The Efficacy of Biomarkers as Predictors For Transfusion Need and Survival in Veterinary Settings

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Abstract

In veterinary trauma cases there is a need to quickly identify high risk patients. Past studies have shown there are several biomarkers in canines which may be associated with the need for transfusion, and in extreme cases survival. However, these studies have not been extensive. In this observational study of the VetCot Registry, which houses more than 30,000 veterinary records of canine trauma, the relationship between 8 predictive biomarkers (animal trauma triage cumulative score, abdominal fluid score, blood lactate concentration, base excess, ionized calcium, packed cell volume, total solids, and blood glucose) and the outcomes of transfusion need and survival are explored with the goal of establishing recommendations for cut-points where particular biomarkers may indicate a need for transfusion. Both classic methods (logistic regression) and machine learning (random forest) were employed to explore these relationships. For each outcome, univariate models (with each of the 8 predictors) and multivariate models (with all or subsets of the predictors, along with potential covariates for survival) were analyzed. The random forest and logistic regression approaches performed comparably, though random forest established more strict cut-off points for transfusion. Based on AUROC, ATT was the best predictor of both transfusion and survival and performed better than even multivariate models, while ionized calcium was the worst predictor. Other biomarkers (such as PCV, base excess, and total protein) could be promising in indicating transfusion need and survival. While this is an encouraging start in exploring these biomarkers, further study will be needed to establish cutpoints for transfusion with high enough sensitivity/specificity to be used in clinical settings where lives are at risk.

Introduction

Dogs are our family members, and they can be victims of traumatic injuries, just like us. In veterinary trauma clinics, there is a need to quickly determine triggers for transfusion in dogs suffering traumatic injuries. Delayed hemorrhagic resuscitation causes dire consequences, including increased risk for mortality.

To date, there have not been studies with large enough sample sizes to make sound conclusions about cut-off points for transfusion criteria. There is research to suggest total plasma proteins, packed cell volume, base excess, lactate, abdominal fluid score, total trauma score, and perhaps glucose are independent predictors of transfusion need. These will be explored within the veterinary registry, along with overall survival of patients. The ultimate goal of this work is to establish point of care “transfusion triggers” that any hospital can use to administer timely transfusions. For example, it was well documented that packed cell volume (PCV) will not decrease until hours after hemorrhage. In contrast, a decrease in total plasma protein (TPP) typically occurs within fifteen minutes after traumatic injury; thus predicting acute hemorrhage more accurately and rapidly (Buseman et al). By studying these eight biomarkers, we can begin to understand the relationship to patients' risk for mortality and need for blood transfusion.

This is the first observational retrospective study of an international veterinary registry with over 30,000 trauma patients, although effective samples are much smaller in many cases. The study objectives include modeling the two dichotomous outcomes of survival and transfusion against the 8 quantitative variables of interest (animal trauma triage cumulative score, abdominal fluid score, blood lactate concentration, base

excess, ionized calcium, packed cell volume, total solids, and blood glucose). In particular the study aims include:

1) Creating univariate models for each of the 8 predictors against each outcome
    a) For transfusion, to establish cutoff points for each predictor, which may provide guidelines on when a transfusion is needed
    b) Predictive univariate modeling of survival, without concern for cutoff points
2) Exploration of multivariate models for each outcome with
    a) Combinations of the 8 predictors of transfusion
    b) Possible covariates (sex, age, trauma type, weight, and transfusion) along with *each* of the 8 univariate predictors of survival, as well as possible combinations of the 8 predictors.

Additionally, researchers were interested in summary statistics for the 8 predictors, 2 outcome variables, and 4 possible covariates.

Summary Statistics

The VetCot registry contains 30,617 observations of dog trauma, 95 variables and many missing values. We focused on analysis with only the 8 biomarkers, 2 possible response variables, and 4 covariates for survival (sex, age, trauma type, and weight). When modeling, only complete cases were considered. As a result, each univariate model had a different effective sample size once NAs and outliers were removed. For the multivariate models, we took complete cases (for all variables). Additionally, 4 observations were removed from all analyses as they were missing a value for either survival or transfusion.

	ATT score	Abdominal Fluid Score	Blood Lactate	Base Excess	Ionized Calcium	Packed Cell Volume	Total Solids	Blood Glucose	Multivariate models
Mean	1.84	0.20	2.80	-4.54	1.27	46.90	6.57	121.33	
Standard Deviation	2.15	0.67	2.24	3.92	0.1	8.03	1.01	45.1	
Outliers	0	0	1	0	359	3	7	16	
Total NAs	30	24,034	23,585	24,770	24,150	20,737	20,839	20,079	
Effective Sample Size	30,583	6,579	7,027	5,847	6,105	9,873	9,767	10,518	2280

When considering the response variables, it is important to note that 379 of the 30,617 (1.24%) dogs in this dataset received blood transfusions and 2,018 dogs passed away (376 died, 1,642 euthanized). This represents 6.59% of the dogs in the sample. The imbalances in these response variables present unique challenges addressed later in the report. Additionally, different types of blood products were administered in various settings. Differences among types of blood transfusion were not explored in the analysis (as the sample sizes would be too small), but are summarized below as some *may* have higher efficacy in treating patients than others.

Transfusion Status by Survival

Transfusions	Lived	Died	Euthanized	Unknown
Yes	240	66	73	0
No	28355	310	1569	1
Unknown	3	0	0	0

Types of Transfusions

Trans_Type	Type_Counts
Whole Blood	40
Plasma	173
PRBC	262
Platelet	3
Lyo Albumin	12
Other	21

Transfusion status cross-tabulated with survival, types of transfusion

Additionally, for the survival models with covariates, summaries of the breakdown of the full sample by the demographics of the patients is provided below. Age and weight were treated as numeric within the models, while sex and trauma were treated as categorical variables.

Counts of Dogs by Size

Dog_Sizes	Weight_Categories	Dog_Counts
Toy	<= 5 kg	5578
Small	> 5 and <= 10 kg	6573
Medium	> 10 and <= 20 kg	5857
Large	> 20 and <= 45 kg	11826
Giant	> 45 kg	724
NA	NA	59

Counts of Dogs by Sex

Dog_Sex	n
In Tact Male	5367
Neutered Male	11102
In Tact Female	3661
Spayed Female	10415
Unkown	69
NA	3

Counts of Dogs by Trauma Type

Trauma_types	n
Blunt	12878
Penetrating	16205
Both	1532
NA	2

Counts of Dogs by Age Range

Dog_Ages	Dog_Counts
0-5	17623
5-10	8669
10-15	3948
15-20	356
20-24	3
NA	18

Breakdown of sample by weight, age, and sex, and trauma type

For a more detailed overview of the distribution of each predictor and its relationship to the two outcomes, see appendix A.

Statistical Methods

In all cases, we treated modeling our response variables as a binary classification problem. Both outcomes were dichotomous (non-transfusion vs transfusion and passed away vs survived). For transfusion, the positive class (i.e received transfusion) was the one of interest, while the negative class (passed away) was of interest for survival. Since there is a large imbalance in our predictors, we refer to the majority class (non-transfusion/survival) and minority classes (transfusion/passed-away) when describing our statistical models.

Logistic regression

Initially, univariate logistic regression models were run on each of the 8 point-of-care variables with both of the response variables, which resulted in sixteen models. Ultimately, 5 different logistic regression methods were employed for a total of 80 univariate models.

First a classic logistic regression was fit using the generalized linear model function (glm) within R. This is the model upon which the four subsequent methods are built. Each predictor variable was regressed on each response variable. Initially, we used the default classification threshold of 0.5 in order to make our predictions. Our predictions range from zero to one on the log-odds scale. Our response of interest is either zero (no transfusion/passed away) or one (had transfusion/survived). A predictive value > 0.5 is classified as one, while a prediction ≤ 0.5 will be assigned a value of zero. These initial models produced extremely skewed results that heavily favored the majority class. They had high overall accuracy, but poor accuracy of the minority class.

The second method expands on the basic model by changing the classification threshold. The threshold for classifying observations is adjusted from 0.5 to a value commensurate with proportion of each class. For example, if dogs who received transfusions represent 10% of the effective sample size for the predictor variable, then the classification threshold is lowered to 0.10. In these cases, we classified predictions >0.10 (or the relevant value for their dataset) as one, and those $\leq$0.10 as a zero. This method generally lowered the model accuracy but increased the accuracy of our predictions for our minority class.

This next method is similar, in that it uses the initial baseline univariate model. However, we change the prior weights when fitting the model. This changes the weight that each observation contributes to the model. To continue with the example in which 10% of the dogs received transfusions; we assign a weight of ten to observations in which the dogs received a transfusion, and a weight of one to the observations with dogs who did not receive a transfusion. Since the weighting is used during the execution of the model, the classification threshold used is the traditional 0.5. This method also improved classification of the minority class.

The next two methods experimented with sampling to balance the classes. The fourth model employs "upsampling," where observations from the minority class are randomly sampled with replacement. We do this until we have an equal number of observations of dogs from the minority and majority class. Therefore observations from the minority class may be included in the sample multiple times. This method also serves to give us more realistic sensitivity/specificity and PPV/NPV.

The last method utilizes "downsampling." We randomly sample a subset of observations from the majority class without replacement. This is done until we have an equal number of observations from the minority and majority class. This might under-utilize or "throw out" observations from the majority class. For example, if the sample of the particular point-of-care variable has 275 cases of dogs who received transfusion, then we sample 275 unique cases from the non-transfusion group. There was concern about using so few cases in which dogs didn't have a transfusion. An "exploratory" method was employed in which the non-transfused dogs were randomly subdivided into groups of 275. Then the process of "down sampling" was repeated by pairing the group of transfused dogs with each random group of non-transfused dogs, and then running the model on each of these pairings. The results across models are surprisingly consistent, and an added bonus: all data were used. As in previous methods, the aim is to obtain better sensitivity/specificity and PPV/NPV.

In addition, multivariate logistic models were fit for each predictor. This was done using the default generalized linear regression model for logistic regression (i.e. weighting and sampling were not adjusted).

Random forest

In addition to the logistic regression, potential machine learning models were explored. Random forest was a natural choice as it is well-suited for binary classification and would allow easy exploration of "cut-points." All 28 models reported here were fit using the "randomForest" package and function within R. All random forest models were split into 80% training data and 20% testing data with the ratio of majority to minority class for predictors in each dataset remaining consistent from the overall effective sample. The test data was used to evaluate the models.

For the univariate models (of both transfusion and survival) each of the 8 predictors were used to classify the 2 outcomes (resulting in 16 models). To force a binary decision and establish cut-off values, the number of decision nodes was set to two. In all cases the number of trees was set to 50, with the sample size of the

majority to minority class set in a 3:10 ratio. Samples were taken without replacement to minimize potential duplicates within the samples, and improve modeling. These parameters were consistent among models to ease in comparison and reporting, though these could be more finely tuned. Blood transfusion was explored initially within the univariate models for survival but did not improve modeling when compared to the univariate cases.

For the multivariate models, the parameters previously described remained consistent, but the number of nodes was not predetermined as cut points were of less interest. In the case of transfusion, two multivariate models were fit, one with all 8 predictors, and one containing the top 3 predictors as a simplified multi-variate model. These included ATT score, PCV, and total solids.

Since survival was more difficult to accurately classify (possibly because there are more background variables impacting survival), we explored models with the possible covariates (sex, age, trauma type, weight, and transfusion) for each of the 8 individual predictors. Additionally, two "full models" were explored, one with the 8 predictors alone, and one with the 8 predictors plus the covariates.

For both logistic regression and random forest models, cut points were only explored for the univariate models of transfusion. Both logistic regression and random forest rely on the assumption of independent observations, and the multivariate models assume there is no collinearity among predictors. It is safe to assume the cases within the dataset are independent. To assess collinearity, we looked at the correlation matrix for the 8 predictors. The highest correlation (between base excess and blood lactate) was moderate with an absolute value of 0.63, which assures us collinearity should not be a problem.

Limitations and Alternatives

The greatest challenge is the extreme imbalances in the binary response variables. We applied a few techniques to account for this (i.e. adjusting probability weights and sampling), though there are more possible methods to explore. These imbalances present challenges in the realm of statistical analysis. A classification algorithm could achieve falsely high accuracy by labeling everything as the dominant class. Additionally, there could be difficulty identifying the minority class with limited data. The mortality data in our sample are (happily) quite imbalanced, as only 6.5% of the dogs in the study passed away. There is a more severe imbalance for transfusion, with only about 1.25% of the dogs receiving blood transfusions. The transfusion imbalance is quite unusual because we see higher rates of transfusions in other studies. For example, 15%, 8 of 52 dogs **(Stillion),** 18%, 8 of 44 dogs **(Stillion),** 36%, 45 of 125 dogs **(Lynch)** and 42%, 11 of 26 dogs **(Buseman)** are among a few examples of studies reporting higher percentages of their sample trauma patients receiving transfusions.

It is necessary to make the distinction that we are not predicting which dogs need transfusions; we are predicting which dogs *received* transfusions. This is a subtle distinction, but it may be the case that the data we are using to train our models do not contain completely accurate classifications. An alternative approach to balancing the data through statistical methods could be to have a veterinary expert identify cases where a transfusion *should* have been administered to an injured dog and ensure accuracy of the classification within the dataset.

The high prevalence of missing data is another challenge as it limits power. Our sample sizes shrunk considerably from the original ~30,000. It is possible that the performance of ATT as a top predictor could partially be due to the fact that there was the most complete dataset for ATT compared to other predictors.

It is important to keep in mind that an advantage of experimental studies is the possibility to randomly assign different subjects to different testing groups, and it is this randomization that removes the effects of confounding. We have to be cognizant of the fact that "association is not causation," as instructed by every professor in the statistics department. In an observational study, it's possible to have confounding, where-in the relationship between two variables of interest is compromised because both of these variables can be impacted by other, unobserved variables.

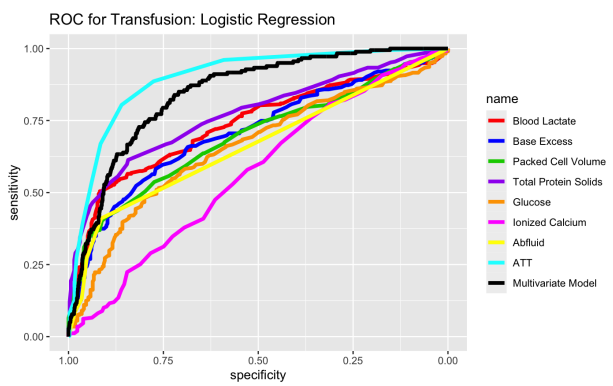
Additionally, models and cut-points could be further explored. In our consideration of cut-points we assumed dichotomous cutoffs, suggesting that a transfusion might be necessary at greater than/less than a particular value. However, it may be the case for some variables either extreme is problematic and indicative of dire health consequences, and this is a potential alternative to explore. Other modeling approaches could prove useful. For example, alternative machine learning algorithms could be promising, as well as alternative approaches to data-balancing.

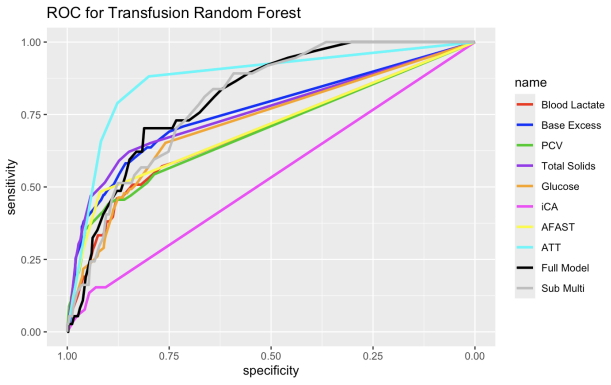
Results and Conclusions

In order to make comparisons and have the ability to identify the "strongest" individual variables, with potentially the strongest associations to the response variables (Blood Transfusions and Survival), the eight variables were individually run on the same dataset with effective sample size described in the summary table. For multivariate models, we used the dataset in which all eight point-of-care variables have complete cases. This is because we need to be consistent and compare the metrics on the same dataset to ensure equitable comparisons. The effective sample size of the multivariate dataset is just over 2,200 cases. The variables compared for model selection were judged by highest AUROC. For logistic regression, lowest AIC, as well as p-values of their performance within models were considered. We're looking for common patterns among many metrics across many settings.

Transfusion

For the logistic regression models, the resampling methods improved the sensitivity/specificity and NPV/PPV more than the two re-weighting methods. We reported the top logistic regression models below. Based on AUROC, the consistently top performing 3 biomarkers for the transfusion case in random forest are ATT score, total protein solids, and base excess. For logistic regression the top 3 biomarkers are ATT score, total protein solids and abdominal fluid score. So two (ATT and total protein solids) of the top 3 performers, derived independently from different methods, concur. This might suggest that these biomarkers are particularly important to monitor when evaluating canine trauma patients.





For the multivariate models, it is interesting to note that in both cases the multivariate models containing all 8 predictors of interest did not perform as well as the univariate model containing ATT alone. This is true for both logistic regression and the random forest.

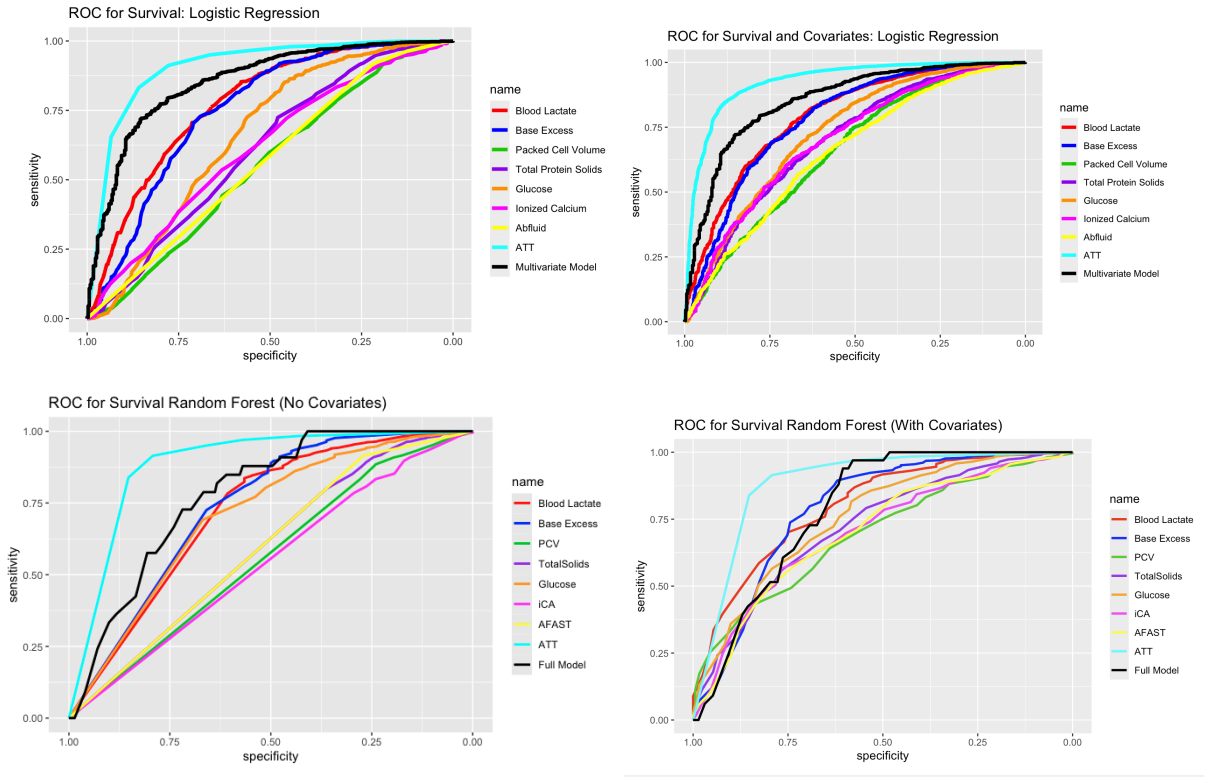
For the random forest, a subset of variables were explored. The 3 highest ranking variables on the variable importance plot based on mean GINI decrease were included. These varied slightly from the highest ranking univariate variables and included, in order of importance ranking: packed cell volume, total solids, and ATT score. It is interesting to note that the random forest model with these three predictors performed comparably to the model containing all 8 variables, suggesting that these might be important to monitor when considering transfusion needs.

	ATT score	**Abdominal Fluid Score**	**Blood Lactate**	**Base Excess**	**Ionized Calcium**	**Packed Cell Volume**	**Total Solids**	**Blood Glucose**
Best LR Method	Down sampling	Up Sampling	Down sampling	Down sampling	Up Sampling	Up Sampling	Up Sampling	Down sampling
LR cutpoint	≥ 3	≥ 2	≥ 4.5	< -5.85	1.27	< 37	< 5.95	≥ 139
LR AUROC	0.90	0.72	0.72	0.72	0.58	0.69	0.76	0.70
RF cutpoint	≥ 4	≥ 2	≥ 5.05	< -6.08	< 1.485	< 28.5	< 4.575	≥ 189
RF AUROC	0.88	0.70	0.69	0.73	0.53	0.69	0.75	0.66

When compared with the overall mean of each predictor, the random forest model tended to provide stricter cut-off points (i.e. further away from the mean). This would mean, if those were followed as guidelines fewer patients would receive transfusion, which could be advised if the transfusion is a procedure that is costly and risky. However, if veterinary clinics want to take quick decisive action, the cut points for logistic regression might be of more interest. In any case, ATT is the only variable with both sensitivity and specificity greater than 80%, which may be high enough to use in clinical settings. Conversely, ionized calcium was the worst predictor in each model, and non-informative in the logistic regression model, as it labeled all cases as non-transfusion. Therefore, no cut-points were established in the logistic regression case.

Survival

Survival proved more difficult to accurately predict. As such, we examined how the inclusion of the covariates of sex, age, weight, trauma type, and blood transfusion status affected the models. Based on the variable importance plot for random forest and p-values for predictors within the logistic regression, age and weight were consistently, though not always, ranked of greater importance when predicting survival. Based on the ROC plots and AUROC as a metric, adding the covariates to the univariate models of the biomarkers improves said models, particularly with those obtained via random forest. It also seems that the same 3 variables (ATT score, blood lactate, and base excess) seem to be the top predictors of survival in both random forest and logistic regression. For random forest, these ranked highest on the variable importance plot for survival and were the top-performing univariate variables. It's also encouraging to see that these variables are consistent.



We see this in our own analyses, and we see parallels to earlier studies. Stillion and Fletcher focused on the potential for both ATT score and Base Excess, particularly together, as predictors of blood transfusion and survival (Stillion et al). Meanwhile, Buseman notes the efficacy of Total Plasma Protein (TPP) as a predictor of transfusion requirement, and TPP featured prominently in both our logistic regression and random forest results (Buseman). Lynch also found TPP as well as blood lactate levels to be indicators of transfusion need (Lynch). Blood Lactate featured more prominently in our survival analyses. Conversely, however, Holowaychuck focused heavily on ionized calcium and considered it to be a "prognostic indicator" of transfusion requirements. Our analyses found the opposite to be true; in all models ionized calcium was the worst predictor of both survival and transfusion. This might suggest that ATT score, base excess, total protein, and blood lactate are particularly important to monitor.

Discussion

In all cases ATT models performed best, this may be because it had the largest effective sample size. It may be the case that since ATT score is a qualitative evaluation of trauma severity, it naturally correlates most highly with transfusion need and survival. The "cut points" with logistic regression tend to be looser than those derived with the Random Forest method. A possibility is to view them as an "action range." When a dog seems reasonably stable, then perhaps Veterinarians decide to go with the stricter "cut point" levels computed via Random Forest. However, if a dog is less stable, then perhaps a judgment call to be more cautious will result in adopting the "cut point" found through Logistic Regression. In either case, more exploration is needed to establish cut points that will be suitable for patient care recommendations.

Our analyses discovered some important information that can help in determining the need for transfusions, and hopefully, decrease mortality in dogs who are victims of traumatic injuries. There are infinite opportunities to build upon this work. Naturally, more of the many variables within the VetCot registry can be considered, interactions can be evaluated, more combinations of 2+ variable multivariate models along

with condition exploration of cut-points can be conducted. There may be additional statistical methods to consider as well. Perhaps mixed models could be explored, especially if the site variable is available. We could also utilize advances in machine learning. There is no shortage of life-saving information that can be gleaned over time from this extensive, international repository of veterinary data.

Author's Statement

Both authors contributed to statistical analysis and writing for this report. Shannon led the logistic regression analysis, while Valerie led the random forest analysis. Each author cross-validated the other's work and collaborated on the analytical approach, final report, and code appendix.

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Appendix A - Additional Tables and Graphs

RESULTS SUMMARIES

Univariate associations with receipt of Blood Transfusions for Logistic Regression

	ATT	Abfluid	Total Protein Solids	Packed Cell Volume	Blood Lactate	Base Excess	Ionized Calcium	Glucose
Best Method	Down sampling	Up Sampling	Down sampling	Down sampling	Up Sampling	Up Sampling	Up Sampling	Down sampling
Correlation w/ transfusions	0.643	0.337	-0.453	-0.323	0.379	-0.366	-0.124	0.328
Odds Ratio	2.05	0.829	0.45	0.928	1.377	0.829	0.072	1.017
Lower CI	1.81	0.820	0.38	0.911	1.355	0.82	0.050	1.012
Upper CI	2.19	0.837	0.453	0.944	1.399	0.837	0.103	1.021
AUC	0.903	0.721	0.76	0.686	0.716	0.721	0.577	0.695
Confusion Matrix Accuracy	0.841	0.7	0.718	0.669	0.705	0.696	0.594	0.665
Sensitivity	0.804	0.638	0.668	0.592	0.53	0.638	0.530	0.553
Specificity	0.879	0.727	0.734	0.719	0.852	0.727	0.586	0.797
PPV	0.869	0.7	0.715	0.678	0.743	0.700	0.564	0.724
NPV	0.818	0.668	0.688	0.638	0.686	0.668	0.558	0.631
Cut Point	3	2	< 5.95	< 37	> 4.5	< -5.85	< 1.27	> 139

Univariate associations with Survival for Logistic Regression

	ATT	Abfluid	Total Protein Solids	Packed Cell Volume	Blood Lactate	Base Excess	Ionized Calcium	Glucose	Trans-fusion
Best Method	Down sampling	Changed Threshold	Changed Prior Weights	Changed Prior Weights	Down sampling	Up Sampling	Up Sampling	Changed Threshold	Changed Prior Weights
Correlation w/ Survival	-0.652	-0.151	0.14	0.084	-0.47	0.404	0.199	-0.262	-0.265
Odds Ratio	0.442	0.637	1.458	1.029	0.652	1.24	47.65	0.988	0.114

Lower CI	0.42	0.589	1.42	1.026	0.617	1.227	30.21	0.987	0.1
Upper CI	0.465	0.688	1.498	1.033	0.688	1.255	64.64	0.989	0.13
AUC	0.91	0.663	0.625	0.68	0.775	0.762	0.625	0.664	0.53
Confusion Matrix Accuracy	0.852	0.807	0.603	0.553	0.72	0.713	0.594	0.795	0.931
Sensitivity	0.859	0.914	0.710	0.563	0.853	0.721	0.555	0.829	0.992
Specificity	0.846	0.218	0.492	0.542	0.601	0.705	0.634	0.461	0.069
PPV	0.848	0.865	0.593	0.552	0.678	0.711	0.603	0.938	0.938
NPV	0.857	0.315	0.62	0.554	0.789	0.716	0.588	0.214	0.367

Univariate associations with Survival for Logistic Regression (with covariates)

(note the base model was used (i.e. no weighting or re-sampling); Sensitivity/PPV will be high; Specificity/NPV will be low)

	ATT	Abfluid	Total Protein Solids	Packed Cell Volume	Blood Lactate	Base Excess	Ionized Calcium	Glucose
Best Method	Base glm()	Base glm()	Base glm()	Base glm()	Base glm()	Base glm()	Base glm()	Base glm()
Correlation w/ Survival	-0.567	-0.149	0.139	0.083	-0.407	0.336	0.128	-0.262
Odds Ratio	0.525	0.661	1.574	1.017	0.689	1.254	21.34	0.989
Lower CI	0.513	0.608	1.46	1.012	0.668	1.227	10.03	0.988
Upper CI	0.538	0.72	1.697	1.348	0.711	1.282	45.47	0.99
AUC	0.931	0.668	0.724	0.69	0.803	0.792	0.72	0.749
Confusion Matrix Accuracy	0.951	0.844	0.91	0.908	0.892	0.891	0.893	0.908
Sensitivity	0.989	0.993	0.996	0.997	0.986	0.987	0.995	0.992
Specificity	0.397	0.021	0.026	0.01	0.12	0.172	0.031	0.079
PPV	0.848	0.848	0.914	0.91	0.901	0.9	0.897	0.914
NPV	0.857	0.35	0.026	0.265	0.655	0.634	0.435	0.5

Associations with receipt of Blood Transfusions for Random Forest

	ATT	Abfluid	Total Protein Solids	Packed Cell Volume	Blood Lactate	Base Excess	Ionized Calcium	Glucose	Multivariate with all 8 Predictors	Multivariate with top 3 Predictors
AUC	0.8733	0.7036	0.7576	0.6919	0.6888	0.7345	0.5318	0.6625	0.8111	0.8029
Confusion Matrix Accuracy	0.8759	0.9301	0.9258	0.9397	0.8782	0.923	0.9574	0.9096	0.8684	0.8662
Sensitivity	0.9970	0.9671	0.9807	0.9750	0.9688	0.9646	0.9574	0.9748	0.9499	0.9409
Specificity	0.0747	0.2500	0.2199	0.2258	0.1538	0.2388	NA	0.1187	0.2982	0.2600
PPV	0.8770	0.9595	0.9417	0.9622	0.9016	0.9542	NA	0.9306	0.9045	0.9117
NPV	0.7895	0.2931	0.4697	0.3088	0.3810	0.2909	NA	0.2794	0.4595	0.3514
Cut Point	≥ 4	≥ 2	≥ 5.05	< -6.08	< 1.485	< 28.5	< 4.575	≥ 189		

Associations with Survival for Random Forest

	ATT	Abfluid	Total Protein Solids	Packed Cell Volume	Blood Lactate	Base Excess	Ionized Calcium	Glucose	Multivariate with all 8
AUC	0.8876	0.5927	0.5921	0.5601	0.7565	0.7373	0.6088	0.7074	0.8441
Confusion Matrix Accuracy	0.9125	0.8313	0.8991	0.8997	0.8616	0.8690	0.8935	0.8939	0.5702
Sensitivity	0.4079	0.3333	0.3143	0.2121	0.4286	0.4460	NA	0.3636	0.2744
Specificity	0.9812	0.8539	0.9209	0.9114	0.9291	0.9261	0.8935	0.9232	0.9842
PPV	0.7475	0.0936	0.1287	0.0391	0.4850	0.4493	NA	0.2073	0.9605
NPV	0.9241	0.9659	0.9731	0.9855	0.9126	0.9252	NA	0.9633	0.4921

Associations with Survival for Random Forest (With covariates)

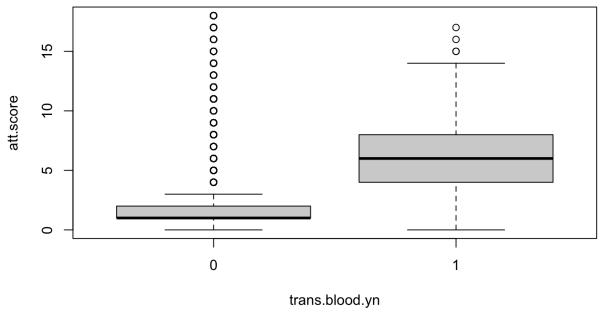
	ATT	Abfluid	Total Protein Solids	Packed Cell Volume	Blood Lactate	Base Excess	Ionized Calcium	Glucose	Multivariate with all 8
AUC	0.9293	0.7029	0.7245	0.6955	0.8011	0.7901	0.7039	0.7582	0.8052
Confusion Matrix Accuracy	0.9294	0.8377	0.8934	0.8813	0.8766	0.8962	0.8754	0.9015	0.5965

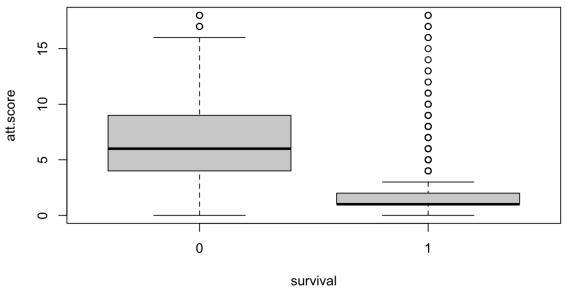
Sensitivity	0.4698	0.4000	0.3238	0.2200	0.4803	0.5762	0.3115	0.4428	0.2840
Specificity	0.9791	0.8586	0.9258	0.9167	0.9248	0.9275	0.9051	0.9320	0.9757
PPV	0.7089	0.1194	0.1988	0.1236	0.4371	0.4380	0.1473	0.3021	0.9342
NPV	0.9447	0.9676	0.9601	0.9565	0.9360	0.9573	0.9615	0.9618	0.5289

SUMMARY GRAPHS

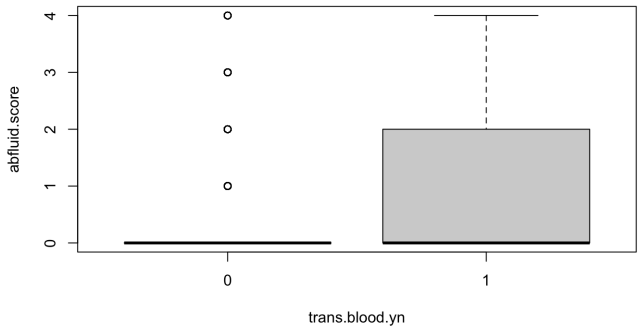
Note: For transfusion: 0 = Non-Transfusion, 1= Transfusion
For survival: 0 = Passed away, 1= Survived to discharge

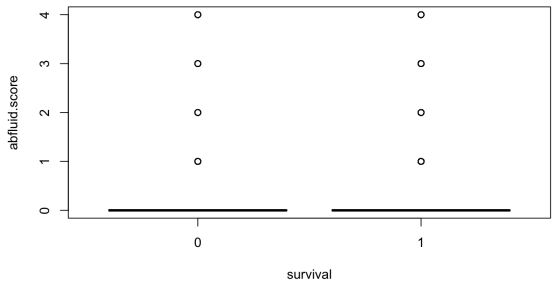
ATT TRANSFUSION AND SURVIVAL



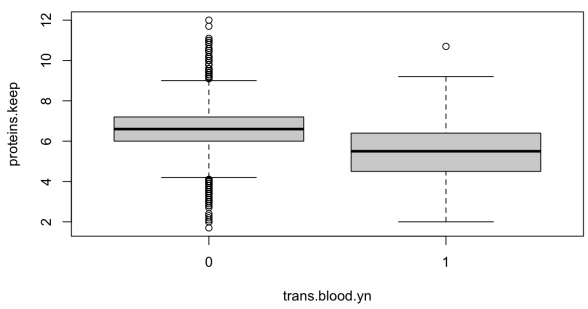


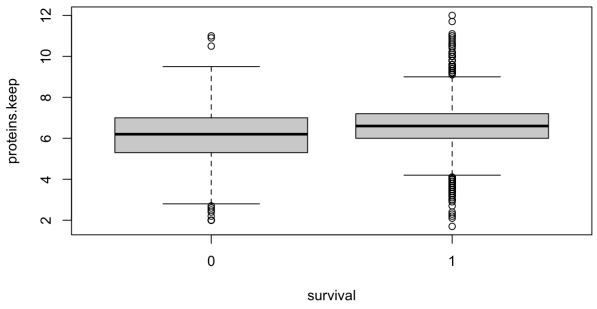
ABDOMINAL FLUID TRANSFUSION AND SURVIVAL



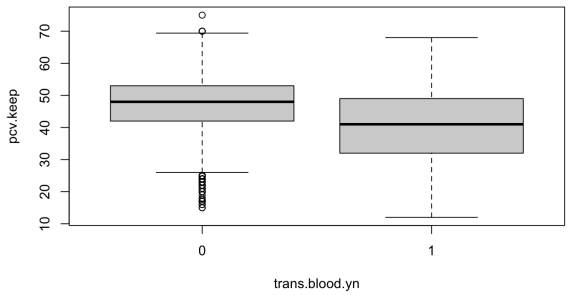


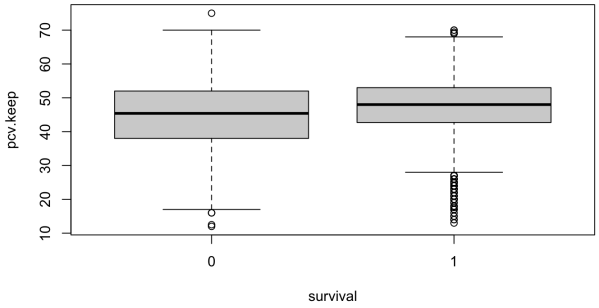
TOTAL PROTEIN SOLIDS TRANSFUSION AND SURVIVAL



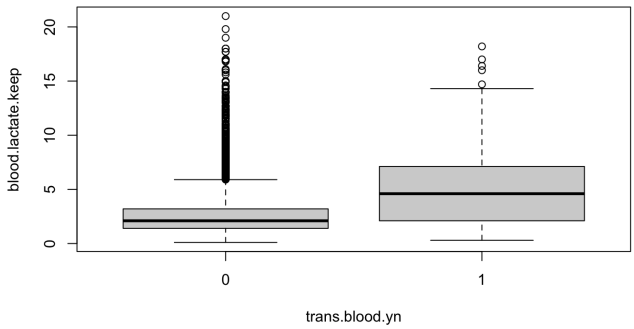


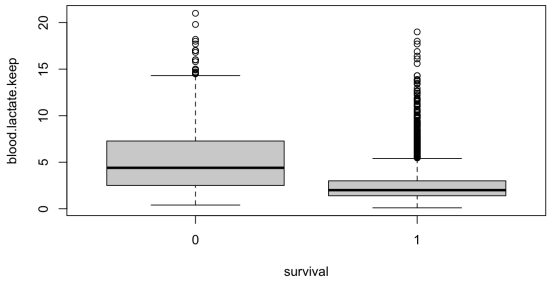
PACKED CELL VOLUME TRANSFUSION AND SURVIVAL



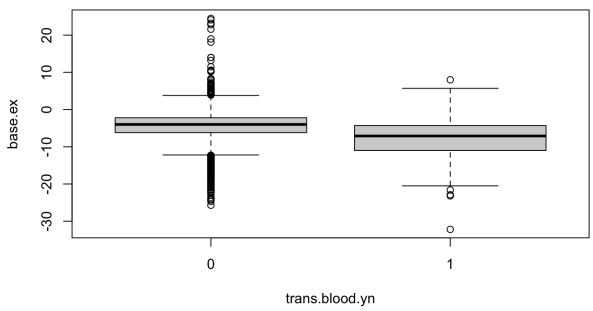


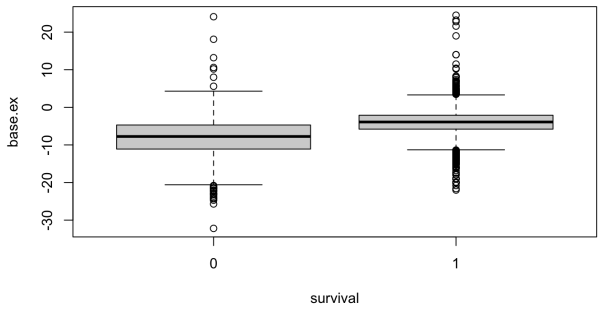
BLOOD LACTATE TRANSFUSION AND SURVIVAL



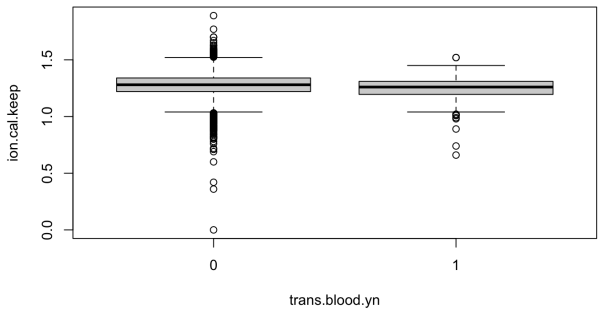


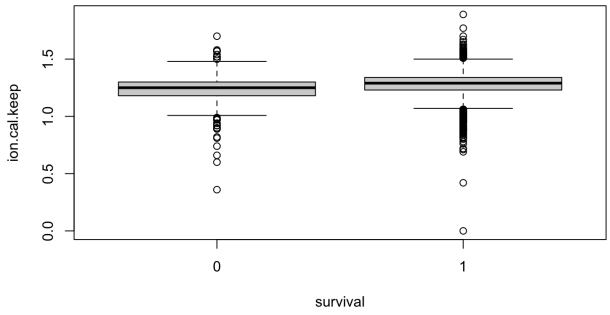
BASE EXCESS TRANSFUSION AND SURVIVAL



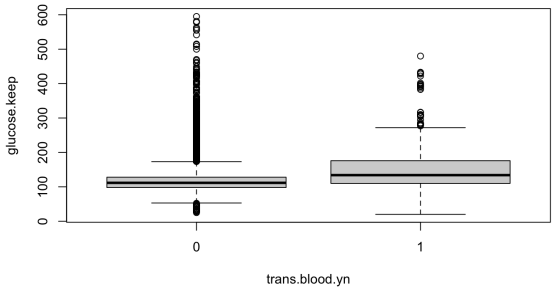


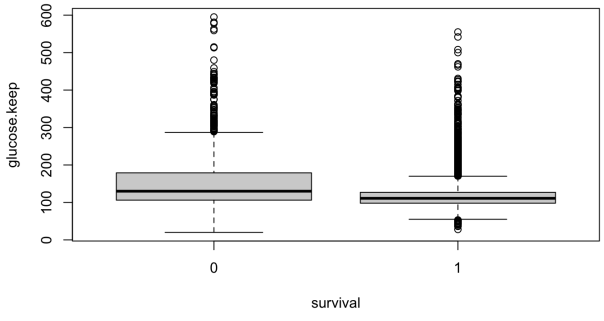
IONIZED CALCIUM TRANSFUSION AND SURVIVAL





GLUCOSE TRANSFUSION AND SURVIVAL





Transfusion and Survival Counts by ATT Score

ATT_score	Counts	Transfusion	Trans_Percent	Survived	Surv_Percent
0	5639	2	0.04	5596	99.24
1	13108	13	0.10	13020	99.33
2	5442	28	0.51	5290	97.21
3	2390	31	1.30	2228	93.22
4	1288	51	3.96	1063	82.53
5	825	51	6.18	608	73.70
6	573	54	9.42	350	61.08
7	387	44	11.37	186	48.06
8	283	34	12.01	110	38.87
9	185	22	11.89	52	28.11
10	134	17	12.69	37	27.61
11	78	10	12.82	10	12.82
12	88	11	12.50	4	4.55
13	38	4	10.53	4	10.53
14	24	2	8.33	2	8.33
15	30	2	6.67	2	6.67
16	19	1	5.26	8	42.11
17	14	1	7.14	7	50.00
18	42	1	2.38	10	23.81

Appendix B - Exploration of Logistic Regression

See attached R markdown

Appendix C - Exploration of Random Forest

See attached R markdown