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Characterizations of Temporal Postoperative Pain Signatures with Symbolic Aggregate Approximations

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Abstract

Objectives—The primary aim was to characterize the temporal dynamics of postoperative pain intensity using symbolic aggregate approximation (SAX). The secondary aim was to explore the effects of sociodemographic and clinical factors on the SAX representations of postoperative pain intensity.

Materials and Methods—We applied SAX to a large-scale time series database of 226,808 acute postoperative pain intensity ratings. Pain scores were stratified by patient age, gender, type of surgery, home opioid use, and postoperative day (POD), and co-stratified by age and gender. Cosine similarity, a metric that measures distance using vector angle, was applied to these motif data to compare pain behavior similarities across strata.

Results—Across age groups, SAX clusters revealed a shift from low-to-low pain score transitions in older patients to high-to-high pain score transitions in younger patients, whereas analyses stratified by gender showed that males had a greater focus of pain score transitions among lower intensity pain scores compared to females. Surgical stratification, using cardiovascular surgery as a reference, demonstrated that pulmonary surgery had the highest cosine similarity at 0.855. With POD stratification, POD 7 carried the greatest cosine similarity to POD 0 (0.611) after POD 1 (0.765), with POD3 (0.419) and POD4 (0.441) carrying the lowest cosine similarities with POD 0.

Discussion—SAX offers a feasible and effective framework for characterizing large-scale postoperative pain within the time domain. Stratification of SAX representations demonstrate unique temporal dynamic profiles on the basis of age group, sex, type of surgery, preoperative opioid use, and across postoperative days 1-7.

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Keywords

postoperative pain; symbolic aggregate approximation; time domain

Each year, over 100 million surgeries are performed in the United States, and between 40% and 60% of surgical patients suffer from severe acute postoperative pain.¹ Chapman and others have demonstrated that for over one-third of surgical patients, postoperative pain will remain steady, or even increase, over the first 7 days after surgery when measured via daily averages.^{2,3} Poorly managed postoperative pain has been associated with a number of adverse cardiac, pulmonary, and thromboembolic events.⁴⁻⁶

Furthermore, while severe acute postoperative pain has been associated with the development of persistent postsurgical pain (PPP), Althaus et al. have shown that the slope of a linear postoperative pain trajectory predicts development of PPP, independent of acute pain severity.⁷⁻¹¹ This suggests that the acute pain trajectory may join, or even be mediated by, a host of other biological, psychological, and social factors that modulate the risk of developing PPP.^{9,12}

While providing important experimental findings, the methodologies used to collect and analyze these previous data suffer from limitations inherent to different stages of translational clinical research.¹³ Importantly, the above studies relied upon daily pain assessments, and thus were unable to account for intra-day variations in acute pain intensity. This is a significant limitation given that postoperative pain assessments often occur on an hourly basis, and because of pharmacokinetics, most commonly used analgesics impact pain ratings on an hourly rather than a daily basis.¹⁴ Thus, there is a critical need to extend these findings at a higher temporal resolution while accounting for both clinical and sociodemographic patient factors.

Among the general themes in time series research are anomaly detection, clustering, classification indexing, and visualization of massive datasets.¹⁵ During preprocessing, time series are usually converted to some meaningful representation appropriate for the desired analysis.¹⁶ Some of the more ubiquitous methods include the Discrete Fourier Transform,¹⁷ Discrete Wavelet Transform,¹⁸ Piecewise Linear and Piecewise Constant models,¹⁹ Adaptive Piecewise Constant Approximation (APCA),¹⁹ and Singular Value Decomposition.¹⁹ A modern technique, Symbolic Aggregate Approximation (SAX), represents the time series in terms of normalized discrete symbols, or “musical notes” of the time series.²⁰ Similar to “musical notes” that encode a discrete representation of the music audio signal, SAX allows for a discrete representation of time series data in general. This property has the benefit of being a gateway to borrow techniques from the natural language processing literature and apply them within the time series domain. In particular, SAX simultaneously reduces the length of a time series and the number of possible values for each time point. Furthermore, SAX offers a lower bounding property, guaranteeing that, when comparing time series, the SAX representation is the most accurate reproduction of the original signal. Within the healthcare field, SAX has proven itself useful for analyzing vital sign time series data in many ways. Oates et al. showed that it is possible to predict patient outcomes using classification strategies with SAX “bags of words.”²¹ A SAX-based anomaly detection

algorithm, published by Keogh et al., was shown to be capable of spontaneously discovering physiologically relevant medical events in vital sign signals.²²

Here, we explore the use of SAX-based representations of 226,808 acute postoperative pain intensity ratings from 5,737 surgical patients measured at an hourly, rather than a daily, time frame after surgery. The analysis was inspired by a technique developed by Keogh et al. called “Intelligent Icons” (also called Time-Series Bitmaps) that aligns common meaningful patterns – or motifs – in time series data into an icon format for visualization and further analysis.^{23,24} We made a few modifications to the technique to maximize its utility, in particular to the normalization and pixel alignment strategies. This improved the interpretability of the icons and allowed us to identify the inter-relationship between numerous short motifs simultaneously. Furthermore, our use of a nonparametric normalization strategy added a distribution-free quality to the technique, vastly improving its versatility. Our primary aim was to define several facets of SAX with respect to postoperative pain intensity ratings, thereby tailoring the prototypical SAX algorithm to demonstrating the temporal dynamics of acute pain. Our secondary aim was to explore the effects of age, gender, type of surgery, opioid status, and postoperative day (POD) on the temporal nature of postoperative pain through co-stratification of SAX representations.

MATERIALS AND METHODS

Description of Data

This study, approved by the University of Florida Institutional Review Board, was a retrospective cohort study conducted in accordance with the STROBE guidelines.²⁵ Surgical case data were obtained from the University of Florida's Integrated Data Repository. This repository is a large database of validated fields obtained from electronic medical record systems used for patient tracking, billing, surgery, and hospital documentation purposes. Subjects were those patients aged 21 and over undergoing non-ambulatory surgery at UF Health at the University of Florida over a 1-year period beginning in May 2011. Surgical case exclusion criteria included obstetric surgery, as well as those patients who received multiple separate surgeries within the study period in order to avoid contamination of pain scores from the effects of surgeries preceding or following the case of interest.

All pain scores were documented by clinical staff using the numeric rating scale (NRS) on an 11-point system ranging from 0 to 10. Pain scores were entered using the EPIC electronic medical record system; this particular implementation provides education on the administration of the NRS query at the point of data entry to improve the veracity of collected data. Pain scores were generally recorded every 4 h per nursing protocol, with a repeat query within 1 h following administration of analgesic medications for breakthrough pain. Structured analgesic frameworks were used for each surgical population. When the clinical staff documented a pain score as “patient asleep,” the pain score was converted to a missing value rather than 0/10 to account for the fact that some patients had received additional sedatives that may have facilitated sleep despite an otherwise large nociceptive load. All pain scores were labeled with a corresponding date/time stamp, as were the start and end times of the patient's surgical procedure. End-of-surgery times generally reflected closure of skin and emergence from anesthesia. For each pain score, the time in minutes

following the end of surgery was calculated to enable a common reference point from which to calculate pain trajectories. Pain scores were filtered to include only those obtained after the listed end-surgery time through the end of POD 7. Patients were included in the analysis only if their first pain score was recorded within 2 h of the end of surgery to exclude those subjects with prolonged emergence from anesthesia. A histogram of recorded scores included in the analysis can be seen in Appendix A (Part A). Pain scores reported as zero were greatly over-represented likely due to hourly measurements within the intensive care units. In agreement with prior findings by Dexter and Chestnut, Lilliefors test for normality demonstrated substantial non-Gaussian behavior for the set of all scores as well as the set of non-zero scores (P indistinguishable from 0 for both).²⁶

The types of surgery were identified using current procedural terminology (CPT) codes. Given the large number of possible CPT codes, surgeries were grouped into separate categories based upon their anatomic location according to the first digits of the CPT code. For patients with multiple CPT codes, only the primary CPT code was used for definition of the type of surgery. Gender was defined as male or female. Age was defined as a categorical variable consisting of the following empirically selected age groups: 21 to 39, 40 to 64, 65 to 84 years, and 85 years or greater.

Observations with missing pain scores or missing measurement time points for pain scores were removed from the analysis set given the interpolation methods described below.

Management of Outliers

Records of pain scores for most of the patients included in the study began shortly after surgery, with approximately 80% starting within 2 h after the end of surgery. However, there was a non-trivial subset of patients whose pain score recordings started up to several days after their surgeries, as shown in Appendix A (Part B). These delays were potentially attributable to a number of factors, including intensive care unit stay, use of non-NRS measures of pain assessment, and/or data entry issues. In the interest of analyzing pain profiles along a standard postoperative time interval, data were disregarded for those patients whose pain score records began more than 2 h after their procedure. Appendix A (Part C) shows the set of start times that were less than 2 h after surgery.

Interpolation

Given the irregular timing of clinical pain assessments, data were preprocessed for each patient to linearly interpolate their pain scores and establish derived pain intensity ratings at regular time intervals. An interval of 10 min was chosen as the standard interval between scores to guarantee robust oversampling and avoid aliasing. Figure 1A illustrates the transformation of sample scores.

Dimensionality Reduction and Discretization

Although interpolation to 10-min intervals resulted in a very fine resolution of the data, it is desirable to analyze longer-term changes in pain levels. A major benefit of SAX is that multiple adjacent data points can be compressed into individual quantities that closely approximate aggregate trends. Within the SAX literature, this procedure is referred to as

Piecewise Aggregate Approximation (PAA) and is a part of a larger class of methods used for dimensionality reduction.²⁷ Dimensionality reduction refers to techniques, such as principal component analysis (PCA), whereby a large number of features, or variables, are compressed into a smaller number of core variables that represent the information from the original variables in a more condensed manner. The time length within which measurements are compressed is an adjustable parameter referred to as the PAA frame length, and we found that a value of 5 hours captured the most salient trends for all stratification analyses except POD. The PAA values were further discretized by assigning to them alphabetical letters that symbolically represent multiple subsequent measurements (see Fig. 1, B and C). This final representation of a time series is called a SAX word. The number of letters available for discretization is a parameter, denoted β , which indicates the final amount of discrete pain levels and determines the resolution of the visualization icons.

Identifying Motifs

Motifs are subsequences of specific letters within a SAX word that may indicate a pattern in the data. For example, if $\beta = 3$ (that is, the set of possible SAX letters is {a,b,c}), then the motif *cba* indicates a steady downward trend from highest to medium to lowest pain. As another example, the motif *cab* represents a downward trend followed by an upward trend. We are interested in the number of times any given motif appears in the SAX word representing a patient's postoperative pain scores.

Stratification

We stratified patients by gender, age group, surgery type, and home opioid use, and stratified patients using age and gender to investigate motif differences between patient characteristics. We also stratified recoveries by POD to investigate motif differences over time. To determine the importance of a motif m within a particular stratum C_{κ} , the number of occurrences of the motif m among patients within the stratum were divided by the total occurrences for all motifs among patients within C_{κ} , stratum. We denote this importance of motif m to stratum C_{κ} as $x_{C_{\kappa},m}$.

Normalizing of Strata Motif Importance

Because motif importance values followed a similar distribution between all strata, it was necessary to further normalize the within-stratum motif importance to elucidate subtle motif variations between the investigated strata. This was accomplished by comparing each within-strata motif importance with the empirical cumulative distribution function (ECDF) of motif importance values. The ECDF offers a simple and effective nonparametric method for normalization while making no assumptions about the underlying distribution, and was calculated via bootstrapping by randomly assigning patients into artificial groups and then comparing the observed value against the ECDF of the resampled values. When $x_{C_{\kappa},m}$ was renormalized in this manner across strata, we denoted this as $\hat{F}_{C_{\kappa},m}$, which indicated the proportion of potential motif importance values that the observed motif importance value was greater than.

The ECDF has the benefit of being bound to the interval [0,1]. As shown below, when comparing strata ("Computing Similarity between Strata"), this allows us to assign a

similarity between 0 and 1. In addition, when generating an intelligent icon for a given strata (“Generating Intelligent Icons”), knowing the boundary makes it easier to assign a color to that value.

Computing Similarity between Strata

It is often useful to determine how similar patient strata are to each other. Here again, each motif represents one of the many ways in which pain scores can step up or down during a time series of pain assessments. From this, we used a measure called the *cosine similarity*²⁸ to estimate similarity between strata.

The cosine similarity score considers the similarity between two intelligent icons based on the cosine of the angle of their corresponding ECDF vectors, where each vector component represents the normalized importance of a particular motif. The cosine similarity is bound to the interval [0,1], where 1 represents perfect agreement between the two vectors and 0 indicates that there is no similarity. Altogether, the cosine similarity metric gives a quantitative measure of temporal pain behavior similarity across different strata (e.g., gender, age, type of surgery, etc.).

Generating Intelligent Icons

The normalized motif importance vectors can be reshaped to square icons, as shown in Figure 2A.²⁴ This has the effect of positioning in close vicinity those motifs that indicate similar patterns, as shown in Figure 2B. Figure 2C demonstrates the icon generated using the following parameters: five severity levels of pain (i.e., $\beta = 5$), two-step sequences, and stratification labeled as cardiothoracic surgery patients.

When plotting icons, a stratum is chosen first and the associated icon is then plotted. Icons for other strata are plotted from left to right, typically in descending cosine similarity flowing over to subsequent rows.

Statistical Analyses

Following demographic characterization, we first characterized individual strata according to age, gender, type of surgery, and opioid status. A separate analysis was conducted of changing motif distributions by POD. Next, we performed a series of experiments for co-stratification of age and gender. In each analysis, 1000 random patient groups were used to bootstrap the output of the ECDF during normalization. Pain scores were discretized into 2, 5, and 10 categories, corresponding to $\beta \in \{2,5,10\}$. Cosine similarities were reported for $\beta = 10$.

All analyses were conducted using Python 2.7.5; a python script describing all code used in these analyses is included in the online supplement.

RESULTS

A total of 297,140 pain scores from 7,174 patients was examined. Of these, 226,808 scores belonged to patients whose first score was collected less than 2 h postoperation (5,737 qualifying patients) and were thus included in the analysis. Linear interpolation of these

scores to consistent 10-min intervals yielded 2,867,471 total scores. Of those included patients, there were slightly more females than males (51.6% and 48.4%, respectively). The mean age was 55.5 ± 16.1 years, with 98% of patients below 85 years old (Table 1).

Stratification by Age Group

Strata analysis of age groups revealed a shift from low-to-low pain score transitions (e.g., aa, ab, ba, bb, and other transitions found in the left upper quadrant of the intelligent icon for age group) in older patients to a high-to-high pain score transition (e.g., right lower quadrant of the intelligent icon) in younger patients (Fig. 3). Notably, the preponderance of off-diagonal scores in the upper right and lower left quadrants increased and converged away from the central diagonal with increasing age, showing that patients in the 85 years or greater category were more likely to experience the extremes in transition from lowest to highest or highest to lowest pain scores. Cosine similarity measures were 0.888 between age groups 21 to 39 and 40 to 64 years, 0.180 between 21 to 39 and 65 to 84 years, and 0.258 between age groups 21 to 39 and 85 or greater years given $\beta = 10$.

Stratification by Gender

Males had a focus of motifs in the left upper quadrants, suggesting transitions among lower-intensity pain scores without off-diagonal foci, which would indicate transitions from extremes of low to high or high to low (Fig. 4). The cosine similarity between the male and female icons was 0.401 given $\beta = 10$, suggesting notable dissimilarity across gender in temporal transitions of pain.

Stratification by Type of Surgery

The intelligent icons for cardiovascular, pulmonary, and urinary surgeries demonstrated increased foci of sustained low pain score transitions, as shown in the left upper quadrants of each icon (Fig. 5). The icons for urinary, digestive, and female genital surgeries demonstrated increased signal at the left margin, indicating increased frequency of motifs, suggesting pain transitions decreasing toward minimal pain scores. Contrariwise musculoskeletal surgeries indicated increased frequencies of motifs with an ascending pain score pattern toward maximal pain intensity ratings. Nervous system surgeries showed an increased signal along the off-diagonals, suggesting moderate transitions to higher or lower pain states. The icon for integumentary surgery was predominantly found in the right lower quadrant, suggesting a preponderance of foci within high-pain intensity states. With cardiovascular surgery as a reference, pulmonary surgery had the highest cosine similarity at 0.855, followed by urinary at 0.814, and digestive at 0.683. Musculoskeletal and integumentary surgeries had the lowest cosine similarities with cardiovascular surgery at 0.477 and 0.368, respectively.

Stratification by Home Opioid Medication Status

Patients on home opioid therapy had a grossly increased foci of motif representation in the right lower quadrant, suggesting sustained elevated acute pain scores with transitions to other high-intensity pain states (Fig. 6). Cosine similarity given $\beta = 10$ was 0.240 between home opioid status.

Stratification by POD

Stratification by POD was differentiated from other stratification processes given that the same patient was represented across multiple strata rather than exclusively within a single strata definition. To correct for this, the procedure was altered slightly so that strata would contain subsequences of a patient's pain records specific to the POD to which the stratum referred, therefore prohibiting temporal overlap of patient scores between strata. In addition, PAA frame sizes were set to include 1 h of pain scores rather than the 5 h used for other analyses. POD 0 and 1 demonstrated a high concentration of motifs in the right lower quadrant, with off-diagonal (POD 0) and diagonal (POD 1) representations, suggesting a high pain intensity rating with intermittent relief on POD 0, transitioning to lower intensity but more sustained pain intensity ratings on POD 1 (Fig. 7). This trend continued on POD 2 and 3, with a shift toward the left upper diagonals giving way to dispersion across lower intensity ratings. Despite this trend, POD 7 carried the greatest cosine similarity to POD 0 (0.611) after POD 1 (0.765), with POD 3 (0.419) and POD 4 (0.441) carrying the lowest cosine similarities to POD 0.

Stratification of Age and Gender

To simultaneously examine the motif distribution across age and gender, patients were co-stratified by age group and gender categories, and icons were created for each combination. Given a reference of males aged 21 to 39 years, females aged 21 to 39 years had the greatest cosine similarity (0.895), followed by females aged 40 to 64 (0.869) years and then males aged 40 to 64 (0.799) years. For each age group stratification, female gender had greater cosine similarity with the baseline male 21 to 39 year stratum than did the male gender stratum at that age group. In general examination of motif distribution with each co-stratification, the age group effects generally predominated those of gender; that is, males and females within the same age group shared similar cosine similarity to the reference icon (Fig. 8). The reason for this is that the importance of motifs varied more between different age group strata than between the two genders, thus age group had a stronger effect during the normalization procedure than did gender.

Impact of Initial Pain Assessment Selection Criterion

To examine the impact of the exclusion of subjects with an initial pain assessment greater than 2 h after surgery, data were reanalyzed with removal of this selection criterion. Aggregate pain scores were slightly lower in the all-subject cohort compared with the selected patient cohort [4.082 ± 3.308 (mean $\pm$ SD) for selected cohort vs. 3.850 ± 3.318 for all-subject cohort, mean difference 0.232 ± 0.0092 , $P < 0.0001$], although no gross changes in the structure of the intelligent icons were detected for the analyzed strata (Appendix B).

DISCUSSION

Here, we report the results of a novel approach to examining postoperative pain score changes over time with respect to age, gender, type of surgery, and home opioid status. Our results demonstrate substantial heterogeneity in how pain scores change over time following surgery. Additionally, our results suggest that the observed temporal patterns differ by age, gender, type of surgery, and opioid status. The distribution of pain state transitions differs by

POD, although it remains unclear how this may be confounded by other effects such as type of surgery.

Our study focused on two specific characterizations of the time series signal: motif characterization and proportional representation of motifs within demographic and clinical strata. Motifs in this context refer to the pairs of sequential pain intensity ratings that define a transition from one pain state to another. Here, SAX offered two important advantages over other representations of time series data: dimensionality reduction and lower-bounding guarantee. Dimensionality reduction refers to the ability of SAX to represent the same amount of temporal information with fewer variables, similar to the use of principal component analysis.²⁹⁻³² The lower-bounding guarantee specifies that the SAX representation approximates the original time series signal as closely as possible. These advantages of SAX allowed us to identify, characterize, and compare motifs, which represented temporal transitions in pain ratings in a computationally feasible manner.

Our results on the distribution of motifs suggested that younger patients had a greater proportion of motifs with higher pain intensity ratings, and that they were more likely to transition from a high pain intensity to another high pain intensity rating compared with older patients. These findings are notable given prior work suggesting that postoperative pain is especially poorly controlled in older patients.^{33,34} However, work by Althaus suggested that age has no impact on the postoperative pain trajectory in a multivariate model that included sociodemographic and psychometric variables.⁷ This discrepancy highlights the importance of examining the characteristics of the time series themselves; while a linear trajectory may not be influenced by age, it is important to recognize that a given linear trajectory can be defined according to many different arrangements of motifs. For instance, a lowest-highest, highest-lowest, middle-middle, and low-high-high-low arrangement of motifs would each yield a flat trajectory on average. Additionally, it is certainly feasible that this discrepancy may be due to the univariate, rather than multivariate, nature of the analyses applied in this report.

The observed distribution of motifs in females versus males is in general agreement with prior findings from a number of investigators, suggesting that females are more likely to suffer from severe postoperative pain compared with male patients.³⁵⁻³⁸ Interestingly, younger male patients had greater cosine similarity with the female versus male subjects within each increasing age-gender stratification in the co-stratification analysis, suggesting that young males may have more in common with the females versus males in older age group/gender strata combinations. Males with home opioid use also had greater cosine similarity with females whether or not the females were on opioids compared with males not on opioids. The stratification results reported here suggest that the general motif distribution may follow the effects of age more so than gender, although both of these effects may be trumped by home opioid use.

Our analyses strongly associate the type of surgical tissue injury with the manner in which patients move from one pain state to another after surgery. For instance, cardiovascular and thoracic surgery had very high cosine similarity scores, likely reflecting the intrathoracic nature of this surgery. Urinary, digestive, and female genital surgeries had similar motif

profiles, and each reflects a mix of open and laparoscopic abdominal surgeries. The icons for integumentary and musculoskeletal surgeries also had similar motif profiles, likewise reflecting a predominance of soft tissue and periosteal surgical tissue trauma. The distribution of motifs along the right border of the icon suggests that many patients will experience a transition from moderate to high pain, which may be explained by the sometimes drastic change in pain intensity following resolution of an otherwise successful nerve block. The inability of a predominantly opioid-based analgesic approach to musculoskeletal surgeries to offer satisfactory relief from pain compared with the analgesia achievable with opioids for abdominal surgery is in agreement with prior work examining the effects of opioids on abdominal versus musculoskeletal surgeries.³⁹ These findings may suggest the role of postoperative tuning of continuous perineural analgesia, or the need for further research in optimizing the timing of resolution of intraoperative neuraxial blockade and transition to a lower level block postoperatively.

Our results on pain transition motifs by POD offer unique insights into how pain scores change at different time scales. In general, the data demonstrate that the distribution of pain score transitions are heavily focused on moving to or from the highest pain intensity ratings on the day of surgery. As patients transition from POD 1 through 4, these pain scores generally shift toward transitions to or away from low intensity pain ratings. The path of this transition occurs along motifs suggesting a relatively steady state of pain intensity ratings within each POD. After POD 4, however, the motif distribution disperses to the corners of the intelligent icon of pain transitions representing the extremes of low-low, high-low, and low-high. These findings may represent confounding by censorship given that those patients remaining in the hospital through POD 7 may have received more painful surgeries or may be those patients who remain in the hospital due to poor pain control stemming from patient – rather than procedural – factors. It is possible that this dispersion may explain the large subset of patients in prior work by Chapman and others who reported postoperative pain trajectories that were flat or even positive in slope.

These results may eventually lead to new insights into the clinical management of acute pain. For instance, SAX analyses could inform future efforts to more closely tie the pharmacokinetic profile of analgesic interventions to the intra- and inter-day temporal variation of postoperative pain. Although typically considered agents for management of chronic pain, extended-release/long-acting formulations of opioids can offer substantial improvements in postoperative pain in select applications.⁴⁰⁻⁴² Catheter-based regional anesthetics now permit extension of these important acute pain management techniques from an interval of hours to days or even weeks, and the development of extended-release/long-acting formulations of local anesthetics will likely add to the armamentarium of acute pain management techniques.⁴³⁻⁴⁵ These results offer a basis for developing patient-specific temporal postoperative pain signatures to better personalize analgesic interventions in the postoperative period. Moreover, the methods described here may prove useful to explore the transition between the acute to chronic postoperative pain state by examining novel indices of variability of acute pain scores early after surgery, potentially identifying at-risk patients early after surgery.

Given the clinical nature of the data collection, as opposed to a research-oriented process using robust data collection protocols, it is important to note that this study relied upon the assumption that the pain ratings were psychometrically valid. While a widespread research-oriented pain data collection process would be ideal, such approaches are unfortunately unlikely to enjoy widespread use in clinical settings. Our analyses thus far were limited to univariate stratification analyses, although our inclusion of co-stratification begins to account for multivariate relationships among the examined features. Additionally, our current approach relied on linear interpolation of pain score assessments; although this represents a standard approach to time series analyses, it requires the assumption of at least a mean transition between sequential pain states. The original SAX algorithm assumes that the time series data has a Gaussian distribution, which is not true in our problem. A more sophisticated way of handling the non-Gaussian distribution with SAX representation is to use adaptive breakpoints.⁴⁶ However, we found that the optimal solution for our data was to set breakpoints to values that separated scores into equal-sized bins (quantiles), thus satisfying SAX's expectation that any arbitrary score has an equal probability of being assigned to any of the bins. Another limitation of this study regards the single-site origins of the dataset. Hence, the findings may reflect the particular pain management practices used at this single clinical site, which may limit the generalizability of the findings to other healthcare systems. In addition, more research is necessary to place these findings within the context of relevant patient and procedural factors, an effort that may require substantially more observations of postoperative pain and additional information related to patient characteristics to satisfy the large number of patient-procedure-time combinations that characterize surgical patients.

In conclusion, SAX offers a feasible and effective framework for characterizing postoperative pain within the time domain. These initial findings already demonstrate the considerable heterogeneity of pain transition motif distribution within and across demographic and clinical strata. Although much work is necessary to further develop this framework, our results reinforce prior work emphasizing the importance of time-domain analyses of postoperative pain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

Overview of symbolic aggregate approximation of postoperative pain scores. (A) Illustration of interpolation procedure. Recorded pain scores are connected via a linear function of time from which interpolated scores are predicted at consistent, 10-min intervals. (B) Example of piecewise aggregate approximation (PAA) being used to reduce the interpolated scores to five approximated measurements. Interpolated measurements are represented as crosses, and PAA levels are shown as thick horizontal lines. (C) Discretization to the SAX word, *ccbac*. Motifs of length 2 are *cc*, *cb*, *ba*, and *ac*.

FIGURE 2.

Motif determination. (A) Illustration of motif placement repositioning from vector format to icon. (B) Arrangement of motifs within an icon along with the discrete pain score patterns that the motifs represent. Each motif is associated with a pixel in the icon, and pixels are colored based on their relative importance as determined via bootstrapping. Pixels with values closer to 1 (pink color range) indicate motifs that carry greater importance, where importance reflects their relative over-representation both within and between icons of different strata. (C) Sample icon for the stratum of patients that underwent cardiovascular surgery, with text overlaying each pixel describing how the color was calculated.

FIGURE 3.

Motif distribution by age group. Three sets of icons (symbolic aggregate approximations using 2, 5, and 10 letters) for strata of patients based on age group. Here, β represents the number of pain intensity level such that $\beta = 2$ would represent a 2×2 matrix with pain levels reflecting low vs. high, while $\beta = 10$ would reflect 10 levels of increasing pain intensity. Labels underneath the $\beta = 10$ icons indicate how similar the stratum is from the stratum of patients aged 21 to 39 years, and icons are sorted in descending similarity.

FIGURE 4.

Motif distribution by gender. Three sets of icons (symbolic aggregate approximations using 2, 5, and 10 letters) for patient strata based on gender. The $\beta = 10$ icon corresponding to female patients is labeled to indicate its similarity to the male patient stratum.

FIGURE 5.

Motif distribution by type of surgery. Three sets of icons (symbolic aggregate approximations using 2, 5, and 10 letters) for patients' strata based on type of surgical procedure. Labels underneath the $\beta = 10$ icons indicate how similar the stratum is from the stratum of patients that underwent cardiovascular surgery, and icons are sorted in descending similarity.

FIGURE 6.

Motif distribution by home opioid status. Three sets of icons (symbolic aggregate approximations using 2, 5, and 10 letters) for strata of patients based on home opioid status. The $\beta = 10$ icon representing patients not on an opioid is labeled to indicate how similar the stratum is from the stratum of patients on an opioid.

FIGURE 7.

Motif distribution by postoperative day. Three sets of icons (symbolic aggregate approximations using 2, 5, and 10 letters) for strata of pain records within individual POD. Labels underneath the $\beta = 10$ icons indicate how similar the icon is to the POD = 0 icon, icons are sorted by ascending POD.

FIGURE 8.

Motif distribution by age group and gender. Three sets of icons (symbolic aggregate approximations using 2, 5, and 10 letters) for patient strata based on gender and age group. The $\beta = 10$ icons are labeled to indicate their similarity to the stratum of male patients aged 21 to 39 years, and strata are sorted in descending similarity.