±1.4	1.6+1.2	.36
ADL, median (lower-upper quartile) (range, 0-6)	5 (5-6)	6 (5-6)	.48
Instrumental ADL, median (lower-upper quartile) (range, 0-8)	6 (3-8)	6 (5-8)	.29
Living independently[e]	32 (56)	42 (74)	.08
Inouye risk, median (lower-upper quartile) (range, 1-3)[f]	2 (2-2)	2 (2-2)	.91

Note. From "Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair," by F. E. Sieber, K. J. Zakriva, A. Gottschalk, M. R. Blute, H. B. Lee, P. B. Rosenberg, & S. C. Mears, 2010, *Mayo Clinic Proceedings, 85*(1), p. 22.

[a]Data are No. (percentage) unless indicated otherwise. ADL = activities of daily living; ASA = American Society of Anesthesiologists. [b]For education level, 1 indicates grade school; 2, some high school; 3, high school graduate; 4, vocational training or some college; 5, college graduate; 6, some graduate school; and 7, completed degree. [c]As determined by clinical assessment or Mini-Mental State Examination score of less than 24. [d]Coronary artery disease, congestive heart failure, cerebrovascular disease, diabetes mellitus, chronic renal insufficiency or failure, chronic obstructive pulmonary disease, or malignant neoplasm. [e]Lives in own home. [f]For Inouye risk, 1 indicates low risk (0 points); 2, intermediate risk (1-2 points); and 3, high risk (3-4 points), in which 1 point is assigned for each of the 4 risk factors (visual impairment, severe illness, cognitive impairment, high blood urea nitrogen-creatinine ratio).

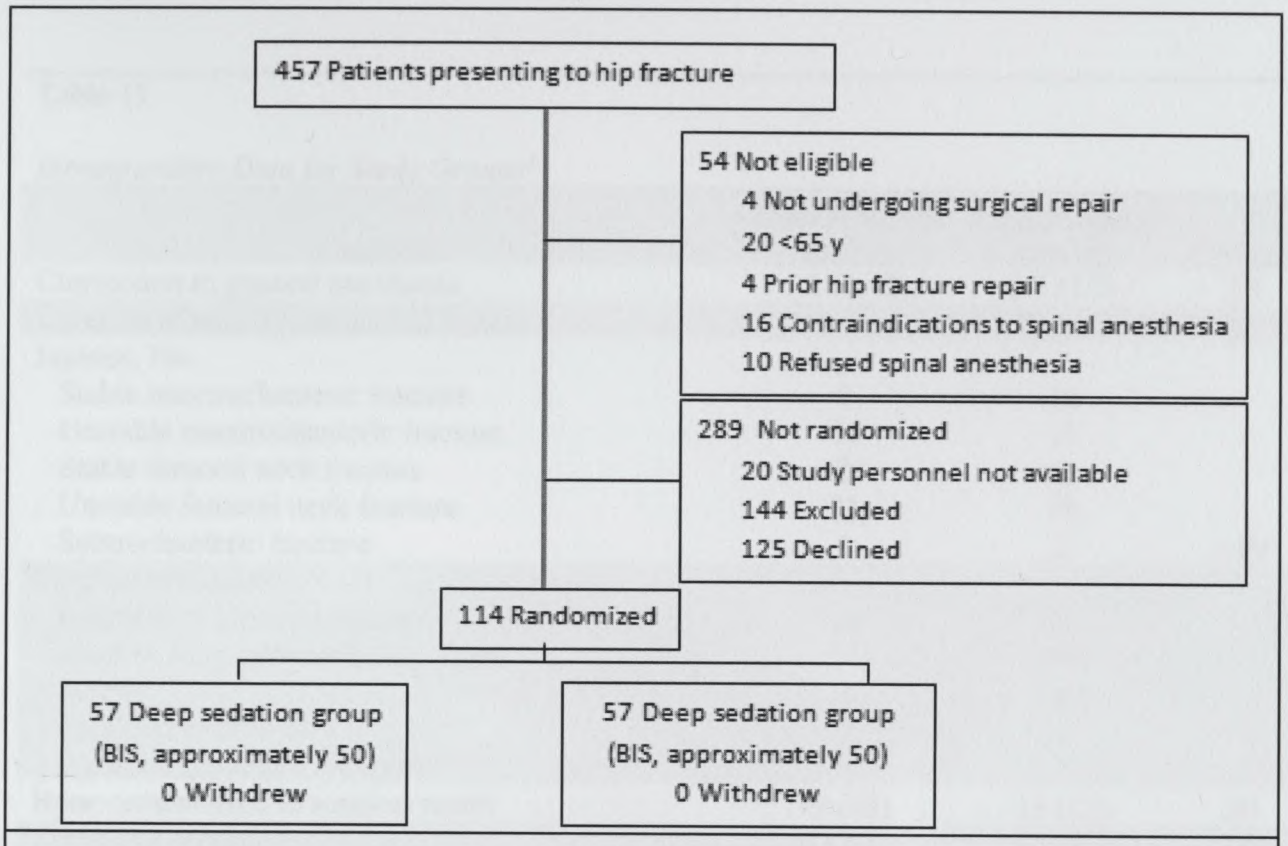

Figure 2. Study flow. The only contraindication to spinal anesthesia encountered was concurrent use of clopidogrel bisulfate at the time of injury. Patients were excluded from the study because they could not speak English (n=4), met exclusion criteria for dementia (Mini-Mental State Examination score, <15) preoperatively (n=42), met exclusion criteria for delirium (positive results on the Confusion Assessment Method) preoperatively (n=37), or simultaneously met the exclusion criteria for dementia and delirium (n=61). The indicated number of patients who declined to participate includes 1 who consented but withdrew before randomization. Although 4 patients in the deep sedation group and 6 in the light sedation group required conversion to general anesthesia because of incomplete or insufficient duration of spinal blockade, all data were analyzed on an intention-to-treat basis. BIS = bispectral index. Reprinted from "Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair," by F. E. Sieber, K. J. Zakriva, A. Gottschalk, M. R. Blute, H. B. Lee, P. B. Rosenberg, & S. C. Mears, 2010, *Mayo Clinic Proceedings, 85*(1), p. 21.

Table 11

Intraoperative Data for Study Groups[a]

Category	Deep sedation (n=57)	Light sedation (n=57)	*P* value
Conversion to general anesthesia	1.8 (1.42)	1.6 (1.5)	.52
Duration of surgery, mean ± SD (min)	93 ± 44	79 ± 33	.05
Injuries, No.			
Stable intertrochanteric fracture	9	10	
Unstable intertrochanteric fracture	14	17	
Stable femoral neck fracture	2	8	
Unstable femoral neck fracture	31	20	
Subtrochanteric fracture	1	2	>.99
Surgical procedures, No.			
Unipolar or bipolar implant	28	21	
Short or long intramedullary screw	24	25	
Screws	3	6	
Total hip arthroplasty	2	2	
Dynamic hip screw and plate	0	3	>.99
Bone cement used in surgical repair	19 (33)	13 (23)	.30
Receiving propofol	57 (100)	52 (91)	.06
Propofol dose, mean ± SD (mg/kg)	10.2 ± 5.6	2.5 ± 2.7	<.001
Receiving midazolam	3 (5)	11 (19)	.04
Midazolam dose, mean ± SD (mg/kg)	1.26 ± 6.36	5.53 ± 12.42	.02
Receiving intraoperative opioids	46 (81)	46 (81)	>.99
Average BIS, mean ± SD (range, 0 -100)	49.9 ± 13.5	85.7 ± 11.3	<.001

Note. Adapted from "Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair," by F. E. Sieber, K. J. Zakriva, A. Gottschalk, M. R. Blute, H. B. Lee, P. B. Rosenberg, & S. C. Mears, 2010, *Mayo Clinic Proceedings, 85*(1), p. 22.

[a]Data are No. (percentage) unless otherwise indicated. BIS = bispectral index.

Table 12

Hospitalization Data for the Study Groups[a]

Category	Deep sedation (n=57)	Light sedation (n=57)	*P* value
Postoperative delirium	23 (40)	11 (19)	.02
Duration of delirium for all patients, mean ± SD[b]	1.4 ±4.0	0.5 ± 1.5	.01
Duration of delirium for those with delirium, mean ± SD[b]	3.4 ± 5.7	2.8± 2.3	.77
Time from surgery until discharge, mean ± SD (d)	4.5 ± 2.3	4.7 ± 3.1	.69
MMSE score on POD2, mean ± SD (range, 0-30)	20.0 ± 9.3	23.1 ± 5.5	.08
MMSE score on POD2 vs. preoperative day score, mean ± SD	-4.4 ± 6.1	-2.1 ± 3.4	.06
Patients with ≥1 complication(s)	30 (53)	26 (46)	.57
Patients with postoperative complications (range, 0-11)[c]	1.0 (1.8)	0.8 (1.4)	.44

Note. Adapted from "Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair," by F. E. Sieber, K. J. Zakriva, A. Gottschalk, M. R. Blute, H. B. Lee, P. B. Rosenberg, & S. C. Mears, 2010, *Mayo Clinic Proceedings, 85*(1), p. 23.

[a] Data are No. (percentage) unless indicated otherwise. POD = postoperative day, MMSE = Mini-Mental State Examination. [b] Data on duration of delirium are provided for both the entire population of each group and just those experiencing delirium in each group. [c] Postoperative complications averaged over the entire population of each group include the following: urinary tract infection, discharge with urinary drainage catheter, acute renal failure, pneumonia, congestive heart failure, myocardial infarction, new dysrhythmia, fall, return to surgery, pulmonary embolus or deep venous thrombosis, or wound infection.

Table 13

Adverse Events in the Hospital and After Discharge [n (%)]

	In Hospital	After Discharge
Oxygen desaturation	6 (1.6)	N/A
Inadequate/failed sedation	43 (12)/28 (8)	N/A
Gastrointestinal effects	9 (2)	87 (23)
Agitation	9 (2)	72 (19)
Motor Imbalance	NA	117 (31)
Restlessness	NA	52 (14)
Escalation of care/parent seeks medical advice or follow-up	3 (<1)	15 (4)[a]

Note. NA indicates not applicable. From "Prolonged Recovery and Delayed Side Effects of Sedation for Diagnostic Imaging Studies in Children" by S. Malviya, T. Voepel-Lewis, G. Prochaska, and A. R. Tait, 2000, *Pediatrics, 105*(3), p. 2.

[a]Includes 3 admissions to emergency department for excessive sedation.

Table 14

Adverse Events in Relation to Medications Administered [n (%)]

	Chloral Hydrate (CH) (302)	CH + Benzodiazepine (34)	Benzodiazepine (40)
Respiratory events	5 (<2)	0	1 (3)
Inadequate/failed sedation	23 (8) / 16 (5)	11 (32) / 7 (21)	10 (25) / 5 (13)
Agitation			
In hospital	3 (1)	5 (15)	1 (3)
At home	55 (18)	13 (38)	3 (8)
Gastrointestinal effects			
In hospital	8 (3)	0	0
At home	78 (26)	5 (15)	3 (8)
Motor imbalance	93 (31)[a]	17 (50)	7 (18)
Restlessness	42 (14)	7 (21)	3 (8)

Note. From "Prolonged Recovery and Delayed Side Effects of Sedation for Diagnostic Imaging Studies in Children" by S. Malviya, T. Voepel-Lewis, G. Prochaska, and A. R. Tait, 2000, *Pediatrics, 105*(3), p. 3.

[a]$P = .05$ compared to children who received a benzodiazepine as a sole sedative.

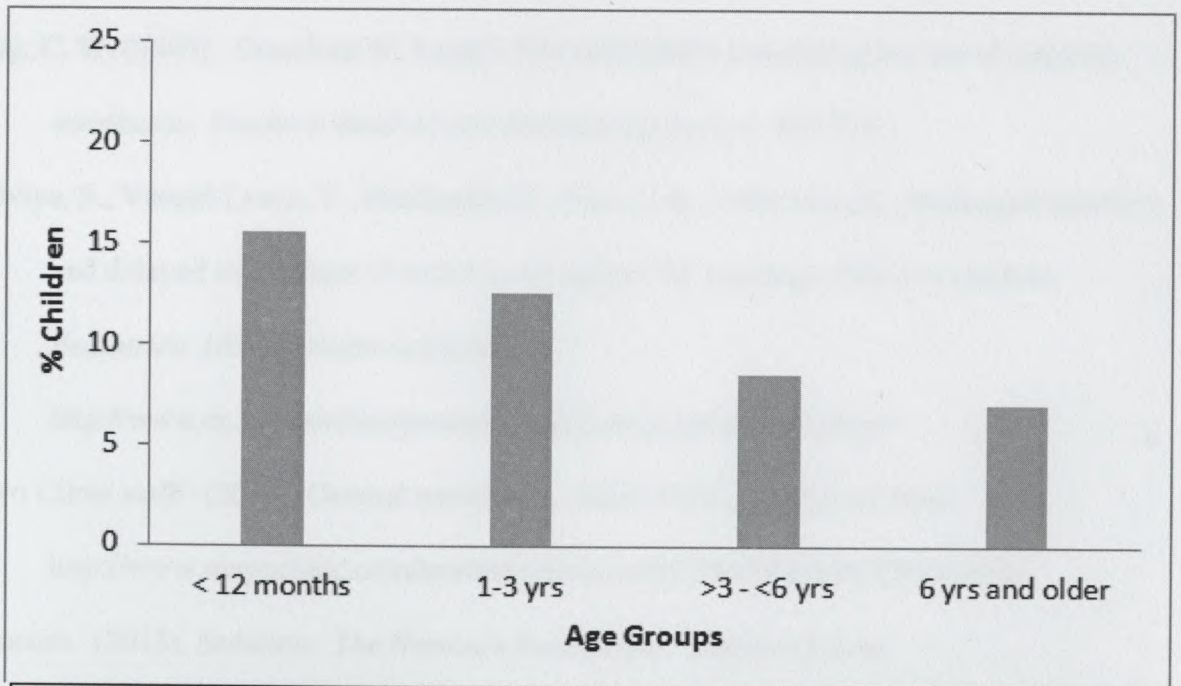

Figure 3. Delayed Recovery (ie, >24 hours) related to age. From "Prolonged Recovery and Delayed Side Effects of Sedation for Diagnostic Imaging Studies in Children" by S. Malviya, T. Voepel-Lewis, G. Prochaska, and A. R. Tait, 2000, *Pediatrics, 105*(3), p. 4. Copyright 2000 by *Pediatrics*.

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