

UNIVERSITI PUTRA MALAYSIA

BAYESIAN NETWORK MODELING OF GASTROINTESTINAL BLEEDING

NAZZIWA AISHA

FS 2013 73



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By

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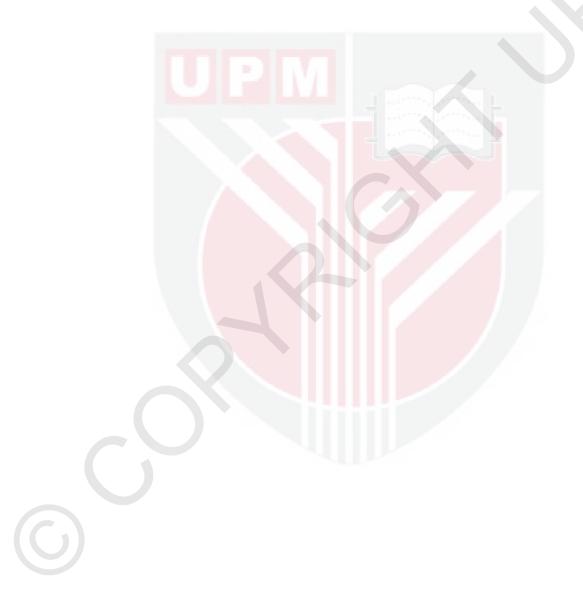
Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science.

November 2013

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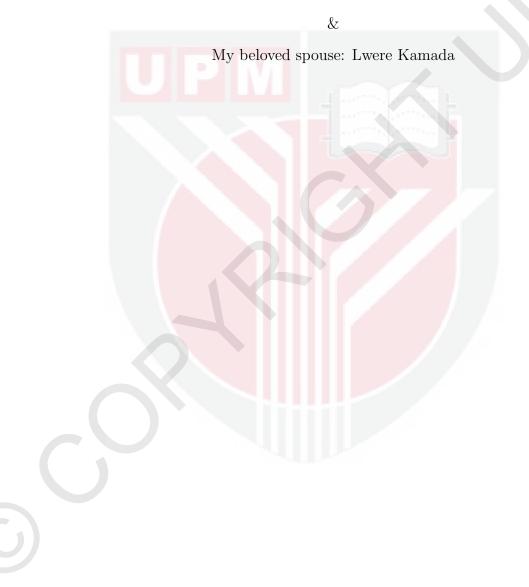
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In the name of Allah, Most Gracious, Most Merciful

Dedicated to:

My beloved father & mother



Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master of Science

BAYESIAN NETWORK MODELING OF GASTROINTESTINAL BLEEDING

By

NAZZIWA AISHA

November 2013

Chair: Mohd Bakri Adam, Ph.D. Faculty: Science

Acute gastrointestinal bleeding (GIB) is a common medical emergency with 50-150 per 100,000 people admitted per year. Although 80 percent of GIB cases stop spontaneously, it is important to determine the source of bleeding and establish a diagnosis such that possible recurrences are prevented and that the most suitable management may be given in future episodes. In the emergency room, when a patient shows signs of hematemesis (vomiting of red blood), it is obvious that the patient has upper gastrointestinal bleeding. In the absence of hematemesis however, the source of bleeding remains unclear. While the diagnosis of GIB is best done by a gastroenterologist, it is not always feasible, due to scarcity of resources and time. A reliable classification model would be very helpful in diagnosing patients more efficiently and effectively targeting the scarce resources.

Current review of the literature, did not reveal any model that predicts the source of GIB in the absence of hematemesis. This thesis uses a graphical modeling approach, specifically Bayesian networks, to model the different outcomes of GIB. One key advantage of Bayesian network models in this context is their ability to predict the outcome with partial observations on variables or attributes. The four outcome variables predicted are: source of bleeding, need for urgent blood resuscitation, need for urgent endoscopy, and disposition. Performance of the models is assessed by classification or prediction accuracy, area under curves, sensitivity and specificity values. The Bayesian network models provide good accuracy for the prediction of the source of bleeding and need for urgent blood resuscitation but did not do well on predicting need for urgent endoscopy, and disposition. The models require further validation if they are to be used in clinical settings.



Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Sarjana Sains

PEMODELAN RANGKAIAN BAYESIAN PENDARAHAN GASTROUSUS

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Pendarahan gastrousus akut (GIB) adalah penyakit kecemasan biasa dengan 50-150 daripada 100,000 orang dimasukkan ke wad dalam tempoh setahun. Walaupun 80 peratus daripada kes-kes GIB berhenti secara spontan, adalah penting untuk menentukan punca pendarahan dan melakukan diagnosis supaya dapat menghalang perkara yang sama berulang dan langkah yang paling sesuai diambil pada masa akan datang. Di dalam bilik kecemasan, apabila pesakit menunjukkan tanda-tanda hematemesis (muntah darah merah), ia adalah jelas bahawa pesakit mempunyai pendarahan gastrousus atas. Walaubagaimanapun, ketiadaan hematemesis menyebabkan punca pendarahan tidak jelas. Walaupun diagnosis GIB adalah lebih baik dilakukan oleh gastroenterologi, ia tidak kerap dilaksanakan kerana kekurangan sumber dan masa. Satu model klasifikasi yang boleh dipercayai akan banyak membantu dalam mendiagnosis pesakit dengan lebih cekap dan berkesan berdasarkan kepada sumber-sumber yang terhad.

Berdasarkan literatur yang terkini, di mana ianya tidak menunjukkan sebarang model yang meramalkan sumber GIB dengan ketiadaan hematemesis. Tesis ini menggunakan pendekatan model grafik, iaitu rangkaian Bayesian untuk memodelkan hasil GIB yang berbeza. Kelebihan utama model rangkaian Bayesian dalam konteks ini adalah keupayaannya untuk meramalkan hasil dengan menggunakan pemerhatian separa ke atas pembolehubah. Empat hasil ramalan pembolehubah adalah punca pendarahan, keperluan untuk bantuan pernafasan darah kadar segera, keperluan untuk endoskopi kecemasan, dan permisahan. Prestasi model ini dinilai dengan klasifikasi atau ramalan ketepatan, kawasan di bawah lengkungan, sensitiviti dan nilai-nilai spesifikasi. Model rangkaian Bayesian ini memberikan kejituan yang bagus bagi meramalkan punca pendarahan dan keperluan untuk bantuan pernafasan darah pada kadar segera, tetapi, model ini tidak mununjukkan kejituan yang baik dalam meramalkan keperluan untuk endoskopi kecemasan dan permisahan. Model-model ini memerlukan pengesahan yang selanjutnya sekiranya hendak digunapakai dalam penetapan klinikal.



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LIST OF ABBREVIATIONS

ACC	Prediction accuracy
ANB	Augmented naive Bayes
AUC	Area under receiver operating characteristic curves
BAN	Bayes net augmented naive Bayes
BN	Bayesian network
BNCs	Bayesian network classifiers
BUN/CR	Ratio of blood urea nitrogen to creatinine.
CPT	Conditional probability table
Cr	Creatinine
CV	Cross validation
DAG	Directed acyclic graph
DBP	diastolic blood pressure
ED	Emergency department
GI	Gastro intestinal
GIB	Acute gastrointestinal bleeding
Hct	Hematocrit
HGIB	history of gastrointestinal bleeding
HR	Heart rate
ICD-9	International Statistical Classification of Diseases
ICU	Intensive care unit
J48	Decision tree
KNN	K nearest neighbour
LGIB	Lower gastrointestinal bleeding
MAP	Maximum a posteriori
MGIB	Middle gastrointestinal bleeding
NB	Naive Bayes
NBC	Naive Bayes Classifier
NGlavage	Naso gastric lavagePlatelet count
NPV	Negative predictive value
NSAID	Non steroidal anti-inflammatory drug
NSAIDs	Nonsteroidal anti-inflammatory drugs
Plt	Platelet count
PPV	Positive predictive value
RF	Random forrest
ROC	Receiver operating characteristics
SBP	systolic blood pressure
SN	Sensitivity
SP	Specificity
TAN	Tree augmented naive Bayes
UGIB	Upper gastrointestinal bleeding
Weka	Waikato Environment for Knowledge Analysis

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CHAPTER 1

INTRODUCTION

1.1 Background

Acute gastrointestinal bleeding (GIB) is a potentially life-threatening abdominal emergency that remains a common cause of hospitalization (Fallah et al., 2000; Cerulli, 2013). According to Kanwal et al. (2010) nonvariceal upper gastrointestinal bleeding results in 400,000 hospital admissions per year, costing more than \$2 billion annually in the US. The rising incidence of GIB is associated with increasing non steroidal anti-inflammatory drug (NSAID) use such as aspirins and the high prevalence (64 percent) of Helicobacter pylori infection in patients with peptic ulcer bleeding (Sánchez-Delgado et al., 2011; Simon et al., 2013). Previous research has shown that the use of NSAIDs, for doses $\geq 325 \text{ mg/d}$ increases the risk of bleeding from peptic ulcer disease up to fivefold (Lanas et al., 2006). The advent of new drugs and endoscopic interventions have however reduced the number of surgeries for bleedings from peptic ulcer, but not mortality (Di Fiore et al., 2005). GIB is twice as common in men as in women and increases in prevalence with age (Longstreth, 1995).

The signs of GIB depend on the rate of blood loss. Patients with GIB will show signs of iron-deficiency anemia or hemoccult-positive stools when there is microscopic blood loss (Manning-Dimmitt et al., 2005). Some GIB patients will have coffee-ground emesis, which is the vomiting of altered black blood, hematemesis which is defined as the vomiting of fresh blood, melena which is the passing of black tarry stools or hematochezia which is is the passing of red blood via the rectum (usually from the lower gastrointestinal tract, but sometimes from a briskly bleeding upper gastrointestinal source) (Watson and Church, 2013; Palmer, 2002). These presentation signs are important in the diagnosis of GIB. When patients arrive in the emergency room with GIB, they are often met by a front line physician (not a gastroenterologist). The physician must make a prompt and accurate clinical assessment of the patient. This assessment involves checking the severity of the bleeding, its acuity, activity and location or source of bleeding. The source of bleeding could be from the upper part of the gastrointestinal tract or digestive tract (esophagus, stomach, and first part of the small intestine) as shown in Figure 1.1, and is known as upper gastrointestinal bleeding (UGIB) or from the lower part (includes much of the small intestine, large intestine or bowels, rectum, and anus) known as lower gastrointestinal bleeding (LGIB). Physician's make several decisions based on their prediction of the source of bleed (UGIB or LGIB). The source of bleed will determine the management of bleed i.e., consultant to be assigned and the timing for consultation.

When UGIB is suspected, the diagnostic tool of choice is esophagogastroduodenoscopy or upper endoscopy and is done by a gastroenterologist while if LGIB is suspected, a colonoscopy or lower endoscopy is done, Figure 1.2, or arteriography if the bleeding is too brisk (Zuccaro, 1998; Eisen et al., 2001). The evaluation and management of LGIB may also necessitate consultation with a nuclear medicine specialist, a general surgeon or an intervention radiologist (Brackman et al., 2003).

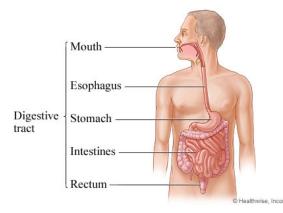


Figure 1.1: Gastrointestinal Tract.

(Adam, 2010)

Taking into consideration the numerous diagnostic and management options, an incorrect prediction of the source of bleeding can result in unwarranted consultations and procedures and in delays in delivery of proper care. Jensen et al. (1988) found out as many as 11 percent of patients suspected initially to have LGIB are ultimately found to have UGIB. Physicians also make several other

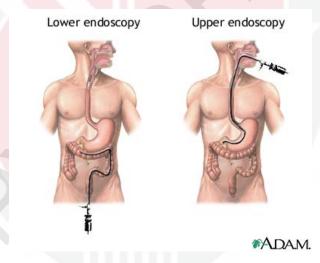


Figure 1.2: Endoscopy.

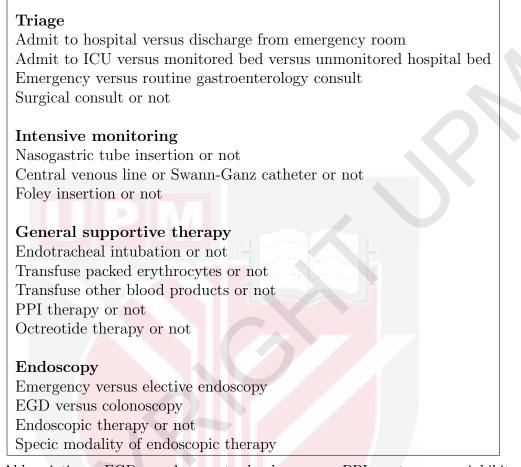
(Dugdale and Longstreth, 2009)

decisions based on the initial assessment. They determine the endoscopy timing, consultation requirements, resuscitation requirements, triage, and prognostication (Kollef et al., 1997). Other decisions are listed in Table 1.1, (Cappell and Friedel, 2008).

Although a gastroenterologist would be the most preferred to diagnose every single case of GIB, this is not always feasible due to time and cost constraint. Physicians are thus left to the task of identifying patients who are at risk of adverse outcomes (re bleeding, death) and to make key decisions on preventing these adverse outcomes. There are several clinical and laboratory variables that are available in the first few hours of evaluation in the emergency department

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Table 1.1: Key early decisions in the medical management of acute upper gastrointestinal bleeding.



Abbreviations: EGD, esophagogastroduodenoscopy; PPI, proton pump inhibitor. (Cappell and Friedel, 2008)

that can be used to identify patients at risk of adverse outcomes. (Adamopoulos et al., 2003) found that variables like haemoglobin level, haemodynamic status, that are available at presentation can be used to distinguish between patients in need of urgent endoscopy and those who don't. Using symptoms alone however, physicians can predict the location of GIB with only 40 percent accuracy compared to endoscopy on other studies. Physicians use scoring systems to help them identify patients who are at risk of adverse outcomes and their fore in need of urgent treatment. i.e., urgent blood resuscitation or endoscopy. Several scoring systems and models have been developed to identify patients at risk of adverse outcomes. The Rockall score (Rockall et al., 1996b) uses clinical data from endoscopic findings to identify UGIB patients who are at high risk. The Blatchford score (Blatchford et al., 2000), is applicable for UGIB patients as well.

Although a number of scoring systems have been developed, these scoring systems have focused on identifying patients with UGIB that are at risk of adverse outcomes. Little attention has been given to the identification of LGIB patients that are at risk of adverse outcomes. Classification or prediction models need to



be developed to help identify those patients in need of urgent resuscitation and endoscopic intervention (Baradarian et al., 2004; Jensen et al., 2000). There are several classification models that have been developed that can be used to predict several outcomes of GIB in patients (Chu et al., 2008). The Bayesian network (BN) models have however not been considered as predictors of outcomes of GIB. In this thesis, Bayesian network (BN) models are developed, to help in the diagnosis or prediction of outcomes of GIB. BNs have the following advantages over other methods.

- 1. BN's represent powerful tools for graphically representing the relationships among a set of variables and for dealing with uncertainties.
- 2. The graphical structure of the BN provides a simple way to visualize the relationships between the variables.
- 3. BN's are interactive and offer a graphical modeling mechanism that researchers can use to understand the behavior of a system or situation. When variables are observed or more evidence is obtained, the information can be propagated throughout the model and the effects on particular variables of interest can be inspected .

1.2 Objectives of the thesis

The objectives of the thesis are to:

- 1. Develop BN models for predicting the source of bleeding, need for urgent endoscopy, need for urgent blood resuscitation and disposition in patients with GIB.
- 2. Develop a naive Bayes model (NB) to predict the source of bleeding in GIB patients presenting without hematemesis.
- 3. Compare the NB model for predicting the source of bleeding in patients presenting without hematemesis with other classification models.

1.3 Methods

In order to achieve the objectives, a BN approach to modeling GIB is selected after a broad review of numerous approaches which include; rule induction, traditional statistics, random forest, and other modeling algorithms. Three BN models are considered: the naive Bayes (NB) model, tree augmented naive Bayes model (TAN), and Bayes network augmented naive Bayes (BAN). These models are developed with the help of two modeling shells. The first is Weka modeling shell which is selected because of its ability to incorporate case files, provide the classification accuracy and because it has a variety of other classifiers with which we can use to compare our model. Weka cannot perform sensitivity analysis and provides no option for updating the model. These two functions are found in the Netica (Norsys) modeling shell. Netica solves the network by performing standard belief updating which looks for the marginal posterior probability for each node . In BN modeling, a prior probability is the likelihood of some input parameters being in a particular state e.g. a patient having a history of GIB. A conditional probability is the likelihood of a state of a parameter given the states of other parameters that affect it, i.e., how the presence of a history of UGIB affects the current presence of GIB. A posterior probability is the likelihood of a certain parameter being in a particular state e.g. the patient having UGIB given the input parameters, conditional probabilities and the rules governing the combination of the probabilities (Marcot et al., 2001). A network is solved when the nodes are updated.

1.4 Expected outcome

The expectation of this thesis is that the BNs developed will assist the physician in the emergency room to diagnose the patients more efficiently and effectively. BN models have the potential to identify patients with both UGIB and LGIB and ascertain their need for urgent treatment or disposition. The model can be used to predict the source of bleeding, disposition and need for intervention (endoscopy and resuscitation) in patients with UGIB or LGIB.

1.5 Limitations of the study

In order to use the BN model, it would need to be validated on larger real datasets and more simulation studies done. It takes time to get approval for use of a large established datasets from organizations. This has limited the testing of the BN models on datasets from other clinics. This study has thus been based on two datasets. A BN model is interactive. It would need to be developed as a web interface so that its performance be compared to the prediction of a physician at the hospital. Due to time and cost constraint, the web interface is not developed.

1.6 Organization of the thesis

This thesis is divided into five chapters. Chapter 1, explains the motivation of the thesis and how the contents throughout the document are organized. Chapter 2, introduces the methods used in the thesis beginning with the most general concepts and gradually focusing on those most related to the remaining chapters. First the general concept of BN is explained, and then details of the modeling process and their construction is given. Finally a specific type of BNs, called Bayesian network classifiers (BNCs) which is the main theme of the thesis, are emphasized. In Chapter 3, BNCs for predicting the four outcomes of GIB are developed. In Chapter 4, BNs for the special case of predicting the source of GIB in the absence of hematemesis are developed and the BNs are compared with other classification models. Finally, Chapter 5 summarizes the main contributions of the thesis and gives the future work.

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