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CONTRIBUTION OF RECURRENCE GRAPHS IN THE PROGNOSTIC ASSESSMENT OF INTENSIVE CARE UNIT PATIENTS

CONTRIBUIÇÃO DOS GRÁFICOS DE RECORRÊNCIA NA AVALIAÇÃO PROGNÓSTICA DE PACIENTES DE UNIDADE DE TERAPIA INTENSIVA

CONTRIBUCIÓN DE LOS GRÁFICOS DE RECURRENCIA EN LA EVALUACIÓN PRONÓSTICA DE PACIENTES EN LA UNIDAD DE CUIDADOS INTENSIVOS

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ABSTRACT

This study evaluated heart rate variability (HRV) in patients admitted to an intensive care unit using recurrence graphs. This is a quantitative, qualitative, prospective, and longitudinal study and the selected patients were divided into a group of survivors and a group of deaths. Time series of heartbeats were used with the Polar Advanced RS800CX frequency meter, for 30 minutes. The analysis of the recurrence data used the following selected parameters: dimension = 2, delay = 2, radius = 70, line = 2, and Volcano as the color scheme. The classic variables of the recurrence charts were selected: ApEn, SamPEn, Alpha 1, % Recurrence, Det%, Laminarity, TT, and LDmax. Continuous quantitative variables with Gaussian distribution were analyzed using Fisher's exact test and unpaired Student's t-test, with p values < 0.05 being considered significant. Heart rate time series data were filtered and subsequently analyzed using Kubios HRV Analysis software and Visual Recurrence Analysis software. A total of 92 patients were studied, with the group of deaths comprising 32 patients and the group of survivors comprising 60. There was no significant difference in the quantitative aspect and in the qualitative analysis of the recurrence graphs, geometric patterns, and a greater number of “dark rectangles” were demonstrated, indicating greater linearity (greater impairment of homeostasis). HRV analysis with the aid of recurrence charts allowed the differentiation of health states and could act as a marker of severity and probable death.

KEYWORDS: Intensive care unit. Heart rate variability. Linear domain. Non-linear domain. Autonomic nervous system.

RESUMO

Este trabalho avaliou a variabilidade da frequência cardíaca (VFC) em pacientes internados em unidade de terapia intensiva com auxílio de gráficos de recorrência. Trata-se de um estudo quantitativo, qualitativo, prospectivo e longitudinal e os pacientes selecionados foram divididos em grupo de sobreviventes e grupo de óbitos. Foram utilizadas séries temporais de batimentos cardíacos com o frequencímetro *Polar Advanced RS800CX*, por 30 minutos. A análise dos dados de recorrência utilizou-se dos seguintes parâmetros selecionados: dimensão = 2, atraso = 2, raio = 70, linha = 2 e como esquema de cores o *Volcano.* Foram selecionadas as variáveis clássicas dos gráficos de recorrência, sendo: *ApEn, SamPEn, Alfa 1, % Recurrence, Det%, Laminaridade, TT e LDmax*. As variáveis quantitativas contínuas com distribuição gaussiana, foram analisadas com auxílio do teste exato de Fischer e *Test t Student* não pareado, sendo considerados significantes os valores de p < 0,05. Os dados de séries temporais de batimentos cardíacos foram filtrados e posteriormente analisados com o *software Kubios HRV Analysis* e o *software Visual Recurrence Analysis*. Foram estudados 92 pacientes, sendo o grupo de óbitos composto por 32 pacientes e o grupo de sobreviventes por 60. Não houve diferença significativa no aspecto quantitativo e na análise qualitativa dos gráficos de recorrência, foi

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demonstrado padrões geométricos e maior quantidade de “retângulos escuros”, indicando maior linearidade (maior comprometimento da homeostase). A análise da VFC com o auxílio dos gráficos de recorrência permitiu a diferenciação dos estados de saúde, podendo atuar como um marcador de gravidade e provável morte.

PALAVRAS-CHAVE: Unidade de terapia intensiva. Variabilidade da frequência cardíaca. Domínio linear. Domínio não linear. Sistema nervoso autônomo.

RESUMEN
Este estudio evaluó la variabilidad de la frecuencia cardíaca (VFC) en pacientes ingresados en la unidad de cuidados intensivos con la ayuda de gráficos de recurrencia. Se trata de un estudio cuantitativo, cualitativo, prospectivo y longitudinal y los pacientes seleccionados se dividieron en grupo de supervivientes y grupo de muerte. Se utilizaron series temporales de latidos con el medidor de frecuencia RS800CX de Polar Advanced durante 30 minutos. El análisis de los datos de recurrencia utilizó los siguientes parámetros seleccionados: dimensión = 2, retraso = 2, radio = 70, línea = 2 y como esquema de color el Volcán. Se seleccionaron las variables clásicas de las gráficas de recurrencia: ApEn, SamPEn, Alfa 1, % Recurrencia, Det%, Laminaridad, TT y LDmax. Las variables cuantitativas continuas con distribución gaussiana se analizaron con la ayuda de la prueba exacta de Fischer y la prueba t de Student no pareada, y los valores de $p < 0,05$ se consideraron significativos. Los datos de la serie temporal de latidos del corazón se filtraron y luego se analizaron con el software Kubios HRV Analysis y el software Visual Recurrence Analysis. Se estudiaron un total de 92 pacientes, con 32 pacientes y 60 supervivientes. No hubo diferencia significativa en el aspecto cuantitativo y en el análisis cualitativo de los gráficos de recurrencia, se demostraron patrones geométricos y un mayor número de "rectángulos oscuros", indicando mayor linealidad (mayor deterioro de la homeostasis). El análisis de la VFC con la ayuda de gráficos de recurrencia permitió la diferenciación de los estados de salud, que pueden actuar como un marcador de gravedad y muerte probable.

PALABRAS CLAVE: Unidad de cuidados intensivos. Variabilidad de la frecuencia cardíaca. Dominio lineal. Dominio no lineal. Sistema nervioso autónomo.

INTRODUCTION

The Intensive Care Unit (ICU) was designed based on the actions of Florence Nightingale. During the Crimean War, in 1853, soldiers died due to precarious conditions, but the mortality rate was reduced with more complex and specialized care interventions, that is, they were classified according to the state of severity, where the most serious ones were monitored to be continued. The basic objective of the Intensive Care Unit is to recover or support the vital functions of patients (BORSON, 2021).

Thus, the ICUs are intended for the care of high-risk patients, performing uninterrupted assistance from a multidisciplinary team with specific equipment. These units demand increasing costs, requiring accurate data on the severity and prognosis of patients, enabling interventions by the health team, both for assistance and resource planning (MAGALHÃES, 2021; CIAMPONE, 2006).

According to Souza (2019), knowledge of established parameters in different clinical states is definitive for decision-making. These parameters have provoked continuous discussions regarding therapeutic investments related to costs and without transgressing the ethics of equal care, which patients these investments should be used in the face of reduced prospects of survival or decreased quality of life after hospital discharge unit. Thus, defining a prognostic marker in this scenario is of paramount importance (NOGUEIRA, 2012).

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HEART RATE VARIABILITY

The Autonomic Nervous System (ANS) exerts influence on various organs, devices, and systems of the human body. This system plays an important role in regulating physiological processes both under normal and pathological conditions and is essential for maintaining the internal physiological balance and the body's interaction with the environment. The ANS supplies afferent and efferent nerves to the heart in the form of sympathetic endings throughout the myocardium and parasympathetic to the sinus node, atrial myocardium and atrioventricular node (TAKAKURA, 2013).

The autonomic nervous system regulates heart rate through sympathetic and parasympathetic responses to different stimuli. A decrease in Heart Rate Variability (HRV) is a marker of reduced parasympathetic tone and increased sympathetic tone, long thought to have a negative impact on the prognosis of cardiovascular disease (HUIKURI, 2013).

Second Godoy (2019) the human body is a complex system, its behavior is typically non-linear or deterministic in the short term and has low predictability in the long term. HRV has been considered an effective marker of the presence or absence of adequate homeostasis (VANDERLEI, 2009). Recurrence charts are useful for assessing the autonomic nervous system, as they allow for quantifying and qualifying HRV (NAYAK, 2018; MARWAN, 2002).

Marwan (2007) describes that recurrence is a fundamental property of many dynamical systems, hence of many processes in nature. In phase space, recurrence can be described by recurrence graphs (Recurrence Plot, RPs). For the construction of Recurrence Graphs, a time series is needed that is generated by an experiment or by numerical simulations carried out on a computer. Recurrence Graphs are highly effective and widely accepted methods as tools for investigating time series, being restricted to a series of a single dimension or path over time (GODOY, 2011).

To build, we have a square, in this, the x-axis as the y-axis contains the elements of the time series arranged sequentially. Starting from this, according to the pre-established values, size of measurement intervals (dimension), and distances (radius), it is verified whether there is a recurrence of values (GATTI, 2015).

Recurrence quantification measures are considered important methods for describing and analyzing complex systems (MARWAN; KURTHS, 2007). The measures used are the Recurrence Rate (RR), which corresponds to the probability of a state occurring in phase space (MARWAN, 2003); If the recurrence rate values are high, they are specific to states with a high probability of recurrence; low values indicate less likelihood of recurrence (MARWAN; KURTHS, 2004).

Recurrence graphs can be interpreted visually and by quantitative analysis of recurrence in phase space (GATTI, 2015). According to Marwan et al., (2002), the qualitative evaluation of recurrence graphs has a presentation with homogeneity of colors, and more geometric patterns, called “big dark rectangles” in cases with decreased autonomic activity.

Thus, the objective of this study was to evaluate the HRV in patients admitted to the ICU for different diagnoses, considering changes in the clinical status and their respective autonomic alterations,

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with the aid of recurrence graphs. Quantitatively and qualitatively demonstrate the higher probability of death and/or worse prognosis in a short period.

METHOD

The research carried out was quantitative and qualitative, longitudinal, and prospective. The sample was selected for convenience. Adult male and female patients hospitalized for different diagnoses in an Intensive Care Unit of a Teaching Hospital in the interior of the State of São Paulo were studied after signing an informed consent form. As exclusion criteria were patients diagnosed with cardiac arrhythmias of non-sinus rhythms, use of pacemakers and/or defibrillators, minors, and refusal to participate in the study. The study was approved by the Research Ethics Committee of the Faculty of Medicine of *São José do Rio Preto* with an opinion embodied in CAAE number 89505218.4.0000.5415.

For clinical data collection, a questionnaire was used with data from the medical records (diagnosis, comorbidities, age, gender, ethnicity, vital signs, length of stay, and type of discharge). Patients were studied for analysis of intercurrences until the day of hospital discharge and/or death.

To obtain cardiac data and HRV analysis in the time, frequency, and non-linear domains (chaos), an electrocardiographic record was used for 30 minutes with the aid of the Polar Advanced RS800CX equipment. This equipment consists of a transmitter module coupled to a belt and a watch, where the time series is stored for later analysis of the R-R intervals. The recordings were performed with the monitoring of the responsible researcher, with the individual in the ICU bed, in the supine position with the hands resting beside the body. The transmitter module and the watch were positioned on the xiphoid process and on the wrist, respectively. The results of the variables were analyzed along with the clinical profile data of each patient. Patients were divided into two groups: a group of survivors and a group of deaths.

Time series of heartbeats were used for about 30 minutes. Recurrence data analysis was performed using parameters selected according to the method validated by Iwanski and Bradley (1998): dimension = 2, delay = 2, radius = 70, line = 2, and Volcano as the color scheme. The classic variables of the recurrence charts were selected.

Continuous quantitative variables with Gaussian distribution were analyzed using Fisher's exact test and unpaired Student's t-test. An alpha error of 5% was admitted, p values < 0.05 being considered significant. Statistical analyzes were performed using Stats Direct Statistical Software version 3.3.3 (07/20/20).

Heart rate time series data were filtered and subsequently analyzed using the Kubios HRV Analysis software. Visual Recurrence Analysis software (VRA - Version 5.01, Eugene Kononov, http://visual-recurrence-analysis.software.informer.com) was used.

The graphic characterization was done with Box-Plot graphics. In the qualitative analysis, the appearance of evident geometric patterns and a greater number of “dark squares” indicate greater linearity and, therefore, greater impairment of homeostasis.

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RESULTS

A total of 92 patients were studied, where the group of deaths consisted of 32 patients with a mean age of 66.9 years, with a predominance of males (68.8%). The group of survivors consisted of 60 patients with a mean age of 59.6 years, with a predominance of females, representing 56.7%. The mean length of stay was not significantly different between groups.

Among the comorbidities presented by the groups, smoking appears more prevalent in the group of deaths (50%) compared to the group of survivors (18.3%). In the group of deaths, 68.8% were hypertensive and 25% had Diabetes Mellitus and more deaths occurred in patients on mechanical ventilation (78.1%).

After constructing and evaluating the quantitative aspects in the comparative analysis of time series based on heart rate variability, it was not possible to verify significant differences in any of the analyzed variables when the groups were compared to each other (p-value > 0.05).

After constructing and evaluating the qualitative aspects of the Recurrence Graphs in the comparative analysis of time series based on heart rate variability, significant differences were observed in the qualitative analysis when comparing the groups. In the group of deaths, there was a predominance of geometric shapes, a greater number of dark squares, and a homogeneity of colors **(Figure 1)**, in relation to the group of survivors **(Figure 2)**. To present the graphic analysis, 12 patients from each group were randomly selected.

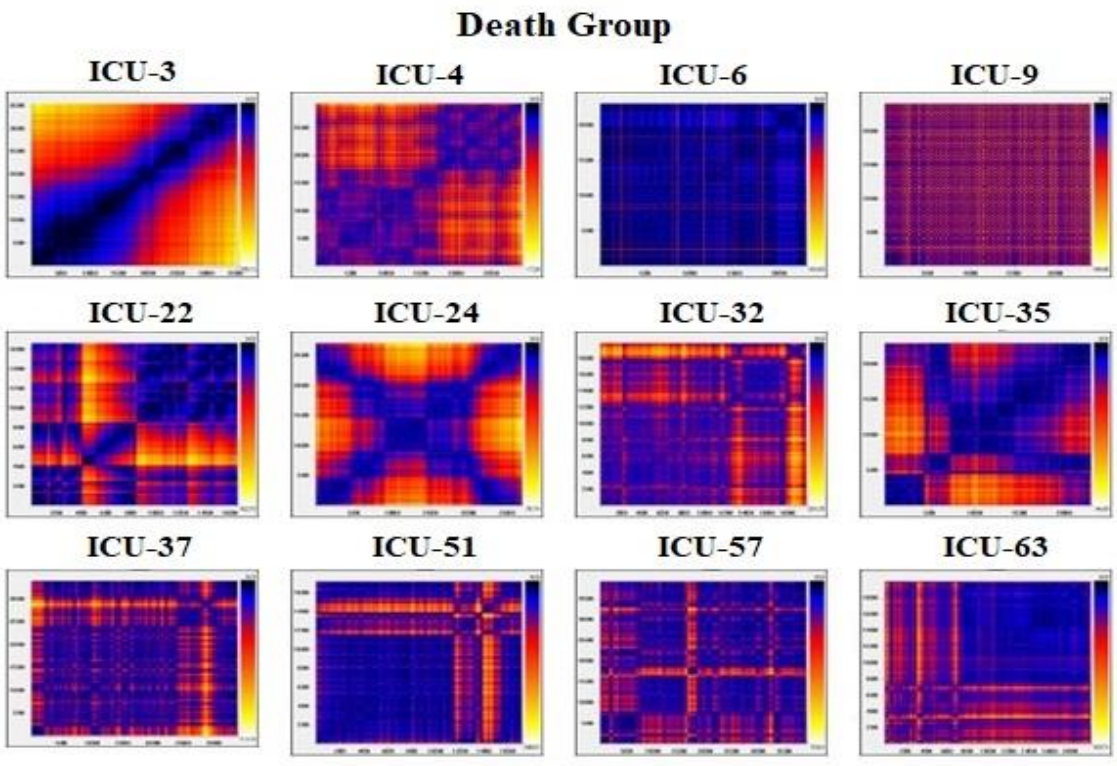

Figure 1: Visual analysis of the Recurrence Graphs (Volcano Schema) of 12 individuals from the death group.

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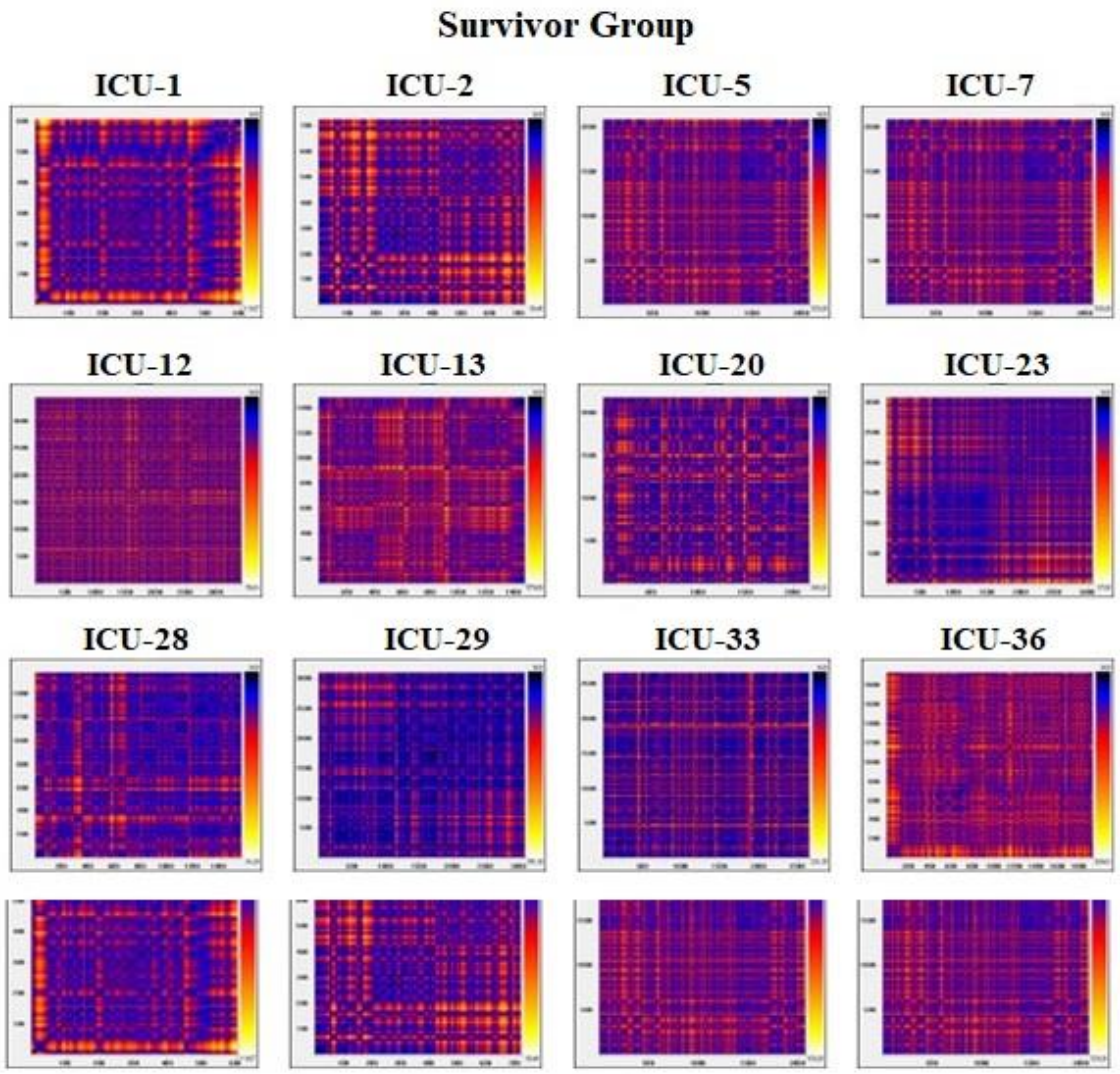

Figure 2: Visual analysis of the Recurrence Graphs (Volcano Schema) of 12 individuals from the survivor group.

DISCUSSION

In this study, it was evidenced that the Heart Rate Variability analyzed with the aid of the Recurrence Graphs allows the identification of individuals with a higher probability of death and/or worse prognosis in the short term. This finding supports the hypothesis that changes in HRV patterns demonstrate that the decrease in cardiac autonomic function is significantly greater in the group of deaths compared to the group of survivors, there is a predominance of geometric shapes and greater homogeneity of colors in the Charts of Recurrence, indicating a decrease in parasympathetic activity, as well as a predominance of sympathetic tonus in patients with the outcome of death. The analysis of the severity of pathological conditions through Recurrence Graphs proves to be very effective, as they are simple and effective tools for analyzing data in a time series of a system under study (BIANCHI, 2016). The methods in question are established to detect transitions in system dynamics, as well as to

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predict the behavior of biological systems (ECKMANN, 1995). In addition, graphs are also an excellent method of analyzing oscillations in the intervals between two consecutive beats, showing them as characteristics of each individual (GODOY; GREGÓRIO, 2019).

Godoy and Gregório (2019) characterizing health, disease, or death in humans using recurrence graphs, demonstrated that the quantitative and qualitative aspects allow the differentiation between states of health, advanced disease, and imminent death throughout the life cycle. In this research, these alterations were not evidenced in the quantitative analysis, however, the qualitative analysis of the graphs produced similar results. In the group of deaths, there was a predominance of geometric patterns and the dominance of dark squares, demonstrating greater linearity, greater dysfunction of the autonomic nervous system, and, consequently, an indicator of death.

Research related to a study based on the analysis of the RR interval signal obtained from the electrocardiogram and, with the construction of graphs of recurrences, sought to establish a predictor of an episode of paroxysmal atrial fibrillation (AF). The qualitative assessment of the recurrence charts was similar to the patterns we observed across groups. A more homogeneous pattern was observed in the electrocardiogram segments before paroxysmal AF and more heterogeneous in the distant segments of paroxysmal AF, demonstrating that there is greater linearity (less chaotic pattern) before arrhythmia episodes (MOHEBBI, 2011). Arrhythmias are considered important mortality factors, so we can associate the predominant geometric patterns and homogeneity in the group of deaths with greater worsening of autonomic control and, consequently, greater severity and death outcome.

Takakura et al., (2013) seeking to verify the behavior of HRV after heart transplantation with Recurrence Charts, used charts constructed with the time series of heart transplant patients with time series charts of mathematical models (random, chaotic, periodic, and linear) and clinical models (young adult, child, premature newborn and patient with brain death), there was a similarity between the patients in the postoperative period of the most recent heart transplantation with the linear mathematical model and the clinical model of a patient with brain death. In patients in the postoperative period of late heart transplantation, a periodic tendency to chaotic mathematical models and clinical models of newborns or premature children was observed. The evolutionary qualitative analysis of the recurrence of the graphs tends to a linear pattern, or to training patterns on repetitive color characteristics, less diffuse and more homogeneous when there is low variability and less time elapsed from the transplant. On the other hand, with the longer time elapsed after transplantation, there was a clear tendency to present a more diffuse pattern of color heterogeneity, suggesting a change in the linear reduction of meaning and, the physiologically, partial return of autonomic control.

These results are similar to those found in the analysis between the groups of deaths and the group of survivors, where more diffuse patterns of heterogeneity predominate in the survivor group (improvement in the clinical picture) and a predominance of geometric shapes and linearity characteristics in the group of deaths, demonstrating the greater deterioration of the autonomic nervous system in these patients and consequent death.

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The increased autonomic dysfunction of patients in the death group probably occurs in response to long-standing chronic comorbidities. The underlying diseases found in patients directly interfere with the balance to maintain the homeostasis of systems functioning.

It appears that the qualitative evaluation of the Recurrence Graphs has a potential role as prognostic markers in the face of the occurrence of death. In the analysis comparing the groups of deaths and survivors, we showed that there is less action of the autonomic nervous system in the group of deaths, demonstrated by greater linearity in the recurrence graphs, indicating greater homeostatic impairment in these patients.

Nursing care in the Intensive Care Unit is developed by complex care activities, which require technical and scientific competence and immediate decision-making (SILVA, 2021), thus, it is believed that this research collaborates with the validation of a non-invasive, low-cost, and efficient method easy to interpret both for the nursing team and for the multidisciplinary team in decision-making regarding the management and therapeutic approaches of critically ill patients. Some limitations should be pointed out, such as the cross-sectional nature of the study, which made it impossible to follow up with the individuals for a longer period, not allowing us to know whether the surviving group would deteriorate in the long term. However, considering the small number of studies with this population using qualitative methods, new research should be encouraged, so that more information can be disseminated about this method in other age groups and populations.

CONCLUSION

It is concluded that HRV analysis with the aid of Recurrence Graphs allows short-term differentiation in identifying severity and/or death in ICU patients and may act as an early marker of injuries in these patients. Because it is a resource with visual interpretation and easy to differentiate, it can act in an important way in the management of critically ill patients for risk stratification and monitoring of therapeutic procedures.

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