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Subcutaneous nerve activity is more accurate than the heart rate variability in estimating cardiac sympathetic tone in ambulatory dogs with myocardial infarction

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Abstract

Background—We recently reported that subcutaneous nerve activity (SCNA) can be used to estimate sympathetic tone.

Objectives—To test the hypothesis that left thoracic SCNA is more accurate than heart rate variability (HRV) in estimating cardiac sympathetic tone in ambulatory dogs with myocardial infarction (MI).

Methods—We used an implanted radiotransmitter to study left stellate ganglion nerve activity (SGNA), vagal nerve activity (VNA), and thoracic SCNA in 9 dogs at baseline and up to 8 weeks after MI. HRV was determined based by time-domain, frequency-domain and non-linear analyses.

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Disclosures

Drs Shien-Fong Lin and Peng-Sheng Chen have equity interest in Arrhythmotech, LLC. Indiana University has filed patent application related to this work. Cyberonics Inc., Medtronic Inc. and St. Jude Medical Inc. donated research equipment to Dr. Chen's research laboratory.

Results—The correlation coefficients between integrated SGNA and SCNA averaged 0.74 (95% confidence interval (CI), 0.41–1.06) at baseline and 0.82 (95% CI, 0.63–1.01) after MI ($P<.05$ for both). The absolute values of the correlation coefficients were significant larger than that between SGNA and HRV analysis based on time-domain, frequency-domain and non-linear analyses, respectively, at baseline ($P<.05$ for all) and after MI ($P<.05$ for all). There was a clear increment of SGNA and SCNA at 2, 4, 6 and 8 weeks after MI, while HRV parameters showed no significant changes. Significant circadian variations were noted in SCNA, SGNA and all HRV parameters at baseline and after MI, respectively. Atrial tachycardia (AT) episodes were invariably preceded by the SCNA and SGNA, which were progressively increased from 120th, 90th, 60th to 30th s before the AT onset. No such changes of HRV parameters were observed before AT onset.

Conclusion—SCNA is more accurate than HRV in estimating cardiac sympathetic tone in ambulatory dogs with MI.

Keywords

heart rate variability; autonomic nervous system; subcutaneous nerve activity; myocardial infarction; atrial arrhythmia

Introduction

Heart rate variability (HRV) is a method frequently used to estimate autonomic tone.[1] Depressed HRV is a powerful predictor of sudden cardiac death and arrhythmic complications in patients following acute myocardial infarction (MI) independent of left ventricular ejection fraction. Its importance is also supported by the fact that 11,980 articles in the PubMed data base contain the exact phrase “heart rate variability” as of January, 2014. The most commonly used HRV methods include either time-domain or frequency-domain analyses.[1] In addition, recent studies showed that non-linear analysis of HRV may detect abnormal patterns of RR fluctuations more efficiently than standard HRV measurements.[2] Among these new methods is the phase-rectified signal averaging (PRSA),[3] which is used to quantify the quasi-periodic accelerations and decelerations in short-term heart rate. The latter is normally masked by nonstationarities (such as ectopic beats and changes in activity), noise, and artifacts. PRSA characterizes how the heart behaves around points of deceleration (deceleration capacity (DC)) and acceleration (acceleration capacity (AC)) under a given recording condition. Bauer et al. found that a low DC was a stronger predictor of mortality after MI than traditional HRV techniques.[4, 5] Recently, we demonstrated that the left thoracic subcutaneous nerve activity (SCNA) could be used to accurately estimate left stellate ganglion nerve activity (SGNA) in normal ambulatory dogs and to predict susceptibility to ventricular tachycardia (VT) and ventricular fibrillation (VF) in a canine model of ventricular arrhythmia and sudden cardiac death.[6, 7] However, whether the SCNA can be used as a marker of cardiac sympathetic tone in ambulatory dogs with MI remained unknown. In a previous study from our laboratory, Han et al simultaneously recorded left SGNA, left thoracic vagal nerve activity (VNA) and the subcutaneous electrocardiogram (ECG) in 9 ambulatory dogs at baseline and after MI.[8] That data set gave us an excellent opportunity to study the relationship between HRV, SGNA and SCNA in dogs with MI without the need to use additional animals for experiments. The purpose of the

present study was to perform further analyses of that data set to test the hypothesis that SCNA is better than HRV in estimating cardiac sympathetic tone in ambulatory dogs with MI.

Materials and methods

We re-analyzed data in nine ambulatory dogs with MI from a previous study.[8] The study protocols were approved by the Institutional Animal Care and Use Committee of the Indiana University School of Medicine and the Methodist Research Institute, Indianapolis, Indiana, and conformed to the Guide for the Care and Use of Laboratory Animals. Data Sciences International (DSI, St Paul, MN) D70-EEE radio transmitters with 3 bipolar recording channels were implanted in 9 mongrel dogs. The first pair of bipolar electrodes was used to record from the left stellate ganglion and the second pair was used to record from the left vagal nerve at the level 4 to 5 cm above the aortic arch. A third pair of bipolar leads was placed in the subcutaneous space of left thorax and left abdomen for electrocardiogram (ECG) recording. Signals from the latter electrodes were high pass filtered at 150 Hz to reveal nerve signals.[6] Subcutaneous inter-electrode distance was not measured at the time of the study, but in similar sized dogs it is estimated at around 28 cm.[7] After baseline recording, acute MI was created and recording continued for an additional 8 weeks.

HRV analysis based on time-domain, frequency domain and PRSA methods

The R peak of QRS complex in the 5-min window of each ECG signal was automatically detected based on the Pan Tompkins algorithm[9] and RR interval tachogram was then obtained beat-by-beat (Online supplement Figure 2). The time-domain, frequency domain, and PRSA analysis of the HRV were all performed using the Matlab 2013 software (@MATLAB). The standard deviation of NN intervals (SDNN), the square root of the mean of the squares of the successive differences between adjacent NNs (RMS) and the proportion of the number of pairs of successive NNs that differ by more than 50 ms (NN_{50}) divided by total number of NNs (pNN_{50}) calculated over 5 min were used to represent the HRV measures based on time domain method. For the frequency domain analysis, spectral power for HRV was analyzed on 5-min ECG recording segments and an autoregressive algorithm was used to analyze digitized signals from the ECG recordings (Online supplement Figure 2). The total power (TP), very low frequency (VLF) (0.003 to 0.04 Hz), low frequency (LF) (from 0.04 to 0.15 Hz), high frequency (HF) (from 0.15 to 0.4 Hz) components, LF normalized unit (LF_{nu}), HF normalized unit (HF_{nu}) and LF-HF ratio were calculated based on the frequency domain analysis. LF_{nu} was calculated as LF/(TP-VLF)*100. HF_{nu} was calculated as HF/(TP-VLF)*100.[1] The PRSA was calculated according to methods published elsewhere.[4] Detailed methods are available in an Online Supplement.

Statistical analysis

Unless otherwise indicated, all data are expressed as mean and 95% CI. Data with skewed distribution are given as median and interquartile range (25^{th} percentile – 75^{th} percentile). For each dog, each HRV parameter was calculated from the total beats within each 5-minute window. The SGNA, VNA and SCNA were also obtained by integrating the nerve activities in the same 5-min window. Therefore, there were a total 288 recordings per day in each dog

at baseline or after MI, respectively. Shapiro-Wilk test was used to assess if the parameters in Table 1 and Table 2 were in normally distributed. Paired T test was used to compare for normally distributed variables. Wilcoxon test was used to compare non-normally distributed variables at baseline and after MI. Pearson correlation coefficient was used to measure the correlations among all HRV parameters or SCNA vs the SGNA or VNA in each dog. The significance of the consecutive values for SGNA, VNA, SCNA, SDNN, LF_{nu} and DC in Figure 2 (baseline, 2, 4, 6, and 8 weeks after MI) and Figure 4 (−120, −90, −60, and −30 s prior onset of atrial tachycardia) were checked with repeated-measure one-way ANOVA. Cosinor tests were used to detect and quantify significant 24-hour circadian variations in the 9 dogs. Statistical analysis was performed using IBM SPSS Statistics 19. A two-sided $P < .05$ was considered significant.

Results

Presence and characteristics of subcutaneous nerve discharges

The morphology of SCNA resembles that of the SGNA in all dogs studied both at baseline and after MI. In addition, SCNA morphology was similar to filtered skin and muscle sympathetic nerve activity obtained in microneurography studies (Online supplement Figure 1).[10, 11] The SCNA signals are more likely to contain unfiltered ECG signals as compared with the SGNA channel.

SCNA and HRV analysis after MI

We manually screened all data and discarded data windows with recording artifacts or noises. Among the 288 5-min windows within a 24-hr period, 269 [223 to 314] and 267 [226 to 311] windows at baseline and at 8 weeks after MI, respectively, were adequate for analyses. We calculated SGNA, VNA, SCNA and all HRV parameters for each 5-min window. Averaged SGNA, SGNA/VNA ratio and SCNA were all significantly increased after 8 weeks of MI as compared to baseline in the 9 dogs: the SGNA increased from 81 [95% CI, 33 to 128] to 151 mV-sec [95% CI, 53 to 249] ($P < .001$), the SGNA/VNA ratio increased from 2.2 [95% CI, 0.9 to 3.4] to 3.4 [95% CI, 0.5 to 6.4] ($P = .043$), and the SCNA increased from 116 [95% CI, 41 to 190] to 165 mV-sec [95% CI, 107 to 223] ($P < .001$). The VNA also showed significant change after MI ($P = .021$). In comparison, all HRV measures showed no obvious change at 8 weeks after MI in these 9 dogs (Table 1).

Pearson correlation between the analyzable 5-min segments of the SGNA or VNA and all HRV profiles or SCNA was calculated for each dog at baseline and at 8 weeks after MI. Table 2 summarizes the average correlation coefficient for all dogs. We used SDNN, low frequency normalized unit (LF_{nu}), and deceleration capacity (DC) to represent the HRV measures based on time domain, frequency domain and non-linear methods in the following sections, respectively. At baseline, the average correlation coefficient of SCNA vs SGNA (0.74 [95% CI, 0.41 to 1.06]) is significantly higher than the absolute values of the correlation coefficient of SGNA vs SDNN (−0.59 [95% CI, −0.94 to −0.24]), LF_{nu} (−0.07 [95% CI, −0.58 to 0.44]), and DC (−0.63 [95% CI, −0.98 to −0.28]) for all dogs ($P < .05$ for all). At 8 weeks after MI, the average correlation coefficient of SCNA vs SGNA (0.82 [95% CI, 0.63 to 1.01]) is also significantly higher than the absolute value of correlation

coefficient of SGNA vs SDNN (−0.57 [95% CI, −0.88 to −0.25]), LF_{nu} (0.17 [95% CI, −0.34 to 0.68]), or DC (−0.63 [95% CI, −0.95 to −0.32]) for all dogs ($P < .05$ for all). The correlation coefficient of DC vs SGNA is significantly higher than the correlation coefficient of SDNN or LF_{nu} vs SGNA for all dogs at baseline and after MI (both $P < .05$). It is noted that the SCNA showed weak positive correlation with the VNA at baseline (0.27 [95% CI, −0.12 to 0.65]) and 8 weeks after MI (0.29 [95% CI, 0.02 to 0.58]), respectively. In general, the absolute values of correlation coefficient between the VNA and all HRV parameters were low at either baseline or after 8 weeks of MI.

SCNA, SGNA and HRV analysis retained circadian variation

We plotted hourly SGNA, VNA, SCNA, SDNN, LF_{nu} and DC over 24-hour period for all dogs at baseline and 8 weeks after MI. The 24-hour tracing was averaged from each dog's 24-hour tracing (Figure 1). The SGNA and SCNA after MI was higher than baseline throughout the 24-hr period, but the increased SGNA and SCNA were mainly observed during daytime. During the 2 days analyzed, SGNA was significantly higher in the nine different hours 8 weeks after MI than at baseline (1:00, 6:00, 7:00, 8:00, 11:00, 12:00, 16:00, 17:00, 19:00, all $P < .05$). The SCNA reached similar higher significant values in nine hours as well as the SGNA (1:00, 5:00, 6:00, 7:00, 8:00, 10:00, 12:00, 17:00, 19:00, all $P < .05$). The VNA reached higher significant values in two hours after MI (7:00 and 18:00, both $P < .05$). For the HRV measures, the LF_{nu} showed lower significant values in three hours as well as the SGNA (0:00, 1:00, 20:00, all $P < .05$). The SDNN and DC did not show any significant difference in all hours at 8 weeks after MI. The SGNA, SCNA, SDNN, LF_{nu} and DC all showed circadian variation at either baseline or 8 weeks after MI (all $P < .01$). The VNA did not show any circadian variation at either baseline or 8 weeks after MI.

SGNA, SCNA but not HRV parameters changed after MI

We calculated 24-h averaged SGNA, VNA, SCNA, SDNN, LF_{nu}, and DC values for each dog at baseline, 2, 4, 6, and up to 8 weeks after MI. As shown in Figure 2, there was progressive increment of SGNA at 2, 4, 6 and 8 weeks after MI ($P < .01$). The SGNA reached maximal values at 6 to 8 weeks after MI. The SGNA was significantly increased at 2, 4, 6 and 8 weeks after MI as compared to baseline, respectively (all $P < .05$ vs baseline). Similar to SGNA, SCNA was significantly higher at 2, 4, 6 and 8 weeks after MI, respectively, than baseline (all $P < .05$ vs baseline). VNA was significantly increased at 6 and 8 weeks after MI (both $P < .05$ vs baseline). In contrast, none of the HRV parameters showed significant changes after MI except for LF_{nu} and DC, which were significantly decreased at the 2 and 4 weeks after MI as compared with baseline, respectively.

SGNA, SCNA, and HRV analysis before atrial arrhythmia episodes at baseline and 8 weeks after MI

We did not find any sustained ventricular tachycardia (VT) episodes (VT lasting > 5 sec with a heart rate > 150 beats per min (BPM)) at baseline or 8 weeks after MI in any dog studied.[8] Instead, we found frequent paroxysmal atrial tachycardia (AT) episodes (defined as an abrupt (>20 BPM) increase in the heart rate to >150 BPM that persisted for at least 5-s) in all 9 dogs (Figure 3). We documented a total of 48 AT episodes (5.3 episodes/dog [95% CI,

−5.3 to 15.9]) at baseline and 117 AT episodes (13.0 episodes/dog [95% CI, −2.6 to 28.6]) at 8 weeks after MI ($P = .03$). Integrated SGNA, VNA, SCNA, and ultra-short term HRV measures with SDNN, LF_{nu}, and DC were calculated in four 30-s intervals for 120 s prior to the onset of AT episodes. At baseline, there was progressive increase in integrated SGNA, VNA, and SCNA prior AT episodes (all $P < .01$). Of note, the incremental effect was further augmented for integrated SGNA and SCNA 8 weeks after MI (both $P < .001$). For the HRV measures, only the DC showed progressive decrement before AT episodes after MI (Figure 4) ($P < .01$).

Discussion

We found that SCNA can be used to provide an estimate of sympathetic activity in ambulatory dogs before and after MI. The correlation coefficient of the SCNA and SGNA is significantly higher than the absolute values of correlation coefficients of any HRV parameters. Both SCNA and SGNA showed clear incremental changes at 2, 4, 6 and 8 weeks after MI, but no changes were found in HRV parameters. There was progressive increment of SCNA and SGNA before the onset of AT episodes, but no such changes were found for HRV parameters except for the DC value. We conclude that the SCNA is more accurate than the HRV parameters in estimating cardiac sympathetic tone in ambulatory dogs with MI.

HRV and cardiac autonomic function after MI

Without direct cardiac sympathetic recording, evaluating the cardiac autonomic tone in clinical practice mainly relied on the noninvasive analysis of HRV.[1, 12] Novel non-linear methods assessing HRV have shown new insights into abnormalities in heart rate behavior in various pathological conditions, providing additional prognostic information when compared with traditional HRV measures.[2] However, the HRV analyses based on either traditional or non-linear method had several limitations. Because HRV measures RR interval variations, it is limited to patients in sinus rhythm with intact sinoatrial nodal response to autonomic outflow and to those with few ectopic beats. Approximately 20 to 30% of high risk post-MI patients are excluded from HRV analysis due to frequent ectopy or cardiac arrhythmias, including atrial fibrillation and frequent premature ventricular beats.[13] In patients with advanced heart diseases or old age, heart rate may become invariate and refractory to analysis by conventional HRV techniques. Also, respiratory parameters like respiratory frequency, tidal volume or static lung volume can profoundly alter heart rate and RR interval variability independent of changes in cardiac autonomic regulation.[12] The above limitations had resulted in skepticism when considering HRV changes as indicators of autonomic outflow to the heart in the patient groups, and raised the question of how HRV may be effectively employed in patients with advanced heart diseases.[13, 14]

By using the direct recording of SGNA as the “gold standard” measures in representing the cardiac sympathetic outflow, we found that the HRV measures based on time domain (i.e. SDNN) and nonlinear methods (i.e. DC) had a significant correlation with the SGNA at baseline and 8 weeks after MI (Table 2). In the contrast, none of the frequency domain parameters showed good correlations with the SGNA at either baseline or after MI.

Traditionally, LF and HF components of HRV measures are often assumed to correspond to cardiac sympathetic and parasympathetic activity, respectively. However, accumulating evidence clearly demonstrates this assumption is not necessarily correct.[15–17] Interventions that would be expected to increase cardiac sympathetic tone, such as acute exercise, myocardial infarction, or heart failure, actually provoked significant reduction of LF components.[16] Accordingly, LF power should not be used as an index of cardiac sympathetic regulation. Specifically, the nonlinear HRV measures (DC) showed a higher correlation than the traditional HRV measures (SDNN or LF_{nu}) with the SGNA (Table 2), supporting the rationale of using novel HRV measures as a more robust indicator to represent the cardiac sympathetic tone as compared to traditional HRV analysis.[4, 5]

A major problem of HRV is that it was not very sensitive to detect the chronic changes of cardiac autonomic tone as shown in our study (Figure 2). There are several possible mechanisms to explain the phenomenon: The daily HRV measures is influenced not only by the level of intrinsic autonomic activity but also by the daily physical activity, humoral response, respiratory changes, and even mental status as the dogs experienced from the baseline, acute to chronic phase of MI. All of those factors may affect the heart rate dynamics diversely. Therefore, the HRV measures based on heart rate dynamics lacked the specificity to identify the evolutional changes of cardiac autonomic activity after MI. Another issue is the change of sinoatrial nodal sensitivity after MI. All HRV measures showed 24-hour circadian variation that paralleled the 24-hour SGNA changes both at baseline and 8 weeks after MI. However, it was noted that the magnitude of day-night HRV changes are all similar between baseline and after MI, even though the magnitude of day-night SGNA change was obviously augmented after MI (Figure 1). Previous studies demonstrated several pathophysiological processes, such as aging and congestive heart failure, render the sinoatrial node itself less efficient in responding to autonomic impulses.[16, 18, 19] Our result also indicated that the heart rate response modulated by sympathetic outflow is blunted after MI. HRV changes therefore may not truly reflect cardiac autonomic tone after MI due to the dysfunction of the sinoatrial node.

SCNA and cardiac autonomic function after MI

Instead, we demonstrated that SCNA was more accurate than the HRV in estimating cardiac sympathetic activity in ambulatory canines with MI. The histological studies of human skin biopsy confirmed the presence of abundant sympathetic nerves in arteriovenous anastomoses, arrector pilorum muscles, and arterioles.[20] Because of the direct and extensive connections among the cardiac and skin sympathetic innervation demonstrated in previous studies,[21, 22] it is possible for the sympathetic nerves in the various structures to activate simultaneously. Using bipolar electrodes located in the chest wall, we aimed to obtain good ECG signal for heart rate analyses and, in the meantime, record nerve signals over a wide area in the left lateral thorax. Sources of recordings from the subcutaneous space of the thorax could include multiple signals, including autonomic nerve activities, motor and sensory nerves, respiratory muscle activities, cardiac electrocardiogram and low frequency movement artifacts. High pass (150 Hz) filtering eliminates a significant amount of low frequency electrical activities including muscle contractions, motion artifacts and residual ECG signals. When excluding frames with artifacts or noises, our collective findings suggest

that the majority of signals recorded from the subcutaneous space after high pass signal filtering are sympathetic in origin.

Study Limitations

The significant limitation of this study is that incomplete filtering of ECG signal was observed in the subcutaneous channel. The degree of signal contamination appeared to vary between dogs. Further studies should be aimed at improving signal processing, eliminating ECG artifacts from SCNA recordings, and determining the optimal recording electrode location and inter-electrode distance. Second, none of these dogs developed ventricular arrhythmias during the chronic phase of MI, making it difficult to assess the importance of SCNA and SGNA in ventricular arrhythmogenesis.[8] However, Doytchinova *et al.* recently demonstrated that SCNA can be used as a surrogate for SGNA to predict susceptibility to ventricular tachyarrhythmias in a canine model with sudden cardiac death.[7]

Conclusions

We provided direct evidence that left thoracic SCNA was more accurate than the HRV parameters in estimating cardiac sympathetic activity in ambulatory dogs with MI. It is possible that SCNA may be used as a method to measure of sympathetic tone for risk stratification in patients with MI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations and Acronyms

AC	acceleration capacity
AT	atrial tachycardia
DC	deceleration capacity
ECG	electrocardiogram
HF	high frequency
HF_{nu}	high frequency normalized unit
HRV	heart rate variability
LF	low frequency
LF_{nu}	low frequency normalized unit
MI	myocardial infarction

pNN_{50}	the proportion of NN_{50} divided by total number of NNs
PRSA	phase-rectified signal average
RMSSD	root mean square of successive differences
RRI	RR interval
SCNA	subcutaneous nerve activity
SDNN	the standard deviation of normal to normal beat intervals
SGNA	stellate ganglion nerve activity
TP	total power
VLF	very low frequency
VNA	vagal nerve activity
VT	ventricular tachycardia

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Clinical Perspectives

Cardiac autonomic tone is important in cardiac arrhythmogenesis. HRV is a commonly used method to estimate autonomic nerve activity. However, it has significant limitations because HRV relies on the sinus node response to autonomic modulation. In patients with abnormal function of the sinus node (such as in patients with heart failure or AF), HRV may not adequately reflect sympathetic tone. In addition, HRV cannot be used in patients with AF or frequently ventricular arrhythmias. We showed that SCNA increased significantly in a canine model of MI while the HRV did not show consistent changes. These findings show that SCNA is more accurate than HRV in estimating cardiac sympathetic tone in ambulatory dogs with MI. Our findings indicate that SCNA may be more useful than HRV in risk stratification after MI. Implanted cardiac devices (such as pacemaker, implantable cardioverter-defibrillator, or loop recorder) are usually placed in the thoracic subcutaneous pocket which is richly innervated by sympathetic nerves originating from the stellate ganglion. Sympathetic nerve activity recorded directly by the implanted devices may be useful in estimating cardiac sympathetic tone in patients with MI. Prospective clinical studies are needed to determine if it is possible to record sympathetic nerve activities from the subcutaneous tissues in humans, and if the sympathetic nerve activities is more accurate than HRV in risk stratification in patients with MI or other organic heart diseases.

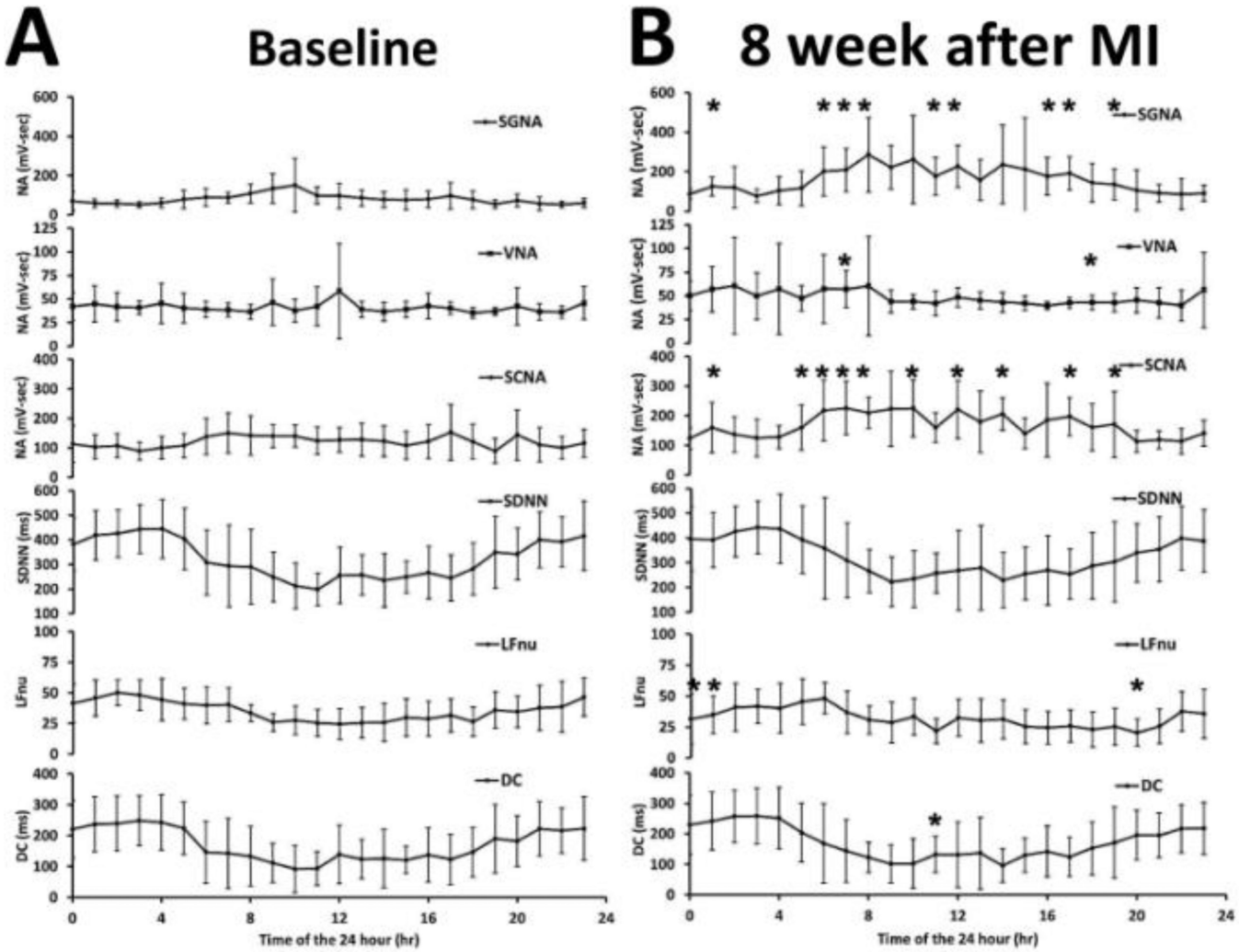

Figure 1. Changes of SGNA, VNA, SCNA, and HRV measures after MI

Daytime change of SGNA, VNA, SCNA, SDNN, LF_{nu}, and DC for the all dogs at baseline **(A)** and 8 weeks after MI **(B).** The SGNA, SCNA, SDNN, LF_{nu}, and DC all showed significantly circadian variation at baseline and after MI. DC=deceleration capacity; HRV=heart rate variability; LF_{nu}=low frequency normalized unit; MI=myocardial infarction; NA=integrated nerve activity; SCNA=subcutaneous nerve activity; SDNN=the standard deviation of normal to normal beat intervals; SGNA=stellate ganglion nerve activity; VNA=vagal nerve activity. * $P < .05$ vs baseline.

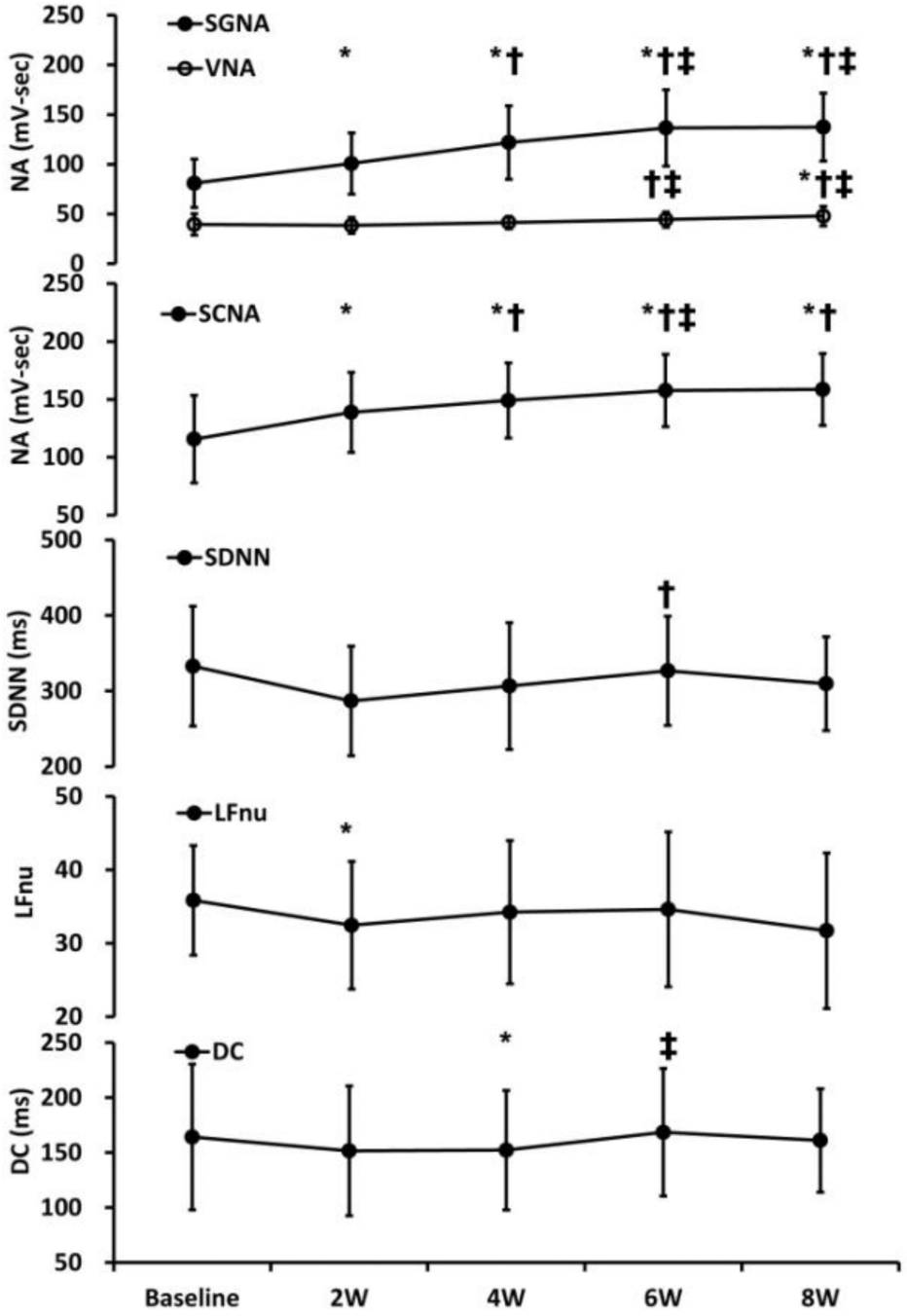

Figure 2. Consequent changes of daily SGNA, VNA, SCNA, and HRV measures at baseline, 2, 4, 6, and 8 weeks after MI

There is a progressive increment of SGNA and SCNA at baseline, 2, 4, 6, and 8 weeks after MI. The HRV measures failed to show progressive increment or decrement that parallel the SGNA changes at baseline, 2, 4, 6, and 8 weeks after MI. The abbreviations as in Figure 1. **P* < .05 vs baseline; †*P* < .05 vs 2 weeks; ‡*P* < .05 vs 4 weeks.

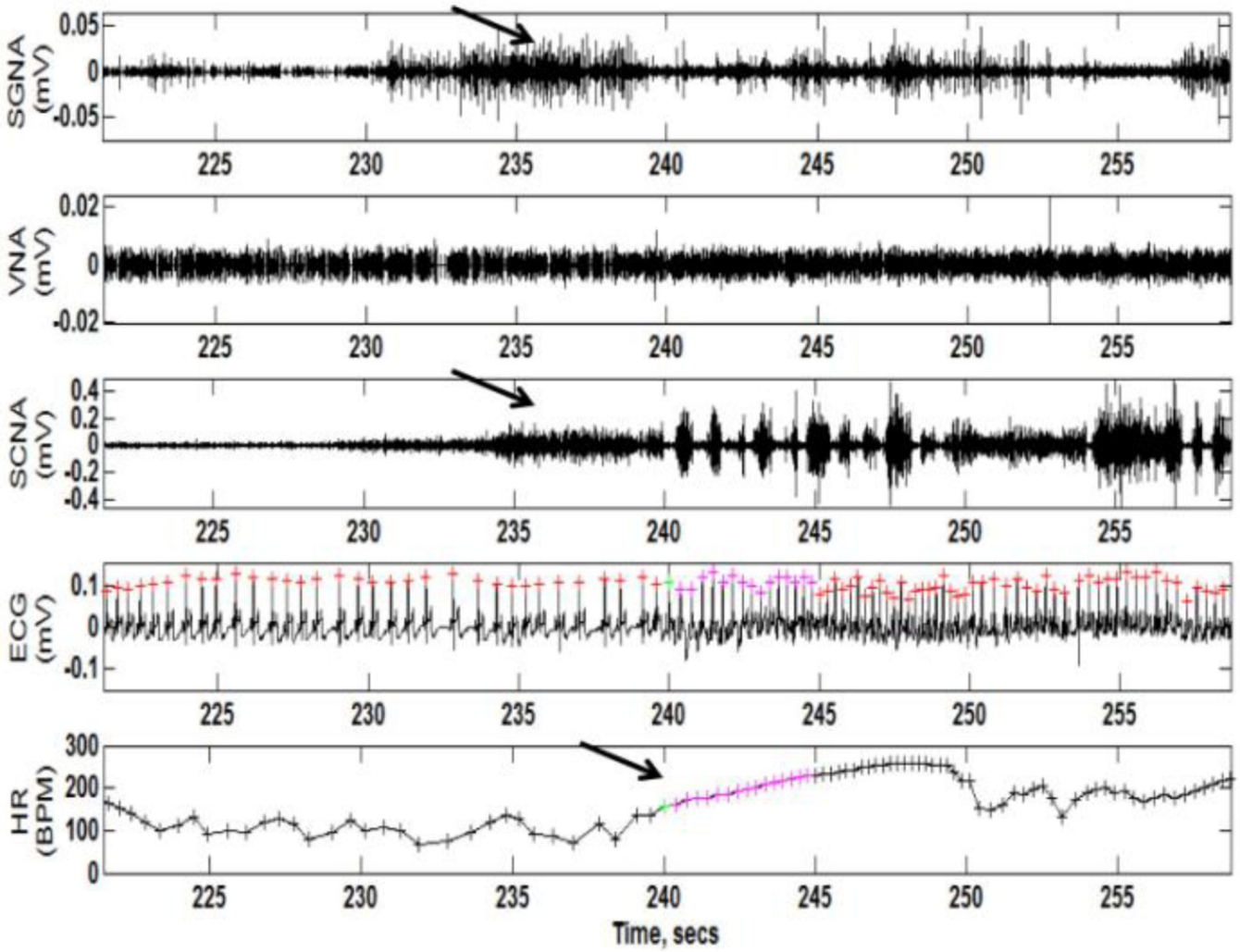

Figure 3. SGNA, VNA, and SCNA prior to the onset of AT

Prolonged low amplitude burst discharge activity (LABDA) recorded from the stellate ganglion and the subcutaneous tissues were present prior to the onset of AT in one representative dog after MI (as arrow heads). AT=atrial tachycardia; ECG=electrocardiogram; HR=heart rate; Other abbreviations as in Figure 1.

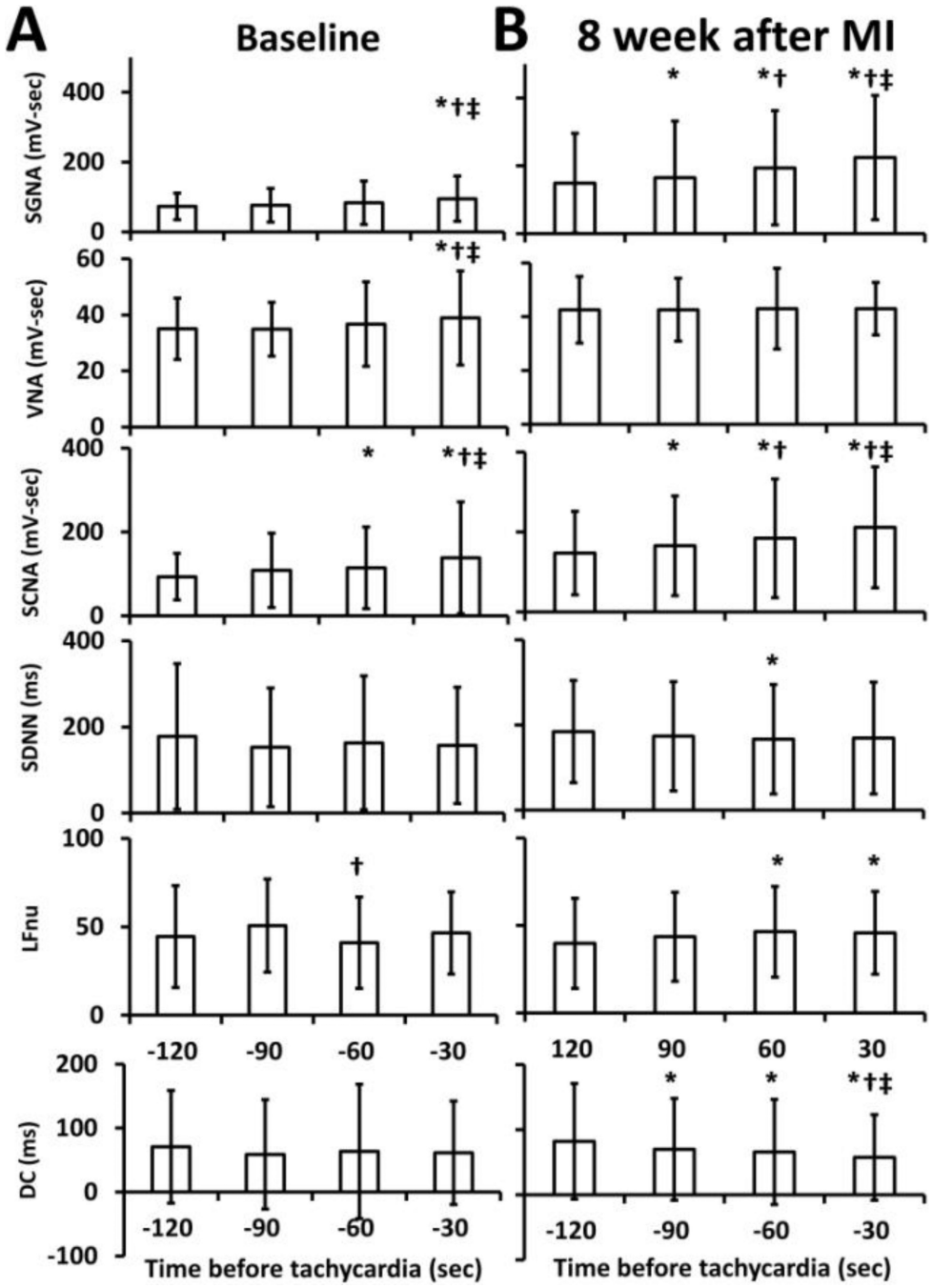

Figure 4. Integrated SGNA, VNA, SCNA, and HRV measures prior to the onset of AT

Progressive increase in both integrated SGNA and integrated SCNA is noted from 30 s intervals measured 120, 90, 60 and 30 s before initiation of AT in 9 dogs at baseline **(A)** and the incremental effects were more obvious at 8 weeks after MI **(B)**. The DC value also showed progressive decrement from 30 s intervals measured 120, 90, 60 and 30 s before initiation of AT in 9 dogs after MI. The abbreviations as in Figure 1 and Figure 3. **P* < .05 vs − 120 s; †*P* < .05 vs − 90 s; ‡*P* < .05 vs − 60 s;.

Table 1

Nerve activity and HRV at baseline and after MI

Variables	Baseline (N=9)	8 week after MI (N=9)	*P* value
SGNA (mv-s)	81±24	151±50	<0.001
VNA (mv-s)	39±11	48±10	0.021
SGNA/VNA ratio	2.2±0.7	3.4±1.5	0.043
SCNA (mv-s)	116±38	165±29	<0.001
RRI (ms)	764±97	781±96	.459
Time domain			
SDNN (ms)	333±79	309±62	.442
RMSSD (ms)	369±87	336±85	.458
pNN50	0.65±0.08	0.63±0.08	.647
Frequency domain			
TP (ln ms^2)	12.2±0.8	11.8±0.7	.324
VLF (ln ms^2)	10.1±0.8	9.8±0.5	.279
LF (ln ms^2)	11.2±0.9	10.6±0.9	.219
HF (ln ms^2)	11.4±0.7	11.2±0.7	.455
LF_{nu}	35.8±7.5	31.7±10.6	.092
HF_{nu}	64.2±7.5	68.3±10.6	.092
LF/HF	0.76±0.26	0.66±0.31	.141
PRSA			
DC (ms)	165±66	160±47	.786
AC (ms)	96±32	93±26	.701

AC=acceleration capacity; DC=deceleration capacity; HF=high frequency; HF_{nu}=high frequency normalized unit; HRV=heart rate variability; LF=low frequency; LF_{nu}=low frequency normalized unit; MI=myocardial infarction; pNN_{50}=the proportion of NN_{50} divided by total number of NNs; PRSA=phase-rectified signal average; RMSSD=root mean square of successive differences; RRI=RR interval; SCNA=subcutaneous nerve activity; SDNN=the standard deviation of normal to normal beat intervals; SGNA=stellate ganglion nerve activity; TP=total power; VLF=very low frequency; VNA=vagal nerve activity.

* $P < .05$ vs baseline.

Table 2

Correlation coefficients among different parameters at baseline and after MI

	Baseline (N=9)		8 week after MI (N=9)	
	vs SGNA	**vs VNA**	**vs SGNA**	**vs VNA**
SCNA	0.73±0.17	0.27±0.19	0.82±0.09	0.29±0.14
Time domain				
SDNN	−0.59±0.18	0.02±0.25	−0.56±0.15	0.11±0.22
RMS	−0.58±0.21	0.02±0.25	−0.59±0.14	0.06±0.21
pNN_{50}	−0.56±0.25	0.08±0.28	−0.59±0.13	0.01±0.21
Frequency domain				
TP	−0.39±0.19	0.03±0.18	−0.36±0.12	0.13±0.22
VLF	−0.12±0.14	0.02±0.12	−0.09±0.15	0.11±0.16
LF	−0.33±0.17	0.01±0.13	−0.26±0.12	0.13±0.22
HF	−0.43±0.19	0.04±0.21	−0.37±0.17	0.08±0.21
LF_{nu}	0.07±0.26	0.04±0.17	0.17±0.26	0.11±0.11
HF_{nu}	−0.07±0.26	0.04±0.17	−0.17±0.26	−0.11±0.11
LF/HF	0.12±0.20	−0.05±0.14	0.09±0.25	0.08±0.11
PRSA				
DC	−0.63±0.18	0.02±0.25	−0.63±0.15	0.15±0.23
AC	0.61±0.18	−0.03±0.25	0.61±0.13	−0.09±0.24

The abbreviations are the same as in Table 1.