Evidence-Based Clinical Update

No evidence for decreased incidence of aspiration after rapid sequence induction

[Aucune donnée probante concernant l'incidence réduite d'inhalation après l'induction en séquence rapide]

David T. Neilipovitz MD FRCPC,*† Edward T. Crosby MD FRCPC*

Purpose: The purpose of this structured, evidence-based, clinical update was to determine if rapid sequence induction is a safe or effective technique to decrease the risk of aspiration or other complications of airway management.

Source: In June 2006 a structured search of MEDLINE from 1966 to present using OVID software was undertaken with the assistance of a reference librarian. Medical subject headings and text words describing rapid sequence induction or intubation (RSI), crash induction or intubation, cricoid pressure and emergency airway intubation were employed. OVID's therapy (sensitivity) algorithm was used to maximize the detection of randomized trials while excluding non-randomized research. The bibliographies of eligible publications were hand-searched to identify trials not identified in the electronic search.

Principal findings: A total of 184 clinical trials were identified of which 163 were randomized controlled trials (RCTs). Of these clinical trials, 126 evaluated different drug regimens with 114 being RCTs. Only 21 clinical trials evaluated non-pharmacologic aspects of the RSI with 18 RCTs identified. A parallel search found 52 trials evaluating cricoid pressure (outside of the context of an RSI technique) with 44 classified as RCTs. Definitive outcomes such as prevention of aspiration and mortality benefit could not be evaluated from the trials. Likewise, the impact on adverse outcomes of the different components of RSI could not be ascertained.

Conclusion: An absence of evidence from RCTs suggests that the decision to use RSI during management can neither be supported nor discouraged on the basis of quality evidence.

Objectif : Cette mise à jour clinique structurée, basée sur des données probantes, avait pour objectif de déterminer si l'induction en séquence rapide est une technique sécuritaire ou efficace pour réduire le risque d'inhalation ou d'autres complications de prise en charge des voies respiratoires.

Source : Une recherche structurée de MEDLINE, allant de 1966 à nos jours, à l'aide du logiciel OVID, a été entreprise en juin 2006 avec l'assistance d'un bibliothécaire documentaliste. Les titres de sujets et les termes de textes médicaux décrivant l'induction ou l'intubation en séquence rapide (RSI), la « crash induction » ou intubation, la pression cricoïdienne et l'intubation des voies respiratoires en urgence ont été utilisés. L'algorithme de thérapie (sensibilité) d'OVID a servi à maximiser la détection d'études randomisées tout en excluant les recherches non randomisées. Les bibliographies des publications admissibles ont été cherchées manuellement pour identifier les études qui n'avaient pas été relevées par la recherche électronique.

Constatations principales : Au total, 184 études cliniques ont été identifiées, desquelles 163 étaient des études randomisées contrôlées (RCT). De ces études cliniques, 126 ont évalué différents régimes médicamenteux, 114 étant des RCT. Seules 21 études cliniques ont évalué des aspects non pharmacologiques de l'induction en séquence rapide, dont 18 étaient des RCT. Une recherche parallèle a mis en évidence 52 études évaluant la pression cricoïdienne (hors du contexte d'une technique de RSI), dont

From the Departments of Anesthesiology* and Critical Care Medicine,† The Ottawa Hospital and the University of Ottawa, Ottawa, Ontario, Canada.
   Address correspondence to: Dr. David T. Neilipovitz, Department of Anesthesiology, The Ottawa Hospital - Civic Campus, 1053 Carling Avenue, Ottawa, Ontario K1Y 4E9, Canada. Phone: 613-798-5555, ext. 14940; Fax: 613-761-5418;
E-mail: dneilipovitz@ottawahospital.on.ca

44 étaient classées comme RCT. Des pronostics définitifs, tels que la prévention d'une inhalation et les bienfaits par rapport à la mortalité, n'ont pas pu être évalués à partir des études. De même, l'impact sur les devenirs indésirables des différentes composantes de la RSI n'a pas pu être déterminé.

Conclusion : *Un manque de données probantes issues de RCT suggère que la décision d'utiliser la RSI pendant la prise en charge d'un patient ne peut être ni recommandée ni déconseillée sur la base de données probantes de qualité.*

Clinical context for literature review

While on duty in your hospital, you are called to manage the airway of a woman with a suspected subarachnoid bleed. She is 45 yr old and was previously well aside from a history of intermittent gastroesophageal reflux that she treated with antacids when symptomatic. Following your assessment, you determine that she requires emergent airway management with endotracheal intubation. You believe that tracheal intubation to isolate the respiratory from the gastrointestinal tract is considered to be the optimum method to prevent aspiration in at-risk patients. Limiting the time that the airway is unprotected during the induction of anesthesia is intuitively advisable and the practice of rapid sequence induction (RSI) with cricoid pressure is widely accepted as the standard of care in this setting.[1] As you contemplate the intervention, you wonder what evidence is available to measure the impact of RSI on the incidence of aspiration, how it should best be performed, and what is its risk-to-benefit profile. These questions are particularly relevant in light of the marked increase use of RSI in situations outside of the operating room. The purpose of this article is to review the current evidence base supporting the use of RSI and its various components in at-risk patients.

Methods

In June 2006 a structured search of MEDLINE from 1966 to present using OVID software was undertaken with the assistance of a reference librarian. The primary question was whether RSI had any impact on the incidence, severity or consequences of pulmonary aspiration. Medical subject headings and text words describing rapid sequence induction or intubation, crash induction or intubation, cricoid pressure and emergency airway intubation were employed (Appendix 1). OVID's therapy (sensitivity) algorithm was used to maximize the detection of randomized trials while excluding non-randomized research. The search was restricted to articles written in English or French. The bibliographies of eligible publications

TABLE I Questions regarding each component of rapid sequence induction (RSI)

1. Does RSI improve outcomes of emergency airway interventions compared with other airway management technique?
2. What is the preferred preoxygenation technique for RSI?
3. Should all drugs be rapidly administered during RSI?
4. Which is the best induction drug for RSI?
5. Which muscle relaxant should be used for RSI?
6. Should adjuvant drugs be routinely employed during RSI?
7. Should cricoid pressure be used routinely in all patients undergoing RSI?
8. Should bag-mask ventilation be routinely avoided during RSI?

were then hand-searched to identify trials not identified in the electronic search. The two investigators independently reviewed the abstracts of the trials to identify eligible research. Additional trials were identified with a similar technique to investigate and answer secondary questions (Table I).

It was readily apparent that any conclusions addressing the primary question would be inadequately supported due to the limited number of studies, most of which were retrospective in nature. As well, the working definition of RSI used by researchers was variable and many of its component parts were of unproven or questionable merits. Thus, we sought to determine whether RSI had measurable benefits beyond aspiration prophylaxis and whether or not a risk-benefit relationship of the component parts of the RSI could be assessed using a list of secondary questions (Table I). This search included studies conducted by non-anesthesiologists and patients in a non-operative setting. In fact, much of the available literature comes from these sources. Although how well this information can be translated to the operative setting may be debatable, the goal of this review was to assess RSI and the various aspects of this technique using the best available literature. The literature review did not exclude pediatric or obstetrical studies but the recommendations mainly pertain to the non-obstetrical adult population.

The definition of RSI is variable and inconsistent in the literature. Though originally described as rapid or crash *induction*,[2,3] RSI was called rapid sequence *intubation* in 182 of the 488 articles identified, and rapid sequence *induction* in 286, while 20 papers used both terms interchangeably (Appendix 1). For the purpose of our review and discussion, we defined RSI as it would be conventionally carried out by practicing
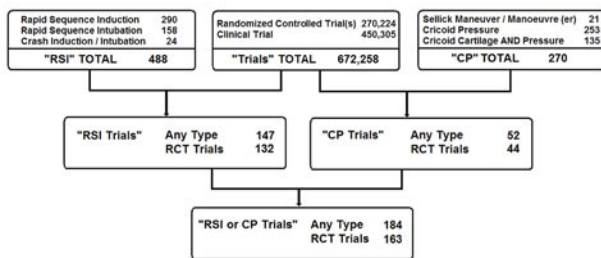
FIGURE Article search algorithm
Simplified algorithm to illustrate search technique for primary question and for cricoid pressure. RSI = rapid sequence induction; CP = cricoid pressure. Totals may not be the sum of individual components because of overlap.

anesthesiologists. The technique evaluated includes preoxygenation, rapid administration of predetermined doses of both induction and paralytic drugs, concurrent application of cricoid pressure, avoidance of bag and mask ventilation, and direct laryngoscopy followed by tracheal intubation.

One hundred and eighty-four eligible studies were identified using the described search strategy (Figure). There were 163 randomized controlled trials (RCTs). The number of clinical trials that evaluated different drug regimens was 126 with 114 being RCTs. Twenty-one clinical trials evaluated non-pharmacologic aspects of RSI with 18 RCTs identified. In a parallel search, there were 52 trials solely evaluating cricoid pressure (outside of the context of an RSI technique) with 44 RCTs identified. The literature was independently ranked by the authors using the Oxford Center for Evidence Based Medicine criteria for both level of evidence and strength of recommendation (Appendices 2 and 3).

Results

Aspiration in contemporary anesthetic practice – incidence and risk factors

Contemporary reports from analysis of large databases demonstrate an overall incidence of aspiration of 1:2,000–3,000 patients administered general anesthesia. Aspiration is more frequent in emergency (1:600–900 cases) than elective (1:3,000–4,000) procedures.[4–6] The factor most commonly associated with an increased incidence of aspiration is emergency surgery.[4–8] The risk of aspiration also increases directly with increasing ASA physical status; there is a sevenfold increase in risk as ASA status increases from I to IV or V.[6,8] Aspiration-associated morbidity

also increases with ASA status and most deaths due to aspiration occur in ASA IV and V patients. Other factors often cited as being associated with a higher incidence of aspiration perioperatively include a history of reflux and hiatus hernia, obesity, difficult intubation, extremes of age, reduced level of consciousness, underlying neurological diseases, gastric obstruction, ileus and bowel obstruction, the recent ingestion of a meal, and critical illness.[4,6–12]

Answering the primary question - the impact of RSI in aspiration prevention

The prevention of aspiration and its related complications by RSI is the primary outcome of interest as this is the reason for performing RSI. However, a number of factors make it difficult to employ aspiration as the outcome variable in studies assessing the impact of RSI. Aspiration is rare and very large numbers of patients would need to be studied to assess the impact of RSI on its occurrence. Morbidity and mortality would also be relevant outcomes for analysis but they are again uncommon and this analysis would also require very large numbers of patients to be studied. For practical reasons, surrogate outcomes, such as ease or success of intubation with RSI, are the most commonly reported, with successful tracheal intubation being the single most common outcome reported in clinical evaluations of RSI protocols. Further, many of the reports assessing RSI outcomes are simulations of RSI conducted in healthy elective populations who may not be representative of the cohorts of patients typically subjected to RSI.

Following our analysis of the literature it was apparent that there was no evidence available that would allow the following question to be answered: "Does RSI reduce either the incidence or the adverse consequences of aspiration during emergency airway management?" In fact, there is no study, randomized, controlled, blinded, or otherwise, that measures the impact of any intervention on the incidence of aspiration, nor is there likely to be a statistically meaningful study conducted on this issue. Assuming that the incidence of aspiration during emergency surgery is 0.15%,[13] a strategy that would simply reduce the incidence by 50% would require a study of approximately 50,000 patients to confirm that benefit (one-tailed hypothesis for improved outcome, $\alpha = 0.05$, $\beta = 0.20$). Thus, the strength of any recommendation favouring the use of RSI for the prevention of aspiration would be Grade D.

Since an evidence-based conclusion regarding the efficacy and safety of RSI as it relates to aspiration or mortality is not possible, the only literature evalua-

tion possible is a determination of the other potential benefits of RSI and a risk benefit assessment of the component parts of RSI as defined in Table I. Thus we now present the evidence addressing the secondary questions in an attempt to determine the evidence supporting the component part(s) of the RSI technique.

Answering the secondary questions

1. Does RSI improve the outcomes of emergency airway interventions compared to other airway management technique?

Only one prospective, randomized comparison of emergency tracheal intubations was found. Succinylcholine-assisted intubation and blind nasal intubation were compared in 52 drug intoxicated patients.[14] Surprisingly, induction or sedative drugs were not used in either group with only topical local anesthetic and vasoconstrictor used in the blind nasal group. One hundred percent of the succinylcholine-assisted direct oral intubations were successful, *vs* 65% of the blind nasal intubations. Mean time to intubation was shorter with succinylcholine and more of the patients in the succinylcholine-assisted group were intubated in < 120 sec. The number of intubation attempts and the complications recorded were also lower with succinylcholine-assisted intubation compared with nasal intubation.

There are three prospective, observational studies evaluating the outcomes between RSI, oral intubation with no sedation, oral intubation with sedation only, and/or blind nasal intubation in emergency room patients.[15–17] Two studies, including one multicentre analysis involving more than 6,000 patients, demonstrated a higher probability of success with RSI than with the other techniques, both on the first attempt and overall (estimated at 85% *vs* 75% for first attempt; and 92% *vs* 82% overall).[15,16] The third report demonstrated that the application of RSI was successful as a rescue technique in all 102 cases where tracheal intubation had failed after being attempted initially orally, with or without sedation, or by blind nasal intubation.[17] None of these three studies analyzed adverse events related to the technique of intubation. There is also one prospective observational study comparing the complications of emergency intubation with and without the use of neuromuscular blocking agents (NMBA).[18] Complications, both minor and severe, were more common in the patients who were managed without NMBA than in those who were paralyzed to facilitate intubation (78% *vs* 28%, *P* < 0.0001). Finally, there are three retrospective studies that assess the impact of the introduction of an RSI

protocol on intubation success in aeromedical transport.[19–21] All three reports documented an increase in the rate of intubation success with fewer intubation attempts and more rapid achievement of intubation with RSI compared with non-NMBA techniques.

Enthusiasm for widespread implementation of RSI protocols is however tempered by the sobering results of studies demonstrating increased mortality and morbidity. The San Diego Paramedic RSI Trial [22] prospectively evaluated the implementation of paramedic performed RSI in head injured patients compared with historic controls. Patients undergoing RSI performed by paramedics had increased mortality (33.0% *vs* 24.2%, *P* < 0.01) and lower incidence of a favourable outcome (45.5% *vs* 57.9%, *P* < 0.01) than controls managed without intubation. A retrospective assessment of the implication of a RSI protocol for air medical personnel by Falcone *et al.*[23] significantly increased transport times without improving intubation success rates. Ochs *et al.*[24] reported only an 84.2% intubation success rate after implementation of paramedic performed RSI. Although this success rate may be higher than with non-paralytic based techniques, it is debatable if the risks of paralysis are acceptable if there is a 15% failure rate.[25]

In the prehospital and emergency room settings, the use of RSI is more likely to result in successful intubation, in less time, and with fewer attempts than will oral or nasal intubation techniques that do not involve the administration of muscle relaxants (Grade B recommendation). However, there is conflicting evidence regarding the incidence of complications and patient outcomes with airway interventions in the prehospital setting and strong recommendations regarding the application of RSI or other techniques in the field cannot be supported at this time.

2. What is the preferred preoxygenation technique for RSI?

The purpose of preoxygenating a patient before RSI is to provide the maximum duration that a patient can safely tolerate apnea so that airway interventions may be undertaken at low threat to the patient, even in situations where unanticipated difficulties arise.[26] It is assumed that the conventional pattern of practice is to refrain from bag-mask ventilation of the lungs in the interval from induction of anesthesia until laryngoscopy and tracheal intubation is performed. A number of outcome variables have been utilized in studies assessing the effectiveness of various preoxygenation techniques. These outcomes include: highest arterial oxygen tension (P_aO_2) achieved; highest fractional end-tidal oxygen ($F_{ET}O_2$) concentrations achieved;

pulmonary nitrogen washout; and time to pulse oxygen desaturation (S_pO_2) to a critical endpoint (defined by the authors as *safe apnea time*). Although there is generally a correlation between oxygen stores and safe apnea times, the most meaningful outcome of interest appears to be the time to a critical oxygen desaturation threshold after induction of anesthesia. The preferred oxygenation technique would thus be the one that provides the longest safe apnea time and the literature was evaluated on this basis. Two strategies have been advocated to provide preoxygenation, tidal volume ventilation (TVV) for three to five minutes (TVV3 - TVV5) or inspiration of a number of deep or vital capacity breaths (DB) over a shorter period of time.

Two RCTs investigated whether preoxygenation before induction of anesthesia improved the tolerance to apnea.[27,28] Both demonstrated that preoxygenation prolonged the time to desaturation milestones and decreased the incidence of hypoxemia during the apneic intervals assessed. Five RCTs reported no difference on oxygen tensions generated with TVV three to five minutes compared with 4DB in 30 sec.[29–33] Four of these studies measured P_aO_2 as the outcome variable and one measured the $F_{ET}O_2$; safe apnea time was not assessed. However, three other RCTs dispute these results; each of these studies compared 4DB with TVV3 and measured safe apnea time.[34–36] All three reported that the time to desaturate to a given S_pO_2 was longer when patients were preoxygenated with TVV than with DB techniques. Two subsequent RCTs have compared the effect of more prolonged period of deep breathing (8DB) with 4DB and TVV.[32,33] Both concluded that 8DB was more effective than 4DB and as good or better than TVV3; one study measured safe apnea time[33] and the other reported $F_{ET}O_2$.[32]

Two RCTs have measured the impact of maximal exhalation on subsequent preoxygenation.[37,38] The measured outcomes were P_aO_2 and $F_{ET}O_2$, rather than safe apnea time but both studies reported better outcomes when preoxygenation was preceded by maximal exhalation.

The role of patient positioning during preoxygenation was assessed in two RCTs in morbidly obese patients.[39,40] Both studies measured safe apnea time after RSI and tracheal intubation and concluded that preoxygenation in a head-up position extends the safe apnea time in obese patients when compared with the supine position.

Preoxygenation of the patient before RSI provides substantial benefit with respect to increasing oxygen stores and extending the duration of safe apnea time following induction. Level 1b evidence supports the conclusion that TVV for at least three minutes or 8DB in 60 sec provides similar durations of safe apnea time (Grade A recommendation). Preoxygenation of obese patients in the head up position compared with the supine position also provides more prolonged safe apnea time after induction and is also supported by level 1b evidence (Grade A recommendation). The use of maximal exhalation before preoxygenation results in increased pulmonary oxygen concentrations; although no data are available regarding safe apnea time at present, it should be considered in cooperative patients (Grade B recommendation).

3. Should all drugs be rapidly administered during RSI?

Conscious patients with intact airway reflexes are able to protect their airways from gastric regurgitation but will not permit airway manipulation. As consciousness is lost (excluding normal sleep states), protection from gastric regurgitation is also lost. Further, most intravenous induction drugs and opioids reduce esophageal sphincter tone, thus increasing the risk of regurgitation.[41,42] The goal of RSI therefore is to achieve a state that allows tracheal intubation but minimizes the time that patients are at risk for regurgitation and aspiration. The generally accepted practice regarding drug administration during RSI is rapid administration of predetermined doses. This practice may result in drug over- or under-dosing precipitating hemodynamic instability. If the hemodynamic consequences of bolus drug administration are severe, they may result in adverse outcomes negating any potential benefit of RSI.

There are no data that allow for a comparison of the risks of a more prolonged interval of reduced airway reflexes before tracheal intubation is achieved resulting from titrated drug administration *vs* the potential for hemodynamic instability resulting from rapid drug administration. Thus, level 5 evidence would suggest that rapid drug administration should be restricted to circumstances and patients with a high risk of aspiration and low potential for untoward responses to rapid drug administration (Grade D recommendation).

4. Which is the best induction drug for RSI?

The ideal induction drug for RSI would be a short-acting agent, free of adverse hemodynamic effects, effective at blunting the sympathetic response to intubation, that reliably ensures anesthesia and amnesia, improves the grade of laryngoscopy in the setting of inadequate paralysis, and is free of other adverse effects. A review of the literature indicates clearly that a single ideal induction drug for all RSI situations does not exist. All presently available induction drugs

have problems or limitations associated with their use. Hypotension, due in large part to the rapid administration of induction drugs, has become the most common complication after emergent intubation.[15,43–45] The challenge of selecting the best induction drug for RSI is further confounded by the marked heterogeneity of patient characteristics and clinical scenarios. Therefore, the evidence was evaluated to determine not only if one drug is best overall but also how induction drugs are presently used and if certain agents may be preferable in certain circumstances to others.

A survey of anesthetists in the UK suggests that thiopental, propofol and etomidate are the induction agents most commonly used for an RSI.[46] The National Emergency Airway Registry phase 2 (NEAR 2) reported that US emergentologists preferred the use of etomidate for RSI (69% of cases) with midazolam and fentanyl the next most commonly used induction drugs (16% and 6% respectively).[15] This prospective, multicentre registry initiated in January 1996 provides observational information on airway interventions performed in affiliated emergency departments in the United States, Canada and Singapore. Observations regarding RSI from NEAR 2 report successful intubation using RSI was achieved in 98.5% of patients with 83% success on initial attempt and 12% on the second.[15] Only 9.1% of patients received more than one drug labelled as *sedative* by the NEAR 2 investigators, although two-thirds of patients also received lidocaine.[15] The use of thiopental, methohexital and propofol were independent predictors of successful intubation on the first attempt.[15] Conversely, etomidate, ketamine and midazolam were less likely to be associated with successful single attempt intubations. The reported difference was attributed to a deeper plane of anesthesia achieved with the barbiturates and propofol that complemented incomplete muscle relaxation although no supporting evidence for this attribution was provided.[15]

Studies directly comparing induction drugs for RSI using real emergency conditions are limited both in number and format. The best available study is the SHRED study, a blinded RCT comparing the use of thiopental (5 mg·kg^{-1}), midazolam (0.1 mg·kg^{-1}) and fentanyl (5 µg·kg^{-1}) in 86 patients requiring intubation in the emergency department.[47] Outcomes were mortality, time until intubation, ease of intubation and hemodynamic stability during the procedure. Induction doses were reduced by 50% if patients were considered to be 'unstable' (heart rate > 100 min^{-1} or systolic blood pressure < 90 mmHg). Despite an overall 24% in-hospital mortality, no differences between groups were found, probably a reflection of the small

sample size. The hemodynamic profile was most stable in the fentanyl group but significant hypotension still occurred in 21 of 86 patients. The thiopental group had the largest decrease in blood pressure (mean of 38 mmHg) but the highest rate of rapid intubation (intubation within 300 sec from start of protocol and within three attempts) compared with the two other agents. The midazolam-treated group was more likely to be deemed inadequately sedated by physicians compared with either the fentanyl or thiopental groups but this difference did not reach significance (6 *vs* 2 *vs* 1; *P* = 0.08). Therefore, level 2b evidence from NEAR and SHRED would suggest that thiopental is the single best overall induction drug (Grade C recommendation). Midazolam does not appear to have clear indications and its role as a sole induction agent for RSI must be questioned (Grade B recommendation).

Analysis of the features of the various induction drugs employed in RSI techniques, with respect to the characteristics of an ideal induction drug outlined above, yields the following results. With the possible exception of midazolam and fentanyl, the commonly used induction drugs including thiopental, propofol, etomidate, ketamine and methohexital all have reasonably short durations of action. Duration of action between these medications are unlikely to be different clinically and thus would not likely influence choice of induction agent for RSI. Likewise, there is insufficient evidence to determine if any of the induction drugs are better or worse for ensuring reliable amnesia or anesthesia. However, fentanyl is an unreliable drug for amnesia and anesthesia and thus cannot be recommended as a sole induction agent for RSI (Grade D recommendation).

Hemodynamic effects of the various induction drugs differ considerably. Etomidate induces minimal hemodynamic changes even in the setting of preexisting hypotension or significant cardiovascular disease.[48–51] Significant decreases in blood pressure occur with thiopental although it is less apt to cause hypotension than propofol.[52–55] Ketamine's stimulating effect on sympathetic output minimizes the hypotension with its use and provides more favourable hemodynamic effects compared with the other induction drugs with the exception of etomidate. Although hypotension and other life threatening complications are not prevented by etomidate use,[50,56,57] etomidate is the preferred drug for patients with limited cardiac reserve or in hemodynamic compromise (Grade C recommendation). Concerns surrounding etomidate's suppression of adrenal cortical function however remain[58–60] and caution is advised with avoidance in patients at risk for sepsis (Grade D recommendation).

The ability to effectively blunt the hypertensive reflex to intubation is particularly important in patients at risk for increased intracranial pressure (ICP). Administration of etomidate does not effectively blunt this reflex.[15,48,61] Barbiturates possess cerebral protective effects, but do not reliably block the hypertensive response to intubation.[15,53,62] Midazolam has neither effective sympathetic blunting effects nor cerebroprotective effects and should not be used in these circumstances.[15,63] Ketamine increases ICP by a small amount, and it should be used with caution in patients at risk for neurologic injury. Propofol, as a single agent, is the most effective at suppressing the hypertensive response to intubation but it does not do so in a completely reliable fashion.[64,65] No induction agent given alone is adequate for patients with increased ICP who are at risk for a hypertensive response to intubation (Grade C recommendation).

If complete muscle paralysis is provided, the effect of an induction drug on the laryngoscopy grade becomes a non-issue. However, in the setting of incomplete paralysis, added blunting of airway and laryngeal reflexes by an induction drug may improve laryngoscopy grade and intubation success. Ketamine tends to preserve these reflexes while etomidate and the barbiturates do not reliably blunt them.[15,53,62] Conversely, propofol is the most effective at blunting airway reflexes and is the preferred induction drug for improving laryngoscopy grade.[47–49,52,64,66–72] Propofol is the preferred induction drug when a non-depolarizing NMBA is used and the use of propofol is not otherwise contraindicated (Grade A recommendation).

5. Which muscle relaxant should be used for RSI?

Succinylcholine has been the conventional choice for muscle relaxant for RSI. Motivated by concerns regarding the potential adverse effects of succinylcholine, a number of authors have assessed whether a non-depolarizing NMBA could provide intubating conditions in a similar time frame for RSI as succinylcholine but in the absence of adverse effects. Advocates for succinylcholine use during RSI primarily base their support on two factors: 1) its speed of onset; and 2) the perception that its duration of action is sufficiently short to allow recovery before oxygen desaturation in the event of failure to intubate the trachea. The validity of this latter assumption was, until recently, not tested.

The dose of succinylcholine necessary for *excellent* intubation conditions within 60 sec during simulated RSI was determined in a RCT which enrolled patients electively presenting for general anesthesia in non-urgent conditions.[73] Succinylcholine 0.39 mg·kg⁻¹ and 1.6 mg·kg⁻¹ provided *excellent* intubating conditions in 50% and 80% of patients studied at 60 sec, respectively. The dose required to provide *acceptable* intubation conditions in 95% of patients within 60 sec was also determined in a similar RCT.[74] Succinylcholine 0.24 mg·kg⁻¹ and 0.56 mg·kg⁻¹ provided *acceptable* intubating conditions in 90% and 95% of patients studied at 60 sec, respectively. Reducing the dose of succinylcholine from 1.0 to 0.60 mg·kg⁻¹ decreased its duration of action by more than 90 sec, but onset times did not differ and intubation conditions were similar with all doses ≥ 0.5 mg·kg⁻¹.[75,76] Apnea time, however was dose-dependent and the time to regular spontaneous reservoir bag movements was shorter in patients who received 0.6 mg·kg⁻¹ (4.0 min) compared with patients given 1 mg·kg⁻¹ (6.16 min).[76]

The short duration of action of succinylcholine compared with non-depolarizing NMBAs has been considered by some to be an advantage should unexpected difficulties with laryngoscopy or ventilation be encountered. The hypothesis is that patients will recover from the effects of succinylcholine and resume spontaneous ventilation before the onset of critical hemoglobin desaturation [defined as a pulse oximetry (S_pO_2) reading that is ≤ 80% and decreasing][77] thus avoiding the consequences of a cannot-intubate, cannot-ventilate scenario. Until recently, this hypothesis had not been tested with scientific rigor. Recovery from the effects of succinylcholine has been defined with a number of measures including a return of some fraction of the twitch response at the adductor pollicis, onset of diaphragmatic movement, recovery of spontaneous respiration with either reservoir bag movement or recordable end-tidal CO_2, and eye opening. The recovery of spontaneous breathing has been termed functional recovery and is estimated to occur at about the same time as 50% recovery of twitch height; this takes an average of 8.5 min after a dose of succinylcholine 1 mg·kg⁻¹ provided that the airway is patent.[77] It is the authors' opinion that functional recovery is the most meaningful clinical measure of recovery and the literature was evaluated on that basis. Critical desaturation will occur more quickly in a number of situations including obesity, increased oxygen consumption, inadequate preoxygenation, critical illness and an obstructed airway.[77,78]

One observational study enrolling 12 healthy volunteers assessed the time to recovery and the impact on hemoglobin saturation with apnea following the administration of succinylcholine 1 mg·kg⁻¹.[79] Following preoxygenation to a $F_{ET}O_2 > 90\%$, induction of anesthesia and administration of succinylcholine 1

mg·kg^{-1}, the facemask was removed and the airway left unsupported, simulating failed ventilation. In four volunteers (25%), the time to recovery of spontaneous respiration averaged seven minutes (five, seven, eight, nine minutes) and oxygen saturation (S_pO_2) deteriorated to < 80% in all of them, requiring airway interventions. Two RCTs have assessed both the time to recovery and the impact on hemoglobin saturation following the administration of succinylcholine 1 mg·kg^{-1}.[73,80] In one RCT, the facemask was removed during apnea and the airway was left unsupported.[73] The time to spontaneous diaphragmatic movement was 4.7 ± 1.3 min and the S_pO_2 deteriorated to < 90% in 85% of the patients. In the second RCT, the airway was supported and the facemask remained in place and was connected to an oxygen source during the apneic period.[80] The average times to diaphragmatic movement, reservoir bag movement, and a recordable ETCO$_2$ were 4.66 min, 4.7 min, and 5.06 min, respectively; in 11% of patients, S_pO_2 decreased to ≤ 90% before resumption of spontaneous ventilation.

To address the concern that critical desaturation may occur in some patients after administration of succinylcholine 1 mg·kg^{-1} if airway management difficulties are encountered, four RCTs have evaluated the effects of smaller doses of succinylcholine (< 1 mg·kg^{-1}) on both intubating conditions and recovery; not all have used functional recovery as the index of recovery.[75,76,81] One RCT compared the impact on intubating conditions and recovery when administering succinylcholine in doses of 0.4, 0.6, and 1.0 mg·kg^{-1}.[75] The 0.6 and 1.0 mg·kg^{-1} doses produced similar degrees of relaxation but the mean time to twitch recovery of 90% was prolonged in the 1.0 mg·kg^{-1} dose group (9.3 ± 1.2 min) compared with the 0.6 mg·kg^{-1} dose group (7.6 ± 1.6 min). The authors acknowledged considerable overlap in the individual recovery times between the two groups and functional recovery was not measured. Two RCTs comparing functional recovery after doses of approximately 0.6 mg·kg^{-1} and 1.0 mg·kg^{-1} have yielded conflicting results.[76,81] In the first study enrolling 20 patients in each group, the average time to spontaneous diaphragmatic movement was not different in patients who had received 0.56 mg·kg^{-1} (4.8 ± 2.5 min) compared with 1.0 mg·kg^{-1} (4.7 ± 1.3 min).[81] In the second RCT, enrolling 23 patients in each group, the average time to spontaneous diaphragm movement was longer in patients receiving 1.0 mg·kg^{-1} (5.3 ± 0.8 min) than in those receiving 0.6 mg·kg^{-1} (4.0 ± 0.5 min).[76] The time to resumption of spontaneous respiration as denoted by a well-formed ETCO$_2$ trace took an average of 35 sec beyond resumption of

spontaneous diaphragm movement in the 0.6 mg·kg^{-1} group and 54 sec in the 1.0 mg·kg^{-1} group.

The use of non-depolarizing NMBA has also been advocated to eliminate succinylcholine-related complications in RSI; the bulk of the current literature in this regard addresses the use of rocuronium. The majority of studies comparing succinylcholine and rocuronium used the achievement of good or excellent conditions and the occurrence of failed intubation as their principal outcome variables. However, failed intubation has not been common in patients treated with either succinylcholine or rocuronium and differences between the groups in this regard are rarely reported. A meta-analysis evaluating whether rocuronium provided intubating conditions equivalent to succinylcholine during RSI intubation included 26 RCTs and controlled clinical trials comparing rocuronium ≥ 0.6 mg·kg^{-1} and succinylcholine ≥ 1.0 mg·kg^{-1}.[69] Succinylcholine was more likely than rocuronium to provide *excellent* intubating conditions although there was no difference when the less stringent endpoint of *acceptable* (excellent or good, not failed) conditions were measured. Again, there were few failed intubations in the studies, and no differences between the two agents in this regard were reported. Conditions were also more likely to be equivalent in studies that employed propofol for induction. The conclusions were that succinylcholine provided *excellent* intubating conditions more often than rocuronium 0.6–0.7 mg·kg^{-1} but rocuronium doses of 0.9–1.2 mg·kg^{-1} were more likely to be equivalent to succinylcholine.[69] Three subsequent RCTs provide additional support for these conclusions regarding the use of rocuronium for RSI.[52,67,82]

Level 1a evidence support the conclusion that the paralytic drug of choice for RSI should continue to be succinylcholine as it is more likely to provide *excellent* intubating conditions in a shorter time frame than does rocuronium (Grade A recommendation). A dose ≥ 1 mg·kg^{-1} is required to ensure *excellent* intubating conditions; doses ≤ 0.5 mg·kg^{-1} are more often associated with poor intubating conditions (level 1b). A dose ≥ 0.6 mg·kg^{-1} is associated with a similar measure of *acceptable* conditions as is 1 mg·kg^{-1} and may result in shorter apnea times but the evidence is conflicting; the duration of effect of either may result in hypoxemia if the patient cannot be intubated or oxygenated through bag-mask ventilation. Rocuronium, at a dose ≥ 0.6 mg·kg^{-1}, is as likely to provide *acceptable* conditions when compared to succinylcholine but will less frequently provide *excellent* conditions; it is an acceptable alternative to succinylcholine for RSI if the latter is contraindicated or unavailable (Grade A rec-

ommendation). Intubation conditions achieved with rocuronium are better if propofol is used and the use of propofol is advocated if there are no contraindications to its use (Grade A recommendation).

6. Should adjuvant drugs be routinely employed during RSI?

In addition to induction and paralytic drugs, several different drugs have been advocated for use during RSI. These so-called *adjuvant* drugs are typically used to blunt the potential for autonomic reflexes in response to intubation and to reduce both the dose and the adverse effects of the larger doses of the primary induction agent. Of the many different adjuvant drugs available, the administration of opioids, lidocaine, and esmolol are the most commonly described.[46,47] Opioids appear to improve control of intraocular, intracranial and hemodynamic variables including attenuation of the hypertensive response to intubation.[64,83] Although not appropriate as a sole induction drug because of the unreliable amnestic and general anesthetic effects,[84] fentanyl use in the SHRED study provided the most neutral hemodynamic profile post-intubation.[15] Lidocaine administered intravenously prior to intubation is reputed to diminish airway reactivity, the hypertensive response to intubation, and the rise in ICP.[85–87] However, three RCTs failed to demonstrate an effect for lidocaine in attenuating the cardiovascular responses to intubation in patients undergoing induction of general anesthesia.[88–90] As well, the evidence available on the efficacy of lidocaine for intubation in status asthmaticus or head injury does not support its use in these scenarios.[87,91,92] Esmolol is a short acting beta-blocker that appears to be more effective than lidocaine or fentanyl for suppressing the pressor response to intubation.[88,93,94]

Level 1b evidence therefore supports the use of adjuvant drug including esmolol or opioids during RSI when a clinical assessment dictates a role (Grade A recommendation). Although lidocaine can suppress the cough reflex and may have an induction agent sparing effect,[95,96] level 2 evidence does not support its routine use for RSI (Grade B recommendation).

7. Should cricoid pressure be used routinely in all patients undergoing RSI?

Application of cricoid pressure (CP) or Sellick's maneuver is considered to be an integral component of RSI.[1,97,98] Surprisingly, despite its wide acceptance, the efficacy and effectiveness of CP in preventing aspiration has remained unproven and spawned debate as to its role in emergency airway management.[1,99–102]

Evidence affirming a role for CP in preventing aspiration is unavailable.[1,98,100] Its continued use during RSI is based on anecdotal evidence and expert opinion; it has likely achieved the status of standard of care and it is unlikely that a large RCT will be forthcoming that assesses its role in high-risk patients.

In the original report assessing the anatomic basis of CP using contrast CT scanning, it was reported that only part of the esophageal lumen was obliterated when pressure was applied, even though the cricoid cartilage and cervical vertebrae were approximated.[102] In a subsequent report, cervical computed tomography scans of normal patients were reviewed to assess the anatomic relationships between the cricoid cartilage and the esophagus; lateral esophageal displacement relative to the cricoid cartilage was evident in half (25 of 51) of the patients studied; 64% of these individuals had esophageal displacement beyond the lateral border of the cricoid cartilage.[103] A later evaluation in 22 volunteers using magnetic resonance imaging reported that the esophagus was laterally displaced relative to the cricoid cartilage in 52.6% of the subjects; this proportion increased to 90.5% with the application of CP.[104] Lateral laryngeal displacement and airway compression were observed in 66.7% and 81% of the patients, respectively, with the application of CP. The potential for lateral positioning and displacement of the esophagus relative to the cricoid cartilage possibly explains a number of case reports where, despite seemingly appropriate application of CP during RSI, regurgitation and aspiration occurred nevertheless.

Cricoid pressure may interfere or prevent ventilation of the lungs with a mask and a bag as well as placement and ventilation with a laryngeal mask airway.[105–110] Although perhaps not a major clinical issue if bag and mask ventilation is to be withheld in the induction-intubation interval, there is also evidence that maintenance of airway patency prolongs the time to desaturation even in the absence of ventilation.[78] At 44 N of applied pressure, cricoid deformation occurs in 90% of patients and 50% have airway occlusion at the level of the cricoid; 43% have cricoid occlusion at 30 N and 23% at 20 N.[111] Associated difficulty in ventilation occurs in 50% of patients. According to some RCTs, the application of CP increases the difficulty experienced during airway management with the direct laryngoscope, the lightwand, and the flexible fibreoptic bronchoscope. Less difficulty has been reported with the Bullard laryngoscope.[112–114] Although CP has been reported to make airway management more difficult, Turgeon *et al.*[115] were unable to confirm such an effect in an RCT of 700 patients. The view at laryngoscopy and the incidence of failed

intubation at 30 sec was not different in control and cricoid pressure groups.

Despite the presence of only level 5 evidence to support a role for CP during RSI, its status as a standard of care ensures its continued and routine use during RSI (Grade D recommendation). Because application of CP may result in airway obstruction and increase the likelihood of difficulty during airway management, its use is advocated primarily in situations where the risk of aspiration is high. Application of lowered pressures or release (partial or complete) of CP should be considered if it is deemed to be obstructing the airway, interfering with bag-mask ventilation, or interfering with tracheal intubation. This appears to be a supportable practice based on the same evidence (Grade D recommendation).

8. Should bag and mask ventilation be routinely avoided during RSI?

The practice of routinely avoiding bag and mask ventilation during RSI is based on the hypothesis that its use would result in gastric insufflation and increase the risk of regurgitation and subsequent aspiration. Avoidance of bag and mask ventilation does hasten the onset and severity of hypoxemia during RSI particularly in the setting of failed intubation. If concurrent application of CP results in some degree of airway obstruction, physiological modeling studies suggest that the onset of hypoxemia will occur earlier in the apneic interval.[78] As well, some critically-ill patients will not tolerate any duration of apnea without further desaturation.[116] Finally, routinely avoiding bag and mask ventilation will subject a significant proportion of patients to hypoxemia during the apneic interval resulting from succinylcholine administration in the setting of failed intubation. Although there is a concern that bag and mask ventilation during the interval between induction and intubation may result in gastric distension and increase the risk for aspiration, there are no data to support this contention. There is an established relationship between the airway pressures required to ventilate the lungs and those which force air into the stomach.[117] During mask ventilation without CP, airway pressures below 15 cm H_2O rarely cause stomach inflation but pressures greater than 25 cm H_2O do so in most patients.[118] Application of CP increases the maximum pressure reached during mask ventilation, without air entering the stomach, to about 45 cm H_2O.[118] Application of CP also reduces gastric insufflation but may result in difficulty with ventilation in some patients and these patients tended to have more air in the stomach than those patients considered easy to ventilate.[119]

Hemoglobin desaturation will occur in a proportion of patients before recovery from succinylcholine-induced apnea if airway management difficulties are encountered during RSI; a fraction of patients will be at risk regardless of the dose of succinylcholine administered and this fraction is likely increased in obese or critically ill patients (level 1b evidence). There is no evidence to support the avoidance of bag-mask ventilation during the apneic interval after the induction of anesthesia to decrease the incidence of aspiration (Grade B recommendation). Keeping peak airway pressures below 15–20 cm H_2O will allow for ventilation without increasing the risk of air entry into the stomach (Grade C recommendation). Application of CP reduces the likelihood of gastric insufflation in most patients during bag and mask ventilation during RSI but may complicate airway management (Grade C recommendation).

Conclusions (Table II)

Aspiration of gastric contents is an uncommon complication of emergency airway management. The recommended approach to prevent aspiration and other complications during emergency airway management is the use of an RSI technique. The question of when to use or not use RSI could not be definitively answered from a review of the literature. Intuitively, patients at moderate to high risk for aspiration should be considered for an RSI technique (Grade C recommendation). If there are concerns about the ability to successfully ventilate the lungs or intubate the trachea of the patient, then avoiding RSI is prudent. The use of induction drugs and particularly NMBAs improve the success of tube placement during tracheal intubation (Grade B recommendation). Since hypotension is the most common complication after RSI, the decision to employ rapid administration of induction drugs should be carefully considered, especially in vulnerable patients, and it is a justified modification to use alternative strategies such as incremental drug administration despite a theoretical increase in the risk for aspiration (Grade D recommendation). The use of RSI as a rescue airway management strategy in the setting of failed intubation from other airway management techniques cannot be supported by existing evidence (Grade D recommendation).

Adequate preoxygenation is most rapidly achieved by TVV for at least three minutes or 8DB using fresh gas flow of 5 L·min^{-1} (Grade A recommendation). The routine practice of rapid administration of drugs is not recommended except in situations when the risks of aspiration are exceptionally high (Grade D recommendation). Review of the evidence does not

TABLE II Recommendations for rapid sequence induction parameters

RSI Parameter	Recommendation	Description
General considerations	Grade B	RSI increases intubation success *vs* non-NMBA techniques
	Grade C	RSI, whole or in part, be used if moderate-high aspiration risk
	Grade D	RSI may reduce aspiration risk
	Grade D	In patients at risk, alternative strategies to avoid RSI-related complications are acceptable
	Grade D	RSI as a rescue strategy cannot be supported by existing evidence
Preoxygenation		
	Grade A	Most rapid preoxygenation is TVV 3+ or 8 DB in 60 sec using FGF of 5 LPM
	Grade A	Preoxygenation of obese patients is best performed in the head up position
	Grade B	Maximal exhalation before preoxygenation should be used
Drug administration	Grade D	Rapid drug administration can be eliminated
Induction drugs	Grade A	Propofol is preferred when a non-depolarizing NMBA is used
	Grade B	Midazolam alone is not an appropriate induction drug for RSI
	Grade C	Thiopental appears to be the single best overall drug
	Grade C	Etomidate is preferred if there is limited cardiac reserve or hemodynamic compromise
	Grade C	No drug alone is adequate if increased ICP or risk of hypertensive response to intubation
	Grade D	Etomidate should be avoided in patients at risk for sepsis
	Grade D	Fentanyl alone is not an appropriate induction drug for RSI
Muscle relaxants	Grade A	The NMBA of choice for RSI is succinylcholine at a dose of ≥ 0.6 mg·kg^{-1}
	Grade A	Rocuronium (≥ 0.6 mg·kg^{-1}) is best available alternative to succinylcholine
Adjuvant drugs	Grade A	Esmolol or opioid use during RSI is acceptable if clinical assessment dictates a role
	Grade B	Evidence does not support the routine use of lidocaine for RSI
Cricoid pressure	Grade C	CP reduces gastric insufflation during bag and mask ventilation during RSI
	Grade D	Routine CP use is a benign practice and should be used during RSI
	Grade D	Reduction or full release of CP is acceptable if it is interfering with airway management
Bag and mask ventilation	Grade B	Routine avoidance of bag and mask ventilation is not recommended
	Grade C	Keep airway pressures ≤ 20 cm H$_2$0 allows for safe ventilation and oxygenation

RSI = rapid sequence induction; TVV = tidal volume ventilation; DB = deep vital capacity breaths; FGF = fresh gas flow; LPM = L·min^{-1}; CP = cricoid pressure; NMBA = neuromuscular blocking agent.

allow recommendation of a single induction agent for all situations. Etomidate is preferable for non-septic hypotensive patients and those with limited cardiac reserve requiring RSI (Grade C recommendation). Propofol is the preferred induction drug when a non-depolarizing NMBA is used (Grade A recommendation). The NMBA of choice for RSI is succinylcholine at a dose of at least 0.6 mg·kg^{-1} (Grade A recommendation). Rocuronium, at a dose ≥ 0.6 mg·kg^{-1}, is the best alternative to succinylcholine for RSI and the use of propofol should be considered if rocuronium is to be used (both Grade A recommendations). The evidence supporting a role for the routine use of esmolol and short acting opioids in RSI is incomplete and prevents strong affirmative recommendations. The best available evidence does not support a role for lidocaine as an adjuvant drug for RSI (Grade B recommendation). Due to its low risk but potential benefit, the routine use of CP would appear to be a benign practice and it continues to be recommended (Grade D recommendation). Reduction of applied pressures during CP or its release if it is deemed to be interfering with airway management is acceptable (Grade C recommendation). The routine practice of avoiding

mask-bag ventilation after the induction of anesthesia to decrease the incidence of aspiration is not recommended (Grade B). Providing bag and mask ventilation while maintaining airway pressures below 15–20 cm H$_2$0 during ventilation allows for oxygenation without increasing the risk of gastric air entry and is recommended (Grade C recommendation).

Recommendations: reapplying evidence to the case

After reviewing the literature, you (our physician described in the clinical scenario) conclude that the RSI technique is not necessary for all patients. In regards to the patient with the suspected subarachnoid bleed however, you decide that application of an RSI technique would likely be beneficial for her. Although her history of reflux likely has a negligible effect on increasing her risk of aspiration, the non-fasting state, her critical illness, decreased level of consciousness and increased ICP all do increase the risk, thus supporting the use of RSI.

You decide to preoxygenate her for at least three minutes of TVV since she will not be compliant to perform a DB technique. The risk of bag and mask

ventilation in the induction-intubation interval is negligible but may provided substantial benefit to this particular patient. You therefore elect to provide bag and mask ventilation after induction as this will help oxygenate her and avoid an increase in ICP due to an increase in P_aCO_2. You decide to use CP and instruct your assistant in placement and application pressure. However, you will ask CP to be reduced or removed if you believe it is interfering with maintenance of the airway or with airway interventions.

Attenuation of the pressor response to intubation is critical but so is avoidance of hypotension in this case. Rapid bolus administration of the induction drug may cause hypotension to threatening levels thus a reasonable approach may be to have a slower titration of the induction drug followed by a bolus administration of a NMDA. You choose to add an adjuvant drug such as fentanyl to attenuate the pressor response to intubation. The theoretical concerns of a slight increase in ICP with succinylcholine are secondary compared with the guarantee of avoiding coughing and the excellent intubation conditions that succinylcholine provides and you elect to administer succinylcholine as the NMDA.

The selective use of RSI, with or without modification of any of its components, awaits further research to provide a more evidence-based approach to guide its use. Until then, the best strategy would appear to use an evidence-based evaluation of each aspect of an RSI technique to determine its applicability in the situations where it is to be intended.

APPENDIX 1 Search results

Database: OVID MEDLINE(R) < 1966 to July Week 1 2006 >
Search strategy:*
1   (rapid adj1 sequence intubation).tw. (158)
2   (rapid adj1 sequence induction).tw. (290)
3   rapid tracheal intubation.tw. (37)
4   (crash adj1 (induction or intubation)).tw. (24)
5   or/1-4 (488)
6   randomized controlled trial.pt. (228355)
7   random$ tw (358104)
8   clinical trial.pt. (450305)
9   clinical trial/ (450305)
10   or/6-9 (649631)
11   exp Randomized Controlled Trials/ (46552)
12   6 or 11 (270224)
13   1 or 2 or 3 (467)
14   10 or 11 (672258)
15   13 and 10 (144)

16   from 15 keep 1-144 (144)
17   4 and 10 (4)
18   5 and 10 (147)
19   from 18 keep 1-147 (147)
20   (sellick$ adj (maneuver or manoeuvre or manoeuver)).tw. (21)
21   cricoid pressure.ti. (155)
22   cricoid pressure.tw. (246)
23   *cricoid cartilage/ (887)
24   pressure/ (43321)
25   23 and 24 (135)
26   20 or 21 or 22 or 25 (270)
27   10 and 26 (52)
28   6 or 7 or 11 (449330)
29   5 and 28 (132)
30   from 29 keep 1-132 (132)
31   28 and 26 (44)
32   from 31 keep 1-44 (44)

*The format of each line is: search number, key words and number of articles found in parentheses. tw = text word; pt = publication type; ti = title; random$ = truncation.

APPENDIX 2 Levels of evidence

Level	Supporting evidence
1a	Systematic review (with homogeneity) of randomized controlled trials
1b	Randomized controlled trials (with narrow confidence intervals)
2a	Systematic review (with homogeneity) of cohort studies
2b	Cohort study or low quality randomized controlled trial
3a	Systematic review (with homogeneity) of case-controlled studies
3b	Case-controlled studies
4	Case-series or poor quality cohort and case-controlled studies
5	Expert opinion

Adapted from Oxford Centre for Evidence Based Medicine. http://www.cebm.net/levels_of_evidence.asp#notes.

APPENDIX 3 Grades of recommendations

Grade	Supporting evidence
A	Consistent level 1 studies
B	Consistent level 2 or 3 studies, extrapolation from level 1 studies
C	Level 4 studies or extrapolation from level 2 or 3 studies
D	Level 5 or inconsistent studies at levels 1-4

Adapted from Oxford Centre for Evidence Based Medicine. http://www.cebm.net/levels_of_evidence.asp#notes.

References

1 *Brimacombe JR, Berry AM*. Cricoid pressure. Can J Anaesth 1997; 44: 414–25.

2 *Morton HJ, Wylie WD*. Anaesthetic deaths due to regurgitation or vomiting. Anaesthesia 1951; 6: 190–201, 205.

3 *Woodbridge PD*. "Crash induction" for tracheal intubation. JAMA 1967; 202: 845.

4 *Warner MA, Warner ME, Weber JG*. Clinical significance of pulmonary aspiration during the perioperative period. Anesthesiology 1993; 78: 56–62.

5 *Mellin-Olsen J, Fasting S, Gisvold SE*. Routine preoperative gastric emptying is seldom indicated. A study of 85,594 anaesthetics with special focus on aspiration pneumonia. Acta Anaesthesiol Scand 1996; 40: 1184–8.

6 *Olsson GL, Hallen B, Hambraeus-Jonzon K*. Aspiration during anaesthesia: a computer-aided study of 185,358 anaesthetics. Acta Anaesthesiol Scand 1986; 30: 84–92.

7 *Kluger MT, Short TG*. Aspiration during anaesthesia: a review of 133 cases from the Australian Anaesthetic Incident Monitoring Study (AIMS). Anaesthesia 1999; 54: 19–26.

8 *Warner MA, Warner ME, Warner DO, Warner LO, Warner EJ*. Perioperative pulmonary aspiration in infants and children. Anesthesiology 1999; 90: 66–71.

9 *Mort TC*. The incidence and risk factors for cardiac arrest during emergency tracheal intubation: a justification for incorporating the ASA guidelines in the remote location. J Clin Anesth 2004; 16: 508–16.

10 *Lockey DJ, Coats T, Parr MJ*. Aspiration in severe trauma: a prospective study. Anaesthesia 1999; 54: 1097–8.

11 *Hardoff R, Sula M, Tamir A, et al*. Gastric emptying time and gastric motility in patients with Parkinson's disease. Mov Disord 2001; 16: 1041–7.

12 *Heyland DK, Tougas G, King D, Cook DJ*. Impaired gastric emptying in mechanically ventilated, critically ill patients. Intensive Care Med 1996; 22: 1339–44.

13 *Mendelson CL*. The aspiration of stomach contents into the lungs during obstetric anesthesia. Am J Obstet Gynecol 1946; 52: 191–205.

14 *Dronen SC, Merigian KS, Hedges JR, Hoekstra JW, Borron SW*. A comparison of blind nasotracheal and succinylcholine-assisted intubation in the poisoned patient. Ann Emerg Med 1987; 16: 650–2.

15 *Sagarin MJ, Barton ED, Chng YM, Walls RM; National Emergency Airway Registry Investigators*. Airway management by US and Canadian emergency medicine residents: a multicenter analysis of more than 6,000 endotracheal intubation attempts. Ann Emerg Med 2005; 46: 328–36.

16 *Sakles JC, Laurin EG, Rantapaa AA, Panacek EA*. Airway management in the emergency department: a one-year study of 610 tracheal intubations. Ann Emerg Med 1998; 31: 325–32.

17 *Bair AE, Filbin MR, Kulkarni RG, Walls RM*. The failed intubation attempt in the emergency department: analysis of prevalence, rescue techniques, and personnel. J Emerg Med 2002; 23: 131–40.

18 *Li J, Murphy-Lavoie H, Bugas C, Martinez J, Preston C*. Complications of emergency intubation with and without paralysis. Am J Emerg Med 1999; 17: 141–3.

19 *Rose WD. Anderson LD, Edmond SA*. Analysis of intubations. Before and after establishment of a rapid sequence intubation protocol for air medical use. Air Med J 1994; 13: 475–8.

20 *Pearson S*. Comparison of intubation attempts and completion times before and after the initiation of a rapid sequence intubation protocol in an air medical transport program. Air Med J 2003; 22: 28–33.

21 *Ma OJ, Atchley RB, Hatley R, Green M, Young J, Brady W*. Intubation success rates improve for an air medical program after implementing the use of neuromuscular blocking agents. Am J Emerg Med 1998; 16: 125–7.

22 *Davis DP, Stern J, Sise MJ, Hoyt DB*. A follow-up analysis of factors associated with head-injury mortality after paramedic rapid sequence intubation. J Trauma 2005; 59: 486–90.

23 *Falcone RE, Herron H, Dean B, Werman H*. Emergency scene endotracheal intubation before and after the introduction of a rapid sequence induction protocol. Air Med J 1996; 15: 163–7.

24 *Ochs M, Davis D, Hoyt D, Bailey D, Marshall L, Rosen P*. Paramedic-performed rapid sequence intubation of patients with severe head injuries. Ann Emerg Med 2002; 40: 159–67.

25 *Wang HE, Yealy DM*. Out-of-hospital rapid sequence intubation: is this the "success" we envisioned? Ann Emerg Med 2002; 40: 168–71.

26 *Benumof JL*. Preoxygenation: best method for both efficacy and efficiency. Anesthesiology 1999; 91: 603–5.

27 *Drummond GB, Park GR*. Arterial oxygen saturation before intubation of the trachea. An assessment of oxygenation techniques. Br J Anaesth 1984; 56: 987–93.

28 *Kashyap L, Yaddanapudi LN, Sandhya*. Arterial desaturation during induction with and without preoxygenation: evaluation of four techniques. Anaesth Intensive Care 1993; 21: 811–3.

29 *Gold MI, Duarte I, Muravchick S*. Arterial oxygena-

tion in conscious patients after 5 minutes and after 30 seconds of oxygen breathing. Anesth Analg 1981; 60: 313–5.

30 *Goldberg ME, Norris MC, Larijani GE, Marr AT, Seltzer JL.* Preoxygenation in the morbidly obese: a comparison of two techniques. Anesth Analg 1989; 68: 520–2.

31 *Norris MC, Dewan DM.* Preoxygenation for cesarean section: a comparison of two techniques. Anesthesiology 1985; 62: 827–9.

32 *Chiron B, Laffon M, Ferrandiere M, Pittet JF, Marret H, Mercier C.* Standard preoxygenation technique versus two rapid techniques in pregnant patients. Int J Obstet Anesth 2004; 13: 11–4.

33 *Baraka AS, Taha SK, Aouad MT, EI-Khatib MF, Kawkabani NI.* Preoxygenation: comparison of maximal breathing and tidal volume breathing techniques. Anesthesiology 1999; 91: 612–6.

34 *Gambee AM, Hertzka RE, Fisher DM.* Preoxygenation techniques: comparison of three minutes and four breaths. Anesth Analg 1987; 66: 468–70.

35 *Valentine SJ, Marjot R, Monk CR.* Preoxygenation in the elderly: a comparison of the four-maximal breath and three-minute techniques. Anesth Analg 1990; 71: 516–9.

36 *McCarthy G, Elliott P, Mirakhur RK, McLoughlin C.* A comparison of different pre-oxygenation techniques in the elderly. Anaesthesia 1991; 46: 824–7.

37 *Baraka AS, Taha SK, El-Khatib MF, Massouh FM, Jabbour DG, Alameddine MM.* Oxygenation using tidal volume breathing after maximal exhalation. Anesth Analg 2003; 97: 1533–5.

38 *Baraka A, Haroun-Bizri S, Khoury S, Chebab IR.* Single vital capacity breath for preoxygenation. Can J Anesth 2000; 47: 1144–6.

39 *Dixon BJ, Dixon JB, Carden JR, et al.* Preoxygenation is more effective in the 25 degrees head-up position than in the supine position in severely obese patients: a randomized controlled study. Anesthesiology 2005: 102: 1110–5.

40 *Altermatt FR, Munoz HR, Delfino AE, Cortinez LI.* Pre-oxygenation in the obese patient: effects of posture on tolerance to apnoea. Br J Anaesth 2005; 95: 706–9.

41 *Cotton BR, Smith G.* The lower oesophageal sphincter and anaesthesia. Br J Anaesth 1984; 56: 37–46.

42 *Vanner RG, Pryle BJ, O'Dwyer JP, Reynolds F.* Upper oesophageal sphincter pressure and the intravenous induction of anaesthesia. Anaesthesia 1992; 47: 371–5.

43 *Tayal VS, Riggs RW, Marx JA, Tomaszewski CA, Schneider RE.* Rapid-sequence intubation at an emergency medicine residency: success rate and adverse events during a two-year period. Acad Emerg Med 1999; 6: 31–7.

44 *Dufour DG, Larose DL, Clement SC.* Rapid sequence intubation in the emergency department. J Emerg Med 1995; 13: 705–10.

45 *Sivilotti ML, Ducharme J.* Randomized, double-blind study on sedatives and hemodynamics during rapid-sequence intubation in the emergency department: The SHRED Study. Ann Emerg Med 1998; 31: 313–24.

46 *Morris J, Cook TM.* Rapid sequence induction: a national survey of practice. Anaesthesia 2001; 56: 1090–7.

47 *Sivilotti ML, Filbin MR, Murray HE, Slasor P, Walls RM; NEAR Investigators.* Does the sedative agent facilitate emergency rapid sequence intubation? Acad Emerg Med 2003; 10: 612–20.

48 *Reynolds SF, Heffner J.* Airway management of the critically ill patient: rapid-sequence intubation. Chest 2005; 127: 1397–1412.

49 *Oglesby A.* Should etomidate be the induction agent of choice for rapid sequence intubation in the emergency department? Emerg Med J 2004; 21: 655–9.

50 *Zed PJ, Abu-Laban RB, Harrison DW.* Intubating conditions and hemodynamic effects of etomidate for rapid sequence intubation in the emergency department: an observational cohort study. Acad Emerg Med 2006; 13: 378–83.

51 *Smith DC, Bergen JM, Smithline H, Kirschner R.* A trial of etomidate for rapid sequence intubation in the emergency department. J Emerg Med 2000; 18: 13–6.

52 *Skinner HJ, Biswas A, Mahajan RP.* Evaluation of intubating conditions with rocuronium and either propofol or etomidate for rapid sequence induction. Anaesthesia 1998; 53: 702–6.

53 *Lindgren L, Yli-Hankala A, Randell T, Kirvela M, Scheinin M, Neuvonen PJ.* Haemodynamic and catecholamine responses to induction of anaesthesia and tracheal intubation: comparison between propofol and thiopentone. Br J Anaesth 1993; 70: 306–10.

54 *Wilmot G, Bhimsan N, Rocke DA, Murray WB.* Intubating conditions and haemodynamic changes following thiopentone or propofol for early tracheal intubation. Can J Anaesth 1993; 40: 201–5.

55 *Vohra A, Thomas AN, Harper NJ, Pollard BJ.* Non-invasive measurement of cardiac output during induction of anaesthesia and tracheal intubation: thiopentone and propofol compared. Br J Anaesth 1991; 67: 64–8.

56 *Sagarin MJ, Chiang V, Sakles JC, et al.* Rapid sequence intubation for pediatric emergency airway management. Pediatr Emerg Care 2002; 18: 417–23.

57 *Sokolove PE, Price DD, Okada P.* The safety of etomidate for emergency rapid sequence intubation of pediatric patients. Pediatr Emerg Care 2000; 16: 18–21.

58 *Fellows IW, Yeoman PM, Selby C, Byrne AJ.* The effect of anaesthetic induction with etomidate on the endocrine response to surgical trauma. Eur J Anaesthesiol 1985; 2: 285–90.

59 *Jackson WL Jr.* Should we use etomidate as an induction agent for endotracheal intubation in patients with septic shock? A critical appraisal. Chest 2005; 127: 1031–8.

60 *Schenarts CL, Burton JH, Riker RR.* Adrenocortical dysfunction following etomidate induction in emergency department patients. Acad Emerg Med 2001; 8: 1–7.

61 *Weiss-Bloom LJ, Reich DL.* Haemodynamic responses to tracheal intubation following etomidate and fentanyl for anaesthetic induction. Can J Anaesth 1992; 39: 780–5.

62 *Brossy MJ, James MF, Janicki PK.* Haemodynamic and catecholamine changes after induction of anaesthesia with either thiopentone or propofol with suxamethonium. Br J Anaesth 1994; 72: 596–8.

63 *Reves JG, Fragen RJ, Vinik HR, Greenblatt DJ.* Midazolam: pharmacology and uses. Anesthesiology 1985; 62: 310–24.

64 *Lavazais S, Debaene B.* Choice of the hypnotic and the opioid for rapid-sequence induction. Eur J Anaesthesiol Suppl 2001; 23: 66–70.

65 *McCollum JS, Dundee JW.* Comparison of induction characteristics of four intravenous anaesthetic agents. Anaesthesia 1986; 41: 995–1000.

66 *Wong AK, Teoh GS.* Intubation without muscle relaxant: an alternative technique for rapid tracheal intubation. Anaesth Intensive Care 1996; 24: 224–30.

67 *Dobson AP, McCluskey A, Meakin G, Baker RD.* Effective time to satisfactory intubation conditions after administration of rocuronium in adults. Comparison of propofol and thiopentone for rapid sequence induction of anaesthesia. Anaesthesia 1999; 54: 172–6.

68 *McKeating K, Bali IM, Dundee JW.* The effects of thiopentone and propofol on upper airway integrity. Anaesthesia 1988; 43: 638–40.

69 *Perry JJ, Lee J, Wells G.* Are intubation conditions using rocuronium equivalent to those using succinylcholine? Acad Emerg Med 2002; 9: 813–23.

70 *Erhan E, Ugur G, Alper I, Gunusen I, Ozyar B.* Tracheal intubation without muscle relaxants: remifentanil or alfentanil in combination with propofol. Eur J Anaesthesiol 2003; 20: 37–43.

71 *Hans P, Brichant JF, Hubert B, Dewandre PY, Lamy M.* Influence of induction of anaesthesia on intubating conditions one minute after rocuronium administration: comparison of ketamine and thiopentone. Anaesthesia 1999; 54: 276–9.

72 *Sparr HJ, Giesinger S, Ulmer H, Hollenstein-Zacke M, Luger TJ.* Influence of induction technique on intubating conditions after rocuronium in adults: comparison with rapid-sequence induction using thiopentone and suxamethonium. Br J Anaesth 1996; 77: 339–42.

73 *Naguib M, Samarkandi AH, El-Din ME, Abdullah K, Khaled M, Alharby SW.* The dose of succinylcholine required for excellent endotracheal intubating conditions. Anesth Analg 2006; 102: 151–5.

74 *Naguib M, Samarkandi A, Riad W, Alharby SW.* Optimal dose of succinylcholine revisited. Anesthesiology 2003; 99: 1045–9.

75 *Kopman AF, Zhak B, Lai KS.* The "intubating dose" of succinylcholine: the effect of decreasing doses on recovery time. Anesthesiology 2003; 99: 1050–4.

76 *EI-Orbany MI, Joseph NJ, Salem R, Klowden AJ.* The neuromuscular effects and tracheal intubation conditions after small doses of succinylcholine. Anesth Analg 2004; 98: 1680–5.

77 *Benumof JL, Dagg R, Benumoff R.* Critical hemoglobin desaturation will occur before return to an unparalyzed state following 1mg/kg intravenous succinylcholine. Anesthesiology 1997; 87: 979–82.

78 *Hardman JG, Wills JS, Aitkenhead AR.* Factors determining the onset and course of hypoxemia during apnea: an investigation using physiological modelling. Anesth Analg 2000; 90: 619–24.

79 *Heier T, Feiner JR, Lin J, Brown R, Caldwell JE.* Hemoglobin desaturation after succinylcholine-induced apnea: a study of the recovery of spontaneous ventilation in healthy volunteers. Anesthesiology 2001; 94: 754–9.

80 *Hayes AH, Breslin DS, Mirakhur RK, Reid JE, O'Hare RA.* Frequency of haemoglobin desaturation with the use of succinylcholine during rapid sequence induction of anaesthesia. Acta Anaesthesiol Scand 2001; 45: 746–9.

81 *Naguib M, Samarkandi AH, Abdullah K, Riad W, Alharby SW.* Succinylcholine dosage and apnea-induced hemoglobin desaturation in patients. Anesthesiology 2005; 102: 35–40.

82 *Sluga M, Ummenhofer W, Studer W, Siegemund M, Marsch SC.* Rocuronium versus succinylcholine for rapid sequence induction of anesthesia and endotracheal intubation: a prospective, randomized trial in emergent cases. Anesth Analg 2005; 101: 1356–61.

83 *Harris CE, Murray AM, Anderson JM, Grounds RM, Morgan M.* Effects of thiopentone, etomidate and propofol on the haemodynamic response to tracheal

intubation. Anaesthesia 1988; 43 (Suppl): 32–6.

84 *Hug CC Jr.* Does opioid `anesthesia' exist? Anesthesiology 1990; 73: 1–4.

85 *Lev R, Rosen P.* Prophylactic lidocaine use preintubation: a review. J Emerg Med 1994; 12: 499–506.

86 *Brucia JJ, Owen DC, Rudy EB.* The effects of lidocaine on intracranial hypertension. J Neurosci Nurs 1992; 24: 205–14.

87 *Robinson N, Clancy M.* In patients with head injury undergoing rapid sequence intubation, does pretreatment with intravenous lignocaine/lidocaine lead to an improved neurological outcome? A review of the literature. Emerg Med J 2001; 18: 453–7.

88 *Feng CK, Chan KH, Liu KN, Or CH, Lee TY.* A comparison of lidocaine, fentanyl, and esmolol for attenuation of cardiovascular response to laryngoscopy and tracheal intubation. Acta Anaesthesiol Sin 1996; 34: 61–7.

89 *Lin PL, Wang YP, Chou YM, Chan HL, Huang HH.* Lack of intravenous lidocaine effects on HRV changes of tracheal intubation during induction of general anesthesia. Acta Anaesthesiol Sin 2001; 39: 77–82.

90 *Chraemmer-Jorgensen B, Hoilund-Carlsen PF, Marving J, Christensen V.* Lack of effect of intravenous lidocaine on hemodynamic responses to rapid sequence induction of general anesthesia: a double-blind controlled clinical trial. Anesth Analg 1986; 65: 1037–41.

91 *Butler J, Jackson R.* Best evidence topic report. Lignocaine as a pretreatment to rapid sequence intubation in patients with status asthmaticus. Emerg Med J 2005; 22: 732.

92 *Butler J, Jackson R.* Towards evidence based emergency medicine: best BETs from Manchester Royal Infirmary. Lignocaine premedication before rapid sequence induction in head injuries. Emerg Med J 2002; 19: 554.

93 *Helfman SM, Gold MI, DeLisser EA, Herrington CA.* Which drug prevents tachycardia and hypertension associated with tracheal intubation: lidocaine, fentanyl, or esmolol? Anesth Analg 1991; 72: 482–6.

94 *Singh H, Vichitvejpaisal P, Gaines GY, White PF.* Comparative effects of lidocaine, esmolol, and nitroglycerin in modifying the hemodynamic response to laryngoscopy and intubation. J Clin Anesth 1995; 7: 5–8.

95 *Poulton TJ, James FM 3rd.* Cough suppression by lidocaine. Anesthesiology 1979; 50: 470–2.

96 *Yukioka H, Yoshimoto N, Nishimura K, Fujimori M.* Intravenous lidocaine as a suppressant of coughing during tracheal intubation. Anesth Analg 1985; 64: 1189–92.

97 *Schwartz DE, Matthay MA, Cohen NH.* Death and other complications of emergency airway management in critically ill adults. A prospective investigation of 297 tracheal intubations. Anesthesiology 1995; 82: 367–76.

98 *Vanner RG, Asai T.* Safe use of cricoid pressure. Anaesthesia 1999; 54: 1–3.

99 *Jackson SH.* Efficacy and safety of cricoid pressure needs scientific validation. Anesthesiology 1996; 84: 751–2.

100 *Kron SS.* Questionable effectiveness of cricoid pressure in preventing aspiration (Letter). Anesthesiology 1995; 83: 431.

101 *Schwartz DE, Cohen NH.* Questionable effectiveness of cricoid pressure in preventing aspiration (Letter, reply). Anesthesiology 1995; 83: 432.

102 *Vanner RG, Pryle BJ.* Nasogastric tubes and cricoid pressure. Anaesthesia 1993; 48: 1112–3.

103 *Smith KJ, Ladak S, Choi PT, Dobranowski J.* The cricoid cartilage and the esophagus are not aligned in close to half of adult patients. Can J Anesth 2002; 49: 503–7.

104 *Smith KJ, Dobranowski J, Yip G, Dauphin A, Choi PT.* Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. Anesthesiology 2003; 99: 60–4.

105 *Allman KG.* The effect of cricoid pressure on airway patency. J Clin Anesth 1995; 7: 197–9.

106 *Moynihan RJ, Brock-Utne JG, Archer JH, Feld LH, Kreitzmand TR.* The effect of cricoid pressure on preventing gastric insufflation in infants and children. Anesthesiology 1993; 78: 652–6.

107 *Vanner RG.* Tolerance of cricoid pressure by conscious volunteers. Int J Obstet Anesth 1992; 1: 195–8.

108 *Lawes EG, Duncan PW, Bland B, Gemmel L, Downing JW.* The cricoid yoke - a device for providing consistent and reproducible cricoid pressure. Br J Anaesth 1986; 58: 925–31.

109 *Hartsilver EL, Vanner RG.* Airway obstruction with cricoid pressure. Anaesthesia 2000; 55: 208–11.

110 *Aoyama K, Takenaka I, Sata T, Shigematsu A.* Cricoid pressure impedes positioning and ventilation through the laryngeal mask airway. Can J Anaesth 1996; 43: 1035–40.

111 *MacG Palmer JH, Ball DR.* The effect of cricoid pressure on the cricoid cartilage and vocal cords: an endoscopic study in anaesthetised patients. Anaesthesia 2000; 55: 263–7.

112 *Hodgson RE, Gopalan PD, Burrows RC, Zuma K.* Effect of cricoid pressure on the success of endotracheal intubation with a lightwand. Anesthesiology 2001; 94: 259–62.

113 *Shulman GB, Connelly NR.* A comparison of the

Bullard laryngoscope versus the flexible fiberoptic bronchoscope during intubation in patients afforded inline stabilization. J Clin Anesth 2001; 13: 182–5.

114 *Wood PR*. Direct laryngoscopy and cervical spine stabilisation. Anaesthesia 1994; 49: 77–8.

115 *Turgeon AF, Nicole PC, Trepanier CA, Marcoux S, Lessard MR*. Cricoid pressure does not increase the rate of failed intubation by direct laryngoscopy in adults. Anesthesiology 2005; 102: 315–9.

116 *Mort TC*. Preoxygenation in critically ill patients requiring emergency tracheal intubation. Crit Care Med 2005; 33: 2672–5.

117 *Lawes EG, Campbell I, Mercer D*. Inflation pressure, gastric insufflation and rapid sequence induction. Br J Anaesth 1987; 59: 315–8.

118 *Ruben H, Krudsen EJ, Carugati G*. Gastric inflation in relation to airway pressure. Acta Anaesthesiol Scand 1961; 5: 107–14.

119 *Petito SP, Russell WJ*. The prevention of gastric insufflation - a neglected benefit of cricoid pressure. Anaesth Intensive Care 1988; 16: 139–43.