To the Editor—Dowd et al.¹ have provided important information about the pharmacokinetics of tranexamic acid (TA) in cardiac surgery with cardiopulmonary bypass. Particularly, they demonstrated the necessity of a continuous infusion of TA to obtain stable therapeutic concentrations. Then, they proposed two different dosage schemes in low- and high-risk patients for bleeding, to obtain TA plasma concentrations of 334 µM and 800 µM, respectively. Considering the patients with low-risk for bleeding, they recommended a loading dose of 12.5 mg/kg (or greater) over 30 min, a continuous infusion of 6.5 mg·kg⁻¹·h⁻¹, and 1 mg/kg (or greater) added to the priming, whereas in patients with high-risk for bleeding they proposed doses about 2.5 higher.

My group published various studies²-⁴ proposing an original pharmacologic protocol for TA that seem very similar to that proposed by Dowd et al. For patients with low-risk for bleeding; that is, a loading dose of 1 g over 20 min before sternotomy (and not 1 g, 20 min before sternotomy, as erroneously reported in the work of my group cited by Dowd 1995; 110:835–42), followed by a continuous infusion of 400 mg/h, and 500 mg added to pump priming. We also applied the same protocol in high-risk patients for bleeding, obtaining a significant reduction of blood loss and allogeneic transfusions.⁵-⁶ One criticism of the study of Dowd et al. is that the need to increase the doses of TA in this type of patient requires further clinical demonstrations, particularly considering (as the same authors report) that TA plasma concentrations of about 200 µM completely inhibit fibrinolysis.

Concerning the administration of TA after surgery, I agree with Dowd et al. regarding benefits in the postoperative period depending on intraoperative dosing techniques, but I do not understand why the authors claim that the efficacy of prolonged TA administration in the postoperative period is an open question. In reality, the authors, applying their pharmacokinetic model to our TA protocol, confirmed the conclusions of our study.³ Our intraoperative TA dosage scheme guarantees therapeutic concentrations for about 12 h, rendering unnecessary postoperative infusion of the drug.

It also seems that the potential thrombotic risk intrinsic to antifibrinolytic drugs is underestimated by Dowd et al. I particularly disagree with their statement, "TA appears to be a very safe medication... Thus our attempt to avoid excessive TA concentrations may not be necessary." An extensive literature search showed cases of thrombosis following the use of hemostatic drugs such as ε-aminocaproic acid, aprotinin, and TA, but it would be sufficient to cite a recent case report describing two fatal cases of thrombosis after the use of ε-aminocaproic acid (very similar to TA with a potency 10 times lower) in cardiac surgical patients operated on with deep hypothermic circulatory arrest, wherein postmortem laboratory analysis revealed the presence of Factor V Leiden. Because it is impossible to identify patients with a procoagulant prothrombotic state, it is appropriate to use the minimal effective doses of hemostatic drugs to avoid amplifying these thrombotic complications. Furthermore, the same authors’ group reported in a previous study seven cases of stroke in cardiac surgical patients with known peripheral vascular disease, treated intraoperatively with high doses of TA. One would speculate that high concentrations of TA facilitated the formation of a thrombus in the presence of blood flow reductions in a diseased vessel.

In conclusion, only large, prospective, blinded studies will establish the real safety and efficacy of the various doses of tranexamic acid in cardiac surgery. Currently, caution is required when using a hemostatic drug.

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References


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In Reply.—We appreciate your interest in our work and would like to take this opportunity to reply to your comments. First, we would like to apologize for misquoting your tranexamic acid (TA) administration regimen. However, we think that the principal behind the administration of a loading dose remains the same (1 g of TA over 20 min).

Regarding the criticism with respect to validity of increased TA dosage for patients undergoing complex cardiac surgery, we would like to emphasize that our previous studies (J Thorac Cardiovasc Surg 1995; 110:855–42) showed that higher TA dose regimens were more effective in reducing postoperative bleeding compared to a lower single-dose regimen.

With respect to safety aspects of TA, we must admit that we have never claimed that the use of any antifibrinolytics during cardiac surgery is a safe practice in the face of circulatory arrest. All information in the literature about vascular thrombosis after the use of antifibrinolytics in cardiac surgery is anecdotal. We have recently reviewed stroke rates (as an indicator of vascular thrombosis) in our prospectively collected database of 18,000 primary coronary artery bypass graft patients with respect to utilization of TA. Stroke rates of 1.2–1.4% were similar between the two groups of patients, regardless of TA assignment. Furthermore, we have conducted a prospective randomized placebo controlled trial that demonstrated that there was no difference in early coronary graft patency between high-dose TA and placebo groups (Can J Anaesth 1999; 46:A29).

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Measurement of the Low-frequency Component of Blood Pressure Variability Can Assist the Interpretation of Heart Rate Variability Data

To the Editor—We congratulate Hogue et al.1 for their excellent investigation of the autonomic effects of dexmedetomidine in humans. Although a good understanding of the hemodynamic effects of different anesthetic drugs in patients is the daily routine for most anesthesiologists, the origin and mechanisms of these drug effects are still confusing and complex. The author’s use of heart rate variability (HRV) in addition to baroreflex responses and systemic catecholamine concentrations in these volunteers exemplifies the need to use multiple measurement techniques when examining the sympathetic and parasympathetic nervous system. We suggest that the addition of blood pressure variability (BPV) to this study would help strengthen the HRV data and expand their measurement techniques. As the authors stated, the low-frequency oscillatory component of the respiratory rate interval is considered a marker of sympathetic activity. Similarly, one can identify low-frequency oscillations that emanate from a different end organ, arterial smooth muscle, known as Mayer waves.5 The simultaneous measurement of HRV and systolic BPV has been described and used by Malliani et al. and showed increases in both low-frequency components with tilt, exercise, mental stress, physical exercise, moderate hypotension, and coronary artery occlusion.7 In conditions that directly affect one of the respective end organs, i.e., heart (HRV) versus peripheral arteries (BPV), a unilateral response may be identified.8 Thus, the low-frequency component of systolic BPV, in addition to that generated by HRV, represents a good marker of sympathetic activity.9 Unfortunately, although the high-frequency component of HRV is considered a marker of parasympathetic activity, the high-frequency component of BPV is not. This is because the high-frequency oscillations in blood pressure are largely influenced by the mechanical changes induced by respiration.9 Therefore, we believe that analysis of the changes in low-frequency oscillations of the systolic blood pressure simultaneously with low-frequency and high-frequency oscillations measured in HRV will help investigators better explore and quantify the effects of anesthetic drugs on neural regulatory mechanisms.

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In Reply.—We thank Introna et al.1 for their kind comments regarding our manuscript.2 The authors correctly point out that a comprehensive approach to assessing the autonomic nervous system effects of anesthetic and sedative drugs provides clinically useful insight into their cardiovascular effects. Measurement of variations in systolic blood pressure is a well-characterized method for measuring peripheral sympathetic nervous system responses to various autonomic stressors, and such data might have furthered our findings.5,5 We chose, however, to focus on the cardiac autonomic effects of sedative doses of dexmedetomidine during clinically common thermal stress. Future investigation along these lines that incorporate measurement of systolic blood pressure variations might prove to be useful.

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CORRESPONDENCE

Pain Significantly Influences Postoperative Wound Oxygen Tension

To the Editor.—Buggy et al. conducted a very interesting study investigating the influence of epidural or intravenous analgesia on postoperative wound oxygen tension. They found significantly increased values in patients who received epidural analgesic techniques when compared with patients who received intravenous analgesia. In my opinion, the two groups were not comparable, because the patients without neuraxial blockade had significantly higher pain scores. It is known that pain is a major determinant of postoperative subcutaneous oxygen partial pressures. It causes an autonomic response with increased adrenergic nerve activity and plasma-catecholamine concentrations. Hence, according to the presented data it seems unjustified to conclude that epidural techniques improve in general postoperative wound oxygen tension.

The role of neuraxial analgesia to improve postoperative outcome remains to be debated. Randomized trials comparing different perioperative analgesic concepts are often unable to demonstrate the superiority of one of the concepts. This is partially attributable to lack of power and a focus on major morbidities. Buggy et al. must be congratulated for the aim of their study, but I suggest repeating the investigation while ensuring that patients in both groups receive comparably effective pain treatments. This is not an easy task because patients recovering from surgical interventions often consider pain as normal. They should, therefore, be instructed to use the patient-controlled devices not only to achieve a tolerable level of analgesia but also to aim for an a priori defined level of analgesia.

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References

In Reply.—We thank Dr. Hübner for his interest in our manuscript, but we think he may have missed the point. Our stated hypothesis was to evaluate whether combined general anesthesia and epidural anesthesia and postoperative analgesia would increase subcutaneous tissue oxygen tension in the wound (PsqO₂) compared with general anesthesia alone followed by postoperative opioid analgesia. It is well recognized that epidural analgesia provides superior analgesia compared with intravenous morphine analgesia, and as Dr. Hübner points out, minimizing pain increases PsqO₂. Therefore, of course our patients with epidural analgesia had less pain: The issue we evaluated was whether the method of analgesia (epidural or intravenously administered opioid) also influences PsqO₂. Furthermore, randomization took place preoperatively, and the distinction between our two groups commenced before the induction of anesthesia, not on emergence.

We believe Dr. Hübner’s proposed repeat study is unworkable, because postoperative patients on intravenously administered opioid patient-controlled analgesia can never realistically expect to achieve similar levels of analgesia after major laparotomy compared with functional epidural analgesia.

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It’s the Colloid, Not the Esophageal Doppler Monitor

To the Editor.—The debate over whether crystalloids or colloid is a better replacement fluid in the perioperative period has been of interest for decades. Gan et al.1 have introduced new data in this debate with their study of 100 patients undergoing major elective surgery with an anticipated 500-ml blood loss. The authors used esophageal Doppler monitor (EDM)-guided colloid administration to improve preload, cardiac output, tissue perfusion, and patient outcome in the treatment group.

In effect, the treatment group has two variables: use of the EDM and use of colloid boluses. The EDM provided guidance for “goal-directed” fluid therapy. Although the EDM may not give an accurate measurement of preload or cardiac output,2–5 as a clinical monitor it enables an assessment of changes in corrected flow time and preload. With regard to the use of colloid boluses, the treatment group received 200 ml of 6% hydroxyethyl starch in saline every 15 min to maximize corrected flow time and stroke volume. The control group received 200-ml “fluid” boluses (more likely crystalloid) to treat changes in hemodynamic parameters (heart rate, blood pressure, central venous pressure) or decreased urinary output.

The better outcomes in the treatment group can be attributed solely to those patients receiving 847 ml of hydroxyethyl starch compared to 282 ml for the control group. Both groups received 4400 ml of lactated Ringer’s solution during roughly 4 h of surgery. Other studies have demonstrated that EDM-guided use of supplemental colloid boluses in cardiac4 and orthopedic surgical patients6 was associated with improved outcomes, including shorter hospital stays. Taken together, the three studies demonstrate significantly improved patient outcomes when larger amounts of colloid were given to patients in the treatment group.

An esophageal Doppler monitor costs $8000, with an additional

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control group. It may be that the earlier administration of hydroyxyethyl starch will provide a more cost-effective patient benefit for relatively healthy patients, without significant cardiovascular disease, who are undergoing major elective surgery.

We agree with the authors that “intraoperative fluid augmentation appears to confer significant benefits compared with customary practice.” Further investigation is required to test whether additional colloid administration without the use of EDM would result in similar patient benefits, because Gan et al. do not directly address this issue. Crystallloid or colloid? The results of this study imply that administration of both may improve patient outcomes after major elective surgery.

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Alternative Method to Deflate the Operated Lung when Using Wire-guided Endobronchial Blockade

To the Editor—In his excellent review, Dr. Campos1 describes clinically relevant lung isolation methods. To deflate the lung when using a wire-guided endobronchial blocker (WEB®; Cook, Bloomington, IN), Dr. Campos proposes withdrawing the loop wire, thus opening a 1.4 mm air channel to the atmosphere. Because the procedure as proposed can be very time-consuming, we use an alternative method to deflate the operated lung when using WEB®: After conventional intubation, we introduce the WEB® catheter in the main stem bronchus of the operated lung but do not inflate it. After patient positioning and thoracotomy, we check and, when needed, correct the position of the WEB® catheter using a fiberscope. To deflate the lung, we then disconnect the ventilator from side port of the WEB® connector and thus open the main airway to the atmosphere. After verifying lung collapse, we inflate the WEB® under fiberoptic control and reconnect the ventilator to the endotracheal tube. This way we avoid removing the flexible wire loop, which is essential for repositioning the WEB® if it

To the Editor—Thank you for allowing us the opportunity to respond to the letter by Horowitz and Kumar. In our study,1 we investigated whether goal-directed intraoperative plasma volume expansion guided by the esophageal Doppler monitor would shorten the length of hospital stay and improve postoperative outcomes. The control and protocol groups consisted of patients undergoing similar procedures. The general anesthetic for both groups was standardized. We did not regiment the type of fluid to be administered in the control group, because we wanted this group to receive, as closely as possible, a routine standard of care. The protocol group received 6% hetastarch in saline to a maximum of 20 ml/kg, based on a fluid challenge algorithm. Patients in the protocol group received, on average, 500 ml more colloid than the control group. Hence, we could not completely rule out that additional colloid may have contributed to the observed results. Based on the present study, we suggest that none of these three methods may be superior in better perfusion of the gastrointestinal tract and, hence, earlier resumption of gastrointestinal motility and return to normal diet.

The type of fluid administered may also be important in postoperative patient outcome. In a recent study,2 we found an improvement in the quality of recovery in patients receiving a combination of colloid (6% hetastarch) and crystalloid (lactated Ringer’s) versus crystalloid alone. Specifically, the colloid/crystalloid patients had a lower incidence of postoperative nausea and vomiting, severe pain, and peripheral edema. Further investigations are therefore needed to study the contribution of these factors.

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Endobronchial Blocker Response

To the Editor—I would like to respond to Dr. Campos’ excellent article on options for one-lung ventilation. The use of a conventional single-lumen endotracheal tube is more efficient in providing ventilation relative to a double-lumen tube, or Univent® endotracheal tube. The internal diameter for ventilation decreases to 3.4 to 3.5 mm and 4.3 to 4.5 mm, respectively. The equivalent diameter Univent® tube would be 32 French, 35 French, 6.0-mm internal diameter, and 7.0-mm internal diameter, respectively. As compared to a single lumen endotracheal tube, the inner diameter is small relative to the outer diameter. When comparing the 32 French and 35 French double-lumen tubes, they have a combined internal diameter of 5.0 to 6.0 mm, respectively. The internal diameter for ventilation decreases to 3.4 to 3.5 mm and 4.3 to 4.5 mm, respectively. The equivalent diameter Univent® tube have an internal diameter of 6.0 to 7.0 mm. The WEB® allows patient management with a large internal diameter endotracheal tube as compared to the Univent® endotracheal tube or double-lumen endotracheal tube with the same approximate outer diameter. The WEB® is now made in a 7 French adult diameter, which makes placement through 7.0 or 7.5 endotracheal tubes relatively easy.

The advantages of the WEB® are several; however, the ability to conserve internal diameter as compared to outer diameter is an important advantage. Both the Univent® and double-lumen endotracheal tube lose a large part of their internal diameter because of the extra plastic material used, which is inherent in their construction.

An Alternative Way to Use Fogarty Balloon Catheter for Perioperative Lung Isolation

To the Editor—We read with great interest the review of current techniques for perioperative lung isolation by Dr. Campos. Use of the Fogarty® balloon catheter (FBC®) (Edwards Lifesciences, Irvine, CA) as a bronchial blocker to achieve lung isolation is reviewed. It is suggested that a standard endotracheal tube (ETT) of at least 6.0-mm internal diameter is required to use the FBC® for lung isolation.

We suggest an alternate way to use the FBC® for lung isolation. In our experience, under direct laryngoscopy it is possible to place the FBC independently through the vocal cords alongside the ETT. A fiberoptic bronchoscope may or may not be required to guide the FBC into the desired position. This alternate technique obviates the need for an ETT larger then 6.0-mm internal diameter and a right-angle connector with self-sealing diaphragm. Introducing the FBC independently alongside the ETT may also preclude the need for ventilation interruption for placement of the FBC in critically ill mechanically ventilated patients requiring high positive end expiratory pressure. Use of the FBC alongside the ETT instead of through the ETT also decreases the risk of dislodging the FBC that may occur when the fiberoptic bronchoscope is withdrawn alongside the FBC.

The FBC is considerably cheaper than double-lumen tubes, Univent® endotracheal tubes, and wire-guided endobronchial blockers (WEB®) for lung isolation and is readily available in operating rooms. The disadvantages include a low-volume, high-pressure cuff, and its lack of hollow center. The FBC, therefore, may increase the risk of tracheal mucosal damage if used for a prolonged time, and it cannot be used to insufflate oxygen, evacuate air, or perform pulmonary toilet.

We also disagree with the author about using a fiberoptic bronchoscope suction port to evacuate air from the lung. We believe that using active suction may collapse the proximal bronchioles and bronchi and leave the distal alveoli distended, thus deteriorating the situation.

We recommend that the size of the ETT may not limit the selection of the FBC for one-lung ventilation. Introducing the FBC independently alongside the ETT may be considered for critically ill mechanically ventilated patients, and to avoid risk of FBC dislodgement.

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Reference


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Reference


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In Reply—I appreciate the suggestion of Dr. Karzai of an alternative method to facilitate lung collapse while using a wire-guided endobronchial blocker (WEB®; Cook, Bloomington, IN). The various methods I discussed in my article for facilitating and/or expediting lung collapse when the WEB® is in use include: (1) Removal of the wire loop after the patient is turned to a lateral decubitus position and fiberoptic confirmation demonstrate that the WEB® is correctly placed in the optimal position, so that air can be evacuated spontaneously along with the absorption atelectasis in the nondependent lung. (2) Use of the low-suction-assisted method, which basically consists of connecting the barrel of a 3-ml syringe to the wire loop site (after the wire loop has been removed) then attaching it to a low-suction device after the cuff of the blocker has been fully inflated. I do not recommend continuous suction through this channel, because of the risk of developing negative pressure pulmonary edema reported with the Univent® endotracheal tube (Vitaids, Lewiston, NY).2

Regardless of the method used to facilitate or expedite lung collapse, variability among time to lung collapse exists when using double-lumen endotracheal tubes (DLT) or bronchial blockers (Univent® and WEB®). In a recent study,3 when comparing the DLT versus Univent® and WEB®, it was found that the majority of patients assigned to the WEB® group required assisted suction and took longer to achieve complete lung collapse when compared to the DLT or Univent® groups (by an average of 7 min). The method proposed by Dr. Karzai raises some concerns How long do we need to stop ventilating the patient until complete collapse is achieved? Has this method been tested in a prospective, randomized, and scientific fashion? I will assume that some patients with severe chronic obstructive pulmonary disease may not tolerate prolonged periods of apnea. Until Dr. Karzai’s method to expedite lung collapse is tested in a scientific fashion defining length of time and oxygenation/saturation measurements, I would not propose using it clinically.

Another important issue that Dr. Karzai mentioned relates to maintaining the wire loop through the operation as long as is needed. In a recent study4 when comparing the left-sided DLT with the Univent® and WEB®, we reported nine total malpositions in 32 patients in the WEB® group. The first six malpositions occurred while changing from the supine to the lateral decubitus position. The wire loop was kept until the WEB® was confirmed to be in its optimal position with the fiberoptic bronchoscope after the blocker cuff was fully inflated. The other three malpositions occurred during one-lung ventilation, after the wire loop was already removed. The WEB® was repositioned under fiberoptic bronchoscopy with no difficulty and was placed in its optimal position. In addition, removing the wire loop allows the opening channel to apply continuous positive airway pressure ventilation or intermittent inflation, if required. Maintaining the wire loop in the WEB® during the operation may potentially damage the membranous airway, or the airway may accidentally be stapled into the bronchial closure, as reported when the bronchial blocker of the Univent® was stapled during a right upper lobectomy.4

I appreciate the comments by Dr. Arndt and would like to address the issue he has raised. I agree with the importance of comparing the inner and outer diameters of the DLT, Univent®, and single-lumen endotracheal tubes. As mentioned in his letter, one of the advantages of the WEB® is the ability to preserve the inner diameter of a single-lumen endotracheal tube while using the WEB®. However, one must consider that a reduction of the cross-sectional area occurs when a WEB® is placed inside a single-lumen endotracheal tube. I would speculate that the presence of the WEB® may also affect air-flow resistance, which at the present time has not been tested scientifically, as opposed to DLT, Univent®, and single-lumen endotracheal tubes.5

I also appreciate the comments by Munir et al. and would like to address the alternative method for using the Fogarty® embolectomy balloon catheter (Edwards Lifesciences, Irvine, CA) through the vocal cords alongside the single-lumen endotracheal tube under direct laryngoscopy. This method of placement has been previously reported in the pediatric literature and is commonplace in some practices.6 I disagree with Munir et al. that a fiberoptic bronchoscope may not be needed for guidance while advancing the Fogarty catheter. I believe it would not be a safe practice to omit the use of the bronchoscope. If a Fogarty catheter is advanced with its stylet in place, there is the potential for tracheobronchial laceration, as previously reported.7 Regarding the cost, Fogarty catheters are cheap, $4.20, when compared to the DLT (the University of Iowa acquisition cost for a left-sided DLT is $79.20, a Univent® is $137, a WEB® is $107 plus $1 for a single-lumen endotracheal tube, and a Fogarty catheter No. 8/14 F is $75). One of the advantages that the Fogarty catheter may offer over the DLT is its balloon durability when compared with DLTs in which the tracheal cuff is more prone to tears in some cases.8

I believe that the use of the fiberoptic bronchoscope suction port to facilitate and expedite lung collapse is justified while using a bronchial blocker. It is doubtful that the negative pressure and flow characteristics used would be sufficient to collapse the cartilage-supported bronchi and bronchioles. Finally, to advance a Fogarty catheter independently alongside the single-lumen endotracheal tube in a patient who is critically ill and mechanically ventilated, as suggested by Munir et al. (usually these patients are intubated for days and have severe edema in the vocal cords), would be difficult because the upper airway would likely be edematous.

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References


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Cricoid Pressure Is Effective in Preventing Esophageal Regurgitation

To the Editor—Cricoid pressure (Sellick’s maneuver) is a routinely used technique for the prevention of pulmonary aspiration of gastric contents during anesthesia in patients at high risk of aspiration. Its effectiveness in preventing regurgitation of esophageal contents has been demonstrated in several studies1,2 and in cadavers.3,4 However, its effectiveness in preventing aspiration in clinical practice is debated.5 The following case scenario clearly demonstrates its effectiveness during clinical anesthesia.

A 21-yr-old, 75-kg man presented for repositioning of an intraocular lens under general anesthesia. He had a history of esophageal reconstruction by gastric pull-through to treat childhood achalasia. General anesthesia about 2 yr earlier for eye surgery had resulted in pulmonary aspiration of gastric contents during induction of anesthesia. No further details were available. Preoperatively, he was apprehensive about recurrent aspiration. On the day of surgery, he was given metoclopramide 10 mg and ranitidine 20 mg intravenously; he had taken nothing by mouth for 15 h previously. In the operating room, he was positioned supine with extension of the neck. The cricoid cartilage was identified while the patient was awake. Following adequate preoxygenation, continuous cricoid pressure was applied immediately before the induction of anesthesia with propofol 200 mg and succinylcholine 120 mg in a rapid sequence manner. Laryngoscopy and tracheal intubation with a 7.5 endotracheal tube were easily accomplished, the endotracheal tube cuff was inflated with 10 ml of air, and cricoid pressure was released. This was followed immediately by the appearance of copious, greenish fluid in the mouth, which was suctioned. There were no further sequelae.

Although no prospective randomized controlled clinical studies can be done to prove its clinical efficacy, the above case illustrates that proper application of cricoid pressure is effective, at least in some patients, in the prevention of gastric aspiration from passive regurgitation.

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