A comparison of ketamine versus etomidate for procedural sedation for the reduction of large joint dislocations

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ABSTRACT

Study Objectives: Ketamine and etomidate are used for procedural sedation (PS) to facilitate the performance of painful procedures. We hypothesized that ketamine produces adequate and comparable sedation conditions for dislocated large joint reduction when compared to etomidate and results in fewer adverse events.

Methods: This Institutional Review Board approved prospective trial compared a convenience sample of subjects, who were randomized to receive either ketamine or etomidate for PS to facilitate reduction of large joint dislocations. Following informed consent, subjects were assigned via a computer-generated algorithm to receive either etomidate (0.1 mg/kg) or ketamine (0.5 mg/kg) intravenously; if PS was not sufficient, subjects received repeat doses of etomidate or ketamine until adequate PS was achieved. The protocol’s primary endpoint was a successful reduction of dislocated, large joints. Secondary endpoints included alteration in blood pressure, vomiting, recovery agitation, hypersalivation, myoclonus, hypoxia, airway assistance with chin lift or jaw thrust, bag-valve-mask ventilation, endotracheal intubation, utilization of additional doses of ketamine or etomidate, and recovery time from sedation.

Results: Total enrollment was eighty subjects, 46 in the ketamine cohort and 34 in the etomidate cohort. The two PS groups were comparable in terms of gender, age, and weight. There was no significant difference in the primary endpoint of large joint dislocation reduction between the ketamine and etomidate cohorts (46/46, 100%; 32/34, 94.1%; P - 0.1). Shoulder, hip, and ankle joints account for the majority of joint reductions in this trial. Titration of PS was necessary for almost half of each cohort as evidenced by the utilization of additional dosages of the sedative agents: ketamine (22/46, 47.8%) and etomidate (14/34, 41.2%; P - 0.56). Among secondary outcome variables, significant differences between ketamine and etomidate cohorts were myoclonus (1/46, 2.2%, 15/33, 45.5%; P - 0.0001), assisted ventilation with airway manipulation (3/45, 6.7%; 9/33, 27.3%; P - 0.01), and pulsoximetry desaturation < 90% (0/46; 7/34, 20.6%; P - 0.002). There was no significant difference in recovery time from PS between the ketamine and etomidate cohorts (11 min vs. 10 min; P - 0.69).

Conclusion: Ketamine produces PS conditions for successful large joint dislocation reduction that are adequate and comparable to etomidate. The increased likelihood of myoclonus, of the requirement for airway assistance, and of hypoxia observed with etomidate suggest potential benefits with the utilization of ketamine for PS for dislocated large joint reduction.

Key Words: Etomidate, joint dislocation, ketamine, procedural sedation
INTRODUCTION

Procedural sedation (PS) is routinely performed in the emergency department (ED) to facilitate potentially painful procedures by alleviating pain, anxiety, and suffering. An ideal medication for PS in the ED has a rapid onset of pharmacologic action, short duration of action sufficient for performance of the procedure, rapid return consciousness, and minimal risk of adverse effects. The shorter duration of action of one PS pharmacologic agent relative to other PS medications with longer durations of action allows for relatively quicker recovery from sedation and faster throughput in the ED, which would be a highly desirable aspect of any PS medication used in the setting of the ED.

Ketamine and etomidate are used for PS to facilitate performance of painful procedures in the ED. While there are multiple case series regarding the utilization of ketamine as a PS agent in children, data on ketamine for PS in adults in the emergency medicine literature are sparse. Ketamine is a phencyclidine derivative that causes dissociation between the cortical and limbic systems, preventing patients from perceiving sensory stimuli. As a dissociative agent, ketamine is amnestic, analgesic, preserves pharyngeal reflexes, and stimulates cardiovascular tone resulting in a rise of blood pressure and myocardial oxygen demand. Etomidate, an imidazole sedative-hypnotic agent that is chemically unrelated to any other pharmacologic agent, is frequently utilized as a PS agent because of its rapid onset of action, short duration of sedation, and minimal hemodynamic effects. It is considered to have the least hemodynamic effect of any of the pharmacologic agents available for PS.

We hypothesized that ketamine produces adequate conditions for dislocation reduction compared to etomidate and result in an analogous number of adverse effects. The primary objective of this single institution, prospective trial compared PS outcomes utilizing either ketamine or etomidate in adults for the reduction of dislocated large joints. Secondary outcomes included the necessity of utilization of additional doses of ketamine or etomidate, the utilization of adjuvant analgesics, the rate of adverse events related to PS, the necessity for clinical interventions related to respiratory depression, and the time required for patients to return to their baseline level of consciousness after PS.

METHODS

Study setting and population
St. Luke’s University Hospital is a suburban medical center with approximately 55,000 ED patient visits per year. In our ED, PS is performed at the discretion of the treating emergency physician. All adult (age > 18 years) ED patients in need of PS for the purposes of reduction of a dislocated large joint (shoulder, hip, knee, ankle, and elbow) were eligible for study enrollment on a convenience sample basis. Exclusion of patients from the study occurred if there was age < 18 years, inability to give informed consent, altered mental status, suspected cocaine or other illicit drug abuse, an American Society of Anesthesiologists Physical Assessment Score of > 2, allergy to etomidate or ketamine, pregnancy, or evidence of illicit drug intoxication prior to the start of the PS.

Study design
This Institutional Review Board approved trial prospectively enrolled a convenience sample of subjects requiring PS for reduction of large joint dislocations to either intravenously administered ketamine or etomidate. After informed consent, subject randomization occurred by selection of sequentially numbered sealed envelopes containing group assignment, which had been predetermined using a computer-generated list of random numbers. Patients could receive pain medication during the initial evaluation of injury; physicians were instructed not to co-administer pain medication with the PS agents. Patients and staff were not blinded to the PS pharmaceutical administered. Etomidate (0.1 mg/kg) or ketamine (0.5 mg/kg) was administered for PS; if sedation was deemed insufficient by the clinician for the dislocation reduction, subjects received additional doses of etomidate (0.1 mg/kg) or ketamine (0.5 mg/kg) until achieving adequate sedation. The protocol’s primary endpoint was a successful reduction of the dislocated joint. Secondary endpoints included alteration in vital signs such as blood pressure and pulsoximetry, recovery agitation, myoclonus, hypersalivation, laryngospasm, vomiting, utilization of additional doses of nonstudy sedative agents, and respiratory depression as manifest by the necessity for assisted ventilation with airway manipulation. Airway manipulation consisted of chin lift or jaw thrust, bag-valve-mask (BVM) ventilation, or endotracheal intubation. Recovery time from sedation was assessed by nursing staff, who were responsible for data collection, utilizing the Aldrete score.

Measures
Data were collected by the patient’s nurse on a standardized data collection worksheet during the procedure and later entered into an Excel (Microsoft Corporation, Redmond, WA) spreadsheet. Pulsoximetry, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse, and respiratory rate were monitored continuously. Airway repositioning with chin lift or jaw thrust, utilization of airway adjuncts, such as BVM-assisted respirations, oral or nasopharyngeal airway placement, and endotracheal intubation were recorded. For exploratory purposes only, given the lack of formal sample size calculation, skewed continuous variables were analyzed using separate
RESULTS

Demographic characteristics of study subjects
Eighty patients, 46 in the ketamine cohort and 34 in the etomidate cohort, met the inclusion and exclusion criteria for the study during the enrollment dates. The characteristics of the enrolled study subjects are presented in Table 1. Table 2 delineates the different types of dislocations that were treated in both cohorts. Shoulder dislocations followed by hip and ankle dislocations were the most common injuries requiring PS. Data were collected over a 3-year period, from January 2011 to January 2014.

Primary outcome: Achieving adequate procedural sedation
There was no significant difference in the primary endpoint of successful joint reduction between the ketamine and etomidate cohorts, as demonstrated in Table 3 (46/46, 100%; 32/34, 94.1%; P = 0.10). The necessity for utilizing more than 1 dose of ketamine or etomidate was not significantly different between cohorts (22/46, 47.8%; 14/34, 41.2%; P = 0.56); however, the median number of extra doses of PS administration per subject when required was lower for ketamine (1, range: 1–2) than for etomidate (2, range: 1–8; P = 0.02). The need for additional dosages of procedural sedative based on joint dislocation type was most common for hip joints: Ketamine 5/8 (62.5%) and etomidate 6/9 (66.7%, P not significant [NS]) in Table 3. Analgesics were administered for 24/46 (52.2%) and 23/33 (69.7%; P = 0.12) to the ketamine and etomidate cohorts, respectively, prior to the administration of PS for pain control during the evaluation of the initial injury. Need for additional sedative dose was not different between the two groups based on the administration of opioid analgesia: Ketamine 11/22 (50%) and etomidate 8/23 (34.8%; P NA). There was no significant difference in recovery time from PS between the ketamine and etomidate cohorts (11 min vs. 10 min; P = 0.69).

Adverse events

Procedural sedation impact on vital signs
Marked alterations of SBP > 200 mmHg or < 100 mmHg were transient and uncommon events in this study for both ketamine (2.2%; 1/46) and etomidate (5.9%, 2/34; P = 0.39) cohorts. There was a > 20% change in postprocedure SBP in 11/36 (29.9%) of the ketamine cohort and 4/34 (11.8%; P = 0.17) of the etomidate cohort. There were no reports of pulsoximetry desaturation episodes to < 90% in the ketamine cohort (0/46); however, 7/34 (20.6%; P = 0.002) of the etomidate cohort had pulsoximetry desaturation episodes to < 90%.

Recovery agitation was not noted in either ketamine or etomidate cohort (0/46, 0/33; P NA). Myoclonus was more prevalent in the etomidate cohort (15/33, 45.5%) than the ketamine cohort (1/46, 2.2%; P < 0.0001). While hypersalivation and vomiting occurred in insignificant numbers for both groups, serious complications such as

**Table 1: Demographic variable**

| Variable                  | Ketamine* (n = 46) | Etomidate* (n = 34) | P**   |
|---------------------------|-------------------|-------------------|-------|
| Age (mean ± SD)           | 46.4 ± 24.4       | 51.6 ± 22.6       | 0.34  |
| Gender (%)                |                   |                   |       |
| Female                    | 19 (42.2)         | 15 (45.5)         | 0.83  |
| Male                      | 26 (57.8)         | 18 (54.4)         |       |
| Weight (kg), median (range)| 70 (50-136)       | 73 (45-122)       | 0.23  |

**Table 2: Type of joint reduction**

| Type of joint reduction | n (%)          |
|-------------------------|----------------|
| Ankle                   | 11/75 (14.7)   |
| Elbow                   | 6/75 (8)       |
| Forearm                 | 1/75 (1.3)     |
| Hip                     | 17/75 (22.7)   |
| Knee                    | 2/75 (2.7)     |
| Mandible                | 1/75 (1.3)     |
| Patella                 | 2/75 (2.7)     |
| Shoulder                | 31/75 (41.3)   |
| Wrist                   | 4/75 (5.3)     |

*Certain variables had missing data, **Age as the sole normally distributed continuous variable analyzed via an independent samples t-test; skewed continuous outcomes analyzed via separate Mann-Whitney rank sums tests; categorical variables analyzed via separate Chi-square or Fisher’s exact tests. SD: Standard deviation

**Table 3: Primary and Secondary Outcome Variables**

| Variable                                           | Ketamine (n = 46) | Etomidate (n = 34) | P**   |
|----------------------------------------------------|-------------------|-------------------|-------|
| Primary outcome                                    |                   |                   |       |
| Successful joint dislocation reduction (%)         | 46/46 (100)       | 32/34 (94.1)      | 0.10  |
| Secondary outcomes                                 |                   |                   |       |
| Additional dose of study sedative (%)              | 22/46 (47.8)      | 14/34 (41.2)      | 0.56  |
| Number of additional doses, median (raw range)     | 1 (1-2)           | 2 (1-8)           | 0.02  |
| Need for additional sedative dose based on joint dislocation type (%) | Hip: 5/8 (62.5) | Hip: 6/9 (66.7)   | NA    |
|                                                    | All other: 16/35 (45.7) | All other: 7/23 (30.4) | NA |
|                                                    | 24/46 (52.2)      | 23/33 (69.7)      | 0.12  |
| Need for additional analgesia administered prior to PS (%) | 90 (30-180) | 86 (30-120)    | NA    |
| Need for additional analgesia time prior to PS, median (range) (min) | 11/22 (50) | 8/23 (34.8) | NA |
| Recovery from sedation, median (range) (min)       | 11 (2-0)          | 10 (2-65)         | 0.69  |

*Certain variables had missing data. **Age as the sole normally distributed continuous variable analyzed via an independent samples t-test; skewed continuous outcomes analyzed via separate Mann-Whitney rank sums tests; categorical variables analyzed via separate Chi-square or Fisher’s exact tests. PS: Procedural sedation, NA: Not available
laryngospasm or invasive airway intervention, such as the need for endotracheal intubation, did not occur at all for either group [Table 4]. A small number of subjects in the ketamine cohort (1/45, 2.2%; P = 0.39) and the etomidate group (3/33, 9.9%) required airway maneuvers to maintain an open airway. No patient required the cessation of PS or admission as a consequence of an adverse event in either group.

**DISCUSSION**

**Primary endpoint**
Both intravenously administered ketamine and etomidate achieved PS conditions that facilitated successful reduction of dislocated, large joints, and the primary outcome of this study. The data in this manuscript support prior published data that shows that ketamine and etomidate reliably produce PS conditions that facilitate the performance of painful procedures.[2] Recovery to consciousness from PS, as measured by the Aldrete score, was rapid for both ketamine and etomidate cohorts, 11 and 10 min, respectively, which mirrors the results of other trials utilizing these agents intravenously.[2,4,5,6]

**Achieving adequate sedation**
The utilization of additional dosages of ketamine (47.8%) or etomidate (41.2%) to achieve PS occurred frequently in this study but was not significantly different between the two cohorts [Table 3]. The necessity for progressive titration of both ketamine and etomidate was anticipated as the dosages administered for PS were chosen in order to achieve PS while limiting the likelihood of adverse pharmacologic effects. Etomidate displays a dose-response continuum observed with all PS agents except ketamine; specifically, that larger dosages of etomidate provide deeper sedation.[12] Alternatively, ketamine sedation manifests at a dosing threshold of approximately 0.5–1.0 mg/kg intravenously. Once the dissociated threshold is reached, administration of additional ketamine does not enhance sedation.[9] The dose continuum effect seen with etomidate versus the more clearly demarcated dosing threshold for ketamine is manifest in this trial’s data by the significantly higher median number of additional doses to achieve adequate PS conditions for etomidate (2, range: 1–8) compared to ketamine (1, range: 1–2) documented in Table 3. Once a critical dosage threshold is achieved for ketamine, typically 0.5–1 mg/kg intravenously, the characteristic dissociative state of ketamine necessary for PS manifests.[10] The reliability of ketamine’s dose response makes ketamine an ideal PS anesthetic for ED patients.

**Secondary outcomes**

**Procedural sedation effect on vital signs**
For the majority of ED patients and procedures, there is no evidence that transient elevations or depressions in blood pressure related to short-acting, intravenously administered PS pharmacological sedatives have clinical significance.[11] Both ketamine and etomidate caused alterations in SBPs and DBPs in a minority of subjects in both cohorts in this study. However, the pharmacologic alterations in blood pressure did not result in conditions that prevented successful reduction of the dislocated joint or caused any morbidity to any of the subjects. Etomidate is known for its hemodynamic neutrality when used for PS, which enhances its popularity as a sedative.[2] Though ketamine impacted both SBPs and DBPs, no adverse events secondary to ketamine-induced transient elevations in blood pressure were reported that precluded the attempted joint reduction.

**Adverse events**
Adverse events are reported to occur in 4–18% of PS attempts.[1,12] Adverse events from PS can manifest as respiratory depression, loss of a patent airway, aspiration, hypotension, agitation, delirium, bradycardia, vomiting, and myoclonus. Fortunately, adverse events from PS tend to be transient can be detected and prevented with careful monitoring and rarely affect the patient outcome or disposition.[13]

**Respiratory complications**
The American College of Emergency Physicians clinical policy document lists respiratory depression as the most concerning of adverse events.[1] Unlike most other PS medications that are respiratory depressants, ketamine is a respiratory stimulant that can induce tachypnea.[3]
However, ketamine can induce respiratory difficulties via laryngospasm and airway obstruction.\[14\] Prior studies of ketamine PS in adults have documented the frequency of hypoxia at 6% and of airway complications at 1.4%, including laryngospasm, aspiration, and bradypnea.\[5,13\] Excessively rapid intravenous administration of ketamine is the most important factor associated with respiratory depression or bradypnea secondary to abrupt elevations of the central nervous system ketamine concentrations. It has been recommended that ketamine is administered slowly intravenously over 60 s to avoid respiratory complications. While 6.7% in the ketamine group required airway maneuvers to maintain ventilation and oxygenation, none of the patients in the ketamine cohort had a pulsoximetry recording of < 90%, an established marker of respiratory compromise and hypoxia.

The etomidate literature demonstrates that respiratory depression resulting in oxygen desaturation < 90% or apnea occurs with etomidate in 10% of patients undergoing PS with or without adjuvant opioid analgesia.\[3\] Etomidate-induced respiratory depression is believed to be due to a decreased sensitivity of the medullary respiratory center to carbon dioxide resulting in decreased minute ventilation, smaller tidal volumes, and bradypnea.\[15\] PS with etomidate in this study resulted in significantly more subjects with hypoxia during the dislocation reduction procedure, 20.6%, than the ketamine cohort, and the need for more airway assistance than in prior studies.\[5,24\] The need for clinical interventions related to respiratory depression during PS including oxygen utilization, airway repositioning, and BVM-assisted respirations has been noted by other trials utilizing etomidate for PS.\[25\] Of note, there were no episodes of hypoxia or airway compromise for any of this study’s subjects that necessitated discontinuation of the PS procedure. There was no difference in the utilization of BVM ventilation between the ketamine and etomidate cohorts, nor did the administration of either agent result in the need for endotracheal intubation. More patients in the etomidate group required assisted ventilation with jaw thrust or chin lift than the ketamine group. The necessity for airway assistance was not related to hypersalivation, laryngospasm, or vomiting as these adverse events occurred either infrequently or not at all in either cohort.

**Myoclonus**

The most common and clinically important pharmacologically induced adverse side effect from either agent in this study was etomidate-induced myoclonus (15/33; 45.5%), which is higher than reported by other studies that utilize etomidate for PS.\[1,3\] Myoclonus occurred only once for ketamine (1/46; 2.2%; \(P < 0.001\)). Etomidate-induced myoclonus can present mildly with focal extremity tremor; alternatively, it can be severe and be associated with full body rigidity or tonic-clonic activity, which is called hypertonus.\[11\] Myoclonus has the potential to be severe enough to prevent the performance of the PS, to necessitate action to prevent the patient from falling off the gurney, and even to potentially induce hypoventilation and hypoxia.\[11\] Ketamine administration has also been reported to induce hypertonus infrequently.\[14\] More commonly, ketamine induces purposeless movements secondary to its generated, dissociative condition; these purposeless movements do not generally interfere with the performance of the necessary procedure.\[9\] In our trial, PS with etomidate did not result in a significantly lower likelihood of successful joint reduction compared to ketamine as a result of the etomidate-induced myoclonus. However, when musculoskeletal relaxation is needed for large joint dislocation reduction, the potential for myoclonus makes etomidate a less desirable procedural sedative in this setting.

**Recovery agitation**

Dysphoric recovery agitation occurs in 10–20% of cases utilizing ketamine for PS; however, benzodiazepine anxiolytics are effective in alleviating these reactions.\[1,4\] Recovery agitation has been reported to be as high as 10–20% incidence in other trials utilizing ketamine for PS.\[10\] Although recovery agitation is a well-known adverse side effect of ketamine, etomidate has also been associated with recovery agitation.\[11\] There were no reports of recovery agitation for either the ketamine or the etomidate cohort in this trial. Other trials that have similar numbers of enrolled subjects to this trial have reported higher incidences of recovery agitation among subjects who received ketamine than those who received alternative PS pharmaceuticals, such as etomidate.\[3\] The lower incidence of dysphoric reactions in this trial may be a result of utilization of lower initial dosages of ketamine and etomidate with the subsequent dose titration to achieve PS.

**Limitations**

The lack of binding of physicians and nursing staff to the pharmacological sedative being administered limits this study by potentially introducing confirmation bias based on the clinicians’ prior experience with these medications. The utilization of preprocedure analgesia during the initial evaluation of the patients was not controlled for, other than the methodology stipulation that the pain medication not be co-administered with the procedural sedative, in terms of pain medication type, timing of administration, and overall quantity. The combination of opioid analgesics and procedural sedatives increase the likelihood of adverse respiratory events related to PS. Table 3 documents that the median time after opioid administration to ketamine and etomidate administration was 90 and 86 min, respectively. Furthermore, the need for additional sedative dose was not affected by administration of prior opioid analgesia for ketamine
11/22 (50%) or etomidate 8/23 (34.8%). Finally, the severity of the myoclonus was not assessed, which can result from either etomidate or ketamine. Because the severity of etomidate and ketamine-induced myoclonus is clinically variable ranging from minor to full body rigidity, the induced myoclonus is an important clinical variable to consider monitoring in any trial of PS because of the potential impact that myoclonus can have on the reduction of large, dislocated joints.[11]

CONCLUSION

Ketamine produced PS conditions for successful joint dislocation reduction that were adequate and equivalent when compared to etomidate. In terms of the secondary outcomes, the relative lack of myoclonus associated with ketamine utilization as compared to etomidate as well as the increased requirement for airway assistance and the risk of hypoxia observed in the etomidate cohort suggest that ketamine for PS is a superior agent to etomidate for the reduction of large dislocated joints.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Bellolio MF, Gilani WI, Barrionuevo P, Murad MH, Erwin PJ, Anderson JR, et al. Incidence of adverse events in adults undergoing procedural sedation in the emergency department: A systematic review and meta-analysis. Acad Emerg Med 2016;23:119-34.
2. Falk J, Zed PJ. Etomidate for procedural sedation in the emergency department. Ann Pharmacother 2004;38:1272-7.
3. Ruth WJ, Burton JH, Bock AJ. Intravenous etomidate for procedural sedation in emergency department patients. Acad Emerg Med 2001;8:13-8.
4. Strayer RJ, Nelson LS. Adverse events associated with ketamine for procedural sedation in adults. Am J Emerg Med 2008;26:985-1028.
5. Miner JR, Gray RO, Bahr J, Patel R, McGill JW. Randomized clinical trial of propofol versus ketamine for procedural sedation in the emergency department. Acad Emerg Med 2010;17:604-11.
6. Miner JR, Danahy M, Moch A, Biros M. Randomized clinical trial of etomidate versus propofol for procedural sedation in the emergency department. Ann Emerg Med 2007;49:15-22.
7. Aldrete JA, Kroulik D. A postanesthetic recovery score. Anesth Analg 1970;49:924-34.
8. Di Liddo L, D’Angelo A, Nguyen B, Bailey B, Amre D, Stanciu C. Etomidate versus midazolam for procedural sedation in pediatric outpatients: A randomized controlled trial. Ann Emerg Med 2004;48:433-40, 440.e1. Epub 2006 Apr 27.
9. Green SM, Roback MG, Kennedy RM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. Ann Emerg Med 2011;57:449-61.
10. Sener S, Eken C, Schultz CH, Serinken M, Oxsarac M. Ketamine with and without midazolam for emergency department sedation in adults: A randomized controlled trial. Ann Emerg Med 2011;57:109-14.e2.
11. Green SM. Research advances in procedural sedation and analgesia. Ann Emerg Med 2007;49:31-6.
12. Sacchetti A, Senula G, Strickland J, Dubin R. Procedural sedation in the community emergency department: Initial results of the ProSCED registry. Acad Emerg Med 2007;14:41-6.
13. Vardy JM, Dignon N, Mukherjee N, Sami DM, Balachandran G, Taylor S. Audit of the safety and effectiveness of ketamine for procedural sedation in the emergency department. Emerg Med J 2008;25:579-82.
14. Green SM, Roback MG, Krauss B, Brown L, McGlone RG, Agrawal D, et al. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: An individual-patient data meta-analysis of 8,282 children. Ann Emerg Med 2009;54:158-68.e1-4.
15. Krauss B, Green SM. Systemic analgesia and sedation for procedures. In: Channugam AS, Chudnofsky CR, Deblieux PMC, Mattu A, Swadron SP, editors. Roberts and Hedges’ Clinical Procedures in Emergency Medicine. 6th ed. Philadelphia: Elsevier Inc.; 2014. p. 2266-357.