Characterization of Postoperative Pain Through Electrocardiogram: A First Approach

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Abstract. Current standard practices to evaluate pain are mainly based on self-reporting instruments. However, pain perception is subjective and influenced by several factors, making objective evaluation difficult. In turn, the pain may not be correctly managed, and over or under dosage of analgesics are reported as leading to undesirable side-effects, which can be potentially harmful. Considering the relevance of a quantitative assessment of pain for patients in postoperative scenarios, recent studies stress out alterations of physiological signals when in the experience of pain. As the Autonomic Nervous System (ANS) functions without conscious control, it is difficult to deceive its reactions, thus it a feasible way to assess pain. The goal of the proposed work is to characterize pain in postoperative scenarios through physiological features extracted from the electrocardiogram (ECG) signal, finding features with the potential to discriminate the experience of pain. Using ECG from 'pain' and 'no-pain' intervals reported from 19 patients during the postoperative period of neck and thorax surgeries, several features were computed and scaled regarding the baseline of each participant to vanish inter-participant variability. Upon, selected features, though pairwise correlation, were analyzed using pairwise statistical tests to infer differences between 'pain' and 'no-pain' intervals. Results showed that 6 features extracted from ECG are able to discriminate the experience of postoperative pain. These initial results open the possibility for researching physiological features for a more accurate assessment of pain, which is critical for better pain management and for providing personalized healthcare.

Keywords: ECG monitoring · Pain · Postoperative · Feature correlation · Feature extraction · Statistical tests

1 Introduction, Motivation and Goals

Pain involves dysregulations in the Autonomic Nervous System (ANS), a primary behavioral system [23], which regulates fundamental physiological states that

are typically involuntary, upregulating, and downregulating various functions within our body. The experience of pain induces reactions in the ANS, and, as it functions without conscious control [5], is a feasible way to assess pain. In the current standard practices to evaluate pain, due to the lack of quantified measures of pain, there are several barriers that can lead to a misleading pain assessment, resulting, therefore, in over or under dosage of analgesics. Either way, the pain may not be correctly managed and the undesirable side-effects of wrong doses can be potentially harmful. An incorrect assessment of pain may lead to undertreatment or overtreatment of pain [6,19], difficult the overall recovery [11,20], and lead to adverse psychological and cognitive effects [9,18]. Indeed, in postoperative scenarios, pain assessment is considered the most important task to ensure patient comfort. Considering that it is of utmost importance to properly measure and assess pain in such cases [8], there are several studies on the alterations of physiological signals when in the experience of pain.

Recent studies have shown that common symptoms associated with pain are increased respiratory activities, cardiac acceleration, a burst of sweat, increased skin conductance and heightened muscle contraction [4,7,10,13–16,21,22]. Thus, it is paramount to process and extract information from these physiological signals in order to present an understandable pain assessment. In the works [13,14], the authors agree that the severity of postoperative pain significantly influences the skin conductance (SC), demonstrating a correlation between the number of fluctuations in SC per second (NFSC) and self-assessed pain measured using a numeric rating scale. Within the same scope, the authors of [7] proposed using changes in the ECG and PPG signals to assess postoperative pain in children, being able to predict moderate to severe postoperative pain from NFSC. Also concerning physiological signals, the authors of [4], based on four pain induction tasks, proposed heart rate variability (HRV) as a biomarker for chronic pain in children.

Embracing this concern, the goal of this work is to characterize postoperative pain through ECG, finding features with the potential to discriminate the experience of pain. For that, it uses pain assessments from 19 patients, who underwent neck and thorax surgeries, collected during the postoperative at the recovery room.

The remainder of this work is organized as follows: Sect. 2 describes the setup for data monitoring and collection, as well as the methods used for data analysis. In Sect. 3 the results are presented and discussed. Final remarks and future research lines are presented in Sect. 4.

2 Materials and Methods

This section describes the setup for data monitoring and collection, as well as the methods proposed to identify ECG-based features which are able to provide a feasible characterization of pain in postoperative scenarios. Data processing was

performed in MATLAB [17] and Python, using the NeuroKit2[1], which provides biosignal processing routines.

2.1 Setup and Data Collection

Twenty participants undergoing elective neck and thorax surgeries at Centro Hospitalar Tondela-Viseu (CHTV) took part in this study. The recruitment was performed on a volunteer basis and after a written informed consent form.

ECG signals were monitored, using minimally invasive equipment, in the recovery room and during the standard clinical practices of analgesia, fulfilling all the clinical aspects and without compromising the patient's well-being. The ECG data was recorded, through the Vital Jacket®t-shirt [2], with a sampling rate 500 Hz, and using two electrodes placed on the right and left side of the participant's ribcage and a reference electrode placed above the pelvic bone.

Besides the ECG signals, this dataset contains information on patient's age, gender, type of surgical intervention, and type of anesthesia protocol. The procedures performed during the postoperative recovery of patients were also registered, including self-reports of pain, pain relief therapeutics, and other medical interventions (such as patient repositioning). These procedures are associated with time triggers that mark the event occurrence in the ECG signal. The evaluation of pain was based on self-report instruments (Numerical Rating Scale - NRS [25]) and several assessments, as necessary according to the clinical team, as obtained until discharge.

From the twenty patients in the dataset one patient was withdrawn from the study because of the lack of pain assessment annotations during the ECG recording, resulting in a total of nineteen patients (60 ±21 years old), ten females.

2.2 ECG Processing

The ECG signals are affected by noise, such as skin-electrode interference (low-frequency noise, which is amplified by motion, movements, and respiratory variation), powerline (with a frequency 50 Hz), and electronic devices (high-frequency noise) interference, namely from the clinical apparatus that concern this specific clinical scenario [3,12]. To attenuate the effects of noise and improve the quality of the signal, the raw ECG was low-pass filtered at a cut-off frequency 40 Hz, as the useful band of frequencies for these research purposes, without clinical relevance, varies between 0.5 Hz 40 Hz. The fundamental frequencies for the QRS complex, which is composed of Q, R, and S waves, are 30 Hz, and for the P-wave and T-wave components are 20 Hz 10 Hz, respectively [24]. Afterward, the baseline wander was removed with a moving average filter.

To achieve the proposed goal of characterizing postoperative pain through ECG-based features, we rely on information from the self-reported pain and from pain analgesia to define intervals related to pain experience. Further, we investigate if features expose differences between 'pain' and 'no pain' intervals, which

[1] https://neurokit2.readthedocs.io/en/latest/

corresponds, respectively, to the intervals of 15-minutes of data before and after these reported instances. Also, the baseline for each participant, which serves as a comparison regarding the pain state, was selected. In this work, it was considered that the last 10 min of useful ECG provide information on the state of the patient without the influence of pain or analgesia for pain management. Therefore, to reduce inter-patient dependency, each feature in both the 15-minutes intervals was divided by the respective feature computed in the baseline.

Table 1 presents a description of the 34 features computed, using the NeuroKit2 package, for the two 15-minutes intervals and for the baseline.

Table 1. Different types of features extracted from monitored ECG signals.

ECG-based features
Heart Rate (**HR**);
Amplitude of peaks: **P**, **Q**, **R**, **S**, and **T**;
Intervals: **PP**, **QQ**, **RR**, **SS**, **TT**, **PR**, **QT**, **ST**, and **QRS**;
HRV-Time domain features
RMSSD: The square root of the mean of the sum of successive differences between adjacent RR intervals;
MeanNN: The mean of the RR intervals;
SDNN: The standard deviation of the RR intervals;
SDSD: The standard deviation of the successive differences between RR intervals;
CVNN: The standard deviation of the RR intervals (SDNN) divided by the mean of the RR intervals (MeanNN);
CVSD: The root mean square of the sum of successive differences (RMSSD) divided by the mean of the RR intervals (MeanNN);
MedianNN: The median of the absolute values of the successive differences between RR intervals;
MadNN: The median absolute deviation of the RR intervals
MCVNN: The median absolute deviation of the RR intervals (MadNN) divided by the median of the absolute differences of their successive differences (MedianNN);
IQRNN: The interquartile range (IQR) of the RR intervals;
pNN50: The proportion of RR intervals greater than 50 ms, out of the total number of RR intervals;
pNN20: The proportion of RR intervals greater than 20 ms, out of the total number of RR intervals.
HRV Frequency-domain features
LF: The spectral power density pertaining to low frequency band;
HF: The spectral power density pertaining to high frequency band
HRV Non-linear features
SD1: index of short-term RR interval fluctuations;
SD2: index of long-term RR interval fluctuations;
SD1/SD2: ratio between short and long term fluctuations of the RR intervals;
HRV Complexity features
ApEn: approximate entropy measure of HRV;
SampEn: The sample entropy measure of HRV;

Thereafter, for each feature, the average in the 15-minutes intervals and in the baseline was calculated and the ratio between each 'pain' and 'no pain' 15-minutes intervals and the baseline was computed.

Moreover, to characterize the postoperative pain through the ratio of averaged features, feature selection was performed to reduce the total number of features, relying upon a filter-based method. At first, the Lilliefors test was applied to all features to decide if data comes from a normally distributed family (with a significance level of 5%). Thus, the pairwise Spearman correlation (as not all of the ratio of averaged features were normally distributed) between the 34 features was computed, and for each pair with an absolute correlation value above 0.9, the feature with lower variance was discarded.

To explore if the selected features differ according to the 'pain' or 'no-pain' experience, an analysis using boxplots, with notched boxes, was performed to visualize the distribution of the features and assess differences between the medians. Afterward, to test which features expose differences between 'pain' and 'no-pain' groups, the pairwise Student's t-test or the Wilcoxon Signed Rank test were applied, depending on the normality of the distribution of the features, to decide if the samples from the 2 groups ('pain' vs. 'no pain') originated from the same distribution, by comparing the mean or the mean ranks of both groups.

3 Results and Discussion

This section presents the results from the approach previously described and summarizes with a discussion with respect to related works.

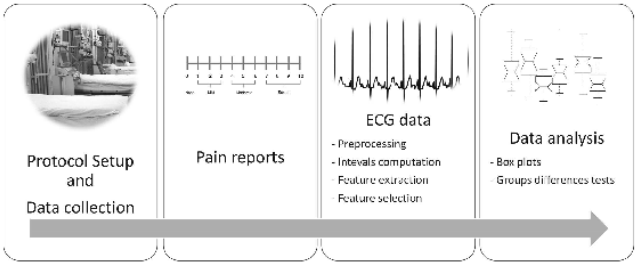

Fig. 1. Data analysis workflow.

3.1 Results

As detailed above, the workflow process for data analysis consisted of several steps, from the collection of data to the evaluation of the results, including the preprocessing of ECG data, the selection of 'pain' and 'no pain' 15-minutes intervals according to the reports, the extraction of features and the computation of ratios with the respective feature in the baseline (from now on referred only

as features), the analysis of the boxplots of the features, the selection of most relevant features, and, finally, the application of pairwise tests (Student's t-test or the Wilcoxon Signed Rank test) to infer which features expose statistical significant differences in between pain groups. This workflow is illustrated in Fig. 1.

From the 34 features extracted, feature selection was performed based on the pairwise correlation of the features and variance analysis, resulting in a total of 19 relevant features. Moreover, and in accordance with the literature, some of the features that report similar measures, and thus, are highly correlated, were discarded. For example, the authors of [1] indicate that although on a different scale, the RMSSD is equivalent to SD1, both representing short-term HRV, and the obtained correlation shows a perfect relation of these features. Thus the selected features were:

ECG-based features: Amplitude of peaks: P, Q, R, S, and T; Intervals: PR, QT, ST, and QRS;

HRV Frequency-domain features: RMSSD, SDNN, MedianNN, IQRNN, pNN50, pNN20;

HRV Frequency-domain features: LF, HF;
HRV Non-linear features: SD1/SD2;
HRV Complexity features: SampEn;

Figure 2 displays a heatmap of the correlation matrix of the selected features, showing that, most of the time, the same type of feature presents a larger correlation in between and lower correlation with other types of features.

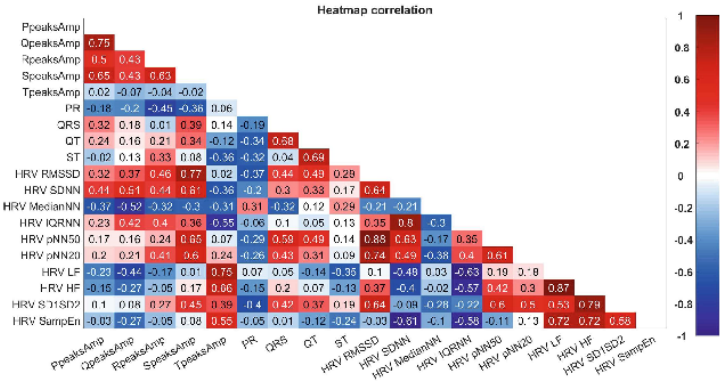

Fig. 2. Heatmap of the correlation matrix of the selected features.

Thereafter, the boxplots of the features were computed to analyze the distribution in both 'pain' and 'no pain' groups. Figure 3 shows the boxplots for 8 of the selected features, namely ECG-based (QT and ST intervals), HRV time-domain (IQRNN and pNN20), HRV frequency-domain (LF and HF), HRV non-linear (SD1/SD2), and HRV complexity (SampEn) features.

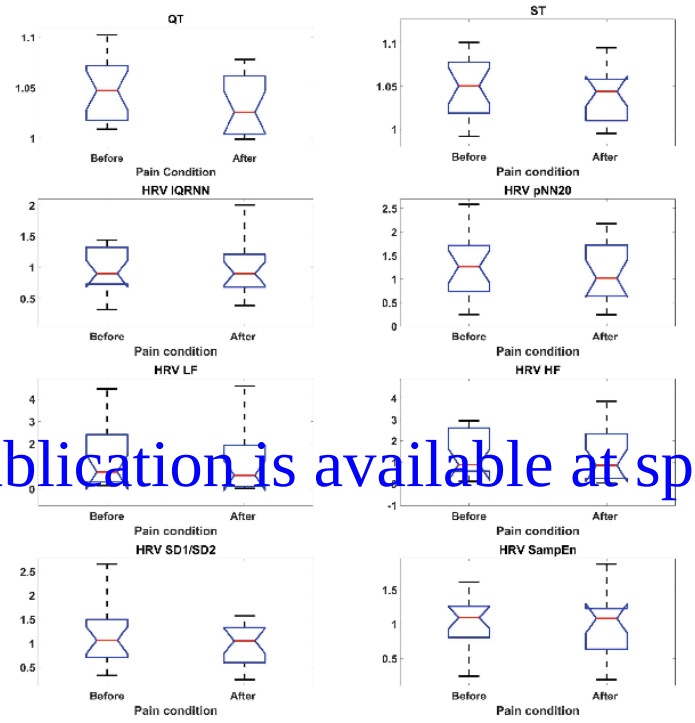

Fig. 3. Boxplots for 8 of the selected features: QT interval, IQRNN, LF and SD1/SD2 (left) and ST interval, pNN20, HF and SampEn (right).

From the boxplots, it can be observed that, with the exception of IQRNN, the median values for the group 'no pain' are lower than for the group 'pain'. Whereas for the dispersion, ST interval, pNN20, LF, and SD1/SD2 presented higher values for the 'pain' group.

With respect to the ECG-based features, there was a statistical difference between both pain groups for the QT and ST intervals ($p = 0.0176$ and $p = 0.0242$, respectively, with a 95% confidence interval (CI)).

Concerning HRV time-domain features, only MedianNN ($p = 0.0176$, 95% CI) shows a significant difference between the groups of 'pain' and 'no-pain'.

For the HRV frequency-domain features, both low and high frequencies were significantly different ($p = 0.0003$ and $p = 0.0112$, respectively, 95% CI) in pain groups.

Whereas for the HRV non-linear features, only the SD1/SD2, associated with the randomness of the HRV signal, shows a statistical difference between 'pain' and 'no-pain' ($p = 0.0367$, 95% CI).

For the remaining selected features, there was no significant difference between 'pain' and 'no-pain' groups.

3.2 Discussion

With a similar protocol to the one presented, the work [13] monitored 25 patients, after minor elective surgeries, in the recovery room. At different time-points, the patients reported the pain on an NRS scale, and SC, HR, and blood pressure were recorded. From the analysis performed, the authors found that while NFSC is significantly different for different groups of pain levels, HR showed no correlation with pain. The same authors have other works regarding HR and HRV responses to postoperative pain [15,16], which report no statistically significant differences in HR, LF, HF, and LF/HF between pain groups (defined according to NRS values). Also assessing effects of postoperative pain in HRV measures, the authors of [21] found that LF and LF/HF were significantly different in moderate/severe pain and that HF did not present statistical differences in pain groups. In the present study, the finding that the response of HR did not show significant differences among pain groups is confirmed by these related works. With respect to HRV measures, the present work showed that several HRV measures presented differences between 'pain'/'no pain' groups. However, these findings can not be directly compared with the results mentioned above, as differences in the HRV responses among different levels of pain were not assessed in this work.

4 Conclusions and Future Work

Pain perception is subjective and influenced by several factors, turning its objective evaluation an added difficulty. Embracing this concern, this work proposes the study of ECG signals of patients in postoperative pain, in order to extract the necessary information for its characterization. Thus, relying on ANS reactions, which are difficult to deceive, this work aims to describe postoperative pain through physiological features extracted from the ECG signal.

The ECG-based features, QT and ST intervals, the MedianNN, an HRV time-domain feature, the low and high frequencies of HRV, and the HRV non-linear SD1/SD2, show to have the potential to discriminate the experience of postoperative pain.

Although the limitations of the used dataset, the encouraging obtained results, sustain the feasibility of these physiological features to serve as pain indicators, enabling a more accurate assessment. Thus, future research should focus on enlarging the number of patients, exploring the responses from other

physiological signals, such as electrodermal activity and electromyogram, and discerning the physiological responses to different levels of pain. Collecting different physiological signals, and considering more patients under study, would also allow learning a classification model for pain recognition. These first results can advise on the most relevant ECG-based features to be included in this pain recognition task.

An assessment of pain based on physiological signals, besides improving the comprehension of pain mechanisms, may provide objective and quantified inputs that could help enhance self-care and promote the health and well-being of patients. Moreover, it can contribute to opening the path of adaptive and personalized therapies, such as adaptive drug adjustment according to the level of pain.

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