International Journal of Gerontology 12 (2018) 271–273

Contents lists available at ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Brief Communication

Heart Rate Variability of a Heart Reviving from Extracorporeal Circulation

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ARTICLE INFO

Article history:
Received 16 May 2017
Received in revised form
10 July 2017
Accepted 2 August 2017
Available online 4 September 2017

Keywords:
complexity,
extracorporeal circulation,
heart rate variability,
multi-scale entropy,
standstill

SUMMARY

Heart rate variability (HRV), analyzed by non-linear methods confer prognostic values. HRV of a heart reviving from extracorporeal circulation (EC) has not been elaborated. We applied Multi-scale entropy (MSE) and Detrended fluctuation analysis (DFA) to study the HRV of patients receiving open-heart surgeries needing EC, during which the heart is standstill. Thirty-four patients were enrolled. ECG was recorded continuously. The analyses were categorized by clinical outcomes. HRV of those without major cardiovascular events (No-MACE) significantly decreased in complexity (4.92 ± 2.80 to 2.94 ± 1.87, $p < 0.001$). Those who suffered post-op MACEs got no changes in all studies of HRV, including MSE and DFA. We postulated that, the decrease of HRV complexity of a heart recovering from EC-induced standstill is probably a vagal-predominant process, implying less stress during the surgery. The absence of such decrement, perhaps a more adrenergic-driven phenomenon, might suggest some unresolved stress. This MSE-derived HRV parameter may be applied in further study of patients recovering from cardiac arrests.

1. Introduction

Heart rate variability (HRV) has been used to assess the activity of autonomic nervous system (ANS). Previous studies have revealed predictive values of HRV in ventricular tachycardia[1], response to therapy[2] and cardiac surgeries[3,4]. Detrended fluctuation analysis (DFA) and Multi-scale entropy (MSE) are sophisticated non-linear analyses.

How does human heart resurrect from standstill? Extracorporeal circulation (EC) renders a controlled environment, in which the heart was standstill during the surgery. We compared the HRV between pre- and post-EC stages, as we hypothesized that peri-op HRV of an EC-assisted open-heart surgery, as an integrated index of systemic and cardiovascular ANS, may confer some clinical interests.

2. Methods

2.1. Patients

This observational cohort study was conducted in the operating theater (OT) of a tertiary-referring center and was approved by the in-house Institutional Reviewer Board (IRB). It also conformed to the 1975 Declaration of Helsinki.

In 3 months, 34 patients of elective open-heart valvular surgery with EC were enrolled. We excluded emergent operations. All enrollee should present their written informed consent before the procedure, either by themselves or by their legitimate delegate.

The electrocardiogram (ECG) was taken as the patient entered the OT, and it continued until the patient left. The endpoints were clinical outcomes: a smooth course (No-MACE) or any major adverse cardiovascular events (MACEs), such as peri-op myocardial infarction (MI), post-op stroke, bleeding necessitating re-open hemostasis, or any resuscitative events during hospital stay.

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http://dx.doi.org/10.1016/j.ijge.2017.08.002

2.2. ECG data acquisition

Continuous ECG was recorded with a sampling rate of 500 Hz by Datex-ohmeda S/Anesthesia Monitor (GE Healthcare®). The duration recording was 2–4.5 h (2.88 ± 0.75 h). It spanned the stage before the EC (pre-EC) and the stage after commencing EC (post-EC). The duration of EC was 1.92 ± 0.67 h, during which the heart was standstill. In other words, the post-EC stage recorded the reviving stage of the heart during and after the wean-off of EC. The signals were translated by the software of Micro-star International (MSI). The algorithm of extracting R-R interval was previously described[5].

2.3. Detrended fluctuation analysis (DFA)

DFA is a non-linear fractal analysis, able to quantify the scaling behavior of a time series and complexity[5]. It requires only 1000 RR intervals to suffice a legitimate DFA. The mathematic basis is illustrated in the literature[5].

The scaling exponents, short term $\alpha 1$ ($\leq$13 beats) and long term $\alpha 2$ were utilized. In a healthy subject, the scaling exponent is approximately 1.0. If totally random, such as white noise or atrial fibrillation, the scaling exponent is 0.5.

2.4. Multi-scale entropy (MSE)

MSE is capable of measuring the real system complexity of the time series[6]. The operation constitutes two main parts: (1) it makes the original time scale into a coarse-grained time series by scale factor, (2) SampEn was calculated in the different time scales. In our study, the RR interval signal was coarse-grained to a scale of 13. The complexity index (CI) was defined as the area under MSE the curve (1–13 scale).

Matlab (2012a, MathWorks®) was adopted to perform DFA/MSE.

2.5. Statistical analysis

The values of $\alpha 1$, $\alpha 2$, and CI were expressed as mean ± standard deviation (SD) and median in parenthesis, and was compared within and between groups of MACEs and No-MACE. Categorical variables were analyzed by Chi-square test (Fisher's exact if number <5). Continuous variables were analyzed by 2-tail *t*-test. Paired Student t-test was applied to the within-group difference of pre- and post-EC stages. $p < 0.05$ was deemed significant. SPSS 12th edition (IBM®) was used.

3. Results

In a period of 3 months, we enrolled 34 patients. The demographics of the enrollee were listed in Table 1. The MACEs included 2 fatalities, 2 re-open surgeries and one peri-op ischemic stroke.

There was no significant difference in basic characteristics. Table 2 illustrated the results of HRV. Before EC, there was no differences between groups (No-MACE vs. MACEs: Pre-EC $\alpha 1$ $p = 0.105$; Pre-EC $\alpha 2$ $p = 0.119$; Pre-EC CI $p = 0.42$).

Regarding DFA, both short term $\alpha 1$ ($p = 0.36$) and long term $\alpha 2$ ($p = 0.47$) did not distinguish between No-MACE and MACEs.

Table 1
Demographics categorized by outcomes.

	No-MACE (n = 29)	MACEs (n = 5)	P-value
Pre-EC			
Age, yr	59 ± 14.1	62.5 ± 3.5	0.36
male/female	24/5	4/1	0.88
DM	5 (17.2%)	1 (20%)	0.88
Hypertension	8 (27.6%)	1 (20%)	0.73
Hyperlipidemia	2 (6.9%)	1 (20%)	0.35
Smoker	3 (10.3%)	1 (20%)	0.54
LVEF%	49.08 ± 14.2	43.1 ± 15.3	0.61
Post-EC time (hr)	1.34 ± 0.49	1.81 ± 0.56	0.07
Post-EC			
Inotrope	29 (100%)	5 (100%)	1.00
Isuprel	4 (13.8%)	1 (20%)	0.72
Pacemaker	5 (17.2%)	1 (20%)	0.54

LVEF: Left ventricular ejection fraction.

Table 2
HRV categorized by outcomes.

	No-MACE (n = 29)		MACEs (n = 5)	
	Pre-EC	Post-EC	Pre-EC	Post-EC
ECG duration (hr)	0.83 ± 0.28	1.33 ± 0.48^{+}	0.89 ± 0.46	1.81 ± 0.55
RR numbers	6689 ± 2609	9855 ± 5548	5809 ± 2462	16638 ± 5131
DFA				
$\alpha 1$	0.741 ± 0.152^{+} (0.704)	0.672 ± 0.105* (0.683)	0.625 ± 0.071^{+} (0.604)	0.652 ± 0.087* (0.630)
$\alpha 2$	0.781 ± 0.118$^{@}$ (0.757)	0.760 ± 0.276$^{\#}$ (0.760)	0.672 ± 0.241$^{@}$ (0.738)	0.898 ± 0.112$^{\#}$ (0.884)
CI (MSE 1–13)	4.92 ± 2.80$^{\%**}$ (4.44)	2.94 ± 1.87$^{\&**}$ (2.74)	7.06 ± 5.25$^{\%}$ (5.57)	4.47 ± 1.03$^{\&}$ (2.62)

** within-group $p < 0.001$.
+,*,@,#,% between-group: no significant differences.
"median" in parentheses.

Referring to complexity index (CI), the CI values in post-EC stage decreased in No-MACE patients (4.92 ± 2.80 to 2.94 ± 1.87, $p < 0.001$), but not in MACEs groups (7.06 ± 5.25 to 4.47 ± 1.03, $p = 0.175$).

4. Discussion

It has been known that conditions, such as aging[6], stroke[5], etc. may cause the loss of complexity. Some authors proposed that high levels of noradrenaline often developed during CABG, and it might result in altered R-R intervals by accentuated sympatho-vagal interactions[3,7]. However, those literature did not address the role of extracorporeal circulation, as CABG nowadays can be performed mostly without EC. Furthermore, there was no knowing how it works from the beginning, resurrection from complete standstill.

The heart was standstill during EC, and regained its electric activities as the weaning of EC commenced. Patients experiencing No-MACE had decreased CI, which may imply that the reviving heart needed less complexity to cope with the prei-op stress. Decreased complexities might be a vagal-predominant phenomenon, meaning less adrenergic-driven. On the contrary, those hearts bearing unchanged complexity may infer some unresolved stress, which demanded more adrenergic drives.

There are some limitations in our study. First, the studied population is small, which disabled further comparisons. The preliminary conclusion should be taken cautiously. Second, the post-EC stage included anesthesia, and its impact on HRV was not addressed.

5. Conclusions

This is a preliminary demonstration of studying the HRV of a heart resurrecting from a controlled standstill. It may be too early to derive any clinical conclusion, but it could become a rudiment to study the post-cardiac- arrest care.

Funding

This research was supported by Center for Dynamical Biomarkers and Translational Medicine, National Central University, Taiwan, and sponsored by the Ministry of Science and Technology (MOST103-2911-I-008-001).

Conflict of interest

All authors have no conflict of interest.

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