System for supporting clinical professionals dealing with chronic disease patients

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Abstract. To deal with the large amount of data produced by telemonitoring of patients with chronic diseases, a decision support system (DSS) was developed. The DSS uses sensor data and the data from a patient's electronic health record as the input. It assesses the risk to the patient's health by exploiting the existing medical knowledge. The risk assessment can show the contribution of the individual monitored parameters to the risk, and can be tailored by the doctor to each patient.

Keywords: Decision support system, Expert knowledge, Risk assessment, Chronic diseases

1 Introduction

The amount of data produced by telemonitoring solutions can be overwhelming, so using it for clinical decision-making is difficult. When telemonitoring data is combined with data obtained by traditional means, the problem becomes even larger. In a European project aiming to integrate telemonitoring into the clinical workflow, we tackle this problem by a decision support system.

In the CHIRON project [1], a patient is equipped with wearable ECG, temperature, sweating and activity sensors. The data produced by the sensors is sent to a user's mobile phone where the data is transformed into several parameters. These are then sent to a central server and are combined with the data from the patient's health record in order to be examined by the doctor. The DSS system uses all the data to automatically assess the risk to the patient's health and helps the doctor understand its assessment. It also offers personalization, allowing the doctor to tailor the risk assessment to each patient. For the most part, the DSS can support the management of any chronic disease. Our test case, however, is the congestive heart failure (CHF), and the choice of sensors and the expert knowledge contained in the DSS reflects that.

The architecture of the DSS is as follows: (i) the system input are sensor values from monitored parameters and electronic health records; (ii) in the risk assessment module, which is designed as an expert system, the input values are

transformed to a risk; (iii) the risk value can be used to trigger alerts (e.g., if the risk is too high, the doctor will receive a notification); and (iv) the configuration module can be used to tailor the risk assessment to each patient.

2 Related work

Pocock et al. [2] conducted an analysis that included individual data on 39,372 patients with heart failure. Using multivariable piece-wise Poisson regression methods with step-wise variable selection, a final model included 13 highly significant independent predictors of mortality. Conversion from real parameter values to an easy-to-use integer-based model was done by translating mortality rate into a risk score. The score facilitates the identification of low-risk patients, e.g. score < 17 has an expected 90% 3-year survival, and very high-risk patients, e.g. score ≥ 33 has an expected 30% 3-year survival.

Yan et al. [3] presented a medical decision support system based on the Multilayer perceptron neural network architecture for heart disease diagnosis. They have identified the 40 input variables critical to the diagnosis of the heart diseases. A heart diseases database consisted of 352 cases in this study. Three assessment methods, cross validation, holdout and bootstrapping, were applied to assess the generalization of the system. The results showed that the proposed system can achieve very high diagnosis accuracy ($> 90\%$) and comparably small intervals ($< 5\%$), proving its usefulness in support of clinic diagnosis decision of heart diseases.

In the Chiron project an observational study is currently undergoing in Italy and United Kingdom and consists of 30 patients diagnosed with CHF. First difference with two above mentioned studies is that Chiron observational study targets only CHF patients. Second difference is that in this study more than 60 parameters will be collected and evaluated at the end of the study, which has not been done at such scale before. Hopefully this will improve above results.

3 Expert system for risk assessment

The expert system is a set of knowledge-based models for risk assessment, which attempts to exploit the large amount of existing medical knowledge. Its construction and the result is first presented in general terms suitable for a range of diseases, and then specifically for the CHF and the CHIRON project. The CHF/CHIRON models will be updated with the knowledge generated during the CHIRON observational study. This is of particular importance for the parameters that have not been studied at such a scale before (for example continuous monitoring of several ECG parameters).

3.1 Selection of parameters

Parameter selection was made by a three-stage process. First a literature search was performed and a list of parameters was made available. There were more

than 60 variables selected including clinical, angiographic, biological, pharmacological, local ambient and electrocardiographic items which were considered in previous published investigations in CHF patients and were deemed relevant as potential short- or long-term risk factors for complications including hospitalization or mortality. A medical expert (reference) initially subdivided all selected variables into baseline Information (for which an agreement exist on the capability of potential long-term predicting value) versus short- or very short-term potential predictors (on which CHIRON will specifically focus in this Expert system construction). The baseline parameters included: demographic and clinical variables including socio-economic status and activity parameters, results obtained from blood sample and electrocardiographic tests, comorbidities and ongoing drug regimen or devices. Short-term parameters included oxygen saturation, skin and ambient humidity and temperature, parameters to monitor movements, electrocardiogram and potassium blood content from high fidelity electrocardiogram. The same medical expert ranked all these variables by giving a synthetic probabilistic value to each potential risk factor, allocating a reliability code: L = low, M = average, H = high.

The second step was to perform a survey among European Opinion Leaders (OL) in cardiology as a means to obtain a comparative evaluation of the value of the selected variables. A questionnaire was constructed and the OL were asked to reply to the questions by giving a semiparametric coded series of responses to specific questions, made such to be adapted to the risk under evaluation. The questionnaire consisted of two parts. The first aimed at questioning on clinical elements not definitely proved in published studies (25 questions), whereas the second part addressed elements to be considered as more definitely proved (41 questions). The semiparametric responses might be given taking the probabilistic nature of the question into account. There were 32 OL respondents from Italy, Slovenia, Spain and UK.

4 Risk modeling

We decided to use three risk models, since the risk within different time horizons is affected by different parameters:

- Long-term, which models static risk, and is mostly affected by the parameters that change rarely
- Medium-term, which primarily models risk with causes in the last three months, and is mostly affected by the parameters that change with a medium frequency
- Short-term, which primarily models risk with causes in the last three days, and is mostly affected by the parameters that change frequently

These three models are tailored to the CHF and the CHIRON observational study, although they are suitable for other settings as well. In principle one could use any number of models and any time horizons, as long as matching parameters are available. In order to include each parameter in one or more models, and assign the risk value to it, the following information is required:

- The importance, which was obtained through the surveys: low, medium, high
- The frequency at which the parameter changes, which roughly corresponds to the frequency at which it is measured: low fairly static (e.g., age); medium measured during regular visits to the doctor (e.g., blood pressure); high measured continuously using sensors (e.g., heart rate)
- The minimum and maximum expected value of the parameter p: p_{min}, p_{max}
- The relation between the parameter value and the risk: (+) - the higher the value, the higher the risk; (-) - the higher the value, the lower the risk; (U) - high risk at low and high values, low risk in between (for such parameters the lowest-risk value p_{mid} is needed in addition to the minimum and maximum expected value)
- The low threshold, which separates the parameter values corresponding to low risk (green) from those corresponding to medium risk (yellow), and the high threshold, which separates the parameter values corresponding to medium risk from those corresponding to high risk (red)

4.1 Parameter value to risk transformation

The value of each parameter is transformed into a risk value, which lies in the [0, 1] interval. If a given parameter p is numeric and has the (+) or (-) relation, this is straightforward:

$$risk(p) = (p - p_{min})/(p_{max} - p_{min}); \qquad p\text{'s relation is } (+)$$

$$risk(p) = 1 - (p - p_{min})/(p_{max} - p_{min}); \qquad p\text{'s relation is } (-)$$

Computing the thresholds on the risk scale is also straightforward. If p_l and p_h are the low and high threshold in terms of parameter values, then the thresholds in terms of risk values are $risk(p_l)$ and $risk(p_h)$, computed using the equations above. If the parameter p has the (U) relation, computing the risk is somewhat more complicated. Each such parameter has two low and two high thresholds in terms of parameter values, one on the left and one on the right side of the U-shaped curve: $p_l^{(left)}$, $p_h^{(left)}$, $p_l^{(right)}$ and $p_h^{(right)}$. Since we wish to have only one low and one high threshold in terms of risk, we assume that $risk(p_l^{(left)}) = risk(p_l^{(right)}) = 1/3$, and $risk(p_h^{(left)}) = risk(p_h^{(right)}) = 2/3$, and transform as

follows:

$$risk(p) = \tfrac{1}{3} \cdot (p - p_{mid})/(p_l^{(right)} - p_{mid}); \qquad p_{mid} < p \leq p_l^{(right)}$$

$$risk(p) = \tfrac{1}{3} + \tfrac{1}{3} \cdot (p - p_l^{(right)})/(p_h^{(right)} - p_l^{(right)}); \qquad p_l^{(right)} < p \leq p_h^{(right)}$$

$$risk(p) = \tfrac{2}{3} + \tfrac{1}{3} \cdot (p - p_h^{(right)})/(p_{max} - p_h^{(right)}); \qquad p_h^{(right)} < p$$

$$risk(p) = \tfrac{1}{3} \cdot (p_{mid} - p)/(p_{mid} - p_l^{(left)}); \qquad p_l^{(left)} < p \leq p_{mid}$$

$$risk(p) = \tfrac{1}{3} + \tfrac{1}{3} \cdot (p_l^{(left)} - p)/(p_l^{(left)} - p_h^{(left)}); \qquad p_h^{(left)} < p \leq p_l^{(left)}$$

$$risk(p) = \tfrac{2}{3} + \tfrac{1}{3} \cdot (p_h^{(left)} - p)/(p_h^{(left)} - p_{min}); \qquad p \leq p_h^{(left)}$$

The transformation is illustrated in Figure 1. If the risk is never high on one side and thus $p_h^{(left)}$ or $p_h^{(right)}$ is not given, we assume that $p_h^{(left)} = p_{min}$ or $p_h^{(right)} = p_{max}$.

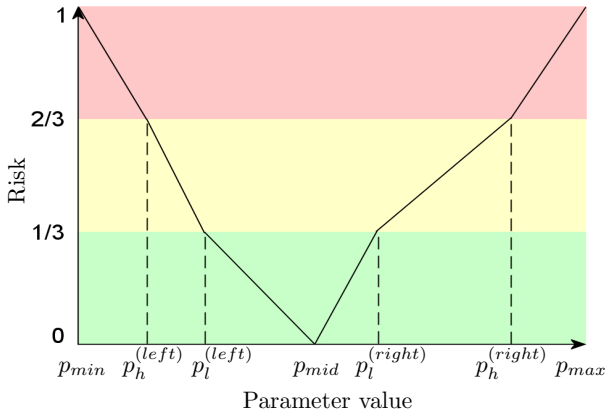

Fig. 1. The graph of the risk with respect to the parameter value.

The parameters with only two values (0 and 1, e.g., gender) also require special treatment. For these, one value is always assigned low risk (0), and the other may be assigned medium risk (1/2) or high risk (1). The thresholds in terms of risk values are $risk(p_l) = 1/3$ and $risk(p_h) = 2/3$.

All above formulas are experimental as there is currently not enough data to evaluate them, but they are still derived from the current medical knowledge about congestive heart failure and use principals for designing clinical decision support system [4]. At the end of the observational study the parameter thresholds and risk thresholds will be evaluated and the model will be updated accordingly.

4.2 Construction of the models

We propose simple additive models, which means that the risk values are added up to the overall risk. In risk modeling, various exponential models are more common [5], but their parameters are typically computed from data. Since we are using expert knowledge, and the risk values are only rough estimates, we believe the transparency and simplicity of additive models is preferable.

Let N be the number of parameters, and let each parameter be associated with a weight. The formula for a model is then as follows:

$$risk = \frac{1}{\sum_{i=1}^{N} w(p_i)} \cdot \sum_{i=1}^{N} w(p_i) \cdot risk(p_i)$$

The weight of a parameter depends on its importance (w_I) and model-specific properties (w_M):

$$w(p_i) = w_I(p_i) \cdot w_M(p_i)$$

The importance weights were set to 1/3 for low-importance parameters, 1 for medium-importance parameters and 3/2 for high-importance parameters by the reference expert. The model-specific weights are 1 by default; the exceptions are specified in the following three paragraphs.

Long term. This model uses parameter values upon enrollment, which is a common point for all the patients.
- Low-frequency parameters: all are included with the enrollment values.
- Medium-frequency parameters: all are included with the enrollment values.
- High-frequency parameters: selected are included with the average values over the first month after the enrollment. The averaging is needed because the impact of the exact time of measurement could otherwise be too large.

Medium term. This model uses recent parameter values, and deemphasizes the low-frequency parameters in order to give a greater weight to the more frequently-changing ones.
- Low-frequency parameters: all are included with the last known values and the model-specific weight of 1/3.
- Medium-frequency parameters: all are included with the averages over the last three months. For those with numeric values, the slope of a linear approximation over the last three months is also included.
- High-frequency parameters: selected are included with the average values over the last month.

Short term This model also uses recent parameter values and deemphasizes both the low-and the medium-frequency parameters.
- Low-frequency parameters: all are included with last known values and the model-specific weight of 1/9.
- Medium-frequency parameters: all are included with the averages and in some cases slopes over the last three months, and the model-specific weight of 1/3.

– High-frequency parameters: all are included with the averages and slopes over the last three days. For those measured continuously, the standard deviations are also included.

As mentioned before, these three models are tailored to the CHF and the CHIRON observational study. For other purposes, one could modify the selection of the attributes (e.g., include all the high-frequency attributes in the medium-term model, or exclude some of the low-frequency attributes from the short-term model) and the model-specific weights ($1/3$ and $1/9$).

5 Prototype

The prototype of the expert system is implemented in Java as a stand-alone PC application, and shown in Figure 2. The upper left window allows the selection of the patient, model and parameter, the upper middle window shows the short-medium- and long-term risk, and the upper right window shows the selected risk over time. The lower two windows show the selected parameters over time.

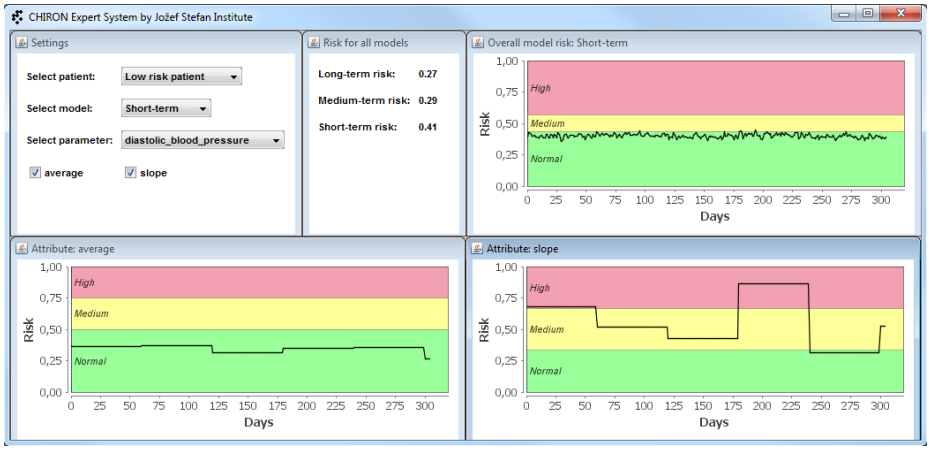

Fig. 2. Prototype of the expert system.

The expert system prototype is fully configurable. Essentially, all parameters are stored in an XML file that can be changed at any time. Parameters (and their averages, slopes and standard deviations) can be removed or added to any of the three models. When the prototype is started, the XML file is loaded and the system configured. Only adding a new type of parameter would require modifying the prototype itself.

To test the prototype, the reference expert defined static parameter values for three imaginary patients: one with low, one with medium and one with high risk. Since data at multiple time points are needed for the models, a year's worth of data was generated by adding normally distributed noise to the static values.

In order to improve user experience and provide data about patients' risks to the medical experts during the observational study, Advanced Medical Expert Support Tool (A-MEST) [6] was developed. It is a step towards achieving the patient-centric approach by incorporating the health information into the Electronic Health Record (EHR). Risk values produced by presented decision support system are also recorded to EHR and therefore made available for use by A-MEST. It also has a Graphical User Interface which shows the visualization of the health status of the patients providing meaningful information to the cardiologists. Furthermore, alert system is incorporated into A-MEST to facilitate the medical experts by prioritizing patients with higher risks and alert them when a certain patient has a critical risk value. Due to the use of EHR by A-MEST, it could also be used by any Hospital Information System using European standard ISO/EN 13606.

Conclusion

In this paper we presented a DSS for the management of chronic diseases using telemonitoring. Since the DSS was designed with CHF in mind, the sensors used for telemonitoring (ECG, temperature, sweating and activity) are suitable for CHF patients, and the expert knowledge contained in the system also pertains to CHF. The DSS is otherwise general.

The main module of the DSS deals with risk assessment. It is designed as an expert system which provides the risk assessment from sensor data values and electronic health record. The risk assessment module is supported by a configuration module which can be used to meet the requirements of a specific patient. The correctness and the accuracy of the risk assessment module proposed in this paper will be evaluated at the end of the observational study. The thresholds will be updated accordingly and the system will hopefully be ready for deployment in real-life environment.

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