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Prospective Evaluation of the Safety and Efficacy of THRIVE for Children Undergoing Airway Evaluation

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Abstract

Background: Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) is a humidified high-flow nasal cannula capable of extending apneic time. Although THRIVE is assumed to stent upper airway soft tissues, this has not been objectively evaluated. Also, there are no prior studies providing safety and efficacy data for those patients undergoing upper airway evaluation using THRIVE. **Methods:** This report is a prospective study of the safety and efficacy of THRIVE in pediatric patients younger than 18 years old undergoing drug-induced sleep endoscopy. We positioned a flexible laryngoscope to view the larynx, and photographs were taken with no THRIVE flow (control) and with THRIVE flow at 10 and 20 liters per minute (LPM). Upper airway patency was measured using epiglottis to posterior pharynx distance, laryngeal inlet area, and modified Cormack–Lehane score at the trialed parameters. Vomiting and aspiration were our primary safety endpoints. **Results:** Eleven patients (6 women) with a mean age of 5.3 ± 2.1 years (2–8 years; SD, 2.05) were enrolled. Measurements of upper airway patency showed a significant THRIVE flow–associated increase in epiglottis to posterior pharynx distance (105 ± 54 at 10 L/min and 199 ± 67 at 20 L/min; $P = 0.007$) and nonsignificant increase of laryngeal inlet area (206 ± 148 at 10 L/min and 361 ± 190 at 20 L/min; $P = 0.07$). Cormack–Lehane score improved significantly at higher THRIVE volumes ($P = 0.006$). **Conclusions:** THRIVE appears to safely improve upper airway patency during sleep endoscopy in the pediatric patient. In this study, we objectively document the flow-dependent increase in laryngeal patency associated with THRIVE. *(Pediatr Qual Saf 2020;5:e348; doi: 10.1097/pq9.0000000000000348; Published online September 25, 2020.)*

INTRODUCTION

Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) is an emerging technique for primary and secondary airway management. THRIVE uses humidified high-flow nasal cannula (HFNC) to oxygenate and ventilate the airway during apnea and has become increasingly popular in the pediatric arena.[1–3] THRIVE is unique because the delivered oxygen is humidified, allowing much higher flow rates than using traditional HFNC.

Previous studies have suggested that THRIVE may contribute to ventilation by clearing upper airway dead space in apneic patients.[4–6] Another possible contribution to gas exchange involves the physical stenting of the upper airway. Intuitively, THRIVE's positive pressure may exert an expanding force on the laryngopharynx's soft tissues, thereby improving upper airway patency. This point remains particularly salient to the pediatric otolaryngologist, who commonly encountered both fixed and dynamic upper airway obstruction.

Although the expansion of the upper airway in the THRIVE setting may be an assumed phenomenon, no prior studies examined the direct effect of THRIVE on the cross-sectional patency of the upper airway. THRIVE has been shown to increase oxygenation for children undergoing intubation, and in pediatric intensive care units, but not in pediatric patients undergoing airway evaluation. In this pilot study, we aimed to assess and potentially characterize upper airway patency changes experienced with THRIVE in children. We hypothesized that an increase in THRIVE flow would result in a visible increase in the patency of the upper airway. As our primary outcome

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measures, we attempted to quantify changes in upper airway patency objectively. Also, as one of the chief concerns of this technology is the theoretical risk of gastric insufflation and aspiration during the surgical suspension, we evaluated rates of vomiting either during or following the procedure.

METHODS

Context

This study was conducted at a quaternary care academic children's hospital in Northern California between January 2019 and August 2019. The University Institutional Review Board provided approval for this study. The team members included 1 attending pediatric otolaryngologist, 2 otolaryngology residents, and 1 attending pediatric anesthesiologist.

Intervention

We conducted a prospective pilot trial of pediatric patients (younger than 18 years old) undergoing drug-induced sleep endoscopy (DISE). We enrolled patients from an outpatient otolaryngology clinic. We considered patients eligible if they were scheduled to undergo DISE in the operating room for airway evaluation. We obtained informed consent from the patients' guardians in the clinic or on the day of the procedure.

In the operating room, patients underwent DISE in the supine position, with standard cardiopulmonary monitoring in the presence of a pediatric anesthesiologist. Following intravenous catheter placement, patients were sedated with a dexmedetomidine and ketamine infusion. We then placed the age-appropriate THRIVE cannula. All patients were maintained spontaneously ventilating throughout the procedure. A single operator then performed transnasal flexible laryngoscopy and a systematic evaluation of the upper airway. We recorded all examinations for data collection. For this study, following DISE (performed in the absence of flow), airway assessment was performed using a camera positioned immediately inferior to the soft palate, with direct visualization of the larynx, pharynx/hypopharynx, and tongue base. We initially maintained THRIVE flow at 0 liters per minute (LPM) for video and photo documentation. We considered this flow as the physiologic baseline. The flow was then increased to 10 LPM, followed by 20 LPM, and never exceeding 2 L/kg/min. Following each flow adjustment, we waited for 10 seconds for equilibration before photo documentation. The camera remained static throughout this process and was positioned at the midline just posterior to the uvula. We took all photographs during a pause between inspiration and expiration. We took no pictures during airway maneuvers, such as jaw thrust, chin lift, or laryngeal manipulation. The entire examination was video-recorded, and static images were taken at the described times for analysis.

Measures

We collected demographic information, including date of birth, body mass index, and gender, of the patients once they were enrolled in the study. As our primary safety outcomes, we also collected the perioperative incidence of vomiting and aspiration.

In an attempt to quantify changes in the hypopharynx appearance while using THRIVE, we chose consistent anatomic landmarks to perform measurements that would reflect airway patency. We evaluated photos at each THRIVE flow rate. We used 3 quantitative measurements to assess the patency of the laryngopharynx: (1) the epiglottis to the posterior pharynx (EPP), measured as the anterior–posterior distance from epiglottis (midline, posterior-most aspect) to the midline pharyngeal wall; (2) the laryngeal inlet cross-sectional area (LIA), bound by the epiglottis anteriorly and by the pharyngeal wall posteriorly; and (3) thickness of the epiglottis at lateral edge. Distances (1) and (2) were measured using anteroposterior and lateral lines that were perpendicular to one another to assess the sagittal and coronal diameters of the larynx. Measurement (3) was used to correct for magnification in the laryngeal inlet measurements (1–2). Figures 1 and 2 demonstrate images illustrating examples of these measurements. We used the retro-epiglottic laryngeal inlet size measurement method previously described by Borek et al.[6] Figure 3 demonstrates the THRIVE nasal cannula that we use for pediatric patients.

We assessed the patency of the upper airway qualitatively using the modified Cormack–Lehane classification score (CLS) (Fig. 2). The CLS was described in 1984 as a classification system of glottic view during direct laryngoscopy, where the laryngeal view shows the whole glottis (grade 1), part of the glottis (grade 2), the epiglottis only (grade 3), or not even the epiglottis (grade 4).[7] Although this scoring system is designed for patients undergoing direct laryngoscopy, previous studies have also applied the CLS to describe the laryngeal view during indirect laryngoscopy.[8,9] We thus felt that this would also be an appropriate system to compare changes occurring during THRIVE use. Figure 2 highlights example images of CLS ranging from grades 1 to 3.

Finally, we checked all operative reports, postoperative notes, progress notes, and telephone encounters to determine emesis and aspiration rates.

Analysis

The research team reviewed and analyzed images using ImageJ image processing software (National Institutes of Health, Bethesda, Md.). We obtained measurements in units of pixels, and the cross-sectional area was measured in units of pixels squared. To account for differences in measurements (in units of pixels) at different camera positions in the same patient, we corrected the measurements by dividing it by the thickness of an epiglottic edge measured in the same still frame. The analysis was performed using both raw and corrected measurements executed by a single operator for consistency (G.S.L).

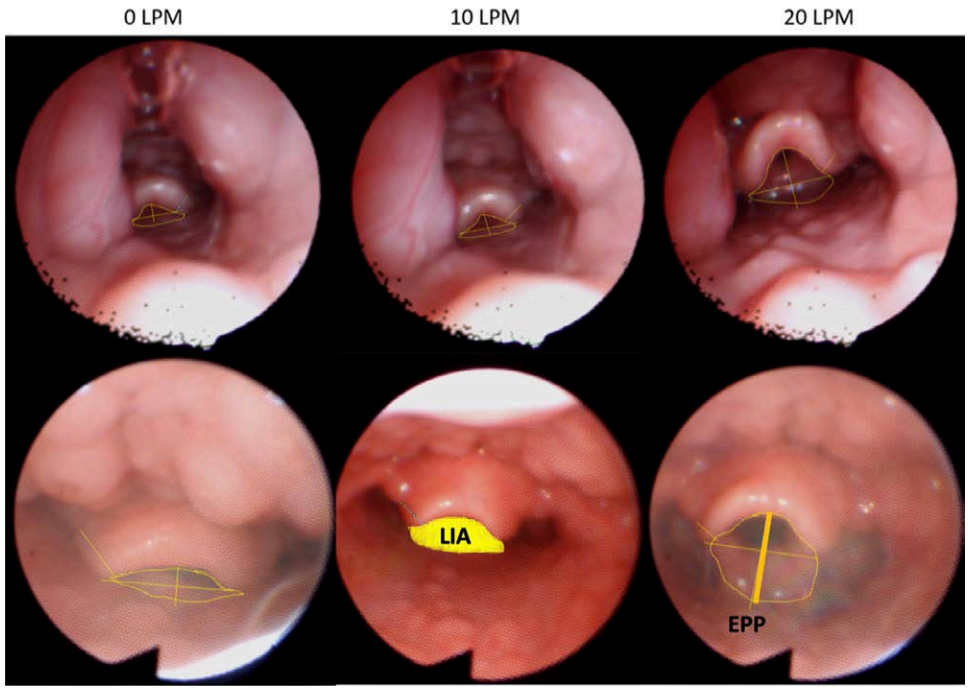

Fig. 1. Measurement of upper airway soft tissue. Representative still images of quantitative measurements made during THRIVE for 2 cases (A and B). Yellow measurements demonstrate the epiglottis to posterior pharynx distance (EPP), lateral diameter, laryngeal inlet area (LIA), and epiglottis edge thickness. Images correspond to high-flow nasal cannula 100% oxygen flow rates of 0 (left), 10 (middle), and 20 (right) liters per minute (LPM).

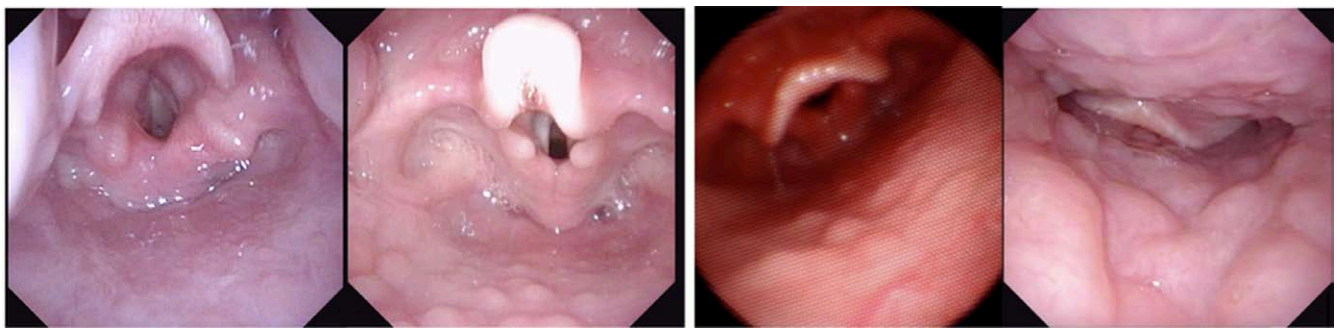

Fig. 2. Examples of modified Cormack-Lehane categories. Examples of the still photographs used to determine modified Cormack–Lehane scores from grade 1 (A, full view of the glottis and vocal folds) to grade 2a (B, partial view of the glottis), grade 2b (C, only arytenoids/posterior glottis visible), and grade 3 (D, only the epiglottis is visible). Although this grading scheme includes a grade 4 view, no patients in this study fell into that category.

Fig. 3. Image of the THRIVE device for pediatric patients: Optiflow (Fisher & Paykel Healthcare Limited, Panmure, Auckland, New Zealand).

We collected demographic and descriptive statistics to evaluate mean, SD, range, and frequency. We analyzed data for statistical differences using Wilcoxon's test or paired *t* test. Computational statistics aided the analysis. We performed statistical analysis in Microsoft Excel. A critical alpha level of 0.05 was used to determine statistical significance. The Benjamini–Hochberg correction was also used to assess statistical significance accounting for multiple hypothesis testing.

RESULTS

Eleven patients met the inclusion criteria, with a mean age of 5.3 ± 2.1 years (range, 2–8 years) and a mean BMI

of 17.3 ± 2.9 kg/m^2. Six patients were women (55%). Table 1 illustrates patient- and case-specific information. There were no cases of perioperative vomiting in any of the patients.

Overall, we noted increases in all gross measurements (uncorrected) of airway patency (EPP, LIA, and CLS), with increases in THRIVE flow (Tables 2 and 3). At 10 LPM, only EPP demonstrated a statistically significant change (+105 ± 54%, $P = 0.03$). At a flow rate of 20 LPM, both EPP (+199 ± 67%, $P = 0.0001$) and LIA increased significantly (+361 ± 190%, $P = 0.006$). CLSs were assessed for all still frames (Table 3), and the scores showed a statistically significant overall improvement with increasing flow rates [$\chi^2 = 18.0$, degrees of freedom (DOF) = 6, $P = 0.006$]. CLS scores improved for eight patients at 10 LPM (72.73%) and for all patients at 20 LPM (100%). Subset analysis of CLS change across pairs of flow rates showed statistically significant improvement from 0 LPM to 20 LPM ($\chi^2 = 15.1$, DOF = 3, $P = 0.002$), but no significant improvement from 0 LPM to 10 LPM ($\chi^2 = 7.4$, DOF = 3, $P = 0.06$) and from 10 LPM to 20 LPM ($\chi^2 = 3.8$, DOF = 3, $P = 0.28$). Figures 1 and 2 demonstrate example images of still frames and their measurements.

By normalizing measurements by the measured thickness of the epiglottis edge in the same still frame for images of the same patient, we corrected for magnification differences. EPP increased significantly at 20 LPM (+183 ± 48%, $P = 0.007$). Although LIA continued to demonstrate an increase in cross-sectional area with increased flow, these changes were not statistically significant at 10 or 20 LPM (+74 ± 29%, $P = 0.08$; and +307 ± 115%, $P = 0.07$, respectively) following epiglottic correction. Determinations of statistical significance were the same when using the Benjamini–Hochberg correction for multiple hypothesis testing.

DISCUSSION

In this study, we demonstrate significant and flow-dependent increases in the anteroposterior glottic view with THRIVE, using both EPP and CLS. We chose these measurements as our primary outcomes because they are proxies for the anteroposterior vector of airway patency, most commonly negotiated by the anesthesiologist and the airway surgeon. Airway view is directly proportional to this vector, and maneuvers such as external laryngeal manipulation (eg, cricoid pressure) or jaw thrust may improve it. We also evaluated LIA to characterize better the 3-dimensional effects of THRIVE on laryngopharyngeal soft tissue. Again, we noted increases in these measurements with THRIVE. While there was no significant

Table 1. Drug-induced Sleep Endoscopy Finding per Patient

Case Number	Preoperative Diagnosis	Other Operations	DISE Findings
1	SDB	Intracapsular tonsillectomy with adenoidectomy	75% OP tonsillar obstruction
2	SDB, adenoid hypertrophy	Bilateral tympanostomy tube placement, adenoidectomy	(1) BOT collapse +, (2) lateral pharyngeal collapse +, (3) minimal tonsillar obstruction < 1+, (4) adenoids 4+
3	Adenoid hypertrophy, OME bilateral, aspiration	MDLB, bilateral tympanostomy tube placement, nasal endoscopy, adenoidectomy	Grade 2 view normal airway. Adenoids 3+ with 85% obstruction and adenoiditis
4	OSA, adenotonsillar hypertrophy, otitis media with effusions	Intracapsular tonsillectomy with adenoidectomy, bilateral myringotomies	Subglottic stenosis, laryngomalacia
5	Adenotonsillar hypertrophy, recurrent epistaxis	Tonsillectomy, revision adenoidectomy, bilateral nasal endoscopy with cautery	Collapsing tonsils, tongue base collapse. 3+ tonsils with severe obstruction on DISE. Adenoids 1+ regrowth. Bilateral nasal cautery with silver nitrate.
6	OSA, nasal turbinate hypertrophy, adenoid hypertrophy, severe allergic rhinitis	Adenoidectomy, ITR	Minimal glossoptosis. No lingual tonsils. No significant palatine tonsillar tissue or obstruction. 3+ adenoid pad (complete obstruction with some achievable patency with jaw thrust and while on inspiration). Moderate-to-severe inferior turbinate hypertrophy.
7	ARDS and ventilator dependence, history of tracheostomy now decannulated with scar tissue adherent to trachea	MDLB, excision of tracheal scar/ tethering with layered closure	Normal supraglottis and glottis. Subglottis had small anterior glottic shelf. Trachea normal. Mild-to-moderate left bronchus malacia.
8	Grade 3 subglottic stenosis, bronchopulmonary dysplasia	MDLB, dilation balloon subglottis, intracapsullar tonsillectomy, and adenoidectomy	Airway obstruction from 4+ palatine tonsils and 4+ adenoid pad, improvement in tonsillar collapse with HFNC at 20 L, normal supraglottis
9	Moderate OSA, prior adenoidectomy, with obstructive symptoms	Intracapsullar tonsillectomy, ITR	2+ tonsils most obstructive on DISE due to A-P dimension and associated collapse at level of palate. Obstruction at level of superior tonsillar poles was partially relieved by application of positive pressure via THRIVE.
10	COM, OSA, adenoid hypertrophy	T&A, bilateral ear exam, ITR	Adenoids 2+ peritubal growth, tonsils minimal obstruction on DISE, occult laryngomalacia (mild–moderate epiglottic prolapse).
11	SDB, turbinate hypertrophy	T&A, ITR	Minimal glossoptosis, 2+ partially obstructive ball valving tonsils. Tonsils 2+, adenoids 4+

ARDS, acute respiratory distress syndrome; BOT, base of tongue; COM, chronic otitis media; ITR, inferior turbinate reduction; MDLB, microdirect laryngoscopy with bronchoscopy; OME, otitis media with effusion; OSA, obstructive sleep apnea; SDB, sleep-disordered breathing; T&A, tonsillectomy and adenoidectomy.

Table 2. Change in Laryngeal Inlet Patency with Increased THRIVE Flow Rates

	Change from 0 L (% mean ± STE)				Paired *t* test *P*			
	Uncorrected		Corrected		Uncorrected		Corrected	
Measurement	**0–10 LPM**	**0–20 LPM**	**0–10 LPM**	**0–20 LPM**	**0–10 LPM**	**0–20 LPM**	**0–10 LPM**	**0–20 LPM**
Epiglottis-posterior pharynx	105 ± 54	199 ± 67	71 ± 29	183 ± 48	0.03*†	0.0001*†	0.05	0.007*†
Laryngeal inlet area	206 ± 148	361 ± 190	74 ± 34	307 ± 115	0.07	0.006*†	0.08	0.07

*$P < 0.05$.
†$P < 0.05$ with Benjamini–Hochberg correction for multiple comparisons.STE, standard error of the mean.

Table 3. Modified Cormack–Lehane Scores per Case

	Modified Cormack–Lehane Score		
Case No.	**0 LPM**	**10 LPM**	**20 LPM**
1	3	3	2a
2	3	2b	2b
3	3	2a	2a
4	2b	2b	2a
5	2b	2a	2a
6	2a	2a	1
7	3	2b	2a
8	2b	1	1
9	2b	2a	2a
10	2b	2a	1
11	2b	2a	1

increase in LIA with increasing flows, there was a trend of increased patency at higher flows.

Despite concerns about gastric insufflation and potential aspiration during surgical suspension with this technology, there were no cases across our patient cohort. However, given the relatively low incidence of this outcome in the pediatric perioperative patient, more extensive studies may be needed to elucidate the overall risk of this phenomenon. Future studies could also evaluate gastric air volume with ultrasound for THRIVE patients, as a surrogate measure.

When compared with adults, pediatric patients experience shorter apneic windows (ie, length of time an individual can maintain oxygen saturation in the absence of mechanical ventilation) due to both increased oxygen consumption and smaller reserve and may desaturate within 3 minutes.[3] THRIVE has been shown to extend the safe apneic window for pediatric patients during general anesthesia without significant change in rates of carbon dioxide (CO_2) clearance when compared with controls.[10] This result is in contrast to that of studies on adults, where THRIVE was associated with a 2- to 3-fold lower rate of end-tidal CO_2.[4] Naturally, this raises questions about whether THRIVE indeed participates in ventilatory exchange, and if this benefit is experienced only by adult patients.

Regardless, the mechanism by which THRIVE promotes ventilation remains incompletely characterized.[12] A recent study by Möller et al[12] suggests that THRIVE clears dead space in the upper respiratory tract through supraglottic flow vortices. Patel et al[4] demonstrated THRIVE may exert positive pressure support of approximately 7 cm H_20, which likely contributes to the observed ventilatory properties of the device. Mechanistically, it seems most likely that both adult and pediatric patients share the ventilatory effects of THRIVE.

A prior anatomical study by Hirano et al[13] noted less dense macula flava fibers in the pediatric larynx, implying less anchoring strength of the laryngeal structures. The laryngeal framework in pediatric patients is softer than in adults, making it less susceptible to blunt trauma. However, it is more at risk of collapse due to negative inspiratory pressures that may develop in the spontaneously ventilating child.[14] For these reasons, the concept of upper airway stenting with THRIVE is particularly engaging in the pediatric population.

This study is the first to provide quantitative evidence of the flow-dependent increase in pediatric upper airway patency relationship when using THRIVE. Implications are broad, but our results may indicate that THRIVE could be especially useful in the difficult pediatric airway. Patients with obstructive sleep apnea, laryngomalacia with structural insufficiencies, or upper airway soft tissue redundancy may especially benefit from THRIVE as an oxygenation source during an intervention. However, whether the impact we documented confers a clinical benefit is unclear, and future studies are needed to fully elucidate the clinical effect of THRIVE on the pediatric airway.

It is also worth mentioning that THRIVE may distort upper airway soft tissues during airway assessment. The senior author's practice is to avoid the use of supplemental oxygen or flow during sleep endoscopy. Otherwise, findings may underestimate the degree of collapse in the evaluation of the sleep apnea patient.

This study's strengths include the prospective nature of data collection, the use of baseline patient airway measurements, and correcting for subtle changes in camera position by correcting each still frame for a constant epiglottic thickness.

There are several limitations to this study that merit mention. First, this is a pilot study, and our data are derived from a small patient cohort. Furthermore, patients included in this study were airway patients who presented for DISE/bronchoscopy and may not be reflective of the general pediatric cohort. THRIVE may be especially useful in specific anatomic phenotypes, and therefore, this particular limitation may have impacted our lack of statistical significance to some degree. There are also technical aspects of this study, which could have impacted our results. Measurement of EPP distance with a flexible

camera is not perfect, and minor movements in the scope during flow changes can alter perspective and measurements. Again, we attempted to counter measurement errors by using epiglottis thickness as a benchmark to correct for each patient's magnification changes at the different flow rates. Finally, the measurements used are not standardized, and their errors cannot be estimated. However, this is consistent with prior studies measuring glottic inlet, as such measurements would likely require CT, not feasible in a pediatric study of airway patients such as this.[6] Although MRI is another imaging modality that may be useful for airway measurements in this population, it is not routinely used for this indication at our institution.

CONCLUDING SUMMARY

We demonstrate a flow-dependent relationship between THRIVE and epiglottis to posterior pharynx distance and modified CLS. The laryngeal inlet cross-sectional area also improved for all patients at higher flows. It may be especially useful in pediatric patients with obstructive sleep apnea or laryngomalacia due to THRIVE's ability to stent upper airway soft tissues. THRIVE oxygen flow may alter upper airway anatomy and therefore confound results during DISE. Further studies are needed to define better the clinical impact of these improved measurements on pediatric patients.

DISCLOSURES

The authors have no financial interest to declare in relation to the content of this article.

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