

Supporting Information

Predicting dynamic clinical outcomes of the chemotherapy for canine lymphoma patients using a machine learning model

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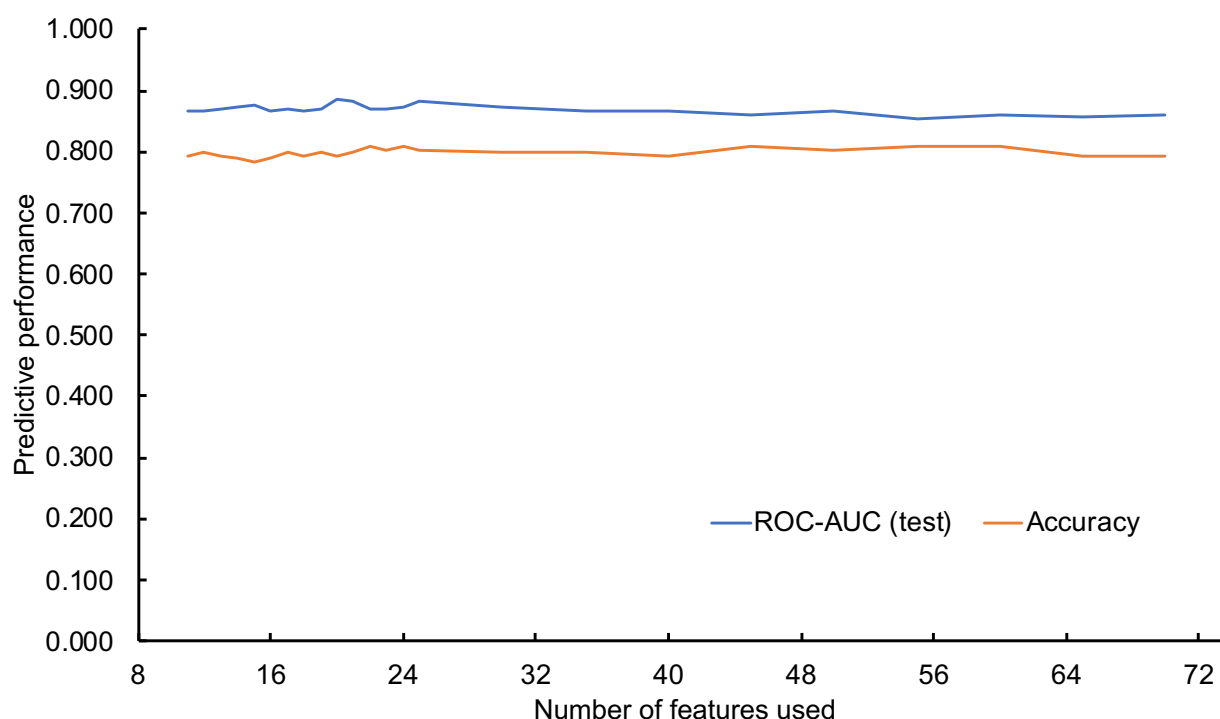


Fig. S1. Changes in the predictive performance of the RF model when the number of selected features k is increased from 7 to all. The top k features were chosen by the mutual information classification algorithm using the nearest neighbors method.

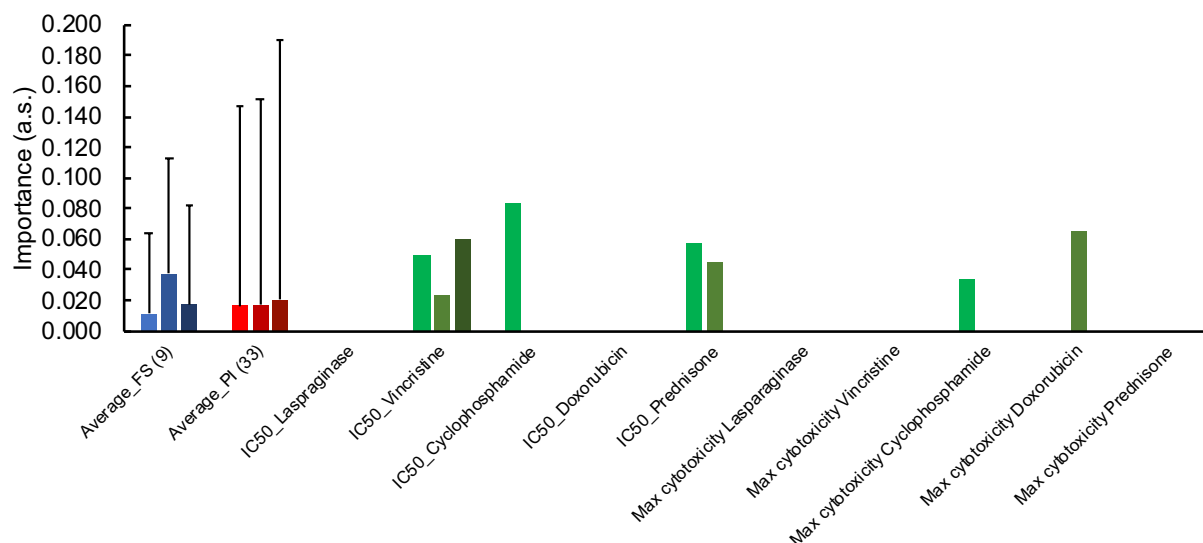


Fig. S2. Importance of the features to the ML models predicting clinical outcome by the 4th, 8th, and 12th week since the initiation of the chemotherapy. The bars represent the importance computed for the models exhibiting the highest predictive performance. For each feature, three bars are drawn that represent the importance for the models predicting clinical outcome by the 4th, 8th, and 12th week (left to right). Instead of showing the importance of every single feature, the average and maximum (represented by the error bar) of all FC and PI data are shown (blue and red colored bars on the left side). In contrast, the importance of each feature (green colored bars) is shown individually for the DS data. As one can see, the number of features selected decreased from 4 to 1 for the DS data when predicting clinical outcome for the 4th vs. 12th week. This is the opposite of the trend observed for the PI data, for which the average and maximum importance increased for the later time points.

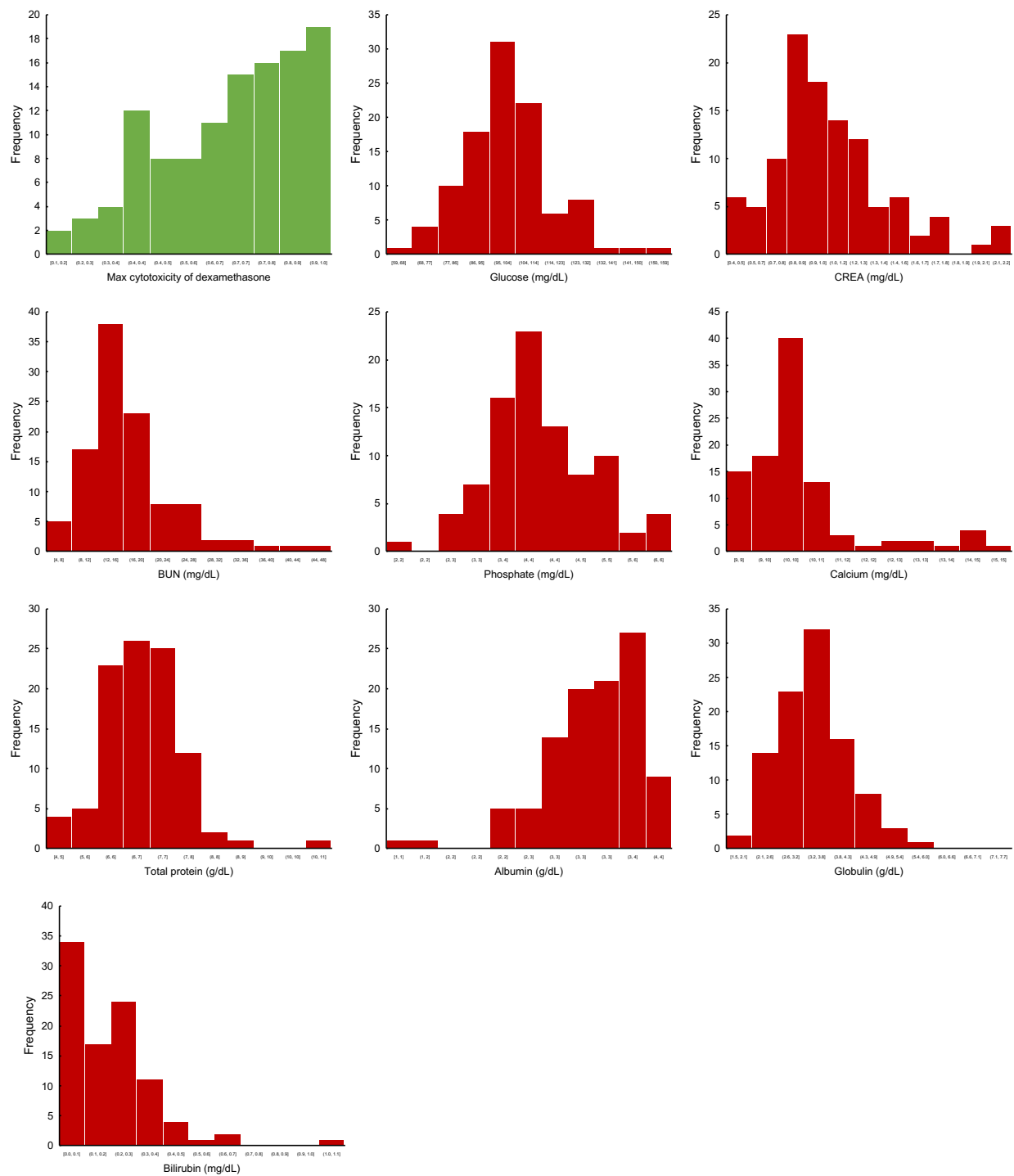


Fig. S3. Distribution of the raw data for the features having high (> 50%) percentages of missing values. The green and red colors of bars indicate that these features are part of the DS or PI data, respectively.

Table S1. List of the 8 additional chemotherapeutic drugs for canine lymphoma considered in this study.

| Drug | Type |
|-----------------|---|
| Mitoxantrone | Anthracenedione antineoplastic agent |
| Vinblastine | Vinca alkaloid that inhibits the assembly of microtubules |
| Actinomycin | Transcription inhibitor |
| Rabacfosadine | Nucleotide analog |
| Chlorambucil | Alkylating agent blocking the formation of DNA and RNA |
| Mechlorethamine | Alkylating agent disrupting DNA replication |
| Lomustine | Alkylating agent disrupting DNA replication |
| Melphalan | Alkylating agent blocking the formation of DNA and RNA |

Table S2. List of the 33 features comprising the PI data.

| Feature | Description | Feature | Description |
|----------------|---|----------------|---|
| Age | age at the time of diagnosis | Lymp | lymphocyte count (K/ μ L) |
| Sex | male or female | Mono | monocytes count (K/ μ L) |
| Breed | retriever, collie, poodle, mix, etc. | EOS | eosinophil count (K/ μ L) |
| IsRelapse | relapse or naïve | Baso | basophil count (K/ μ L) |
| Stage | extent of spread of tumor (1-5) | Glu | blood glucose level (mg/dL) |
| Substage | how patients feel (a or b) | CREA | blood creatine level (mg/dL) |
| Type | B, T, or other | BUN | blood urea nitrogen level (mg/dL) |
| Grade | growth rate of tumor | Phos | blood phosphorus level (mg/dL) |
| WBC | white blood cell count (K/ μ L) | Ca | blood calcium level (mg/dL) |
| RBC | red blood cell count (M/ μ L) | TP | blood total protein level (g/dL) |
| HGB | hemoglobin content (g/dL) | Alb | blood albumin level (g/dL) |
| HCT | proportion of RBC (%) | Glob | blood globulin level (g/dL) |
| MCV | mean corpuscular volume (fL) | Alt | alanine aminotransferase level (U/L) |
| MCH | mean corpuscular hemoglobin (pg) | Alkp | alkaline phosphatase level (U/L) |
| MCHC | mean corpuscular hemoglobin concentration (%) | GGT | gamma-glutamyl transpeptidase level (U/L) |
| PLT | average number of platelets (K/ μ L) | Tbil | total bilirubin level (mg/dL) |
| Neu | neutrophil count (K/ μ L) | | |

Table S3. Performance of the other ML models when predicting clinical outcome across the time points.

| ML method | ROC-AUC (cross-validation) | | |
|------------------------|-----------------------------------|----------------------|-----------------------|
| | 4 th week | 8 th week | 12 th week |
| Random Forest | 0.841 | 0.893 | 0.823 |
| Support Vector Machine | 0.830 | 0.739 | 0.659 |
| Linear Regression | 0.831 | 0.782 | 0.681 |

Table S4. Grid of hyperparameters used to optimize the performance of the RF models.

| Hyperparameter | Grid |
|-----------------------|------------------|
| n_estimators | 30, 50, 100 |
| max_features | auto, sqrt, log2 |
| max_depth | 6, 7, 8, 9 |
| criterion | gini, entropy |
| min_samples_leaf | 3, 4, 5 |