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Ultra-short heart rate variability reliability for cardiac autonomic tone assessment in severe traumatic brain injury

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This study compares heart rate variability (HRV) indices across different time epochs (5 minutes, 1 minute, and 30 seconds) to evaluate the reliability of ultra-short recordings for assessing cardiac autonomic tone 1 year after a severe traumatic brain injury (TBI). Electrocardiogram recordings were obtained from 48 patients 1 year after a severe TBI. Pearson correlation analysis was performed to evaluate the association between ultra-short HRV indices (1 minute and 30 seconds) and the standard 5-minute recordings. Additionally, ANOVA was used to compare the differences in mean HRV indices across the different epochs. The correlation analysis supports that time-domain indices present higher correlation coefficients ($r = 0.63$ to 0.99, $p < 0.05$) when compared with frequency-domain indices ($r = 0.51$ to 0.97, $p < 0.05$). The reduction in recording time increases the percentage variation of all indices. The root mean square of the successive differences of RR intervals (rMSSD) shows higher Pearson coefficient values and lower percentage variation at the 1-minute and 30-second epochs compared with other HRV indices. Ultra-short HRV indices are reliable for assessing cardiac autonomic tone in chronic patients who survived severe TBI. rMSSD was the most reliable HRV index for ultra-short recordings. The value of ultra-short HRV for cardiovascular prognosis after severe TBI remains to be determined in future studies.

Keywords: Cardiac autonomic tone, heart rate variability, rMSSD, TBI, ultra-short recording.

Introduction

Traumatic brain injury (TBI) is a major health and socioeconomic problem worldwide (1, 2). TBI is classified according to the Glasgow Coma Scale (GCS) score into mild, moderate, and severe categories (3). The complex interplay between primary (e.g., trauma-related injuries) and secondary (e.g., inflammatory responses following injury) brain damage influences patient severity (1, 4). Patients with a history of severe TBI commonly develop psychiatric disorders (5, 6), cognitive impairments (7–10), or an increased risk of sudden unexpected death (11). The disability caused by TBI imposes high costs on society, as most affected individuals are young adults who require medical treatment and are often unable to return to work (12, 13). Investigating functional outcome biomarkers after TBI presents an opportunity to develop technologies for monitoring treatment responses, ultimately improving clinical care for patients (14–16).

The sympathetic and parasympathetic branches of the autonomic nervous system (ANS) regulate cardiac rhythm via synapses at the sinoatrial node to produce adaptive responses (17). Heart rate variability (HRV) is a widely used noninvasive measure for assessing cardiac ANS function (18). HRV analysis provides quantitative indices derived from the time intervals between successive heartbeats to evaluate both sympathetic and parasympathetic heart activity (19). The neurovisceral model suggests that cardiac ANS activity, as assessed by HRV, reflects the synaptic interactions between the prefrontal cortex and the amygdala via the vagus nerve (20–22). In this model, the similarities between central nervous system structures that regulate cardiac autonomic tone and cognitive performance suggest that HRV may serve as a peripheral index of the functional integrity of central nervous system networks associated with goal-directed behavior (23). Numerous studies support the association between HRV and cognitive performance (21, 24), emotional regulation (20, 25–27) and functional measures of the central nervous system (22, 28, 29). Consequently, several studies propose that HRV indices may serve as potential biomarkers for functional outcomes in both healthy and clinical populations.

It is now well established, based on a variety of studies, that patients with TBI have lower HRV compared with healthy controls (14, 30–33). The reduction in HRV begins in the acute phase of injury but can gradually recover over the months of rehabilitation (33). Despite the recovery of cardiac autonomic tone, physiological changes may remain permanent even after an extended recovery period (31). Patients with moderate or severe TBI exhibit a more pronounced reduction in HRV compared with those with mild TBI, suggesting that the severity of trauma is associated with the magnitude of cardiac autonomic dysfunction (34). Recently, there has been increased interest in using HRV as a biomarker for monitoring post-TBI outcomes (14). Recent studies suggest that HRV is associated with the prediction of imminent brain death and global patient outcomes (14, 30, 35). Sung *et al.* (2016) reported that HRV was correlated with symptoms of depression and anxiety in patients with TBI. This finding is supported by other studies that have reported an association between HRV and symptoms of depression (36) and anxiety (37). Data from several studies suggest that higher HRV is associated with better functional outcomes (e.g., neurological or psychiatric functioning) after TBI (14). HRV is a well-described method for assessing cardiac autonomic tone with various clinical applications, but at least 5 minutes of recording is necessary to obtain reliable values due to the influence of posture on cardiac autonomic regulation (18). Developing faster recording methods could enhance the applicability of HRV in clinical practice.

Previous research has established that ultra-short HRV recordings ($\leq$1 minute) can provide reliable HRV indices in both healthy (38–40) and clinical populations (41, 42). Melo *et al.* (2018) compared HRV intervals of 1, 2, and 3 minutes with the gold standard period ($\geq$5 minutes) and reported that the ultra-short-term recording method can offer a quick and reliable means of assessing cardiac ANS function. The reliability of ultra-short HRV indices (including recordings of $\leq$1 minute) has been replicated in other studies (39–42). The existing body of research suggests that rMSSD is the most reliable HRV index in ultra-short epochs, but the debate continues regarding the minimum time required to obtain reliable assessments of time or frequency domain indices. Although several reports support the reliability of ultra-short HRV recordings, there are no

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Table 1. Clinical and demographic characteristics of patients with TBI

Variable	Frequency (%) or Mean ± SD
Sex	
Female	9 (18.75)
Male	39 (81.25)
GOS at the Hospital discharge	
2	1 (2.08)
3	27 (56.25)
4	17 (35.42)
5	3 (6.25)
Predominance of lesion side	
Right > Left	18 (37.5)
Left < Right	15 (31.25)
N.A	15 (31.25)
Marshall CT classification	
Marshal I	5 (10.64)
Marshal II	11 (23.40)
Marshal III	21 (44.68)
Marshal IV	6 (12.77)
Marshal V	4 (8.51)
SAH	
No	28 (59.57)
Yes	19 (40.43)
Associated trauma	
No	18 (38.30)
Yes	29 (61.70)
Glasgow Coma Scale	
3	14 (29.79)
4	4 (8.51)
5	3 (6.38)
6	6 (12.77)
7	8 (17.02)
8	12 (25.53)
Pupils	
Isochoric	39 (82.98)
Anisocoric	8 (17.02)
Education, *years*	9.02 ± 2.99
Age, *years*	37.18 ± 15.56
ICU time, *days*	15.00 ± 7.51
Hospitalization time, *days*	30.60 ± 16.49

studies investigating the reliability of these recordings specifically in patients with TBI. The reliability of some ultra-short HRV indices reported in previous studies may not be directly generalizable to patients with TBI. This study compares time and frequency domain HRV indices across different time epochs (5 minutes, 1 minute, and 30 seconds) to evaluate the reliability of ultra-short recordings for assessing cardiac autonomic tone in patients with TBI.

Results

The clinical and demographic data of patients with TBI are shown in Table 1. This study included 9 women (18.75%) and 39 men (81.25%) with a mean age of 37.18 (±15.56) years. The patients had a mean hospitalization duration of 30.60 (±16.49) days, with a mean ICU stay of 15.00 (±7.51) days. Most patients with TBI had associated trauma (61.7%) and were classified as Marshall III (44.68%). GCS distribution showed that 55.32% of patients had scores of 6 (12.77%), 7 (17.02%), and 8 (25.53%), with 82.98% presenting with isochoric pupils. Most patients had a GCS score of 3 (56.25%) at hospital discharge.

The Pearson correlation analysis between 5-minute, 1-minute, and 30-second epochs of HRV indices is shown in Table 2. For 1-minute epochs, time-domain HRV indices (RR, HR, SDNN, rMSSD, and pNN50) exhibited higher mean r values ($r = 0.84$ to 0.99) compared with frequency-domain indices (VLF, LF, HF) ($r = 0.30$ to 0.93) (see Figure 1). Similar results were observed for 30-second epochs (time-domain: $r = 0.80$ to 0.99; frequency-domain: $r = 0.24$ to 0.93) (see Figure 2). The mean r coefficients were higher for 1-minute epochs in both time-domain ($r = 0.84$ to 0.99) and frequency-domain indices ($r = 0.30$ to 0.93) compared with 30-second epochs (time-domain: $r = 0.80$ to 0.99; frequency-domain: $r = 0.24$ to 0.93). rMSSD presented higher r values compared with other HRV indices for both 1-minute and 30-second epochs (all time epochs with $r = 0.99$, $p < 0.05$).

The ANOVA comparison of mean HRV indices between 5-minute, 1-minute, and 30-second epochs is shown in Table 3. ANOVA indicated that there is no significant difference in HRV mean values between the 5-minute and 1-minute epochs ($p > 0.05$). However, the posthoc analysis revealed that the mean VLF differed significantly ($F = 1.95$, $p = 0.08$ for the ANOVA, but $p < 0.05$ for posthoc comparisons of the 1st, 3rd, and 5th epochs). The comparison between 30-second epochs and 5-minute HRV mean values revealed that the mean values of 30-second VLF epochs were significantly different ($F = 10.75$, $p = 0.0001$). The posthoc analysis indicated that some SDNN epochs were significantly different ($F = 1.17$, $p = 0.32$ for ANOVA, but $p < 0.05$ for posthoc comparisons of the 1st and 4th epochs). No significant differences were observed for other indices. rMSSD exhibited lower percentage variations across 1-minute (0.97%) and 30-second (0.46%) epochs compared to other HRV indices (see Figure 3).

Discussion

This study investigated the reliability of ultra-short HRV indices for assessing cardiac autonomic tone in patients with TBI. The results suggest that all HRV indices show significant associations for 1-minute and 30-second epochs (except VLF and the 4th 30-second epoch for LF). Time-domain indices exhibit higher correlation coefficients compared with frequency-domain indices. All HRV indices show a percentage variation in mean values across different time epochs, indicating that positive associations do not necessarily reflect numerical equivalence. The comparison of mean values revealed that VLF values in 30-second epochs were significantly different. The posthoc analysis indicated that some 1-minute VLF epochs and the 4th SDNN 30-second epoch were significantly different ($p < 0.05$). For both 1-minute and 30-second epochs, rMSSD showed higher Pearson correlation coefficients and a lower percentage of mean value variation across the two-time epochs.

This finding is consistent with Nussinovitch *et al.* (2011), who reported that rMSSD exhibits higher reliability for ≤1-minute HRV ultra-short recordings. Similar results were reported by Melo *et al.* (2018), who compared 1-minute, 2-minute, and 3-minute epochs and found that rMSSD had higher Pearson coefficients across all time epochs. Munoz *et al.* (2015) also reported a significant association for rMSSD in 30-second epochs. These results, previously reported in healthy samples (38–40) are replicated in clinical populations, as observed in epilepsy (41) and diabetes (42). The existing body of research on ultra-short HRV suggests that rMSSD is the most reliable index for ultra-short recordings. rMSSD is less influenced by heart rate fluctuations and is more stable during periods of stationary oscillations because it is calculated based on the difference between RR intervals (43, 44). Consistent with the literature, this research found that the reliability of rMSSD reported for healthy samples, as well as for epilepsy and diabetes, can be extended to patients with TBI.

Surprisingly, the comparison between 1-minute and 30-second epochs for other HRV indices showed significant Pearson coefficients for RR, HR, SDNN, pNN50, LF, and HF. This finding contrasts with previous studies (38, 39, 45), which have suggested that longer recordings are required for SDNN and frequency domain indices. However, it corroborates the findings reported by Munoz *et al.* (2015), which demonstrated SDNN reliability for 30-second epochs. Similar results were reported by McNames and Aboy (2006), who demonstrated a significant association between ≤1-minute and 5-minute epochs for HF. The controversy regarding SDNN and frequency domain reliability may arise from the influence of nonstationary artifacts that impair the replicability of ultra-short indices compared with 5-minute recordings. Consequently, selecting only

Table 2. Pearson correlation analysis of HRV indices between time epochs

1-minute epoch	1st epoch	2nd epoch	3rd epoch	4th epoch	5th epoch	Mean *r* coefficient
RR (ms)	0.991*	0.981*	0.991*	0.981*	0.989*	0.986
SDNN (ms)	0.813*	0.855*	0.818*	0.881*	0.877*	0.848
HR (bpm)	0.991*	0.988*	0.991*	0.986*	0.990*	0.989
rMSSD (ms)	0.994*	0.994*	0.995*	0.991*	0.994*	0.993
pNN50 (%)	0.989*	0.988*	0.985*	0.975*	0.980*	0.983
VLF (ms^2)	0.258	0.260	0.176	0.397	0.443	0.306
LF (ms^2)	0.796*	0.891*	0.838*	0.855*	0.849*	0.845
HF (ms^2)	0.939*	0.947*	0.957*	0.879*	0.972*	0.938
30-second epoch	**1st epoch**	**2nd epoch**	**3rd epoch**	**4th epoch**	**5th epoch**	**Mean *r* coefficient**
RR (ms)	0.989*	0.988*	0.976*	0.974*	0.971*	0.979
SDNN (ms)	0.870*	0.843*	0.802*	0.859*	0.673*	0.809
HR (bpm)	0.990*	0.989*	0.983*	0.976*	0.984*	0.984
rMSSD (ms)	0.993*	0.995*	0.995*	0.995*	0.994*	0.994
pNN50 (%)	0.980*	0.985*	0.966*	0.975*	0.978*	0.976
VLF (ms^2)	0.136	0.291	0.355	0.287	0.157	0.245
LF (ms^2)	0.808*	0.818*	0.716*	0.418	0,772*	0.780
HF (ms^2)	0.927*	0.952*	0.874*	0.960*	0.946*	0.931

Mean RR intervals (RR, ms); Mean heart rate (HR, bpm); Standard deviation of RR intervals (SDNN, ms); Root mean square of the successive differences of RR intervals (rMSSD, ms); Percentage of RR intervals with difference in successive RR intervals longer than 50 ms (pNN50, %); Very low frequency (0.01–0.04 Hz, VLF, ms^2); Low frequency (0.04–0.15 Hz, LF, ms^2); High frequency (0.15–0.4 Hz, HF, ms^2); $p < 0.05$ for *Bonferroni* multiple comparison correction (*).

a few (≤3) random epochs from a 5-minute recording may introduce selection bias that affects reliability. The reliability of SDNN and frequency domain indices would benefit from further studies (38). Although SDNN and time-domain indices show significant associations with 5-minute epochs, their mean values exhibit greater variance compared with rMSSD. Therefore, our results should be interpreted with caution. rMSSD, which clearly represents parasympathetic activity (18, 21), shows lower mean value variation across 5-minute recordings and higher Pearson coefficients for ≤1-minute epochs (38–40). Thus, our results support the conclusion that rMSSD is the most reliable index for ultra-short recordings in patients with TBI.

Cardiac autonomic dysfunction, assessed by HRV, has been reported in several diseases. However, the common pathophysiological mechanisms underlying these conditions have been the subject of intense debate within the scientific community (20–22, 26, 27). HRV maintenance is associated with various cardiovascular, physiological, metabolic, and psychological variables (18, 21, 46). Recent trends in HRV clinical applications suggest that HRV can reflect a general state of well-being, serving as a sensitive but nonspecific biomarker for individual symptoms (47). While some researchers have reported normative values for healthy samples, there is no consensus on a "safe zone" for HRV values (48). Developing a generalized normative database can be challenging due to the precise quantitative measurement required for all daily variables associated with HRV fluctuations. A possible strategy for clinical application development might be to use a single-subject model, which compares values with baseline reference values. This model is used for monitoring fatigue and

Table 3. Comparison of mean HRV indices between time epochs

Variable	5-minute epoch	1st epoch 1 minute	2nd epoch 1 minute	3rd epoch 1 minute	4th epoch 1 minute	5th epoch 1 minute	%Δ	*F* (*p*)
RR (ms) ±	961.48 ± 185.14	963.58 ± 186.83	963.31 ± 173.68	963.38 ± 185.49	965.63 ± 183.17	967.24 ± 182.84	0.32	0.01 (1.00)
HR (bpm)	64.89 ± 12.94	64.71 ± 12.80	64.48 ± 12.24	64.73 ± 12.80	64.57 ± 12.84	64.41 ± 12.79	0.47	0.01 (1.00)
SDNN (ms)	41.18 ± 18.35	36.05 ± 15.88	35.79 ± 19.45	36.76 ± 20.02	38.40 ± 19.53	35.35 ± 16.68	11.43	0.69 (0.63)
rMSSD (ms)	27.79 ± 19.20	27.90 ± 19.25	28.41 ± 19.65	27.90 ± 19.20	28.24 ± 19.50	27.85 ± 19.14	0.97	0.01 (1.00)
pNN50 (%)	9.38 ± 15.63	9.38 ± 15.97	9.30 ± 15.80	9.82 ± 16.74	9.79 ± 16.14	9.12 ± 15.26	1.08	0.01 (0.99)
VLF (ms^2)	972.15 ± 1021.88	439.01 ± 409.93*	612.38 ± 1242.56	539.34 ± 636.24*	778.43 ± 1806.73	431.46 ± 432.27*	42.38	1.95 (0.08)
LF (ms^2)	515.54 ± 601.49	491.30 ± 517.42	606.36 ± 1051.67	572.29 ± 717.89	679.92 ± 899.14	417.21 ± 544.70	7.34	0.73 (0.59)
HF (ms^2)	344.12 ± 542.49	351.58 ± 649.52	430.32 ± 712.68	348.52 ± 509.18	341.52 ± 466.31	356.91 ± 575.49	6.29	0.16 (0.97)
Variable	**5-minute epoch**	**1st epoch 30-second**	**2nd epoch 30-second**	**3rd epoch 30-second**	**4th epoch 30-second**	**5th epoch 30-second**	**%Δ**	***F* (*p*)**
RR (ms)	961.48 ± 185.14	966.72 ± 185.21	966.80 ± 180.58	962.30 ± 172.71	956.08 ± 177.7776	972.70 ± 196.13	0.35	0.05 (0.99)
HR (bpm)	64.89 ± 12.94	64.50 ± 13.01	64.36 ± 12.43	64.54 ± 12.11	65.11 ± 12.82	64.25 ± 12.97	0.52	0.03 (0.99)
SDNN (ms)	41.18 ± 18.35	32.91 ± 17.15*	34.09 ± 19.69	36.62 ± 24.21	32.97 ± 18.39*	35.23 ± 21.24	16.55	1.17 (0.32)
rMSSD (ms)	27.79 ± 19.20	28.07 ± 18.70	27.81 ± 19.35	27.93 ± 19.48	27.72 ± 19.21	28.06 ± 19.36	0.46	0.01 (1.00)
pNN50 (%)	9.38 ± 15.63	9.82 ± 18.60	9.57 ± 17.83	9.07 ± 17.09	9.34 ± 17.39	9.71 ± 16.96	1.30	0.01 (1.00)
VLF (ms^2)	972.15 ± 1021.88	193.42 ± 242.25*	255.21 ± 466.27*	384.05 ± 592.01	207.99 ± 283.46	317.95 ± 758.08	72.04	10.75 (0.0001)
LF (ms^2)	515.54 ± 601.49	491.30 ± 517.42	606.36 ± 1051.67	572.29 ± 717.89	679.92 ± 899.14	417.21 ± 544.70	7.34	0.73 (0.59)
HF (ms^2)	344.12 ± 542.49	351.58 ± 649.52	430.32 ± 712.68	348.52 ± 509.18	341.52 ± 466.31	356.91 ± 575.49	6.29	0.16 (0.97)

Results are presented in mean ± sd; mean RR intervals (RR, ms); Mean heart rate (HR, bpm); Standard deviation of RR intervals (SDNN, ms); Root mean square of the successive differences of RR intervals (rMSSD, ms); Percentage of RR intervals with difference in successive RR intervals longer than 50 ms (pNN50, %); Very low frequency (0.01–0.04 Hz, VLF, ms^2); Low frequency (0.04–0.15 Hz, LF, ms^2); High frequency (0.15–0.4 Hz, HF, ms^2); Mean values percentage of variation across epochs (%Δ); $p < 0.05$ for posthoc comparison to 5-minute epoch (*).

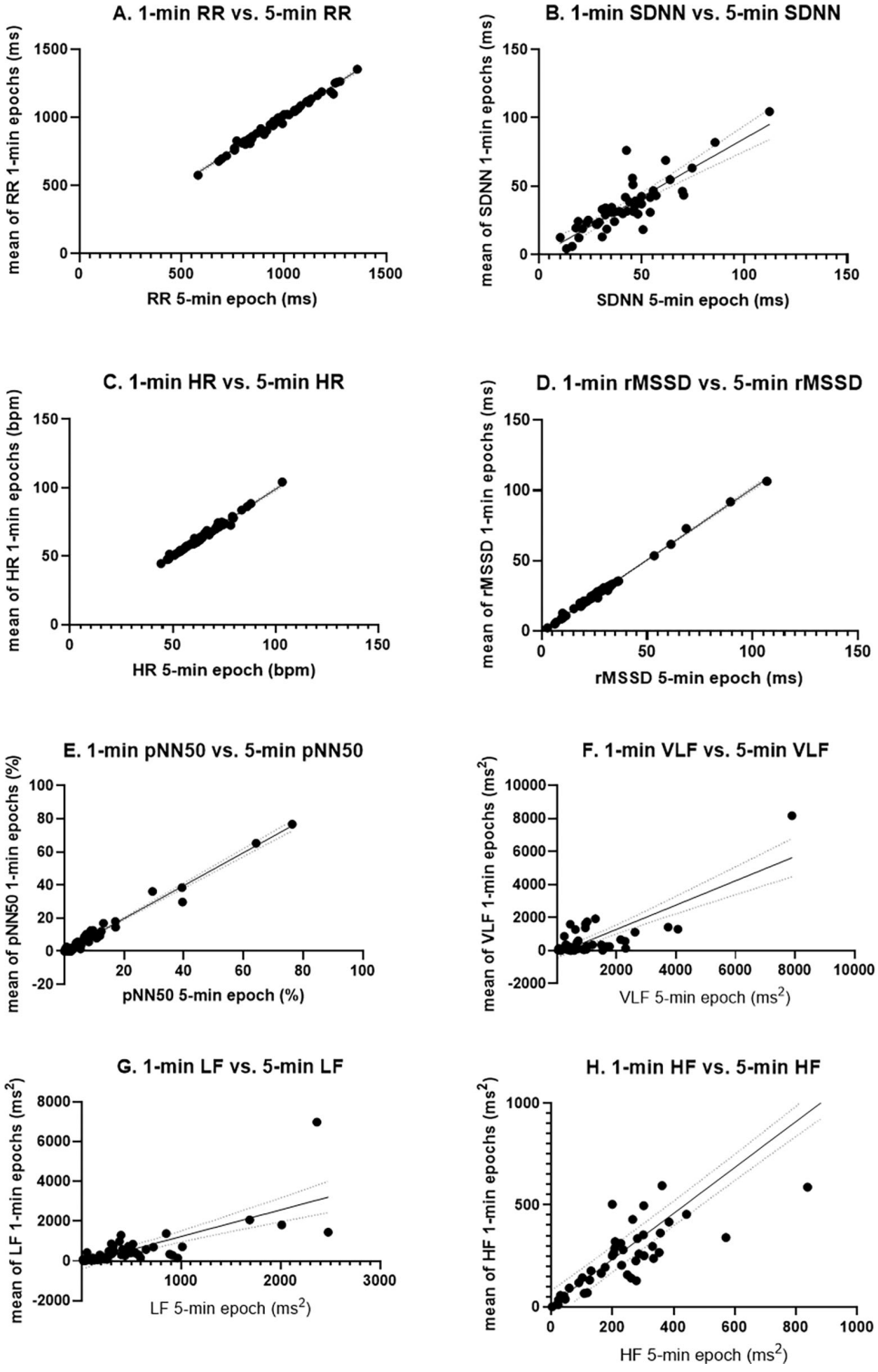

Figure 1. Associations between 1-minute with 5-minute epochs of HRV indices.

training load in high-performance athletes (49). Therefore, ultra-short measurements could enhance patient adherence to daily HRV recording. Our results support that ultra-short HRV recording is a simple, fast, and noninvasive method for evaluating cardiac autonomic tone in patients with TBI, with rMSSD being the most reliable index for ultra-short recordings. The ultra-short recording method could improve the applicability of HRV in clinical settings.

Ultra-short HRV measurements, defined as recordings shorter than 5 minutes, have shown potential as a noninvasive tool for monitoring ANS function. In the context of TBI care, these measurements could provide valuable insights into autonomic dysregulation, which is commonly observed in patients with TBI and is associated with poor outcomes (50). By applying ultra-short HRV measurements in clinical settings, it may be possible to develop more timely and personalized interventions aimed at

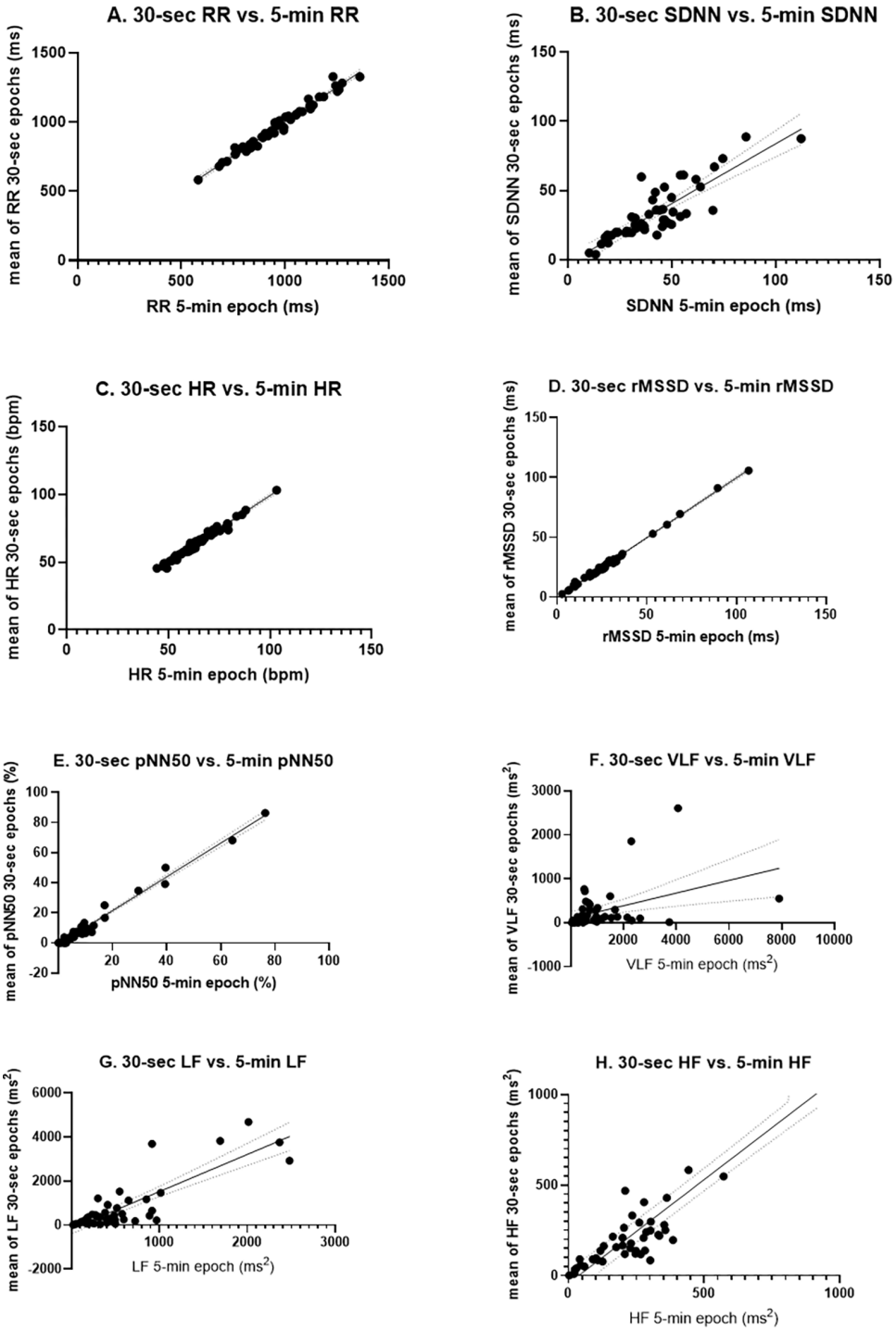

Figure 2. Associations between 30-second with 5-minute epochs of HRV indices.

improving patient outcomes. Future research should focus on validating the efficacy of these measurements in predicting TBI progression and recovery, as well as determining their utility in guiding treatment decisions. This approach aligns with the growing body of evidence supporting the use of HRV as a biomarker for various neurological conditions, including TBI (33, 36, 37, 51–53).

Our results should be interpreted with caution. The HRV data used in these analyses were recorded under controlled conditions (e.g., supine position, quiet room, proper baseline resting period), so these results may not fully reflect typical environmental conditions in various hospitals or clinics where electrocardiogram (EKG) recordings are performed. Addressing measurement issues such as variability and artifact management is crucial for improving the accuracy and reliability of HRV assessments across different populations (54). Moreover, incorporating longitudinal designs could provide valuable insights into the temporal aspects of patient compliance with brain recovery interventions that utilize HRV measurements and training. Such studies would help to better understand how adherence to these methods changes over time and its effect on patient recovery (47, 55). This approach will advance our understanding of the practical integration of HRV metrics into TBI rehabilitation

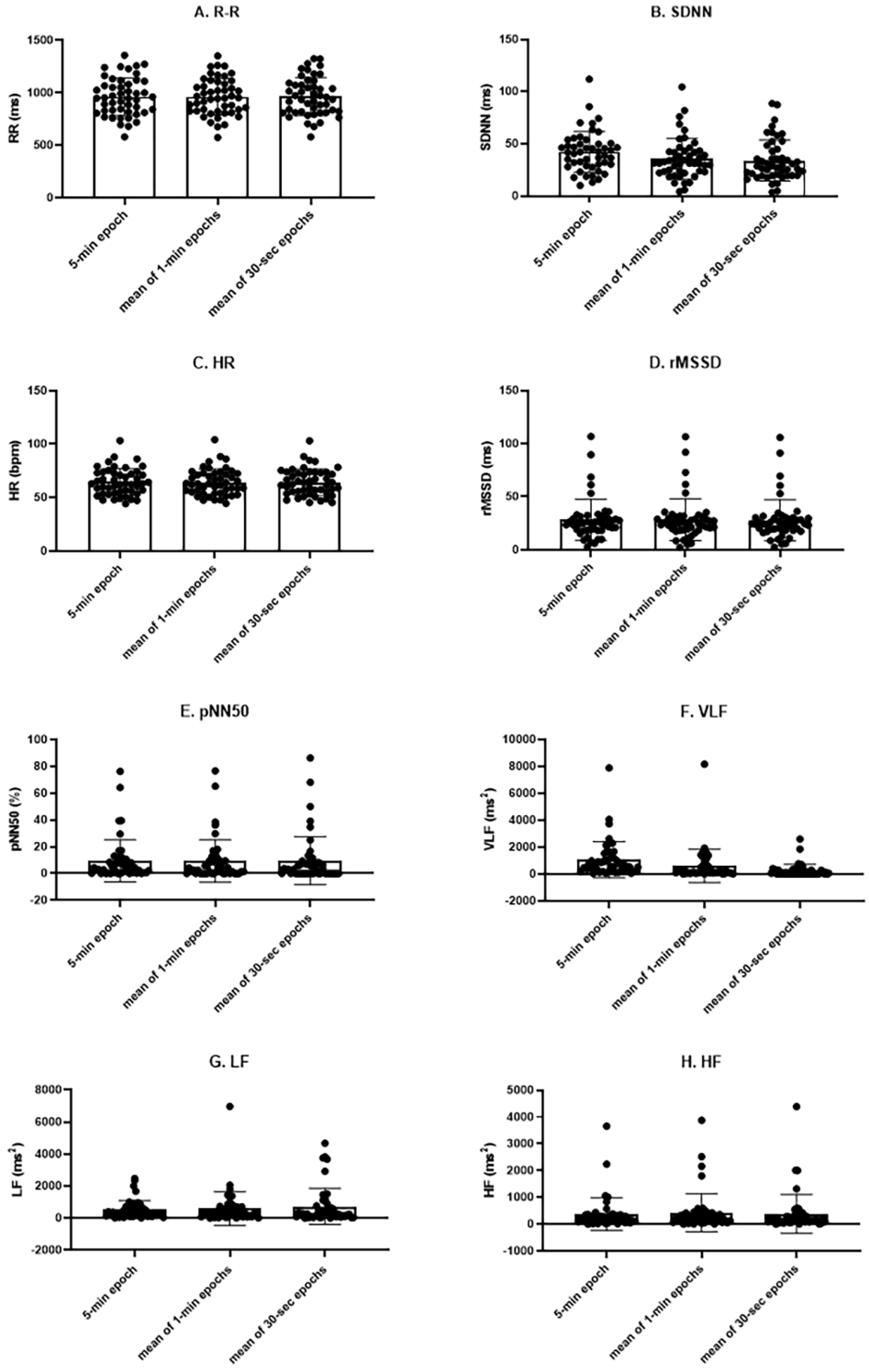

Figure 3. Comparison between mean values of HRV indices in time epochs (5-minute, 1-minute, 30-second).

protocols. Although some HRV indices remain reliable for ultra-short recordings, general precautions for preparing patients for regular EKG recordings should be maintained. The reliability of ultra-short recordings may not be generalizable to uncontrolled environments or situations where proper postural position or baseline resting conditions are not followed. Short HRV assessments may, in the future, offer a practical and efficient method for evaluating patients with TBI, particularly in resource-constrained settings.

Ultra-short HRV indices are reliable for assessing cardiac autonomic tone in patients with TBI. The correlation between ultra-short recordings (1 minute and 30 seconds) and standard time recordings (5 minutes) supports that time-domain indices exhibit higher correlation coefficients compared to frequency-domain indices. The comparison between the results of the 1-minute and 30-second epochs indicates that reducing recording time increases the percentage variation of all HRV indices. rMSSD exhibits higher Pearson coefficient values and lower percentage of variation at both 1-minute and 30-second epochs compared with other

HRV indices. rMSSD is thus the most reliable HRV index for ultra-short recordings in patients with TBI. SDNN and frequency domain indices (e.g., VLF or LF) require longer recording times to provide reliable values. The associations between clinical or sociodemographic variables and HRV indices, as well as the prognostic value of HRV for TBI survivors, remain to be determined in future studies.

Methods

Participants

This study included 48 patients with TBI from Hospital Governador Celso Ramos (HGCR) and Hospital Homero de Miranda Gomes (HHMG), two reference hospitals for brain trauma in the public health system of Santa Catarina state, southern Brazil, between April 2014 and January 2016. The inclusion criteria were a GCS score of 8 or lower after acute neurosurgical resuscitation, without sedation, or a deterioration to that level within 48 hours of hospital admission, and a favorable outcome (Glasgow Outcome Scale 4 or 5) one year after hospitalization, when the EKG was performed. The exclusion criteria were poor quality of the EKG signal during the predetermined sampling period and patients with a history of known cardiac disease (as indicated by medical records and patient oral confirmation). The research protocol was approved by the Ethics Committee for Human Research at Universidade Federal de Santa Catarina (Plataforma Brazil Registration 02832612.6.1001.0121), and written informed consent was obtained from all participants.

Electrocardiographic Recording

The Nihon Kohden amplifier was used for EKG recording, sampled at 512 Hz. All EKG recordings were performed between 2 and 4 PM while the patients were in a supine position. The skin areas where the disposable Ag/AgCl electrodes were applied were cleaned with 70% isopropyl alcohol. The electrodes were placed in a triangular chest configuration. Muscle artifact epochs ($<$2%) were identified through visual inspection and excluded from the analysis. The first 5 minutes of EKG recording, without muscular artifacts, were used for HRV analysis. The QRS complex identification, RR interval extraction, and HRV analysis were performed using Kubios v2.3 software (56). The following time-domain and frequency-domain HRV indices were calculated: a) Mean RR intervals (RR, ms); b) Mean heart rate (HR, bpm); c) Standard deviation of RR intervals (SDNN, ms); d) Root mean square of successive differences of RR intervals (rMSSD, ms); e) Percentage of RR intervals with differences in successive RR intervals longer than 50 ms (pNN50, %); f) Very low frequency (0.01–0.04 Hz, VLF, ms^2); g) Low frequency (0.04–0.15 Hz, LF, ms^2); h) High frequency (0.15–0.4 Hz, HF, ms^2). A fast Fourier transform using a Hanning window of 256 seconds width with 50% overlap was used for frequency domain indices analysis. All HRV indices extraction was based on the Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology guidelines (1996). The 5-minute recordings were reanalyzed in consecutive 1-minute epochs (1st – 1 minute; 2nd – 1 minute; 3rd – 1 minute; 4th – 1 minute; 5th – 1 minute) and 30-second epochs (1st – 30 seconds; 2nd – 30 seconds; 3rd – 30 seconds; 4th – 30 seconds; 5th – 30 seconds). To prevent selection bias, the 30-second epochs were selected from the final portion of the consecutive 1-minute epochs.

Statistical Analysis

All data were normally distributed as assessed by the Shapiro–Wilk test ($p > 0.05$). ANOVA was used to compare the mean values of HRV indices across different time epochs. Pearson correlation was used to evaluate the association between HRV values at different time intervals (5 minutes, 1 minute, and 30 seconds). The p-values from the Pearson correlation analysis were corrected using the Bonferroni multiple comparisons correction. A p-value of <0.05 was considered statistically significant. All statistical procedures were performed using Stata 14.0 (Version 14; StataCorp LLC, Texas, USA).

Author Disclosures

The authors declare no conflicts of interest, sources of funding, or financial ties to disclose. They have no current or past relationships with companies or manufacturers that could benefit from the results of the present study.

Author Contributions

Hiago Murilo Melo: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Beatriz Rangel**: Writing – review & editing, Visualization. **Guilherme Loureiro Fialho**: Writing – review & editing, Validation. **Katia Lin**: Writing – review & editing, Visualization. **Roger Walz**: Writing – review & editing, Visualization, Validation and Supervision.

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Ethical Review

The research protocol was approved by the Ethics Committee for Human Research at Universidade Federal de Santa Catarina (Plataforma Brazil Registration 02832612.6.1001.0121), and written informed consent was obtained from all participants.

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