Network representation of cardiac interbeat intervals for monitoring restitution of autonomic control for heart transplant patients.

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Abstract—The aim is to present the ability of a network of transitions as a nonlinear tool providing a graphical representation of a time series. This representation is used for cardiac RR-intervals in follow-up observation of changes in heart rhythm of patients recovering after heart transplant.

Index Terms—heart transplant, heart rate variability, graphical representation

I. INTRODUCTION

The patient’s life is usually endangered before the decision to transplant the heart is taken. On the other hand, in many cases it is amazing how the patient’s organism recovers after heart transplant (HTX) [1].

It is generally believed that the time intervals between subsequent heart contractions (so-called RR-intervals) carry the information about the cardiac control system mainly driven by autonomic nervous system [2]. However, heart transplantation interrupts the possibility of autonomic control over the heart beating. Therefore, heart rate variability (HRV) in patients after HTX is low, regardless of the time elapsed since surgery. It is controversial whether the cardiac reinnervation occurs after HTX [1]. But it is expected that progressive reinnervation sets in and it is a good prognosis for survival.

We believe that the changes that occur in heart rhythm may provide the first signals of the recovery of cardiac control. Furthermore, these signals should be connected with the increasing influence of the sympathetic nervous system. Therefore we hope that observing these changes, with the help of carefully selected tools, we can describe the process of cardiac reinnervation.

The considerable success of the network theory in various fields of research (see, e.g., [3], [4]) motivated us to explore these ideas in the analysis of HRV time series. Tools of the complex networks allow one to resolve important and complementary properties of a dynamical system. For example, it is possible to study spatial dependencies between individual observations instead of temporal correlations. In the following we continue our earlier studies (see [5]) on networks of transitions applied to study recordings of time intervals between subsequent cardiac contractions in patients after HTX.

We will also raise the question whether these transitions build a monotonic sequence of accelerations or decelerations. We are of opinion that sequences of monotonic accelerations or decelerations may indicate response of the cardiac system to some special needs of the organism. Hence, these studies may have a chance to offer additional insights into the emergence of the heart regulatory control.

It must be emphasized that all graphical representations of the discussed networks are produced with the Pajek software package [7].

II. METHODS

A. The patient group

We analyze 24-hour sequences of 23 ECG signals comprising of the intervals between two successive R waves of sinus rhythm. These signals were taken from 11 patients recovering after heart transplantation in the First Cardiology Clinic of Gdańsk Medical University. The recordings were taken from the same patients within different periods after surgery. Therefore, we have 3 recording from two patients, 2 recordings from 8 patients and 1 recording from one patient. We considered signals taken from two weeks to 38 months after HTX.

From each RR-signal we have carefully selected a sequence of 15,500 points corresponding to nocturnal rest of a patient. There are two reasons why we investigate the nocturnal heart rhythm. The first one is that during the sleep the central nervous system is less dependent on the patient’s intentions, and therefore we may have a more direct insight into reflexes regulating the cardiac rhythm. Moreover, the nocturnal recordings appear to be less perturbed by artifacts what enables us to study sufficiently long and consistent signals.

To avoid influence of artifacts (errors in detecting the R-wave) the consecutive RR-intervals were thoroughly reviewed. The parts, which consist of at least 500 normal-to-normal intervals, were identified. If two such parts were separated by artifacts or ectopic beats of the length smaller than 10, then the gap was edited manually. To preserve time chronology, the corresponding RR-intervals were interpolated by the value of median from the last normal-to-normal seven events. Additionally, the value of median was confronted with the total length of the edited gap.

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B. Network representation of RR-signal

In general, the construction of the transition network is based on the concept of phase space. The phase space represents all possible values of studied dynamical system partitioned into mutually disjoint sets. Since the recorded values of RR-intervals have well-separated magnitudes then partitioning of the value space of RR-intervals is natural. Assuming these values as vertices of a network, we represent each pair of consecutive in time RR-intervals as a transition between these vertices.

| RR series: | Phase space: |
|------------|--------------|
| t | 820 | v |
| i | 830 | a |
| m | 840 | l |
| e | 850 | u |
| n | 860 | e |
| e | 870 | n |
| i | 880 | e |
| n | 890 | o |
| e | 900 | h |
| o | 910 | r |
| r | 920 | s |
| s | 930 | t |
| s | 940 | u |

Fig. 1. Construction of a network from a time series. Left: space values from a time series discretized at \( \Delta = 10 \text{ms} \). Right: a time series as a path on a network of values of phase space.

More precisely, the \( N \) values of a recording with RR-intervals \( \{RR_1, RR_2, \ldots, RR_N\} \) are uniformly discretized (rounded) with accuracy \( \Delta = 10 \text{ms} \). Then, in order to determine the phase space, a set of ordered distinct values \( RR_{MIN} = RR(1) < RR(2) < \ldots < RR(K) = RR_{MAX} \) is extracted. These \( K \) different values label different vertices in the network. This is depicted in Fig. 1 left where the first column gives the sequence of RR intervals (already discretized), the second column gives the ordered values from \( RR_{MIN} \) to \( RR_{MAX} \), thus constituting the phase space of the signal. The right panel shows the studied time series as a transition network. Here, the labels of vertices correspond to values from the phase space. Vertices are arranged from \( RR_{MIN} \) (top) to \( RR_{MAX} \) (bottom). An arrow between two vertices is plotted if the corresponding two RR-intervals represent a pair of the consecutive values in the time series.

It appears that neighbors in time are often also neighbors in values what results that the transition network takes the linear shape. But to improve the visualization of the transition properties we propose a ladder presentation of the network. Namely, vertices are placed alternatively in the left and right columns.

Moreover, to classify differences among the transitions we use the following coloring scheme:

- no change in the value, i.e., \( RR_i = RR_{i+1} \) : violet;
- to a nearest neighbor, i.e., \( |RR_i - RR_{i+1}| = \Delta \) : green;
- to a next neighbor, i.e., \( |RR_i - RR_{i+1}| = 2\Delta \) : blue;
- to a second neighbor, i.e., \( |RR_i - RR_{i+1}| = 3\Delta \) : red;
- to other neighbors, i.e., \( |RR_i - RR_{i+1}| > 3\Delta \) : black.

Fig. 2 shows two transition networks obtained for a patient called loj. The left network represents heart rhythm after 4 months elapsed after HTX, the right one 34 months later. The important message of this example is that when the time after HTX increases the number of transitions other than to nearest neighbors also increases (in the right panel there are more red and black arrows). We believe that it is a good symptom.

It should be explained that widths of the transition arrows in Fig. 2 and all further network plots are determined by logarithms of the frequencies of particular transitions.

Study of the transitions between RR-intervals can be compared to investigations of RR increments – the popular measure of HRV. However, the adopted scheme additionally serves as a classification with respect to the size of increments. Therefore, due to the network representation we learn not only what kind of increments dominates in a signal but also when these events take place.

III. RESULTS

A. Group study: healthy versus patients after HTX

The classification of transitions scheme introduced in Sec. II.B leads to clear distinction between the heart rhythm of healthy individuals and those of people after HTX. This is shown in Fig. 3. For example, the transitions to the second and farther neighbors, in the case of healthy young persons, occur with probability 0.5 (upper part of the left bar), while in case of people after HTX these events are quite rare.

The majority of transitions in patients after HTX can be described as no change events. Moreover the deceler-
Fig. 3. Distributions of changes in consecutive RR-intervals for healthy young people (of age: 18–26, 21 women and 14 men) and the group of considered patients after HTX. Abbreviations \textit{acc} and \textit{dcc} refer to acceleration and deceleration. For other details, see the main text.

Fig. 4. Probability to find a given type of transition in a signal for different patients after HTX: \textit{top} – no change or transitions to nearest neighbors; \textit{bottom} – transitions to the next neighbors.

B. Transitions in individuals

Statistics of one-step mono-transitions found for each recording separately are presented in Fig. 4. They are compared to the corresponding values calculated for young, healthy young persons (the first entry on horizontal axis).

The first observation from Fig. 4 top is that plotted values seem to be independent of the time elapsed after the HTX. As already observed, the no-change or transitions to the nearest neighbor dominate. It means that almost all increments are less than 10 ms. The transitions to the next-neighbors shown in Fig. 4 bottom (the increments are greater than 10 ms but lower than 20 ms) do not provide any regular picture. Moreover also differences between number of accelerations and decelerations are statistically not significant. However, concentrating on characteristics for each patient individually, we get hints whether the changes are evolving towards the healthy people characteristics or not.

The results obtained for the carefully selected two-step mono-transitions are reported in Fig. 5. We classified the monotonic changes with respect to the total size of the transition. Namely, the consecutive three RR-intervals \(RR_i\), \(RR_{i+1}\) and \(RR_{i+2}\) are quantified as:

- double loop:  \(RR_i = RR_{i+1} = RR_{i+2}\);
- slow deceleration:  \(RR_i < RR_{i+1} < RR_{i+2}\) and \(|RR_{i+2} - RR_i| = 2\Delta\);
- mid deceleration:  \(RR_i < RR_{i+1} < RR_{i+2}\) and \(|RR_{i+2} - RR_i| = 3\) or \(4\Delta\).

The classification of the corresponding acceleration events goes with the changed directions of the above inequalities.

Probabilities of the occurrence of such two-step mono-transitions, shown in Fig. 5, are ordered with respect to the patient name, and restricted to recordings from patients being less than about 12 months after the surgery. This ordering helps to track alternations in the cardiac rhythm in the particular patient. The entry corresponding to healthy young people is added for comparison. Note that the plots are in log-scale.

The data presented in Figs 4 and 5 give a total picture of changes in heart rhythm of a patient. Both analysis: one-step mono-transitions and two-step mono-transitions may be useful in assessing the progress of patient’s recovery, and possibly to produce an alarming signal that the progress is not satisfactory.

For example, Figs 4 and 5 does not provide the clear picture for the direction of changes of patients \textit{daw} and \textit{boc}. Therefore, via the network presentation we get the eye catching and easily readable additional information on quality and quantity of changes. In Figs 6, 7 we present network representation for these two patients.

The networks of \textit{daw} patient (Fig. 6) show the rhythm after 1 and 2 months after surgery. We see that networks are quite similar, what indicates that the picture is stable. On the other hand, the networks obtained for \textit{boc} patient (Fig. 7) show gradual simplification of the cardiac rhythm structure. It is worth noting that our predictions based on the analysis of the constructed networks (Figs 6 and 7) coincide with the clinical
Fig. 5. Log plots of the probability to observe double loop, slow (top) and mid (bottom) transitions in signals of patients after HTX. To observe restitution of cardiac control in a patient, the results are collected by a patient name. In the case of sit patient after a month after HTX no mid transitions occur.

Fig. 6. Networks for daw patient obtained from signals recorded after 1 and 2 months after HTX. Transitions with probability less than 0.1% are omitted but all vertices which correspond to all recorded RR-intervals are plotted. The widths of arrows represent logarithms of counts of the particular transitions.

Fig. 7. Networks for boc patient obtained from signals recorded after 2 and 6 months after HTX.

state of these two patients.

IV. CONCLUSIONS

The network of transitions provides yet another way to assess the heart rhythm. It appears that RR-series leads to the transition network with the specific shape. Therefore one can classify typical properties of these networks, and then construct a measure of heart rhythm changes. The network representation, first of all, offers a total assessment of increments between the consecutive RR-intervals by quantifications and qualification of their values. Additionally, it gives the eye-catching picture of RR-intervals as a map from which one can read at what RR-interval and how frequently the particular increase occur. In this work we used this approach to observe the restitution of cardiac control in patients after heart transplantation.

The arguments supporting the decision to perform HTX were different for each patient. The clinical state of every patient was specific and, therefore, each time series should be analyzed individually, and also the progress in the process of the acceptance of the graft had to be evaluated for each patient separately. This evaluation was attempted due to quantification and classification of transitions in the phase space of his/her RR-intervals. We propose to interpret the alternations in the number of particular type transitions, here towards corresponding values found in the healthy people rhythms, in the prognosis for individual patient. Moreover, since sequences of accelerations and decelerations of heart rate are considered as a sign of autonomic control [6], then consecutive intervals with fixed acceleration or deceleration rates give us additional insights into the activity of the control mechanisms.

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