Does objective measurement of tracheal tube cuff pressures minimise adverse effects and maintain accurate cuff pressures? A systematic review and meta-analysis

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Summary

Correct inflation pressures of the tracheal cuff are recommended to ensure adequate ventilation and prevent aspiration and adverse events. However there are conflicting views on which measurement to employ. The aim of this review was to examine whether adjustment of cuff pressure guided by objective measurement, compared with subjective measurement or observation of the pressure value alone, was able to prevent patient-related adverse effects and maintain accurate cuff pressures. A search of PubMed, Web of Science, Embase, CINAHL and ScienceDirect was conducted using keywords 'cuff pressure' and 'measure*' and related synonyms. Included studies were randomised or pseudo-randomised controlled trials investigating mechanically ventilated patients both in the intensive care unit and during surgery. Outcomes included adverse effects and the comparison of pressure measurements. Pooled analyses were performed to calculate risk ratios, effect sizes and 95% confidence intervals. Meta-analysis found preliminary evidence that adjustment of cuff pressure guided by objective measurement as compared with subjective measurement or observation of the pressure value alone, has benefit in preventing adverse effects. These included cough at two hours (odds ratio [OR] 0.42, confidence interval [CI] 0.23 to 0.79, $P=0.007$), hoarseness at 24 hours (OR 0.49, CI 0.31 to 0.76, $P<0.002$), sore throat (OR 0.73, CI 0.54 to 0.97, $P<0.03$), lesions of the trachea and incidences of silent aspiration ($P=0.001$), as well as maintaining accurate cuff pressures (Hedges' g 1.61, CI 2.69 to 0.53, $P=0.003$). Subjective measurement to guide adjustment or observation of the pressure value alone may lead to patient-related adverse effects and inaccuracies. It is recommended that an objective form of measurement be used.

Key Words: airway, intubation, tracheal, tracheostomy, intensive care

Many patients in the intensive care unit (ICU) or operating theatre (OT) will require intubation with either an endotracheal or tracheostomy tube. Cuff inflation is important to secure the tube position, to provide an adequate seal for ventilation and to prevent the aspiration of gastric and oral secretions. Currently a range of 20 to 30 cmH₂O is regarded as safe; however out-of-range tracheal cuff pressures are common in patients with intratracheal intubation¹. Over-inflation of the cuff can potentially impair tracheal mucosal blood flow². This has been associated with tracheal injuries including mucosal inflammation, mucosal ischaemia, tracheal ulceration, stenosis, tracheo-oesophageal fistula, tracheomalacia and tracheal rupture³⁻¹⁰. Conversely, under-inflation of the cuff is associated with inadequate ventilation and microaspiration^{9,11-13}, which may result in ventilator-acquired complications including pneumonia¹⁴.

Routine cuff pressure measurement and adjustment to keep the pressure within a recommended range has been claimed to be important in the prevention of adverse effects to the intubated patient¹⁵⁻¹⁷. However among the methods utilised, there is much variability ranging from subjective estimation techniques¹⁸⁻²³, to more objective measures²⁵⁻²⁸. Despite this recommendation for routine measurement, cuff pressure monitoring is varied across sites, and recent literature has shown that dedicated guidelines or protocols and documentation are lacking^{15,29}.

The objective of this systematic review was to examine whether adjustment of cuff pressure guided by objective measurement, as compared with subjective measurement or observation of the pressure value alone, was able to prevent patient-related adverse effects in mechanically ventilated patients with an artificial airway. Secondly, the review compared the ability of the two forms of measurements to maintain accurate cuff pressure, despite variability in the target range between studies. Accurate cuff pressure was defined as a significant difference in cuff pressure between the two measurement groups.

Materials and methods

A systematic review of the published literature was conducted to investigate the effects of adjustment of cuff

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pressure guided by objective measurement, as compared with subjective measurement or observation of the pressure value alone, in mechanically ventilated patients in both the intensive care unit (ICU) and in the operating theatre (OT). Inclusion and exclusion criteria were determined and are listed in Table 1. As it was anticipated there would not be a large number of papers, it was decided a priori to include all studies fulfilling the inclusion criteria, regardless of the quality score. A protocol for this systematic review was registered and published on the PROSPERO database (42015016652). The PRISMA statement³⁰ was followed to assure the quality of the reporting.

Search strategy

A comprehensive search strategy of the electronic databases PubMed, Web of Science, Embase, CINAHL and ScienceDirect was conducted. All databases were searched from 1970 to March 2015. Only studies after 1970 were reviewed to exclude older low volume, high pressure tracheal and tracheostomy tubes, which were replaced with high

volume, low pressure (HVLP) cuffs in the early 1970s. The keywords or search terms were as follows: ('cuff pressure' OR 'cuff volume' 'mechanically ventilated' OR 'mechanical ventilation' OR 'ventilated patient' OR ventilat* OR intubat* OR tracheostom* AND measure* OR record* OR monitor* OR observe* OR manage*). In addition we scanned citations from articles sourced within the database search. For the purpose of this review we defined cuff pressure measurement as any objective measure such as using a manometer/direct intracuff pressure gauge or pressure–volume loop closure. Subjective cuff pressure included estimation techniques such as pilot balloon palpation, auscultation technique, and measuring but not adjusting the cuff pressure within an appropriate range. Language limits were set to English and French. Animal studies were excluded.

Selection criteria

Studies selected for the meta-analysis were confined to those investigating mechanically ventilated patients both within the ICU and the OT with either an endotracheal tube or tracheostomy tube. Primary outcomes were associated adverse effects including self-reported sore throat, hoarse voice, tracheal mucosal injury visualised via fiberoptic bronchoscopy, and cough post-extubation at various timepoints. Secondary outcomes of interest were cuff pressures within the recommended range. In order to calculate 95% confidence intervals (CI) and effect sizes, the studies were required to report means, standard deviations and sample size or sample size and *P*-value. To calculate odds ratios the studies were required to report numbers and percentages. To assess eligibility, two independent assessors (CH, JP) independently examined the titles and abstracts of the studies and consulted in case of disagreement. Figure 1 illustrates the article selection process.

Assessment of methodological quality

The quality of the methodological features of the nine studies were independently assessed and rated using the Physiotherapy Evidence Database (PEDro) scale. Criteria include specification of eligibility criteria (not scored), random allocation, concealed allocation, baseline similarity, therapist blinding, assessor blinding, measure of key outcomes >85% of subjects, intention to treat, between-group statistical comparison and point measures, and measures of variability³². Only criteria two to 11 are scored in the PEDro scale. This is a reliable instrument for rating quality of randomised controlled trials (RCTs)^{32–33}, based on a 0–10 point scale where a score of six or more indicates a trial of moderate to high quality. Following independent scoring and assessment, both reviewers (CH, JP) then discussed and verified the results. Consensus was achieved with open discussion between the investigators. The quality scoring for the included studies is shown in Table 2 (next page).

Table 1
Inclusion/exclusion criteria for review

	Inclusion	Exclusion
Design	Prospective randomised controlled trials Pseudo-randomised controlled trials Systematic reviews	Case studies Narrative reviews Guidelines Audits Studies published <1970 Studies other than in English or French
Participants	Adults or children mechanically ventilated with an artificial airway (tracheal tube or tracheostomy tube) including during surgery and in the intensive care unit	Animal models Intubated with a laryngeal mask airway
Comparison	Comparing objective cuff pressure measurement and adjustment to either no, or subjective measurement (based on human decision) Comparing objective cuff pressure measurement and adjustment to observation of the pressure without adjustment	Comparing two objective cuff pressure measurements Comparing personnel ability to accurately inflate cuff Comparing continuous monitoring to single objective measurement
Outcome measures	Primary Associated adverse effects including sore throat, dysphagia, dysphonia, hoarse voice, bleeding of the tracheal mucosa, cough post-extubation Rates of cuff over-inflation/under-inflation Rates of silent aspiration Secondary Cuff pressures within the recommended range

Figure 1: Flow diagram outlining the selection of studies for the review.

Data Extraction and Analysis

Two reviewers (CH, JP) independently performed and then cross-checked the data with regard to study design, intervention, and outcome measures. To compare results between trials, for continuous outcomes the unbiased effect size estimators (Hedges' *g*) with 95% confidence intervals were calculated, using Comprehensive Meta-analysis software. Dichotomous outcomes were expressed as risk ratios with 95% confidence intervals. The data was pooled using the fixed effects model, however where heterogeneity was statistically significant (Q statistic $P < 0.01$), the data was reanalysed using the random effects model. Meta-analysis was not possible for some outcomes due to heterogeneity in the method of measurement and infrequent outcome measures included in the studies. The data for these outcomes was reported descriptively. A summary of information is included in Tables 2 and 3, together with the score for quality assessment.

Results

From 1009 papers identified, 985 were eliminated on abstract review due to duplicate copies or meeting the a

priori exclusion criteria (Figure 1). The 24 remaining studies were full-text reviewed and excluded if they were non-randomised controlled trials^{25,26,34-37}, not available in English³⁸, full text not available^{39,40} or not on the actual topic^{23,41-44}. This systematic review was based upon nine studies including seven RCTs⁴⁵⁻⁵¹ and two pseudo-randomised controlled trials where interventions were compared but participants were not randomly allocated to groups^{52,53}.

Demographics and setting

Specific details for selected studies are shown in Table 2. Studies were in either adult tertiary intensive care settings (2)^{52,53}, operating theatre (6)⁴⁵⁻⁵⁰, both operating theatre and intensive care setting⁴⁷, or intubated in medical wards (1)⁵¹. Mean age overall was 43 years (range 22–70). The ratio of males to females was approximately 1:1 (Table 3). Intubation time varied from 1.76 to 98.4 hours with the mean being 21.7 hours. Intubation time for ICU, OT and ICU, and ward patients was longer (range 8–98.4 hours) compared to intubation time in the OT (range 1.76–4.15 hours). The overall number of subjects was 1077 (n ranging from 24 to 509).

Methodology

The control groups used a variety of subjective measurement techniques and occasional objective measurements but adjustments were not guided by frequent objective measurement of pressures. The intervention group had objective measurements, most commonly using a manometer, and the pressures were either frequently or continuously adjusted using this method.

Study quality and design

Most prospective randomised controlled trials were well conducted but did not report the blinding of assessors⁵¹⁻⁵⁵. Faults noted in lower scoring papers were nonspecification of eligibility criteria, lack of reporting of random allocation or concealed allocation, inequality at baseline, or blinding of assessors. As patients were heavily sedated or anaesthetised at this stage they were assumed to be blinded. Quality scores for the comparative studies are provided in Table 2. All studies except one⁴⁹ were single-centre which decreases external generalisability.

Summary of findings

Results are presented with Table 4 summarising the effect sizes. Meta-analysis was performed for differences in cuff pressures between groups (presented as a forest plot in Figure 2), incidence of cough at two and 24 hours, incidence of hoarseness at two and 24 hours, and incidence of sore throat at 24 hours.

Cuff pressure measurement

Six studies recorded the difference in intra-cuff pressure between the groups and a random effects model ($i^2 = 95.3$, $P < 0.001$) found significantly lower cuff pressures in the

Table 2
Physiotherapy Evidence Database (PEDro)³¹ scores of reviewed studies

Study	Random allocation	Concealed allocation	Baseline similarity	Subject blinding	Therapist blinding	Assessor blinding	Measure of key outcomes >85% of subjects	Intention to treat	Between-group statistical comparison	Point measures and measures of variability	Physiotherapy evidence database score (/10)
Almarakbi et al 2014 ⁴⁶	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	9
Ansari et al 2014 ⁴⁵	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	9
Liu et al 2010 ⁴⁹	✓	X	✓	✓	X	✓	✓	✓	✓	✓	8
Morris et al 2007 ⁵²	X	X	X	✓	X	X	✓	✓	✓	X	4
Rubes et al 2014 ⁴⁷	✓	✓	X	✓	X	✓	✓	✓	✓	✓	8
Ryu et al 2013 ⁴⁸	✓	✓	✓	✓	X	✓	✓	✓	✓	✓	9
Sajedi et al 2002 ⁵⁰	✓	X	✓	✓	X	✓	✓	✓	✓	✓	8
Sridermma et al 2007 ⁵¹	X	X	X	✓	X	X	✓	✓	✓	✓	5
Zand et al 2008 ⁵³	X	X	X	✓	X	X	✓	✓	✓	✓	5

intervention group (Hedges' g 1.61, confidence interval [CI] 2.69 to 0.53, $P=0.003$) (Figure 2).

Cough, hoarseness

Random effects models found a significant effect for incidence of cough at two hours (odds ratio [OR] 0.43, CI 0.23 to 0.79, $P=0.007$) but not for 24 hours, (OR 0.80, CI 0.33 to 1.99, $P=0.64$). Although two studies^{46,48} found no difference between groups in hoarseness at two hours postoperatively (OR 0.67, CI 0.39 to 1.16, $P=0.15$), overall there was a significant decrease in hoarseness at 24 hours in the intervention group (OR 0.49, CI 0.31 to 0.76, $P<0.002$).

Sore throat, pain and dysphagia

Three studies^{46,48,49} found significantly increased incidence of sore throat in the control group at 24 hours (OR 0.55, CI 0.41 to 0.75, $P=0.00$). Another study established pain by the visual analog scale (VAS) and found a significantly greater score for pain at two and six hours but not at 24 hours⁴⁵ (Table 4). One study investigated dysphagia at two and 24 hours and found no difference between groups⁴⁸ (Table 4).

Tracheal lesions

Of the two studies that looked for tracheal injury, Liu et al ($P=0.043$)⁴⁹ and Sajedi et al ($P<0.001$)⁵⁰ found an increased incidence of tracheal injury in the control group. There was also a higher incidence ($P=0.002$) of blood-streaked expectoration in the control group⁴⁹ (Table 4).

Silent aspiration

A significant incidence of silent aspiration was found in the intervention group ($P<0.001$) of one study⁴⁷ (Table 4).

Rates of over-inflation

One study⁵² examined rates of over-inflation (>25 cmH₂O) and severe over-inflation (>40 cmH₂O) and found no difference between groups (Table 4).

Intubation time and possible risk of bias

The majority of the studies^{46,48-50} had intubation times of approximately two hours, including all studies included in the meta-analyses reporting pain, sore throat, hoarseness, dysphagia and cough. The only outliers were Zand et al (98 hours)⁵³ and Rubes et al (50 hours)⁴⁷. Two studies^{45,51} reported an approximate intubation time for both groups, and one study⁵² did not report any time. Within studies, times between groups were homogeneous, except in the study by Rubes et al where there was a non-significant difference between groups ($P=0.038$) (Table 3).

Discussion

This review provided preliminary evidence that adjustment of cuff pressure guided by objective measurement, as compared with subjective measurement or observation of the pressure alone can prevent adverse effects including hoarseness, sore throat, lesions of the trachea, and

Table 3
Characteristics of reviewed studies

Study	Number (control/ intervention) Sex distribution (M/F) Age (control/ intervention)	Intubation time (hours)	Recommended cuff pressure range (cmH ₂ O)	Sample population	Control arm (no measurement/ estimation)	Intervention arm (objective measurement)	Outcome measures	Major findings
Almarakbi et al 2014 ⁴⁶	100 Control (26/24) Intervention (26/24) Control 42.5 (37–51) Intervention 41 (36–50) $P=0.417$	Control (1.83+/-1.58–2.16) Intervention (1.76+/-1.55–2.13)	No range outlined Lower end, with minimal volume	Adult patients with ASA physical status I or II, elective surgery requiring tracheal intubation	Cuff inflated using JS technique	Cuff inflation guided by PVL	Incidence of postoperative cuff-related complications Difference in cuff pressures	PVL associated with lower cuff pressure than JS group PVL associated with less incidence of cuff-related complications than JS group
Ansari et al 2014 ⁴⁵	43 (23/20) Control (14/6) Intervention (12/11) Control 28.6 (6.1) Intervention 25.8 (3.5)	2–4	20–30	Adult patients having maxillofacial procedure under GA	Cuff pressure estimated and adjusted by palpation of pilot balloon at beginning of operation	Cuff pressure measured and adjusted using pressure gauge at intubation and every subsequent hour	Difference in cuff pressures Incidence of throat pain at 1, 6 and 24 hrs postoperatively	Control group final mean cuff pressure higher than study group Throat pain scores lower in study group at 1 and 6 hours but not at 24 hrs
Liu et al 2010 ⁴⁹	509 Control (112/116) Intervention (81/155) Control (52+/-17) Intervention (53+/-17) $P=0.617$	Control (2.8+/-1.35) Intervention (2.7+/-1.3)	20–34	Adult patients with ASA physical status I or II from 4 tertiary university hospitals in China scheduled for GA	Cuff inflated by anaesthesiologist using pilot balloon palpation but not adjusted throughout procedure	Cuff inflated by anaesthesiologist then adjusted with manometer within range 15–25 mmHg	Mean cuff pressure difference in study group after palpation vs. adjustment Incidence of sore throat, cough, hoarseness and blood-streaked expectoration at 24 hrs Degree of injury, measured via fiberoptic bronchoscopic examination	Estimation group mean cuff pressure higher than group using manometer Control group associated with more incidences of post procedural sore throat, hoarseness and blood-streaked expectoration than study group More severe degree of mucosal injury associated with control group than study group
Morris et al 2007 ⁵²	115 M/F (numbers in groups not stated) Age not reported	Not reported Not reported	Lower range not reported – 25	Adult medical and surgical ICU patients ventilated via cuffed TT or Trache	Cuffs assessed by palpation and adjusted once every 12 hrs	Cuffs measured with manometer every 1–2 days, informally palpated every shift and adjusted	Rates of over-inflation (>25 cmH ₂ O) Rates of severe over-inflation (>40 cmH ₂ O) Difference in cuff pressures	Incidence of over-inflation (38%) was identical between both groups
Rubes et al 2014 ⁴⁷	24 Control (7/5) Intervention (8/4) Control (63.2+/-8.9) Intervention (51.3+/-11.6) $P=0.028$	Control 50.0 (28.5 to 93.5) Intervention (32.0 (19.5 to 39.8) $P=0.038$	20–30	Adult patients from Sept 2008 to Nov 2009 undergoing PEA with CPB and DHCA	Cuff pressure monitoring with manometer without adjusting cuff volume or pressure	Cuffs measured with manometer and reinflated when pressure dropped below 20 cmH ₂ O, up to starting value (25 cmH ₂ O). During rewarming, pressure checked at various temperature points and cuff deflated if pressure exceeded 30 cmH ₂ O	Difference in cuff pressures Silent aspiration (Blue dye test)	Intervention group associated with less frequent silent aspiration than control group Control group associated with lower cuff pressures at several timepoints during cooling, just before DHCA and at all time points during rewarming

Ryu et al 2013 ⁴⁸	90 Control (12/32) Intervention (14/30) Control 46.3 (11.3) Intervention 47 (14.5)	Control (2+/- 0.87) Intervention (1.96+/- 1.045)	25–50	Adult patients with ASA physical status I or II, 19–70 yrs of age, scheduled for elective thyroidectomy under GA	Cuff pressure set to 25 cmH ₂ O, continuously monitored with manometer, not adjusted	Cuff pressure set to 25 cmH ₂ O, monitored and continuously maintained at 25 cmH ₂ O during surgery via manometer	Difference in cuff pressures Incidence and degree of POST as reported by patient in questionnaire Incidence of hoarseness, dysphagia and cough	Control group cuff pressures were higher over time than those of study group Incidences of POST was lower in the study group at 2 and 24 hrs Severity of POST at 2 hrs was lower in study group No differences in hoarseness, dysphagia and cough
Sajedi et al 2002 ⁵⁰	80 Control (18/22) Intervention (21/19) Control (36+/-13) Intervention (36+/- 11)	Control (2.03+/-0.93) Intervention (1.96+/-0.67)	No range outlined Used MOV as baseline value	Adult patients with ASA physical status I or II scheduled for elective surgery under GA with tracheal intubation	Cuff pressure measured every 15 minutes, average recorded at conclusion of procedure	Cuff pressure set to point of no leak pressure via water manometer Cuff pressure maintained at constant pressure throughout procedure	Mean cuff pressure in loose control group vs. set pressure TMLS >0 Incidence of sore throat	Loose control group associated with higher mean cuff pressures than tight control group Loose control group associated with a significantly higher proportion of patients with TMLS >0 than tight control group Loose control group associated with a higher incidence of sore throat than tight control group
Sridharan et al 2007 ⁵¹	59 M/F (Number in groups not stated) Ages not reported	8	20–30	Adult patients with indwelling TT in general medical wards	Cuff pressure estimated by finger palpation of pilot balloon or inflating 5 ml of air	Manometer used as guide to inflate cuff until pressure was 30 cmH ₂ O every eight hours	Number of measurements within cuff pressure recommended range	Manometer group associated with higher proportion of measurements within recommended range than estimation group
Zand et al 2008 ⁵³	57 Control (35/10) Intervention (10/2) Control (53.5+/- 18.8) Intervention (36.5+/-17) P=0.007	Control (98.4+/- 122.4) Intervention (96+/- 67.2)	No range outlined	Adult ICU patients requiring tracheal intubation	Pressure monitored by 'no leak test' and manual palpation of the pilot balloon and adjusted	Pressure monitored by CPG and adjusted	Difference in cuff pressures	The estimation group was associated with higher cuff pressures than the CPG group

American Society of Anesthesiologists (ASA), just seal (JS), pressure-volume loop (PVL), general anaesthetic (GA), hours (hrs), tracheal tube (TT), tracheostomy tube (Trache), tracheal mucosal lesion score (TMLS), postoperative sore throat (POST), intensive care unit (ICU), pulmonary endarterectomy (PEA), cardiopulmonary bypass (CPB), deep hypothermic circulatory arrest (DHCA), years (yrs), minimal occlusive volume (MOV), cuff pressure gauge (CPG).

Figure 2: Differences in cuff pressures between groups. CI = confidence interval.

incidences of silent aspiration, as well as maintaining accurate cuff pressures.

Multiple factors that contribute to patient-related adverse effects have been implicated in the literature. These include tracheal tube size, cuff position, type of tube, cuff contours, multiple attempts at tracheal intubation, duration of intubation, type of surgery, use of nasogastric tubes and, throat packs, some forms of lubrications, and downfolding of the epiglottis⁵⁴⁻⁵⁸. However the studies in this group were relatively homogeneous as regards intubation times and type of surgeries within groups. Other factors, while a source of variability, should have been counteracted by randomisation. However there is a need for larger studies with the analysis adjusted for confounders.

Only one study reported dysphagia as an outcome and found no difference between the two measurement groups at either two or 24 hours. These results were similar to a study of patients undergoing anterior cervical spine surgery, where dysphagia was related to the duration of neck retraction rather than cuff pressure⁵⁹.

Sore throat is a common postoperative complaint following tracheal intubation. Causative factors reported in the literature include tracheal tube size⁵⁶, cuff design⁶⁰, certain lubricants containing local anaesthetic agents and steroids⁶¹, and high cuff pressures⁶². This review demonstrated a significant decrease in reports of sore throat or pain, suggesting a role of objective measurement. It is postulated that over-inflation may cause an increase in the cuff–tracheal contact area⁶², and as such a larger area of damage to the mucosa, due to ischaemia⁶³. The incidence of sore throat has been shown to be relative to the area of cuff–tracheal contact⁶² with the literature suggesting that cuff-pressure limitation may reduce the incidence of postoperative sore throat⁶².

All adverse effects reported in the included studies were within the first 24 hours post-extubation. Conclusions therefore are unable to be drawn about any long-term effects

that high cuff pressures may have.

All nine studies included in this review compared cuff measurements between groups. Meta-analysis of six studies demonstrated that objective cuff pressure measurement has a significant role in maintaining a lower cuff pressure, as compared to subjective techniques or observation of the pressure value alone.

Of note, whilst most of the studies reported cuff pressures as a direct comparison between the measurement groups, few of them reported a direct comparison between adverse events and targeted pressures. The one study that did look at the incidences of cuff pressure measurements within a recommended range, favoured the use of objective measurement in maintaining accurate cuff pressures⁵¹. There was significant variability among the recommended cuff pressure ranges within the studies included in this review. This variability is reflected in the literature, where there is no clear consensus of target cuff pressures²⁹. It is often recommended to be between 20 and 30 cmH₂O^{2,14,64}, however benchtop studies have suggested that cuff pressures may need to be much higher (up to 60 cmH₂O) in order to limit microaspiration⁶⁵. The application of higher pressures (>30 cmH₂O) is of concern because of the risk of tracheal injury resulting from the obstruction of bloodflow in the tracheal mucosal wall^{2,66}. These upper ranges have mostly been informed by animal studies, which conclude that cuff pressure monitoring is essential to avoid serious injury to the trachea^{63,67}.

Tracheal cuff pressure tends to fluctuate with time. Diffusion of nitrous oxide during anaesthesia into the cuff of the tracheal tube results in an increase in cuff pressure almost immediately⁸, whilst prolonged surgical procedures (>4 hours) have been shown to result in significant variations in cuff pressure⁶⁸. Using intermittent monitoring, Sole et al^{69,70} noted decreases in tracheal cuff pressure within four to 12 hours after adjustment of the pressure to 20 cmH₂O. Similar findings were noted when cuff pressure was monitored

Table 4
Summary of results

Outcome Measure	Author	Results (study vs. control)	Favours
Adverse effects			
Rates of over-inflation	Morris et al 2007 ⁵²	20/52 (38%) vs. 24/63 (38%) $P=0.99$	NS
Rates of severe over-inflation	Morris et al 2007 ⁵²	21% vs. 17% $P=0.83$	NS
Dysphagia at 2 h	Ryu et al 2013 ⁴⁸	39 (89) vs. 36 (82) $P=0.367$	NS
Dysphagia at 24 h	Ryu et al 2013 ⁴⁸	31 (71) vs. 34 (77) $P=0.467$	NS
Pain 1 h after extubation (VAS)	Ansari et al 2014 ⁴⁵	3.9 (1.5) vs. 5.3 (1.1) $P=0.002$	Study group
Pain 6 h after extubation (VAS)	Ansari et al 2014 ⁴⁵	3.1 (1.5) vs. 4.5 (1.3) $P=0.002$	Study group
Pain 24 h after extubation (VAS)	Ansari et al 2014 ⁴⁵	1.6 (1.2) vs. 1.9 (1.1) $P=0.4$	NS
Blood-streaked expectoration	Liu et al 2010 ⁴⁹	9% (4) vs. 30% (11) $P=0.002$	Study group
Fibreoptic bronchoscopic examination (degree of injury)	Liu et al 2010 ⁴⁹	$P=0.043$	Study group
TMLS >0	Sajedi et al 2002 ⁵⁰	28% vs. 77.5% $P<0.001$	Study group
Intra-cuff Measurements			
Mean TT CP difference in study group after palpation vs. adjustment (mmHg)	Liu et al 2010 ⁴⁹	43+/-23.3 vs. 20+/-3.1 $P<0.001$ N = 236 N = 273	Study group
Mean CP in loose control group vs. set pressure (cmH ₂ O)	Sajedi et al 2002 ⁵⁰	81+/-17 vs. 23.4+/-3 $P<0.001$ N = 40 N = 40	Study group
Number of measurements within CP recommended range	Sridermma et al 2007 ⁵¹	181 (90.5%) vs. 123 (31.8%) $P<0.001$ (95% CI 2.44–3.32) N = 20 N = 39	Study group

Tracheal tube (TT), cuff pressure (CP), hours (h), visual analog scale (VAS), tracheal mucosal lesion score (TMLS), non-significant (NS).

continuously^{1,71}. Longer duration of intubation has been associated with greater decreases in pressure over time^{1,72} and this is thought to be due to the cuff becoming less compliant⁷³. This change in pressures has implications for the

timing of measurements. A recent qualitative review of cuff measurement practices found wide variability in frequency ranging from four-hourly to once a day²⁹. This variability was reflected in this review with frequency of measurements ranging from continuous measurement to once every one to two days.

Two studies in the review reported on lesions of the trachea. It is thought that high cuff pressures affect perfusion of the tracheal mucosa, resulting in inflammation, ischaemia, ulceration, stenosis, necrosis, and ultimately, rupture of the tracheal mucosa^{74,75}. Both studies directly visualised the tracheal mucosa via fibreoptic bronchoscopy, and reported mucosal injury. In addition Liu et al⁴⁹ reported incidences of blood-streaked expectoration as a measure of tracheal damage. Both studies reported some degree of mucosal injury to the trachea in both measurement groups but found that the injury was more severe in the non-objectively measured group. Post mortem specimens of intubated patients have demonstrated extensive laryngeal and tracheal epithelial damage occurring as a result of both the intubation itself and the presence of the tracheal tube with an intubation period as short as one hour^{76,77}. Damage was greatest in those patients who had been intubated the longest⁷⁸. Intubation time in the studies included in this review ranged from one hour to five days. The times were homogeneous between the measurement groups in all studies. There appeared to be no association between length of intubation and reported adverse effects or tracheal damage. All studies included in meta-analysis of these outcomes came from the OT group and as such had relatively short intubation times, meaning that no comparisons could be made between the shorter intubation groups (OT) and the patients requiring longer intubation times (longer cases in OT and prolonged ICU and ward stays).

Only one study in the review looked at the incidence of silent aspiration as a reported adverse effect. They found objective cuff pressure measurement to be beneficial in preventing silent aspiration. Similarly Nseir and colleagues⁷⁹ demonstrated that continuous cuff pressure monitoring was effective in reducing the risk of microaspiration and subsequently ventilator-associated pneumonia (VAP). Cuff pressure control to prevent microaspiration is often included in the bundle of care to prevent VAP^{80,81}. The results from this review support the use of regular objective cuff measurement as part of a VAP prevention strategy.

From the overall results of this review there is strong evidence that adjustment of cuff pressure guided by objective measurement as compared with subjective measurement or observation of the pressure alone has beneficial effects in maintaining accurate cuff pressures, despite the lack of a clear consensus regarding a recommended cuff pressure range. There does appear to be some moderate evidence that objective measurement is beneficial in preventing

cough, hoarseness, sore throat, lesions of the trachea, and incidences of silent aspiration. The results clearly support that cuff pressure adjustment be guided by use of an objective device as it has a direct impact on patient-related outcomes for the prevention of adverse effects.

This systematic review and meta-analysis has some limitations, namely the small number of participants included in the studies and heterogeneity of both methodology and outcome measures. Initial criteria excluded comparison of continuous or automated monitoring. These forms of monitoring are becoming more common and need to be investigated further. Generalisation of results may be limited as most of the trials were conducted within a theatre, where intubation time is shorter relative to stays in the ICU. This review did not seek to outline the specifics of recommended cuff pressure range, frequency of measurements or objective device used. Further definitive studies are required to inform the specifics associated with this practice.

Future trials should focus on specific measurable targets, such as a recommended cuff pressure range, and be powered for meaningful short- and long-term outcomes. It is important to include a priori a more diverse population of intubated patients in order to investigate which population of patients receives most benefit from cuff pressure measurement.

This review has found preliminary evidence that adjustment of cuff pressure guided by objective measurement as compared with subjective measurement or observation of the pressure alone, can prevent adverse effects including hoarseness, sore throat, lesions of the trachea and incidences of silent aspiration, as well as maintaining accurate cuff pressures.

Conclusion

Adjustment of cuff pressures guided by subjective measurement, or observation of the pressure value alone, may lead to patient-related adverse effects and inaccurate cuff pressures. It is recommended that an objective device be used.

References

- Nseir S, Brisson H, Marquette C-H, Chaud P, Di Pompeo C, Diarra M, Durocher A. Variations in endotracheal cuff pressure in intubated critically ill patients: prevalence and risk factors. *Eur J Anaesthesiol* 2009; 26:229-234.
- Seegobin RD, van Hasselt GL. Endotracheal cuff pressure and tracheal mucosal blood flow: endoscopic study of effects of four large volume cuffs. *Br Med J (Clin Res Ed)* 1984; 288:965-968.
- Rubio PA, Farrell EM, Bautista EM. Severe tracheal stenosis after brief endotracheal intubation. *South Med J* 1979; 72:1628-1629.
- Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy. A prospective study of 150 critically ill adult patients. *Am J Med* 1981; 70:65-76.
- Bouattour K, Prost-Lapeyre A, Hauw-Berlemont C, Diehl J-L, Guerot E. [A post-intubation tracheal rupture in intensive care unit]. *Ann Fr Anesth Reanim* 2014; 33:590-592.
- Lim H, Kim JH, Kim D, Lee J, Son JS, Kim DC, Ko S. Tracheal rupture after endotracheal intubation—a report of three cases. *Korean J Anesthesiol* 2012; 62:277-280.
- Alvarez-Maldonado P, Vidal E, Ceron-Diaz U. Tracheal ulcers due to endotracheal tube cuff pressure. *J Bronchology Interv Pulmonol* 2011; 18:288-289.
- Combes X, Schaulvliege F, Peyrouset O, Motamed C, Kirov K, Dhonneur G, Duvaldestin P. Intracuff pressure and tracheal morbidity: influence of filling with saline during nitrous oxide anesthesia. *Anesthesiology* 2001; 95:1120-1124.
- Terashima H, Sakurai T, Takahashi S, Saitoh M, Hirayama K. [Postintubation tracheal stenosis; problems associated with choice of management]. *Kyobu Geka* 2002; 55:837-842.
- Hameed AA, Mohamed H, Al-Mansoori M. Acquired tracheoesophageal fistula due to high intracuff pressure. *Ann Thorac Med* 2008; 3:23-25.
- Estes RJ, Meduri GU. The pathogenesis of ventilator-associated pneumonia: I. Mechanisms of bacterial transcolonization and airway inoculation. *Intensive Care Med* 1995; 21:365-383.
- Hamilton VA, Grap MJ. The role of the endotracheal tube cuff in microaspiration. *Heart Lung* 2012; 41:167-172.
- Lau ACW, So HM, Tang SL, Yeung A, Lam SM, Yan WW. Prevention of ventilator-associated pneumonia. *Hong Kong Med J* 2015; 21:61-68.
- Rello J, Sonora R, Jubert P, Artigas A, Rue M, Valles J. Pneumonia in intubated patients: role of respiratory airway care. *Am J Respir Crit Care Med* 1996; 154:111-115.
- Curiel Garcia JA, Guerrero-Romero F, Rodriguez-Moran M. [Cuff pressure in endotracheal intubation: should it be routinely measured?]. *Gac Med Mex* 2001; 137:179-182.
- Vyas D, Inweregbu K, Pittard A. Measurement of tracheal tube cuff pressure in critical care. *Anaesthesia* 2002; 57:275-277.
- Peters JH, Hoogerwerf N. Prehospital endotracheal intubation; need for routine cuff pressure measurement? *Emerg Med J* 2013; 30:851-853.
- Maboudi A, Abtahi H, Hosseini M, Tamadon A, Safavi E. Accuracy of endotracheal tube cuff pressure adjustment by fingertip palpation after training of intensive care unit nurses. *Iran Red Crescent Med J* 2013; 15:381-384.
- Velasco Sanz TR, Ronda Delgado de la Fuente M, Sanchez de la Ventana AB, Reyes Merino Martinez M. [Cuff pressure control at the intensive care unit: influence of nursing professionals' training]. *Enferm Intensiva* 2015; 26:40-45.
- Jiang N, Del Signore AG, Illoreta AM, Malkin BD. Evaluation of a teaching tool to increase the accuracy of pilot balloon palpation for measuring tracheostomy tube cuff pressure. *Laryngoscope* 2013; 123:1884-1888.
- Michlig SA. Anaesthetic staff cannot identify extremely high tracheal tube cuff pressures by palpation of the pilot balloon. *Br J Anaesth* 2013; 111:300-301.
- Hoffman RJ, Parwani V, Hahn IH. Experienced emergency medicine physicians cannot safely inflate or estimate endotracheal tube cuff pressure using standard techniques. *Am J Emerg Med* 2006; 24:139-143.
- Parwani V, Hoffman RJ, Russell A, Bharel C, Preblich C, Hahn IH. Practicing paramedics cannot generate or estimate safe endotracheal tube cuff pressure using standard techniques. *Prehosp Emerg Care* 2007; 11:307-311.
- Ganner C. The accurate measurement of endotracheal tube cuff pressures. *Br J Nurs* 2001; 10:1127-1134.

25. Stewart SL, Secrest JA, Norwood BR, Zachary R. A comparison of endotracheal tube cuff pressures using estimation techniques and direct intracuff measurement. *AANA J* 2003; 71:443-447.
26. Braz JR, Navarro LH, Takata IH, Nascimento Junior P. Endotracheal tube cuff pressure: need for precise measurement. *Sao Paulo Med J* 1999; 117:243-247.
27. Fernandez R, Blanch L, Mancebo J, Bonsoms N, Artigas A. Endotracheal tube cuff pressure assessment: pitfalls of finger estimation and need for objective measurement. *Crit Care Med* 1990; 18:1423-1426.
28. Galinski M, Treoux V, Garrigue B, Lapostolle F, Borron SW, Adnet F. Intracuff pressures of endotracheal tubes in the management of airway emergencies: the need for pressure monitoring. *Ann Emerg Med* 2006; 47:545-547.
29. Talekar CR, Udy AA, Boots RJ, Lipman J, Cook D. Tracheal cuff pressure monitoring in the ICU: a literature review and survey of current practice in Queensland. *Anaesth Intensive Care* 2014; 42:761-770.
30. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Br Med J* 2009; 339:b2535.
31. Physiotherapy Evidence Database Scale. 1999 Physiotherapy Evidence Database website. From <http://www.pedro.org.au/english/downloads/pedro-scale/>. Accessed March 2015.
32. Tooth L, Bennett S, McCluskey A, Hoffmann T, McKenna K, Lovarini M. Appraising the quality of randomized controlled trials: inter-rater reliability for the OTseeker evidence database. *J Eval Clin Pract* 2005; 11:547-555.
33. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther* 2003; 83:713-721.
34. Ramadan M, Pushpanathan E, Sultan P. Should endotracheal cuff pressure be routinely measured during elective surgery? *Br J Hosp Med (Lond)* 2012; 73:538.
35. Valles J. Monitoring intra-cuff pressure in subglottic aspiration. *Crit Care Med* 2005; 33:1469-1470.
36. Nagdeve NG, Kelly K. Audit of tracheal tube cuff pressure measurement with a minimal occlusion technique of cuff inflation in a theatre setting. *Br J Anaesth* 2011; 107:294P.
37. Gopalan P, Browning ST. Accuracy of finger-tip palpated tracheostomy tube cuff pressure readings among otolaryngologists. *J Laryngol Otol* 2005; 119:461-464.
38. Muñoz VE, Mojica S, et al. Comparison of the orotracheal tube cuff pressure estimated by palpation vs. the measurement taken with a manometer. *Revista Ciencias de la Salud* 2011; 9: 229-236.
39. Jain MK, Tripathi CB. Endotracheal tube cuff pressure monitoring during neurosurgery—manual vs automatic method. *J Anaesthesiol Clin Pharmacol* 2011; 27:358-361.
40. Kovaceric M, Pavicic AM et al. Monitoring tracheal tube cuff pressure reduces postoperative sore throat symptoms. *Eur J Anaesthesiol* 2013; 30: 54.
41. Arndt M, Hofmockel R, Benad G. [Sore throat after use of the laryngeal mask and intubation]. *Anaesthesiol Reanim* 1998; 23:44-48.
42. Goyal R, Kumar G, Waghray MR. Endotracheal tube cuff pressure monitoring in peripheral hospitals. *Med J Armed Forces India* 2006; 62: 243-245.
43. Modirian E, Ghafouri HB, Saeedi H, Yasinzadeh M, Famouri S. Excessive endotracheal tube cuff pressure: is there any difference between emergency physicians and anesthesiologists? *Signa Vitae* 2012; 7:17-20.
44. Srinivasan D, Halsnad S, Anand R, Parmar S. Intraoperative tracheostomy tube cuff pressures: Pilot balloon palpation versus manometry. Accessed from *Oral Oncol Supplement* 2009; 3: 169.
45. Ansari L, Bohluli B, Mahaseni H, Valaei N, Sadr-Eshkevari P, Rashad A. The effect of endotracheal tube cuff pressure control on postextubation throat pain in orthognathic surgeries: a randomized double-blind controlled clinical trial. *Br J Oral Maxillofac Surg* 2014; 52:140-143.
46. Almarakbi WA, Kaki AM. Tracheal tube cuff inflation guided by pressure volume loop closure associated with lower postoperative cuff-related complications: Prospective, randomized clinical trial. *Saudi J Anaesth* 2014; 8:328–334.
47. Rubes D, Klein AA, Lips M, Rulisek J, Kopecky P, Blaha J et al. The effect of adjusting tracheal tube cuff pressure during deep hypothermic circulatory arrest: a randomised trial. *Eur J Anaesthesiol* 2014; 31:452-456.
48. Ryu JH, Han SS, Do SH, Lee JM, Lee SC, Choi ES. Effect of adjusted cuff pressure of endotracheal tube during thyroidectomy on postoperative airway complications: prospective, randomized, and controlled trial. *World J Surg* 2013; 37:786-791.
49. Liu J, Zhang X, Gong W, Li S, Wang F, Fu S, Zhang M, Hang Y. Correlations between controlled endotracheal tube cuff pressure and postprocedural complications: a multicenter study. *Anesth Analg* 2010; 111:1133-1137.
50. Sajedi P, Maaroffi V. The macroscopic changes of tracheal mucosa following tight versus loose control of tracheal tube cuff pressure. *Acta Anaesthesiol Sin* 2002; 40:117-120.
51. Sridemma S, Limtangturakool S, Wongsurakiat P, Thamlikitkul V. Development of appropriate procedures for inflation of endotracheal tube cuff in intubated patients. *J Med Assoc Thai* 2007; 90 Suppl 2:74-78.
52. Morris LG, Zoumalan RA, Roccaforte JD, Amin MR. Monitoring tracheal tube cuff pressures in the intensive care unit: a comparison of digital palpation and manometry. *Ann Otol Rhinol Laryngol* 2007; 116:639-642.
53. Zand F, Nekooeian AA, Rohani M. Endotracheal tube cuff pressure monitoring in intensive care units. *Iran Red Crescent Med J* 2008; 10: 223-227.
54. Ayoub CM, Ghobashy A, Koch ME, McGrimley L, Pascale V, Qadir S et al. Widespread application of topical steroids to decrease sore throat, hoarseness, and cough after tracheal intubation. *Anesth Analg* 1998; 87:714-716.
55. Hahnel J, Treiber H, Konrad F, Mutzbauer T, Steffen P, Georgieff M. Performance characteristics of a novel reusable intermediate-volume low-pressure cuffed endotracheal tube. *Acta Anaesthesiol Scand* 1994; 38:363-367.
56. Stout DM, Bishop MJ, Dwersteg JF, Cullen BF. Correlation of endotracheal tube size with sore throat and hoarseness following general anesthesia. *Anesthesiology* 1987; 67:419-421.
57. Edomwonyi NP, Ekwere IT, Omo E, Rupasinghe A. Postoperative throat complications after tracheal intubation. *Ann Afri Med* 2006; 5: 28–32.
58. van Zundert A, van Zundert T, Brimacombe J. Downfolding of the epiglottis during intubation. *Anesth Analg* 2010; 110:1246-1247.
59. Ratnaraj J, Todorov A, McHugh T, Cheng MA, Laurysen C. Effects of decreasing endotracheal tube cuff pressures during neck

- retraction for anterior cervical spine surgery. *J Neurosurg* 2002; 97:176-179.
60. Loeser EA, Hodges M, Gliedman J, Stanley TH, Johansen RK, Yonetani D. Tracheal pathology following short-term intubation with low- and high-pressure endotracheal tube cuffs. *Anesth Analg* 1978; 57:577-579.
61. Stride PC. Postoperative sore throat: topical hydrocortisone. *Anaesthesia* 1990; 45:968-971.
62. Jensen PJ, Hommelgaard P, Sondergaard P, Eriksen S. Sore throat after operation: influence of tracheal intubation, intracuff pressure and type of cuff. *Br J Anaesth* 1982; 54:453-457.
63. Nordin U, Lindholm C E, Wolgast M. Blood flow in the rabbit tracheal mucosa under normal conditions and under the influence of tracheal intubation. *Acta Anaesthesiol Scand* 1977; 21:81-94.
64. Dullenkopf A, Gerber A, Weiss M. Fluid leakage past tracheal tube cuffs: evaluation of the new Microcuff endotracheal tube. *Intensive Care Med* 2003; 29:1849-1853.
65. Pitts R, Fisher D, Sulemanji D, Kratochvil J, Jiang Y, Kacmarek R. Variables affecting leakage past endotracheal tube cuffs: a bench study. *Intensive Care Med* 2010; 36:2066-2073.
66. Bernhard WN, Cottrell JE, Sivakumaran C, Patel K, Yost L, Turndorf H. Adjustment of intracuff pressure to prevent aspiration. *Anesthesiology* 1979; 50:363-366.
67. Touzot-Jourde G, Stedman NL, Trim CM. The effects of two endotracheal tube cuff inflation pressures on liquid aspiration and tracheal wall damage in horses. *Vet Anaesth Analg* 2005; 32:23-29.
68. Kako H, Goykhman A, Ramesh AS, Krishna SG, Tobias JD. Changes in intracuff pressure of a cuffed endotracheal tube during prolonged surgical procedures. *Int J Pediatr Otorhinolaryngol* 2015; 79:76-79.
69. Sole ML, Combs SM, Willis J. Changes in endotracheal cuff pressures over time. *Crit Care Med* 2003; 31: A144.
70. Sole ML, Poalillo FE, Byers JF, Ludy JE. Bacterial growth in secretions and on suctioning equipment of orally intubated patients: a pilot study. *Am J Crit Care* 2002; 11:141-149.
71. Sole ML, Penoyer DA, Su X, Jimenez E, Kalita SJ, Poalillo E et al. Assessment of endotracheal cuff pressure by continuous monitoring: a pilot study. *Am J Crit Care* 2009; 18:133-143.
72. Fu Y, Xi X. [Analysis on risk factors of endotracheal cuff under inflation in mechanically ventilated patients]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2014; 26:870-874.
73. Sole ML, Su X, Talbert S, Penoyer DA, Kalita S, Jimenez E et al. Evaluation of an intervention to maintain endotracheal tube cuff pressure within therapeutic range. *Am J Crit Care* 2011; 20:109-117.
74. Nseir S, Duguet A, Copin M-C, De Jonckheere J, Zhang M, Similowski T, Marquette C-H. Continuous control of endotracheal cuff pressure and tracheal wall damage: a randomized controlled animal study. *Crit Care* 2007; 11:R109.
75. Tu HN, Saidi N, Leiutaud T, Bensaid S, Menival V, Duvaldestin P. Nitrous oxide increases endotracheal cuff pressure and the incidence of tracheal lesions in anesthetized patients. *Anesth Analg* 1999; 89:187-190.
76. Hilding AC. Laryngotracheal damage during intratracheal anesthesia. Demonstration by staining the unfixed specimen with methylene blue. *Ann Otol Rhinol Laryngol* 1971; 80:565-581.
77. Donnelly WH. Histopathology of endotracheal intubation. An autopsy study of 99 cases. *Arch Pathol* 1969; 88:511-520.
78. McHardy FE, Chung F. Postoperative sore throat: cause, prevention and treatment. *Anaesthesia* 1999; 54:444-453.
79. Nseir S, Zerimech F, Fournier C, Lubret R, Ramon P, Durocher A, Balduyck M. Continuous control of tracheal cuff pressure and microaspiration of gastric contents in critically ill patients. *Am J Respir Crit Care Med* 2011; 184:1041-1047.
80. Palmer LB. Ventilator-associated tracheobronchitis. *Curr Respir Med Rev* 2010; 6: 58-64.
81. Alvarez Lerma F, Sanchez Garcia M, Lorente L, Gordo F, Anon JM, Alvarez J et al. Guidelines for the prevention of ventilator-associated pneumonia and their implementation. The Spanish 'Zero-VAP' bundle. *Med Intensiva* 2014; 38:226-236.