

Transnasal Endoscopy for Children and Adolescents With Eosinophilic Esophagitis: A Single-Center Experience

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Abstract

Background: Transnasal endoscopy (TNE) has been introduced in the care of pediatric patients with eosinophilic esophagitis (EoE) who require repeated esophagoscopies. TNE, as compared to conventional endoscopy, is less invasive and avoids sedation or anesthesia allowing for frequent assessments of the esophageal mucosa when making management decisions. The aim of this study is to review our early experience with TNE.

Methods: We extracted data from all patients with EoE who underwent TNE at UH Rainbow Babies & Children's Hospital, Cleveland, Ohio from December 2018 to April 2021. We assessed total visit time, procedure time, success rate, and complications. Data are presented as percentages or medians with interquartile ranges (IQRs). Comparisons were made using Chi-square (and Fisher's exact) test for categorical data, Mann-Whitney test and the unpaired *t*-test for non-normally distributed and normally distributed data, respectively.

Results: Thirty-three patients underwent 65 TNE procedures during our study period. The male-to-female ratio was 4.5:1 and median age was 13 years (IQR: 10 - 15 years; range: 4 - 20 years). Sixty-three (96.9%) of 65 procedures were completed. Distraction methods were used in all procedures (virtual reality goggles in 19.3% and television in 80.7%). Isolated elevated blood pressure (BP) measurements prior to the procedure were more frequent in those undergoing TNE as compared to sedated esophagogastroduodenoscopy ($P = 0.04$). We also calculated the heart rate (HR) for patients undergoing TNE and sedated upper endoscopy;

no difference was noted ($P = 0.71$). Only minor adverse events occurred with TNE: nosebleed ($n = 1$), pre-syncope ($n = 1$), and pain ($n = 4$). None of the patients who underwent a sedated upper endoscopy developed an event. Two TNE procedures were not completed due to an inability to traverse the upper esophageal sphincter.

Conclusions: We demonstrate TNE is an efficient and well-tolerated means of monitoring patients with EoE. Various straight forward distraction methods may contribute to the successful completion of the procedure. The safety as compared to conventional esophagoscopy requires large multicenter studies.

Keywords: Transanal endoscopy; Unsedated; Eosinophilic esophagitis; Children; Adolescents

Introduction

Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory disease of the esophagus resulting in symptoms and signs of esophageal dysfunction. Since its initial identification in the early 1990s, the number of patients with EoE has been rising, with a reported incidence of 1 - 20 new cases per 100,000 population per year and a prevalence between 13 and 49 cases per 100,000 [1]. Due to the risk of complications secondary to EoE if not managed in a timely fashion, it requires prompt evaluation and treatment. To date, the only reliable method of evaluating the response to therapy in EoE is via direct visualization and sampling of the esophageal mucosa via endoscopy [2]. The need for frequent endoscopies requires recurrent exposure to anesthetic agents, which may introduce patients with EoE to potential side effects, patient and family inconvenience, increased cost, time consumption, and the need for intravenous (IV) access [3-10]. The search for novel, less invasive methods to evaluate the response of treatment to EoE has been a major goal for gastroenterologists who manage patients with this disease. Several different methods have been evaluated including sampling of the esophageal mucosa with sponges, strings, and brushes, and measuring plasma and urine biomarkers [6-9]. The most successful in monitoring response to EoE management has been unsedated transnasal endoscopy (TNE) [11-13]. In this study, we aimed to evaluate the feasibility, tolerance, and success rate of TNE in children and adolescents at our institution.

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Materials and Methods

We reviewed data from all patients with EoE who underwent a TNE at UH Rainbow Babies & Children's Hospital, Cleveland, Ohio from December 2018 to April 2021. Endoscopy reports, video recordings, intake forms, progress notes, and pathology reports were reviewed. We calculated the total visit time, procedure time, success rate, and complication rate. The arrival time to the endoscopy suite or operating room, procedure start time, procedure end time, and departure time from the endoscopy suite or operating room were obtained from information documented in the medical record. We compared TNE procedure times, vital signs, and adverse events to the most recent sedated esophagogastroduodenoscopy (sEGD) with sufficient data in the same patient prior to the first TNE. Data are presented as percentages or medians with interquartile ranges (IQRs). Comparisons were made using Chi-square (and Fisher's exact) test for categorical data, Mann-Whitney test and the unpaired *t*-test for non-normally distributed and normally distributed data, respectively. The University Hospitals Institutional Review Board approved our study (IRB number: STUDY20190620, approved September 4, 2019). This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

One pediatric gastroenterology attending physician (RS) and one fellow (AB) under supervision (by RS) performed the procedures, both observed pediatric and adult otolaryngologists perform flexible laryngoscopy multiple times prior to initiating the TNE program to become familiar with handling a bronchoscope. One of the pediatric otolaryngologists (JS) was available to assist with nasal intubation if needed for the first five procedures. All patients and their guardians were provided information regarding the TNE procedure by RS during a clinic visit or by telephone prior to the procedure being scheduled. An initial subset of patients was sent an email with instructions to download the Google Cardboard application (Google LLC, Mountain View, CA) on their smart phone and choose a video for the visual reality (VR) goggles (Onn, Walmart Corporate, Bentonville, AR) to watch during the procedure if they opted for VR goggles. We changed VR systems in 2020 (Cinema ProMED, Orion, MI) after which time patients were informed that they would be offered a VR goggle system for distraction and can choose a video on the day of the TNE procedure. Patients were instructed: 1) to use a nasal saline spray for 7 days prior to the TNE in preparation for the lidocaine nasal spray on the day of the TNE; and 2) not to eat or drink for 2 h prior to their scheduled procedure. After our first procedure which resulted in a minor nosebleed, patients were instructed to use an oxymetazoline hydrochloride spray for 2 days prior to and on the day of the TNE.

On the day of the procedure, consent for the procedure was obtained from the patients or their guardians, then VR goggles were offered and tested. If television (TV) was chosen as a distraction method, patients choose a movie to view. Immediately prior to the procedure, topical anesthetics lidocaine 4% and benzocaine 20% were applied to the nasal and pharyngeal mucosa, respectively. Bronchoscopes were used for the TNE. For the

first 45 procedures, we used an Olympus BF-P190 (Olympus America, Center Valley, PA) bronchoscope (4.1-mm insertion tube, 4.2-mm outer diameter (OD), 60 cm long, 2.0-mm working channel) and Olympus EndoJaw FB-221D biopsy forceps (1,150 mm in length, minimum channel 2.0 mm, cup opening size 5.0 mm). As we expanded our program and our minimum age was decreased, we transitioned to an Olympus BF-XP190 bronchoscope (2.8-mm insertion tube, 3.1-mm OD, 60 cm long, 1.2-mm working channel) and Olympus FB-56D-1 biopsy forceps (1,150 mm, minimum channel 1.2 mm, cup opening size 7.3 mm). All patients were called the day after the procedure to screen for adverse events related to the procedure.

Results

We attempted TNE in 33 individual patients during our study period (Table 1). The male-to-female ratio was 4.5:1 and median age was 13 years (IQR: 10 - 15 years; range: 4 - 20 years). In these patients 65 TNEs were attempted in total. Eleven (33%) patients underwent more than one TNE (the highest number in a single patient was 9). The Olympus BF-P190 bronchoscope was used in 45 TNEs (19 patients, median age: 13.5 years, range: 7 - 20) and the Olympus BF-XP190 bronchoscope in 20 TNEs (19 patients, median age: 11 years, range: 4 - 18). The vast majority of TNEs (60, 92.3%) were completed with the desired number of biopsies obtained. Three of the 65 procedures (4.6%) of the TNEs were partially successful (three of 33 patients). Among the three partially successful TNEs, the first patient developed pre-syncope during the procedure; only two of six planned biopsies were obtained. The second was a 4-year-old child whose movement did not allow for safe completion of the procedure. Distal esophageal biopsies, but not the planned mid esophageal biopsies were obtained. The third cried prior to and throughout the procedure due to paresthesia in the back of the throat secondary to the anesthetic sprays, which resulted in increased secretions and progressively poor visualization during the procedure. Biopsies were not obtained. Two procedures were not successful due to an inability to traverse the upper esophageal sphincter (both patients were 6 years of age). One of those two patients underwent a successful TNE on a later date using the newer, smaller VR system as a distraction method.

The median TNE total visit time was 33.5 min (IQR: 29.8 - 42.3 min; range: 17 - 60 min; data available for 48 completed procedures) and was less than the sEGD total visit time of 158 min (IQR: 124 - 197 min, range: 66 - 250 min) ($P < 0.0001$). There was no difference in the time of the procedures (TNE: median 7 min, IQR: 6 - 8.3 min; range: 5 - 13 min, data available for 58 completed procedures; sEGD: median 7 min, IQR: 5 - 9.5 min, range: 4 - 21 min; $P = 0.96$).

VR distraction during the TNE was offered to all patients and used in 19.3% of procedures (six of 33 patients, 4 - 15 years of age). TV was used during all other TNEs mainly due to patient preference of not having their eyes covered during the procedure or because the goggles did not fit well due to the smaller head size of two young patients (6 years of age).

Blood pressure (BP) and heart rate (HR) obtained prior

Table 1. Study Information

Age	Mean = 12.62 (4 - 20) Median = 13 (IQR: 10 - 15; range: 4 - 20)
Gender	6 F (18.2%) and 27 M (81.8%) = 33 total patients, 1 F and 1 M failed included
TNE procedures/patient	22 underwent one, 3 underwent two, 2 underwent three, 4 underwent four, 1 underwent six, 1 underwent nine
TNE success rate	93.9% (31/33 patients) 96.9% (63/65 procedures)
Total TNE visit duration	Mean = 35.5 min; 48 procedures with available times Median = 33.5 min (IQR: 29 - 43 min; range: 17 - 60 min)
Total sEGD visit duration	Mean = 162.3 min (31 procedures) Median = 158 min (IQR: 124 - 197 min; range: 66 - 250 min)
Total TNE procedure time	Mean = 7.4 min; 58 procedures with available times Median = 7 min (IQR: 6 - 8.3 min; range: 5 - 13 min)
Total sEGD endoscopy procedure time	Mean = 8.2 min Median = 7 min (IQR: 5 - 9.5 min; range: 4 - 21 min)
Bronchoscope used	BF-XP190 = 30.8% (20/65 procedures) BF-P190 = 69.2% (45/65 procedures)
Elevated BP prior to TNE	Yes 54.2% (32/59 procedures; 23/31 patients = 74.2%) No 45.8% (27/59 procedures; 8/31 patients = 25.8%)
Elevated BP prior to sEGD	Yes 45.2% (14/31 procedures; 14/31 patients = 45.2%) No 54.8% (17/31 procedures; 17/31 patients = 54.8%)
Elevated HR prior to TNE	Yes 13.3% (8/60 procedures; 5/31 patients = 16.1%) No 86.7% (52/60 procedures; 26/31 patients = 83.9%)
Elevated HR prior to sEGD	Yes 9.7% (3/31 procedures; 3/31 patients) No 90.3% (28/31 procedures; 28/31 patients)
Adverse events with TNE procedures	
Pain from procedure	Yes = 7.8% (4/51 available procedures) No = 92.2% (47/51 available procedures)
Nose bleed	1.5% (1/65 procedures; failed ones included)
Other complications	No hypoxia, bleeding, or infection
VR goggles in TNE procedure	Yes = 16.7% of patients (5/30 patients with available data) No = 83.3% of patients (25/30 patients with available data) Yes = 19.3% of procedures (12/62 procedures with available data) No = 80.7% of procedures (50/62 procedures with available data) 3/33 patients = N/A
Versed with TNE procedures	Yes = 7.7% (5/65 procedures; 1/33 patients) No = 92.3% (60/65 procedures; 32/33 patients)
Fellow participation in TNE procedure	9.1% of all patients (3/33 patients) 7.7% of total procedures (5/65 procedures: 4/65 completed by fellow and 1/65 fellow unsuccessful, completed by attending)

TNE: transnasal endoscopy; BP: blood pressure; HR: heart rate; VR: visual reality; sEGD: sedated esophagogastroduodenoscopy; F: female; M: male; IQR: interquartile range.

to TNE and sEGD were reviewed. Considering the TNE procedures, overall, 32 of the 63 procedures and 23 of the 31 patients had an elevated BP reading (age-based standards). One of the 23 patients who had an elevated BP had used VR goggles

and the remaining 22 used TV for distraction. The median age for patients with an elevated BP was 17.5 years (range: 9 - 20). None of these patients had a previous diagnosis of hypertension, suggesting anxiety prior to the procedure. Only one

Table 2. Correlation Between Elevated BP, Number of TNE and Distraction Methods

	Total number of TNEs	Elevated BP	Number of TNEs with elevated BP	Elevated BP for all TNEs	Elevated BP on subsequent TNEs but not initial TNE	Elevated BP then no elevated BP	Distraction method
1	9	Yes	1 (7)	No	Yes	Yes	TV
2	4	No	0	No	No	No	VR goggles
3	4	Yes	1 (3)	No	Yes	Yes	TV
4	4	Yes	3 (2, 3, 4)	No	Yes	No	TV
5	4	Yes	4 (1, 2, 3, 4)	Yes	No	No	VR goggles
6	1	Yes	1 (1)	Yes	No	No	TV
7	1	Yes	1 (1)	Yes	No	No	TV
8	2	Yes	1 (2)	No	Yes	No	TV
9	6	Yes	3 (4, 5, 6)	No	Yes	No	TV
10	3	No	0	No	No	No	TV
11	3	Yes	1 (3)	No	Yes	No	TV
12	2	Yes	2 (1,2)	Yes	No	No	TV
13	2	Yes	2 (1,2)	Yes	No	No	TV
14	1	Yes	1 (1)	Yes	No	No	TV
15	1	Yes	1 (1)	Yes	No	No	TV
16	1	Yes	1 (1)	Yes	No	No	TV
17	1	No	0	No	No	No	VR goggles
18	1	No	0	No	No	No	TV
19	1	Yes	1 (1)	Yes	No	No	TV
20	1	Yes	1 (1)	Yes	No	No	TV
21	1	Yes	1 (1)	Yes	No	No	TV
22	1	No	0	No	No	No	VR goggles
23	1	No	0	No	No	No	VR goggles
24	1	Yes	1 (1)	Yes	No	No	TV
25	1	Yes	1 (1)	Yes	No	No	TV
26	1	Yes	1 (1)	Yes	No	No	TV
27	1	No	0	No	No	No	TV
28	1	No	0	No	No	No	VR goggles
29	1	Yes	1 (1)	Yes	No	No	TV
30	1	Yes	1 (1)	Yes	No	No	TV
31	1	Yes	1 (1)	Yes	No	No	TV
32	1	N/A	N/A	N/A	N/A	N/A	TV
33	1	N/A	N/A	N/A	N/A	N/A	TV

TNE: transnasal endoscopy; BP: blood pressure; TV: television; VR: visual reality; N/A: not available.

patient who had more than one TNE did not have an elevated BP (patient #10); TV distraction was used in this case. Patients who underwent more than one TNE had an elevated BP prior to all or only on follow-up procedures but not the initial one (Table 2).

Isolated elevated BP measurements prior to any procedure were more frequent in those undergoing TNE as compared to sEGD (74.2% vs. 45.2%, $P = 0.04$) (Table 1). Of the 23 patients who had an elevated BP prior to their TNE, 13 also had an elevated BP prior to their sEGD. One patient who did not

develop an elevated BP prior to his TNE did develop an elevated BP prior to a sEGD (Table 3). There was no significant difference in the number of patients who had an elevated HR prior to TNE as compared to sEGD (16.1% vs. 9.7%, $P = 0.71$) (Table 1).

There were no serious adverse events associated with the TNEs or sEGDs. The first patient who underwent TNE developed a nosebleed from the anterior nares during the procedure, which resolved with application of pressure, and four patients reported pain immediately after the TNE prior to discharge

Table 3. Correlation Between Elevated BP Prior to TNE and sEGD

	Elevated BP before TNE	Elevated BP before sEGD
1	Yes	No
2	No	No
3	Yes	Yes
4	Yes	Yes
5	Yes	Yes
6	Yes	Yes
7	Yes	Yes
8	Yes	No
9	Yes	No
10	No	No
11	Yes	No
12	Yes	Yes
13	Yes	No
14	Yes	Yes
15	Yes	No
16	Yes	No
17	No	No
18	No	No
19	Yes	No
20	Yes	Yes
21	Yes	Yes
22	No	N/A
23	No	No
24	Yes	Yes
25	Yes	Yes
26	Yes	Yes
27	No	No
28	No	Yes
29	Yes	Yes
30	Yes	No
31	Yes	No
32	N/A	N/A
33	N/A	N/A

TNE: transnasal endoscopy; BP: blood pressure; sEGD: sedated esophagogastroduodenoscopy; N/A: not available.

but the location of the pain was not recorded. One patient developed pre-syncope during the TNE. All symptoms resolved with provision of minor supportive measures.

Discussion

Over the past few years, various less invasive methods of

evaluating the esophagus for EoE have been explored in children. Among those, unsedated TNE has been the most successful as it offers visual evaluation as well as histologic sampling, allowing the endoscopist to obtain all the information a sEGD would provide [11-13]. Our study is the second largest and our center is the second one reporting TNE use in children and adolescents. Our study adds to the literature demonstrating TNE can be used in the care of children and adolescents with EoE. We also found that a simple distraction method (viewing a movie on a TV) can be effective in enabling the endoscopist to complete the procedure. We also report that elevated BP readings are common and suggest that this reflects anxiety prior to the procedure. This was also evident almost half of the patients prior to a sEGD, suggesting baseline anxiety around procedures regardless of them being awake.

Unsedated generally and TNE specifically have been evaluated for over two decades. Studies in adults comparing transnasal to transoral unsedated endoscopy report pain or discomfort with the insertion of the endoscope when the transnasal route is used as compared to the transoral route, but with less gagging [14-18]. In pediatrics, Hargrove et al in 1984 reported their experience with unsedated EGD in 22 children under 2 years of age. One critically ill patient with an upper gastrointestinal bleed developed transient bradycardia during the procedure, but the remainder had no adverse events [19]. In 2002, Bishop et al prospectively evaluated transoral unsedated EGD in 8- to 18-year-old children using a 9.8 mm in diameter gastroscop (GIF 130, GIF 140, Olympus, Melville, NY). They applied topical anesthesia in all patients using pharyngeal benzocaine (Cetacaine, Cetylite Industries, Inc., Pennsauken, NJ) before introducing the endoscope orally. They were successful in completing 95% without the need for sedation. Eighty percent of the children who underwent the unsedated EGD reported they would undergo another unsedated EGD if needed [20]. Since these initial reports, there had been a paucity of research in children until Friedlander et al published in 2016 their experience with unsedated TNE for EoE patients. They successfully performed unsedated TNEs with intranasally applied lidocaine in 21 patients from 8 to 17 years of age without serious adverse events [13]. More recently, Nguyen et al from the same group published a larger experience with 300 attempts in 190 patients, with a 98% success rate and no major adverse events. In these patients they used aerosolized lidocaine or aerosolized benzocaine nasally and orally [11]. The bronchoscopes used in both studies included those with outside diameters of 2.8 mm (Olympus, BF XP160), 3.1 mm (Olympus, BF XP190), 4.0 mm (Olympus BF MP160F), 4.2 mm (Olympus BF P190), and 4.9 mm (Olympus N180).

The more recent studies utilizing TNE in children report the use of VR goggles for distraction during TNE [11-13]. We used two VR systems during our study period. We initially used a low-cost system (Onn, Walmart Corporate, Bentonville, AR) designed to be used with an individual's smart phone. Since these goggles could not be cleaned appropriately between patients, they were given to the patient at the end of the procedure. The goggles are relatively large, similar to the majority of VR goggles on the market; thus, they did not fit well on younger patients. We transitioned to

a medical grade VR system (Cinema ProMED, Orion, MI). These goggles are smaller than the Onn system, do not utilize a smart phone, and are able to be cleaned and used on subsequent patients. We achieved similar results to those published utilizing VR goggles for distraction. Additionally, our study demonstrates that simply watching TV may be an alternative to VR goggles. Approximately 20% of our patients used the VR goggles as a distraction method while the majority (80%) used TV. All, except for two patients who used TV as a distraction method completed the TNE procedure. Younger age and possibly inadequate endoscopist experience with the smaller bronchoscope at that time contributed to the inability to complete the procedures in those two patients. We obtained the smaller VR goggle system to accommodate the younger population who prefer to use VR distraction which helped us expand our minimum age criterion from 8 years to 4 years and helped a 6-year-old patient whose initial TNE was unsuccessful to be distracted enough on the second attempt and successfully complete the procedure.

Anxiety has been reported as a reason to refuse unsedated TNE in adult studies [18]. Stress prior to TNE has been reported in a recent small pediatric study [21]. An elevated BP in more than half of our procedures (54%) and the majority of our patients (23 of 31 successful TNEs) suggests that anxiety is a major issue prior to undergoing TNE. This was more evident on repeat TNEs suggesting that anticipation of TNE after experiencing it once could trigger anxiety prior to follow-up procedures. Although the majority of our population used TV as a distraction method and provided enough distraction to complete the procedure, we did see a higher rate of elevated BP in those children. One of 23 patients who developed elevated BP used VR distraction while the other 22 patients used TV distraction. Despite the elevated BP, the procedures were successful in those patients. This suggests that TV is an adequate means of a distraction for patients to undergo TNEs, but VR goggles seem to provide a less apprehensive experience. This also could be biased as most patients who opted for TV distraction wanted to avoid having their eyes covered during the procedure suggesting the possibility of having baseline anxiety prior to the procedure contributing to the elevated BP and anxiety seen in those patients when they came for their TNE. The fact that the majority of those patients developed elevated BP prior to sEGD supports the presence of baseline anxiety. This is consistent with prior studies in children supporting the use of distraction methods especially VR goggles to improve the TNE experience [11-13], and possibly other sedated and unsedated procedures.

The strengths of our study include adding an alternate distraction method to VR goggles that is an easier and more accessible distraction method for TNE use in children and young adults. Given the cost and technical difficulties that can arise surrounding the use of VR goggles, TV is another reliable option to distract patients undergoing TNE. Another strength of our study is that we are the second largest TNE study in children and young adults, and the only other center in the world other than Colorado Children's Hospital to report a TNE experience in children and young adults [11-13]. Our data add to and extend the literature to support the use of TNE in children. Additionally, we report elevated BP in patients prior to under-

going TNE and sEGD, which we used as a surrogate of anxiety. This finding supports the importance of addressing anxiety prior to any endoscopic procedure. This will allow TNE centers and endoscopists to explore different forms of anxiety relief prior to procedures and sets the ground for further studies in the field.

The limitations of our study include the retrospective nature of the study resulting in some information missing for evaluation, most commonly this included procedure and total visit times, vital signs and pain associated with TNE. Another limitation is that we did not survey the patients to assess anxiety, tolerability of the procedure, and willingness to undergo repeat unsedated TNE in the future, but this has been already reported in children and in adults with high rate of readiness to undergo repeat unsedated TNE if needed [11-13, 18].

In summary, TNE is a feasible, and time-saving procedure in children and adolescents with EoE requiring multiple follow-up endoscopies. Various distraction methods can be successfully used including VR and TV. More of our younger patient population opted for the VR goggles over the TV. The safety as compared to conventional upper endoscopy requires large multicenter studies. Furthermore, additional studies are needed to further evaluate different techniques to improve the TNE experience based on current literature and address stress prior to the procedure.

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None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Informed consent was obtained.

Author Contributions

Alaa Elzayat, Ali Khalili and Ramy Sabe contributed to data collection. Ramy Sabe contributed to drafting the paper. All authors contributed to the conception of the study, interpretation of data, revising the work critically for important intellectual content, and gave final approval of the version to be published. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Abbreviations

EoE: eosinophilic esophagitis; TNE: transnasal endoscopy; IQR: interquartile range; BP: blood pressure; HR: heart rate; TV: television; VR: virtual reality; sEGD: sedated esophago-gastroduodenoscopy; N/A: not available

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