Gait & Posture 71 (2019) 32–37

Contents lists available at ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Full length article

Spatiotemporal gait parameters and tremor distribution in essential tremor

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ARTICLE INFO

Keywords:
Principal component analysis
Movement disorders
Walking

ABSTRACT

Background: Essential Tremor is characterized by an action tremor of the upper extremities, which may or may not be accompanied by a head, voice, leg or trunk tremor. Problems with gait and balance have also been identified in persons with Essential Tremor. Therefore, understanding gait performance is an important area of focus for clinicians and researchers.
Research question: We sought to 1) conduct a factor analysis on a broad spectrum of spatiotemporal gait parameters 2) build upon the normative database of gait measures in persons with Essential Tremor 3) understand the influence of age on gait speed in persons with Essential Tremor and 4) identify the relationships between gait performance and clinical measures of disease severity.
Methods: Gait data and Tremor Rating Scale scores were retrospectively collected from one hundred and forty-two ambulatory participants with a diagnosis of Essential Tremor. A factor analysis was used to characterize spatiotemporal gait parameters and regression models were applied to associate tremor scores to gait performance factors.
Results: Three domains of gait performance factors were identified in persons with Essential Tremor. Specifically, we observed a pace, rhythm, and stability factor. In sum, these factors accounted for 91.9% of the variance in gait performance. Only the pace and stability factors were associated with disease severity, suggesting these factors are most sensitive to disease severity compared to the rhythm factor. Our linear regression analysis revealed a significant influence of age on gait speed. Gait speed decreased with age significantly by 0.64 cm/s/year.
Significance: Reference values for 12 gait parameters will be highly useful for assessing gait performance in individuals with Essential Tremor. Our observations suggest that a clinical assessment of gait and balance would be an important measure to consider in routine clinical practice when treating persons with Essential Tremor.

1. Introduction

Essential tremor (ET) is one of the most prevalent adult-onset movement disorders, with over 7 million people diagnosed in the US [1,2]. ET is fundamentally characterized by an action tremor of the upper extremities, which may or may not be accompanied by a head, voice, leg or trunk tremor [3,4]. Specifically, 19% of persons with ET exhibit a hand tremor [5], and 45% exhibit an intention tremor (a tremor produced at the terminal portion of a movement) [6]. More recently, problems with gait, balance, and lower extremity function such as limb and gait ataxia have also been identified as complications of ET [4,7].

Previous studies have described distinct characteristics of gait alterations during normal and tandem gait in persons with ET. Specifically, lower velocity and cadence, increased time spent in double support, and gait asymmetry have been observed in persons with ET compared to healthy controls [1,8]. When performing a tandem walk test, where the feet are placed sequentially in front of and in close proximity to each other, persons with ET demonstrated lower velocity and cadence, as well as more missteps compared with healthy controls [9]. For this reason, spatiotemporal characteristics of gait are important to understand because they are key predictors of meaningful clinical outcomes such as increased risk of falls [10].

Increasing volumes of investigations have evaluated spatiotemporal gait values that are considered important for clinical and functional behavior in persons with ET. To date, the vast majority of studies on

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https://doi.org/10.1016/j.gaitpost.2019.04.004
Received 24 October 2018; Received in revised form 26 March 2019; Accepted 7 April 2019
0966-6362/

gait performance in persons with ET have a limited (around 13–30 participants) sample of persons with ET compared to a small sample of age-matched healthy participants [11,12]. Although the literature provides normative values of spatiotemporal gait data from healthy young, older adult, and patient populations [10,14–16], only one study exists which summarized gait impairments in a large population of persons with ET (104 participants) [9]. Further, only one study has assessed the relationship of clinical disease severity to gait performance in a large sample size [1]. Louis and colleagues [1] established that persons with ET who are older, possess cranial (head, jaw) tremors and displayed an older age at tremor onset are more likely to experience deficits in tandem gait performance. In this study, gait performance was measured by the number of mis-steps taken, rather than relating the clinical values of tremor severity to quantitative, spatiotemporal gait data. Because a broad range of gait characteristics can be measured with gait performance and are often related, applying a technique that can reduce the number of related variables can prove useful to both researchers and clinicians in order to simplify results of gait analysis. Utilizing a technique such as principal component analysis (PCA) allows distinct features of gait to be described by detecting sources of variability from a large set of spatiotemporal gait variables.

Reducing the data set by using PCA helps to explain the more prominent characteristics (underlying structure) of gait, and understanding this would allow clinicians and researchers to better target gait specific alterations in persons with ET. Previous studies have used principal component analyses for data reduction as well as to detect discrete features of gait to target clinical gait analysis [17–19]. PCA has already been successfully applied in studies of healthy older adults, where analysis yields four domains of gait that include pace, rhythm, stability, and phases of the gait cycle [10,13]. Additionally, previous research has demonstrated that specific factors can explain the contribution of underlying cognitive and other nonmotor features to gait disturbance [10,20]. In persons with movement disorders, PCA has identified fewer factors compared to healthy older adults, suggesting disease states may modify how the variables are combined [16]. Thus, information regarding the factors identified using PCA would shed light upon the control of overground walking in ET and further inform clinicians on the relationship between clinical symptomatology and gait performance.

The purposes of this study were to: 1) identify the distinct features of spatiotemporal parameters during gait in persons with ET, 2) contribute to the normative database of gait parameters from persons with ET, 3) provide information that quantifies the influence of age on gait speed in persons with ET, and 4) identify the relationships between gait performance and clinical measures of disease severity in persons with ET. Based upon previous observations that normal gait speed decreased with age significantly in persons with ET but not healthy controls [12], we expected age to predict gait speed. Additionally, we used individual items from the Fahn-Tolosa-Marin Tremor Rating Scale (TRS) [21] as predictors of characteristics of gait in persons with ET. As recent evidence suggests an association between gait impairment and midline tremor severity in ET [1,12,22] we hypothesized that worse gait performance (e.g. increased velocity, cadence, double support time, step width, and decreased step length) represented by the domains identified by PCA, would be predicted by greater severity of midline tremors (face, tongue, voice, head, and trunk). We particularly expected that if a domain was identified that represented stability, this domain would be predicted by greater severity of any midline tremor.

2. Methods

2.1. Participants

A retrospective analysis was utilized to assess data collected from one hundred and forty-two consecutive ambulatory persons with a diagnosis of ET confirmed by a fellowship trained movement disorders neurologist. The total general sample number was 262 participants, prior to screening participants out for exclusion criteria. Data were collected during the participant visit to their clinician, as a part of their routine exam from April 1, 2011 to April 08, 2015 utilizing an IRB-approved database and all participants provided written informed consent prior to participating. Participants unable to walk across the walkway independently, with deep brain stimulation or other related surgeries were excluded. The demographics of all participants can be found in Table 1.

Table 1
Demographic and clinical information for the sample (n = 142).

	Average ± Standard Deviation	*Range*
Age (years)	67 ± 13	23–90
Sex	Male = 90 Female = 52	
Side of first symptom	Right = 32% Left = 17% Both = 39% Unsure = 12%	
Years since first symptom	18 ± 17	< 1–68
Tremor Rating Scale Motor	23 ± 18	0–61
Activities of Daily Living	10 ± 16	0–25
Total	28 ± 18	0–83
Distribution of Tremors (items 1-14)		
Midline (rest, postural, action)	15%, 25%, 47%	
Extremity (rest, postural, action)	17%, 52%, 53%	

2.2. Equipment

Gait data were measured while walking over GAITRite instrumented walkway system (CIR systems Inc., Havertown, PA). The 5.8 m × 0.9 m pressure sensitive walkway is composed of 18,432 sensors which were activated at foot contact and deactivated at toe-off. The walkway was centered within an isolated 12.2 m × 1.37 m collection hallway free from distraction. Data were collected at 120 Hz and processed within the GAITRite Platinum software. In order to obtain a set of spatiotemporal measures of gait that researchers and clinicians may consider measuring to further understand gait performance, we evaluated data from 12 spatial and temporal gait parameters (Table 2). The 12 spatial and temporal gait parameters were chosen because they are easily obtainable from the GaitRite software. Although the GaitRite software can

Table 2
Quantitative gait parameters of the patients with ET and Factor loading of twelve quantitative variables on the three independent gait factors with varimax rotation and extracted by factor analysis. Bold numbers indicate variables that met the loading criteria indicating an important contribution for the factor.

Gait Variable	Mean (+/− SD)	Pace Factor	Rhythm Factor	Stability Factor
Velocity (m/s)	0.96 (.23)	**0.903**	−0.362	−0.039
Cadence (steps/min)	99.00 (11.00)	0.450	**−0.863**	−0.179
Single Support (% Cycle)	33.9 (2.50)	**0.819**	−0.187	−0.360
Stride Length (m)	1.15 (.21)	**0.954**	0.012	0.059
Step Length (m)	0.58 (.11)	**0.953**	0.030	0.060
Step time (s)	0.62 (.08)	−0.445	**0.863**	0.173
Double Support (% Cycle)	32.25 (5.02)	**−0.852**	0.240	0.353
Stance Time (s)	.81 (.13)	**−0.574**	**0.773**	0.197
Double Support Time (s)	.40 (.11)	**−0.73**	**0.585**	0.268
Step Width (m)	.11 (.03)	−0.089	0.031	**0.924**
Swing Time (s)	.41 (.04)	0.103	**0.928**	−0.050
Single Support Time (s)	.41 (.04)	0.058	**0.948**	−0.064

also provide a Functional Ambulatory Score and a value for the left and right leg, we did not evaluate these parameters. Instead, values for each left and right leg were averaged for each parameter.

2.3. Procedures

Participants were asked to walk on the mat in a well-lit hallway at their normal walking speed four times. Participants began and terminated their walks at least 1.5 m before and after the walkway to minimize acceleration/deceleration effects. Data from all four walks were combined for analysis by averaging across the four trials. On average, the time it took to complete a trial was 6 s, and 27 steps per participant were used in the gait assessment.

A fellowship trained movement disorders neurologist administered the Fahn-Tolosa-Marin Tremor Rating Scale (TRS). At the time of the clinical visits, the TRS was the standard scale used by the clinic to assess tremor in persons with ET. The psychometric properties of the TRS have been previously evaluated as fair (motor sections) to poor (activities of daily living), with very good intrarater reliability in repeated assessments [21]. The TRS consists of 21 individualized items that uses a 5-point scale to rate tremor severity based on tremor amplitude, from 0 (no tremor) to 4 (severe tremor) in each part of the body, and includes assessments of functional disability and specific abilities. The motor sections (items 1–14) evaluate tremor at specific anatomical locations (face, tongue, voice, head, right and left upper extremity, trunk, right and left lower extremity) as well as specific motor tasks (handwriting, spiral drawing, pouring) involving the upper extremity. Four of the items on the motor section are scored at rest, with posture, and with action. Three of the items on the motor section are scored at rest and with posture. Four of the items on the motor section are scored for the right and the left side. The activities of daily living (ADL) section (items 15–21) assess tremor and it's patient-reported interference with activities of daily living (speaking, feeding, bringing liquids to mouth, hygiene, dressing, writing, and working). The total TRS score is the sum of the motor and ADL scores, such that the TRS total minimum score is zero and the maximum score is 144. During the clinical visit, years since first symptom, side of first symptom, and years since diagnosis was determined by subtracting the date of the evaluation from the respective date of symptom onset/diagnosis with ET from the participant's medical record.

2.4. Data analysis

In order to characterize the gait performance of our participants, a principal components factor analysis with varimax rotation with Kaiser normalization was used. Varimax rotation was selected in order to minimize the number of gait variables loading highly onto more than one factor [16,23–25]. This analysis was selected because this method allows a reduction of many gait variables to be grouped into a smaller subset based on the amount of variance in the original data set it explains. Further, this method does not require any expectations regarding the underlying structure of the data set, or assumptions of which variables are most important to study [26]. Factors with eigenvalues exceeding 1.0 and parameters with correlation loadings of 0.5 or higher were considered to be significant contributors to the observed behavior [16,19,27]. Multivariate hierarchical regression models with sex and age included in the first block and stepwise regression with clinical measures of tremor severity in the second block were applied to assess TRS items as predictors of the coefficients of determination (R^2) for each factor (Pace, Rhythm, and Stability). Multicollinearity tests with tolerance and variance inflation diagnostics was performed (a tolerance value of > 0.5 was considered acceptable to exclude multicollinearity). Finally, to understand the influence of age on gait speed in persons with ET, we performed a linear regression analysis with age as the predictor for gait speed. The level of significance was set at $p < 0.05$ and all statistical analyses were performed using IBM SPSS 24 (IBM Corporation, Armonk, NY).

3. Results

Three factors accounted for 91.9% of the variance in gait performance. The first factor accounted for 61.0% of the variance in gait performance and loaded highly on parameters quantifying velocity, double support % and time, stride length, step length, and single support time. The factor loading of the twelve quantitative variables, comparative normative values, along with the Scree plot can be observed in Table 2 and Fig. 3. We have also provided the factor loading of the twelve variables with a direct oblimin rotation, and a correlation matrix of the original variables (see supplementary files). In accordance with previous work [9,10,12] we labeled this as the pace factor. The second factor accounted for 22.4% of the variance loading primarily on variables reflecting gait rhythm such as swing time and single support time. We labeled this factor as the rhythm factor. The third factor accounted for 8.5% of the variance and loaded only on step width, and was therefore labeled as the stability factor. Finally, our linear regression analysis revealed a significant influence of age on gait speed. Gait speed decreased with age significantly by 0.64 cm/s/year, ($R = 0.351$, $p < 0.001$) (Fig. 1).

There were significant associations between TRS scores and the pace factor and stability factor, but not for the rhythm factor. The regression models for each factor are displayed as follows: (1) Pace Factor = β1 (age) + β2 (sex) + β3 (Head Tremor-posture) + β4 (Left Lower Extremity Tremor-resting) + β5 (Left Lower Extremity-posture) + β6 (Feeding Tremor). (2) Rhythm Factor = β2 (sex). (3) Stability Factor = β1 (age) + β2 (sex) + β3 (Right Lower Extremity Tremor-Resting) + β4 (Activities of Daily Living Tremor) (Fig. 2). The TRS item measuring head postural tremor severity significantly predicted the pace factor ($p < 0.001$). Additionally, postural tremor severity of the left leg, resting tremor severity of the left leg, and tremor severity during feeding activities significantly predicted the pace factor, (all $p < 0.01$). Only sex significantly predicted the Rhythm factor ($p < 0.01$). No TRS scores were significant predictors of the Rhythm factor. The TRS ADL score and items measuring lower extremity resting tremor severity of the right leg were significant predictors of the stability factor ($p = 0.023$, $p = 0.026$, respectively) (Fig. 2). Specifically, greater severity of tremors during ADL and resting tremor of the right leg resulted in a significantly higher stability factor (wider step width) (Fig. 2).

4. Discussion

While several studies [2,4,11] have provided values for gait parameters in ambulatory individuals with ET, most are limited by sample size and none have investigated the underlying structure (principal

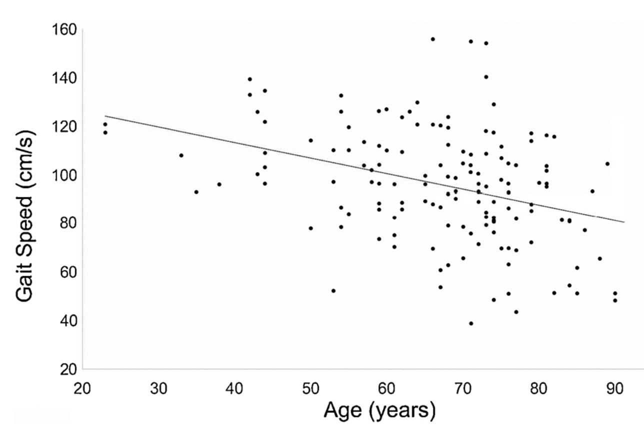

Fig. 1. Relationship between age and gait speed in patients with essential tremor. The regression model equation is as follows: Gait speed = −.64 (age) + 139; $r^2 = .123$.

	Pace Factor		Rhythm Factor		Stability Factor	
	P	R^2	P	R^2	P	R^2
	<0.01	0.47	0.02	0.087	<0.01	0.56
	P	β	P	β	P	β
Age		0.03				-0.02
Sex		-0.49		-0.60		-0.97
TRS-1 Face						
TRS-2 Tongue Rest						
TRS-2 Tongue Posture						
TRS-3 Voice						
TRS-4 Head Rest						
TRS-4 Head Posture		0.37				
TRS-5 RUE Rest						
TRS-5 RUE Posture						
TRS-5 RUE Action/Intention						
TRS-6 LUE Rest						
TRS-6 LUE Posture						
TRS-6 LUE Action/Intention						
TRS-7 Trunk Rest						
TRS-7 Trunk Posture						
TRS-8 RLE Rest						0.854
TRS-8 RLE Posture						
TRS-8 RLE Action/Intention						
TRS-9 LLE Rest		-1.09				
TRS-9 LLE Posture		0.485				
TRS-9 LLE Action/Intention						
TRS ADL (15-21)						0.040
TRS-15 Speaking						
TRS-16 Feeding		-0.249				
TRS-17 Liquids to mouth						
TRS-18 Hygiene						
TRS-19 Dressing						
TRS-20 Writing						
TRS-21 Working						

p<.05
p<.01
p<.001

Fig. 2. Regression analysis results. Clinical measures of tremor severity as predictors of the three independent gait factors extracted by factor analysis. RUE- right upper extremity, LUE-left upper extremity, RLE- right lower extremity, LLE-left lower extremity, ADL-activities of daily living.

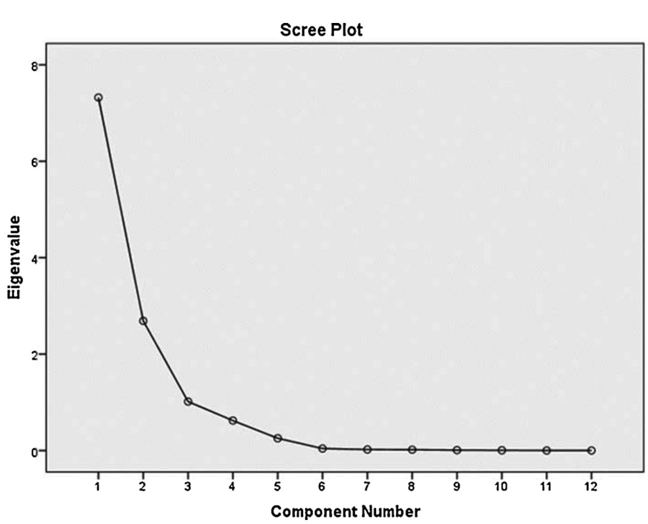

Fig. 3. Scree plot of principal components for gait performance.

components) of objective gait measures in this population. The relationship of clinical measures of tremor severity and their relationship to characteristics of gait has yet to be investigated in a large sample of persons with ET. Our study yields a comprehensive analyses of normative spatiotemporal values in a large cohort of individuals with ET that will further our understanding of gait performance and clinical measures in this population.

Our factor analysis results demonstrate congruency with earlier studies, which used similar methods in community dwelling healthy older adults, individuals with cognitive decline and dementia, and in persons with Parkinson's disease [10,13,15,16]. Each of these studies identified a pace factor characterized by velocity and length measures, and a rhythm factor distinguished mostly by temporal gait measures. These gait characteristics are important parameters to investigate in older populations, as all of these variables directly relate to fall risk, quality of life, and mortality [15,28]. Understanding characteristics of gait such as speed is important for decreasing the risk of falling in older adult populations, including those with movement disorders. Below, we discuss these characteristics and their importance as they relate to gait performance in persons with Essential Tremor.

In the present study, persons with ET walked slower and spent more time in double support compared to the healthy older adult normative data reported previously in the literature [13]. We observed that persons with ET walk at a velocity of .96 m/s while healthy older adults within the age range of 60–70 are reported to walk at a velocity of 1.24–1.34 m/s [29]. Our results are in agreement with Rao et al. [2], who also observed that persons with ET exhibit decreased gait speed and increased percent double support time when compared to age-matched healthy adults. This decrease in gait speed has been previously associated with an increase in falling and fear of falling in persons with ET [2,22]. Indeed, this relationship highlights the concern for our observation that individuals diagnosed with ET show a steeper reduction in gait speed with age (0.64 cm/s/year) compared to age matched controls (0.04 cm/s/year) [12]. Likewise, the increase in percent double support time in ET persons suggest a shift towards more conservative gait which spends comparatively longer amounts of time in the most mechanically stable phase of gait. Taken together, these results suggest that as persons with ET enter into advanced age, impairments in balance and gait are beyond those observed in normal aging despite walking with a more cautious (increased double support) gait.

The notion of impaired balance control in ET is further supported by the result that on average persons with ET walked with a step width of .11 m, while normative data for healthy older adults report a step width of .07 (females) and .097 (males) [13]. Presumably, persons with ET walk with an enlarged step width as a result of impaired balance control or decreased balance confidence [4]. Louis and colleagues [22] have previously described that participants with ET reported greater subjective functional gait and balance impairments than their age-matched controls. Specifically, individuals with ET experience a loss of confidence in balance, and those with head tremor report more gait and balance difficulty, as close to 50% experience at least one near fall or fall over the course of a year [22]. Our observations of decreased gait speed and increased step width support previous research linking these patterns to underlying cerebellar pathology [30,31].

Interestingly, the pace and stability factors were predicted by clinical measures of tremor severity. Tremor severity of the head significantly predicted the pace factor. These results are substantiated by other observations that indicate a strong link between severity of cranial tremors to gait and balance difficulties in persons with ET [13,32,33]. Previous evidence has suggested that the observed gait impairment and cranial tremors (head, jaw, voice) are likely a shared disturbance of cerebellar regulation of the midline, distinct from regulation of the limbs [1,34]. We observed that tremor severity of the legs significantly predicted both the pace factor and stability factor. This observation is contrary to previous studies [1,34], who observed that tandem gait difficulty and cadence during overground gait was not correlated with severity of limb tremors. The observed differences could be related to the walking task and measures of gait performance executed in each of the respective studies. Louis et al. [1], utilized a tandem walking task and counted the number of mis-steps and Rao et al. [22], investigated step time and cadence during overground walking. The main differences between the prior studies and the current one, is that we measured traditional overground walking and examined features of twelve quantitative spatiotemporal parameters (cadence, velocity, step length, double support time, step time, etc.) jointly. Thus, the present study has identified additional discriminating measures of gait impairment in ET. Finally, it is important to note that in our investigation, the rhythm factor (loaded highly on cadence) was not predicted by any of the clinical measures of tremor severity. These findings are unanticipated, as disturbances in rhythm generation of the upper extremity have been noted as abnormal in persons with ET [35]. However, it is possible that in combination some of the clinical measures of the TRS scale do predict rhythm. A full discussion of possible interactions of clinical measures of the TRS and their effects on pace, rhythm and stability lies beyond the scope of this study. Based on our observations, interventions meant to enhance gait performance should seek to improve aspects of pace and stability factors (for example, gait speed and step width).

We were unable to more discretely evaluate the influence of level of disability (i.e. moderate, mild, and severe), as this information in relation to the TRS score does not currently exist. Future research should develop classifications for certain ranges of TRS scores or utilize other measures of disability, so that disease severity can be accounted for when reporting gait parameters. Further, the number of factors produced by PCA may shed light on disease severity. Additionally, our analysis only consisted of participants walking at their preferred self-selected speed, not at their maximum possible speed or while using stressors such as a walking while talking test. Therefore, these results may not represent the true breadth of capacity of an individual with ET, which may have provided further insight into the relationship between clinical measures of tremor and gait impairments. Finally, individuals who had undergone deep brain stimulation were excluded from this analysis, and may or may not share the characteristics of the population included here.

5. Conclusions

A pace, rhythm, and stability factor were identified in a large cohort of persons with ET. Only the pace and stability factors were associated with disease severity, suggesting these factors are most sensitive to disease severity compared to the rhythm factor. Taken together, these results of gait performance in ET to suggest that a clinical assessment of gait and balance would be an important measure to consider in routine clinical practice when treating persons with ET. Particularly, parameters associated with the pace and stability factors would be important markers for researchers and clinicians to observe in persons with ET particularly with more severe axial and leg tremors.

Conflict of interest

None.

Acknowledgements

The authors would like to thank all laboratory students for their help with compilation of data and all volunteers for their participation in this study.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.gaitpost.2019.04.004.

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