Naive Bayesian Prediction of Bleeding After Heart By-Pass Surgery

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Excessive post-operative bleeding occurs in approximately one out of eight patients who undergo heart bypass surgery. Earlier workers have identified laboratory parameters that are correlated with post-operative blood loss but these correlations are not strong enough to be clinically useful. This paper describes a predictor that combines several of these parameters using Naive Bayesian Reasoning, to produce a clinically useful predictor of blood loss.

1. Introduction

Excessive post-operative bleeding complicates cardio-pulmonary bypass surgery. Bleeding occurs for two broad reasons: physiological (i.e., diminished haematological function) or technical (e.g., a surgical problem such as suturing). The major dilemma in treating a patient for bleeding is deciding which of these two broad reasons is dominant.

A number of earlier studies have attempted to find a way of predicting physiological bleeding using one or more laboratory parameters. A major study concluded that the performance of multivariate linear models did not justify routinely screening all patients [1]. Other previous studies looked for single laboratory parameters that correlated (non-linearly) with blood loss [2-4]. The degree of correlation, however, is not high enough to justify the use of just one of these parameters as a predictive tool.

We have applied Naive Bayesian Reasoning (NBR) to predicting which patients will bleed excessively. It is a well-established technique, with a heritage in intelligent systems dating back to the Prospector expert system [5], and more recently has been applied to medical intelligent information systems [6].

2. Materials and Methods

2.1 The Data

Our database of 83 patients contains 8 patients who bled excessively (i.e. more than 80 ml per litre of total blood volume, in the three hours after surgery). An advantage of NBR is that it has few free parameters, and thus can be applied to the small datasets so common in medicine.

It would be ideal if a patient's potential to bleed could be estimated prior to surgery. In practice, however, it is known that the preoperative tests alone cannot achieve this [4]. A viable clinical approach is to assess a patient risk in two phases. In the first phase, pre-operative tests are used in a screening process to eliminate patients with a very low risk of blood loss. In the second phase, the remaining patients are reassessed by a second system that uses parameters collected during and immediately after surgery.

The six pre-operative parameters considered were: Whole Blood Aggregation (WBAG), Bleeding Time, Platelet Count, Fibrinogen, Mean Platelet Volume, and Prothrombin Time. The eight post-operative parameters used in this study were: Haemodilution, Prothrombin Time, Collagen Aggregation, Platelet Count, Activated Partial Thromboplastin Time, Change in Mean Platelet Volume, Bypass Time, and Platelet Volume.

2.2 Naive Bayesian Reasoning

Naive Bayesian Reasoning obtains an estimate of the *posterior probability* P_H of an hypothesis H by combining the probabilities of one or more pieces of evidence e_i. In this study, the hypothesis being tested is "*the patient will bleed above the 80 ml/l/hr threshold following CPB surgery*". The e_i are the pre- and post-operative parameters. The particular Naive Bayesian approach used in this study is a standard text book approach [7].

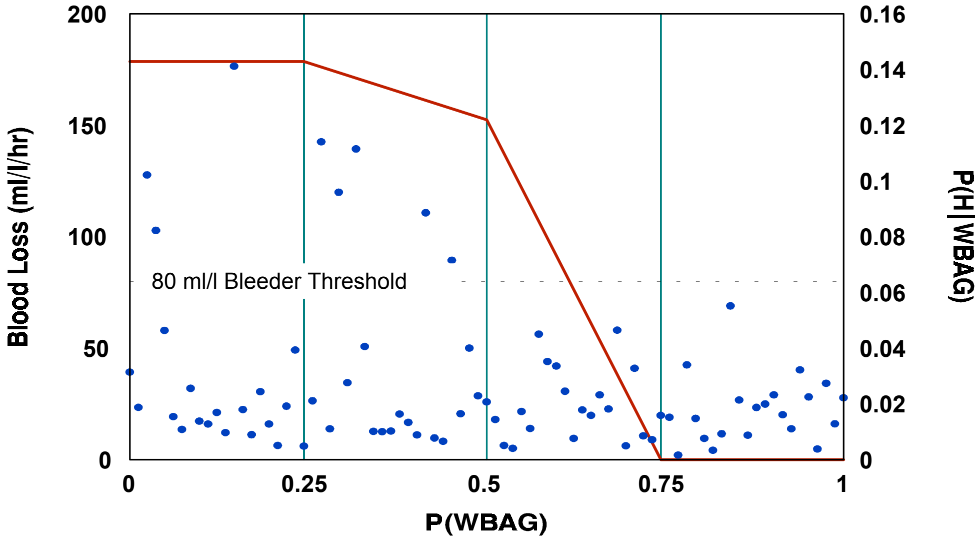

Figure 1: Relationship between blood loss, P(WBAG) and high bleeding P_c(H|WBAG)

We will use whole blood aggregation (WBAG) to illustrate the process used on each parameter for estimating the conditional probability $P_c(H|e_i)$. Figure 1 shows the relationship between blood loss and WBAG over the 83 patients. The horizontal axis expresses each WBAG value as its percentile ranking within the database (i.e. the median WBAG value has a P(WBAG) of 0.5). The left vertical axis shows blood loss (ml/l/hr). The right vertical axis shows our estimation of P_c(H|WBAG), the probability of the hypothesis conditioned on whole blood aggregation.

For the leftmost and rightmost quartiles of the WBAG population, the estimation of the probability of the hypothesis is a constant; the proportion of bleeders in each of those quartiles. The estimate for intermediate WBAG values is a piecewise linear interpolation. The mid-point for the interpolation is the proportion of bleeders in the middle two quartiles.

2.3 The Best Set of Parameters

There are 63 possible combinations of the 6 pre-operative parameters, and 255 possible combinations of the 8 post-operative parameters. Since a Naive Bayesian system can be constructed and tested very quickly (in a single pass through the data), all possible combinations of pre-operative and post-operative parameters can be assessed in a few seconds.

2.4 Prediction Thresholds

A Naive Bayesian system outputs a number in the range from 0 to 1, the estimated probability that the patient will bleed excessively. In a deployed system, it might be appropriate to present the clinician with that output. Such a number, however, is not suitable for a formal performance assessment of the system. A classification into "predicted excessive bleeder" or "predicted normal bleeder" is more suitable for formal performance assessment. For this reason, a probability threshold is used, so that when the output probability is above the threshold the patient is deemed to be at risk of bleeding. Given that pre-operative parameters are weak indicators of bleeding potential, and the aim of the pre-operative system is only to reduce the number of patients that need to be assessed after surgery, a conservative threshold of 0.1 was used for the pre-operative system. A threshold of 0.5 was used for the post-operative system.

2.5 Cross Validation

With a dataset of only 83 patients, the performance of any predictive system (Naive Bayesian or otherwise) may vary significantly if even one patient record is added or deleted to the database. For example, the P_c(H|WBAG) value for the lower quartile of WBAG, as illustrated in Figure 1, would change significantly if one of the three high bleeders record in that quartile was deleted.

Cross-validation is a well established test methodology that can provide an indication of system performance variability due to variation in the data used to construct the system. First, the entire data available is assigned at random into two subsets, a *training set* and a *test set*. Second, the training set is used to construct a predictive system. Third, the test set is used to assess the performance of that predictive system. To assess performance variability of a specific parameter combination due to variations in the training set, we repeated this three-step process one hundred times. The variation in system performance over one hundred repetitions gives an indication of the adequacy of the available data.

3 Results and Discussion

3.1 Pre-Operative Parameters

The best performing combination of pre-operative parameters was the triplet whole blood aggregation, fibrinogen, and bleeding time. The results for this triplet are presented in Figure 2. Each dot represents a patient. The horizontal axis shows the actual rate of bleeding of each patient. The vertical axis shows the predicted probability that each patient would bleed excessively. Each dot is placed to show the mean predicted probability value on a particular patient, over 100 cross validation runs. All 8 high bleeders correctly lie in the upper right quadrant.

The bar associated with each dot shows the 67% confidence interval (ie. standard deviation) of probability values over the 100 validation runs. For the 8 bleeders note that, for the most part, their entire confidence interval is above the 0.1 threshold. The degree of variation for most normal bleeders is also modest.

If the pre-operative predictor was perfect, all normal bleeders would lie in the bottom left quadrant, but in fact 21 normal bleeders are false positives, and lie within the top left quadrant. However, this pre-operative Naive Bayesian predictor eliminates 54 patients (approximately two thirds) as potential high bleeders.

3.2 Post-Operative Parameters

In a deployed system, only patients identified as potential bleeders by the pre-operative system would be reexamined by the post-operative system. It follows that experiments with combinations of post-operative parameters should be done on data typically selected by pre-operative systems built from a specific combination of pre-operative parameters. The data used is the 29 patients, including all 8 actual bleeders, with the mean probability values above the 0.1 threshold in Figure 2.

The best performing combination of post-operative parameters was prothrombin time, activated partial thromboplastin time, and haemodilution. The results are presented in Figure 3. Note that the entire confidence interval of each of the 8 high bleeders lie above the 0.5 threshold. The degree of variation for most normal bleeders is also modest.

The post-operative Naive Bayesian predictor was not perfect, with 6 false positives in the top left quadrant. However, approximately half of the patients lie in the bottom left quadrant, and thus have been judged as being at low risk of bleeding excessively. The 14 patients above the prediction threshold, less than 20% of the original 83, could be afforded special treatments, such as the use of expensive drugs that cannot be justified as a preemptive treatment on all patients.

4. Conclusion

The results of experiments presented here indicate that Naive Bayesian reasoning can combine several parameters to produce a clinically useful predictor of blood loss, even though each parameter alone is a weak indicator of blood loss.

The use of a cross-validation testing strategy indicates that these encouraging results are probably not due to chance patterns in a small dataset, but training and testing on a larger dataset is necessary before this approach could be routinely applied in the clinical environment. The conduct of a large clinical trial is an expensive undertaking, but the results of this study justify such a major study.

5. References

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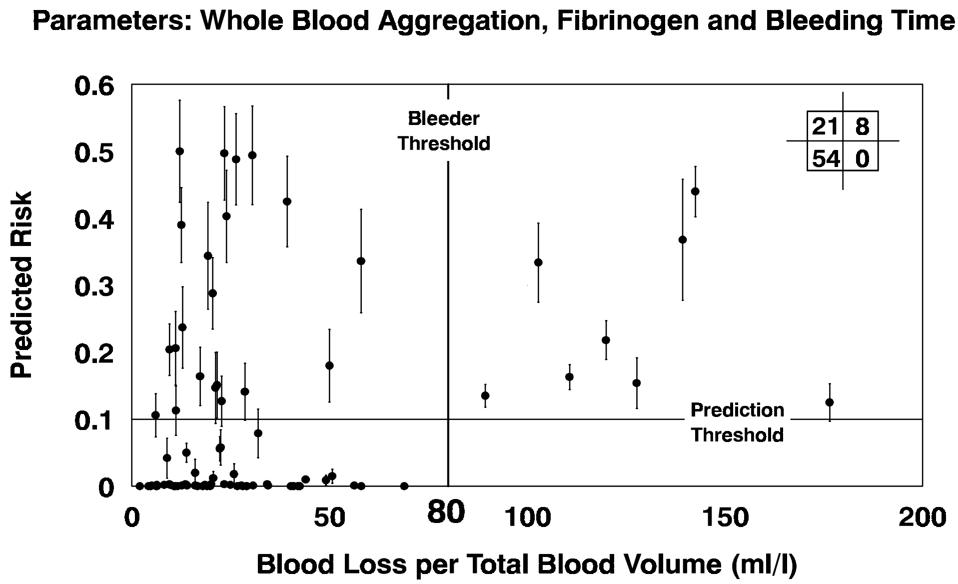

Figure 2: Performance of the combination of pre-operative parameters, Whole Blood Aggregation, Fibrinogen, and Bleeding Time.

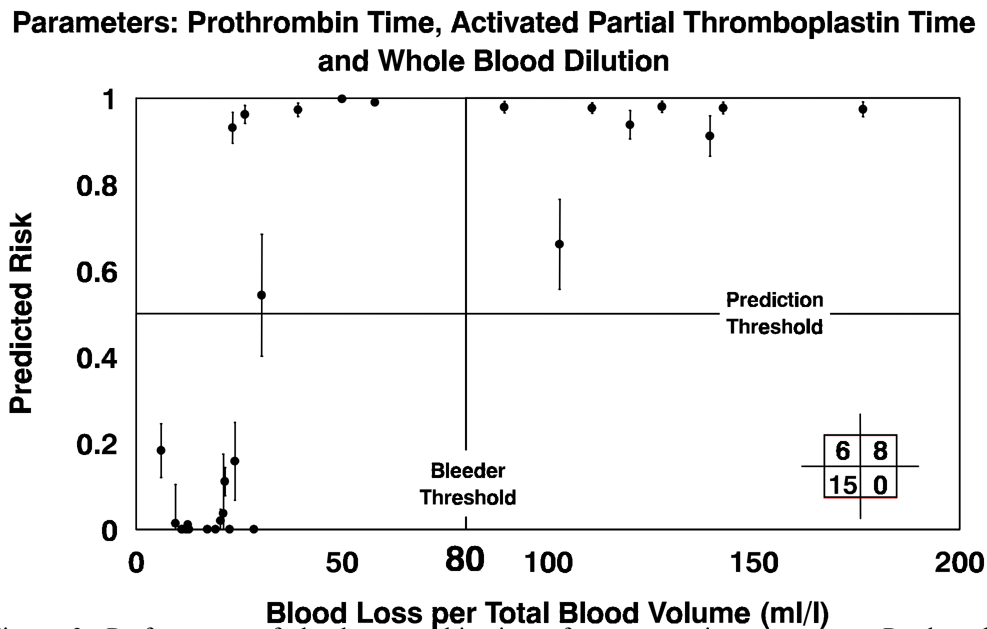

Figure 3: Performance of the best combination of post-operative parameters Prothrombin Time, Activated Partial Thromboplastin Time and Haemodilution.