The Method for Describing Changes in the Perception of Stenosis in Blood Vessels Caused by an Additional Drug

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Abstract. The decision making depends on the perception of the world and the proper identification of objects. The perception can be modified by various factors, such as drugs or diet. The purpose of this research is to study how the disturbing factors can influence the perception. The idea was to introduce the description of the rules of these changes. We propose a method for evaluating the effect of additional therapy in patients with coronary heart disease based on the tree of the impact. The leaves of the tree provide cross-decision rules of perception changes which could be suggested as a solution to the problem of predicting changes in perception. The problems considered in this paper are associated with the design of classifiers which allow the perception of the object in the context of information related to the decision attribute.

Key words: classification, perception interference, cross-decision rules, tree of impact

1 Introduction

One of the aspects of the data mining is learning about the surrounding world by assigning meanings to received impressions, i.e. information provided by sensors. The way in which we perceive and interpret the real world significantly determines the identification of the objects and their classification, which affects the decision-making. The classifiers, based on the available features (conditional attributes), describe the value of the decision attribute and may be treated as approximate descriptions of concepts (decision classes)[3],[10]. Therefore, the classifiers allow the perception of the tested object in the context of information related to the value of the decision attribute.

As a perception we understand a cognitive process that involves assigning the meanings to the received information [12]. We consider the perception associated with medical problems, namely the problem of the coronary artery stenosis in patients with stable coronary heart disease (CHD, see Section 2).

We study how the disturbing factors can influence the perception of stenoses in blood vessels. We show that some disturbing factors can be managed using data mining algorithms based on well-known statistics combined with cross-decision rules. Our approach is illustrated using data representing medical treatment of the patients with stable CHD. The dataset, collected by the Second Department of Internal Medicine, Collegium Medicum, Jagiellonian University, Krakow, Poland, relates to 70 patients subjected to elective coronary angiography with possible percutaneous angioplasty. The decision problem, however, requires approximation of especially designed complex decision attribute, corresponding to the analysis of perception interference.

1.1 Perception and Classification

There are a number of factors that can modify the behavior of the tested object and change the way it is perceived, although generally the state of the object is not changed. The state is stable in the sense that its affiliation to the concept does not change. Sometimes we have no influence on the disturbing factor, for example, in the case of the environment or the weather. But sometimes it may be intentionally introduced or even managed, if we know how to do it (eg. drugs, type of therapy, diet).

If we assume that the perception is achieved by the classifier, this means that if a disturbing factor occurs, the classifier must be redesigned. In this situation, one can build a classifier using additional conditional attribute, representing the information about the occurrence of the disturbing factor. As a result, the classifier can be effective both when the agent is present or when it is not. It is also possible to construct two classifiers: the first one when there is no disturbing factor and the other one in the presence of it.

Another issue is, however, the question how does the disturbing factor change the perception of test objects using the classifier and whether the change affects all test subjects in the same way? If we could get to know the rules of these changes, this factor could be used to control the object perception and indirectly its behavior.

It is known from practical observations, that disturbing factors may often cause various changes in the perception of the observed object. For example, consider the situation when perception refers to the condition of the patient described by four states: A, B, C, D, associated with the severity of disease which may be life-threatening. The condition A indicates the lowest severity of the disease, B - slightly more advanced disease, C - yet slightly more and D - the most advanced disease. Suppose also that perception is based on the attributes describing the results of symptomatic tests, which describe the actual level of critical illness (eg. ECG signal). Let the administration of the Z drug be a factor interfering with perception. Let K1 and K2 are classifiers that have been constructed based on the training data to predict the A, B, C or D state, without the interfering factor and with its presence, respectively. If the K1 classifier assignes the particular patient P1 to state B, it turns out that the K2 classifier may classify P1 to each state: A, B, C or D.

This is so, because the distortion of perception causes the misrepresentation of patient's image, which sometimes is perceived as if he/she had more advanced disease than it really is, and sometimes as if he/she had less advanced disease. At the same time, the misstated picture does not concern the real severity of the disease, but the current degree of threat to life, which this disease causes. Thus, if one could predict what kind of change in the disease perception the Z drug will trigger for a given patient, it could be used to support the acute treatment (eg. on the way to the hospital, awaiting surgery and so on).

Note, however, that the standard method of a classifier construction is not useful for predicting changes in the perception caused by a disturbing factor, because there is no possibility to construct a decision attribute that represents the changes of the perception of the disease for a given patient. This would require the experiments involving patients who had to be treated both without and with the use of the additional drug. Such a situation appears to be technically difficult and unethical, because it can generate a risk of less effective treatment (treatment extended in time).

The former work on this issue concerned the influence of two methods of surgical treatment of the throat and larynx cancers on the survival of patients ([2]). This work led to the discovery of a data mining method, which calculates the so-called cross-decision rules in medical data. Each cross-decision rule, for the group of patients described by its predecessor, gives the consequent likelihood of success of the treatment (patient survival) for both studied treatments. However, the method is based on the symbolic data attributes. This limitation comes from the need to count the specific reducts with regard to the complex decision, which in [2] are calculated for symbolic data. However, in many applications there is a need to analyze data with numerical attributes or mixed ones (symbolic and numeric). We therefore need rules whose predecessors can have ranges of values rather than specific attribute values.

Therefore, in this paper we propose a method based on the so-called tree of the impact, which is a binary tree. The impact tree is constructed so that the leaves contain descriptions of patient groups (patterns) whose perception of the disease changes in a similar way after the application of a disturbing factor. In some leaves a large change in perception is observed, while in some others the small one. Some leaves are characterized by a beneficial change, while certain other by an adverse one. With the patterns assigned to the leaves, the perception changes of the test objects can be predicted. Therefore, each leaf of the tree provides a single cross-decision rule, which in this work will be called a cross-decision rule of perception changes. The rules could be suggested as a solution to the problem of predicting changes in perception. For this purpose, the consequent of the rule would bring the information about the perception both without and with the disturbing factor.

2 Medical Background

Our considerations apply to the patients with stable coronary heart disease. The disease is characterized by reduced blood supply to the heart caused by atherosclerosis. The atherosclerosis is usually present in blood vesells even when their lumens appear normal in angiography. The CHD touches people all over the world and is one od the leading cause of deaths ([7]). Treatment may include medication or invasive revascularization. Treatment is aimed at reducing or eliminating symptoms and reducing the risk of a heart attack. The standard pharmocotherapy includes such classes of medications as: beta blockers, nitrates, calcium channel blockers/calcium antagonists or ACE inhibitors.

Recently a heated discussion on the inflammatory theory underlying the coronary artery disease is conducted ([4],[6]). Inflammatory mediators are involved in the development, progression and destabilization of atherosclerotic plaques ([1]). Some of the strongest pro-inflammatory mediators are leukotrienes. Increased generation of leukotrienes is observed during acute myocardial ischemia, coronary angiography or angioplasty ([17]).

In this context, the studies on the use of anti-inflammatory drugs in CHD were conducted (eg. [13], [16]). In [16] the effect of pharmacological inhibition of leukotriene production on the electrical activity of the heart was assessed using an inhibitor of 5-lipoxygenase (zileuton). It has been shown that pharmacological inhibition of leukotriene biosynthesis in patients with stable CHD subjected to intracoronary interventions causes: reduction of the 24 hours average heart rate, increase in parameters of rhythm variability, and an improvement in the conduction of electrical impulses in the conduction system during intracoronary procedures. No effects on either arrhythmias or ECG patterns of ischemia were noted.

In view of the above results, it would be advantageous to indicate patients with beneficial effects of anti-inflammatory therapy. Commonly used methods based on global statistics such as the average or standard deviation, does not allow for selection of individual patients. Therefore, it is necessary to develop additional methods for evaluating the effect of treatment in individual patients. So we propose the use of a novelty data mining method using the tree measuring the impact of the factor interfering the perception. As a disturbing factor we use here an inflamatory drug - zileuton.

3 Tree Measuring the Impact of the Factor Interfering the Perception

The proposed cross-decision rules of perception changes are the kind of decision rules. A decision rule takes the form of implication, in which the left side consists of presumptions (conditions) expressed as a logical formula, and the right side contains a conclusion (thesis). In classical decision rules, the thesis identifies the decision class, while in the cross-decision rules it is a description of groups of objects from different decision classes.

For the problem of the coronary disease, the descriptors represent the expected value of the number of stenoses for different types of treatment. The Formula 1 presents an exemplary cross-decison rule of perception changes:

$$a = v_1 \wedge b = v_2 \Rightarrow \left| \begin{array}{l} E(S \,\text{after}\, A) = x_1 \\ E(S \,\text{after}\, B) = x_2 \end{array} \right. \tag{1}$$

where $a, b \in A$ (the set of attributtes), E designates expected value, S - the number of significantly narrowed coronary arteries and A, B - therapy with placebo and with the disturbing factor.

For example, let the pattern $a = 1$ and $b > 2$ indicate a stable condition in ECG (without the danger). Then the cross-decision rule of perception changes can be as in Formula 2:

$$a = 1 \wedge b > 2 \Rightarrow \left| \begin{array}{l} E(S \,\text{after}\, P) = 0 \\ E(S \,\text{after}\, Z) = 2 \end{array} \right. \tag{2}$$

where P designates a treatment with placebo and Z - with the disturbing factor (zileuton). Rule 2 means that the treatment causes a misrepresentation of the real state, determined by coronary angiography (number of stenoses). Despite two significantly narrowed coronary arteries, patients receiving zileuton have an ECG indistinguishable from placebo-treated patients without vascular changes.

The cross-decision rules are therefore a way of the knowledge presentation in an intelligible form that facilitates its interpretation. For the case of the CHD, they can be used to decide on the continuation of pharmacotherapy in a designated group of patients.

In order to generate the cross-decision rules of perception changes, we will use the impact tree. It is a binary tree constructed by the greedy algorithm in a top-down recursive divide-and-conquer manner. It takes a subset of data as an input and evaluates all possible splits. The best split is chosen to partition the data into two subsets (divide-and-conquer) and the method is called recursively. The algorithm stops when the stop conditions are met.

3.1 Construction of the Tree of Impact

As a criteria for selecting the best split, we propose a measure based on the distance between the groups. The measure is calulated using probability theory and statistical techniques, such as expected value, well-known from the literature [9],[14, 15].

Suppose that a set of objects includes two groups of subjects. One group was treated with a disturbing factor and the other not (patients received placebo). We are interested in the behavior of a certain characteristic in both groups. Its assessment is carried out according to the following steps:

1. Determination of the probability distributions of chosen feature in both groups, designated as A and B
2. Definition of a variable representing the difference of the feature between the two groups: $X = |A - B|$
3. Denotation of the distribution of X variable
4. Determination of the expected value of X.

The expected value of the difference makes it possible to quantify the variation of the characteristic in both groups. Such a measure used to construct an impact tree, allows the assessment of the degree of influence of disturbing factor on the behavior of objects.

For the concept of CHD, the chosen characteristic may be the number of significantly narrowed coronary arteries which accepts four values: 0, 1, 2 and 3. Then, the distributions of the characteristic in both groups are presented in Tables 1 and 2.

The distribution of X variable (difference of the characteristics between groups) is presented in Table 3, where the probability p_i, for $i = 0, 1, ..3$ is calculated using the

Table 1. Distribution of the chosen characteristic in placebo-treated group

A	**0**	**1**	**2**	**3**
n	n_0	n_1	n_2	n_3
P(A)	a_0	a_1	a_2	a_3

Table 2. Distribution of the chosen characteristic in group subjected to a disturbing factor

B	**0**	**1**	**2**	**3**
m	m_0	m_1	m_2	m_3
P(B)	b_0	b_1	b_2	b_3

fomulas in equations 3-6.

$$p_0 = P(X = 0) = a_0b_0 + a_1b_1 + a_2b_2 + a_3b_3 \quad (3)$$

$$p_1 = P(X = 1) = a_0b_1 + a_1b_0 + a_1b_2 + a_2b_3 + a_2b_1 + a_3b_2 \quad (4)$$

$$p_2 = P(X = 2) = a_0b_2 + a_1b_3 + a_2b_0 + a_3b_1 \quad (5)$$

$$p_3 = P(X = 3) = a_0b_3 + a_3b_0 \quad (6)$$

Table 3. Distribution of X variable

X	**0**	**1**	**2**	**3**
P(X)	p_0	p_1	p_2	p_3

The expected value of X is calculated afterwards according to Formula 7.

$$E(X) = 0 * p_0 + 1 * p_1 + 2 * p_2 + 3 * p_3 \quad (7)$$

The stop condition of a tree construction is satisfied when the expected value of X variable exceeds a certain preset threshold th. In addition, the divisions can be completed also in a situation where the number of objects in a given node falls below a certain level. The value of th was set to 1.75 for the impact tree in the figure 1.

The idea is to separate the groups of patients, with a large change in perception from those with little change. So the quality of the cut is defined by the Formula 8:

$$Q = max|E(X_{left}) - E(X_{right})| \quad (8)$$

The construction of the impact tree proceeds according to the algorithm 1.

In a particular node of the impact tree, we determine the effect of a disturbing factor on the basis of the relationship between the expected number of stenoses in the untreated group and that value in treated one. The expected impact of the disruption is calculated by the Formula 9:

Algorithm 1: Construction of impact tree

Step 1 Sort the values of the numerical attribute a
Step 2 Browsing the values of a attribute from the smallest to the largest
for each appearing cut c designate
Euclidean distance between the expected values of X feature
Step 3 Select division among the possible divisions,
such that $|E(X_{left}) - E(X_{right})| = max$
Step 4 Split the table $\mathbf{DT}$ into two subtables
$\mathbf{DT}(T_p)$ i $\mathbf{DT}(\neg T_p)$ such that
$\mathbf{DT}(T_p)$ includes objects matching the pattern T_p, and
$\mathbf{DT}(\neg T_p)$ includes objects matching the pattern $\neg T_p$.
Step 5 **IF** the tables $\mathbf{DT}(T_p)$ and $\mathbf{DT}(\neg T_p)$ meet the stop conditions,
then terminate tree construction
else repeat 1-4 for all tables which do not meet the stop condition

$$\delta = E(B) - E(A) \tag{9}$$

The factor interfering the perception may be deemed as beneficial, if the value of δ is greater than or equal to some assumed value x. When the δ value falls below a certain value y, than the factor can be regarded as an adversely affecting agent. In the case of CHD, we set the value of x on 1.5, and y on -1.5.

Due to the necessity of sorting attributes values done in time $O(n \cdot log\ n)$, the computational complexity of the algoritm 1 is of the order $O(n \cdot m \cdot log\ n)$.

4 Experiments and Results

The experiments have been conducted on dataset obtained from the Second Department of Internal Medicine, Collegium Medicum, Jagiellonian University, Krakow, Poland. The baseline and angiographic characteristics of the studied subjects are given in Tables 4 and 5. No significant differences with respect to age, gender or the angiographic characteristics were found between the study groups.

Table 4. Baseline characteristicts of the studied groups

	Placebo(n=33)	**Zileuton(n=37)**
Age average	59.4	61.6
Female/Male	22(66.7%)/11(33.3%)	20(54.1%)/17(45.9%)

Using the proposed methodology we achieved the tree of impact as shown in Fig. 1. The tree contains six leaves. An example of the beneficial effect of the additional therapy (zileuton) in CHD represents the rule in one of the leaves shown in Formula

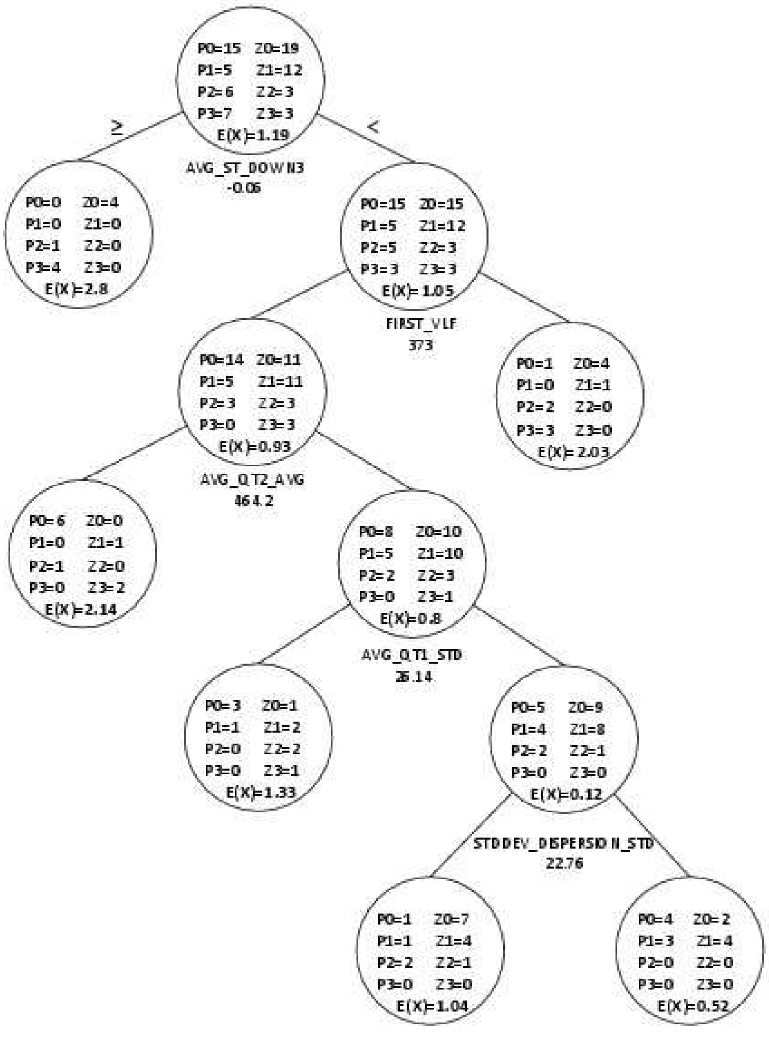

Fig. 1. An example of the impact tree for CHD

10. The parameter AVG_ST_DOWN3 signifies a daily average of the maximum ST segment depression in particular hours $[mV]$, $FIRST\_VLF$ - heart rate variability (HRV) power spectrum $[ms^2]$ in the range of very low frequencies $(0.0033 - 0.04Hz)$ in the first hour of the ECG Holter recording and AVG_QT2_AVG - a daily average of the QT interval duration average in particular hours $[ms]$. The pattern based on Holter ECG parameters is common to untreated patients without coronary stenoses and the patients with significant stenoses treated with zileuton. In terms of the ECG features, they are indistinguishable. Therefore, additional treatment modifies the ECG, such as found in untreated patients without stenosis.

Table 5. Angiographic characteristics of the study groups

	Placebo(n=33)	**Zileuton(n=37)**
0-vessel coronary disease	15(45.5%)	19(51.4%)
1-vessel coronary disease	5(15.2%)	12(32.4%)
2-vessel coronary disease	6(18.2%)	3(8.1%)
3-vessel coronary disease	7(21.2%)	3(8.1%)

$$\begin{array}{r} AVG\_ST\_DOWN3 < -0.06 \wedge FIRST\_VLF \geq 373 \\ \wedge AVG\_QT2\_AVG \geq 464.2 \end{array} \Rightarrow \left| \begin{array}{l} E(S \text{ after } P) = 0.29 \\ E(S \text{ after } Z) = 2.33 \end{array} \right. \quad (10)$$

The opposite case represents, for example, the cross-decision rule given by the Formula 11. The patients with such parameters do not benefit from the additional treatment. Despite the additional treatment, their ECG is the same as in untreated patients with significantly narrowed vessels.

$$AVG\_ST\_DOWN3 < -0.06 \wedge FIRST\_VLF < 373 \Rightarrow \left| \begin{array}{l} E(S \text{ after } P) = 2.17 \\ E(S \text{ after } Z) = 0.2 \end{array} \right. \quad (11)$$

For patients who match the exemplary pattern from the rule presented in Formula 12, using our method, we have no basis for determining whether the anti-inflammatory treatment is beneficial. In this rule, AVG_QT1_STD signifies a daily average of the QT interval standard deviation in particular hours $[ms]$.

$$\begin{array}{r} AVG\_ST\_DOWN3 < -0.06 \wedge FIRST\_VLF \geq 373 \\ \wedge AVG\_QT2\_AVG < 464.2 \wedge AVG\_QT1\_STD \geq 26.1 \end{array} \Rightarrow \left| \begin{array}{l} E(S \text{ after } P) = 0.25 \\ E(S \text{ after } Z) = 1.5 \end{array} \right. \quad (12)$$

5 Conclusions

We discussed the method for describing the effect of a disturbing factor on perception. We considered the influence of anti-inflammatory therapy on perception of narrowing in the blood vessels modeled by the tree of impact. The presented solution may be used in the case of CHD for maintaining momentary stability in the ambulance or in the preoperative period after myocardial infarction.

Our method chooses ECG parameters which are of great clinical importance, such as ST-segment depression associated with myocardial ischemia, very low frequency (VLF) oscillations in the power spectra of HRV or duration and dispersion of QT interval.

Interestingly, the method selects the parameters of ST-segment, on which anti-inflammatory treatment had no effect according to previous studies [13],[16]. The reason may lie in the use of global statistics, which do not distinguish between individual patients.

In the literature, HRV turned out to be a predictive factor of a cardiac death related to myocardial infarction and diabetic angiopathy ([5],[8]). Suppressed HRV, especially within its high frequency component, was found predictive for myocardial infarction or unstable coronary artery disease. While the prolongation of QT interval can predispose to a potentially fatal ventricular arrhythmia [11]. The factor interfering perception could be administered continuously in the case of proven efficacy for specific cases described by the proposed rules.

The novelty of our method is the use of well-known statistics as an innovative measure of a cut quality and the application of the cross-decison rules of perception changes to represent different behaviours of groups of patients.

However, this method is not free from disadvantages. One of them is the need to match a particular type of data, that is diversified within the concept (e.g. different number of stenoses). Another threat is a manual adjustment of the threshold values, which is always a risk of a misapplication. The weak point of the experiment is small data set.

In future we are going to continue the experiments concerning the considered medical problem, in purpose of extending the results of this paper. We also intent to strengthen the reliability of the method for its clinical use. We plan to develop a general approach to describing the influence of a disturbing factor on the perception.

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