Computers in Biology and Medicine 60 (2015) 66–73

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Multifractality in heartbeat dynamics in patients undergoing beating-heart myocardial revascularization

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ARTICLE INFO

Article history:
Received 7 August 2014
Accepted 14 February 2015

Keywords:
Heart rate variability
Autonomic nervous system
Off-pump CABG
Circadian rhythm

ABSTRACT

Background: The multifractal approach of HRV analysis offers new insight into the mechanisms of autonomic modulation of the diseased hearts and has a potential to depict subtle changes in cardiac autonomic nervous control not revealed by conventional linear and non-linear analyses in various conditions like heart failure or stable angina pectoris. The aim of this study was to employ the multifractality approach in cardiac surgery patients and evaluate the multifractality before and after beating-heart myocardial revascularization (off-pump CABG).
Methods: Twenty-four hour Holter recordings were performed pre- and postoperatively in 60 patients undergoing off-pump CABG. Selected conventional time- and frequency-domain linear HRV indices were calculated from the 24 h and 5 min ECG segments, and preselected multifractal parameters $\tau(q=2)$, $\tau(q=3)$, h_top and Δh were determined for daytime (12:00–18:00) and nighttime (00:00–06:00) periods of the ECG recordings using Ivanov's method. Mean differences over time were tested using paired-samples t-test and exact Wilcoxon matched-pairs test. The results are reported as mean ± SD and median with interquartile range. A p value of <0.05 was considered statistically significant.
Results: All selected conventional linear HRV parameters decreased significantly after off pump CABG (p from <0.001–0.015). Preoperatively, multifractal parameter $\tau(q=2)$ was -0.60 ± 0.12 and -0.54 ± 0.12, $\tau(q=3)$ -0.52 ± 0.18 and -0.49 ± 0.17, h_top 0.20 ± 0.07 and 0.15 ± 0.07 and Δh 0.31 ± 0.14 and 0.17 ± 0.14 for daytime and nighttime periods, respectively. Postoperatively, $\tau(q=2)$ and $\tau(q=3)$ were significantly higher for daytime (-0.49 ± 0.15, $p<0.001$ and -0.43 ± 0.23, $p=0.015$), whereas h_top and Δh were significanly higher for both daytime and nighttime (0.25 ± 0.07, $p<0.001$ and 0.19 ± 0.06, $p=0.002$ for h_top and 0.41 ± 0.20, $p=0.003$ and 0.31 ± 0.19, $p<0.001$ for Δh, respectively). All pre- and postoperative parameters, except $\tau(q=2)$ and $\tau(q=3)$ preoperatively, were significantly lower for nighttime as compared to daytime periods.
Conclusions: A significant breakdown of multifractal complexity and anti-correlation behavior with a significant sympathetic overdrive and a concomitant parasympathetic withdrawal occurs after off-pump CABG. The circadian pattern of multifractality regains its day–night variation in the first week after the surgical procedure.

1. Introduction

Heart rate variability (HRV) has been conventionally determined with linear time- and frequency-domain analyses, using spectral and statistical techniques to measure the overall magnitude of R–R interval fluctuations around its mean value or to calculate the magnitude of fluctuations in some predetermined frequencies [1]. Subsequently, recognizing the intrinsic fractal-like features of a human heartbeat, a notable number of nonlinear HRV methods, derived from the mathematics of fractal geometry and confined to second-order linear characteristics, have emerged, assessing the self-similarity of ECG signals by calculating a single correlation exponent and thus delineating the monofractal properties of RR time series [2–5]. However, in 1999 Ivanov et al. have found that a healthy human heart beat displays not only monofractal but also multifractal behavior, which defies the basic mathematical principles of nonlinear methodologies [7,8]. In contrast to homogenous monofractal signals, multifractal signals display such an extraordinary complexity and self-similarity over multiple time and space scales that they cannot be indexed by a single global Hurst exponent. Therefore, a multifractal approach of HRV analysis, utilizing numerous (theoretically countless) local Hurst exponents to fully and adequately characterize the scaling properties of a multifractal signal, was introduced [7,8]. Multifractal methodology

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http://dx.doi.org/10.1016/j.compbiomed.2015.02.012
0010-4825/

possesses the ability to illuminate abnormalities of heart rate behavior in various pathological conditions, not evident with conventional linear and nonlinear HRV techniques. Compared to established HRV methods, multifractal analysis has been shown to be superior in differentiating healthy subjects from patients with congestive heart failure or coronary artery disease [1,7–11]. However, only few attempts have been made so far to evaluate multifractal dynamics in patients undergoing different cardiac procedures such as percutaneous coronary intervention or coronary artery bypass graft (CABG) surgery [12,13]. Using linear and nonlinear HRV approaches by several authors a significantly deranged autonomic modulation with vagal withdrawal and sympathetic predominance was observed following both beating and arrested heart procedures [14,15], however, currently it remains unsettled whether such medical interventions can substantially affect also the multifractal behavior and if doing so, what are the direction and the degree of potential disturbances.

Numerous epidemiological studies are highlighting the existence of a circadian pattern in the onset of adverse cardio- and cerebrovascular events (such as acute myocardial infarction, sudden death, malignant arrhythmias and stroke), which have a peak occurrence rate in the morning hours just after awaking [1,6,16]. Although the exact physiological mechanisms underlying this phenomenon are far from being clearly identified, it is believed, that the transition between the sleep and wake phases is a period of potentially increased neuroautonomic instability because it requires a transition from a more to a less dynamic regulation of the heart [16–18]. Using established nonlinear HRV methods, loss of circadian rhythm in chaotic behavior of RR time series was observed in patients with (un)stable coronary artery disease, heart failure or following myocardial infarction and in survivors of cardiac arrest [1,4,17,19–21]. Furthermore, a growing body of evidence suggests that also multifractal behavior of human heart beat is closely related to control mechanisms that follow the circadian profile. Using multifractal HRV analysis, the majority of authors have implied, that in healthy individuals a higher degree of complexity and stronger anti-correlation with vagal predominance exist during the night (nighttime period), whereas a lesser degree of complexity and a weaker anti-correlation behavior with sympathetic domination occurs during the day (daytime period) [6,16,17,20]. Whether invasive medical or surgical procedures can affect the circadian patterns as assessed my multifractal approach and thus subjecting patients to additional risk by enhancing neurohumoral instability with additionally pronounced transitions between more and less anti-correlated states, remains unveiled [18,21,22].

Our aim in this study was to observe the multifractal behavior of the heart rate dynamics and its circadian pattern in patients undergoing myocardial revascularization on the beating heart (off-pump CABG) whereby cardiac function and autonomic nervous modulation is maintained in surgically less aggressive and more physiological manner.

2. Methods

2.1. Study population

Sixty consecutive patients undergoing off-pump CABG surgery in a single medical center were enrolled in the study. A written informed consent was obtained from all patients prior to the measurements. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki (Finland, 1975) and was approved by Slovenian national human research committee. Inclusion criteria were isolated stable multivessel coronary artery disease, sinus rhythm before the surgical procedure as confirmed by a 12-lead electrocardiographic (ECG) recording and chronic therapy with β-blockers. Exclusion criteria were emergency operation, conversion to on-pump CABG, concomitant valvular disease, any rhythm other than sinus rhythm prior to the procedure or permanent pacemaker, diabetes mellitus with late neurological impairment, kidney, liver, thyroid, systemic or malignant disease, sleeping disorders (including central and obstructive sleep apnea, insomnia, restless legs syndrome, narcolepsy and night terrors), new myocardial infarction within one month and $<95\%$ of pure sinus beats in the recordings. Preoperative clinical data were collected and recorded.

2.2. Operative procedure and postoperative care

Induction of general anesthesia was performed in a standardized manner with fentanyl, midazolam and vencuronium bromide. For maintaining narcosis a continuous infusion of propofol was given. All operations were carried out through median sternotomy on the beating heart without cardiopulmonary bypass by the same surgical team. The details of off-pump CABG surgery have been described in depth elsewhere [23]. After the procedure all patients were transferred to the intensive care unit and continuously monitored for the first four days. Later clinical observation was performed. β-blocker therapy was discontinued on the day of the procedure and continued again postoperatively, guided by hemodynamic criteria but in no patient later than on the third postoperative day.

2.3. Study protocol

24-h Holter recordings were obtained one day before surgery and on the seventh postoperative day by portable three-channel digital recorders (Aspel AsPEKT 702 and Schiller MT-101) with sampling rate of 128-Hz. The subjects were requested not to smoke or drink any caffeinated beverages 24 h prior to measurements. During the Holter data acquisition all patients were hospitalized and accommodated in the surgical ward under continuous medical surveillance. Normal in-hospital bedside activity was allowed from 6:00 to 22:00 and bed rest (i.e. sleeping) was requested from 22:00 to 6:00.

2.4. Data analysis

Digitally collected electrocardiographic data was transferred to a computer and processed with commercially available software (HolCard 24W, Aspel, Poland). The location of the R-wave peak was determined with a resolution of 1 ms through interpolation. Each beat was classified and labeled with the respect to its site of origin using template-matching technique. Later, all events were visually labeled by an experienced observer and corrected, if necessary. Editing eliminated all abnormal beats, including the ones succeeding ventricular or supraventricular ectopic beats without any interpolation attempted for eliminated intervals. To eliminate outliers due to missed beat detections, a moving-window average filter was applied next. For each set of five contiguous NN intervals, a local average was computed excluding the central interval. If the value of the central interval was 20% greater or smaller then the local average, it was considered to be an outlier and replaced by the local average. Finally, HRV analyses were performed only from the RR time series with more than 95% of qualified sinus beats [7]. Time-domain analyses were calculated from the entire 24-h data set, frequency-domain analyses from 5-min segments and multifractal analysis from both daytime (12:00–18:00) and nighttime (0:00–6:00) periods or the ECG recording [1,7].

2.5. Time- and frequency-domain analysis

Time- and frequency-domain analyses included the calculation of conventional and well established HRV parameters.

For time-domain HRV assessment, SDNN (standard deviation of all NN intervals, an estimate of overall HRV), SDANN (standard deviation of the averages of NN intervals in all 5-min segments of