Computer Methods and Programs in Biomedicine 219 (2022) 106754

Contents lists available at ScienceDirect

Computer Methods and Programs in Biomedicine

journal homepage: www.elsevier.com/locate/cmpb

IPOscore: An interactive web-based platform for postoperative surgical complications analysis and prediction in the oncology domain

Hugo Mochão [a], Daniel Gonçalves [a,b,f], Leonardo Alexandre [a,b,f], Carolina Castro [e], Duarte Valério [a], Pedro Barahona [h], Daniel Moreira-Gonçalves [k], Paulo Matos da Costa [i,j], Rui Henriques [f,g], Lúcio L. Santos [c,d,e], Rafael S. Costa [b,a,*]

[a] IDMEC, Instituto Superior Tecnico, Universidade de Lisboa, Lisboa, Av. Rovisco Pais 1, Lisboa, 1049-001, Portugal
[b] LAQV-REQUIMTE, DQ, NOVA School of Science and Technology, Universidade NOVA de Lisboa, Campus da Caparica, Caparica, 2829-516, Portugal
[c] Surgical ICU of the Portuguese Institute of Oncology, Porto, Portugal
[d] Surgical Oncology Department, IPO-Porto, Porto, Portugal
[e] Experimental Pathology and Therapeutics Group of Portuguese Institute of Oncology of Porto FG, EPE (IPO-Porto), Porto, Portugal
[f] INESC-ID, Lisboa, Portugal, R. Alves Redol 9, Lisboa, 1000-029, Portugal
[g] Instituto Superior Tecnico, University of Lisbon, Lisbon, Portugal
[h] NOVA LINCS, Dept. Informatica Faculdade de Ciencias e Tecnologia, Universidade NOVA de Lisboa, Campus da Caparica, Caparica, 2829-516, Portugal
[i] General Surgery Service, Hospital Garcia de Orta, E.P.E., Portugal
[j] Faculdade de Medicina da Universidade de Lisboa, Portugal
[k] Research Centre in Physical Activity, Health and Leisure, Faculdade de Desporto, Universidade do Porto, Porto, Portugal

A R T I C L E I N F O

Article history:
Received 12 October 2021
Revised 7 March 2022
Accepted 11 March 2022

Keywords:
Web-based platform
Decision support tool
Intelligent systems engineering
Postsurgical risk stratification
Cancer
Data management
Data mining
Machine learning

A B S T R A C T

Background: The performance of traditional risk score systems to predict (post)-operative outcomes is limited. This weakness reduces confidence in its use to support clinical risk mitigation decisions. However, the rapid growth of health data in the last years offers principles to deal with some of these limitations. In this regard, the data allows the extraction of relevant information for both patients stratification and the rigorous identification of associated risk factors. The patients can then be targeted to specific preoperative optimization programs, thus contributing to the reduction of associated morbidity and mortality. *Objectives*: The main goal of this work is, therefore, to provide a clinical decision support system (CDSS) based on data-driven modeling methods for surgical risk prediction specific for cancer patients in Portugal. *Results*: The result is IPOscore, a single web-based platform aimed at being an innovative approach to assist clinical decision-making in the surgical oncology domain. This system includes a database to store/manage the clinical data collected in a structured format, data visualization and analysis tools, and predictive machine learning models to predict postoperative outcomes in cancer patients. IPOscore also includes a pattern mining module based on biclustering to assess the discriminative power of a pattern towards postsurgical outcomes. Additionally, a mobile application is provided to this end. *Conclusions*: The IPOscore platform is a valuable tool for surgical oncologists not only for clinical data management but also as a preventative and predictive healthcare system. Currently, this clinical support tool is being tested at the Portuguese Institute of Oncology (IPO-Porto), and can be accessed online at https://iposcore.org.

1. Introduction

The ageing of populations worldwide will lead to an unprecedented increase in cancer cases and casualties. By 2030, 70% of all cancers will occur among adults over 65 years old [1], leading also to an unparalleled rise in surgeries. Due to the heterogeneity among the elderly, with its variation in physiological reserve, comorbidity and geriatric conditions, differences in (side) effects of therapy, like postoperative complications, are expected. Postoperative complications can impose a significant burden, increasing morbidity and mortality, in-hospital length of stay and need for a greater level of care at discharge [2,3]. Moreover, postoperative complications are associated with delays in chemotherapy leading

* Corresponding author at: LAQV-REQUIMTE, DQ, NOVA School of Science and Technology, Universidade NOVA de Lisboa, Campus Caparica, 2829-516, Caparica, Portugal.

E-mail address: rs.costa@fct.unl.pt (R.S. Costa).

https://doi.org/10.1016/j.cmpb.2022.106754
0169-2607/

to worse disease-free and overall survival rates [4]. Presumed fear of greater postoperative morbidity and mortality in these high-risk patients often results in sub-optimal delivery of cancer surgery (the most efficient curative approach for solid tumors [5–7]). To facilitate perioperative risk assessment to support the decision about which patients will mostly benefit from surgery, scoring systems incorporating traditional risk factors such as ASA [8], P-POSSUM [9], ARISCAT [10], and ACS score [11] have been developed. However, it is becoming clear that these tools are often not robust to support clinical decisions, particularly in the geriatric population, since predicted and observed rates significantly differ [12].

Recent advances in machine learning (ML) [13] and subspace clustering [14] offer principles to deal with some of these challenges, by unraveling relationships and patterns from complex datasets to predict future outcomes. Moreover, the constant growth of health data has created an urgent need for platforms based on intelligent algorithms that can be easily applied to extract clinical insights and improve outcomes [15].

In what follows, the IPOscore, a web-based clinical decision support system (CDSS) based on data-driven modeling methods for surgical risk prediction specific for cancer patients in Portugal, is presented. This is the structure of the remainder of this manuscript: section 2 covers related contributions and justifies the need for an innovative approach to assist clinical decision-making in the surgical oncology domain; the implementation of the platform is described in Section 3, and the discussion in Section 4, indicating the usefulness of the developed platform. Section 5 draws main conclusions and presents the limitations of the platform.

Despite the efforts described above, the existing clinical decision support web services and their use in the context of surgical oncology to predict postoperative outcomes have limitations: only relevant for specific surgeries; low to medium patient-level accuracy and precision; require trained clinicians in dealing with EHR; difficult transmission between data and model applications to enable the rapid implementation of validated models; and often are not based in machine learning algorithms (harder to maintain) [29]. In addition, these tools were primarily developed attending to the regularities of specific cohort studies, and therefore their applicability is limited to specific populations, with none targeting the Portuguese population. Therefore, our aim is to develop a powerful, intuitive and computationally scalable web platform based on ML and pattern mining to assist physicians in the interpreting and predicting of cancer surgery outcomes. Specifically, IPOscore can be divided into three major groups of facilities: i) a database of structured clinical data contributing to the definition of guidelines for long term preservations; ii) predictive ML models based on heterogeneity data for several cancer surgery outcomes (i.e. the predictive tool visually frames recommendations for a given individual against the overall population) and iii) pattern mining tools (i.e., to trace patterns in the target population satisfying strict statistical significance and discriminative power of surgical outcomes) in a single user-friendly web-based system. The combination of these features into a single web-based platform is novel, and in accordance with utility evidence in the surgical unit of IPO, IPOscore has been considered to aid pre-surgical, surgical and post-surgical care protocols/decisions.

2. Related work

The number of risk-prediction tools developed and validated in the medical context is increasing [16–18]. One example of a simple and widely used tool is the aforementioned P-POSSUM risk calculator [9] to identify patients at high risk of surgical complications. Other scoring system, developed by Virginia Mason Medical Center, predicts postoperative complications in the first 30 days after spinal deformity surgeries [19]. In the oncology domain, decision support systems (DSS) have been available for over ten years [20]. The IBM Watson for Oncology initiative proposed a platform based on artificial intelligence (AI) that recommends treatments for several types of cancer [21,22]. Another example of successful application of a web tool based on supervised ML algorithms can be found in Alabi et al. [23], who used neural networks to predict recurrences in early-stage oral cell carcinoma. Wang et al. [24] predict 5-year mortality of radical cystectomy by seven ML methods. More recently, clinical decision support based on AI and ML algorithms for the prediction of surgical outcomes have also been proposed. Sheikhtaheri et al. [25] proposed a clinical DSS to infer the complications of gastric bypass surgery. In another study, Soguero-Ruiz et al. [26] complemented Electronic Health Records (EHR) free text data with blood samples values and patient vital signs data to predict gastrointestinal surgical complications in colorectal cancer patients. Merath et al. [27] used a large national database to build predictive models for patient risk of developing complications following liver, pancreatic, or colorectal cancer surgery. Bihorac and co-workers [28] developed an automated analytics framework (*MySurgeryRisk*), a tool for a preoperative risk prediction using ML modeling of clinical data. However, the inherent potentialities of this tool are limited by the lack of a systematic comparison of different ML models, their applicability is restricted to only two outcomes (complications and death after surgery), and a user-friendly web-based platform of the algorithm has not been developed. Other web-based risk tools have also been emerging to aid surgical outcome predictions (e.g. [18]).

3. Implementation

3.1. Platform architecture

IPOscore is provided as a web platform and mobile app with a user-friendly interface through which healthcare professionals can manage and explore cancer patients data, and the prediction of surgical outcomes. The platform architecture has been generated with three major components as shown in Fig. 1, including: 1) the server backend, that stores the database and manages the requests to access its information; 2) the web frontend; and 3) the mobile application. The web platform is hosted at our own server and the mobile app is available at the Google Play store.

IPOscore is a platform developed using several open-source technologies. The backend was built upon Flask [30]. The Flask-HTTPAuth extension was used for user authentication and access control through token-based authentications. Additionally, the data was stored in an SQLite3 database [31] and a REST API was designed to allow access to the patients information by the web and mobile system. Finally, the web application was implemented using the Dash python framework, while the Dash Bootstrap Components [32] provided the website design and the integration with the Bootstrap open-source toolkit. The Flutter framework (https://flutter.dev) was used for the mobile application.

The data exploration and feature ranking module were implemented using statistical testing facilities [33–35] from *scipy* and *scikit-learn* Python (version 3.8) libraries [36], and visualization facilities from *plotly* library.

The pattern mining module was also implemented using *plotly*, and the discriminative patterns discovered from an extensive search as described in [37] using BicPAMS (Biclustering based on Pattern Mining Software) [38]. This search was expanded to all the outcomes of clinical interest. The patterns are stored in the database, each disclosing a subset of patients with coherent values across a subset of variables with guarantees of outcome-specific discriminative power and statistical significance.

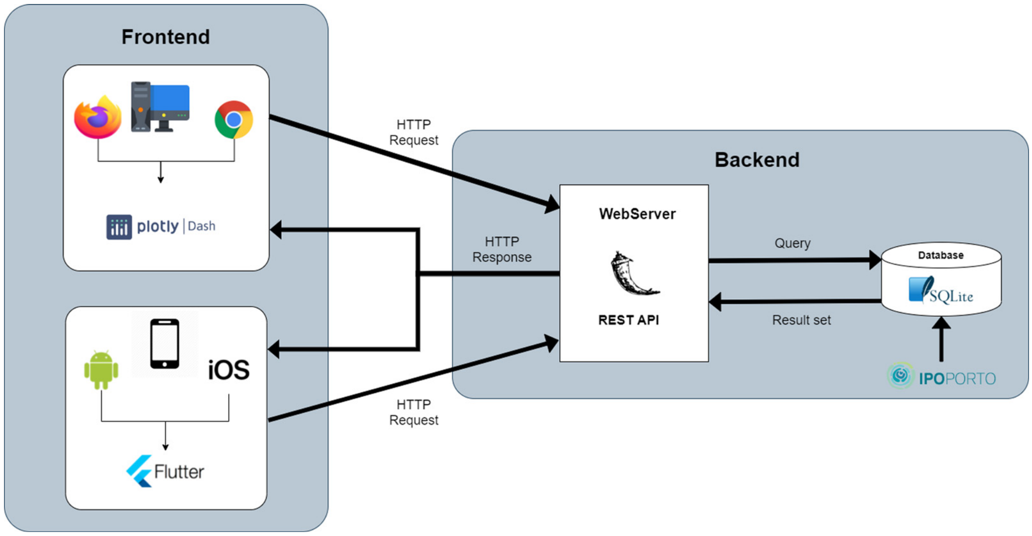


Fig. 1. Overview of the IPOscore platform architecture. The backend consists of the SQLite3 database with the IPO-Porto patients' data and their respective variables, and also the Flask REST API that processes the requests to manage and query the data. The frontend consists of a web application, that can be accessed in a web browser, and a mobile application. The communication between the frontend and backend is done by HTTP protocol.

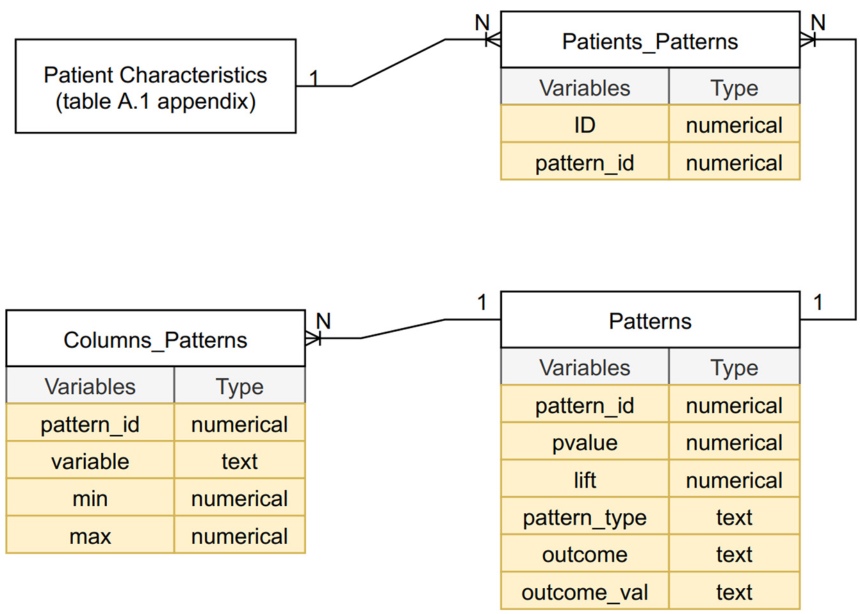


Fig. 2. Illustration of the database structure using Crow's Foot notation [43]. Table *Patient Characteristics* represents the current and future patients inserted by health professionals (for more information view Table A.1 in Appendix). Each patient may be associated with 1 or more patterns (to associate multiple patterns to multiple patients we created an additional table called *Patients_Patterns*). Table *Patterns* represents current and future patterns in the database. Each pattern is formed by a set of characteristics (statistical significance, discriminative power, pattern type, target outcome, and corresponding value), 1 or more patients, and 1 or more patient characteristics (this information is stored in tables *Patterns*, *Patients_Patterns* and *Columns_Patterns*, respectively).

The implementation of the surgical risk score module was employed using the Python language with the *scikit-learn* library [36]. Additionally, two independent packages were used for the XGBoost (version 1.3.3) [39] and CatBoost (version 0.24.4) [40] algorithms. Hyperparameter tuning was performed using the Bayesian approach through *hyperopt* (version 0.2.5) [41]. Moreover, the statistical exploration of the dataset was conducted with the *seaborn* (version 0.11.1) and *matplotlib* (version 3.4.2) libraries for the visualization, as well as *numpy* (version 1.19.2) and *pandas* (version 1.2.1) for data handling. The best predictive models resulting from our previous work [42] were serialized for usage in the web platform. Further information such as preprocessing, features and/or model selection, hyperparameter optimization and the models performance results are described in [42].

3.2. Data source and organization

The anonymized data was initially collected in an Excel spreadsheet from 2016 to 2018 at the Portuguese Institute of Oncology, Porto (IPO-Porto), a comprehensive cancer center in Portugal. Only surgical patients aged 18 years or older were included and were followed up for at least one year (or until death). The cohort of 805 eligible patients contains data from a range of variables (demographic, physiological, cancer location, histopathological, traditional risk score variables, surgical procedures and outcomes of interest). The available cohort is constituted by four major surgical types: thoracic (13.66%), digestive (44.10%), head and neck (24.22%), and others (17.02%). The surgeries type was mainly elective and only 8.57% of the procedures corresponded to emergency surgeries. The

Fig. 3. The components of the platform available after login. IPOscore provides four main modules: patients search & registry, data exploration & feature ranking, discriminative patterns discovery and surgical outcomes prediction.

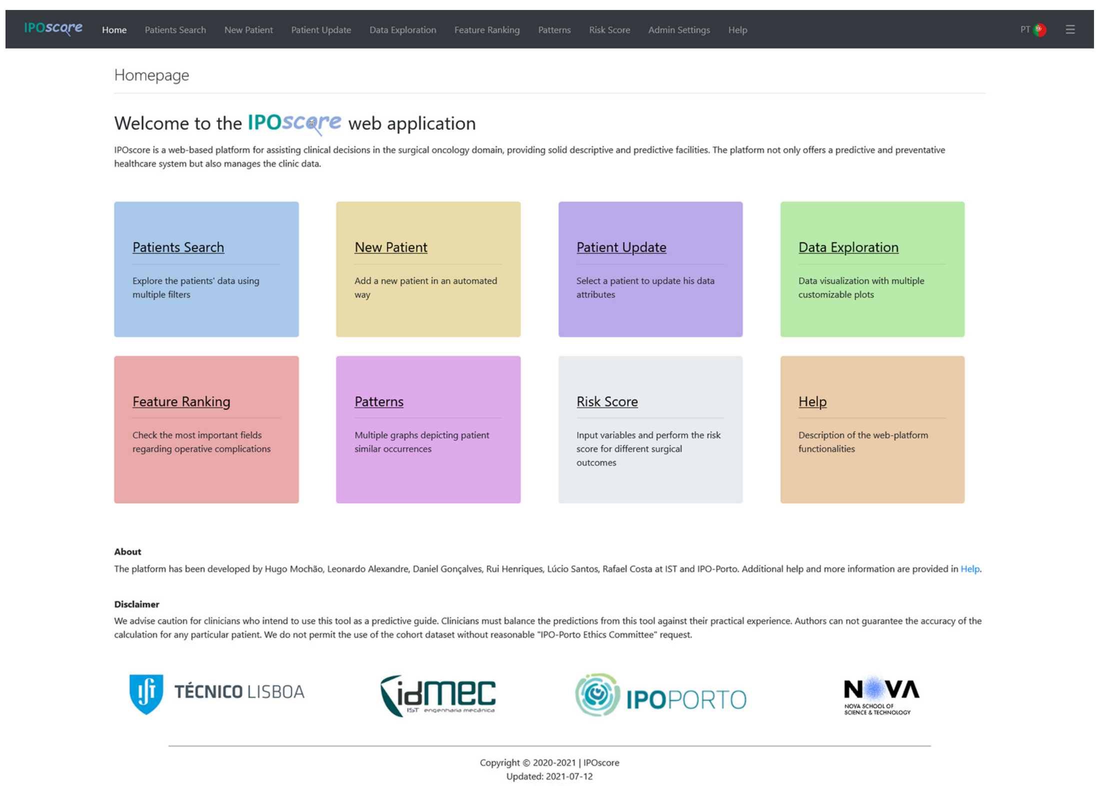


Fig. 4. IPOscore main user interface after login. Screenshot of the basic "Home" tab displays all the available modules. When the user clicks in a module, the system forwards him to the corresponding page.

anonymized dataset was approved by the IPO-Porto Ethics Committee (CES IPO:91/019) and the details for the variables available in the database can be observed in Table A.1 (Appendix). Furthermore, details of data processing are described in [42].

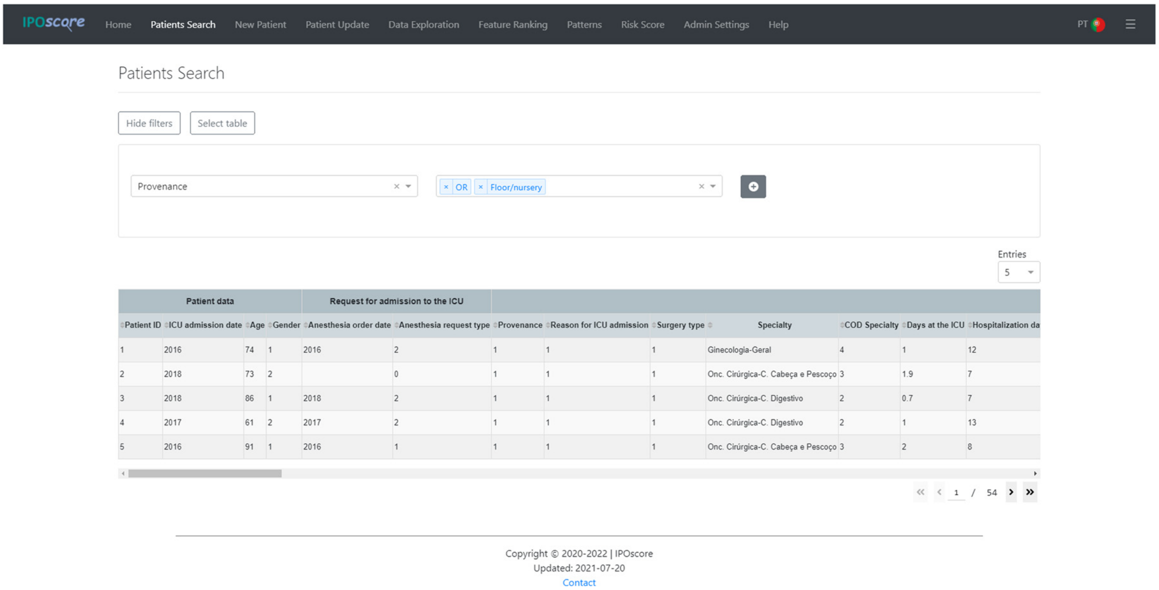
To accommodate the pattern mining module, additional tables had to be created. They store all the information relevant about each pattern to later be displayed to the user Fig. 2). The stored information corresponds to the patients data, the aforementioned variables, statistics, the type of pattern, and the postoperative outcome that the pattern discriminates.

3.3. Web-platform access

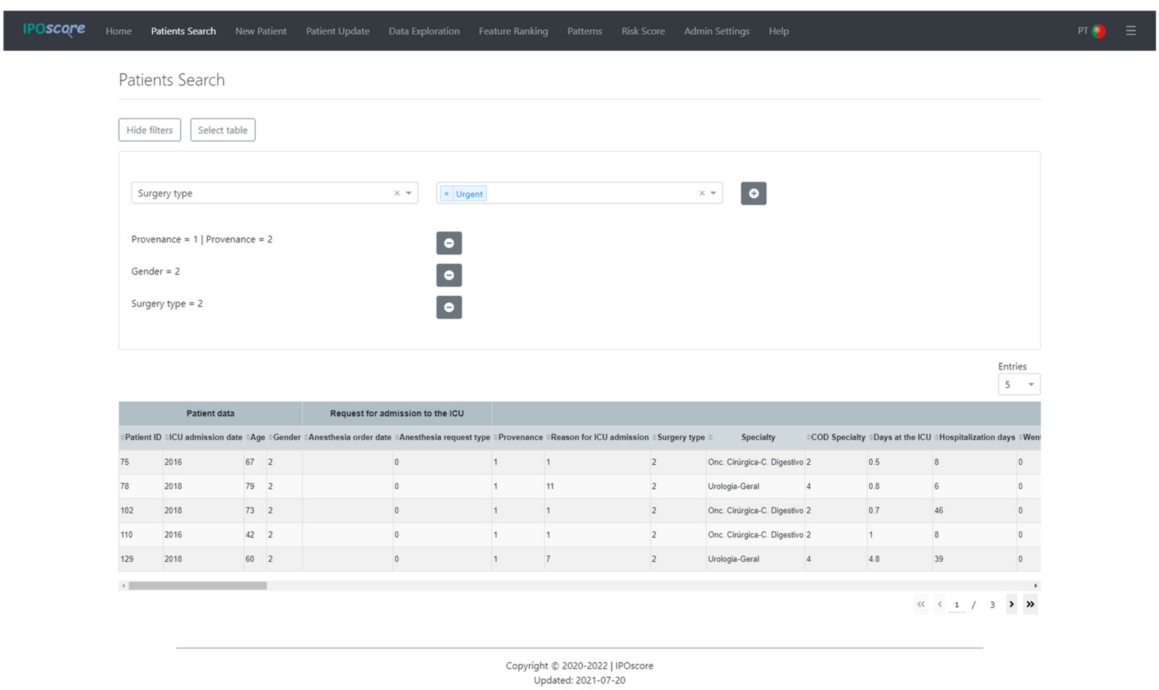
The user can access the platform using a web browser on www.iposcore.org. The Dash framework handles the navigation through the platform. Accessing or managing patients data triggers an HTTP request to the server using the REST API. Then, the server processes the request and accesses the database, retrieving or modifying the necessary data. Finally, it produces the corresponding HTTP response. The database will be routinely backed up and to access all the functionalities of the platform the user needs an account, which can only be created by the system administrator.

4. Results

The data integrated within IPOscore provides several opportunities for analysis and prediction in the oncology domain. IPOscore main functionalities (patients data access, data exploration and the clinical decision support) can be grouped into distinct modules



(a)



(b)

Fig. 5. a) User interface of the “Patient Search” function: attribute to query and its patients table. The highlighted panel shows the search module implemented in the database to obtain specific information. b) An example interface of a typical search and associated results table. Search by “Provenance”, “Gender” and “Surgery type”.

that will be described in the next sections. Figure 3 shows the main components that can be performed within the platform.

4.1. Web-interface

The web-based platform was designed to be used by registered healthcare professionals and consists of the login option and ten tabs (Fig. 4): 1) Home, 2) Patients Search, 3) New patient, 4) Patient update, 5) Data exploration, 6) Feature ranking, 7) Patterns, 8) Risk Score, 9) Admin Settings and 10) Help.

Before login, only the “Home”, “Risk Score” and “Help” tabs are freely available. To access all the platform panels and features it is necessary to have an account. The interactive interface was designed for three types of registered users: 1) basic user, 2) advanced user and 3) administrator. The basic user can explore the patients data but cannot modify it. Hence, this user type has access to the “Patients Search”, “Data Exploration”, “Feature Ranking”, “Patterns”, and “Risk Score” tabs. In addition to the basic user permissions, the advanced user can manage the patient data. After login, the advanced user has access to the “Patients Search” tab to search/filter the patients available data and in the “Patient update” tab to modify their data. For new patients not registered in the database, the advanced user can register a new patient entry. The admin can manage the entire system.

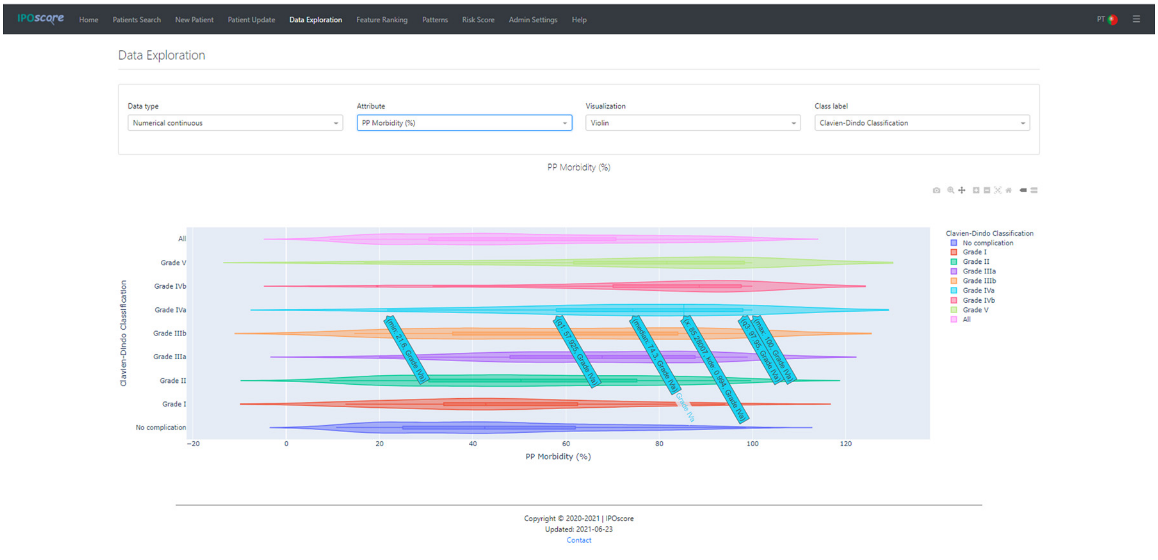


Fig. 6. Screenshot of the violin plot with the following configurations: Clavien-Dindo classification outcome (class label) and PP Morbidity(%) variable (atribute). Each violin represents a grade from the Clavien-Dindo classification.

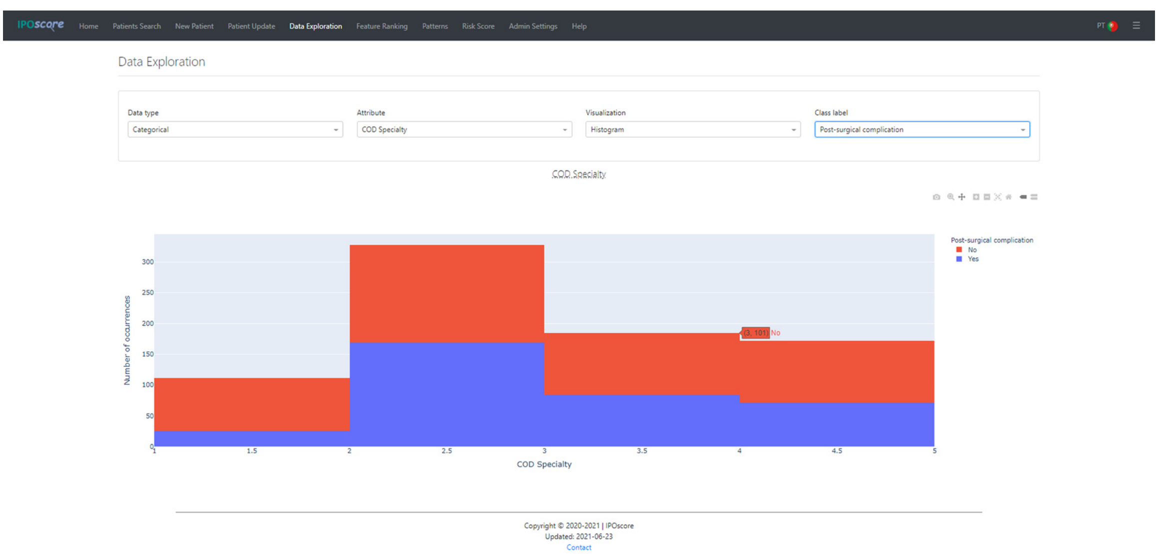


Fig. 7. Screenshot of the data exploration histogram with the configurations: *postsurgical complication outcome* and *COD Speciality*.

The “Data exploration” tab provides several interactive plotting types designed to offer a better understanding and visualization options of the data, while “Feature ranking” tab displays an ordered bar plot of the most statistically significant variables. Visualizations such as violin charts [44] and histogram allow the user to inspect the distribution of the data (Figs. 6 and 7). Violin charts provide the user a clean view of the distribution if the variable is continuous, but if the variable is discrete or categorical it can be better assessed when visualized as a histogram. The interactive histogram allows the user to see the occurrence of each value/category. The aforementioned visualizations show the user both the variable distribution as well as the conditional variable distribution considering a selected patient outcome after surgery (postsurgical complications, ranking of postsurgical complication, survivability aspects or hospitalization needs). Finally, the parallel coordinates [45] visualization allows the user to see how each patient in the database, with a range of values for one or multiple variables (categorical or numerical), varies among other variables and postsurgical outcomes.

In IPOscore, the “Patterns” page provides an insightful view on patients entities that have similar conditions. Firstly, a more general view is displayed where the user can observe how many patterns, of each postsurgical outcome, matched the criteria. This criteria is defined either by inputting patients’ variables, or by selecting a patient in the database. Secondly, a more specific view can be obtained by specifying the postsurgical outcome. This view displays a list of the matched patterns as well as the corresponding plot of the selected pattern.

The “Risk Score” page allows to predict eight surgical outcomes. Additionally, the “Admin Settings” tab is where the platform is administered. Finally, the “Help” panel collects a set of frequently asked questions.

All these interfaces allow data visualization and analysis for the physicians without the need of any programming skills.

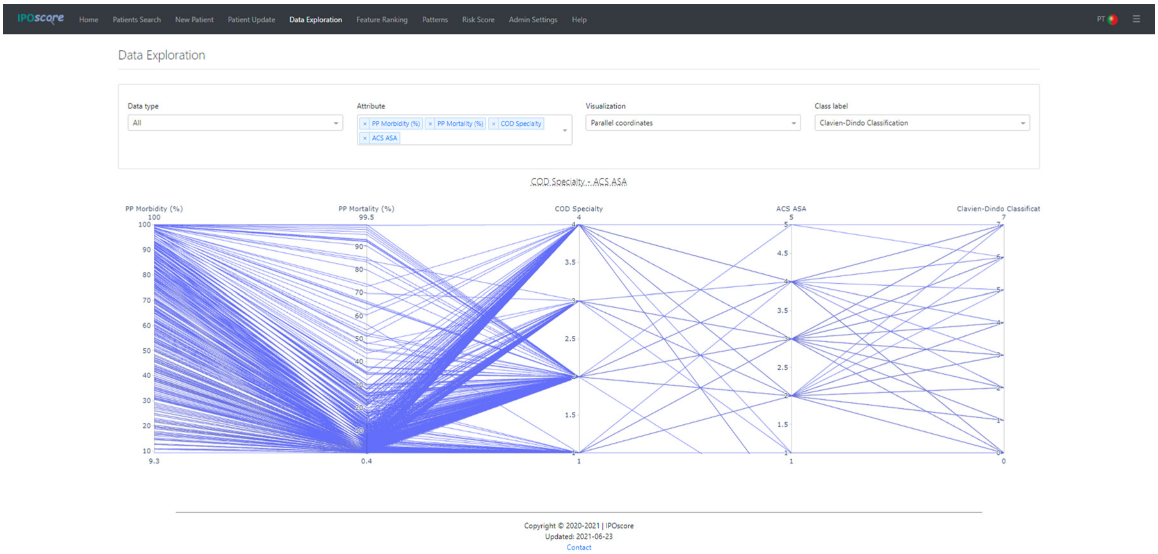


Fig. 8. Screenshot of the parallel coordinates visualization with the following configurations: PP Morbidity (%), PP Mortality(%), COD Speciality, ACS ASA, and Clavien-Dindo classification outcome. Each blue line represents a patient.

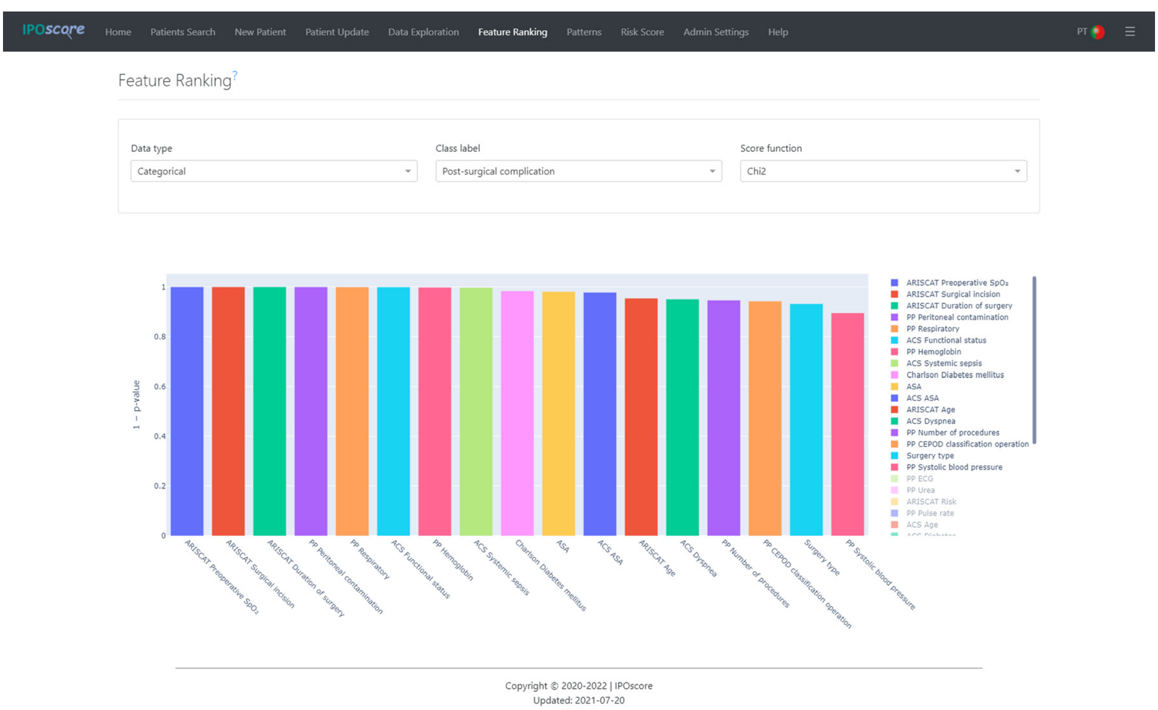


Fig. 9. Feature ranking bar chart visualization using categorical data, postsurgical complication (yes/no) outcome, and χ^2 test. Each bar represents a categorical variable that was matched with postsurgical complication outcome in the χ^2 test. The variables are ordered from most correlated (first left bar) to less correlated (last right bar).

4.2. Search queries and patients registry

Viewing raw data can be extremely difficult if they are not rightly grouped or described. Hence the need to provide a user-friendly graphical interface in which the users can search and filter all these complex data. In IPOscore, the interface includes a wide range of attributes, divided by several categories.

From the “Patients Search” page, the user finds a table with the registered patients entities data grouped by categories: 1) Request for admission to the Intermediate Care Unit, 2) Patient data, 3) Hospitalization characteristics, 4) Surgery data, 5) P-Possum Score, 6) ACS Risk Calculator, 7) ARISCAT Score, 8) Charlson Score, 9) Postsurgical complications, and 10) Discharge Information. Several types of queries may be of interest to the physicians. These data allow users to search the data by simple and multiple queries, where the user selects the filters to obtain a specific table result (Fig. 5a). The query depicted by its multiple Boolean operators (AND/OR) appears below to inform the user which filters are active (Fig. 5b). To facilitate data readability, the user can also select which categories

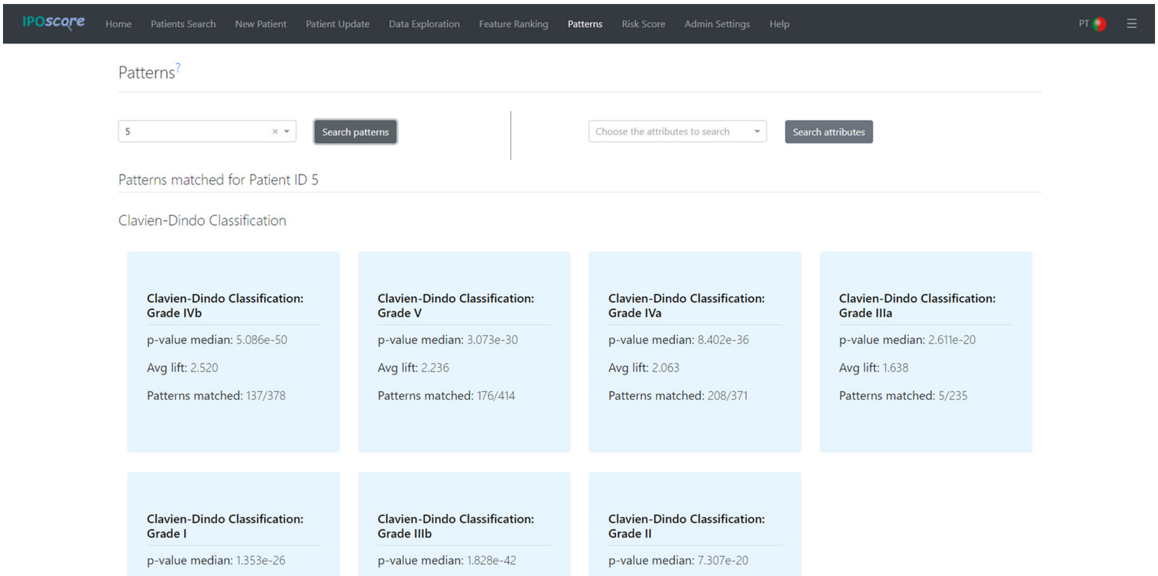


Fig. 10. General screenshot visualization of the "Patterns" page for a specific patient. The user is able to either select a patient from the database or input specific variables (and customize the value). The profile is then matched with existing patterns, and a list of postsurgical outcomes and other logistic outcome variables is displayed, with the respective metrics (number of patterns matched, statistical significance and discriminative power).

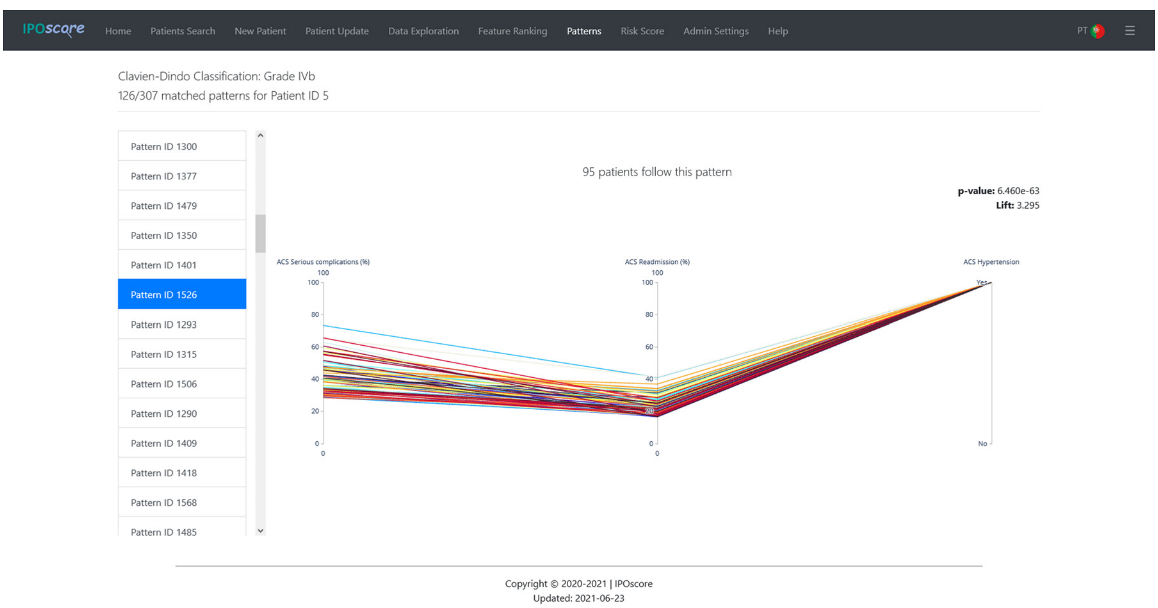


Fig. 11. Final visualization of a single pattern. A list of patterns of Clavien-Dindo classification grade IVb, and a parallel coordinates visualization, are presented in order to better analyse the patterns that matched with a patient. The parallel coordinates displays a group of patients who presented an ACS serious complication (%) variable between 28.5 and 73.4, an ACS readmission (%) between 16.6 and 41.3, and ACS hypertension (yes). Each axis represents a variable and each line represents the patients within the pattern and their respective profile (along the axis).

of variables are displayed and the patients table will be changed accordingly.

To register a new patient an electronic data-submission form is provided ("New Patient" tab). The online form was divided by the attribute categories in nine groups of variables. To prevent mistakes and standardize the patient registration, most of the attributes values were predefined and available to be selected in dropdowns. To facilitate the completion of forms, the result outcomes of the traditional scores (Charlson, ARISCAT and P-Possum score) were automated. The "Update Patient" tab uses the same data-submission form, with the form data being automatically filled with the attributes of the selected patient.

4.3. Data exploration and feature ranking

IPOscore offers a variety of plotting types like violin, histograms and parallel coordinates. To interact with the data exploration module the user is presented with four input options: 1) type of data, 2) patients profile characteristic, 3) visualization type to explore the data, and 4) the postsurgical outcome to change the class conditional part of the visualization.

The violin visualization creates multiple violin plots showing the difference in distribution when considering all the patients (Fig. 6). By hovering the violin plots the user can also inspect statistics such as the minimum value, median, and maximum value.

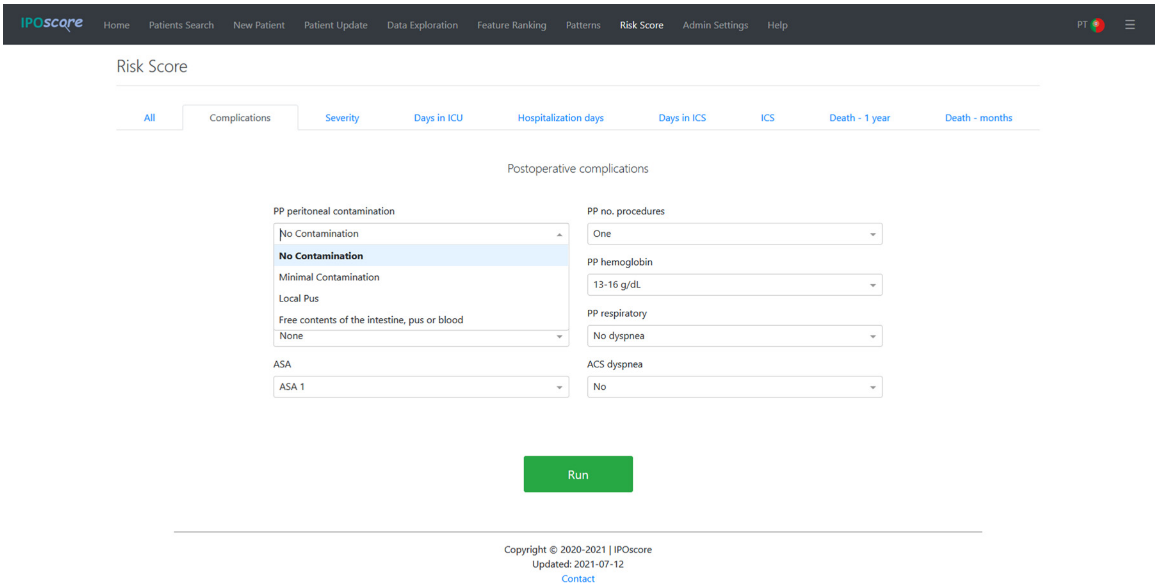


Fig. 12. Example of the risk score interface for the surgical complications outcome prediction. The eight input variables are selected based on dropdown boxes.

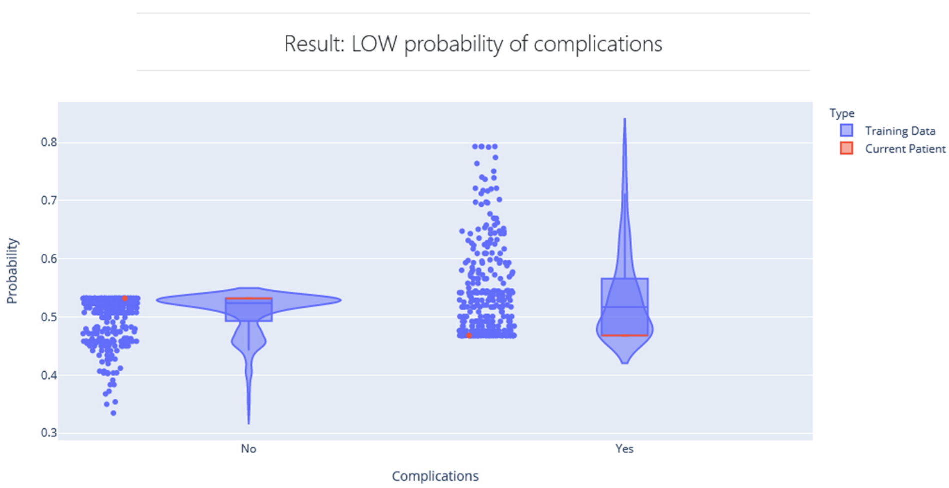


Fig. 13. Screenshot example for the "Complications" outcome showing: i) a text message with the model's outcome and ii) a violin plot with the probabilities predicted for every patient used in training (blue dots) and the probabilities predicted for the current patient (red dot).

The histogram will break into multiple overlapped bars with the red bars representing only patients who did not suffer postsurgical complications and blue bars representing patients who suffered (Fig. 7).

The parallel coordinates visualization allows the user to select at least one variable matched with an outcome and can be observed in Fig. 8. Additionally, characteristics can be added in order to explore how the patients profile characteristic reflects on other characteristics, as well as correlate with specific outcomes. The parallel coordinates also allows the user to select a range in each characteristic, highlighting the patients who belong to that range throughout the characteristics.

Other properties of the data can be explored by using the "Feature Ranking" page. In this module the user can select the data type (which automatically uses all the variables that match that data type), the postsurgical outcome, and the statistical test (χ^2 test [33] for nominal variables, Kruskal-Wallis test [34] for discrete variables, and ANOVA or F-Test for continuous variables [35]). The outcomes of the tests are ranked according to their p-values (Fig. 9). The interface allows users to inspect their value, and interact with the list of variables presented by clicking the name, to hide or show the corresponding bar in the chart.

4.4. Pattern mining module

Given the database, defined by a set of observations (patients), $X = \{x_1, \ldots, x_n\}$, variables, $Y = \{y_1, \ldots, y_m\}$, and elements a_{ij} observed for observation x_i and variable y_j, all relevant patterns, $\mathcal{B} = \{B_1, \ldots, B_s\}$, are maintained in the platform, where a pattern $B = (I, J)$ is associated with a subset of variables, $J = (j_1, \ldots, j_k) \subseteq Y$, and a subset of patients, $I = (i_1, \ldots, i_l) \subseteq X$, yielding specific homogeneity, statistical significance and dissimilarity criteria. A sound statistical testing of the patterns of surgical risk is key to guarantee their occurrence probability (against a null model) deviates from expectations. To this end, the statistical tests proposed in BSig [46] are used to minimize false positives (extracted patterns that

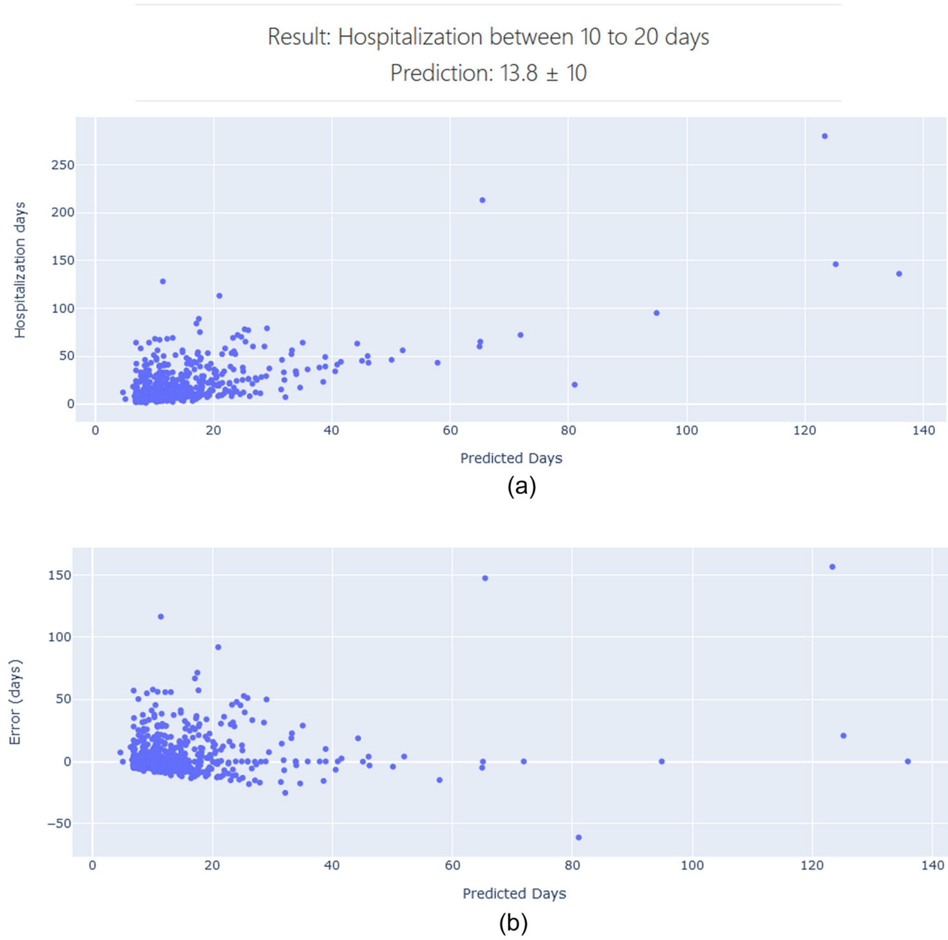


Fig. 14. Screenshot example of a continuous surgical outcome prediction. a) "Hospitalization Days" outcome showing a message with the standardized interval of stay, the exact predicted length ± the model's mean absolute error, complemented by a plot with the actual vs. predicted length of stay for all the patients used for training; b) Residuals plot with the prediction error for every prediction made for the patients used in training.

appear by chance on the cohort data). This is done without considerably increasing the risk of excluding relevant patterns (false negatives) since the pursued statistical tests place non-conservative corrections (Holm and Hochbert corrections) to satisfy the family-wise error rate. In this work the patterns show coherence across individuals, as such, binomial tails can be used to approximate the probability of a bicluster $B = (I, J)$ with pattern φ_B to occur for a given number of individuals, $p_B = P(Z \geq |I|)$, and $Z \sim Bin(p_{\varphi_B}, |X|)$, where $|I|$ is the number of individuals with pattern φ_B, $|X|$ is the total number of individuals, and p_{φ_B} is the occurrence probability of pattern, which essentially depends on the variable distributions approximated from the available cohort data. Lift, a well-established characteristic in association rules [47], was used to assess the discriminative power of a pattern towards a postsurgical outcome.

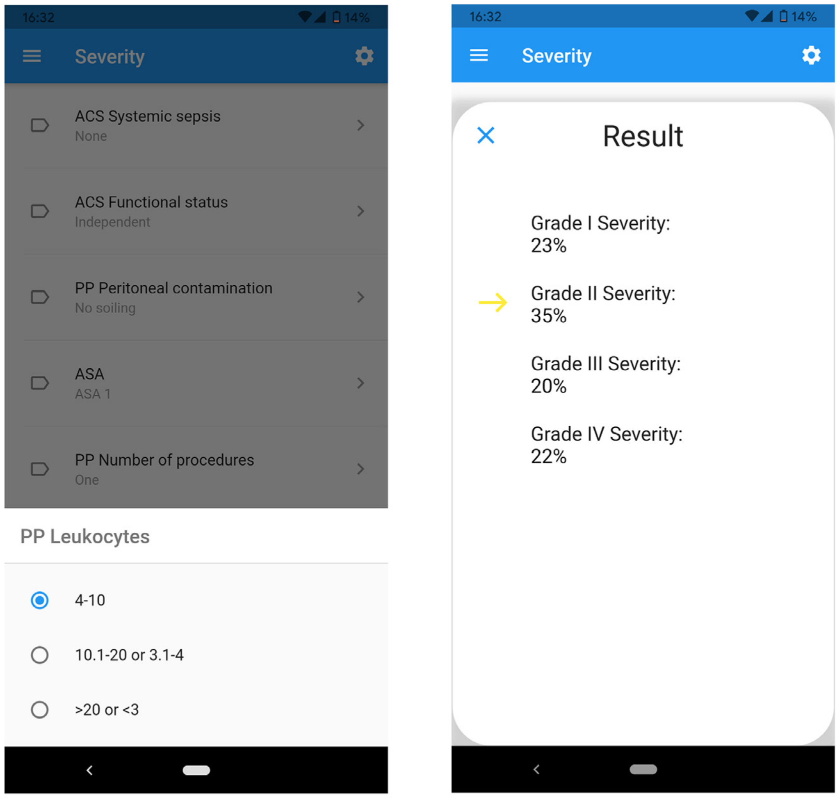
The user can interact with this module by selecting a patient or a set of variables. Figures 10 and 11 display an example case for a 91-year-old female patient with a history of diabetes, hypertension, dementia, asthma and a pacemaker. The set of variables are matched with the available patterns, of each postsurgical outcome, and a general visualization is presented (Fig. 10). Each container in this visualization presents the postsurgical outcome, average lift of matched patterns (discriminative measure), median p-value of matched patterns (statistical significance), and the number of patterns that match the patient's profile. The containers are ordered by discriminative power. When one of the containers is selected another visualization will be presented to the user (Fig. 11). In this interface, a list of patterns that match the selected patient (or inputted variables), as well as a parallel coordinates visualization for single pattern visualization are presented. From all the surveyed tools, only IPOscore is able to perform this descriptive analysis i.e., to trace patterns in the target population satisfying strict statistical significance and discriminative power of surgical outcomes.

4.5. ML-based risk score

The risk score module includes predictive models for eight main surgical outcomes in cancer patients: i) postoperative complications, ii) severity of complications, iii) number of days in the intermediate care unit (ICU), iv) if the patient requires intensive unit care, v) number of days in the intensive care unit (ICS), vi) total number of days in the hospital, vii) one-year mortality after surgery, and viii) time of death after surgery (Fig. 12).

A postoperative complication is defined as a deviation from the ideal postoperative course, which is deemed clinically connected to the surgery prior, requiring any intervention, and happening within the first 90 days after the surgery for cancer treatment. Such outcome is binary, therefore a classification approach is used, with a discrete and well defined set of labels to attribute to a certain patient. Moreover, the Clavien-Dindo system [48] was used to classify the severity of a complication. In this case, a multi-class classification approach is performed.

Due to the continuous and purely numeric nature of the number of days spent in the intermediate care unit, regression models



(a) (b)

Fig. 15. Printscreen examples of the mobile app. a) Input interface. The user chooses the input variables that will be used to predict a risk score outcome; b) Output panel. Snapshot of the risk score for the severity complication outcome. Each value is presented along with an icon that represents the prediction.

are used. Whether or not a stay in an intensive care unit is expected to be required is also crucial information in preoperative time. This prediction is binary and addressed by classification. To complement it, we predict the amount of days in the intensive care unit with a regression model. The total number of days in the hospital is another important outcome. This outcome is addressed by regression models.

We conducted the mortality outcome as a classification problem with the objective of predicting one-year mortality. Death can also be narrowed down to certain post surgical periods. The time frames comprehend: the first 30 days, the period between 30th day and the 90th, the period between the 90th day and 1 year, and also the death past 1 year from surgery. These are four different periods, predicted by classification models.

In order to provide a clinical intuitive interface to the developed predictive models, the platform includes a page dedicated to this module providing graphical facilities to the user. This page includes eight sub-tabs, one for each outcome prediction, providing a mean to input the required variables and to intuitively assess the results of each model. The process of the outcome predictions is facilitated by the input of specific variables (maximum of twenty to obtain all outcomes on the "All" sub-tab) selected in the feature selection process (see more details in [42]).

To illustrate the risk score module (discrete outcome), an example case is shown here that considers a patient with the following inputs: no peritoneal contamination, independent ACS functional status, no sepsis, ASA 1, one PP procedure, hemoglobin 13–16 g/dL and no dyspnea (Fig. 13). This results in a message with the most probable outcome. The output is chosen based on the probabilities dealt by the predictive model, by choosing the outcome with the highest probability among the range of possibilities. Meaning that there is no specified threshold or cutoff value for this decision to happen. A plot with the training set probabilities is also obtained. The patients in the training set are displayed by the blue colored dots and the current patient is displayed in red (Fig. 13). This information offers insight into the confidence of the model when making a decision, both with familiar instances in the training set and the new patient inserted. Moreover, the results can be downloaded. Note that when we have a missing input variable this has to be filled by the user, providing an estimate or default value in order to enable the outcome prediction. The selected inputs have been carefully selected in our previous study [42] and their input is mandatory. By incorporating user knowledge on the estimation of missing data the tool effectively allows for the introduction of expert knowledge. By default, the interface already pre-fills all the input fields.

Regarding the continuous outcomes (e.g. "Hospitalization Days"), a message with the interval (and exact value) of the outcome is obtained, which is useful in clinical practice. This outcome also contains a graphical interface with the model performance. Two plots are displayed: one with the actual versus predicted values (Fig. 14a), and another with a residual plot (Fig. 14b). Together they offer two different perspectives into the predictive performance achieved by the predictive models and allow the users for a better interpretation of the results.

4.6. Mobile application

IPOscore also allows the "Risk Score" module calculation provided by a smartphone health app. Similarly to the web application, it provides a simple user interface to select the input values and predict the outcomes (Fig. 15a). The results are shown with icons that change according to the outcome results (Fig. 15b).

5. Discussion

IPOscore is, to the best of our knowledge, the first tool that provides both predictive ML models and pattern mining in the surgical oncology domain using a user-friendly web-based platform. There are decision support tools available [9,23,28,49] that are able to perform some of the tasks mentioned above. However, IPOscore is able to address some of the shortcomings of these existing systems, offering a broader view of individual needs by accommodating an enlarged set of clinical outcomes together with explainability principles. In particular, the predictive tool visually frames recommendations for a given individual against the overall population, thus providing a trustworthy context for professionals to assess the confidence of the recommendations. In addition, the platform comprehensively traces patterns in the target population satisfying strict statistical significance, discriminative power of postoperative outcomes, and actionability guarantees. For clinical practice, this module has not only been important to confirm medical knowledge and intuition on postoperative outcome prediction, yet as well expanding their current knowledge with less trivial findings.

The platform yields additional unique properties of interest: i) ensures full access control, privacy, and security aspects while offering the advantages and convenience of browser access at both desktop and mobile devices; ii) adjusts itself to the continuously arriving patients, allowing dynamic database updates which are then reflected in the provided visualization ("Data Exploration" module) and statistical facilities ("Feature Ranking" module); iii) respects extensibility principles for the easy incorporation of new modules and facilities; and iv) further satisfies interoperability and availability requirements.

The statistical framing of recommendations and usability guarantees of IPOscore have been acknowledged by healthcare professionals at IPO-Porto. In particular, its descriptive and predictive facilities have paved the way to relevant clinical initiatives, primarily related with the establishing of personalized presurgical habilitation, bedside monitoring and home care protocols.

Looking forward, IPOscore will be updated routinely with health data from new cancer patients and different regions of Portugal (i.e. from multicenter studies). In the presence of data updates, the predictive ML models will also be routinely retrained.

6. Concluding remarks

In this work, we introduced IPOscore, a web-based platform for assisting clinical decisions in the surgical oncology domain, providing descriptive and predictive facilities. The platform is currently in use at the Portuguese Institute of Oncology, IPO-Porto, one of the largest oncological hospitals in Portugal. The primary users are surgeons, intensive care physicians, nurses, and anesthetists. Altogether, the descriptive, predictive and optimization facilities provided by the presented platform offer a trustworthy context for the multifaceted design of surgical interventions, as well as establishing pre and postoperative care protocols.

A few limitations can be noted: i) The safety feature of restricting access to the full features to users may hinder occasional use by some professionals; ii) By design, IPOscore addresses postsurgical outcomes prediction for cancer patients; it can in the future be extended to other cohorts of patients, if available data and interest from healthcare professionals exist. iii) Data comes from a single centre. In the future, data from other healthcare units may be incorporated, providing more accurate predictions. iv) Serialized predictive models used by IPOscore have been validated by the clinicians who are using it, but further external validation is necessary to ensure the quality of this tool; and v) Currently, the patients are individually inserted in the database, and although the input is done with predefined values, this process could be improved by performing batch inserts to identify potential mistakes through outlier detection.

Funding

This work was supported by Fundação para a Ciência e a Tecnologia (FCT), through IDMEC, under LAETA project (UIDB/50022/2020) and IPOscore with reference (DSAIPA/DS/0042/2018). This work was further supported by the Associate Laboratory for Green Chemistry (LAQV), financed by national funds from FCT/MCTES (UIDB/50006/2020 and UIDP/50006/2020), INESC-ID plurianual (UIDB/50021/2020), the FCT individual PhD grant to LA (2021.07759.BD) and the contract CEECIND/01399/2017 to RSC.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

CRediT authorship contribution statement

Hugo Mochão: Software, Writing – review & editing. **Daniel Gonçalves:** Software, Writing – review & editing. **Leonardo Alexandre:** Software, Writing – review & editing. **Carolina Castro:** Data curation. **Duarte Valério:** Writing – review & editing. **Pedro Barahona:** Writing – review & editing. **Daniel Moreira-Gonçalves:** Data curation. **Paulo Matos da Costa:** Data curation. **Rui Henriques:** Software, Writing – review & editing. **Lúcio L. Santos:** Conceptualization, Data curation. **Rafael S. Costa:** Conceptualization, Software, Supervision, Writing – review & editing.

Acknowledgments

The authors thank IPO-Porto for providing the anonymized data.

Appendix A. Database variables

Table A.1
Database variables. Contains the set of variables that describe each patient (outcome variables are star-marked).

domain	variable	type	domain	variable	type
PATIENT DATA	ICU admission date	date	ACS RISK	ACS procedure	text
	age	numerical		ACS age	categorical
	genre	binary		ACS functional status	categorical
	preoperative comorbidities	text		ACS emergency	binary
HOSPITAL STAY	provenance	categorical		ACS ASA	categorical
	reason for ICU admission	categorical		ACS steroids	categorical
	surgery type	binary		ACS ascites	binary
	specialty	categorical		ACS systemic sepsis	categorical
	days at the ICU*	numerical		ACS ventilation dependency	binary
	days at IPOP*	numerical		ACS disseminated cancer	binary
	destination after ICU*	categorical		ACS diabetes	categorical
	NAS points*	numerical		ACS hypertension	binary
	surgery recurrence	binary		ACS ICC	binary
	preoperative QT	binary		ACS dyspnea	categorical
	ICU readmission*	binary		ACS smoker	binary
SURGERY DATA	ASA	categorical		ACS DPOC	binary
	location	categorical		ACS dialysis	binary
	preoperative diagnosis	text		ACS acute renal failure	binary
	surgery date	date		ACS height	numerical
	surgery class	text		ACS weight	numerical
	interventions: ICD10	text		serious complications (%)	numerical
	procedures: COD	text		any complication (%)	numerical
POST SURGICAL COMPLICATION	postsurgical complication*	binary		pneumonia (%)	numerical
	complication description*	text		cardiac complications (%)	numerical
	main complication: COD*	text		surgical infection (%)	numerical
	secondary complications: COD*	text		ITU (%)	numerical
	ACS general complications*	binary		venous thromboembolism (%)	numerical
	ACS specific complications*	categorical		renal failure (%)	numerical
	Clavien-Dindo classification*	categorical		anastomotic leak (%)	numerical
ADMISSION REQUEST	anesthesia request date	date		readmission (%)	numerical
	anesthesia type	categorical		reoperation (%)	numerical
ARISCAT	ARISCAT age	categorical		death (%)	numerical
	ARISCAT SpO2	numerical		discharge to nursing/rehab (%)	numerical
	ARISCAT resp. infection	binary		ACS forecast of hosp. days	numerical
	ARISCAT preoperative anemia	binary	P-POSSUM	PP age	categorical
	ARISCAT surgical incision	categorical		PP respiratory	categorical
	ARISCAT surgery duration	categorical		PP ECG	categorical
	ARISCAT emerging procedure	binary		PP systolic blood pressure	categorical
	ARISCAT score	categorical		PP arterial pulse	categorical
CHARLSON	Charlson age	categorical		PP hemoglobin	categorical
	Charlson diabetes mellitus	categorical		PP leukocytes	categorical
	Charlson liver disease	categorical		PP urea	categorical
	Charlson malignity	categorical		PP sodium	categorical
	Charlson AIDS	binary		PP potassium	categorical
	Charlson chronic kidney disease	binary		PP glasglow scale	categorical
	Charlson heart failure	binary		PP type of surgery	categorical
	Charlson myocardial infarction	binary		PP number of procedures	categorical
	Charlson COPD	binary		PP blood loss	categorical
	Charlson peripheral vascular	binary		PP peritoneal contamination	categorical
	Charlson AVC/transient ischemic	binary		PP state of malignancy	categorical
	Charlson dementia	binary		POSSUM physiological score	numerical
	Charlson hemiplegia	binary		PP CEPOD-classification	categorical
	Charlson connective tissue	binary		PP cardiac	categorical
	Charlson peptic ulcer	binary		PP surgical severity score	numerical
	Charlson comorbidity index	numeric		POSSUM physiological score	numerical
	% estimated 10-year survival	numeric		PP CEPOD-classification	categorical
DISCHARGE	destination after IPO*	categorical		PP cardiac	categorical
	death up to 1 year*	binary		PP surgical severity score	numerical
	surgery-to-death time (<1year)*	categorical		PP % morbidity	numerical
				PP % mortality	numerical

References

[1] M.C. White, D.M. Holman, J.E. Boehm, L.A. Peipins, M. Grossman, S.J. Henley, Age and cancer risk: a potentially modifiable relationship, Am. J. Prev. Med. 46 (3) (2014) S7–S15.

[2] V.A. Ferraris, M. Bolanos, J.T. Martin, A. Mahan, S.P. Saha, Identification of patients with postoperative complications who are at risk for failure to rescue, JAMA Surg. 149 (11) (2014) 1103–1108.

[3] M. Vester-Andersen, L.H. Lundstrøm, M. Møller, T. Waldau, J. Rosenberg, A.M. Møller, D.A. Database, Mortality and postoperative care pathways after emergency gastrointestinal surgery in 2904 patients: a population-based cohort study, Br. J. Anaesth. 112 (5) (2014) 860–870.

[4] R.P. Merkow, D.J. Bentrem, M.F. Mulcahy, J.W. Chung, D.E. Abbott, T.E. Kmiecik, A.K. Stewart, D.P. Winchester, C.Y. Ko, K.Y. Bilimoria, Effect of postoperative complications on adjuvant chemotherapy use for stage III colon cancer, Ann. Surg. 258 (6) (2013) 847–853.

[5] B. Ten Wolde, M. Kuiper, J.H. de Wilt, L.J. Strobbe, Postoperative complications after breast cancer surgery are not related to age, Ann. Surg. Oncol. 24 (7) (2017) 1861–1867.

[6] R.A. Audisio, H. Ramesh, W.E. Longo, A.P. Zbar, D. Pope, Preoperative assessment of surgical risk in oncogeriatric patients, Oncologist 10 (4) (2005) 262–268.

[7] H.S.J. Ramesh, D. Pope, R. Gennari, R.A. Audisio, Optimising surgical management of elderly cancer patients, World J. Surg. Oncol. 3 (1) (2005) 1–14.

[8] M. Saklad, Grading of patients for surgical procedures, Anesthesiology 2 (3) (1941) 281–284.

[9] M. Whiteley, D. Prytherch, B. Higgins, P. Weaver, W. Prout, An evaluation of the possum surgical scoring system, Br. J. Surg. 83 (6) (1996) 812–815.

[10] J. Canet, L. Gallart, C. Gomar, G. Paluzie, J. Valles, J. Castillo, S. Sabate, V. Mazo, Z. Briones, J. Sanchis, Prediction of postoperative pulmonary complications in a population-based surgical cohort, Anesthesiology 113 (6) (2010) 1338–1350.
[11] K.Y. Bilimoria, Y. Liu, J.L. Paruch, L. Zhou, T.E. Kmiecik, C.Y. Ko, M.E. Cohen, Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons, J. Am. Coll. Surg. 217 (5) (2013) 833–842.
[12] J. Watt, A.C. Tricco, C. Talbot-Hamon, P. Rios, A. Grudniewicz, C. Wong, D. Sinclair, S.E. Straus, et al., Identifying older adults at risk of harm following elective surgery: a systematic review and meta-analysis, BMC Med. 16 (1) (2018) 1–14.
[13] J.A. Cruz, D.S. Wishart, Applications of machine learning in cancer prediction and prognosis, Cancer Inform. 2 (2006) 117693510600200030.
[14] J. Lobo, R. Henriques, S.C. Madeira, G-Tric: generating three-way synthetic datasets with triclustering solutions, BMC Bioinf. 22 (1) (2021) 1–28.
[15] E.J. Topol, High-performance medicine: the convergence of human and artificial intelligence, Nat. Med. 25 (1) (2019) 44–56.
[16] A. Jović, I. Stančin, K. Friganović, M. Cifrek, Clinical decision support systems in practice: current status and challenges, in: 2020 43rd International Convention on Information, Communication and Electronic Technology (MIPRO), IEEE, 2020, pp. 355–360.
[17] C.J. Kelly, A. Karthikesalingam, M. Suleyman, G. Corrado, D. King, Key challenges for delivering clinical impact with artificial intelligence, BMC Med. 17 (1) (2019) 1–9.
[18] S.H. Woo, J. Zavodnick, L. Ackermann, O.H. Maarouf, J. Zhang, S.W. Cowan, Development and validation of a web-based prediction model for AKI after surgery, Kidney360 2 (2) (2021) 215–223.
[19] Q.D. Buchlak, V. Yanamadala, J.-C. Leveque, A. Edwards, K. Nold, R. Sethi, The seattle spine score: predicting 30-day complication risk in adult spinal deformity surgery, J. Clin. Neurosci. 43 (2017) 247–255.
[20] B. Séroussi, J. Bouaud, É.-C. Antoine, ONCODOC: a successful experiment of computer-supported guideline development and implementation in the treatment of breast cancer, Artif. Intell. Med. 22 (1) (2001) 43–64.
[21] N. Zhou, C.-T. Zhang, H.-Y. Lv, C.-X. Hao, T.-J. Li, J.-J. Zhu, H. Zhu, M. Jiang, K.-W. Liu, H.-L. Hou, et al., Concordance study between IBM Watson for oncology and clinical practice for patients with cancer in China, Oncologist 24 (6) (2019) 812.
[22] S.H. Yu, M.S. Kim, H.S. Chung, E.C. Hwang, S.I. Jung, T.W. Kang, D. Kwon, Early experience with watson for oncology: a clinical decision-support system for prostate cancer treatment recommendations, World J. Urol. 39 (2) (2021) 407–413.
[23] R.O. Alabi, M. Elmusrati, I. Sawazaki-Calone, L.P. Kowalski, C. Haglund, R.D. Coletta, A.A. Mäkitie, T. Salo, I. Leivo, A. Almangush, Machine learning application for prediction of locoregional recurrences in early oral tongue cancer: a web-based prognostic tool, Virchows Arch. 475 (4) (2019) 489–497.
[24] G. Wang, K.-M. Lam, Z. Deng, K.-S. Choi, Prediction of mortality after radical cystectomy for bladder cancer by machine learning techniques, Comput. Biol. Med. 63 (2015) 124–132.
[25] A. Sheikhtaheri, A. Orooji, A. Pazouki, M. Beitollahi, A clinical decision support system for predicting the early complications of one-anastomosis gastric bypass surgery, Obes. Surg. 29 (7) (2019) 2276–2286.
[26] C. Soguero-Ruiz, K. Hindberg, I. Mora-Jiménez, J.L. Rojo-Álvarez, S.O. Skrøvseth, F. Godtliebsen, K. Mortensen, A. Revhaug, R.-O. Lindsetmo, K.M. Augestad, et al., Predicting colorectal surgical complications using heterogeneous clinical data and kernel methods, J. Biomed. Inform. 61 (2016) 87–96.
[27] K. Merath, J.M. Hyer, R. Mehta, A. Farooq, F. Bagante, K. Sahara, D.I. Tsilimigras, E. Beal, A.Z. Paredes, L. Wu, et al., Use of machine learning for prediction of patient risk of postoperative complications after liver, pancreatic, and colorectal surgery, J. Gastrointest. Surg. 24 (8) (2020) 1843–1851.
[28] A. Bihorac, T. Ozrazgat-Baslanti, A. Ebadi, A. Motaei, M. Madkour, P.M. Pardalos, G. Lipori, W.R. Hogan, P.A. Efron, F. Moore, et al., Mysurgeryrisk: development and validation of a machine-learning risk algorithm for major complications and death after surgery, Ann. Surg. 269 (4) (2019) 652.
[29] D.M. Gonçalves, R. Henriques, R.S. Costa, Predicting postoperative complications in cancer patients: a survey bridging classical and machine learning contributions to postsurgical risk analysis, Cancers 13 (13) (2021), doi:10.3390/cancers13133217.
[30] F.A. Aslam, H.N. Mohammed, J.M. Mohd, M.A. Gulamgaus, P. Lok, Efficient way of web development using python and flask, Int. J. Adv. Res. Comput. Sci. 6 (2) (2015) 54–57.
[31] R.D. Hipp, SQLite, 2020, https://www.sqlite.org/index.html.
[32] T.C. Nokeri, Web app development and real-time web analytics with python., 2022
[33] R.J. Tallarida, R.B. Murray, Chi-square test, in: Manual of Pharmacologic Calculations, Springer, 1987, pp. 140–142.
[34] W.H. Kruskal, W.A. Wallis, Use of ranks in one-criterion variance analysis, J. Am. Stat. Assoc. 47 (260) (1952) 583–621.
[35] L. St, S. Wold, et al., Analysis of variance (ANOVA), Chemom. Intell. Lab. Syst. 6 (4) (1989) 259–272.
[36] F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, M. Blondel, P. Prettenhofer, R. Weiss, V. Dubourg, et al., Scikit-learn: machine learning in Python, J. Mach. Learn. Res. 12 (Oct) (2011) 2825–2830.
[37] L. Alexandre, R.S. Costa, L.L. Santos, R. Henriques, Mining pre-surgical patterns able to discriminate post-surgical outcomes in the oncological domain, IEEE J. Biomed. Health Inform. (2021).
[38] R. Henriques, F.L. Ferreira, S.C. Madeira, BicPAMS: software for biological data analysis with pattern-based biclustering, BMC Bioinf. 18 (1) (2017) 82.
[39] T. Chen, C. Guestrin, XGBoost: a scalable tree boosting system, in: Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, ACM, 2016, pp. 785–794.
[40] L. Prokhorenkova, G. Gusev, A. Vorobev, A.V. Dorogush, A. Gulin, CatBoost: unbiased boosting with categorical features, arXiv:1706.09516 (2017).
[41] J. Bergstra, D. Yamins, D.D. Cox, et al., Hyperopt: a Python library for optimizing the hyperparameters of machine learning algorithms, in: Proceedings of the 12th Python in Science Conference, vol. 13, Citeseer, 2013, p. 20.
[42] D.M. Gonçalves, R. Henriques, L. Santos, R.S. Costa, On the predictability of postoperative complications for cancer patients: a portuguese cohort study, BMC Med. Inform. Decis. Mak. 21 (1) (2021) 200.
[43] I. Puja, P. Poscic, D. Jaksic, Overview and comparison of several elational database modelling metodologies and notations, in: 2019 42nd International Convention on Information and Communication Technology, Electronics and Microelectronics (MIPRO), IEEE, 2019, pp. 1641–1646.
[44] J.L. Hintz, R.D. Nelson, Violin plots: a box plot-density trace synergism, Am. Stat. 52 (2) (1998) 181–184.
[45] M. d'Ocagne, Coordonnées Parallèles et Axiales: Méthode de transformation géométrique et procédé nouveau de calcul graphique déduits de la considération des coordonnées parallèlles, Gauthier-Villars, 1885.
[46] R. Henriques, S.C. Madeira, BSig: evaluating the statistical significance of biclustering solutions, Data Min. Knowl. Discov. 32 (1) (2018) 124–161.
[47] G. Piatetsky-Shapiro, Discovery, analysis, and presentation of strong rules, Knowl. Discov. Databases (1991) 229–238.
[48] D. Dindo, N. Demartines, P.-A. Clavien, Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey, Ann. Surg. 240 (2) (2004) 205.
[49] K.M. Corey, S. Kashyap, E. Lorenzi, S.A. Lagoo-Deenadayalan, K. Heller, K. Whalen, S. Balu, M.T. Heflin, S.R. McDonald, M. Swaminathan, et al., Development and validation of machine learning models to identify high-risk surgical patients using automatically curated electronic health record data (Pythia): a retrospective, single-site study, PLoS Med. 15 (11) (2018) e1002701.