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INTEGRATED ARTIFICIAL INTELLIGENCE-BASED CLASSIFICATION APPROACH FOR PREDICTION OF ACUTE CORONARY SYNDROME

NADER SALARI

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By

NADER SALARI

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirement for the Degree of Doctor of Philosophy

November 2014

DEDICATION

To:

My father and mother's soul and my precious wife and son.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in Fulfillment of the Requirement for the Degree of Doctor of Philosophy

INTEGRATED ARTIFICIAL INTELLIGENCE-BASED CLASSIFICATION APPROACH FOR PREDICTION OF ACUTE CORONARY SYNDROME

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November 2014

Chairperson: Shamarina Shohaimi, PhD
Faculty: Science

Coronary heart disease (CHD) is one of the most life-threatening diseases all over the world. One of the common medical emergencies and the leading cause of hospitalization, morbidity and mortality is known as acute coronary syndrome (ACS). ACS, which refers to a wide range of acute myocardial ischaemic conditions, is a dynamic and unstable process. The failure in timely diagnosis and prompt treatment of ACS may lead to fatal outcomes. The existing gap of knowledge in "timely and accurate" diagnosis and classification of the patients with suspected ACS is an extremely challenging issue for the practicing emergency physicians. Therefore, application of an innovative approach is required. Using "AI-based" classification models could be considered as an innovative, creative, and multi-disciplinary strategy.

Recently, the "hybrid AI-based" classification models have gained more attraction due to the inefficiency of conventional "single AI-based" models in accurate classification. Accordingly, the present study attempts to introduce a novel hybrid classification model for the prediction of ACS to fill the multi-stages gaps.

To this end, as the initial stage, the pros and cons of the "single AI-based" were evaluated toward providing a strategy in development of the best classification models for prediction of heart failure based on the Perth data set. In the second stage, a registry entitled "Acute Coronary Syndrome Event — in Kermanshah, Iran (ACSEKI)" was designed and established as the first ACS registry in Iran. The following results were obtained when classification of the ACS types used the conventional "single AI-based" methods. The comparison results of the classifiers showed the highest accuracy of 83.2% and 82.9% for the Feed-forward back-propagation neural network (FFBPNN) and K-nearest neighbors (K-NNs) methods respectively. Although FFBPNN classifier is slightly more accurate than K-NN, there are some advantages such as simple implementability, understandability and interpretability for the latter. In the development of the "hybrid AI-based" classification models, the proposed model (K_1-K_2- NN), was basically introduced through combining AI approaches of modified K-NN, genetic algorithm (GA), Fisher's discriminant ratio (FDR) and class separability criteria (CSC). The classification performance of K_1-K_2-NN model was benchmarked against 13

commonly used classification models using repeated random sub-sampling cross-validation on ACSEKI data set. The optimized K_1-K_2-NN model (3-5-NN) demonstrated higher performance accuracy with an average of 94.4% ± 0.9%.

As the core component of the present study, the previous models were improved by introducing a "Developed Feed Forward Back Propagation Neural Network" (DFFBPNN). Performance evaluation of the proposed model were conducted by comparing 13 well-known classification models based on various commonly used evaluation criteria on seven data sets (ACSEKI data set as well as six data sets taken from the University of California Irvine (UCI) machine-learning repository). Statistical analysis was performed using the Friedman test followed by post-hoc tests. Finally, the performance results of the proposed model was benchmarked against the best ones reported as the state-of-the-art classifiers in terms of classification accuracy for the same data sets. The experimental findings indicated that the novel proposed hybrid model resulted in significantly better classification performance compared with all 13 classification methods. The classification accuracy of the "hybrid model" and "K_1-K_2-NN" on ACSEKI data set were 95.2% and 94.2%, respectively, showing 0.08% improvement for the "hybrid model". Furthermore, substantial findings of the comprehensive comparative study revealed that performance of the proposed model in terms of classification accuracy is desirable, promising, and competitive to the existing state-of-the-art classification models. Accordingly, the proposed "hybrid model" demonstrated to be applicable for classification problems in different medical areas, particularly for early detection of ACS.

To recapitulate, the study demonstrated that an integrated AI-based classification approach could be a significant potential for prediction of ACS. Thus, the proposed model could be effectively used for a clinician with less experience or as a second opinion for an experienced senior clinician to their quickly, timely, and accurately decision making process. The model could also be utilized for classification tasks in the other medical fields such as breast cancer and diabetes. This model is expected to make a significant contribution to the literature of integrated AI-based approach for classification of ACS with high accuracy and efficiency.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Doktor Falsafah

PENDEKATAN PENGELASAN BERASASKAN KECERDASAN BUATAN BERSEPADU UNTUK MERAMAL SINDROM KORONARI AKUT

Oleh

NADER SALARI

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Penyakit jantung koronari (CHD) adalah salah satu penyakit yang paling mengancam nyawa di seluruh dunia. Salah satu daripada kecemasan perubatan yang biasa dan penyebab utama kemasukan ke hospital, morbiditi dan mortaliti dikenali sebagai sindrom koronari akut (ACS). ACS, yang merujuk kepada pelbagai keadaan iskemia miokardium akut, adalah satu proses yang dinamik dan tidak stabil. Kegagalan dalam diagnosis yang tepat pada masanya dan rawatan segera ACS boleh membawa maut. Jurang yang sedia ada dalam pengetahuan dalam diagnosis ACS yang "tepat pada masanya dan tepat" dan pengelasan pesakit yang disyaki menghidap ACS merupakan satu isu yang amat mencabar bagi pakar perubatan kecemasan. Oleh itu, penggunaan pendekatan yang inovatif adalah diperlukan. Menggunakan model pengelasan berasaskan kecerdasan buatan boleh dianggap sebagai satu strategi yang inovatif, kreatif, serta merangkumi pelbagai disiplin.

Kebelakangan ini, model pengelasan berasaskan kecerdasan buatan hibrid telah mendapat perhatian lebih disebabkan oleh ketidakcekapan model konvensional berasaskan kecerdasan buatan tunggal dalam pengelasan yang tepat. Oleh itu, kajian ini memperkenalkan model pengelasan hibrid baru bagi meramalACS bagi mengisi jurang pelbagai aras.

Untuk tujuan ini, pada peringkat awal kebaikan dan keburukan model pengelasan berasaskan kecerdasan buatan tunggal telah dinilai bagi menyediakan satu strategi dalam pembangunan model pengelasan terbaik untuk meramal kegagalan jantung berdasarkan set data yang diperolehi daripada Perth. Langkah kedua melibatkan pembangunan sebuah *registry* bertajuk "Kejadian Sindrom Koronari Akut- di Kermanshah, Iran (ACSEKI)" yang merupakan*registry* ACS pertama di Iran. Hasil dapatan daripada pengelasan jenis ACS menggunakan kaedah konvensional berasaskan kecerdasan buatan tunggalmenunjukkan ketepatan tertinggi iaitu 83.2% dan 82.9% bagi kaedah Feed-Hadapan rangkaian neural perambatan balik (FFBPNN) dan K-jiran terdekat (K-NN) masing-masing. Walaupun pengelas FFBPNN adalah sedikit lebih tepat daripada K-NN, terdapat beberapa kelebihan K-NN seperti kaedah pelaksanaan, memahami dan mentafsir yang lebih mudah berbanding pengelas FFBPNN. Dalam pembangunan model pengelasan berasaskan kecerdasan buatan hibrid, model yang dicadangkan (K1-K2-NN), pada asasnya diperkenalkan melalui penggabungan pendekatan kecerdasan buatan iaitu K-NN

yang diubahsuai, algoritma genetik (GA), nisbah diskriminan Fisher (FDR) dan kriteria kelas dapat dipisahkan (CSC). Prestasi pengelasan model K1-K2-NN telah ditanda aras dengan 13 model pengelasan yang biasa digunakan menggunakan sub-pensampelan rawak berulang pengesahsahihan silang pada set data ACSEKI. Oleh itu, model K1-K2-NN yang dioptimumkan (3-5-NN) telah menunjukkan prestasi ketepatan yang lebih tinggi dengan purata 94.4% ± 0.9%.

Sebagai komponen teras kajian ini, model-model sebelum ini ditambah baik dengan memperkenalkan rangkaian neural perambatan balik (DFFBPNN). Penilaian prestasi model yang dicadangkan telah dijalankan dengan membandingkan 13 model pengelasan terkenal berdasarkan pelbagai kriteria penilaian yang lazim pada tujuh set data (data ACSEKI yang ditetapkan serta enam set data yang diambil daripada University of California Irvine (UCI) repositori mesin-pembelajaran). Analisis statistik dilakukan dengan menggunakan ujian Friedman diikuti dengan ujian post-hoc. Akhirnya, keputusan prestasi model yang dicadangkan telah ditanda aras dengan pengelas terbaik yang telah dilaporkan dari segi ketepatan pengelasan untuk set data yang sama. Hasil dapatan kajian menunjukkan bahawa novel model hibrid yang dicadangkan telah menghasilkan prestasi pengelasan yang jauh lebih baik berbanding semua ketigabelas kaedah pengelasan. Ketepatan pengelasan model hibrid dan K1-K2-NN pada set data ACSEKI adalah 95.2% dan 94.2%, masing-masing, menunjukkan peningkatan 0.08% bagi model hibrid. Tambahan pula, penemuan besar kajian perbandingan komprehensif mendedahkan bahawa prestasi model yang dicadangkan dari segi ketepatan pengelasan adalah wajar dan berdaya saing dengan model pengelasan terbaik yang sedia ada. Oleh itu, model hibrid yang dicadangkan menunjukkan bahawa ia boleh dipakai untuk masalah pengelasan perubatan dalam bidang yang lain, terutamanya bagi pengesanan awal ACS.

Sebagai kesimpulan, kajian ini menunjukkan bahawa pendekatan pengelasan berasaskan kecerdasan buatan bersepadu boleh menjadi potensi yang besar untuk meramalkan ACS. Oleh itu, model yang dicadangkan boleh digunakan dengan berkesan untuk pakar klinikal yang kurang berpengalaman atau sebagai pendapat kedua untuk doktor senior yang berpengalaman dalam proses membuat keputusan mereka yang cepat, tepat pada masanya, dan tepat. Model ini juga boleh digunakan dalam bidang perubatan lain seperti kanser payudara dan diabetes. Model ini dijangka akan memberi sumbangan yang besar kepada pengetahuan tentang pendekatan pengelasan berasaskan kecerdasan buatan bersepadu bagi pengelasan ACS dengan ketepatan yang tinggi dan cekap.

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I certify that a Thesis Examination Committee has met on 27 November 2014 to conduct the final examination of Nader Salari on his thesis entitled "Integrated Artificial Intelligence-Based Classification Approach for Prediction of Acute Coronary Syndrome" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

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LIST OF ABBREVATIONS

APM	Accuracy Probability Matrix
ACS	Acute Coronary Syndrome
ACSEKI	Acute Coronary Syndrome Event — in Kermanshah, Iran
AMI	Acute Myocardial Infarction
ANFIS	Adaptive Network Fuzzy Inference System
AI	Artificial Intelligence
ANN	Artificial Neural Network
AUC	Area Under the receiver/relative operating characteristic Curve
BA	Bootstrap Aggregation
Bagging-ID3	Bootstrap Aggregation -ID3
CSC	Class Separability Criteria
CM	Confusion Matrix
CAD	Coronary Artery Disease
CHD	Coronary Heart Disease
CPM	Correctness Probability Matrix
CK	Creatine Kinase
CK-MB	Creatine Kinase-Muscle/Brain
DWK-NN	Distance Weighted K-NN
DFFBPNN	Developed feed-forward back-propagation neural network
EOHF	Early-Onset Heart Failure
ECG	Electrocardiogram
FFBPNN	Feed-Forward Back-Bropagation Neural Network
FDR	Fisher’s Discriminant Ratio
GLM	Generalized Linear Model
GA	Genetic Algorithm
ID-3	Iterative Dichotomiser-3
HF	Heart Failure
K_1-K_2-NN	K_1-K_2- nearest neighbor
K-NN	K-Nearest Neighbor
MLP	Multilayer Perceptron
MI	Myocardial Infarction
NPV	Negative Predictive Value
NB	Naive Bayes
NSTEMI	Non-ST-segment Elevation Myocardial Infarction
PDK-NN	Partial Distance K-Nearest Neighbor
PPV	Positive Predictive Value
PCA	Principal Component Analysis
RBF	Radial Basis Function
ROC	Receiver/Relative Operating Characteristic
STEMI	ST-segment Elevation Myocardial Infarction
UCI	University of California Irvine
UA	Unstable Angina
WBC	Wisconsin Breast Cancer
WDBC	Wisconsin Diagnostic Breast Cancer

CHAPTER 1

INTRODUCTION

1.1 General Introduction

Diseases are one of the leading causes of death among human beings, have always-threatened human health. Some diseases such as plague, cholera, malaria and tuberculosis were pandemic in different periods, and they inflict devastating casualties(Cliff et al., 2004). On the one hand, due to significant improvements in the public health systems and advances in therapeutic methods the mortality rates of some diseases have been decreased over times which in turn resulted in longer life expectancy(Armstrong et al., 1999). On the other hand, other lethal and chronic conditions, such as cardiovascular disease and cancer, which are mostly caused by modern life style, have been emerged as a new challenge. So that, such diseases have become the most serious community health problems (Lippi et al., 2006).

During the last century, Coronary Heart Disease (CHD) has burgeoned from a relatively minor disease to one of the most life-threatening diseases and a leading cause of morbidity and mortality(Levenson et al., 2002; Guilbert, 2003). Studies indicate that at the beginning of the 20th century, CHD has been accounted for less than 10 percent of all deaths worldwide. At the beginning of the 21st century, CHD accounts for nearly half of the deaths in the developed countries and a quarter of those in the developing ones(Guilbert, 2003).

CHD is currently the leading cause of morbidity and mortality in Iran(Hatmi et al., 2007), Malaysia(Raihan and Azmawati, 2013), the United States (U.S.)(Roger et al., 2012), and the United Kingdom (UK)(Bhattarai et al., 2012), as in the all over the world(Mendis et al., 2011). The prevalence of CHD in the US in 2008 was 7 percent or 16.3 million adults (20 years and older)(Roger et al., 2012). Furthermore, it has been projected to almost double during the 21st century(Guthrie, 2003).

World Health Organization (WHO) estimates that 7.3 million people (i.e. 12.66% out of 58.66 million) died globally due to CHD in 2008(Mendis et al., 2011). CHD is the cause of more than 40 percent of all deaths (i.e. approximately 138,000 deaths) in Iran each year(Naghavi and Jafari, 2007). In addition, CHD is the cause of over 405,300 deaths(Roger et al., 2012), (i.e. about one in six deaths) in the US and over 88,000 deaths(Bhattarai et al., 2012),(i.e. one in five male and one in seven female deaths) in the UK in 2008. CHD is responsible for 22.2 percent of total deaths in Malaysia in 2011(WHO, 2011).

Acute Coronary Syndrome (ACS) is a term, which encompasses the clinical manifestations of CHD. The spectrum of clinical presentations of ACS ranges from unstable angina (UA) and non-ST-segment elevation myocardial infarction (NSTEMI) to ST-segment elevation myocardial infarction (STEMI). Of the eight million patients who visit emergency departments suffering from chest pain each year, five millions are diagnosed with ACS(Rosamond et al., 2008). According to a conservative estimate, the number of hospital discharges with ACS as the primary diagnosis was 671,000 in the U.S in 2007. Whereas secondary diagnoses for ACS were included, the number of hospital discharges was 1,172,000(Sangkachand et al., 2012).

In spite of the fact that the vast majority of cardiologists and primary care physicians have a low threshold for diagnosing ACS, about 5% of patients are misdiagnosed and discharged inappropriately (with potentially fatal consequences) (Pope et al., 2000; Harrison and Kennedy, 2005). Although this figure may appear to be relatively low, misdiagnosis and inappropriate early discharge of patients will inevitably result in significantly increased mortality rate. So that, it was demonstrably shown that in hospitalized patients the mortality rate is approximately 1.7 to 1.9 times less than in such patients(Ho and Reddy, 2010). Innovative approaches are therefore needed to facilitate the predictive decision making process of early diagnosing and classification of ACS patients more accurately, rapidly and efficiently.

On the other hand, medical knowledge is complex and dynamic. It is increasingly growing and expanding exponentially to such an extent that even those who are expert in medicine have difficulties in following the latest advances and new challenges. In addition, in this high-tech world, computers surpass humans in the capability to remember. This important property can be very valuable in the practice of medicine and, in fact, computer-aided systems can lead to important improvements in the diagnosis, classification and treatments of diseases. Consequently, researching in system development for classification purposes is a very popular area in Artificial Intelligence (AI).

AI is one of the most powerful approaches for classification purposes, especially in various medical fields (Fayyad et al., 1996). In the last decade, the impact of AI-based classification models on decision making processes in various scientific domains, including medicine, have attracted a lot of attention. Among the numerous AI approaches, K-Nearest Neighbor (K-NN) algorithms, genetic algorithms (GAs), and Artificial Neural Networks (ANNs) are considered as the most common and effective methods.

However, these methods have often been used separately in classification approaches in numerous studies. While it seems that the focus of research carried out on traditional “single AI- based” technologies has mostly been productive, it could be considered to be sub-optimal in practice due to the limitation of the technologies. This is mainly caused by ignoring the advantage of the synergies among the technologies. In other words, concerns have arisen from the fact that each of AI methods has its specific advantages and disadvantages. In effect, due to the individual strengths and weaknesses associated with the various AI approaches , their potential can merely be realized by taking advantage of the synergy among them.Thus, incorporating these AI-based technologies can capitalize extraordinarily on their strengths and compensating for their deficiencies.

In this context, hybrid models is an innovative approach, which could be considered as one of the best possible strategies in addressing the above-mentioned challenge. During the last few years, researchers increasingly noticed the hybrid models. The main idea behind these models is to benefit from the synergy, which will be emerged from the combined technologies. These are relatively new approaches, which include innovative, creative, and appropriate combination of several models in achieving a final common goal with a performance far better than traditional models based on single technology. This characteristic provides the opportunity to take advantage of the exclusive strengths of each technology and can be used as a means for compensating the deficiencies, and overcoming the limitations of each technology(Shapiro, 2002; Hur and Kim, 2008).

1.2 Problem Statement

The existing gap of knowledge in "timely and accurate" diagnosis and classification of the patients with suspected ACS is an extremely challenging issue for the practicing emergency physicians(Theroux, 2010). In practice, the vast majority of cardiologists and primary care physicians have a low threshold for diagnosing ACS and about 5% of patients with potentially fatal consequences are misdiagnosed and discharged inappropriately(Pope et al., 2000; Harrison and Kennedy, 2005). On the other hand, in numerous studies the traditional AI methods have been used separately in classification of ACS. That is, although the focus of research on traditional "single AI- based" technologies on the basis of "its own individual strengths" has mostly been productive, in practice it could be considered to be sub-optimal due largely to the limitation of each technology. Thus, the studies are constrained and opportunities are lost to take advantage of the synergies between current technologies.

Providing an appropriate strategy to improve the model's classification accuracy as a challenging issue plays an important role to facilitate the predictive decision making process. Recently, in order to achieve higher classification accuracy, the "hybrid AI-based" approaches have gained more attention than conventional "single AI-based" approaches(Gorunescu and Belciug, 2014). This is because, on the basis of the advantages and disadvantages of each of the AI methods, incorporating the "single AI-based" technologies in a "hybrid AI-based" model can capitalize extraordinarily on their strengths and compensating for their deficiencies. It could be considered as one of the best possible strategies and innovation in addressing these multistage gaps.

Accordingly, application of an innovative approach appears to be required in facilitating such a predictive clinical decision making process. In spite of the above-mentioned facts about various aspects of this multi-disciplinary challenge, there are few comprehensive studies in the literature concerned with ACS classification, which are based on only "single AI-based" approaches rather than the "hybrid AI-based" approaches. To the best of our knowledge, no measure has been taken for proposing a hybrid model in this context. So, it is imperative to use "hybrid AI-based" classification models that are considered to be innovative, creative, and multi-disciplinary strategy. In other word, there is a need for developing a more accurate, efficient and broadly applicable "hybrid AI-based" model for ACS classification to fill the multi-stages gaps.

1.3 Objectives

The overall aim of the present project was to develop the hybrid AI-based models in order to more accurately and efficiently classify ACS.

Specific objectives of the study were:

1. To classify ACS types using the conventional “single AI-based” methods.
2. To develop classification models, with introducing novel “hybrid AI-based” models, in order to achieve more accurate, efficient, and broadly applicable classification models.
3. To compare the performance of the novel “hybrid AI-based” model with conventional classification methods.

1.4 Development of Study

The first part of the study will evaluate the pros and cons of the “single AI-based” methods toward providing a strategy in development of the best classification models (chapter 3) for prediction of heart failure on Perth data set. In fact, this will reveal limitation of the “single AI-based” methods and the need to look into “hybrid AI-based” models. To this end, the second part of the study is to develop novel hybrid AI-based methods using the six data sets taken from the University of California Irvine (UCI) machine-learning repository along with other data set derived from a registry entitled “Acute Coronary Syndrome Event — in Kermanshah, Iran (ACSEKI)” (Chapter 4, 5 and 6).

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