Journal of Vessels and Circulation
Qom University of Medical Sciences
July 2022. Volume 3. Number 3

Review Paper

The Promising Options of Heart Rate Variability (HRV) for stroke- a Narrative Review of the Literature and Clinical Translation

Hassan Bafandeh Qaramaleki [1], Masumeh Zamanlu[2], Ezzatollah Ahmadi[1], Parisa Mohammadzadeh[1*], Ehsan Sharifipour[3]

1. Department of Psychology, Faculty of Education & Psychology, Azarbaijan Shahid Madani University, Tabriz, Iran.
2. Neuroscience Research Center, Qom University of Medical Sciences, Qom, Iran.
3. Department of Neurology, School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran.

Use your device to scan and read the article online

Please cite this article as Bafandeh Qaramaleki H, Zamanlu M, Ahmadi E, Mohammadzadeh P, Sharifipour E. The Promising Options of Heart Rate Variability (HRV) for stroke- a Narrative Review of the Literature and Clinical Translation. J Vessel Circ. 2022; 3(3):117-124. http://dx.doi.org/10.32598/JVC.3.3.47.4

: http://dx.doi.org/10.32598/JVC.3.3.47.4

Article info:
Received: 15 May 2022
Accepted: 09 Jun 2022
Publish: 01 Jul 2022

Keywords:
Stroke, Nervous system, Heart rate determination, Neurophysiology, Ischemic stroke

ABSTRACT

Background and Aim: This article is an attempt to summarize the most updated information on heart rate variability (HRV) in ischemic stroke and to contribute to the clinical translation of this field. A wide range of pathologies, including vascular diseases (with stroke as a hallmark), are related to HRV. The parameters of this phenomenon can open a window to improve clinical approaches. The interval between two consecutive heartbeats is changed by the autonomic nervous system and these changes are called heart rate variability or HRV. Higher range and complexity of HRV fluctuations indicate better and more effective vascular and autonomic self-regulation and repair capacities.

Materials and Methods: The keywords including "heart rate variability", stroke, and "cerebrovascular event" were used and PubMed, Scopus, SID, and Google Scholar databases were searched. Reference books on neurology and clinical neurosciences were also used. Researchers checked the relevance of the documents and excluded irrelevant findings.

Results: Several book chapters, together with 50 related reports and journal articles were identified, all of which were studied. The important and acceptable concept line of this field was extracted and reported here.

Conclusion: HRV fluctuations decrease after ischemic stroke, therefore, they show autonomic impairments leading to an increase in sympathetic activity and a decrease in parasympathetic activity in the acute stage of stroke. These changes may persist and be associated with an increased risk of subsequent mortality. In patients with acute ischemic stroke, HRV could be a biomarker with prognostic value and may differentiate favorable and unfavorable outcomes of treatments. Moreover, HRV parameters have a predictive value for the occurrence of ischemic stroke, especially in normal people or patients with significant vascular risks. Overall, HRV recording can be valuable not as an independent tool but as a complement to remove barriers and gaps in the clinical management of stroke; and perform the task of objectifying the patients' vascular conditions and alterations. Recording these parameters is practical, inexpensive, portable, and therefore, easily implemented in various clinical situations.

*** Corresponding Author:**
Parisa Mohammadzadeh.
Address: *Department of Psychology, Faculty of Education & Psychology, Azarbaijan Shahid Madani University, Tabriz, Iran.*
Phone: *+98 (25) 36122547*
E-mail: *diamonddd1997@yahoo.com*

Journal of Vessels and Circulation
Qom University of Medical Sciences

1. Introduction

Heart rate variability is the physiological phenomenon of changes in the time interval between two heartbeats. The heart rate is changed by the autonomic nervous system (sympathetic and parasympathetic) and these changes are called heart rate variability or HRV. These changes are a reflection of the interaction between the sympathetic and parasympathetic branches of the autonomic nervous system [1]. HRV is one of the most important physiological phenomena in our body, functioning not only to increase the quality of physical health and active repairs in the body (especially in the heart and blood vessels) but also to reduce stress and anxiety [1]. To understand the concept of HRV, it is reminded that the R waves indicate the contraction of the ventricles (the main part of a heartbeat); while the R-R interval (sometimes called Normal to Normal - NN or inter beat interval - IBI) indicates the interval between two heartbeats, which, similar to other biologic functions, keeps changing and is not constant. The decreases or increases in the R-R intervals are called HRV [1].

It should be explained that there is a difference between pulse and HRV. The heart rate estimate (HR), which is presented as pulse, indicates the number of ventricular contractions of the heart per unit of time (usually a minute), which is an average over this period. Pulse assumes heartbeats occur with intervals somewhat constant for one minute, and this pulse estimate is easily measurable. But HRV is calculated in each ventricular contraction and cannot be measured except by precise technologic instruments [1]. Heart rate variability, though often mentioned in the literature with the known term of HRV, has several other equivalents, such as cycle length variability [2, 3], R–R variability, and heart period variability [4]. Various devices can detect the beat-to-beat interval and be used to calculate HRV, including advanced electrocardiographs [5], ballistocardiographs [6, 7], blood pressure sensors [8], derived pulse signals from photoplethysmography [9], and recently emerging smart watches or wearable devices applied both in clinical settings and sports exercises or researches.

The purpose of this review is an attempt to summarize the most updated information on HRV in ischemic stroke and to contribute to the clinical translation of this field. A wide range of pathologies, including vascular diseases (with stroke as a hallmark), are related to HRV. The parameters of this phenomenon can open a window to improve clinical approaches.

2. Materials and Methods

The keywords including "heart rate variability", stroke, and "cerebrovascular event" were used and PubMed, ScienceDirect, Scopus, SID, and Google Scholar databases were searched. Reference books on neurology and clinical neurosciences were also used. Researchers checked the relevance of the documents and excluded irrelevant findings.

Search results

Several book chapters, together with 50 related reports and journal articles were identified, all of which were studied. The important and acceptable concept line of this field was extracted and reported here.

Heart rate variability and clinical approaches

The range and complexity of HRV fluctuations indicate the regulation ability of the body in vascular and autonomic biology. The greater fluctuations appear, the better and more effective the physiological and restorative conditions would be, both physiological and mental [1]. A wide range of pathologies, including vascular and non-vascular, psychosomatic, or mental are related to HRV, and the parameters of this phenomenon can open a window to aid related clinical management [10]. Among these important clinical conditions, we can mention cardiac arrhythmia, in which HRV is correlated with high risk and life threat [11] or HRV related to chronic coronary heart disease [12] or high risk in hypertension [13], or association with diabetic neuropathy [14]. Moreover, reports demonstrate clinical neurosciences interventions for increasing HRV successfully led to the improvement of symptoms of various diseases, including coronary artery disease [15-17], heart failure [18], blood pressure in hypertension [19-21], respiration in asthma [22], chronic obstructive pulmonary disease [23], irritable bowel syndrome [24, 25], migraine headache symptoms [1], fibromyalgia [26], post-traumatic stress disorder [27, 28], functional anxiety [29], and major depression [30, 31]. It is worth mentioning that currently the most outstanding and well-known clinical point for HRV can be summarized as a core in neurophysiology and psychophysiology related to psychobiologic arousal where impairment occurs by continuous tension.

Stroke and heart rate variability

Stroke, in terms of the standard terminology of Medical Subject Headings - MeSH is located between the central nervous system and the cardiovascular system, taking

into account both the biological and clinical fields, as the so-called biomedical classification of diseases. Stroke is known as "cerebrovascular accident-CVA" in clinical environments, conveying such meaning. Therefore, it is not surprising that similar to cardiovascular diseases, stroke is associated with autonomic nervous system disorders and HRV impairments [32, 33]. The study of HRV changes in ischemic stroke patients does not show a long time gone by, initiated since the early 1990s [34]. It was in 1994 that Baron et al. first observed HRV spectral indices reduced in patients, assessed 4 to 11 days after stroke, compared to healthy subjects. cardiovascular dysfunction in the acute stage of stroke passes the process of autonomic activity towards an increase in sympathetic activity and a decrease in parasympathetic (vagal) activity [35]. HRV is impaired immediately after the stroke, and may not return to previous values until several months after the event [36]. Although data on HRV impairment in the non-acute phase are conflicting, it was reported in 1997 that these autonomic disturbances may be reversible within 6 months after ischemic stroke [37]. It has been reported that HRV spectral indices were disturbed within 10 hours of the onset of stroke symptoms in patients with arrhythmia, with significant changes once more after 3 days [36]. Although gradual improvement of HRV parameters is observed between 2 and 6 months after stroke, survivors still present with impaired HRV indices in follow-ups (compared to healthy subjects) [37]. In elderly patients with stroke, a very obvious decrease in HRV (HRV depression) is observed. In 2005, a case-control study on HRV impairment of 76 stroke patients compared to 70 matched healthy controls reported continuation of impairment more than 9 months after stroke. Therefore, deeper damage and slower repair might be present in elderly stroke patients [38].

HRV and mortality in stroke patients

Several studies have investigated HRV and its impact on predicting mortality in stroke survivors. It should be noted that death in most of these patients is sudden and due to cardiac arrest, which occurs after cardiac arrhythmias. The incidence of sudden cardiac death in stroke patients is estimated at 6% [39]. The core of this pathophysiology is a vascular complication: either a cerebrovascular event has taken a malignant course, or another cardiovascular complication has occurred, and a small proportion of patients deteriorate with extravascular processes (e.g. infection) [40-42]. Autonomic imbalances are evaluated in various ways, more evident in the acute stage of stroke. However, these changes may persist and be associated with an increased risk of subsequent mortality. Similar to myocardial infarction, autonomic imbalances may indicate a higher risk for arrhythmia and sudden death in the early post-stroke period. Although the exact pathophysiology of these interactions has not been fully elucidated, data are suggesting that such autonomic imbalances are associated with an increased risk of future arrhythmias and sudden death [40-42].

Several clinical studies have shown that decreased HRV may be considered a marker of morbidity and mortality after ischemic stroke. In a study of 84 stroke patients who were followed up until 7 years, the slope of the strength of changes in various HRV parameters was a multivariate predictor of mortality, and specific HRV parameters did not show any prognostic value [43]. In the most extensive study of this field, 327 patients with acute ischemic stroke were studied in 2010. HRV parameters were obtained on the second day after the hospitalization of patients, which were significantly associated with mortality during the 1-month follow-up [41]. As seen for other vascular diseases, abnormal HRV in stroke patients is associated with increased mortality [43], yet the aspects of this association seem more complicated.

HRV and brain regions involved in stroke

Several studies have addressed regions involved in stroke, affecting HRV parameters. Orlandi et al. observed a higher percentage of arrhythmias and autonomic alterations in patients with right-hemisphere stroke compared to left-hemisphere stroke [42]. Other authors approved that right-sided stroke is associated with a greater decrease in HRV and a higher rate of sudden in-hospital deaths [44]. In the study of Tukgozoglu et al. in 1999, the greatest reduction in HRV spectral indices in stroke patients occurred when the affected area was the right insular cortex [44]. These data were confirmed in another study in 2004, illustrating a very obvious drop in heart rate variability (HRV depression) in patients with right hemisphere infarcts in the insula [45].

HRV as a biomarker in stroke clinical care

Early detection of autonomic dysfunction may provide information about potential adverse outcomes of vascular events. In patients with acute ischemic stroke, heart rate variability has prognostic value as a biomarker [46], and reduced HRV is associated with early neural deterioration (END) and recurrent ischemic stroke [47]. Moreover, the increase in sympathetic nervous activity during movement, documented by HRV parameters, is associated with neurological deterioration [48]. The facts about patients at high risk of mortality mentioned in the previous sections can be added to this informa-

Journal of Vessels and Circulation
Qom University of Medical Sciences

tion. HRV is an objective tool to help predict depression after stroke [49]. It has been reported that the presence of an autonomic imbalance in the cardiovascular system, identified by HRV, is associated with poor outcomes after initial rehabilitation in ischemic stroke [50]. At the same time, paradoxically, another study reported that the outcome of rehabilitation after an ischemic stroke has no significant relationship with HRV [51].

Various studies have shown that HRV can have a predictive value for the occurrence of stroke, especially in conditions where there is a significant cardiovascular risk or in patients who are under close cardiovascular monitoring. An interesting example is a report demonstrating stroke predicting the value of HRV in sleep apnea, by a combination of HRV data in addition to the systemic effects of the disease (apnea disease burden) [52]. A marked decline in HRV, assessed during the night, has been reported to be significantly associated with stroke risk in apparently healthy individuals [52]. It has been shown that HRV parameters in patients with atrial fibrillation arrhythmia contain important clinical information, including a risk prediction of ischemic stroke in patients with no prior history of stroke [46]. Moreover, HRV drop is a predictor of complications after hip fracture surgery, including stroke, myocardial infarction, and pneumonia during a 6-month follow-up [53]. As mentioned above, the risk of recurrent stroke in patients with a previous history of stroke is related to HRV, which provides additive evidence of HRV predictive value for cerebrovascular events.

Important parameters of HRV in stroke

HRV parameters mainly include temporal analyses (calculations on R-R intervals) and frequency analyses. Heart rate frequency classification includes high frequency (HF), low frequency (LF), and very low frequency (VLF). The changes in each HRV parameter can have an interesting physiological meaning [54], in which detailed discussions of basic science, especially autonomic neurotransmitter mechanisms, can be presented and can add to the knowledge of the pathophysiology of stroke. However, here, the main focus is on clinical translation, and pathophysiologic details are overlooked.

The simplest and most widely used HRV parameter is the standard deviation of all intervals between consequent heartbeats or standard deviation of all NN intervals (SDNN), which is often calculated over a long period (and of course, ideal recording in these conditions is difficult and among the limitations of this parameter). SDNN is believed to reflect the general variability of interbeat intervals. There are two other parameters, rMSSD and pNN50, which reflect heart rate variability in a way that is known to be a strong correlate to parasympathetic activity (cardiovascular branches) [55]. rMSSD is the root mean square of successive R-R differences. Besides, pNN50 is the percentage of successive R-R (or N-N) intervals that differ by more than 50 milliseconds.

If we refer to the frequency parameters of HF, LF, and VLF in stroke, we should consider the following study in particular: Gujjar et al. in 2004 [56], reported the powers of LF and VLF significantly correlating with mortality in 25 acute stroke patients. After adjusting the analyses for the clinical confounding variables, LF power remained a significant and independent risk indicator. Both temporal and frequency parameters of HRV could be considered in stroke patients. Some authors showed lower values of SDNN together with rMSSD and higher values of LF/HF ratio associated with more frequent and more complex arrhythmias in patients with right hemisphere insula infarcts. The same group observed that SDNN reduction, along with right hemisphere stroke and non-sustained tachycardias, were predictors of mortality during follow-up [57]. Bassi et al. showed that lower SDNN values and older age, along with stroke severity, were independently associated with adverse outcomes in patients undergoing rehabilitation programs. Therefore, the authors suggested that HRV analysis may provide more information about the possibility of functional improvement in stroke victims [58]. Interestingly, a few years later, the same group showed SDNN predicting adverse rehabilitation functional outcomes only in men [59]. Therefore, there may be a gender influence in HRV correlation with rehabilitation outcomes. The Copenhagen study, including 678 patients without a history of cardiovascular disease, showed an independent association of SDNN with stroke risk during a mean follow-up of 76 months, and this effect was significant as much as every 10 milliseconds of SDNN differences. Overall, 81% of strokes in this study occurred in patients with night admission and previously low SDNN (<38 ms) [58].

Future trends

HRV parameters literally open a window to vascular biological information, which is difficult to obtain otherwise. Considering HRV as an independent tool might be misleading in a variety of clinical situations; nevertheless, as a complementary tool, it benefits from removing barriers and gaps in stroke care. The most outstanding ambiguity in the clinical setting of stroke is that the physician manages the care mostly by mental summation of patients' vascular condition without much quantitative

and objective data. HRV can perform the task of objectifying this summation. Recording these parameters is very practical, and inexpensive, with a portable device that can be easily implemented in different clinical environments, and can be equivalent to applying pulse oximetry monitoring, continued as much as needed.

At the stroke onset, HRV can confirm that a significant vascular disorder has occurred to complete the diagnostic panel. While the guided application of HRV data can have high diagnostic sensitivity, its specificity is questionable. As far as we reached in the literature, no comparison of HRV abnormalities has been reported in the differential diagnosis of stroke. At the same time, during the course of the disease, while the vascular biology of the patient often goes through critical stages, HRV can be a valuable monitoring tool and with predictive, a few steps before catastrophic processes become irreversible. For instance, strokes with progressive symptoms may take some time to show themselves clearly to the clinician. There are also situations in which the clinician might be up to immediate decisions about the intensity of the cardiorespiratory monitoring, the decision to continue or cancel thrombolytic therapy, the diagnosis of the change of ischemic stroke to cerebral hemorrhage, and so on. HRV parameters can provide appropriate warnings for such situations.

3. Conclusion

HRV parameters change after a stroke. These changes present both deep physiopathological information about this disease as well as clinical applications. These parameters can be considered as one of the biomarkers of stroke; though their diagnostic value alone could be limited, they can be valuable as complementary paraclinical monitoring to overcome obstacles and gaps in the clinical management of stroke, performing the task of objectifying the summation of the patient's vascular condition. Recording these parameters is practical, and inexpensive, with a portable device that can be easily implemented in different clinical environments, and can be equivalent to applying pulse oximetry monitoring, continued as much as needed.

Ethical Considerations

Compliance with ethical guidelines

This article is a review without human or animal samples.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualization and design: Masumeh Zamanlu; Funding acquisition and resources, Ultimately, and writing–original draft: Parisa Mohammadzadeh; Data analysis and interpretation of literature, writing–review & editing, and approving the final version of the manuscript: All authors.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

We wish to thank Elaheh Habibitabar for useful comments.

References

[1] Gilbert C. The clinical handbook of biofeedback: A step-by-step guide for training and practice with mindfulness. Inna Z. Khazan, PhD, BCB (2013), chichester, UK: John Wiley & Sons. Biofeedback. 2014; 42(3):130-2. [DOI:10.5298/1081-5937-42.3.05]

[2] Kleiger RE, Miller JP, Krone RJ, Bigger JT Jr. The independence of cycle length variability and exercise testing on predicting mortality of patients surviving acute myocardial infarction. The multicenter postinfarction research group. Am J Cardiol. 1990; 65(7):408-11. [DOI:10.1016/0002-9149(90)90801-7] [PMID]

[3] Fotuhi P, Combs W, Condie C, Theres H, Schneider T, Stangl K, et al. R-wave detection by subcutaneous ECG. Possible use for analyzing R-R variability. Ann Noninvasive Electrocardiol. 2001; 6(1):18-23. [DOI:10.1111/j.1542-474X.2001.tb00081.x] [PMID] [PMCID]

[4] Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Kleiger RE, Rottman JN. Frequency domain measures of heart period variability and mortality after myocardial infarction. Circulation. 1992; 85(1):164-71. [DOI:10.1161/01.CIR.85.1.164] [PMID]

[5] Goy JJ, Stauffer JC, Schlaepfer J, Christeler P. Electrocardiography (ECG). Sharjah: Bentham Science Publishers; 2013. [DOI:10.2174/97816080547941130101]

[6] Brüser C, Stadlthanner K, de Waele S, Leonhardt S. Adaptive beat-to-beat heart rate estimation in ballistocardiograms. IEEE Trans Inf Technol Biomed. 2011; 15(5):778-86. [DOI:10.1109/TITB.2011.2128337] [PMID]

Journal of Vessels and Circulation
Qom University of Medical Sciences

[7] Brüser C, Winter S, Leonhardt S. Unsupervised heart rate variability estimation from ballistocardiograms. IntJ Bioelectromagn. 2013; 15(1):1-6. [Link]

[8] Frattola A, Parati G, Cuspidi C, Albini F, Mancia G. Prognostic value of 24-hour blood pressure variability. J Hypertens. 1993; 11(10):1133-7. [DOI:10.1097/00004872-199310000-00019] [PMID]

[9] Elgendi M. On the analysis of fingertip photoplethysmogram signals. Curr Cardiol Rev. 2012; 8(1):14-25. [DOI:10.2174/157340312801215782] [PMID] [PMCID]

[10] Burlacu A, Brinza C, Popa IV, Covic A, Floria M. Influencing cardiovascular outcomes through heart rate variability modulation: A systematic review. Diagnostics. 2021; 11(12):2198. [DOI:10.3390/diagnostics11122198] [PMID] [PMCID]

[11] La Rovere MT, Pinna GD, Hohnloser SH, Marcus FI, Mortara A, Nohara R, et al. Baroreflex sensitivity and heart rate variability in the identification of patients at risk for life-threatening arrhythmias: implications for clinical trials. Circulation. 2001; 103(16):2072-7. [DOI:10.1161/01.CIR.103.16.2072] [PMID]

[12] Bigger JT Jr, Fleiss JL, Steinman RC, Rolnitzky LM, Schneider WJ, Stein PK. RR variability in healthy, middle-aged persons compared with patients with chronic coronary heart disease or recent acute myocardial infarction. Circulation. 1995; 91(7):1936-43. [DOI:10.1161/01.CIR.91.7.1936] [PMID]

[13] Schroeder EB, Liao D, Chambless LE, Prineas RJ, Evans GW, Heiss G. Hypertension, blood pressure, and heart rate variability: the atherosclerosis risk in communities (ARIC) study. Hypertension. 2003; 42(6):1106-11. [DOI:10.1161/01.HYP.0000100444.71069.73] [PMID]

[14] Skinner JE, Weiss DN, Anchin JM, Turianikova Z, Tonhajzerova I, Javorkova J, et al. Nonlinear PD2i heart rate complexity algorithm detects autonomic neuropathy in patients with type 1 diabetes mellitus. Clin Neurophysiol. 2011; 122(7):1457-62. [DOI:10.1016/j.clinph.2010.12.046] [PMID]

[15] Cowan MJ, Pike KC, Budzynski HK. Psychosocial nursing therapy following sudden cardiac arrest: Impact on two-year survival. Nurs Res. 2001; 50(2):68-76.[DOI:10.1097/00006199-200103000-00002] [PMID]

[16] Del Pozo JM, Gevirtz RN, Scher B, Guarneri E. Biofeedback treatment increases heart rate variability in patients with known coronary artery disease. Am Heart J. 2004; 147(3):E11. [DOI:10.1016/j.ahj.2003.08.013] [PMID]

[17] Nolan RP, Kamath MV, Floras JS, Stanley J, Pang C, Picton P, et al. Heart rate variability biofeedback as a behavioral neurocardiac intervention to enhance vagal heart rate control. Am Heart J. 2005; 149(6):1137. [DOI:10.1016/j.ahj.2005.03.015] [PMID]

[18] Swanson KS, Gevirtz RN, Brown M, Spira J, Guarneri E, Stoletniy L. The effect of biofeedback on function in patients with heart failure. Appl Psychophysiol Biofeedback. 2009; 34(2):71-91. [DOI:10.1007/s10484-009-9077-2] [PMID]

[19] McCraty R, Atkinson M, Tomasino D. Impact of a workplace stress reduction program on blood pressure and emotional health in hypertensive employees. J Altern Complement Med. 2003; 9(3):355-69. [DOI:10.1089/107555303765551589] [PMID]

[20] Joseph CN, Porta C, Casucci G, Casiraghi N, Maffeis M, Rossi M, et al. Slow breathing improves arterial baroreflex sensitivity and decreases blood pressure in essential hypertension. Hypertension. 2005; 46(4):714-8. [DOI:10.1161/01.HYP.0000179581.68566.7d] [PMID]

[21] Nolan RP, Floras JS, Harvey PJ, Kamath MV, Picton PE, Chessex C, et al. Behavioral neurocardiac training in hypertension: A randomized, controlled trial. Hypertension. 2010; 55(4):1033-9. [DOI:10.1161/HYPERTENSIONAHA.109.146233] [PMID]

[22] Lehrer P, Carr RE, Smetankine A, Vaschillo E, Peper E, Porges S, et al. Respiratory sinus arrhythmia versus neck/trapezius EMG and incentive inspirometry biofeedback for asthma: a pilot study. Appl Psychophysiol Biofeedback. 1997; 22(2):95-109.[DOI:10.1023/A:1026224211993] [PMID]

[23] Giardino ND, Chan L, Borson S. Combined heart rate variability and pulse oximetry biofeedback for chronic obstructive pulmonary disease: Preliminary findings. Appl Psychophysiol Biofeedback. 2004; 29(2):121-33.[DOI:10.1023/B:APBI.0000026638.64386.89] [PMID]

[24] Humphreys PA, Gevirtz RN. Treatment of recurrent abdominal pain: Components analysis of four treatment protocols. J Pediatr Gastroenterol Nutr. 2000; 31(1):47-51. [DOI:10.1097/00005176-200007000-00011] [PMID]

[25] Sowder E, Gevirtz R, Shapiro W, Ebert C. Restoration of vagal tone: A possible mechanism for functional abdominal pain. Appl Psychophysiol Biofeedback. 2010; 35(3):199-206. [DOI:10.1007/s10484-010-9128-8] [PMID]

[26] Hassett AL, Radvanski DC, Vaschillo EG, Vaschillo B, Sigal LH, Karavidas MK, et al. A pilot study of the efficacy of heart rate variability (HRV) biofeedback in patients with fibromyalgia. Appl Psychophysiol Biofeedback. 2007; 32(1):1-10. [DOI:10.1007/s10484-006-9028-0] [PMID]

[27] Zucker TL, Samuelson KW, Muench F, Greenberg MA, Gevirtz RN. The effects of respiratory sinus arrhythmia biofeedback on heart rate variability and posttraumatic stress disorder symptoms: A pilot study. Appl Psychophysiol Biofeedback. 2009; 34(2):135-43. [DOI:10.1007/s10484-009-9085-2] [PMID]

[28] Tan G, Dao TK, Farmer L, Sutherland RJ, Gevirtz R. Heart rate variability (HRV) and posttraumatic stress disorder (PTSD): A pilot study. Appl Psychophysiol Biofeedback. 2011; 36(1):27-35. [DOI:10.1007/s10484-010-9141-y] [PMID]

[29] Thurber MR, Bodenhamer-Davis E, Johnson M, Chesky K, Chandler CK. Effects of heart rate variability coherence biofeedback training and emotional management techniques to decrease music performance anxiety. Biofeedback. 2010; 38(1):28-40. [DOI:10.5298/1081-5937-38.1.28]

[30] Karavidas MK, Lehrer PM, Vaschillo E, Vaschillo B, Marin H, Buyske S, et al. Preliminary results of an open label study of heart rate variability biofeedback for the treatment of major depression. Appl Psychophysiol Biofeedback. 2007; 32(1):19-30. [DOI:10.1007/s10484-006-9029-z] [PMID]

[31] Siepmann M, Aykac V, Unterdörfer J, Petrowski K, Mueck-Weymann M. A pilot study on the effects of heart rate variability biofeedback in patients with depression and in healthy subjects. Appl Psychophysiol Biofeedback. 2008; 33(4):195-201. [DOI:10.1007/s10484-008-9064-z] [PMID]

[32] Norrving B. Stroke and cerebrovascular diseases. In: Ropper AH, Sumuels MA, Klein JP, Prasad S, editors. Adams and Victor's manual of neurology. New York: McGraw Hill; 2019. [Link]

[33] Norrving B. Oxford textbook of stroke and cerebrovascular disease. Oxford: Oxford University Press; 2014. [DOI:10.1093/med/9780199641208.001.0001]

[34] Cygankiewicz I, Zareba W. Heart rate variability. Handb Clin Neurol. 2013; 117:379-93. [DOI:10.1016/B978-0-444-53491-0.00031-6] [PMID]

[35] Barron SA, Rogovski Z, Hemli J. Autonomic consequences of cerebral hemisphere infarction. Stroke. 1994; 25(1):113-6. [DOI:10.1161/01.STR.25.1.113] [PMID]

[36] Lakusic N, Mahovic D, Babic T. Gradual recovery of impaired cardiac autonomic balance within first six months after ischemic cerebral stroke. Acta Neurol Belg. 2005; 105(1):39-42. [PMID]

[37] Bar-Ilan A, Weizmann K. Circadian rhythm of heart rate variability is reversibly abolished in ischemic stroke. Stroke. 1998; 29(11):2447. [DOI:10.1161/01.str.29.11.2447] [PMID]

[38] McLaren A, Kerr S, Allan L, Steen IN, Ballard C, Allen J, et al. Autonomic function is impaired in elderly stroke survivors. Stroke. 2005; 36(5):1026-30.[DOI:10.1161/01.STR.0000160748.88374.ce] [PMID]

[39] Silver FL, Norris JW, Lewis AJ, Hachinski VC. Early mortality following stroke: A prospective review. Stroke. 1984; 15(3):492-6. [DOI:10.1161/01.str.15.3.492] [PMID]

[40] Korpelainen JT, Sotaniemi KA, Mäkikallio A, Huikuri HV, Myllylä VV. Dynamic behavior of heart rate in ischemic stroke. Stroke. 1999; 30(5):1008-13. [DOI:10.1161/01.STR.30.5.1008] [PMID]

[41] He L, Li C, Luo Y, Dong W, Yang H. Clinical prognostic significance of heart abnormality and heart rate variability in patients with stroke. Neurol Res. 2010; 32(5):530-4. [DOI:10.1179/174313209X431110] [PMID]

[42] Orlandi G, Fanucchi S, Strata G, Pataleo L, Landucci Pellegrini L, Prontera C, et al. Transient autonomic nervous system dysfunction during hyperacute stroke. Acta Neurol Scand. 2000; 102(5):317-21. [DOI:10.1034/j.1600-0404.2000.102005317.x] [PMID]

[43] Mäkikallio AM, Mäkikallio TH, Korpelainen JT, Sotaniemi KA, Huikuri HV, Myllylä VV. Heart rate dynamics predict poststroke mortality. Neurology. 2004; 62(10):1822-6. [DOI:10.1212/01.WNL.0000125190.10967.D5] [PMID]

[44] Tokgözoglu SL, Batur MK, Topçuoglu MA, Saribas O, Kes S, Oto A. Effects of stroke localization on cardiac autonomic balance and sudden death. Stroke. 1999; 30(7):1307-11. [DOI:10.1161/01.STR.30.7.1307] [PMID]

[45] Colivicchi F, Bassi A, Santini M, Caltagirone C. Cardiac autonomic derangement and arrhythmias in right-sided stroke with insular involvement. Stroke. 2004; 35(9):2094-8. [DOI:10.1161/01.STR.0000138452.81003.4c] [PMID]

[46] Buitrago-Ricaurte N, Cintra F, Silva GS. Heart rate variability as an autonomic biomarker in ischemic stroke. Arq Neuropsiquiatr. 2020; 78(11):724-32. [DOI:10.1590/0004-282x20200087] [PMID]

[47] He L, Wang J, Zhang L, Zhang X, Dong W, Yang H. Decreased fractal dimension of heart rate variability is associated with early neurological deterioration and recurrent ischemic stroke after acute ischemic stroke. J Neurol Sci. 2019; 396:42-7. [DOI:10.1016/j.jns.2018.11.006] [PMID]

[48] Nozoe M, Yamamoto M, Kobayashi M, Kanai M, Kubo H, Shimada S, et al. Heart rate variability during early mobilization in patients with acute ischemic stroke. Eur Neurol. 2018; 80(1-2):50-4. [DOI:10.1159/000492794] [PMID]

[49] He L, Wang J, Zhang L, Wang F, Dong W, Yang H. Admission heart rate variability is associated with poststroke depression in patients with acute mild-moderate ischemic stroke. Front Psychiatry. 2020; 11:696. [DOI:10.3389/fpsyt.2020.00696] [PMID] [PMCID]

[50] Scherbakov N, Barkhudaryan A, Ebner N, von Haehling S, Anker SD, Joebges M, et al. Early rehabilitation after stroke: Relationship between the heart rate variability and functional outcome. ESC Heart Fail. 2020; 7(5):2983-2991. [DOI:10.1002/ehf2.12917] [PMID] [PMCID]

[51] Belli TR, Souza LAPS, Bazan SGZ, Bazan R, Luvizutto GJ. Effects of rehabilitation programs on heart rate variability after stroke: A systematic review. Arq Neuropsiquiatr. 2021; 79(8):724-31. [DOI:10.1590/0004-282x-anp-2020-0420] [PMID]

[52] Binici Z, Mouridsen MR, Køber L, Sajadieh A. Decreased nighttime heart rate variability is associated with increased stroke risk. Stroke. 2011; 42(11):3196-201. [DOI:10.1161/STROKEAHA.110.607697] [PMID]

[53] Chairina G, Yoshino K, Kiyono K, Watanabe E. Ischemic stroke risk assessment by multiscale entropy analysis of heart rate variability in patients with persistent atrial fibrillation. Entrop. 2021; 23(7):918. [DOI:10.3390/e23070918] [PMID] [PMCID]

[54] Zali A, Arefian NM. [Heart rate variability (Persian)]. Res Med. 2012; 36(3) :163-6. [Link]

[55] Camm AJ, Malik M, Bigger JT, Breithardt G, Cerutti S, Cohen RJ, et al. Heart rate variability: Standards of measurement, physiological interpretation and clinical use. Task Force of the European society of cardiology and the North American society of pacing and electrophysiology. Circulation. 1996; 93(5):1043-65. [DOI:10.1161/01.CIR.93.5.1043]

[56] Gujjar AR, Sathyaprabha TN, Nagaraja D, Thennarasu K, Pradhan N. Heart rate variability and outcome in acute severe stroke. Neurocrit Care 1, 347–353 (2004). [DOI:10.1385/NCC:1:3:347]

[57] Colivicchi F, Bassi A, Santini M, Caltagirone C. Prognostic implications of right-sided insular damage, cardiac autonomic derangement, and arrhythmias after acute ischemic stroke. Stroke. 2005; 36(8):1710-5. [DOI:10.1161/01.STR.0000173400.19346.bd] [PMID]

[58] Bassi A, Colivicchi F, Santini M, Caltagirone C. Cardiac autonomic dysfunction and functional outcome after ischaemic stroke. Eur J Neurol. 2007; 14(8):917-22.[DOI:10.1111/j.1468-1331.2007.01875.x] [PMID]

[59] Bassi A, Colivicchi F, Santini M, Caltagirone C. Gender-specific predictors of functional outcome after stroke rehabilitation: potential role of the autonomic nervous system. Eur Neurol. 2010; 63(5):279-84. [DOI:10.1159/000287583] [PMID]

This Page Intentionally Left Blank