Linking Bayesian Network and Intensive Care Units Data: A Glycemic Control Study

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***Abstract*—Health informatics in glycemic control is visibly a promising research area. However, this applied science requires more intelligent mechanisms by which user requirements for more accurate prediction can be fulfilled. Such mechanisms must provide very flexible and user friendly procedures to enable complicated decision support functions. This article presents the linking process of per-patient demographic and admission to intensive care unit data with their glycemic control performance using probabilistic causal Bayesian Network models (BNs). Data from two glycemic control protocols are exploited to test the feasibility. The identified steps crucial in building a dependable model are variable selection, state discretization, and structure learning. Different BNs can be generated with more than 83.73% overall precision rate and 93.4% overall calibration index with the combination of these steps. A network with a 95.36% precision was obtained with an equal distance discretization algorithm dataset and Maximum Weight Tree Spanning unsupervised structure learning. The study was the first testing phase in which the results generated by selected data and process is proposed as a benchmark. The resulting network is centred on 'Hypertension' status to predict BG mean and number of measurements as a result of the prediction interest. This co-morbidity is proposed to be considered systematically in the modelling of any glycemic control to optimize its function in the intensive care units.**

***Index Terms*—Glycemic Control, Intensive Care Units, Bayesian Network, Discretization Technique, Performance Prediction**

I. Introduction

Since the birth of intensive care medicine, researchers tend to study the cause and effect result on patients with similar signs and symptoms while trying to integrate individual characteristics such as age, comorbidities condition and individual variations, in response to treatment. As the health informatics and awareness of improved intensive care medicine has progressed, an increasingly personalized medicinal approach is entering ICUs. However, it is only beginning in glycemic control (GC) and the judgements are often left to expert opinion.

In glycemic control and treatment strategies, as across all other Intensive Care Unit (ICU) therapies, more and more control models are being computerized [1]. To obtain more efficient and safer control, an increasing number of ICUs are starting to use validated and computerised algorithms with patient-specific physiological models, such as EndoTool, LOGIC and STAR [2]–[5]. These GCs are based on improved clinical guidelines, but none systematically consider per-patient demographic background and admission condition, such as comorbidities. Furthermore, despite the growing number of computerized patient-specific control, a majority of hospitals around the world, especially in less developed countries still use manual sliding scales based on generalised rules to control glycemic, such in Malaysian ICUs [6].

In any case, all these ICU data need to be exploited to make the best decisions for critically ill patients. These data must be more than written records and documentation tool. Instead of regular measurement, some of these data are one time information and don't have any pattern to signal patient variability, nevertheless they may add value that can support and enhance clinical decision support.

Bayesian Network [7], [8], a probabilistical and graphical model often used to model uncertainty and causality, with applications ranging from medical diagnosis [9], detection [10], prediction [11] to decision-making systems [12], offer a potential solution. Due to their directed graphical structure, Bayesian networks (BNs) are intuitively interpretable, thus assisting and expediting human decision support in ways generalized machine learning cannot. In essence, BN structure helps 'explain' its outputs. BN provides an efficient factorization of the joint probability distribution over a set of random variables. Patient-specific data that often contains a combination of discrete and continuous variables, can be deployed in structured learning and inference to perform diagnosis, prognosis or simply find the causal relationship between variables. Continuous variables are often discretized, and the

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choice of discretization technique has striking impact on the prediction precision, computation speed, and interpretability of the resulting networks.

The objective of this paper is to study the integration of demographic and admission data, which are a one off input value, with glycemic control performance variables using BN and to interpret the possible relationship between these variables. In this view, this paper focuses on the choices of discretization techniques towards all continuous variables and the structured learning steps.

II. Methods

A. Glycemic Control data

The study was conducted on retrospective data from 368 Malaysian critically ill patients treated under sliding-scale intensive insulin infusion approach (210 patients) and computerized STAR glycemic control (158 patients) protocols from the Hospital Tengku Ampuan Afzan (HTAA) and International Islamic university Malaysia Medical Centre (IIUMMC) ICUs respectively.

1) HTAA Intensive Sliding Scale Approach: In this protocol, medical staff perform treatment based on rules. The adopted rules chart in HTAA can be referred to in Fig. 1. Basically, the BG target range is between 5.1 - 8.0 mmol/L. BG monitoring and treatment is performed hourly once insulin is started to be administered. When there is no requirement of insulin rate change for two consecutive hours, BG is then measured 2-hourly. Frequency of monitoring is reduced once the patient is considered stable.

2) IIUMMC STAR control: STAR (Stochastic TARgeted) is a glycemic control protocol that is based on insulin sensitivity to automatedly characterize and forecast changes in per-patient metabolic state and designed to be used in real-time bedside care. Its prediction is based on a stochastic model over the 1-3 hours subsequent potential variation in patient-specific insulin sensitivity [13]–[15]. STAR has shown promising results, and is the default treatment in Christchurch, New Zealand, and Gyula, Hungary hospitals ICU [16]. Since December 2016, it has been implemented in the IIUMMC ICU in Malaysia as part of a Malaysian pilot trial [17].

The adaptability of STAR includes BG level target range, measurement frequency, patient safety within a predefined desired hypoglycemia risk and local nutrition practices [5], [18]. The data from this ICU comes from two BG target range of 4.4 - 8.0 mmol/L and 6.0 - 10.0 mmol/L.

B. Bayesian Network

A Bayesian Network (BN) models a variable as node and the potential causal relationship between two variables as a directed arc. These create the BN structure, while to complete it, a conditional probability table (CPT) is assembled to each node to represent the probabilities of each values of a node, given the conditions of its parents. The structure along with the CPT can be built from human knowledge, machine learned from training datasets, or a combination of both.

In this study, the structure is proposed to be learned with an 80:20 ratio of learning and testing over random data sampling. The structure learning and testing are performed multiple times between different discretizations of continuous variables algorithms, as well as the unsupervised structure learning methods. While BNs can be trained from continuous variables directly, it is common to discretize the variables into states to prepare a dataset that enables the Bayesian network structure learning. Purpose is to minimize computation speed by avoiding having to consider variable interactions complexities. In the discrete states case and provided the probability of an event B does not equal 0, Bayes theorem is used to relate the conditional and marginal probabilities of two events A and B (Equation 1) :

$$P(A \mid B) = \frac{P(B \mid A)P(A)}{P(B)} \tag{1}$$

- $P(A \mid B$ is the conditional probability of A, given B. It is also called the posterior probability.
- $P(B \mid A)$ is the conditional probability of B given A. It is also called the likelihood.
- $P(B)$ is the prior or marginal probability of B, and acts as a normalizing constant.

Data discretization algorithms that were used in this study includes the K-Means, Multivariate, GenOpt, Equal distance, normalized equal distance and Equal frequency. For each of the algorithms, discretization brings out different variable states that translate into multiple datasets. These datasets are then feed to the structure learning step.

Structure learning step was performed using unsupervised algorithms based on score-based learning algorithms. As opposed to the constraint-based algorithms that use independence tests to add or remove arcs between nodes, the Minimum Description Length score [19] or Pearson Correlation score were deployed to measure the quality of network candidates corresponding to the available datasets.

For the purpose of this initial study, discretization for each variable was limited between 2 or 3 states only. Performance evaluations were done using multi-target analysis system with the basis to consider each node in the network as a target node, and final performance is based on the overall performance. For each node as a target, the quantitative performance of all candidates were evaluated using the test dataset with the following two metrics: (i) overall precision; and (ii) overall calibration index.

III. Results and Discussion

The process began with the identification of variables to be used in the modelling. Common variables that were available from 2 ICUs provided data, using two different glycemic controls (GC) were used. 10 variables were extracted, which included age, gender, height, weight, Diabetes Mellitus and hypertension status upon admission to ICU, the total hours under respective GC treatment, the number of measurements involved, the initial BG level, and the mean BG under control. Amongst these variables, only gender, Diabetes Mellitus and

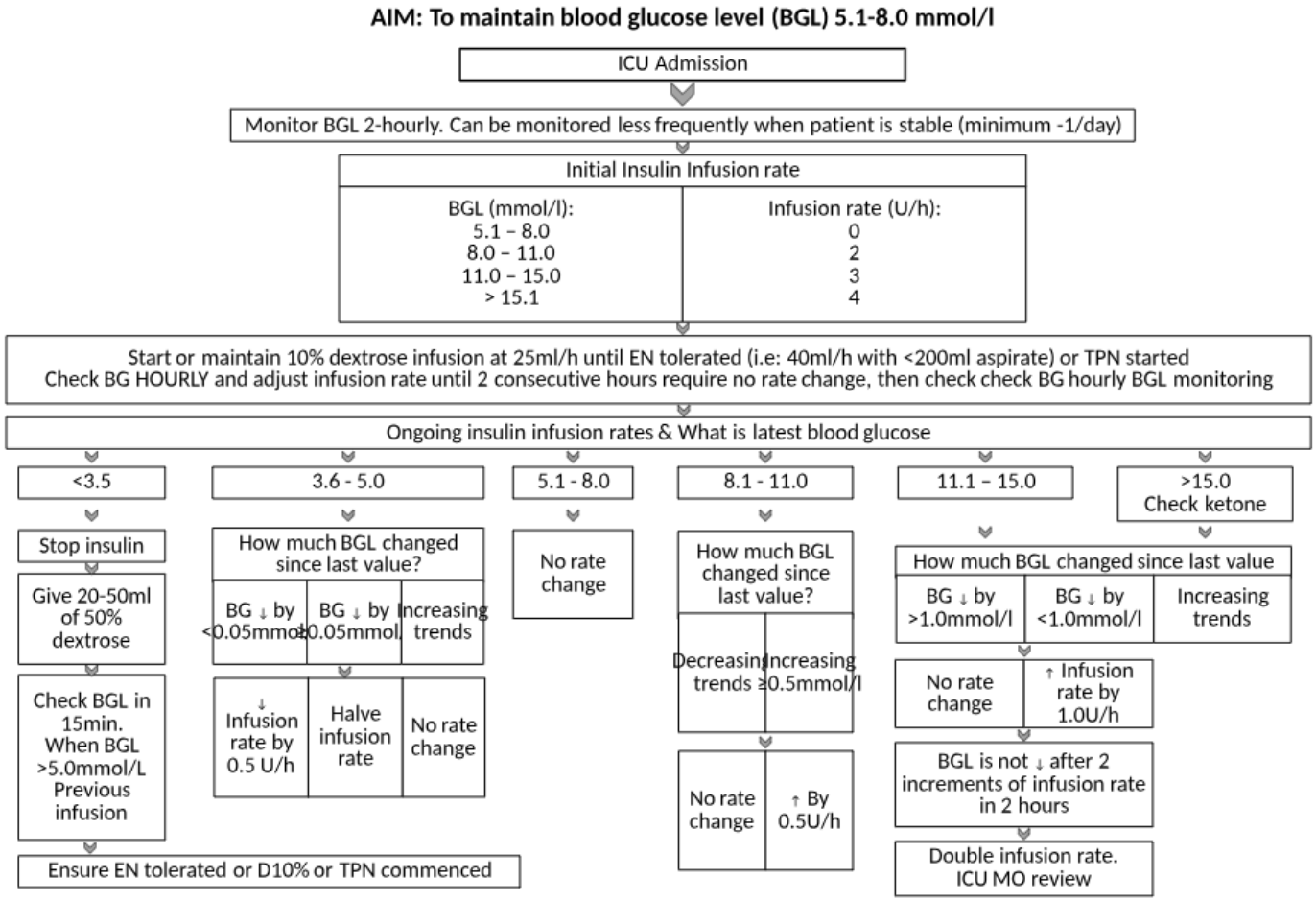

Fig. 1. HTAA Sliding scale protocol chart.

hyprtension status are discrete and binary. All others need to be discretized before being used in the model. Results are presented and discussed based on the final networks with best prediction score first and then the discretization algorithm that produce them.

The comparative performance between networks using different datasets are presented in Table I. Based on this results, BNs built from Equal Distance and Normalized Equal Distance algorithm datasets score the overall highest precision (95.93%) and with the highest calibration index (95.36%). However, if comparisons are only between the discretization by 3 algorithm datasets, K-Mean algorithm displays the best performance (87.46% precision; 96.67% calibration index).

BNs from equal distance by 2 and K-Means by 3 are presented in Figures 2 - 3. Both networks were generated using the unsupervised Maximum Weight Spanning Tree (MWST) approach that uses Pearson correlation coefficients for every pair of nodes. These coefficients are then used as weights to build a network maximizing the total sum of their squared values. MWST using Pearson Correlation, and not using MDL score as an objective function is the only technique consistently providing a final network with all nodes connected to each other. This result is explained by the fact the MDL score considers the correlation plus the structural complexity of the network, thus establishing ”automatic significance thresholds”. However, Pearson’s Correlation is only based on correlation, without any significance threshold. Thus, it always returns networks in which all the nodes are connected, even in the case of very weak relationships, which may not be accurate or desired.

Overall, in terms of quantitative performance, overall precision and calibration index results are not remarkably different between the discretized datasets. Furthermore, the Equal Distance and Normalized Equal Distance performed exactly the same. Equal distance algorithms approaches directly compute the equal distances based on the range of the variable, while the normalized equal distance first uses a smoothing algorithm to ”clean the outliers” and then computes the equal distances. Interestingly, for these data, the normal and normalized algorithms resulted in exactly the same discretization, indicating there were no outliers in the data.

Qualitatively, a closer look into the two networks reveals one common point, which is the proximity of hypertension status control’s to total hours, number of measurements and

TABLE I
SUMMARY OF PERFORMANCE RESULTS COMPARING THE DIFFERENT NETWORKS BUILT UNDER DIFFERENT DATASET FROM MULTIPLE DISCRETIZATION ALGORITHMS

Precision

Discretization by 2	Equal distance	K-Mean	Multi-variate	Normalized equal distance	GenOpt		Discretization by 3	Equal distance	K-Mean	Multi-variate	Normalized equal distance	GenOpt
Mean	82.74%	80.93%	76.49%	82.74%	80.25%		Mean	69.50%	70.72%	69.90%	69.50%	71.30%
Standard Deviation	13.43%	5.79%	7.02%	13.43%	6.92%		Standard Deviation	13.00%	11.88%	9.47%	13.00%	11.65%
Minimum	61.69%	70.41%	64.41%	61.69%	67.69%		Minimum	46.44%	46.44%	55.44%	46.44%	47.46%
Maximum	95.93%	90.85%	89.15%	95.93%	91.86%		Maximum	84.41%	87.46%	83.73%	84.41%	83.73%

Calibration Index

Discretization by 2	Equal distance	K-Mean	Multi-variate	Normalized equal distance	GenOpt		Discretization by 3	Equal distance	K-Mean	Multi-variate	Normalized equal distance	GenOpt
Mean	81.56%	78.82%	78.60%	81.56%	84.06%		Mean	88.80%	89.39%	84.91%	88.80%	87.06%
Standard Deviation	11.39%	8.15%	14.64%	11.39%	68.24%		Standard Deviation	5.20%	6.39%	6.68%	5.20%	5.56%
Minimum	55.73%	67.51%	43.90%	55.73%	69.48%		Minimum	76.51%	76.62%	70.74%	76.51%	77.69%
Maximum	95.36%	93.40%	95.36%	95.36%	95.36%		Maximum	96.58%	96.67%	95.36%	96.58%	95.50%

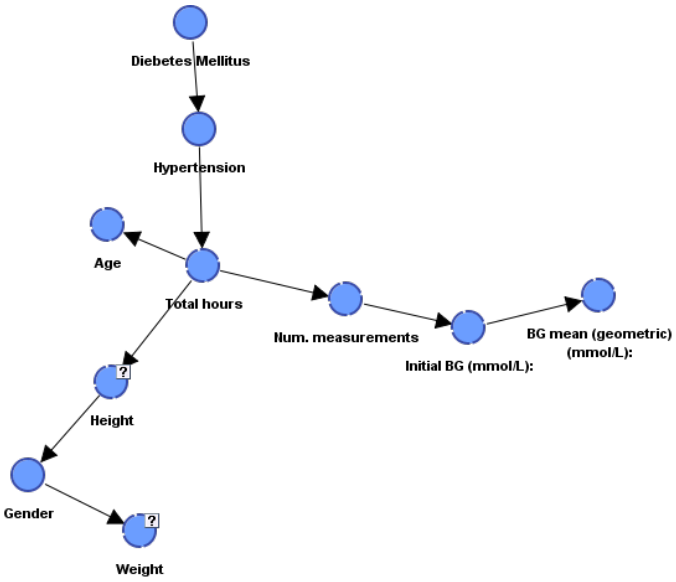

Fig. 2. The network based on equal, all 2 distance discretization.

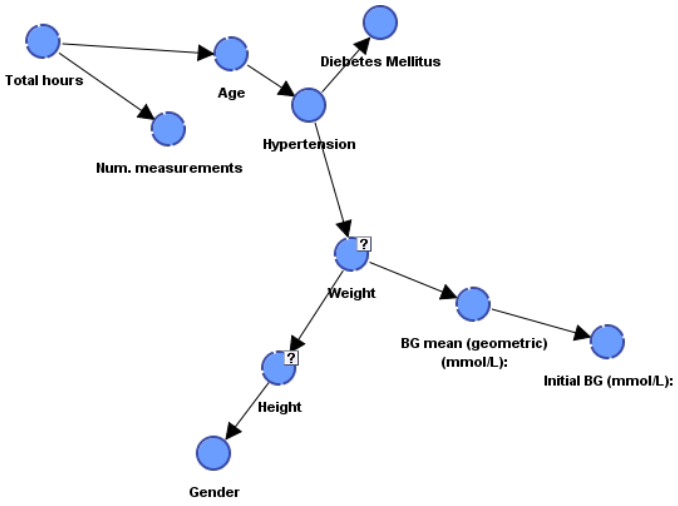

Fig. 3. The network based on equal, all 3 distance discretization with K-Means tehcnique.

BG mean if compared to Diabetes Mellitus status. This result may signal priotizing investigation and potential incorporation of per-patient hypertension status in modelling the overall approach for efficient glucose control, before Diabetes Mellitus status. Second, the arrows in generated BNs need to be approved by medical opinions to adjust the potential causality because with MWST structure learning based on Pearson correlation, the arrows only signify the strength of correlation between 2 nodes, and not necessarily the causal relationship between them. Hence, clinical model verification is necessary.

The node bars (Figures 4 - 5) display the normalized conditional probabilities to have a maximum value of 100 for both networks. From the bar, the states for each node can be extracted. However, the maximum and minimum values are not given in the generated figures, but can be referred to in Table II. Based on this discretization, the results imply difference in BN structures comes directly from the difference in discretized states of each node. This result is important as the choice of states can impact the resulting structure, which we hope can translate into increased interpretability for clinical decision support, which is critical for clinical uptake [20].

IV. CONCLUSION

The paper presents the results from linking the data coming from patients background and their glycemic control treatment in ICU using Bayesian Network. It focuses on the structural machine learned process which we think may gain some relevance for the future research and practical applications of BN in the ICUs. The performance of BN is compared within its building algorithms such as the discretization and the structure learning process. Experiments with real retrospective data revealed that many algorithms to support the building of Bayesian Network from these type of data have

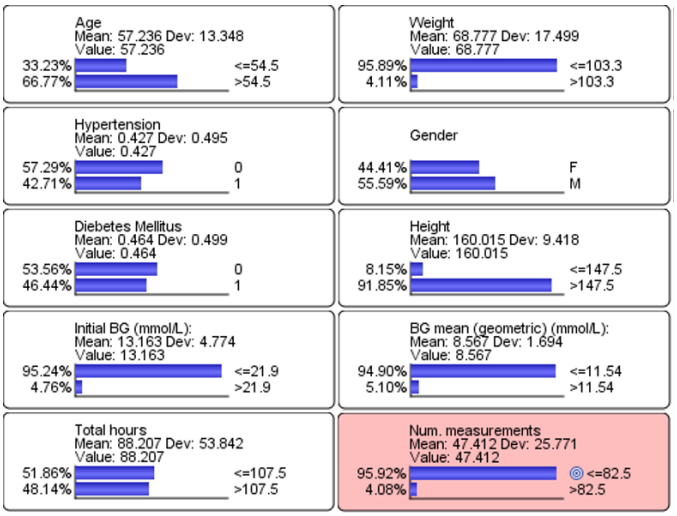

Fig. 4. The initial probability distribution for equal frequency, discretization by 2.

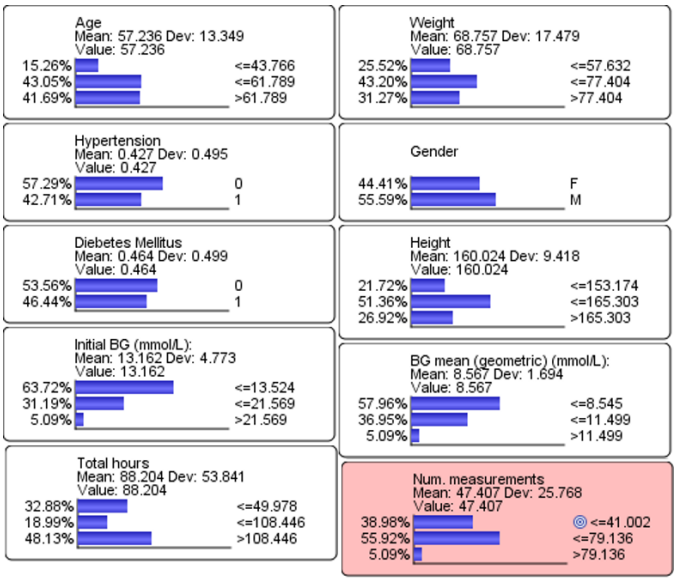

Fig. 5. The initial probability distribution for k-means, discretization by 3.

TABLE II
THE MINIMUM AND MAXIMUM VALUES OF THE VARIABLES COMING FROM THE DATASET

Nodes 10	Variables	Minimum	Maximum
Age	Continuous	18.0	91.0
Gender	Discrete	Aggregates: F or M	
Height	Continuous	109.0	186.0
Weight	Continuous	36.6	170.0
Diebetes Mellitus	Discrete	Aggregates: 0 (No) or 1 (Yes)	
Hypertension	Discrete	Aggregates: 0 (No) or 1 (Yes)	
Total hours	Continuous	2.0	213.0
Num. measurements	Continuous	3.0	162.0
Initial BG (mmol/L):	Continuous	4.8	39.0
BG mean (geometric) (mmol/L):	Continuous	5.55	17.53

statistical validity to provide an excellent prediction of control performance.

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