Computational and Structural Biotechnology Journal xxx (2016) xxx–xxx

COMPUTATIONAL AND STRUCTURAL BIOTECHNOLOGY JOURNAL

journal homepage: www.elsevier.com/locate/csbj

Mini Review

Heart Failure: Diagnosis, Severity Estimation and Prediction of Adverse Events Through Machine Learning Techniques

Evanthia E. Tripoliti [a,b], Theofilos G. Papadopoulos [a], Georgia S. Karanasiou [a,b], Katerina K. Naka [c,d], Dimitrios I. Fotiadis [a,b,*]

[a] Department of Biomedical Research, Institute of Molecular Biology and Biotechnology, FORTH, GR 45110 Ioannina, Greece
[b] Unit of Medical Technology and Intelligent Information Systems, University of Ioannina, GR 45110 Ioannina, Greece
[c] Michaelidion Cardiac Center, University of Ioannina, GR 45110 Ioannina, Greece
[d] 2nd Department of Cardiology, University of Ioannina, GR 45110 Ioannina, Greece

ARTICLE INFO

Article history:
Received 9 July 2016
Received in revised form 12 November 2016
Accepted 14 November 2016
Available online xxxx

Keywords:
Heart failure
Diagnosis
Prediction
Severity estimation
Classification
Data mining

ABSTRACT

Heart failure is a serious condition with high prevalence (about 2% in the adult population in developed countries, and more than 8% in patients older than 75 years). About 3–5% of hospital admissions are linked with heart failure incidents. Heart failure is the first cause of admission by healthcare professionals in their clinical practice. The costs are very high, reaching up to 2% of the total health costs in the developed countries. Building an effective disease management strategy requires analysis of large amount of data, early detection of the disease, assessment of the severity and early prediction of adverse events. This will inhibit the progression of the disease, will improve the quality of life of the patients and will reduce the associated medical costs. Toward this direction machine learning techniques have been employed. The aim of this paper is to present the state-of-the-art of the machine learning methodologies applied for the assessment of heart failure. More specifically, models predicting the presence, estimating the subtype, assessing the severity of heart failure and predicting the presence of adverse events, such as destabilizations, re-hospitalizations, and mortality are presented. According to the authors' knowledge, it is the first time that such a comprehensive review, focusing on all aspects of the management of heart failure, is presented.

Contents

1. Introduction . . . 0
2. Detection of HF . . . 0
3. HF Subtypes Classification . . . 0
4. Severity Estimation of HF . . . 0
5. Prediction of Adverse Events . . . 0
5.1. Destabilizations . . . 0
5.2. Re-Hospitalizations . . . 0
5.3. Mortality . . . 0
6. Summary and Outlook . . . 0
Acknowledgment . . . 0
References . . . 0

1. Introduction

Heart failure (HF) is a complex clinical syndrome and not a disease. It prevents the heart from fulfilling the circulatory demands of the body,

* Corresponding author at: Unit of Medical Technology and Intelligent Information Systems, Department of Materials Science and Engineering, University of Ioannina, GR 45110 Ioannina, Greece.
E-mail addresses: dimitris.fotiadis30@gmail.com, fotiadis@cc.uoi.gr (D.I. Fotiadis).

http://dx.doi.org/10.1016/j.csbj.2016.11.001

Please cite this article as: Tripoliti EE, et al, Heart Failure: Diagnosis, Severity Estimation and Prediction of Adverse Events Through Machine Learning Techniques, Comput Struct Biotechnol J (2016), http://dx.doi.org/10.1016/j.csbj.2016.11.001

since it impairs the ability of the ventricle to fill or eject blood. It is characterized by symptoms, such as breathlessness, ankle swelling and fatigue that may be accompanied by signs, for example elevated jugular venous pressure, pulmonary crackles, and peripheral edema, caused by structural and/or functional cardiac or non-cardiac abnormalities. HF is a serious condition associated with high morbidity and mortality rates. According to the European Society of Cardiology (ESC), 26 million adults globally are diagnosed with HF, while 3.6 million are newly diagnosed every year. 17–45% of the patients suffering from HF die within the first year and the remaining die within 5 years. The related to HF management costs are approximately 1–2% of all healthcare expenditure, with most of them linked with recurrent hospital admissions [1–3].

The increased prevalence, the escalated healthcare costs, the repeated hospitalizations, the reduced quality of life (QoL) and the early mortality have transformed HF to an epidemic in Europe and worldwide and highlight the need for early diagnosis (detection of the presence of HF and estimation of its severity) and effective treatment. In clinical practice, medical diagnosis, including carefully history and physical examination, is supported by ancillary tests, such as blood tests, chest radiography, electrocardiography and echocardiography [4]. The combination of data produced by the above procedure of diagnosis resulted in the formulation of several criteria (*e.g.* Framingham, Boston, the Gothenburg and the ESC criteria) determining the presence of HF [5]. Once the diagnosis of HF is established, the experts classify the severity of HF using either the New York Heart Association (NYHA) or the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines classification systems, since this classification allows them to determine the most appropriate treatment (medication treatment, guidelines regarding nutrition and physical activity exercising) to be followed [6].

Although there is a significant progress in understanding the complex pathophysiology of HF, the quantity and complexity of data and information to be analyzed and managed convert the accurate and efficient diagnosis of HF and the assessment of therapeutic regimens to quite challenging and complicated tasks. Those factors, in combination with the positive effects of early diagnosis of HF (which allows experts to design an effective and possibly successful treatment plan, prevents condition worsening, affects positively the patient's health, improves patient's QoL and contributes to decrease of medical costs) are the reasons behind the enormous increase of the application of machine learning techniques to analyze, predict and classify medical data. Classification methods are among the data mining techniques that have gained the interest of research groups. Accurate classification of disease stage or etiology or subtypes allows treatments and interventions to be delivered in an efficient and targeted way and permits assessment of the patient's progress.

Focusing on HF, different data mining techniques have been employed to differentiate the patients with HF from controls, to recognize the different HF subtypes (*e.g.* HF with reduced ejection fraction, HF with preserved ejection fraction) and to estimate the severity of HF (NYHA class) (Fig. 1). Additionally, data mining techniques can be advantageous even if HF is being diagnosed at a late stage, where the therapeutic benefits of interventions and the prospect of survival are limited, since they allow the timely prediction of mortality, morbidity and risk of readmission. Data recorded in the subjects' health record, expressing demographic information, clinical history information, presenting symptoms, physical examination results, laboratory data, electrocardiogram (ECG) analysis results, are employed. An extended review of the studies reported in the literature addressing the above mentioned issues (HF detection, severity estimation, prediction of adverse events) through the utilization of machine learning techniques is presented in this paper.

The systematic literature review was based on sources like i) PubMeD, ii) Scopus, iii) ScienceDirect, iv) Google Scholar, v) Web of Science (WoS) using as keywords the phrases “detection of HF”, “severity estimation of HF”, “HF subtypes classification”, “prediction of HF destabilizations”, “prediction of HF relapses”, “prediction of HF mortality”, “prediction of HF re-hospitalizations”.

The studies reported in the literature were selected based on the following criteria: i) focus on heart failure and no any other heart disease, ii) are written in English language, iii) are published from 2000 (inclusive) until present, iv) cover different geographical locations, v) are employing machine learning techniques, vi) employ Electronic Health Records, published databases, observational, trial, *etc.* for the development and validation, vii) provide information regarding the evaluation measures and the validation method that was followed and, viii) the response feature is either differentiation of subjects to normal and HF or differentiation of subjects to different HF subtypes or estimation of the severity of HF or estimation of the destabilization or estimation of re-admission or estimation of mortality. There is no restriction regarding the time frame of the prediction. Furthermore, studies addressing both aspects of HF management (*e.g.* detection and severity estimation of HF) were also

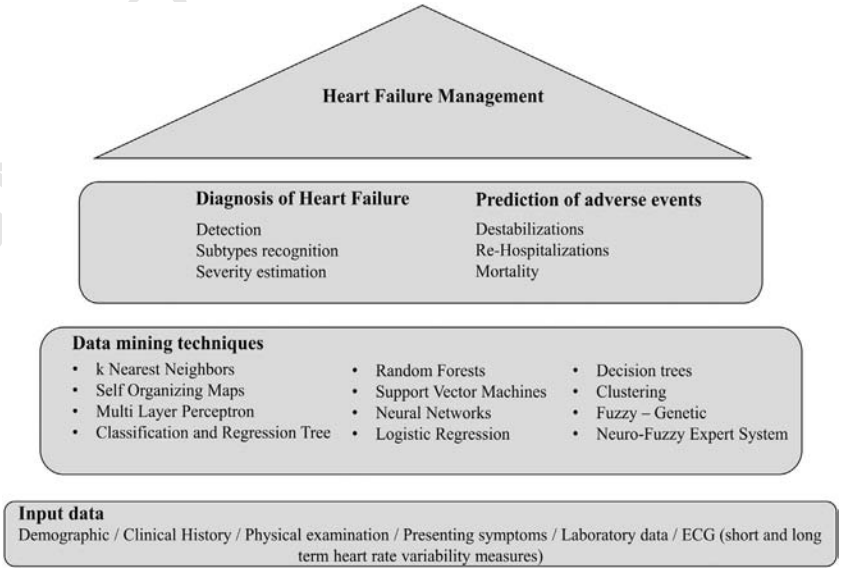

Fig. 1. Overview of studies on heart failure management.