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Significant reduction in ventilator-associated pneumonia with the Venner-PneuX System in high-risk patients undergoing cardiac surgery: the Low Ventilator-Associated-Pneumonia study[†]

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Abstract

OBJECTIVES: This study assessed whether the Venner-PneuX endotracheal tube (ET) system, which has sub-glottic suction as well as irrigation ports and continuous cuff-pressure monitoring, is associated with a reduction in ventilator-associated pneumonia (VAP) when compared with the standard ET in high-risk patients undergoing cardiac surgery.

METHODS: This was a single-institution, prospective, randomized control trial. Patients were categorized as either Group A (Venner-PneuX ET tube, $n = 120$) or Group B (Standard ET tube, $n = 120$). Inclusion criteria included patients over the age of 70 years and/or impaired left ventricular function (LVEF <50%) undergoing cardiac surgery. Patients were monitored for VAP for up to 48 h post extubation and the diagnosis of VAP was according to the centres for disease control definition.

RESULTS: There were no significant differences in the patients' demographics. The mean (SD) ages for the two groups were 72.4 (8.2) and 72.1 (7.4) years ($P = 0.6$), respectively. The mean EuroSCORE was 6.39 (2.2) for Group A and 6.48 (2.6) for Group B ($P = 0.9$). The median intubation times were 14.7 (7.3, 2927.2) h and 13 (2.5, 528.7) h, respectively. VAP incidence was significantly lower in the Venner-PneuX ET group, being 10.8% when compared with 21% in the standard ET group ($P = 0.03$). There was no significant difference between the two groups in terms of intensive care unit stay ($P = 0.2$) and in-hospital mortality ($P = 0.2$). A binary logistic regression analysis (type of ET tube, age, LVEF, history of lung disease, smoking history, surgical procedure, EuroSCORE, cardiopulmonary bypass time, blood transfusion, intubation duration among others) confirmed that the Venner-PneuX ET tube was associated with significant VAP reduction (Odds ratio 0.45, $P = 0.03$).

CONCLUSIONS: The Venner-PneuX VAP prevention system is associated with a significant reduction in VAP. This can potentially lead to significant cost reductions and should be implemented as part of the VAP reduction bundle.

Keywords: Ventilator-associated pneumonia • Sub-glottic suction drainage and irrigation

INTRODUCTION

Ventilator-associated pneumonia (VAP) is defined as pneumonia in patients who had a device to assist or control respiration continuously through an ET or tracheostomy tube within a 48-h period before the onset of infection [1]. VAP is a common complication of mechanical ventilation and may even be the most common infection occurring in the intensive care unit (ICU) [2, 3].

The risk of VAP on the ICU ranges from 9 to 27% with an incidence of 5–10 cases per 1000 ventilator days [4]. In patients undergoing cardiac surgery, the risk of VAP has been reported at 3.2–8.3% [5]. However, sub-groups of these patients are at a particularly high risk for developing VAP. This sub-group includes elderly patients over the age of 70 years, those with impaired ventricular function and those patients who remain on mechanical ventilation for more than 48 h [6, 7].

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VAP accounts for significant morbidity including increased length of hospital stay and significant increase in cost. It is estimated that each episode of VAP may cost as much as $40 000 [8]. It is also attributable to an increase in mortality, which may be as high as 20–60% [8].

Pathogens colonize the pooled secretions in the oropharynx and sub-glottic space in mechanically ventilated patients. Microaspiration of these colonized secretions occurs past the inflated cuff of the ET and into the lower respiratory tract and cause infection of the lung parenchyma and subsequent pneumonia [9]. Standard ETs made up of PVC are used during anaesthesia and in the ICU, and they have high-volume low-pressure cuffs. These cuffs are designed to provide an airtight seal and prevent aspiration of solid contents into the lower respiratory system while, at the same time, preventing excessive pressure on the tracheal wall mucosa [10]. However, an apparently adequately inflated and well-positioned cuff has folds and creases which still allow micro-aspiration of secretions into the lower respiratory tract [11]. There is good evidence that aspirating secretions from the sub-glottic space is effective and reduces the risk of developing VAP [12]. Aspiration of sub-glottic secretions is a level I recommendation in the Centers for Disease Control and Prevention guidelines [13].

The pathogens/microbes easily adhere to the inner surface of ET and form a bio-film. This is not accessible to antibiotics and serves as a source for reinfection in ventilated patients.

The Venner-PneuX VAP prevention system (Figs 1 and 2) (Intavent Direct, Berkshire, UK) has recently been licensed for use on patients who need to be intubated and supported on a mechanical ventilator as part of their treatment. These ETs have sub-glottic suction ports to suction secretions pooled in the sub-glottic space. The low-volume low-pressure cuff of these tubes inflates without folds/creases and the tracheal seal monitors and maintains optimal cuff pressures. The non-stick lining of these tubes prevents microbial attachment and bio-film formation.

The efficacy of the Venner-PneuX VAP prevention system in reducing VAP has only been evaluated in small case series but not in a randomized, controlled trial [14, 15]. This study has been set up to assess the benefit of VAP reduction when comparing the Venner-PneuX VAP prevention system to a standard ET tube (Portex Tracheal Tube, Smiths, Kent, UK).

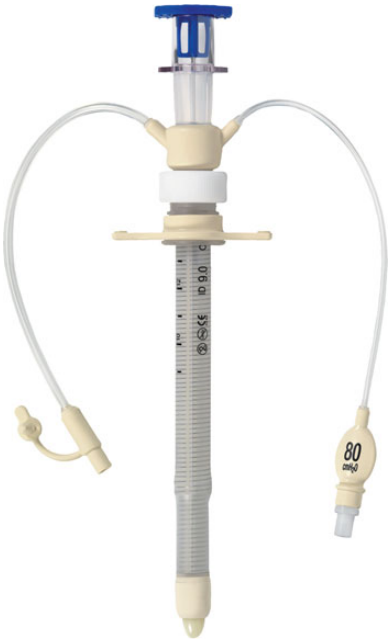

Figure 1: The Pneux-Venner tube.

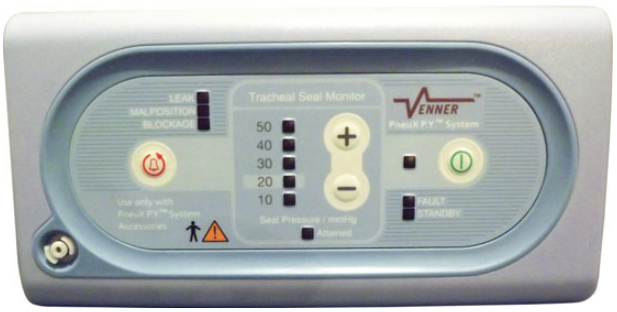

Figure 2: The tracheal seal monitor.

MATERIALS AND METHODS

This was a single-institution, prospective, randomized control trial. This study was funded by the Department of Health in the UK. It was authorized by the Ethical committee (10/H1208/42) and was registered with the ISRCT (ISRCTN 45757289). The study was also supported by the United Kingdom National Institute of Healthcare Research (NIHR) and registered on the NIHR portfolio of studies (UKCRN ID 9831). Trial patients were treated according to the Declaration of Helsinki 1964 (amended Edinburgh 2000).

Power calculations to achieve a power of 0.9 and an alpha of 0.01 suggested that at least 107 patients were needed per group. Inclusion criteria included patients over the age of 70 years and/or impaired left ventricular function (LVEF <50%) undergoing elective and urgent cardiac surgery.

Recruitment was completed within 11 months and the Consort Flow Diagram is shown in the Supplemental Material section.

The Venner-PneuX VAP prevention system consists of an ET with ports for subglottic suction and irrigation as well as a port to attach the Venner™ Tracheal seal monitor. The ET is a flexible armoured tube made up of silicone. It has a low-volume low-pressure cuff made up of silicone that inflates uniformly without folds or creases. The tracheal seal monitor system component is connected to the cuff to continuously maintain and monitor the preset cuff pressure. It has three sub-glottic suction ports around the circumference to ensure that at least one port is patent for suctioning. Sub-glottic suction ports facilitate irrigation and aspiration of secretions from the subglottic space. The tube has a non-stick lining that inhibits the adhesion of microbes and formation of a microbial bio-film. Venner-PneuX tube is available in various sizes. Venner-PneuX tracheostomy tubes are also available. The primary aim of this trial was to determine whether the Venner-PneuX VAP prevention system reduces the risk of developing VAP compared with conventional ETs in the study group. Thus, the primary end-point was to determine the incidence of VAP between the two groups.

The secondary outcomes included postoperative complications, the duration of ICU stay and in-hospital stay for two groups of patients and the in-hospital mortality.

Consented patients were randomized using a computer-generated randomization software program developed by the Trans European Network for Clinical Trial Services, (TENALEA, Amsterdam, Netherlands). Patients were randomized to be intubated with either a standard ET or a Venner-PneuX ET. At

induction of anaesthesia, patients were orotracheally intubated as per randomization. The size of the ET was at the discretion of the consultant anaesthetist. The cuff was inflated until there was no air leak in the conventional ET tubes and the pressure was maintained at the manufacturer's recommended pressures (20–30 mmHg) throughout the procedure with the tracheal seal monitor. Postoperatively, both groups of patients were transferred to the ICU. Patients remained sedated and mechanical ventilation continued via the ET. Both groups of patients received the same routine respiratory care on the ICU as per the ventilator care bundle. This included appropriate hand hygiene, changing of ventilator circuits when soiled, or at 7 days whichever was sooner, semi-recumbent positioning whenever clinically possible and chlorhexidine 2% oral mouthwash every 6 h while intubated. All patients routinely received gastric stress ulcer prophylaxis with Ranitidine 50 mg I.V. every 8 h.

In addition to routine respiratory care, patients randomized to receive the Venner-PneuX VAP prevention system were connected to the Venner™ tracheal seal monitor on arrival to the ICU. Cuff inflation pressures were monitored and maintained at the manufacturer's recommended pressures (20–30 mmHg). This pressure was under continuous monitoring. The sub-glottic ports were irrigated every 6 h as recommended by the manufacturer with 10 ml of distilled sterile water, or as per the clinical judgement of the attending nurse. Irrigation continued until the aspirate ran clear.

If a patient was extubated but subsequently required reintubation, the patient received the same type of ET as had been assigned at randomization. Similarly, if a patient required a tracheostomy tube to facilitate respiratory support and mechanical ventilation, the patient received the same type of tracheostomy tube as that assigned at randomization, namely a standard tracheostomy tube or a Venner-PneuX tracheostomy tube.

Patients were observed and assessed for clinical evidence of VAP for the duration of their period of intubation and for 48 h after extubation. A diagnosis of VAP was confirmed via the Hospitals in Europe Link for Infection Control through Surveillance (HELICS) definition [16].

Statistics

Categorical data are expressed as percentage and differences between the two groups assessed using the (χ^2) test of independence. Continuous variables are expressed as mean [standard deviation (SD)] or median (range) for Gaussian- and skewed-distributed data, respectively. Likewise, group comparison was carried out using the *t*-test or non-parametric test accordingly. The tests were considered significant at $P \leq 0.05$. SPSS version 14.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Binary logistic regression analysis was performed to assess the probability or odds of a patient developing VAP as the dependent variable using a list of predictor variables including the following: type of ET tube, age, LVEF, history of lung disease, smoking history, diabetes, recent MI, urgency of surgery, type of cardiac surgery, EuroSCORE, cardiopulmonary bypass time, re-exploration for bleeding, blood transfusion and duration of intubation. The model was refined using backward elimination.

RESULTS

One hundred and twenty patients were recruited in each group (Total, $n = 240$). There were no significant differences in the patients' demographics with the mean (SD) ages for the two groups being 72.4 (8.2) and 72.1 (7.4) years ($P = 0.6$), respectively. The mean EuroSCORE was 6.39 (2.2) for Group A and 6.48 (2.6) for Group B ($P = 0.9$). There were also no differences between the two groups in terms of cardiac procedures carried out. Preoperative characteristics of the two groups are given in Table 1.

The median intubation times were 14.7 (7.3, 2927.2) h and 13 (2.5, 528.7) h, respectively. Only 6% (15/240) of all the patients who were recruited required ventilation for more than 48 h. The blood transfusion rate was 22% (26/120) for the Venner-PneuX group and 20% (24/120) in the control group, with the majority of these transfused patients receiving less than 2 units of blood.

The incidence of VAP was significantly lower in the Venner-PneuX group, being 10.8% when compared with 21% in the standard ET group ($P = 0.03$). The VAP incidence density was 52 episodes of VAP for 1000 ventilator days for the Venner-PneuX tube and 184 episodes of VAP for 1000 ventilator days for the standard ET tube.

There was no difference between the two groups in terms of ICU stay ($P = 0.2$) and in-hospital mortality ($P = 0.2$) (Table 2).

A binary logistic regression analysis (factors that were entered as predictor variables in the binary logistic regression model include: type of ET tube, age, LVEF, history of lung disease, smoking history, diabetes, recent MI, urgency of surgery, type of cardiac surgery, EuroSCORE, cardiopulmonary bypass time, re-exploration for bleeding, blood transfusion and duration of intubation) confirmed that the use of the Venner-PneuX ET tube was associated with a significant VAP reduction (Odds ratio 0.45, $P = 0.03$).

Overall, there were three deaths in the study: 2 patients in the Venner-PneuX group (cardiac tamponade, coagulopathy/bleeding) and 1 in the standard ET tube group (multiorgan failure). None of the 3 patients who died had VAP. Moreover, 5 patients had tracheostomies: 2 from the standard ET tube group and 3

Table 1: Preoperative characteristics of patients in the two groups

	Standard ET tube	Venner-PneuX tube	*P*-value
n	120	120	
Age[a] (years)	72 (7)	72 (8)	0.5
EuroSCORE[a]	6.4 (2.6)	6.4 (2.2)	0.9
Male, *n* (%)	91 (77%)	83 (69%)	0.2
Elective, *n* (%)	78 (65%)	81 (67%)	0.8
Lung disease, *n* (%)	22 (18%)	20 (17%)	0.7
Recent MI[b], *n* (%)	28 (25%)	18 (21%)	0.2
PVD, *n* (%)	31 (26%)	20 (17%)	0.08
Diabetes, *n* (%)	31 (26%)	44 (37%)	0.07
Impaired LV, *n* (%)	46 (39%)	44 (37%)	0.09
Isolated CABG, *n* (%)	73 61%)	62 (52%)	0.3
Preoperative stay[c] (days)	11 (8, 18)	11 (7, 18)	0.9

[a]Mean (SD).
[b]Denotes surgery carried out within 30 days of an MI (NSTEMI or STEMI).
[c]Median (interquartile range)—in-hospital stay prior to surgery for the urgent cases.
MI: myocardial infarction; PVD: peripheral vascular disease; LV: left ventricular; CABG: coronary artery bypass grafting; SD: standard deviation.

Table 2: Postoperative data

	Standard ET tube	Venner-PneuX tube	*P*-value
n	120	120	
CPB time (min)[a]	105 (62)	110 (58)	0.3
Intubation time (h) [b]	13	15	0.5
ICU stay (days)[b]	1.5	2	0.2
Re-exploration, *n* (%)	10 (8%)	17 (14%)	0.2
Survival	99%	98%	0.2
VAP incidence, *n* (%)	25 (21%)	13 (11%)	0.03
VAP incidence density[c]	184	52	<0.01

[a]Mean (SD).
[b]Median.
[c]Number of VAP episodes per 1000 ventilator days.
CPB: cardiopulmonary bypass; ICU: intensive care unit; VAP: ventilator associated pneumonia.

from the Venner-PneuX tube group. The respective tracheostomy tubes were used for each group.

DISCUSSION

The present study is based on the original Centers for Disease Control definition of VAP: VAP is defined as pneumonia in patients who had a device to assist or control respiration continuously through an ET or tracheostomy tube within a 48-h period before the onset of the infection [1]. It is now well recognized that there is an issue with the development of chest infection when a patient is ventilated [17]. However, there is still ongoing debate regarding the actual diagnosis and hence the recently updated guidelines from the centres for disease control attempt to ensure more objectivity rather than subjectivity in the definition [18]. Moreover, it is also now recognized that ventilated patients can develop lung parenchymal infections even when their intubation period is less than 48 h—a concept sometimes referred to as ventilator-associated condition or ventilator-associated complications (VAC) [17, 18]. Whether it is labelled as VAC or VAP, the problem is the same, i.e. a parenchymal lung infection that developed while the patient was intubated as shown in this study.

Although the ventilator seems to be at blame in the labelling of this clinical condition—ventilator-VAP, there is evidence to show that, in fact, the source of the infection is from the contaminated oropharyngeal secretions trickling past the cuff of the ET [11, 14]. Hence, some authors have suggested the term gravity-tube pneumonia [9]. Thus, it makes sense to drain the sub-glottic region in an attempt to reduce VAP. A systematic review by Muscedere *et al.* [19] concluded that in those patients at risk of VAP, the use of sub-glottic secretion drainage is effective in (i) preventing VAP (risk ratio 0.55), (ii) reducing the duration of mechanical ventilation (by 1.08 days), (iii) reducing days of ICU stay (by 1.52 days) and (iv) increasing the time lapse to the development of VAP by 2.66 days.

There has been a number of factors that have been demonstrated to be associated with VAP in patients undergoing cardiac surgery, namely age (over 70 years), impaired LVEF, duration of intubation, blood transfusion postoperatively, organ-failure index of 3 or greater, need for reintubation and EuroSCORE [20]. However, most of these factors are postoperative factors. Therefore, while setting up the LoVAP study, patients who were at 'high-risk' for developing VAP, i.e. patients who were over 70 years and/or had impaired LV were recruited. On average, the EuroSCORE was at least 6 for each group.

Most of the studies that have reported on VAP and the benefit of sub-glottic suction drainage (SSD) used a continuous suction system [12, 19, 21]. There is emerging evidence that intermittent suctioning may also be of benefit in reducing VAP, ICU stay and mortality [14, 15, 22]. Lacherade *et al.* showed in their study that microbiologically confirmed VAP occurred in 14.8% of the SSD group and in 25.6% of the control group ($P = 0.02$), yielding a relative risk reduction of 42.2% (95% confidential interval, 10.4–63.1%) [22]. In our study, intermittent sub-glottic suctioning was performed at 6-hourly intervals. This was deemed adequate due to the special design feature of the Venner-PneuX tube cuff which prevents any liquid from trickling distally once appropriately inflated in the trachea and its pressure monitored by the Venner™ tracheal seal monitor. Several studies have reported on the benefit of appropriate ET cuffs and their effect on development of VAP [23, 24]. The benefit of the Venner-PneuX VAP prevention system is that it not only allows for intermittent sub-glottic suctioning and irrigation, but it also ensures continuous cuff-pressure monitoring and maintenance. Moreover, the cuff material does not create folds upon contact with the tracheal wall, ensuring a complete seal. In a previously published bench-top study where the Venner-PneuX tube cuff was compared with other ETs in maintaining a water-tight seal, the Venner-PneuX tube was the only device to prevent the leakage of dye past the cuff.

The present study also shows the benefit of subglottic suctioning drainage and irrigation even when the intubation time duration is less than 24 h. So far, reports on VAP in cardiac surgical patients have been focusing on longer ventilation time such as over 48 h [5–7]. In this study, most patients were extubated within 18 h, with only a small proportion being ventilated beyond 48 h (6%). Despite such a short duration for intubation, a 50% reduction in VAP was demonstrated.

Given that this is the first study to objectively assess the efficacy of the Venner™ PneuX VAP Prevention system in a randomized control trial, the incidence of complications relating to the use of the PneuX tube was also recorded. As the tube is armoured, it requires a bougie or intubation stylet to facilitate intubation. The anaesthetists reported no difficulties in intubating patients with the PneuX tube. There were no reports of accidental tube displacement or dislodgement. There was one report of a patient desaturating following suctioning and irrigation. This resulted in a transient increase in oxygen requirement. The patient was subsequently extubated uneventfully 12 h later. The incident was reported to the trial data monitoring and steering committee. An independent clinician from an external organization was also asked to comment on whether the patient had potentially aspirated the sterile water during the reported episode. The independent clinician was given access to all the available clinical material. The external report concluded that it was impossible to state with any certainty that the patient had aspirated the sterile water during the period of suction and irrigation. There were no reports of failure of the continuous cuff-pressure monitoring device.

The incidence of VAP was 10% even in the Venner-PneuX group (elective and urgent patients). This may reflect the fact that a third of the patients had their cardiac surgery as an urgent case. These patients would have been admitted initially with an NSTEMI and thereafter referred for surgery within the same admission. It is a recognized fact that patients are more at risk of developing chest infections the longer they stay in hospital, especially preoperatively. The incidence of VAP in the Venner-PneuX group was 12.8% (5/39).

Additionally, the binary logistic regression analysis showed that in this population group undergoing cardiac surgery, the use of the Venner-PneuX tube was the only significant factor contributing to a halving of VAP incidence (Odds ratio 0.45, $P = 0.03$). This confirms the benefit of both the design of the Venner-PneuX tube (ensuring a proper tracheal seal) and the suction and irrigation ports, which reduce the 'pathogen' burden.

The reported mortality rate in this study was low, being 1.6% in the Venner-PneuX group when compared with 0.8% in the control group ($P = 0.2$) and none of the deaths were related to VAP. However, VAP has been reported with a high mortality rate (up to 50%) [5, 7, 20].

Finally, although no direct cost analysis is reported, the reduction in VAP is associated with a cost benefit. In a recent review, Wyncoll *et al*. reported that the cost of VAP treatment in the USA is around $40 000/patient [25]. In the LoVAP study, there were 12 less patients with VAP in the Venner-PneuX group compared with the standard endotracheal group, amounting to a potential cost saving of $480 000. Given that the cost of using the Venner-PneuX VAP prevention system per patient is around $100, this implies that 4800 patients could have been intubated using this VAP prevention with at least a halving of the VAP rate. Wyncoll also reported that, for a VAP reduction of 45%, the numbers needed to treat (NNT) is only 28 to achieve a cost benefit [25].

CONCLUSION

The LoVAP study has confirmed that VAP (or VAC) is a common postoperative problem in cardiac surgical patients even when the intubation duration is short (<24 h). The Venner-PneuX VAP prevention system significantly reduces the incidence of developing VAP in patients at high risk. Given that this could be associated with significant cost benefits, it is now being implemented in our practice.

SUPPLEMENTARY MATERIAL

Supplementary Material is available at *EJCTS* online.

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Conflict of interest: none declared.

REFERENCES

[1] Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health-care associated infection and criteria for specific types of infection in the acute care setting. Am J Infect Control 2008;36:309–32.

[2] Bouza E, Hortal J, Munoz P, Pascau J, Pérez MJ, Hiesmayr M. Post-operative infections after major heart surgery and prevention of ventilator-associated pneumonia: a one day European prevalence study (ESGNI-008). J Hosp Infect 2006;64:230–4.

[3] Zuschneid I, Schwab F, Geffers C, Behnke M, Rüden H, Gastmeier P. Trends in ventilator-associated pneumonia rates within the German nosocomial infection surveillance system (KISS). Infect Control Hosp Epidemiol 2007;28:314–18.

[4] Chastre J, Fagon JY. Ventilator associated pneumonia. Am J Resp Crit Care Med 2002;165:867–903.

[5] Bouza E, Perez A, Munoz P, Jesús Pérez M, Rincón C, Sánchez C *et al*. Ventilator associated pneumonia after heart surgery: a prospective analysis and the value of surveillance. Crit Care Med 2003;31:1964–70.

[6] Hortal J, Giannella M, Perez MJ, Barrio JM, Desco M, Bouza E *et al*. Incidence and risk factors for ventilator-associated pneumonia after major heart surgery. Intensive Care Med 2009;35:1518–25.

[7] Hortal J, Munoz P, Cuerpo G, Litvan H, Rosseel PM, Bouza E. Ventilator associated pneumonia in patients undergoing major heart surgery: an incidence study in Europe. Crit Care 2009;13:R80.

[8] American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with Hospital-acquired, ventilator-associated and healthcare-associated pneumonia. Am J Resp Crit Care Med 2005;171:388–416.

[9] Mietto C, Pinciroli R, Patel N, Berra L. Ventilator associated pneumonia: evolving definitions and preventive measures. Respir Care 2013;58:990–1003.

[10] Seegobin RD, van Hasselt GL. Endotracheal cuff pressure and tracheal mucosal blood flow: endoscopic study of four large volume cuffs. BMJ 1984;288:965–8.

[11] Seegobin RD, van Hasselt GL. Aspiration beyond endotracheal cuffs. Can Anaesth Soc J 1986;33:273–9.

[12] Dezfulian C, Shojania K, Collard HR, Kim HM, Matthay MA, Saint S. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. Am J Med 2005;118:11–8.

[13] Healthcare Infection Control Practices Advisory Committee; Centres for Disease Control and Prevention (US). Guidelines for preventing health-care-associated pneumonia, 2003 recommendations of the CDC and the Healthcare Infection Control Practices Advisory Committee. Respir Care 2004;49:926–9.

[14] Young PJ, Pakeerathan S, Blunt MC, Subramanya S. A low-volume, low pressure tracheal tube cuff reduced pulmonary aspiration. Crit Care Med 2006;34:632–9.

[15] Fletcher A, Carter J, Blunt M. Incidence of ventilator associated pneumonia in patients undergoing elective tube exchange to LoTrach™ endotracheal tubes. Crit Care 2009;13(Suppl 1):P295.

[16] Hospitals in Europe Link for Infection Control through Surveillance. http://helics.univ-lyon1.fr/ (16 December 2009, date last accessed).

[17] Kollef MH. Prevention of ventilator associated pneumonia or ventilator associated complications: a worthy, yet challenging goal. Crit Care Med 2012;40:271–7.

[18] Centers for Disease Control and Prevention. Device-associated events. Ventilator-associated event (VAE) for use in adult patients >18 years. http://www.cdc.gov/nhsn/PDFs/psc Manual/10-VAE_FINAL.pdf (accessed 9 August 2014).

[19] Muscedere J, Rewa O, Mckechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. Crit Care Med 2011;39:1985–91.

[20] Fitch ZW, Whitman GJR. Incidence, risk and prevention of ventilator-associated pneumonia in adult cardiac surgical patients: a systematic review. J Card Surg 2014;29:196–203.

[21] Bouza E, Perez MJ, Munoz P, Rincón C, Barrio JM, Hortal J. Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. Chest 2008;134:938–46.

[22] Lacherade JC, De Jonghe B, Guezennec P, Debbat K, Hayon J, Monsel A *et al*. Intermittent subglottic secretion drainage and ventilator-associated pneumonia: a multi-centre trial. Am J Respir Crit Care Med 2010;182:910–7.

[23] Valencia M, Ferrer M, Farre R, Navajas D, Badia JR, Nicolas JM *et al*. Automatic control of tracheal tube pressure in ventilated patients in semirecumbent position: a randomized control trial. Crit Care Med 2007;35:1543–9.

[24] Nseir S, Zerimech F, Fournier C, Lubret R, Ramon P, Durocher A *et al*. Continuous control of tracheal cuff pressure and microaspiration of gastric contents in critically ill patients. Am J Crit Care Med 2011;184:1041–7.

[25] Wyncoll D, Camporota L. Number needed to treat and cost-effectiveness in prevention of ventilator-associated pneumonia. Crit Care 2012;16:430–1.