Awake videolaryngoscopic orotracheal intubation in patients with laryngeal tumour using the C-MAC D-Blade

Address for correspondence:

Dr. Swati Jindal,
Department of Anaesthesia
and Intensive Care,
Government Medical College
and Hospital, Sector 32,
Chandigarh - 160 062, India.
E-mail: swatirohit604@gmail.

Submitted: 17-Jan-2022 Revised: 03-Aug-2022 Accepted: 03-Aug-2022 Published: 22-Aug-2022 Selwin R. Selvam, Swati Jindal¹, Lakesh K. Anand², Manpreet Singh Dawar¹, Ariun Dass³

Department of Critical care Medicine, Christian Medical College, Vellore, Tamil Nadu, ¹Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Sector 32, Chandigarh, ²Department of Anaesthesia and Intensive Care, MMIMSR, Mullana, Ambala, Haryana, ³Department of ENT, MAX Hospital, Mohali, Punjab, India

ABSTRACT

Background and Aims: This study assessed the applicability of C-MAC videolaryngoscope (VL) D-blade for awake intubation in patients with laryngeal tumour. The primary study objective was to determine the rate of successful intubation in the first attempt. The other parameters recorded were number of attempts required for intubation, duration of different stages of intubation, haemodynamics, ease of intubation and patient comfort on visual analogue scale (VAS) postoperatively. Methods: Thirty patients were studied. Patients were sedated with dexmedetomidine and fentanyl as a slow bolus (over 20 min) and Ramsay sedation score was assessed. Topicalisation of the oropharynx, tonsillar pillars and base of the tongue was done with lignocaine 10% spray. Four ml of 4% lignocaine using MADgic atomiser was used for anaesthetising the glottis and the tracheal lumen. Results: Successful intubation was achieved in 86.6% patients in first attempt and 13.3% in two attempts. Total time for all intubations was less than 30 seconds. Fremantle score was F-1-C-MAC D-blade (easy intubation with full view) in 60% patients, while 23.3% had F-2-C-MAC D-blade (full view and either required more than one attempt or a modified technique), 13.3% had P-1-C-MAC D-blade (partial view with easy intubation) and 3.3% had P-2-C-MAC D-blade (partial view and required more than one attempt or a modified technique). The VAS score for anaesthesiologist's ease and for patient's experience was 85.83 ± 7.20 and 86.66 ± 14.46, respectively. Conclusion: C-MAC VL D-blade-assisted awake intubation is an effective and safe method to manage the airway of patients with laryngeal tumour once adequate topicalisation is ensured before the procedure.

Key words: Dexmedetomidine, glottis, intubation, laryngeal neoplasm, visual analogue scale

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.ija_54_22

Quick response code



INTRODUCTION

Airway management in the form of intubation in patients with laryngeal tumour is associated with high-risk. A supraglottic tumour may obstruct the view of the larynx, whereas the glottis is the narrowest point for passage of an endotracheal tube (ETT). There is an inherent risk of losing control of the airway in these patients on the induction of general anaesthesia (GA) before tracheal intubation either due to loss of hypopharyngeal muscle tone or dynamic/complete airway obstruction. [1]

In the presence of such predicted difficult airways, awake tracheal intubation (ATI) is considered the technique of choice. ATI is performed

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

 $\textbf{For reprints contact:} \ WKHLRPMedknow_reprints@wolterskluwer.com$

How to cite this article: Selvam SR, Jindal S, Anand LK, Dawar MS, Dass A. Awake videolaryngoscopic orotracheal intubation in patients with laryngeal tumour using the C-MAC D-Blade. Indian J Anaesth 2022;66:579-84.

using either a fibreoptic bronchoscope (FOB) or videolaryngoscope (VL). FOB-guided ATI is skill dependent, requires time, complex equipment and may not be always successful.^[2] Front of neck access (FONA) with awake tracheostomy under local anaesthesia is another option, but this does not seem pragmatic and is avoided if possible.

There has been a paradigm change in the airway management with the introduction of a variety of VLs.^[3] VL-aided ATI is faster, safer, and has higher success rate as it allows visualisation of both, the larynx and the upper airway. There is avoidance of the red out and cork in screw phenomenon seen with FOB-guided intubation. Gentle traction with a VL helps in creating space in the upper airway for suction of secretions and might lift the tumour away from the laryngeal inlet, thereby relieving the obstruction and making the patient more comfortable.^[4] Markova et al.^[1] conducted a feasibility study where 23 out of 25 patients with laryngeal tumours for surgery were intubated awake using King Vision VL (KVVL) with a channelled blade.

The C-MAC®VL has a hyperangulated (40°) D-blade with 1 mm thickness, an elliptical tapered half-moon shape and a facility for paraoxygenation. These features make it an attractive option in difficult intubations, provided the mouth opening is more than 18 mm.^[5,6] However, the use of D-blade in laryngeal tumours is not well documented with only few cases reported in the literature.^[4] This study was conducted to evaluate the use of C-MAC VL D-blade (adult size) for awake orotracheal intubation in patients with laryngeal tumours undergoing elective surgery under GA.

METHODS

This observational study took place at a medical college hospital from March 2019 to August 2020. The study was approved by the Institutional Review Board [IRB number - ECR/658/Inst/PB/2014/RR-2017] and the institutional ethics committee (on 27-12-2018). It was registered in the Clinical Trial Registry, India [CTRI/2019/03/018123], and was performed in accordance with the principles of the Declaration of Helsinki.

For sample size calculation, previous one year data from the department of ear, nose and throat in patients with diagnosed laryngeal tumours was collected. A total of 50 patients with laryngeal tumours had undergone procedures. Considering the exclusion criteria, we planned to enrol 30 patients in our study using convenient sampling in the study period.

Patients older than 18 years, of American Society of Anesthesiologists (ASA) physical status I-III undergoing diagnostic or radical surgery for laryngeal tumour, were included. The exclusion criteria were patients with mouth opening ≤18 mm, at risk of aspiration and pregnant patients. Patients with complete airway obstruction, and those having tumour of airway other than the larynx (tongue or tracheal) were also excluded.

Preoperative anaesthetic evaluation was done a day prior to surgery. Airway difficulty score (ADS) was recorded in all the patients.^[7] Alternatives to awake VL, such as awake FOB guided intubation and FONA were informed.

In the operation room, heart rate (HR), non-invasive blood pressure (NIBP), continuous electrocardiogram and oxygen saturation (SpO $_2$) were recorded before the induction of anaesthesia. All patients received intravenous (IV) glycopyrrolate 0.2 mg, dexamethasone 8 mg, ondansetron 4 mg and an IV infusion of 1 μ g.kg $^{-1}$ dexmedetomidine and 1 μ g.kg $^{-1}$ fentanyl diluted in 50 ml saline, over 20 min for sedation.

An experienced anaesthesiologist performed all the intubations with the patient in the semi-recumbent position. Topicalisation of the airway was done with lignocaine 10% sprayed during inspiration over the oropharynx, tonsillar pillars and base of the tongue (two puffs on each side). Four millilitres of 4% lignocaine was administered during inspiration through a laryngotracheal mucosal atomisation device, for anaesthetising the glottis and tracheal lumen. The adequacy of oral and oropharyngeal topicalisation was checked by gentle suction at the posterior pharyngeal wall before introducing the blade. The total local anaesthetic dose was estimated and was kept below 9 mg.kg⁻¹.^[9]

Paraoxygenation was done via a catheter inserted into the half open-guide rail on the blind side of C-MAC D-blade and attached to an oxygen source with a flow rate of 10-15 L.min⁻¹. A polyvinyl chloride tracheal tube with a soft tip was used to secure the airway. The Fremantle score was used to assess the view, ease and device used for laryngoscopy. Fremantle score is calculated using a three part numerical scoring system

based on the laryngeal view [full (F), partial (P) or no view (N)], ease of endotracheal intubation [easy (1), modified (2) or unachievable (3)] and the VL including blade and its size (here CMAC-D size 3).^[10] Standard anaesthetic drugs were used for the induction and maintenance of GA.

The success of intubation and the duration of stages of intubation were recorded by another anaesthesiologist. The following durations were assessed and recorded using a smart phone: 1) duration of visualising the vocal cord - the time from picking up the VL to noticing the vocal cords (percentage of glottic opening (POGO) score at least 75%); 2) duration of intubation: time from observing the vocal cords up to the passage of ETT through the vocal cords; 3) duration of first ventilation: the time taken to inflate the ETT cuff and to identify the first square wave capnograph on the monitor; and 4) total intubation duration: the time from picking up the VL to the appearance of the first square wave capnograph on the monitor. Failure of intubation was considered if patient did not tolerate the procedure, or if more than three attempts were required.

The cough was assessed by the cough and gag score and patient comfort was assessed by comfort score during the intubation procedure. Ramsay sedation score (RSS) was used to assess sedation in the patients. The anaesthesiologist performing the ATI rated the procedure between 0, if it was very difficult, to 100, if very easy. Similarly postoperatively, the patients in the postanaesthesia care unit were asked about their experience during ATI and they rated between 0, if they had worst possible discomfort, to 100 if comfortable and would not mind having the procedure again.

The primary study objective was to determine the rate of successful intubation in the first attempt. We also recorded the number of attempts (removal of the C-MAC D-blade VL from the airway and re-insertion), HR, NIBP and SpO_2 at baseline, after topicalisation, during VL, immediately after intubation, at 1, 2, 5 min after intubation, before extubation, immediately after extubation, and at 5 and 10 min after extubation. Other findings like damaged teeth, soft tissue oedema, bleeding from the gums or lips were recorded post operatively.

Statistical Package for Social Sciences was used to conduct the statistical analysis (SPSS Inc., Chicago,

version 16.0 for Windows). For the descriptive statistics, categorical variables, that is, gender distribution, ASA physical status, operative procedure, site of tumour, Fremantle score, number of attempts to intubate, additional laryngeal manipulation and coughing/movements of hands were presented as numbers and percentages. Age, weight, height, body mass index (BMI), ADS, duration of topicalisation, POGO score, duration of procedure, cough and gag score, comfort score, RSS, visual analogue scale (VAS), haemodynamics and SpO₂ were presented as the mean and standard deviation.

RESULTS

Out of the 40 patients considered eligible, 30 patients were enroled for the study after obtaining written informed consent [Figure 1]. Patient details such as age, gender, ASA grading, weight, height and BMI were recorded [Table 1]. Out of these 30 patients, 29 (96.7%) underwent direct laryngoscopy with biopsy and 1 (3.3%) had micro-laryngeal surgery. There were 14 (46.7%) patients with supraglottic tumours, 14 (46.7%) with glottic tumours and two (6.6%) patients with subglottic tumours in the present study.

The mean duration of topicalisation was 6.57 ± 2.4 min with 60% of the patients achieving topicalisation in 3-5 min. POGO score 90-100% was noted among majority of the patients (83.3%). Majority (86.7%) of the

Table 1: Patient details					
Parameter	Number (%)	Mean±SD (range)	95% CI		
Age (years)					
<50	6 (20%)	57.47±11.04 (35-75)	53.34-61.59		
50-60	11 (36.7%)				
61-70	10 (33.3%)				
>70	3 (10.0%)				
Gender					
Male	26 (86.7%)				
Female	4 (13.3%)				
ASA grade					
1	3 (10%)				
II	24 (80%)				
III	3 (3%)				
Weight in kg		59.7±12.23 (30-89)	55.13-64.27		
Height in cm		163.63±7.32 (145-178)	160.90-166.37		
BMI in kg/m ²		22.16±3.73 (14.27-30.84)	20.76-23.54		
ADS					
6	4 (13.3%)	7.17±0.69 (6-9)	6.91-7.43		
7	18 (60.0%)				
8	7 (23.3%)				
9	1 (3.3%)				

ASA – American Society of Anesthesiologists, SD – standard deviation.

ADS – Airway difficulty score, CI – confidence interval, BMI – body mass index

patients were intubated in a single attempt. 13.3% of the patients were intubated in two attempts [Table 2].

Sixty percent of the patients had Fremantle score F-1-C-MAC D-blade, 23.3% of the patients had F-2-C-MAC D-blade, 13.3% of the patients had P-1-C-MAC D-blade and 3.3% of the patients had P-2-C-MAC D-blade.

The mean duration to visualising the vocal cords and intubation was 12.02 ± 4.34 s and 9.02 ± 3.84 s respectively. The mean duration of first ventilation and total duration was 4.33 ± 1.51 s, and 25.38 ± 5.88 s, respectively [Table 3]. Additional laryngeal manipulation was performed in 16.7% of patients and 83.3% of the patients did not require it.

Coughing/movements of hand were present in 16.7% patients while 83.3% of the patients did not cough at all during intubation. Majority (86.6%) of the patients had a comfort score 1-2 while 13.3% needed to be pacified (score3). The RSS ranged between 1 and 3 in all patients throughout the intubation procedure [Table 2].

There were no wide fluctuations in any of the haemodynamic variables like HR, blood pressure and oxygen saturation measured at baseline, after topicalisation, during videolaryngoscopy, immediately after intubation, at 1, 2, 5 min after intubation, before extubation, immediately after extubation, at 5 and 10 min after extubation.

None of the patients suffered from damage to teeth or bleeding from gums or soft tissue oedema. The median VAS for anaesthesiologist's ease of intubation was

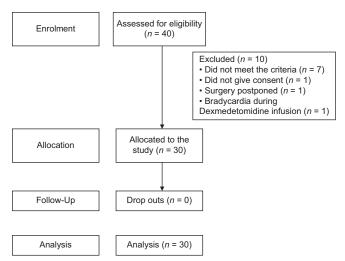


Figure 1: Flow diagram

90 [inter quartile range (IQR) 70-100] and for patient's experience was 90 (IQR 60-100).

DISCUSSION

The results of our observational study validate that C-MAC VL D-blade successfully facilitated ATI in patients with laryngeal tumours.

Intubation was highly successful on the first try (86%) and was accomplished in less than half a minute in all patients [Table 2]. Sahajanandan *et al.*^[13] have reported first attempt success rate of intubation using C-MAC D-blade and channelled KVVL to be

Table 2: Intubation parameter	ers with C-MAC	VLD-blade
	Number of Patients	Percentage
Duration of topicalisation (min)	Patients	(%)
3-5	18	60
	12	40
6-10	12	40
POGO score	0.5	
90-100%	25	83.3
75-89%	5	16.7
Number of attempts to intubate		
One	26	86.7
Two	4	13.3
Cough and Gag score		
1	25	83.33
2	1	3.33
3	4	13.33
4	0	0
5	0	0
Comfort score		
1	19	63.33
2	7	23.33
3	4	13.33
4	0	0
5	0	0
Ramsay sedation score		
1	2	6.67
2	15	50
3	13	43.33
4	0	0
5	0	0
6	0	0

VL - videolaryngoscope, POGO - percentage of glottic opening

	Table 3: Dura	Table 3: Duration of the procedure			
	Mean±SD (s)	Range (s)	95%CI (s)		
D1	12.02±4.34	5.21-30.32	10.39-13.64		
D2	9.02±3.84	3.41-20.30	7.59-10.46		
D3	4.33±1.51	2.01-9.33	3.76-4.90		
D4	25.38±5.88	14.34-41.74	23.18-27.58		

D1=Duration to visualising the vocal cords; D2=Duration of intubation; D3=Duration of first ventilation; D4=Total intubation duration. SD – standard deviation, CI –confidence interval

84.3% and 74.1% respectively in obese patients with anticipated difficult airway. Because of its flat profile and elliptical form, the D-blade may give a better glottic visibility and higher first attempt success. Additionally, it is less bulky, easy to introduce into the mouth with the capability of manoeuvring the ETT within the oral cavity, if required. The fixed wider view of the glottis and surrounding structures, including the tumour, provided by the D blade, aids in recognition of the airway landmarks. Markova et al., in their study on patients with periglottic tumours, had used KVVL and found a first attempt success rate of 74%. In our study, the mean duration to visualise the vocal cords was 12.02 ± 4.34 s [Table 3] (less than half a minute) which was lower compared to the findings of Markova et al.,[1] where the median duration to achieve the glottic view was 19 s. The lower success rate while using the channelled KVVL appears to be due to its thicker cross section making it more difficult to introduce into the mouth. The monitor of KVVL needs to be detached from its blade at the time of introduction into the mouth and the preloaded ETT is known to impinge on the right arytenoids and requires manoeuvres to negotiate the ETT into the glottis.

There were no failures in our study. Two (13.3%) patients required second attempt for intubation, and in them, repetition of topicalisation with the MADgic atomiser was done. Markova *et al.*^[1] encountered a failure rate of 8% with KVVL and Kramer *et al.*^[14] had failure of attempts in two patients with C-MAC D-blade, due to gag reflex. It has been highlighted that for awake VL intubation, adequate topical anaesthesia is critical. Lack of familiarity with VL is also cited as another important reason for failure to intubate.^[13]

Studies where VL has been used either alone or compared with FOB in difficult airways^[1,13,15-17] show a high degree of heterogeneity in the total intubation time for ATI using VL, accentuating the need for a more consistent generalisable approach.

Preoperative administration of dexmedetomidine and fentanyl induced appropriate level of sedation with the score of ≤ 3 without compromising the airway. This relieved anxiety, made the patients cooperative enough to allow awake intubation. It has been shown that dexmedetomidine provided better and safe intubating conditions than fentanyl-midazolam during FOB guided ATI with lesser haemodynamic variations, more favourable cough score and comparable sedation scores. [18,19]

The mean duration of topicalisation (time of topicalisation to the time of laryngoscopy) was 6.57 ± 2.4 min in our study. This corroborates with the fact that the onset of lidocaine topicalisation starts within 5 min.^[9] Further studies need to establish the significance of this duration along with comparison between different local anaesthetics as well as different techniques of topicalisation.

The median VAS was 90 for both, the anaesthesiologist's ease of the procedure and the patient's experience, indicating high levels of acceptance for the ATI. In the study by Mendonca et al.,[20] FOB guided awake intubation was compared with ATI using Pentax AWS VL in patients with anticipated difficult airway, wherein the anaesthesiologist's impression of the ease of procedure for VL, on VAS was 87 (61-100) [mean (range)] and the patient's reported comfort was 79 (59-100). In our study, adequate level of sedation and adequate topical anaesthesia made the patients comfortable. Also there was some amount of difficulty in breathing in these patients due to laryngeal mass obstructing the airway. Moving the tube into the trachea under VL guidance might have relieved the obstruction and made it easier for the patient to breathe. This seemed to increase the patient's acceptance of the whole procedure of intubation.

Minimal cough and high acceptance of the ATI diminished the potential for mucosal injury while suctioning the secretions in the patients in the current study. VL enables clear visualisation and effective suction of secretions from the area under observation. [1] In the randomised controlled trial by Kramer et al., [14] ATI was done either with C-MAC VL D-blade or FOB guided nasal intubation. They reported slight nasopharyngeal haemorrhage in 9 of 50 patients in the C-MAC D-blade group, which required no intervention. The McGrath VL and C-MAC D-blade have been reported to have the highest success and lowest tissue trauma rates, this being attributed to the blade design. [21]

The limitation of our study is its small sample size. All the procedures were carried out by an experienced anaesthesiologist. More trials can be carried out in the future to confirm the superiority of awake videolaryngoscopic intubation over FOB intubation, as well as the superiority of the C-MAC VL D-blade over other VLs for safe and effective airway management in patients with laryngeal tumours.

CONCLUSION

Awake videolaryngoscopic intubation using C-MAC VL is a safe and effective strategy to control the airway in patients with laryngeal tumours. Due to the design, the D-blade offers benefit in awake intubation by inflicting minimal/no tissue injury. The technique is more comfortable for a conscious but sedated patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Markova L, Stopar- Pintaric T, Luzar T, Benedik J, Hodzovic I. A feasibility study of awake videolaryngoscope-assisted intubation in patients with periglottic tumour using the channelled King Vision videolaryngoscope. Anaesthesia 2017;72:512-8.
- Wilson WM, Smith AF. The emerging role of awake videolaryngoscopy in airway management. Anaesthesia 2018;73:1058-61.
- 3. Shruthi AH, Dinakara D, Chandrika YR. Role of videolaryngoscope in the management of difficult airway in adults: A survey. Indian J Anaesth 2020;64:855-62.
- Gaszyński T. The use of the C-MAC videolaryngoscope for awake intubation in patients with a predicted extremely difficult airway: Case series. Ther Clin Risk Manag 2018;14:539-42.
- Xue FS, Li HX, Liu YY, Yang GZ. Current evidence for the use of C-MAC videolaryngoscope in adult airway management: A review of the literature. Ther Clin Risk Manag 2017;13:831-41.
- Vaishnavi BD, Syal R, Vyas R, Bihani P. Awake intubation with C-MAC videolaryngoscope in a patient with difficult airway. Indian J Anaesth 2021;65:253-4.
- Janssens M, Hartstein G. Management of difficult intubation. Eur J Anaesthesiol 2001;18:3-12.
- Hassan ME, Mahran E. Evaluation of different doses of dexmedetomidine alone versus the combination of

- dexmedetomidine and fentanyl in sedation during awake fiberoptic intubation in oral cancer surgery patients: A prospective, randomized, double blind clinical trial. Saudi J Anaesth 2017;11:196-202.
- 9. Ahmad I, El-Boghdadly K, Bhagrath R, Hodzovic I, McNarry AF, Mir F, et al. Difficult Airway Society guidelines for awake tracheal intubation (ATI) in adults. Anaesthesia 2020;75:509-28.
- Swann AD, English JD, O'Loughlin EJ. The development and preliminary evaluation of a proposed new scoring system for videolaryngoscopy. Anaesth Intensive Care 2012;40:697-701.
- Vasu BK, Rajan S, Paul J, Kumar L. Efficacy of atomised local anaesthetic versus transtracheal topical anaesthesia for awake fiberoptic intubation. Indian J Anaesth 2017;61:661-6.
- Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974:2:656-9.
- Sahajanandan R, Dhanyee AS, Gautam AK. A comparison of King vision video laryngoscope with CMAC D-blade in obese patients with anticipated difficult airway in tertiary hospital in India-Randomized control study. J Anaesthesiol Clin Pharmacol 2019;35:363-7.
- Kramer A, Müller D, Pförtner R, Mohr C, Groeben H. Fibreoptic vs videolaryngoscopic (C-MAC(®) D-BLADE) nasal awake intubation under local anaesthesia. Anaesthesia 2015;70:400-6.
- Mahran EA, Hassan ME. Comparative randomised study of GlideScope® video laryngoscope versus flexible fibreoptic bronchoscope for awake nasal intubation of oropharyngeal cancer patients with anticipated difficult intubation. Indian J Anaesth 2016;60:936-8.
- Rosenstock CV, Thøgersen B, Afshari A, Christensen AL, Eriksen C, Gätke MR. Awake fiberoptic or awake video laryngoscopic tracheal intubation in patients with anticipated difficult airway management: A randomized clinical trial. Anesthesiology 2012;116:1210-6.
- Wahba SS, Tammam TF, Saeed AM. Comparative study of awake endotracheal intubation with Glidescope video laryngoscope versus flexible fiber optic bronchoscope in patients with traumatic cervical spine injury. Egypt J Anaesth 2012;28:257-60.
- 18. Yousuf A, Ahad B, Mir AH, Mir AW, Wani JG, Hussain SQ. Evaluation of effectiveness of dexmedetomidine and fentanyl-midazolam combination on sedation and safety during awake fiberoptic intubation: A randomized comparative study. Anesth Essays Res 2017;11:998-1003.
- Rajan S, Talukdar R, Tosh P, Paul J, Vasu BK, Kumar L. Hemodynamic responses and safety of sedation following premedication with dexmedetomidine and fentanyl during fiberoptic-assisted intubation in patients with predicted difficult airway. Anesth Essays Res 2018;12:11-5.
- Mendonca C, Mesbah A, Velayudhan A, Danha R. A randomised clinical trial comparing the flexible fibrescope and the Pentax Airway Scope (AWS) for awake oral intubation. Anaesthesia 2016;71:908-14.
- Kleine-Brueggeney M, Greif R, Schoettker P, Salvodelli G, Nabecker S, Theiler L. Evaluation of six videolaryngoscopes in 720 patients with a simulated difficult airway: a multi centre randomised controlled trial. Br J Anaesth 2016;116:670-9.