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The Association between Cardiac Autonomic Control System and Motor Performance among Patients Post Stroke: Review of the Literature

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Abstract

This paper reviews the evidence regarding the autonomic heart rate regulation system function in relation to motor, activity and functional performance among patients post stroke. The target population included patients of any severity, post event. Databases searched for English language studies from 1990 to 2014 were PubMed, Cochrane Library, the Physiotherapy Evidence Database (PEDro), and the ClinicalTrials.gov.

Search terms included 'stroke', 'hemiplegic', 'cerebrovascular accident' and `autonomic nervous system` or `heart rate variability` or `sympathetic` or `para sympathetic` and ' motor` or `activity` or `function'. Articles were identified and included if (1) participants were older than 18 years of age, (2) diagnosis of stroke was made (3) autonomic cardiac heart rate regulation system state and response to activity was present by HRV parameters (4) or an association between HRV parameter and motor or function performance was described.

Results: Eight studies were identified as eligible for study criteria; among these, five assessed the possible predictive value of the HRV parameters on function performance two or more month later. Two studies assessed the response of heart rate autonomic control system assessed by HRV values to exercise. One study assessed the possible modification effect of heart autonomic system on the influence of aerobic intervention on walking and functional outcomes among patients at the sub-acute phase post stroke. The main results of the current review suggested a relationship between autonomic HR regulation system and motor and functional abilities among patients post stroke. In addition, it seems that cardiac autonomic system response to activity in these patients. However, the extent of the association and further the benefits of autonomic rehabilitation on motor or functional abilities remain to be evaluated.

Keywords: Post stroke; Motor; Hemiplegic; Cerebrovascular accident; Autonomic nervous system; Heart rate variability

Introduction

Patients post stroke frequently present low tolerance for exercise, which repeatedly explained by the impaired motor abilities due to the brain damage or due to secondary physical conditions. Soft tissue contractures or reduced fitness resulting from prolonged chair bound or bed rest are the prevalent explanations [1,2]. However, this low tolerance may also be due to the primary brain damage affects the cardiac autonomic regulatory system [3].

Autonomic instability is common phenomenon in patients post stroke, with signs and symptoms of hyper stimulation of the sympathetic nervous system. Hypertension, postural or episodic hypotension, hyperhidrosis and coldness of the affected limbs, arrhythmia, bladder and bowel dysfunction and reduced heart-rate variability (HRV) have been frequently observed post event [4,5]. HRV refers to beat-to-beat alterations in heart rate as measured by periodic variation in the R–R interval and provides a non-invasive method for investigating autonomic input into the heart. HRV, as a sign of the impaired autonomic system, found to be associated with adverse clinical outcomes among patients post stroke [5,6].

The association between motor, function and autonomic disturbances may possibly explain by neuroimaging data that have shown a network including the insular cortex, anterior cingulate gyrus, and amygdala which necessary for regulation of the central autonomic nervous system [7]. The insular cortex is located in the region of the middle cerebral arteries. Middle cerebral artery infarct is the most common type among the cerebral vascular territory infarcts [8,9]. It is well known the patients post middle cerebral artery infarct become highly dependent for daily activities [8], which seems to be related to the characteristics of the middle cerebral arteries zone for motor function; the corticospinal tract which involved in fine motor, the corticoreticulospinal tract associated with postural control and locomotor

function, the cortico-fugal fibers responsible for limb-kinetic apraxia, and the anterior portion of superior longitudinal fasciculus which is associated with ideomotor apraxia [9].

Studies concerning the rehabilitation of patients post stroke focus mainly on the motor or cognitive disabilities and outcome. The functioning of the autonomic nervous system has been virtually ignored. In addition, aerobic training which may serve as a rehabilitation method for the heart autonomic system, associate with improved walking performance, while heart rate and blood pressure values did not exhibit constant improvement [10].

To improve the clinical management of patients post stroke with emphasis on the heart autonomic system it is important to first describe this system response to activity and its association with function abilities. This review present the existing evidence regarding the immediate response of the autonomic heart rate regulation system to activity among patients post stroke, and the current evidence relate to the significant of the autonomic heart rate regulation system in prediction motor performance and function abilities among patients post stroke.

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Methods

Search strategy

The following databases were searched for English language studies from 1990 to 2014: PubMed, Cochrane Library, the Physiotherapy Evidence Database (PEDro), and the ClinicalTrials.gov.

The search strategy included a combination of three groups of keywords as follows:

- 'stroke' or 'hemiplegic' or 'cerebrovascular accident' AND
- 'autonomic nervous system' or 'heart rate variability' or 'sympathetic' or 'para sympathetic' AND
- 'motor' or 'activity' or 'exercise' or 'function'

Additional articles were identified through a manual search of the reference lists of relevant articles and through citation tracking and key author searches completed using the Web of Science.

Selection of studies

Articles were included if (1) participants were older than 18 years of age, (2) diagnosis of stroke was made (3) autonomic cardiac heart rate regulation system state or response stimuli was present by HRV parameters (by using time domain analysis and/or frequency domain analysis, Table 1) (4) in relation to motor, exercising or function performance and was described for all participants (5) the article was

written in English; and (6) accessibility was existing to a full-text report of original research.

Two reviewers independently applied the inclusion and exclusion criteria to the titles and abstracts or to the full text if necessary. Doubts regarding the eligibility of an article were resolved by discussion between the two reviewers.

The full-text article was saved if the citation was considered potentially eligible and relevant. Each full-text article was evaluated by the two reviewers whether it fulfilled the inclusion criteria. If any of the inclusion criteria were not present, the article was excluded from the review.

Data items and collection

Information was extracted from each included study and presented in Table 2. The main topics (1) the aim of the study (2) study design; (3) the number and the characteristics of participants (4) HRV assessment and interpretation methods; (5) main results.

Results

The initial searches identified 52 references which closely approximated the inclusion criteria and were requested in full. After further examination, 44 were rejected and 8 included for further analysis. The references not included along with the reasons are listed in Table 3.

Of these, five were follow-up studies [6,8-12], two were cross

Abbreviation	Description	Indication (Sympathetic, Parasympathetic or both)				
RR interval	The time interval in seconds between two nearby R waves on the ECG					
Time Domain						
SDNN (ms)	Standard deviation of the RR intervals	Both				
RMSSD (ms)	Root mean square of differences between adjacent RR intervals	Parasympathetic activity				
Frequency Domain						
LF (ms ²)	Power of low frequency range (0.04-0.15 Hz)	Sympathetic activity or both				
HF (ms ²)	Power of low frequency range (0.15-0.40 Hz)	Parasympathetic activity				
L/H	Ratio of LF/HF power	Balance between Sympathetic and Parasympathetic				

Table 1: Abbreviation for heart rate variability measures which included in the review.

Study type	Aim of the study: To assess the	Participants	HR and HRV assessment	Study protocol and motor/ function measures	Outcome
Follow up	Correlate between HRV spectral parameters & functional performances in patients in a rehabilitation setting	16 patients Time post event 1-6 W Age : 73±10	Short recording during exercise 1-6 weeks post event Frequency domain	Geriatric rehabilitation OC : FIM * 48 to 72 hours after admission * A week before discharge	Admission ↓HRV associate ↓FIM score at discharge
Follow up	Impact of cardiac autonomic impairment on functional outcome.	85 patients Time post event<30 D Age: 60±12.4	24h-Holter At rehabilitation admission Time domain s	60 days rehabilitation 2X day, 6 days a week. OC : Bl, mRS *At admission *The end of rehabilitation.	Admission ↓SDNN and ↓SDANN associate ↓BI score at discharge. SDNN < 100 ms ↓↓ associate ↓↓BI<75
Follow up	Impact of cardiac autonomic derangement on gender- associated functional outcome	126 patients At admission to rehabilitation Age 59.7±11.6	24h-Holter At rehabilitation admission Time domain :	60 days rehabilitation 2X day, 6 days a week. OC :BI, mRS *At admission * The end of rehabilitation	BI<75, ↓ mRS and ↑ age on admission predict BI<75 at discharge. In addition Among man SDNN< 100. Insular damage in women associate with BI<75
Follow up	Contribution of multiple parameters to understand better ANS changes and association with functional outcome.	75 patients Time post event <7 D Age: 62 (30- 87)	Short recording +BP < 7 days post event. Time domain Frequency domain	Stroke unit OC :NIHSS, mRS *day 7th *day 90th from event.	Admission ↓L/H, ↑Respiratory rate predict ↑NIHSS, ↑mRS at discharge.

Age; in years,

W- weeks, OC:-outcomes, HRV- heart rate variability, ANS- autonomic nervous system,

Table 2: Short summery of the included studies.

Page 3 of 6

I itie	Journal/year/ volume	Main reason for not including	
Dynamic Cardiophysiologic Variables Correlate with Lesion Location and FIMTM in Patients with Ischemic Stroke	American Journal of Physical Medicine & Rehabilitation 2002. 81 (8): p. 590-596.	HRV parameters weren't time or friquency domain.	
Study porotocol: prediction of stroke associated infections by markers of autonomic control.	BMC Neurol, 2014:13:p 9-14	Study protocol	
Reappraisal of heart rate variability in acute ischemic stroke.	Kaohsiung Journal of medical Science, 2011. 27(6): p. 215-21	Did not include motor, exercising or function performance	
Relationship between Iscemic stroke location and autonomic cardiac function.	Journal of Clinical Neuroscience, 2013. 20(3): p. 406-9	Did not include motor, exercising or function performance	
Parasympathetic activity correlates with early outcome in patients with large artery atherosclerotic stroke.	J Clin Neurosci 2012 314 (1-2): p. 57-61	Did not include motor, exercising or function performance	
Prognostic implications of right-sided insular damage, cardiac autonomic derangement, and arrhythmias after acute ischemic stroke	Stroke 2005, 36 (8): p.1710-5	Did not include motor, exercising or function performance	
CARDIAC AUTONOMIC DERANGEMENT AND ARRHYTHMIAS IN RIGHT-SIDED STROKE WITH INSULAR INVOLVEMENT	Stroke 2004.; 35 (9): p2094-8	Did not include motor, exercising or function performance	
Heart rate variability	Handbook clinical Neurology,2013. 117 :379-93	A Handbook	
Reproducibility of heart rate variability during rest, paced breathing and light-to-moderate intense exercise in patients one month after stroke.	European Journal of Neurology, 2011. (2) 66 : p. 117-22.	Reliability study	
Heart rate variability- a potential early marker of sub- acute post stroke infections	Acta. Neurologica Scandinavica, 2012. 126 : p. 189-196	Did not include motor, exercising or function performance	
Heart rate variability and outcome in acute severe stroke. Neurocritical Care.	Neurocritical 2004. 1 (3): p. 347-353	Did not include motor, exercising or function performance	
CLINICAL PROGNOSTIC SIGNIFICANCE OF HEART ABNORMALITY AND HEART RATE VARIABILITY IN PATIENTS WITH STROKE	Neurological research 2010.32(5): p 530-4	Did not include time or frequency mesurments.	
Cardiovascular autonomic function in lateral medulary infraction	Neurology Sciance. 2013; 34 (11) 1963-9	Did not include time or frequency mesurments.	
Cardiac autonomic status is associated with spasticity in post-stroke patients.	NeuroRehabilitation, 2014. 377	Assessed spasticity	
Effect of insular injury on autonomic functions in patients with ruptured middle cerebral artery aneurysms.	Stroke, 2013. 44 (12): p. 3350-2.	Did not include motor, exercising or function performance.	
Effects of aerobic cycling training on cardiovascular fitness and heart rate recovery in patiants with chronic stroke.	NeuroRehabilitation 2013; 32 (2):327-35	Did not include time or frequency mesurments.	
Autonomic nervous system disorders in stroke.	Clinical Autonomic Res., 1999. 9(6): p. 325-33	Review article	
Dynamic behavior of heart rate in ischemic stroke.	Stroke, 1999. 30 (5): p. 1008-13.	Did not include motor, exercising or function performance	
Circadian rhythm of heart rate variability is reversibly abolished in ischemic stroke.	Stroke, 1997. 28 : p. 2150-5154.	Did not include motor, exercising or function performance	
Abnormal heart rate variability reflection autonomic dysfunction in brainstem infraction.	Acta. Neurol. Scand., 1996. 94(5): p. 337- 42	Did not include motor, exercising or function performance	
Abnormal heart rate variability as a manifestation of autonomic dysfunction in hemispheric brain infraction.	Stroke, 1996. 27 (11): p. 2059-63.	Did not include motor, exercising or function performance	
Asymmetrical skin temperature in ischemic stroke.	Stroke, 1995. 26 : p. 1543-1547	HRV not included, other autonomic variables were examined	
Cardiovascular autonomic reflexes in brain infarction.	Stroke, 1994. 25 : p. 787-792	HRV not included, other autonomic variables were examined	
Asymmetric sweating in stroke: a prospective quantitative study of patients with hemispheral brain infarction.	Neurolmage, 1993. 43 : p. 1121-1214	HRV not included, other autonomic variables were examined	
Suppressed sympathetic skin response in brain infraction.	Stroke, 1993. 24(9): p. 1389-92	HRV not included, other autonomic variables were examined	
Heart rate dynamics predict post stroke mortality.	Neurology, 2004. 62(10): p. 1822-6	Did not include motor, exercising or function performance	
Autonomic function is impaired in elderly stroke survivors.	Stroke, 2005. 36 : p. 1026-1030	Did not include motor, exercising or function performance	
Autonomic and thermal sensory symptoms and dysfunction after stroke.	Stroke, 1995. 26 (8): p. 1379-85	HRV not included, examin other autonomic variables Did not include motor, exercising or function performance	
Reduced heart rate variability after right- sided stroke.	Stroke, 1996. 27(2): p. 247-51	Did not include motor, exercising or function performance	
Relation between 24-h heart rate variavility and blood pressure fluctuation during exercise in stroke patients	Circulation, 2005. 69: p 717-721	Blood pressure response to exercise as outcome variable	
AUTONOMIC NERVOUS SYSTEM FUNCTION IN PATIENTS WITH ACUTE BRAINSTEM STROKE.	Cerebrovascular diseases, 2001; 11 (1):p2-8	Patients with brainstem stroke Did not include motor, exercising or function performance	
Nocturnal deterioration after ischemic troke and autonomic dysfunction:	Cardiovascular Disease, 2013. 36(5-6): p.	Hypothesis and implications.	
hypothesis and implications.	454-61	Ab	

Page 4 of 6

Decreased heart rate variability is associated with poststroke depression	American journal of Geriatric Psychiatry, 2008. 16 (11): 867-73	Did not include motor, exercising or function performance
Cardiovascular and neurological causes of sudden death after ischemic stroke.	Lancet Neurology, 2012.11(2):179-88	Did not include motor, exercising or function performance
Prediction of early secondary complications in patients with spontaneous subarachnoid hemorrhage based on acceletated sympathovagal ratios.	Acta Neurochir, 2009. 151 (12): p. 1631-7.	Did not include motor, exercising or function performance
Effects of stroke localization on cardiac autonomic balance and sudden death.	Stroke, 1999. 30 (7): p. 1307-11	Did not include motor, exercising or function performance
Lateralization of T-lymphocyte responses in patiant with stroke. Effect of sympathetic dysfunction?	Stroke.1995;26(1):p57-62	Not include HRV
Heart rate variability in neurorehabilitation patients with severe acquired brain injury.	Brain Injury, 2014. 28(2): p. 196-202.	Did not include motor, exercising or function performance as outcome
Examination of cardiovascular and peripheral autonomic function in ICU: a pilot study.	Journal of Neurology 2013.260 (6):1511-7	Patients post Stroke were excluded
The effects of cerebral white matter changes on cardiovascular responses to cognitive and physical activity in a stroke population.	Psychopysiology.2010; 49 (12):p1618-28	Did not include HRV Did not include motor, exercising or function performance as outcome
Cerebral blood flow,sympathetic nerve activity and stroke risk in obstructive sleep apnoea. Is there a direct link?	Blood Press, 2013. 22(1): p. 27-33	Review article
Preliminary findings of the effects of autonomic dysfunction on functional outcome after acute ischemic stroke.	Clinical Neurology and Neurosurgery 2012. 114: p. 316-320.	Did not include motor, exercising or function performance.
Autonomic dysfunction in different subtypes of post -acute ischemic stroke.	Journal of Neurological Science, 2014. 337: p. 141-146	Did not include motor, exercising or function performance

Table 3: List of the non-included studies, and main reason for not including.

sectional data collection method [13,14] and one was a randomized clinical trial. One study used only frequency domain analysis [9] and 3 only time domain analysis [10,11,14].

Heart rate regulation system in prediction motor performance and function abilities

In the five studies which assessed the prediction ability of HRV heart rate assessed between 1-7 days [11] up to 1-6 weeks [12-14] post event. The participants were followed and motor and functional performances two or more month later were recorded [11-14]. The main conclusion of all those studies was that autonomic dysfunction is related to a poor motor and/or functional outcome in patients with ischemic stroke.

Bassi et al. [13] assessed HRV using 24h Holter recording among 85 patients, who admitted to a rehabilitation department up to 30 days post stroke. Barthel Index (BI) and modified Ranking Scale (mRS) were assessed at the beginning and at the end of two month rehabilitation period. It was noted that association exist between autonomic impairment and function and motor performance two month later. In 2010 Bassi et al. [14] assessed by the same method the possible modification effect of sex on the association between autonomic impairment and functional outcome. In this study the author noted that HRV parameters predict function abilities among male but not among women.

Graff et al. [11], assessed the heart autonomic regulation system soon after the event among 75 post stroke patients by using short recording ECG and blood pressure as well as breathing rate. Neurological and motor –functional performances of the patients were assessed at day 7 and 90 post event by the National Institutes of Health Stroke Scale (NIHSS) and by the mRS. Their conclusion was that HRV, but not BP variability distinguishes groups with various neurological outcomes and that respiratory rate in the acute phase associated with poor functional outcome.

Arad el al.[15], used the functional independence measure (FIM) as a measure of the functional ability post stroke at the beginning and end of rehabilitation and measured the HRV during physiotherapy session by frequency domain among 16 patients post a stroke. They concluded that higher HRV is correlated with better function and vice versa. Katz-Leurer et al. described the contribution of HRV parameters in prediction motor and endurance test results. Thirty nine patients were followed for two month. A positive, moderately strong association was noted between RMSSD values and motor abilities two weeks post event which remain significant and moderately strong after 8 weeks of rehabilitation [6].

HRV and exercise among patients post stroke

Two studies assessed HRV change as response to exercise session among patients post stroke [16,17]. Katz-Leurer et al. assessed and compared the response of HR and HRV time domain values to physical activity during physiotherapy session among patients at the sub-acute phase post stroke or post traumatic brain injury. Patients were asked to rest for 10 minutes, to perform a constant effort on cycle for 5 minute and then to continue therapy sessions for 45 minutes. Therapy session include, by mean, 15 minutes of bed exercise, 5 minutes sitting exercise and at the remained time about 25 minutes the patient practice while standing, walking or while practicing stairs climbing etc. The authors noted an increase HR value and decrease RMSSD values during cycling activity and physical treatment as compared to rest time; this was true only for patients post stroke.

Raimundo et al. [16] assessed 38 inactive patients one year or more post stroke, using a stress test on a treadmill. The HR targeted to achieve 50%-70% of the maximum HR and the test last for 25 minutes. Patients were asked to rest for 10 minutes before getting up on the treadmill, to perform a 5 minute warm up session on the treadmill and then to perform the test. The patients were followed for 30 minutes post the test while lying and resting. Both, time and frequency measures were used. All time domain values were significantly influenced by exercising, by reducing their values. The SDNN and HR did not returned to baseline value up to 30 minutes post exercise. The LF value increase significantly during exercise and reduced significantly post exercise and as well did not returned to baseline value up to 30 minutes post exercise. The HF value reduced significantly during exercise but did not significantly differ between rest periods.

Autonomic heart rate control system as a modifier factor

Katz-Leurer et al. assessed whether autonomic impairment

modifies the influence of aerobic training on motor and functional outcome. Sixty four patients were randomized to two comparable groups; both participate in regular rehabilitation program. The study group participates in addition in aerobic exercise session, for 8 weeks. Although HRV at baseline was associated with patients' endurance ability, no modification effect was noted.

Discussion

Within this review, we attempted to summarize the current knowledge regarding the association or the possible prediction value of the cardiac autonomic system soon after event on motor ability and functional performance among patients post stroke. To our knowledge there are no previous published reviews on this topic and the searching methods that used for this review included strategies of further seek out articles beyond simple database searches.

Compared to the large amount of studies on HRV in relation to rehabilitation in patients post cardiac event, studies on HRV among patients post stroke are rare. There is growing body of evidence which supports HRV analysis as a helpful information tool for autonomic and concurrent central nervous system function. Clinical studies among patients post stroke [18,19] and other brain injury populations [20-22], suggest that a reduction in HRV is associated with other autonomic impairments such as cold hand or constipation [23,24]. This review targeted to the heart rate autonomic regulation system only, but it may be important to assess the associations between HRV values and other autonomic signs among this group of patients.

Based on the current review it seems that the heart rate regulation system response to activity among patients post stroke, both, at the subacute phase [17] as well in the chronic phase [16]. At the same time it seems that the system response with some deviation from the "healthy" pattern. In both studies which assessed this topic, the time domain variables were significantly influenced by exercising, by reducing their values. Nevertheless Raimundo et al noted that patients' HR and time domain HRV values did not returned to baseline up to 30 minutes post exercise, and Katz-Leurer et al. did not find any adaptation of HR values to 8 weeks of aerobic exercise. This may raise a question of the autonomic response to effort stimuli among adults post stroke. This is especially important during physical therapy sessions involving different postures and positioning, intense activities, and aerobic interventions.

Moreover, as an association between HRV values and motor and functional ability is another conclusion of the current review [11-14], it seems to be important to assess heart autonomic function at rest and its response exercise especially among the more severely impaired patients before therapy and especially prior to more intense activity. One should be aware to the effort of performing simple task for the impaired patient.

It might be that among patients post stroke the autonomic impairment is due to the primary brain insult but it might be due to other reasons. Many risk factors for stroke can cause autonomic disorders including increased sympathetic modulation at rest and reduced autonomic reactivity, the arterial hypertension and diabetic mellitus are most prevalent. Different drug usage for these conditions, sedentary life style (pre or post event) all can contribute to the observed associations [23].

Despite the fact that this is an obvious essential limitation of the current review two important notes has to be raise. The first is that regardless what the reason is, it seems that the cardiac autonomic system is in somehow invisible during rehabilitation. The second is that this is especially surprising as some rehabilitation techniques for

this system became more popular, for example aerobic intervention for these patients. Nonetheless during these interventions the mean HR is widely used to index for the cardiac system response even if HRV, has the all above mention advances. As HR is a product of the complex interaction of the sympathetic and the para-sympathetic systems, change in mean HR present global information while HRV attempts to present the relative contributions of each system activity and by that might be more appropriate to investigate underlying autonomic reactions.

Another limitation of the current work associate with the fact that the studies which included in this review used different techniques to collect R-R data, for example; differences in the length of recording, Bassi et al. [13,14] used 24 hours of recording while Arad et al. [12] used short term recording technic. The studies also present differences in HRV measures, for example Arad et al. [12] present frequency domains parameters, Bassi et al. [13,14] time domains parameters while Graff et al. [11] present both. Other differences include the sampling rate, the way of preparing data for analysis and in the methods dealing with ectopic or artifact events. Recording and analysis methodology has a vital effect on test reliability and sensitivity. These differences and others may limit the comparability between studies, even if the results seem to be in agreement in between. Additional studies should determine the optimal HRV methods for detecting cardiac autonomic regulation as during activity as well as predictor of abilities; time or frequency domain, duration of recordings, being active, all may play an important role that requires further clarification.

Another important limitation of studies included in the current review was the different between functional evaluations used, the Barthel index, FIM or mRS and MAS. Although each has been used excessively in the literature, and each found to be reliable and valid differences between scales do exist [25].

In summary, the results of the current review suggest a relationship between autonomic HR regulation system and motor and functional abilities among patients post stroke. However, the extent of the association and further the benefits of autonomic rehabilitation on motor or functional abilities remain to be evaluated. HRV analytical techniques have become standard for evaluation of mortality and morbidity risks and for use in multivariate analyses of cardiovascular risk, we have to use this knowledge more in the rehabilitation process of patients post stroke. More methodologically sound studies are needed to increase knowledge about HR autonomic system in patients post stroke and its response to different stimulus in order to help clinicians to select and develop the effective assessment and intervention for this population [26].

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Page 6 of 6