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Recurrence plots for the assessment of patient-ventilator interactions quality during invasive mechanical ventilation

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Inappropriate patient-ventilator interactions’ (PVI) quality is associated with adverse clinical consequences, such as patient anxiety/fear and increased need of sedative and paralytic agents. Thus, technological devices/tools to support the recognition and monitoring of different PVI quality are of great interest. In the present study, we investigate two tools based on a recent landmark study which applied recurrence plots (RPs) and recurrence quantification analysis (RQA) techniques in non-invasive mechanical ventilation. Our interest is in how this approach could be a daily part of critical care professionals’ routine (which are not familiar with dynamical systems theory methods and concepts). Two representative time series of three typical PVI “scenarios” were selected from 6 critically ill patients subjected to invasive mechanical ventilation. First, both the (i) main signatures in RPs and the (ii) respective signals that provide the most (visually) discriminant RPs were identified. This allows one to propose a visual identification protocol for PVIs’ quality through the RPs’ overall aspect. Support for the effectiveness of this visual based assessment tool is given by a RQA-based assessment tool. A statistical analysis shows that both the recurrence rate and the Shannon entropy are able to identify the selected PVI scenarios. It is then expected that the development of an objective method can reliably identify PVI quality, where the results corroborate the potential of RPs/RQA in the field of respiratory pattern analysis. Published by AIP Publishing. https://doi.org/10.1063/1.5020371

A mechanical ventilator is a device that replaces or assists the function of the inspiratory muscles. In these two different ventilation strategies (controlled and assisted), an appropriate quality of the patient-ventilator interaction (PVI) is desirable, which means the matching between the intrinsic rhythms of both the ventilator pressure/flow delivery and the patient effort. The lack of such synchronization, commonly due to an inappropriate setting, can occur and is associated with adverse clinical consequences. Despite the modern technology developed for mechanical ventilators, poor PVI quality still occurs in up to 25% of ventilated patients in intensive care units. Here we investigate the use of recurrence plots as a potential graphical tool for identification of PVI quality in invasive mechanical ventilation. The motivation is to investigate the potential of alternative tools for health care professionals without training in nonlinear dynamics.

I. INTRODUCTION

Appropriate patient-ventilator interactions’ (PVI) quality, which means a prompt response of the ventilators timing and pressure/flow delivery to patient effort,1 is a necessary condition in order to avoid harmful clinical consequences such as patient discomfort, anxiety/fear, increased need of sedative and paralytic agents, and prolongation of mechanical ventilation.2,3 It is achieved through a proper setting of the mechanical ventilator sensitivity to patient inspiratory effort, by knowledge of the actual (i.e., current) PVI quality. One possibility for assessing PVI quality is to use specific invasive measurements (i.e., esophageal balloon catheter, phrenic neurogram, diaphragmatic electrical activity), very uncommon in the clinical routine due to the invasiveness of the measurement or the need of specific dedicated hardware/know-how.4 Another possibility is a careful observation of the patients’ physical signs (e.g., timing and magnitude of respiratory muscles activity) in the respiratory waveforms provided by the ventilator, such as airflow and airway pressure.5 Both approaches would require the critical care professional to constantly monitor the waveforms of the measured signals to detect the occurrence of poor PVI, which is impracticable in a clinical scenario, and prone to errors due to subjectivity. Indeed, almost one quarter of all worldwide ventilated patients (in intensive care units) are under a poor PVI quality condition.5–7 Consequently, several algorithms have been proposed to detect and classify PVI quality.4,8

A promising approach is based on recurrence plots (RPs), a technique initially designed to graphically display recurring patterns and non-stationarity in time series,9 and their respective quantification analysis (RQA).10 Due to no rigid constraints on data set size, stationarity, or statistical distribution,
recurrence plots have been increasingly used for investigating various biological systems. Specifically, in the cardiorespiratory system field, different studies suggested the RPs/RQA as useful tools for heart rate variability analysis and for characterization of breathing patterns in several conditions.\textsuperscript{11–16}

A relevant result and paradigmatic approach for the assessment of PVI quality was presented by Rabarimanontsoa et al. (2007).\textsuperscript{11} The authors argued that (i) the RPs provided a global view of the difference in PVI quality with/without the use of an antibacterial filter during non-invasive mechanical ventilation and that (ii) their respective quantification through the RQA’s Shannon entropy\textsuperscript{17} provided a measure of the rate of asynchronism and breathing rhythm. As well, it was shown that (iii) the RQA’s Shannon entropy computed with the discrete time series obtained from a Poincaré section provides better characterization of the dynamics than the use of the original continuous time series (i.e., maximum of the airway pressure, $P_{max}$, and the associated respiratory cycles duration $T_{tot}$, instead of the airway pressure time series itself)—see Ref. 17 for the introduction of this approach and further discussion regarding the underlying fundamentals of dynamical systems theory.

The goal of the current study is twofold. First, we investigate the use of materials and methods anew to characterize some typical scenarios, regarding PVI quality, observed during invasive mechanical ventilation. A broader range of PVI dynamics exists in invasive ventilation, as compared to non-invasive, that can vary from completely controlled mechanical ventilation (i.e., absence of spontaneous effort) to fully assisted mechanical ventilation, where patients inspiratory effort is present but not always synchronized with the ventilator. That is due to the inherent different features of the two contexts. For example, while non-invasive mechanical ventilation is generally delivered in a home care or hospital ward context using a face mask,\textsuperscript{18,19} invasive ventilation requires intubation and is restricted to intensive care units, emergency, and surgery. It is worth noting that the difference goes beyond the ventilation administration technique: non-invasive ventilation is applied intermittently as a form of support to patients that are capable of spontaneously breathing throughout the procedure, while during invasive mechanical ventilation, sedative, anesthetics, or even muscles paralysis agents are required, which, together with the underlying injury, result in a patient that would not be able to breathe independently without support. Second, we aim to bridge the gap between the typical critical care professionals’ needs in practice and those tools from nonlinear dynamics. In view of this, here we report and explore two tools. First, a visual practice and those tools from nonlinear dynamics. In view of the system behavior/state occurred. This fact is marked by the recurrence plot and is associated with regular dynamics (i.e., regular dynamics have higher recurrence rate values). It is defined as

\[
R_{ij}(\epsilon) = \Theta(\epsilon - \|\vec{x}_i - \vec{x}_j\|), \quad i,j = 1,\ldots,N,
\]

where $\epsilon$ is the threshold distance, $\|\cdot\|$ is a norm, and $\Theta(\cdot)$ is the Heaviside function [which returns 1 (0) if the distance between $\vec{x}_i$ and $\vec{x}_j$ is less (greater) than $\epsilon$]. The RP is a plot of the matrix $R_{ij}$, where usually black and white pixels are used for the 1s (recurrence) and 0s (no recurrence), respectively.

The quantification of the dynamical attributes encoded in the RPs is performed through recurrence quantification analysis (RQA),\textsuperscript{10,17,20,23} In the following, we present the two RQA indexes investigated that best fit the analysis in this study. The first one is the recurrence rate, $RR$ (the motivation is discussed in Sec. III). It measures the density of recurrence points in the RP and is associated with regular dynamics (i.e., regular dynamics have higher recurrence rate values). It is defined as

\[
RR = \frac{1}{N^2} \sum_{i,j=1}^{N} R_{ij}(\epsilon).
\]

The second index is the Shannon entropy $S$, as proposed by Letellier.\textsuperscript{17} This index was successfully applied in the characterization of PVI quality in non-invasive mechanical ventilation.\textsuperscript{11} It quantifies the complexity of the underlying system dynamics and is defined as

\[
S = -\sum_{l=1}^{N} P_m(l) \ln P_m(l),
\]

where $P_m$ is the number of diagonal lines of length $l$ formed by non-recurrent points divided by the number of recurrent points. It is known that this definition provides more
consistent and reliable results than the often estimated entropy of recurrent diagonal lines.\textsuperscript{17,24}

A relevant aspect of RQA is that the use of the discrete time series sampled at a Poincaré section (from the original “continuous” time series) enhances the information provided by the RQA. This was originally suggested and demonstrated with the RQA’s Shannon entropy\textsuperscript{17} and was later applied and corroborated in the context of non-invasive mechanical ventilation\textsuperscript{11} and with other classical RQA variables.\textsuperscript{24}

In view of these recommendations, in the current study, RPs were calculated using a time delay embedding reconstruction of two types of time series, meanwhile the RQA indexes were estimated only with the second type. The first type (“continuous” behavior) corresponds to the times series of airflow \( Q \) and airway pressure \( P \). Both signals are easily accessed by health care professionals, being displayed on the ventilator screen. The second type (“discrete” behavior) are the discrete maps associated with \( Q \):\textsuperscript{17} (i) the peak airflow \( Q_{\text{max}} \), defined as the maximum values of \( Q \) during each respiratory cycle (equivalent to a sampling on a Poincaré section of \( Q \)); (ii) the respiratory cycle duration \( \tau_{Q} \) estimated from the inter-peak time interval of \( Q_{\text{max}} \) (hence it corresponds to the return times of the airflow through its Poincaré section).

Given the dependence of the RP/RQA indexes on some parameters, the criteria used to carefully select such parameters are described next. For the time series of the first type, the embedding dimension \( d_{E} \) and the time delay \( \tau \) were chosen using the false nearest neighbors technique\textsuperscript{25,26} and the first zero of the autocorrelation function followed by visual inspection,\textsuperscript{27,28} respectively, in order to achieve an optimal embedding (the value \( d_{E} = 4 \) was found appropriate for those time series). For the time series of the second type, since they can be considered as a Poincaré sampling of the aforementioned ones (which is a process that reduces the phase space dimensionality by 1), the embedding dimension was \( d_{E} = 3 \). The threshold \( \epsilon \) was chosen for each time series \( Q, P \), and \( \tau_{Q} \) as \( \sqrt{d_{E}} \times 10\% \) of the fluctuation of the signal\textsuperscript{17} and confirmed with visual inspection as approximately 10\% of maximum phase space diameter.\textsuperscript{22} The same threshold of \( Q \) was used for \( Q_{\text{max}} \).\textsuperscript{11} In all cases, the Euclidean norm was applied.

### III. Interpretation of RPS Signatures of the Studied Scenarios

The motivation of this section is twofold. First, to provide a link between the signatures observed in the physiological time series of airway flow \( (Q) \) and pressure \( (P) \) with those of the RPs, due to known features of three different PVI scenarios (to be defined in the following). In a sense, this bridges a gap between the specialized clinician point of view (and actual practice) and the dynamical systems’ theory tools and concepts applied here. Second, the insights provided in this step will allow one to choose the best physiological variables and RP property candidates in order to discriminate these PVI scenarios both visually (in Sec. V A) and quantitatively (in Sec. V B).

We define what we call PVI scenarios I, II, and III, by the following typical and broadly known relevant aspects found in clinical practice during invasive mechanical ventilation: (a) scenario I, characterized by the lack of spontaneous inspiratory efforts, therefore, the same airflow and pressure patterns are repeated at every respiratory cycle by the ventilator, i.e., a periodicity is expected in both time series (airflow and airway pressure); (b) scenario II, after each spontaneous inspiratory effort is detected, the ventilator supplies a constant level of positive airway pressure support,\textsuperscript{29} but not with a constant frequency as in scenario I; (c) scenario III, inspiratory efforts are present as in scenario II, but not always supported by the mechanical ventilator. Unsupported spontaneous efforts are clearly observed in the airflow time series as a positive inflection with a smaller amplitude compared with controlled cycles, while on the airway pressure time series they are characterized by a discrete fluctuation, mainly, on the lower pressure level.

It is worth noting that these aspects are usually identified, in practice, by direct visual inspection of the \( P \) and \( Q \) time series by a specialized clinical staff.\textsuperscript{3} Hence, considering the goals of this work, it is pertinent to discuss the RPs aspects in parallel with the aforementioned ones. Figures 1(a)–1(c) depict 60 s of airflow \( Q \) and airway pressure \( P \) signals of a volunteered patient (P03, see details in Sec. IV). The chosen time length allows a clear visualization of the aforementioned features of each PVI scenario considered. On the top, black stripes mark a representative segment of each studied scenario, while grey stripes correspond to “deviations” of the scenario. The respective RPs are shown in Figs. 1(d)–1(i), along with the RPs computed from the discrete time series peak airflow \( Q_{\text{max}} \) and respiratory cycle \( \tau_{Q} \) [Figs. 1(j) and 1(o)].

The aforementioned characteristics, that define the PVI scenarios, can be identified in the RPs representation of the underlying PVI dynamics as follows. The RPs of the scenario I show the expected periodicity (both in magnitude and time), characteristic of controlled mechanical ventilation. For the continuous type data \( Q \) and \( P \) [Figs. 1(d) and 1(g)], such periodicity is expressed by long recurrent diagonals, where the space between each diagonal corresponds to the time period between successive respiratory cycles, which are equally spaced. The white stripes (both vertical and horizontal) represent an interruption of the periodicity caused by a triggered inspiratory effort. Note that this information is clearly observed in the RP, while it might only be visualized, in the time series, by a respiratory care specialist. Regarding the RPs of the discrete type of time series [Figs. 1(j) and 1(m)], periodicity is represented as entire black domains. This is expected, since all the peaks of \( Q \) are almost equal, and the threshold \( \epsilon \) is evaluated with the size of the phase space \( (\approx \sqrt{3} \times 2 \approx 3.5 \text{l/min}). \) Note that the aforementioned triggered effort is captured only by the \( \tau_{Q} \) (see the vertical and horizontal white stripes, indicating non-recurrence), since it promotes a variation only in temporal behavior.

On the other hand, the RPs of the scenario II are expected to express the high periodicity in magnitude and variability in time, as seen in the representative time series [Fig. 1(b)]. The recurrent behavior is observed as several diagonals, which are now interrupted in several moments and hence having different lengths (corresponding to the duration of the recurrent behavior). The variability in time is represented as the variation of the diagonals distance. The white stripes correspond to
FIG. 1. General patterns of different types of PVI scenarios, illustrated by data from a representative patient: (a) scenario I, (b) scenario II, and (c) scenario III. Recurrence plots derived from airflow ($Q$), airway pressure ($P$), peak airflow ($Q_{\text{max}}$), and respiratory cycle duration ($\tau_Q$) during each studied scenario are depicted in Figs. 1(d)–1(o). Circles at airflow signals represent the peak airflow time series.

Finally, Figs. 1(f), 1(i), 1(l), and 1(o) show the RPs corresponding to the time series of scenario III, characterized by unsupported spontaneous efforts alternated with supported mechanical ventilation. Such features are clearly observed in Fig. 1(f), as several spaced black dots (as a signature of random behavior, i.e., unsupported spontaneous efforts) and some diagonal lines (with spacing greater than the one observed in scenarios I and II), and are easily differentiated from other scenarios [Figs. 1(d) and 1(e)].

These above-mentioned features cannot be observed in the RP derived from $P$ [Fig. 1(i)]. Regarding a separate view of the magnitude and temporal behaviors in scenario III, they are reflected in the RPs from $Q_{\text{max}}$ and $\tau_Q$ as the presence of some recurrence in the magnitude captured in the first one [Fig. 1(l)], and a predominant white domain in the second [Fig. 1(o)]. Comparing the RPs of scenario III with the ones of scenarios I and II, the RP from $Q_{\text{max}}$ makes a unique identification of its specific dynamical behavior. Note that the RP from the discrete time series $Q_{\text{max}}$ provides a clearer differentiation.

Summarizing the results above, the RPs derived from $Q_{\text{max}}$ and $\tau_Q$, together, are capable of differentiating the three PVI scenarios. In Fig. 2, a schematic identification key is proposed (which will be tested in Sec. V A): Scenario I is identified as black and black RPs, respectively, scenario II as black and white, and scenario III as grey and white, where grey means an almost equal number of black and white dots in the RP of $Q_{\text{max}}$. 

the “deviations” of the typical scenario II, i.e., longer respiratory period. Considering the discrete data [Figs. 1(k) and 1(n)], the high periodicity in magnitude is expressed as an almost black domain in the RP of $Q_{\text{max}}$, being almost identical to the respective RP of the scenario I. But the variability of the temporal behavior is clearly seen in the predominant white domain with rare episodes of recurrence in the RP of $\tau_Q$. Hence, the more expressive difference between scenarios I and II is obtained with RP built from $\tau_Q$. 

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IV. MATERIALS AND METHODS

The clinical data used in this study were collected in the intensive care unit of Risoleta Tolentino Neves Hospital (Belo Horizonte, Brazil), after the approval of the Local Ethics Committee (CAAE-26626214.0.0000.5149) and after the written informed consent of a legal representative of the patient was obtained. Demographic and clinical characteristics of each patient enrolled in the present study can be found in Table I.

A. Experimental data

Data collection was performed for 6 patients, after orotracheal intubation and institution of mechanical ventilation with an EVITA XL (Drager Medical AG, Lubeck, Germany) or Servo-i ventilator (Maquet, Getinge Group) using pressure ventilation mode. Airflow \( Q \) and airway pressure \( P \) signals were continuously acquired from the ventilator with a sampling frequency of 125 Hz (or 50 Hz for Servo-i ventilator), through serial interface, and stored on a PC. Data acquisition lasted as long as the patient was connected to the mechanical ventilator. Thirty six segments of ten minutes, which we call benchmark segments, were selected by a respiratory care specialist through a standard offline visual inspection of the airway pressure and airflow time series (see Sec. III). For each patient, six intervals were considered, being: two where PVI was present, as well two for scenario I and two for scenario III.

Afterwards, the respective discrete time series of peak airflow \( Q_{\text{max}} \) and the respiratory cycle duration \( \tau_Q \) were extracted. Finally, the time series of airflow \( Q \) and airway pressure \( P \) were re-sampled at 15 Hz for analysis following.30

Repeating the same blind analysis for all volunteers enrolled in this study, 95% of the scenarios were correctly identified.

RESULTS

A. Visual based assessment tool

Figure 3 illustrates the procedure. It shows the airflow \( Q \) time series of approximately 7 days of mechanical ventilation of P03, in which three segments (marked as black) of 1 h each were extracted by visual inspection being predominantly from scenarios I, II, and III (and avoiding disconnection and noisy data). From each of such segments, two segments of 10 min were selected (the benchmark segments), and the RPs from \( Q_{\text{max}} \) and \( \tau_Q \) were built (only the RPs for one of each benchmark segment are shown for illustration). The RPs clearly match the identification key (Fig. 2), and the respective blind analysis made by the RP/RQA specialist correctly identified the segments as representative from scenarios I, II, and III.

B. RQA-based assessment algorithm

Figure 4 depicts the analysis with the RQA indexes \( RR \) and \( S \), estimated for the 36 benchmark (as previously defined) 10 min segments from each \( Q_{\text{max}} \) and \( \tau_Q \) time series. The scatter plots suggest three sectors characterizing the three PVI scenarios. Such results are supported by statistical analysis as showed in the same figure. Accordingly, the joint use of \( RR_{Q_{\text{max}}} \) and \( RR_{\tau_Q} \), or of \( S_{Q_{\text{max}}} \) and \( S_{\tau_Q} \), successfully distinguished the studied scenarios regarding PVI quality.

VI. DISCUSSION

The main findings are that the joint use of RPs derived from peak airflow and the respiratory cycle duration
FIG. 3. Visual assessment of scenario type, proof of principle. (a) Airflow $Q$ time series observed in a mechanically ventilated patient (P03). Three 1 h segments were selected by a specialist by visual inspection. The criterion for these segments I, II, and III was that they should contain a predominantly (but not necessarily unique) behavior of scenarios I, II, and III, respectively. From each of these segments, one sub-segment of 10 min was selected and the respective RPs computed.

($Q_{\text{max}}$ and $\tau_Q$, respectively) graphically distinguished the studied scenarios of patient-ventilator interactions; such graphical differences have shown to have quantitative support by the joint use of the corresponding recurrence rates or of the Shannon entropies.

Part of the results agree with the previous study, which showed that during non-invasive mechanical ventilation, the entropies computed from $P_{\text{max}}$ and $T_{\text{tot}}$ were useful to discriminate patient-ventilator interactions.\(^{11}\) However, despite similarities between non-invasive and invasive mechanical ventilation, a straight extrapolation of RPs analysis during non-invasive ventilation to the context of invasive mechanical ventilation should be made with caution. According to the current work, distinction between PVI scenarios was not so clear through the visual inspection of the RPs from airway pressure time series. A possible explanation is that in the ventilation mode adopted in this study (pressure controlled ventilation), the delivered airway pressure is the controlled variable and hence there is a control action that greatly reduces its variability. It is worth noting that other clinically used assisted ventilation modes exist in which pressure is only partially controlled, for example, bi-level ventilation, which switches between two pressure levels, at fixed intervals, letting the patient breathe spontaneously without support at any time, causing a negative swing in pressure; assisted controlled ventilation, when a respiratory effort is detected, a fixed airflow is delivered until a target inspired volume is achieved (i.e., airflow is the controlled variable). In these cases, it is likely that RPs based on pressure carry relevant information, while those based on airflow might be less meaningful. In order to allow an easier comparison between these different ventilation modes, future studies shall be focused on RPs based on combined information from airflow and pressure (e.g., mechanical work performed by the ventilator).

As previously reported, data from a Poincaré section could be preferred to the whole time series for RQA analysis\(^{28}\). Such series would significantly reduce the computational load to build the RPs and to perform quantitative analysis whenever required. In fact, features of each PVI scenario can be more easily identified, by visual inspection, using RPs derived from peak airflow ($Q_{\text{max}}$) in comparison with RPs derived from airflow ($Q$). Moreover, when the information regarding temporal behavior is analyzed in combination with the magnitude of airflow, i.e., the joint use of RPs derived from $Q_{\text{max}}$ and $\tau_Q$, an identification of unique signatures of each studied PVI can be performed. Such results permit proposing a schematic identification key that can be used by non-specialist of non-linear dynamics or medical field, since it is based on a color shade code. Applying such identification key to RPs built from 6 mechanically ventilated patients, signatures of each studied PVI were easily recognized. However, it is worth noticing that the alternate coupling patterns between 1:2 and 1:3 rhythms in the result obtained with PVI scenario III, which can be observed directly on the raw time series, are clearly detected by the airflow RP instead of its respective analysis through a Poincaré section. Since the perpendicular distance between the diagonal lines corresponds to periods of the underlying process,\(^{22}\) the two different distances observed in that airflow RP [Fig. 1(f)] reveal the quasi-periodicity in the interaction between the patient and the ventilator. Comparing both the airflow and pressure time series, one can see that it corresponds to the interchange between purely spontaneous breathing and mechanical respiratory cycles.

Despite appealing, graphical interpretation of RPs might be questionable due to its subjectivity. In order to provide a quantitative support for our findings and to corroborate with the above-mentioned discussion, two well-known RQA indexes (as proposed in Ref. \(^{10}\)) were computed from the RPs. Shannon entropy and recurrence rate computed from RPs derived from $Q_{\text{max}}$ and $\tau_Q$ successfully distinguished the three scenarios of PVI. Taking into account the computational time
FIG. 4. Recurrence quantification analysis indexes values for each patient-ventilator interaction (PVI) scenario: I (green), II (blue), and III (red). (a,c) Scatter plots show three sectors regarding the three PVI scenarios. (b,d) show that PVI quality can be distinguished by means of the joint use of $RR_{Q_{\text{max}}}$ and $RR_{\tau_Q}$ or of $S_{Q_{\text{max}}}$ and $S_{\tau_Q}$. In (d) mean value for scenario I is zero for $S_{Q_{\text{max}}}$. Statistical tests were performed using ANOVA and adjusted for multiple measurements by means of Bonferroni’s procedure (values are given as mean and standard deviation).

and the interpretation of the concept by health care professionals, recurrence rate appears to be an appropriate index to be used.\(^8\)

It is important to highlight that the main purpose of current study is to exploit an alternative tool to investigate the dynamics underlying patient-ventilator interaction during invasive mechanical ventilation, rather than to compare with others methodologies, where a larger number of enrolled patients would be necessary. Based on our results, the current study reinforces the idea that respiratory data visualization through RPs provides valuable overall information about the dynamics of the system and, thus, it might be a useful tool to be used in critical care field. In this study, it is not possible to conclude that the PVI scenarios considered in this study are a reflection of the small cohort considered, which includes patients with different underlying diseases, possibly not representative of the general population of mechanically ventilated ICU patients. However, it is important to mention that the PVI scenarios adopted were observed for prolonged periods in all the patients considered and are consistent with ventilation conditions that are consolidated in the literature.\(^3\) We speculate that the PVI scenarios considered represent mainly a reflection of the process of weaning from mechanical ventilation (which includes a progressive reduction of sedation and ventilator support, paralleled by increased respiratory strength and overall health of the patient), rather than the underlying disease. The choice of each scenario was deliberate because the aim in this paper is not to provide a general classification scheme, but rather to recognize the signatures of three typical interactions in RPs, easily found during invasive mechanical ventilation. However, it is known that during invasive mechanical ventilation, a broader range of PVI exists and that the recognition of such interactions has an important impact on the outcome of the patient. Thus, a deeper investigation using RP/RQA for patient-ventilator interactions recognition during invasive mechanical ventilation is still desired.
Additionally, it is worth noting that despite promising, the estimation of RPs and RQA could be considerably influenced by the recorded time series used, as previously discussed, the indexes computed in RQA, and the values of several user-defined parameters, such as embedding dimension and threshold. Due to the lack of agreement in the current literature, the selection of these parameters depends on the previous experience of the users with similar time series and, to some extent, on the experimental conditions (e.g., presence of noise). Thus, we strongly suggest that a preliminary study to standardize the values of the parameters should be performed before applying the method. Such procedure will allow comparability between results and avoid misleading interpretations during within and between subject comparisons. Taking the above-mentioned into account, we attest that the choices of embedding dimension ($d_E$), threshold (and minimum length $l_{min}$) values used in the present study are fairly robust.

This work has some limitations that must be addressed: (a) the clinical data considered come from a small cohort of patients (six). However, it is worth noting that the inter-individual dispersion of most RQA indexes is very small, suggesting that the results are very consistent and the main signatures in the RPs are unlikely to change for a larger cohort; (b) this study focused on three typical pre-selected scenarios, thus our findings cannot be immediately extrapolated to other PVI scenarios. Additionally, all patients enrolled in this study were ventilated using pressure-controlled mode; thus, the use of different invasive mechanical ventilation modes (e.g., volume-controlled modes) might impact the results.

VII. CONCLUSION

The evidence found in the current study attests that, as in non-invasive mechanical ventilation, recurrence plots and recurrence quantification analysis are useful tools to assess interactions between patient and mechanical ventilator during invasive ventilation. Indeed, features from three typical patient-ventilator interactions, commonly observed during invasive mechanical ventilation, were easily identified using RPs derived from peak airflow ($Q_{max}$) and respiratory cycle duration ($\tau_R$) in 95% of the data used. One of the contributions of this work was to establish coarse signatures (Fig. 2) that could be further developed and investigated as an identification key with potential use by health-care professionals without training in nonlinear dynamics. Such signatures were supported by quantitative analysis using RQA (recurrence rate and Shannon entropy). Thus, the present work reinforces the potential of RP/RQA on the analysis of respiratory patterns.

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