Identification of factors related to complications in myocardial revascularization surgery: an approach with multi-target association rules networks

Identificação de fatores relacionados a complicações em cirurgia de revascularização do miocárdio: uma abordagem com redes de regras de associação multialvo

Identificación de factores relacionados con las complicaciones en la cirugía de injerto de derivación aortocoronaria: un enfoque con redes de reglas de asociación multiobjetivo

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Abstract
Myocardial revascularization surgery is one of the recommended approaches for the treatment of chronic coronary disease. Several complications related to mortality, sequelae, length of stay, and hospital costs are also associated with this procedure. Death rates and complications depend on the characteristics of each patient. Knowing the factors related to hospital mortality and complications is paramount to improving outcomes. Association Rules Mining may support the discovery of those factors. In this work we propose a new approach, called Multi-target Association Rules Network (MTARN), to analyze association rules based on networks with a simultaneous focus on two parameters. The use of association rules networks aids the analysis of a high number of association rules and the multi-target strategy allows a complete exploration, explaining which factors directly influence the analyzed set. We evaluated our approach in conjunction with domain experts and compared it to two other approaches: Decision Trees and Filtered-ARNs, a single target approach based on networks for pattern visualization. The results indicates that MTARNs optimize the discovery of knowledge directly linked to complication and death factors in patients undergoing coronary artery bypass grafting. These parameters may be used in the construction of an intelligent monitoring system to aid myocardial revascularization patients.
Keywords: Association rules; Association rules networks; Coronary; Coronary artery bypass surgery; Data mining; Multi-target.

Resumo
A cirurgia de revascularização miocárdica é uma das abordagens recomendadas para o tratamento da doença coronariana crônica. Várias complicações relacionadas à mortalidade, sequelas, tempo de internação e custos hospitalares também estão associadas a esse procedimento. As taxas de mortalidade e complicações dependem das características de cada paciente. Conhecer os fatores relacionados à mortalidade e complicações hospitalares é fundamental para melhorar os resultados. A mineração de regras de associação pode ajudar na descoberta desses fatores. Neste trabalho propomos uma nova abordagem, chamada Multi-target Association Rules Network (MTARN), para analisar regras de associação baseadas em redes com foco simultâneo em dois parâmetros. O uso de redes de regras de associação auxilia a análise de um grande número de regras de associação e a estratégia multialvo permite uma exploração completa, explicando quais fatores influenciam diretamente o conjunto analisado. Avaliamos nossa

abordagem em conjunto com especialistas do domínio e a comparamos com duas outras abordagens: Árvores de Decisão e ARNs Filtrados, uma abordagem de destino único baseada em redes para visualização de padrões. Os resultados indicam que os MTARNs otimizam a descoberta de conhecimentos diretamente ligados a fatores de complicação e óbito em pacientes submetidos à cirurgia de revascularização do miocárdio. Esses parâmetros podem ser utilizados na construção de um sistema de monitoramento inteligente para auxiliar pacientes em revascularização miocárdica.
Palavras-chave: Regras de associação; Redes de regras de associação; Coronária; Cirurgia de revascularização miocárdica; Mineração de dados; Multialvo.

Resumen
La cirugía de revascularización miocárdica es uno de los abordajes recomendados para el tratamiento de la enfermedad coronaria crónica. Varias complicaciones relacionadas con la mortalidad, las secuelas, la estancia hospitalaria y los costos hospitalarios también se asocian con este procedimiento. Las tasas de mortalidad y complicaciones dependen de las características de cada paciente. Conocer los factores relacionados con la mortalidad hospitalaria y las complicaciones es fundamental para mejorar los resultados. La minería de reglas de asociación puede respaldar el descubrimiento de esos factores. En este trabajo proponemos un nuevo enfoque, llamado Multi-target Association Rules Network (MTARN), para analizar las reglas de asociación basadas en redes con un enfoque simultáneo en dos parámetros. El uso de redes de reglas de asociación ayuda al análisis de un gran número de reglas de asociación y la estrategia multiobjetivo permite una exploración completa, explicando qué factores influyen directamente en el conjunto analizado. Evaluamos nuestro enfoque junto con expertos en el dominio y lo comparamos con otros dos enfoques: árboles de decisión y ARN filtrados, un enfoque de objetivo único basado en redes para la visualización de patrones. Los resultados indican que los MTARN optimizan el descubrimiento de conocimiento directamente relacionado con los factores de complicación y muerte en pacientes sometidos a un injerto de derivación de la arteria coronaria. Estos parámetros pueden utilizarse en la construcción de un sistema de monitorización inteligente para ayudar a los pacientes con revascularización miocárdica.
Palabras clave: Reglas de asociación; Redes de reglas de asociación; Coronario; Cirugía de bypass de la arteria coronaria; Procesamiento de datos; Multiobjetivo.

1. Introduction

Patients undergoing myocardial revascularization surgery are subject to numerous complications in the hospital phase, so the analysis of the clinical evolution of the patients is essential to prevent these complications (Egito et al., 2013). The understanding of the individual’s responses to cardiovascular diseases becomes an essential factor in the clinical reasoning for the planning the care to be performed (Rosan et al., 2022; de Almeida et al., 2013; Shahian et al., 2009).

Approximately one in 10 patients undergoing coronary intervention are readmitted within 30 days, and this period is associated with higher mortality risk in one-year (Shah et al., 2018; Hannan et al., 2011). However, Kansagara et al. (2011) state that health cost is associated with worse long-term prognosis, which adds the need for more studies that address the issue and evidences of the importance of research in knowledge gaps. Therefore, to evaluate predictive factors of complications in patients submitted to coronary artery bypass graft surgery, which lead to the readmission to hospital or in intensive care units and, in many cases, the death of the patient, is fundamental to plan the entire therapeutic cycle.

Studies have evaluated predictors of complication and death in an intensive care unit on patients with heart disease (Mori et al., 2020). The hospital complication is considered an indicator of the quality of the health care since it entails expenses to the health system, and extreme risk to the quality of life of the patients when they do not die (Shah et al., 2018, Ricci et al., 2016). The estimated hospital mortality for this procedure is around 2%, which varies depending on the center where it is performed (D’Agostino et al., 2018).

In recent years there has been an increase in studies of the application of machine learning to discovery knowledge from historical medical data (Peek et al., 2015). A recent study indicates that machine learning models obtain effective results for waiting time prediction in an emergency department (Kuo et al., 2020). Some efforts have also been devoted to automated reasoning and knowledge extraction, through data mining, for predictive purposes of complications in patients with heart problems (Kojuri et al., 2015). Considering myocardial revascularization, the use of artificial intelligence techniques may aid the evaluation of patient and allow a better decision on the treatment (Ribas Ripoll et al., 2016; Mahajan et al., 2017).

Data mining can be used as a methodology to discover candidate hypotheses or theories in a knowledge domain (Vinaya and Shah, 2016). The starting point of the mining process may come from the observations of events that trigger the researcher to accelerate the conceptual studies and reach a structure in which the underlying process (which is generating the events) can be elucidated. One way to support researchers in observing these patterns is through association rules. Association rules have been applied in several domains, such as the analysis of crime rate, cyber intrusion, beverage production and medical records Lou et al. (2020), Lakshmi and Vadivu (2017).

Association Rules Mining (Agrawal et al., 1994; Agrawal and Srikant., 1994; Agrawal et al., 1996) is used to find interesting patterns in the form of A ⇒ B rules, in which A (antecedent) and B (consequent) can be attributes, items or more generally “data objects”. If it is known in advance that A and B are correlated, the discovery of the A ⇒ B rule only confirms the prior knowledge. On the other hand, if the correlation between A and B was not previously identified, finding the rule A ⇒ B suggests that A and B are candidate pairs to be validated.

When we conduct studies with health-related data, two essential factors must be taken into account: the transparency and interpretability of the results (Mustaqeem et al., 2017; Tai and Chiu, 2009). The lack of these elements is a significant drawback in many health applications, where the explanation of the model’s decision is a requirement for trust (Dosilovic et al., 2018). The format of the association rules allows the interpretation of the patterns, however, the higher the number of elements in A and B, the smaller is the interpretability of the rule (Delgado et al., 2018). Thus, to fully take advantage of the extracted knowledge and optimize the decision-making process, it is necessary to provide an understandable and friendly representation of association rules (Weng, 2016, Lipton, 2016; Valle et al., 2018).

In this article, we present a new association rule-based method for identifying factors related to complications in myocardial revascularization surgery. A timely diagnosis of cardiac complications in patients who underwent coronary surgery is crucial to avoid a life-threatening event. In this context, our new pattern recognition approach may be applied to detect the main parameters related to complications and deaths in individuals from their clinical data. In order to allow a complete exploration, showing the user which factors influence a set of two items (complications and deaths), we propose the Multi-Target Association Rules Network (MTARN). Through the simultaneous exploration of two objective items, MTARN approach presents an explanation of which factors directly influence the analyzed set.

We compared MTARN to two other approaches: Decision Tree and Filtered-ARNs, which is another technique that makes use of networks for pattern visualization, but in a single target approach. The evaluation of extracted patterns was supported by domain experts. The results of this study suggest that it is possible to optimize the discovery of knowledge directly related to the factors of complications and deaths in patients submitted to cardiac surgery for myocardial revascularization.

The main contributions of this work are: (i) the proposal of MTARN, which may support a multi-target analysis in several domains; and (ii) the identification of knowledge directly related to the factors of complications and deaths in patients undergoing cardiac surgery for myocardial revascularization. The results indicate the feasibility of recommending association rule mining practices using multi-target networks for various clinical studies. We may use these parameters to construct an intelligent monitoring system to aid myocardial revascularization patients. Remote monitoring of patients with heart disease is essential to reduce the number of complications and deaths. The identification of functional requirements for telemonitoring systems are relevant. Furthermore, the health systems were well accepted with high adherence and positive patient experience (Yanicelli et al., 2020; Kauw et al., 2019).

This article is divided as follows. Related work is described in Section 2. In Section 3, we present the fundamental concepts about Association Rule Mining using Filtered-Association Rules Networks. In Section 4, we present the Multi-Target

Association Rules Networks. The methodology used in the study of the factors related to complications in myocardial revascularization surgery is detailed in Section 5. Data mining results with the dataset of patients undergoing myocardial revascularization surgeries are presented and evaluated in Section 6. Finally, the conclusions and future work are listed in Section 7.

2. Related Researches

Amato et al. (2004) developed a study of risk factors for complications in patients who underwent coronary artery bypass grafting. The results demonstrated that older female patients with peripheral vasculopathy, ventricular dysfunction, and renal failure had higher operative mortality. Another factor such as the use of grafts with internal thoracic artery was protective.

Research related to the treatment of patients with the aid of artificial intelligence has intensified in recent years (Peek et al., 2015). Mahajan et al. (2017) propose a novel probabilistic symbolic pattern recognition approach to detect congestive heart failure in subjects from their cardiac interbeat intervals. The results from this study suggest that features obtained with the combination of pattern recognition techniques and long-term heart rate variability measures can be used in developing automated heart failure diagnosis tools.

We identify in Hossain et al. (2021) the combination of network analytics and machine learning for predictive risk modelling of cardiovascular disease in patients with type 2 diabetes. The authors extracted some social network-based features from the disease network and some demographic characteristics directly from the dataset. Then, they used risk factors to develop machine learning prediction models to assess the risk of cardiovascular disease in patients with type 2 diabetes. We observe in this study the relevance of the use of network structures in data mining processes to cardiac problems.

In the previous studies mentioned above, machine learning studies were developed to facilitate decision making about patients with cardiac diseases, which is directly related to the death occurrence. However, none of the researchers used the network structure to extract knowledge automatically. All established conclusions were obtained by the use of classifiers that do not make the results explainable. The use of network structures may assist the knowledge extraction process by allowing results to be visualized and the optimization of the descriptive method.

3. Association Rules Mining with the use of Objective Measure Filters

The purpose of data mining techniques is to find models to predict the future or to understand the past (Aggarwal, 2015). The discovery of association rules is a data mining technique, which seeks to identify specific patterns in datasets, allowing, after their interpretation, to acquire specific knowledge about the problem under analysis (Le and Vo, 2016).

Definition 1: Let I = $\{i_1, i_2, ..., i_n\}$ be a set of objects called items that can assume a binary value of 0 or 1 (false or true), which represent the presence or absence of a particular object, respectively. It is also possible to treat quantitative or qualitative variables in order to create ranges of values for subsequent use as binary values. Let T be a set of transactions, where each transaction D corresponds to a set of items such as $D \subset I$. It is also considered that a set of elements A is contained in a transaction D if all items in the set have a “true” value in the transaction. An expression of the form $A \Rightarrow B$ can represent an association rule R, with $A \subset I$, $B \subset I$ and $A \cap B = Ǿ$. A is called the antecedent or lefthand side (LHS) of the rule and B is the consequent or right-hand side (RHS).

The mining of association rules can be divided into the following three main steps (Aggarwal et al., 2002; Agrawal et al., 1994; Nguyen and Nguyen, 2015):

- **Preprocessing**: the data set is prepared for data extraction where the removal of non-interesting items may occur.

- **Extraction of patterns**: measurements are calculated, before constructing frequent item sets and obtaining the association rules.
- **Post-processing**: the rules of interest are identified to decrease the number of rules that need to be explored. The extracted patterns can be simplified, evaluated, viewed, or simply documented for the end-user.

Definition 2: For each rule (LHS ⇒ RHS) extracted from a set of T transactions (propositional model after data transformation), a support value (sup) is calculated (Equation 1) to verify the strength of the association between the LHS and RHS (probability of transaction occurrence LHS ∪ RHS), and a confidence value (conf) (Equation 2) to measure the strength of the logical implication of the rule (conditional probability of RHS given LHS) (Agrawal et al., 1994).

$$\mathrm{sup}(LHS \Rightarrow RHS) = P(LHS \cup RHS) \tag{1}$$

$$\mathrm{conf}(LHS \Rightarrow RHS) = P(RHS|LHS) \tag{2}$$

The support can be described as the probability that any transaction satisfies both the LHS and RHS, whereas the confidence is the probability that a transaction satisfies the RHS since it satisfies the LHS.

According to Agrawal et al. (1994), the problem of extracting all association rules can be broken down into two parts:

- Find all sets of items that have transaction support above an informed threshold, called frequent itemsets.
- Generate Candidate Rules from the frequent itemsets. We should only select rules that have a minimum degree of support and confidence.

Thus, given a set of transactions, the association rules mining problem is to generate all rules that contain support and confidence equal to or higher than the minimum values determined by the user, referenced as minimum support (minsup), and minimum confidence (minconf), respectively.

Measures of interest play an essential role in the extraction and/or selection of interesting association rules. These measures are used to find patterns based on user’s need, since a large number of association rules generated by the mining algorithm may not be useful as a whole. Therefore, there is a need to filter the rules (Prajapati et al., 2017). We used two important measures in this research, Added Value and Gain.

Definition 3 Added Value [-1;1]: the Added Value (AV) measure, described in Equation 3, indicates how much the frequency of consequent increases in the presence of the antecedent, i.e., it measures the gain of RHS in the presence of LHS (Sahar, 2003). If AV > 0, the frequency of RHS increases in the presence of LHS. It is AV < 0, the frequency of RHS decreases in the presence of LHS. If AV = 0, there is a random coincidence, that is, the frequency of LHS does not change the frequency of RHS.

$$AV = P(RHS|LHS) - P(RHS) = \mathrm{conf}(LHS \Rightarrow RHS) - P(RHS) \tag{3}$$

Definition 4 Gain [0;1]: Gain is a measure proposed by Fukuda et al. (1996) (Equation 4) that forms a tradeoff between support and confidence, helping to select the rules according to their frequency, and value of the minimum confidence.

$$Gain = [\mathrm{conf}(LHS \Rightarrow RHS) - \mathrm{minconf}] \,.\, P(LHS) \tag{4}$$

By means of Equation 4, Fukuda et al. (1996) demonstrate that the objective measure Gain works as a normalization of confidence measure. When the value of Gain = 0 the rule confidence equals the minimum confidence (conf(LHS ⇒ RHS) = minconf).

One of the problems related to a large number of rules is its interpretability, and the use of networks for this purpose is very widespread (Lipton, 2016). In general, a network N is represented as N = (V, E), in which V is a set of vertices (or nodes), and E is a set of edges (or links), which connect some pairs of vertices in V. Statistically, we can characterize a graph by derived values, such as the average degree of the nodes and the average length (path) between the nodes. Additional characteristics such as network diameter, number of triangles, number of isomorphisms and clustering coefficient, can also be analyzed (Nettleton, 2013).

Definition 5: Given a network N = (V, E), several links and auto-connections are not allowed depending on the type of network that is being implemented. If N is a directed network, consider the universal set, denoted by U, containing all |V| * (|V| – 1) potential directed links between pair of nodes in V, which |V| denotes the number of elements in V. If N is a network without direction, the universal set U contains |V| * (|V| – 1) links. In this way, the network representation is directly related to the type of data that it represents (Valverde-Rebaza and De Andrade Lopes, 2014).

Combining the use of networks as an aid to the association rules mining and filtering by asymmetric objective measures, as well as the pruning of the rules for optimization of knowledge extraction, Calçada et al. (2018) presented the Filtered-Association Rules Networks (Filtered-ARN). Filtered-ARNs have a structure that allows synthesizing, pruning, and analyzing a set of association rules to construct candidate hypotheses (Calçada et al., 2018). The central idea of Filtered-ARN is that the association rules discovered by a mining algorithm can be filtered, synthesized, pruned, and integrated into the context of specific research objectives. In particular, if we consider a variable of interest, a network can be produced with the variables that are most strongly related to the aim, before obtaining a structure that can be tested using statistical methods. Filtered-ARNs have the following characteristics:

- Rule filtering: Added Value and Gain measures are calculated for all association rules excluding those that do not generate an influence between rule items.
- Pruning in context: Filtered-ARNs are used to prune rules in the context of a specific goal.
- Network structure: Filtered-ARNs provide a method to determine the relationships between relevant variables and the goal by constructing a network. This technique can assist with analyzing the effects of direct and indirect changes in the mining of association rules.
- Generation and evaluation of hypotheses: Filtered-ARN can provide a bridge between the outputs generated by association rule mining and their assessment.

The following three steps are performed to create a Filtered-ARN.

(1) Step A: similar to the first step of all association rules mining processes. Extraction of rules with minimum support and confidence.

(2) Step B: calculate the asymmetric objective measures Added Value and Gain, performing the exclusion of all rules with AV = 0 and gain < mingain.

(3) Step C: choose a frequent item Z, which is represented as the target node in the rule set, and construct a B-graph that flows recursively to Z.

The first stage consists of the Association Rules Mining phase. The only restriction added to this step, if compared to a conventional Association Rule Mining, is that the rules must have unitary sets in the antecedent and consequent (|LHS| = 1 e |RHS| = 1). This restriction has been added to facilitate the Filtered-ARN modeling.

The second step is the filtering of the rules, i.e., the selection of rules that have elements with statistical dependence and definition of the minimum gain of influence (mingain). This step will guide the entire exploration, as it will define the rules of interest that will be used with the target item from which the network will be built.

In the last step, the user must select the item that he wants to understand in the dataset (target item). Then, the construction of the Filtered-ARN is performed. This step is responsible for getting all rules that are directly or indirectly related to the target item and modeling them. The construction of the Filtered-ARN is done recursively. First, the item selected as the target item is modeled on the graph (L = 0). So, all the rules that the LHS item are not on the graph and have the RHS item at level 0 are modeled on the network. The same process is done for all items in level 1, level 2, and so on until there are no more rules to be modeled. Therefore, Filtered-ARN is constructed according to the levels of its vertices.

Definition 6: The level of a given vertex v ⊂ Filtered-ARN, formed by the Filtered-ARN construct, is the number of edges needed to access item Z.

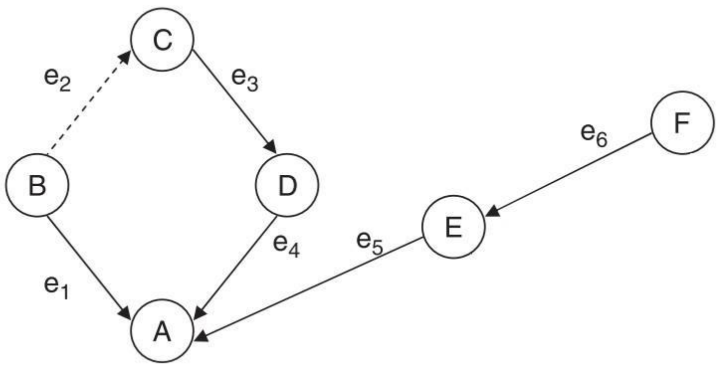
For example, the item Z has zero level (L = 0), since it does not have to go through any edges to reach item Z. Items in the LHS part of rules that have RHS ⊂ Z will have level one (L = 1). They are an edge away from the items in Z.

Definition 7: Given a set of association rules R, containing unit-set rules, and a target item Z, Filtered-ARN is a network that models all rules related to the item in Z, such as:

1. Each edge models a rule r subset R.
2. From any point on the network, it is always possible to reach at least one vertex representing a Z item.
3. Given a vertex v ⊂ Filtered-ARN, such as $v \not\subset Z$. There is no path from any Z item to v.
4. If there is a rule r such as RHS(r) ⊂Z, then the rule r ⊂ Filtered-ARN.

Figure 1 presents an example of a Filtered-ARN where item “A” is selected as the target. All of the rules with “A” as consequent are then selected, i.e., only the rules (B ⇒ A), (D ⇒ A) and (E ⇒ A) in this case. Thus, the items are modeled at ARN level 1. “B”, “D” and “E” are then considered the targets, and the algorithm runs recursively until no more items are left as target at the highest levels. In this case, the rules with “B” as target are modeled, followed by the rules with “D” and then “E,” “C,” and “F”. In this example, no rules have “F” as a consequent. The highlighted hyper-edge “e_2” is one of those eliminated in the pruning process because although it has the “C” item as consequent, the “B” item is already inserted into the Filtered-ARN in the level below, thereby making the use of this rule impossible.

Figure 1 - Example of Filtered-ARN with reverse hyper-edge (e2).



*A Filtered-ARN promotes clear observation of the factors that influence a specific target. In this case, target “A” is directly influenced by items “B”, “D” and “E”. These target-bound elements are called Level 1 items. Source: adapted from (Calçada & Rezende, 2019).

4. Proposed methodology Multi-Target Association Rules Network (MTARN)

In order to allow a complete exploration and taking into account the relationship between a set of target items, in this article, we propose the Multi-Target Association Rules Network (MTARN), which allows the exploration of two target items simultaneously with dependency analysis among the elements of the rules.

In the algorithm proposed for the construction of MTARN, we make use of association rules with consequent of fixed size equal to 2 (|RHS| = 2) and antecedents of sizes 1 or 2 (LHS ≤ 2). We filter the rules using asymmetric objective measures (Added Value and Gain) to construct a graph.

The following three steps are performed to create an MTARN.

The following three steps are performed to create an MTARN.

(1) Step A: similar to the first step of all Association Rules Mining processes, with the restriction of rule formation with consequent formed by 2 items ($|RHS| = 2$) and antecedents formed by 1 or 2 items ($|LHS| \leq 2$).

(2) Step B: calculate the asymmetric objective measures Added Value and Gain, performing the exclusion of all rules with AV = 0 and gain < mingain.

(3) Step C: choose a frequent itemset Z of size equal to 2, which will be represented in the rule set as the target node, and build a targeted network that flows recursively to Z.

Definition 8: Given a set of association rules R, containing rules of itemsets of size equal to 2 in the consequent, and a target item Z, MTARN is a directed network that models all rules related to the item Z (Multi-target), such as:

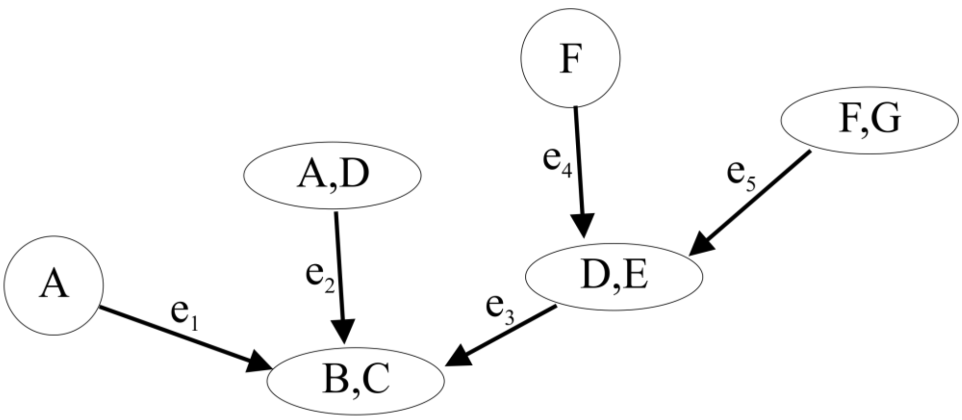
1. Each edge models a rule $r \subset R$.
2. From any point on the network, it is always possible to reach at least one vertex representing a Z item.
3. Given a vertex $v \subset$ MTARN, such as $v \not\subset Z$. There is no path from any Z item to v.
4. If there is a rule r such as $RHS(r) \subset Z$, then the rule $r \subset$ MTARN. Besides, MTARN is constructed according to the levels of its vertices.

Definition 9: The level of a given vertex $v \subset$ MTARN is the number of edges needed to access item Z.

The exclusion of the rules of no statistical dependence (AV = 0) is a fundamental property of the MTARNs since it guarantees that all the items that participate in the network generate some influence in the target item.

Figure 2 presents an example of an MTARN where item "B,C" is selected as the target. All of the rules with "B,C" as consequent are then selected, i.e., only the rules ($A \Rightarrow B,C$), ($A,D \Rightarrow B,C$) and ($D,E \Rightarrow B,C$) in this case. Thus, the items are modeled at MTARN level 1. "A", "A,D" and "D,E" are then the considered the new targets, and the algorithm runs recursively until no more items are left as targets at the highest levels. In this case, the rules with "D,E" as consequent are modeled, being inserted the rules ($F \Rightarrow D,E$) e ($F,G \Rightarrow D,E$). In this example, no rules have "A,D" or "F,G" as consequent. This Multi-target approach consisting of itemsets with $|RHS| = 2$ and $|LHS| \leq 2$ does not allow the formation of rules with the nodes "A" and "F" as a consequent, so these elements will never have antecedents.

Figure 2 - Example of MTARN with "B,C" as target items.

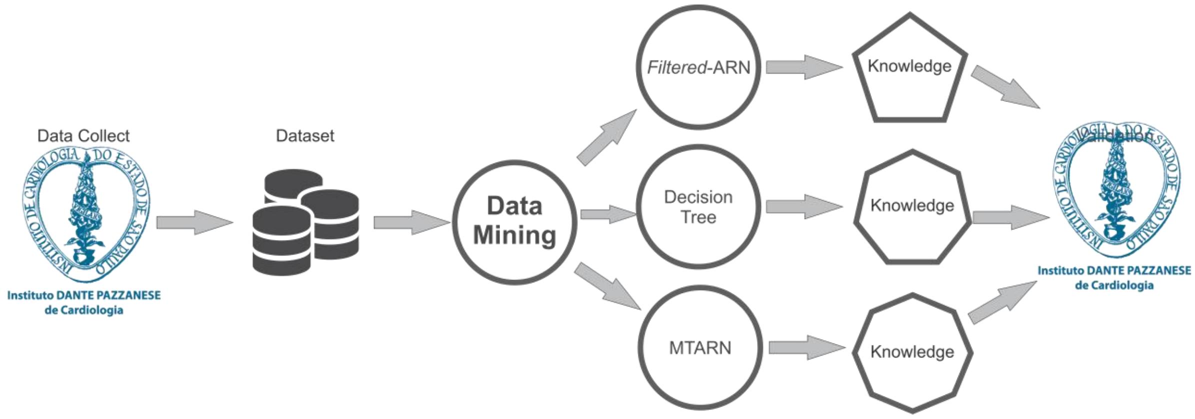


* An MTARN provides the same visualization advantage as a Filtered-ARN, but with the possibility of evaluating two simultaneous target items. The level 1 items of this network ("A", "A,D" and "D,E") are parameters that directly influence the target. Source: authors.

5. Methodology

We performed the entire data mining process comprising the preparation and pre-processing of the data set, before analyzing the extracted association rules, filtering and constructing the MTARNs and Filtered-ARNs to obtain knowledge. The validation of the proposed method was carried out by specialists from Dante Pazzanese Institute of Cardiology[1]. Figure 3 illustrates an overview of this study, including the activities performed.

Figure 3 - Overview of the study.



* The method developed in this research follows the entire process described in the figure, including three techniques. Source: Authors.

5.1 Coronary Dataset

For the construction of the Coronary dataset, we collected the data on myocardial revascularization surgeries performed in patients from the Dante Pazzanese Institute from 1999 to 2015. The information collected was tabulated and divided into three categories: (i) the background of the patient (ap); (ii) the current hemodynamic study; and (iii) the cardiac clinical diagnosis. We also added an attribute referring to the gender of the patient. The "arff" file, available online[2], was built with data related to clinical, preoperative and postoperative aspects.

The study aimed to verify which parameters (or factors) generate complications in patients who underwent coronary revascularization and which of these parameters lead to death. In the Table 1 one can observe the attributes of the dataset. The body surface area attribute (areaCat) of the dataset is calculated by Equation 5 (DuBois and DuBois, 1916).

$$areaCat = \sqrt{\frac{pesoCat * alturaCat}{3600}} \tag{5}$$

The dataset consists of 8.672 instances (patients) and two classes, the first (Complicacoes) represents the occurrence or not of intercurrences, and the second (Obito) represents the death or not of the patient as a result of the performed surgery, in the hospital.

[1] http://www.idpc.org.br/
[2] http://bit.ly/334qu9x

Table 1 - *Coronary* dataset attributes.

ATTRIBUTE	DESCRIPTION
apHAS	Systemic arterial hypertension
apDM	Diabetes mellitus
apAf	Family history
apTabagismo	Smoking habit; interrupted for more than 1 year; or do not smoke
apDPOC	Chronic obstructive pulmonary disease
apCreatinina	Creatinine > 1.5 (Renal Insufficiency)
apColesterol	Cholesterol > 200mg/dl (Dyslipidemia)
apTriglicerides	Triglycerides > 200mg/dl (Dyslipidemia)
apVasculo	Peripheral arterial vasculopathy
apIAMPrevio	Previous acute myocardial infarction
eha ventriculograma	Left ventricular function
dc diag2	Current clinical diagnosis
lesao	Number of affected arteries (Uniarterial; biarterial; or triarterial)
Pontes Mamarias	Revascularization using grafts with mammary artery
QNP	Prior neurological diagnosis
idadeCat	Up to 60 years old (young adult); 60 to 70 years old (intermediate); or 70+ years old (elderly)
pesoCat	Body mass
alturaCat	Height
areaCat	Body surface area
Sexo	Male or female
Complicacoes	Complications during hospitalization
Obito	Patient died

Source: Authors.

The Apriori-TID algorithm was used to extract the association rules. The minimum support value was set to 0.0 in order to initially consider every possible rule. The minimum confidence was set to 0.10 to consider an LHS influence of 10% so that the conditions of the study of complications and deaths in patients were described more broadly.

5.2 Filtered-ARNs construction

Following the methodology of Calçada and Rezende (2019), the Added Value filter removes the rules in which the items do not influence each other. The value assigned to the minimum gain (mingain) was set to 0.01 for the study be as broad as possible since it is data related to patient health. Then, two Filtered-ARNs were constructed, each one considering one of the two classes as the target item ("[Complicacoes]=Sim" (Complications=Yes) and "[Obito]=Sim" (Patient died)). Both complete networks are available online[3].

Filtered-ARNs were plotted using the Gephi software (Bastian et al., 2009). The items of level 1 (L = 1) and level 2 (L = 2) of the network were selected to be evaluated and validated by specialists since they are the elements that have the closest influence of the target items.

5.3 Decision Tree construction

The decision tree method is generally employed for classification and regression tasks in data mining. The decision tree method continually decomposes a data set into smaller subsets according to feature priority until it reaches an appropriate level of disassembly (Nourani & Molajou, 2017).

[3] http://bit.ly/30YB5ke

The final graphical result is a tree with decision nodes and leaf nodes. A decision node comprises non-class attributes and the sub-branches represent all possible values for the attribute. A leaf node represents a specific class considered in a study.

In this study, we built three decision trees, the first with the Complicacoes class; the second with the Obito class; and the third considering the union of the classes Complicacoes and Obito. We only analyzed the final graphical result regardless of the classification accuracy. It was possible that several different configurations could improve the classification accuracy but all methods generated the same final graphic result, and thus we selected the default settings for the search process. We generated the decision trees using the J48 algorithm available from Weka[4] with the default configuration.

5.4 MTARN construction

For the construction of the MTARNs a new process of extraction of association rules was executed so that rules were obtained with consequent of size equal to 2 (Definition 8). The parameters of minsup, minconf and mingain were the same as those used in the construction of Filtered-ARNs, as well as the Added Value filter.

We constructed the MTARN having as a target item the combination of the classes under study "[Complicacoes]=Sim;[Obito]=Sim" in order to analyze the factors leading to both complications and death of patients undergoing revascularization surgery. MTARN was plotted using the Gephi software (Bastian et al., 2009) and its full version is available online[5]. The items of level 1 (L = 1) of the network were selected to be evaluated and validated by specialists because they were the ones that directly influence the target node.

5.5 Expert Validation

After we created the networks, the items connected directly to the target nodes were selected and then inserted into a table so that the experts of the Dante Pazzanese Institute could evaluate the formulated hypotheses.

We prepared three spreadsheets with hypotheses related to the conditions of patients who had complications and/or died after undergoing coronary artery bypass surgery. The first worksheet was formulated with items found at Filtered-ARN levels 1 and 2 with target item "[Obito] = Sim". For the elaboration of the second worksheet, we considered the items found at level 1 of Filtered-ARN with target item "[Complicacoes]=Sim". The third worksheet was prepared with MTARN level 1 items constructed with the target item "[Complicacoes]=Sim;[Obito]=Sim" since they are the items most likely to influence the conditions of these patients. The results of the decision tree experiment were confusing, so we were unable to use them in the construction of a spreadsheet.

Experts assessed the hypotheses of each worksheet, i.e., the items indicated as influencers in one sheet did not interfere with the responses of another worksheet. The experts classified hypotheses as true, false, or suspicious. Suspicious hypotheses are those that do not yet have medical evidence, but there is already some indication that such statement may be true.

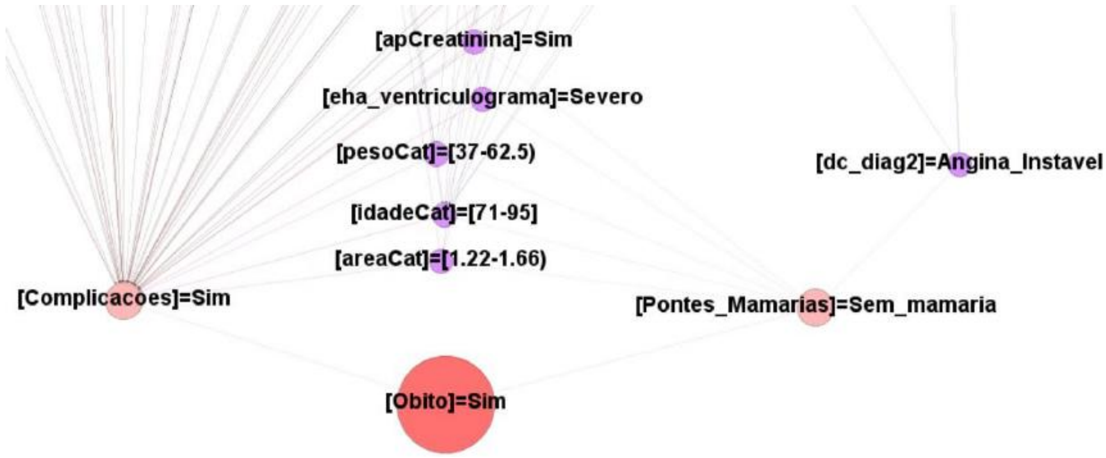
6. Results and Discussion

After the construction of the Filtered-ARN with target "[Obito]=Sim" (Figure 4), we analyzed level one nodes (L = 1). Only two nodes were found "[Complicacoes]=Sim" and "[Pontes Mamarias]=Sem mamaria". With this information, two hypotheses were elaborated. The first one is that "all patients who died had some complication", which is an obvious knowledge, since in medical studies every death comes from a complication, but validates the efficacy of technique used for

[4] http://www.cs.waikato.ac.nz/ml/weka/
[5] http://bit.ly/30YB5ke

pattern discovery. The second hypothesis is that "the patients most likely to die are those who do not have revascularization using grafts with the mammary artery". This hypothesis was confirmed by the specialists validating the network. However, some items related to deaths in patients submitted to revascularization surgery do not appear in the network connected to the target item such as Peripheral Arterial Vascular Disease (apVasculo) and female gender.

Figure 4 - Filtered-ARN with the target "[Obito]=Sim" and levels one (L = 1) and two (L = 2) nodes.



*Only two items were found in Filtered-ARN level 1. Of the two items, the one related to complications is obvious, since every death comes from a complication. Source: authors.

As the number of nodes of level one is small, we observed nodes of level two (L = 2). The total number of elements in Level 2 was 6, and the specialists confirmed all, but without the confirmation of the items of Peripheral Arterial Vascular Disease and female.

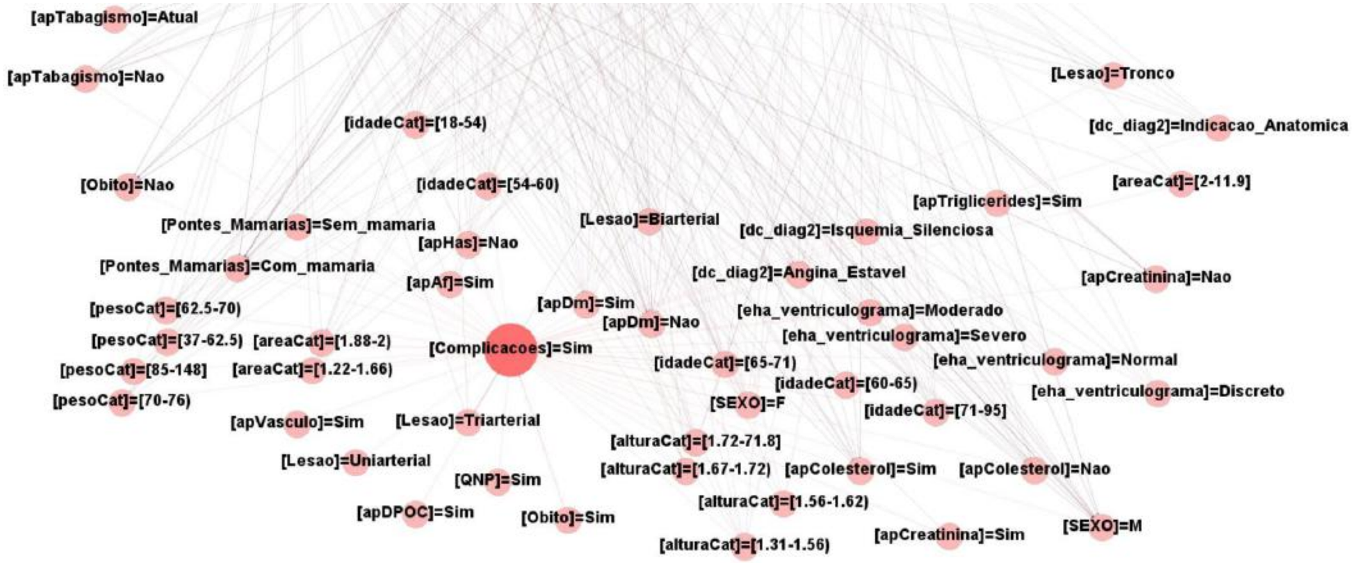
With the analysis of the level one nodes (L = 1) of the Filtered-ARN with target "[Complicacoes]=Sim" (Figure 5), we obtained 47 possibilities of direct influence in postoperative complications, of which 5 do not have a predecessor node, which indicates greater importance to these items.

Level one items without antecedents are:

- "[apDPOC]=Sim": represents that the patient has the chronic obstructive pulmonary disease that was previously diagnosed or at the time of hospitalization.
- "[apVasculo]=Sim": represents a patient with Peripheral Arterial Vascular Disease.
- "[Lesao]=Uniarterial": represents a type of arterial lesion found in the patient.
- "[Obito]=Sim": patient died.
- "[QNP]=Sim": patient with previous cerebral ischemia.

All items with no antecedent were confirmed by the experts, except "[Lesao]= Uniarterial" which represents a false connection.

Figure 5 - Filtered-ARN with the target "[Complicacoes]=Sim" and level one node (L = 1).



*The number of parameters connected to the target of complications is quite high and many of them were not conclusions, as in the example related to death, since affirmative and negative parameters for this item appear. Source: authors.

In addition to items with no antecedent, we studied other level one nodes (L = 1), and experts reported that many items are inconclusive. For example, both female and male patients are connected to death. Attributes such as [apColesterol], [apCreatinina], [apDm], [eha_ventriculograma], [idadeCat], [Lesao], and [Pontes_Mamarias] present all possible values connected to the target item, thus it is not possible to make any affirmation regarding these factors, besides the direct connection of "[Obito]=Nao" to the item of complications. Thus, the network cannot provide more concise information regarding complications in coronary artery bypass graft patients.

When we analyzed the results of the decision trees, we noticed that two of the three trees were formed by only one leaf node (attribute class Obito). The Algorithm performed only the direct classification of the class attribute. The difference between the number of instances of the two values of the class is huge (8,247 [Obito] = No and 425 [Obito] = Yes), and it is not possible to build a Decision tree.

The Decision Tree with the class attribute Complication has a size equal to 867 with 581 leaves. Its visualization is confusing. Although it is not the purpose of this work, the classification accuracy was only 62.1%. When we look at the first three levels of the tree (Figure 6), we notice that the root node is the parameter "[Obito]" connected directly with the attribute [Complicacoes]. However, the other elements that appear are [apCreatinina], [Pontes_Mamarias], and [idadeCat] without direct connection to the target attribute studied. Therefore, the Decision Tree was not able to generate hypotheses that can be used to expand knowledge about patients undergoing coronary surgery.

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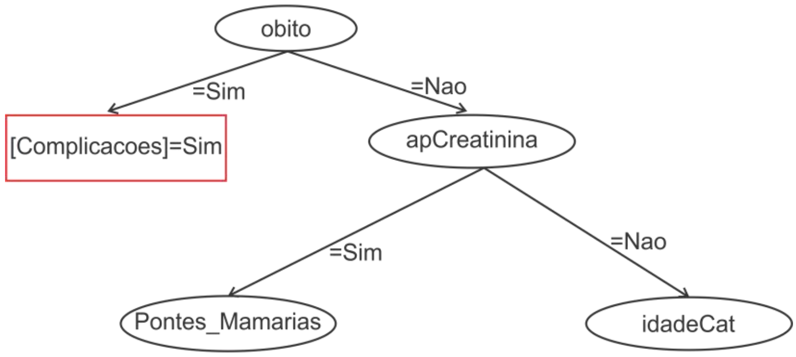
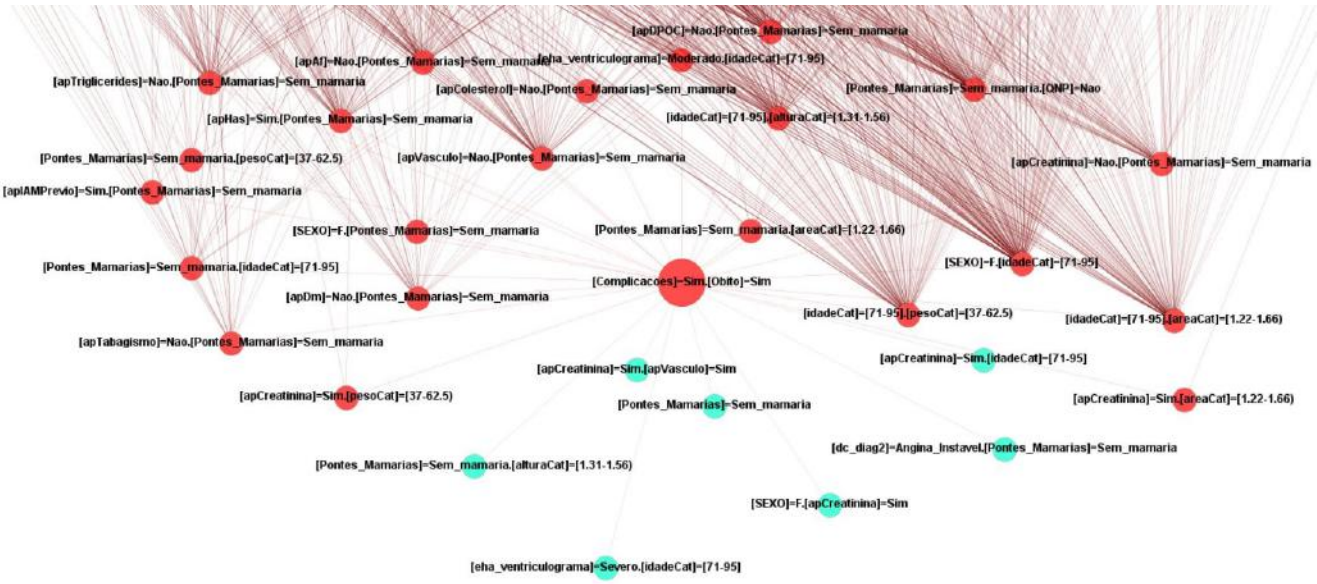
Figure 6 - Complications Class Decision tree (Three firsts levels).



*The first three levels of the decision tree demonstrate only one connection between complications and death, something that is already known. Therefore, it is a method that does not produce innovative knowledge discovery. Source: Authors.

The constructed and plotted MTARN is presented in Figure 7. Analyzing the level one nodes (L = 1), 29 items were obtained, of which 7 do not have predecessor nodes, which may indicate they are attributes of greater importance.

Figure 7 - MTARN with the target "[Complicacoes]=Sim.[Obito]=Sim" and level one node (L = 1).



*The parameters directly connected to the multitarget promote the association of items that directly influence the conditions of complications and death, generating innovative knowledge that can provide the generation of technological products to aid in the care of coronary patients. Source: Authors.

Level one items without antecedents are:

- "[Pontes Mamarias]=Sem mamaria": represents patients who did not undergo revascularization using grafts with the mammary artery.
- "[apCreatinina]=Sim.[apVasculo]=Sim": represents patients with renal insufficiency and Peripheral Arterial Vascular Disease.
- "[apCreatinina]=Sim.[idadeCat]=[71-95]": patients with renal insufficiency and age between 71 and 95 years old.
- "[Pontes Mamarias]=Sem mamaria.[alturaCat]=[1.31-1.56)": patients who did not undergo revascularization using grafts with a mammary artery and had the height between 1.31m and 1.56m.
- "[dc diag2]=Angina Instavel.[Pontes Mamarias]=Sem mamaria": represents patients with unstable angina and no mammary artery grafts.
- "[SEXO]=F.[apCreatinina]=Sim": female patients with renal impairment.

- “[eha_ventriculograma]=Severo.[idadeCat]=[71-95]”: patients with severe left ventricular function and age between 71 and 95 years old.

All items were validated by the specialists, who emphasized the possibility of joint analysis of the known leading factors of complication and death in patients undergoing coronary artery bypass grafting. The knowledge extracted by the MTARN analysis was considered by the experts of high complexity and presenting signs of truth.

By checking the level one items (L = 1) with antecedents, the experts informed that all items that have the “[Pontes_Mamarias] = Sem mamaria” attribute already could be considered true because it is a condition of already proven complication and death. The experts also pointed out that items with an inconsistency in the Filtered-ARN (Figure 5) were presented concisely and together with others such as “[Sexo] = F” indicating that the incidence of complications and deaths is directly connected to female patients.

It is important to note that the application of MTARN enabled the generation of a hypothesis that will be studied in the future in the Dante Pazzanese Institute. The suspicion factor is the non-connection between smoking and postoperative complications ([apTabagismo] = Nao).

The MTARN presented more extensive knowledge. The hypotheses were validated by the experts as true. The MTARN generated more confidence and, mainly, aided in the study of patients’ parameters undergoing myocardial revascularization surgery.

7. Conclusion and Future Work

In this work, we proposed the MTARN for the discovery of multi-target knowledge with the use of Association Rules Networks, which allows two attributes to be simultaneously studied. With the use of MTARNs, it was possible to optimize the discovery of knowledge that is directly related to the factors of complications and deaths in patients submitted to cardiac surgery for myocardial revascularization. We also constructed a dataset on myocardial revascularization surgeries performed in patients from the Dante Pazzanese Institute of Cardiology from 1999 to 2015.

Our proposal was compared to two other methods (Decision Tree and Filtered-ARN). We verify that it was not possible to generate hypotheses with the Decision Tree results. The use of Filtered-ARN allowed the generation of hypotheses that were confirmed by the experts, but many observations were considered inconclusive or even mistaken for each class individually. On the other hand, the findings using the Association Rules Mining technique through the MTARN were confirmed by specialists from the Dante Pazzanese Institute of Cardiology, giving greater credibility to the use of the mining technique in problems with two class attributes.

The MTARN limitation is that some rules generated with only one element and connected directly to the objective node (Level = 1) have a strong influence, so it is possible to create the appearance of more nodes due to these items. For example, the node “[Pontes_Mamarias] = Sem mamaria” is connected directly to the objective node, so other nodes, in which this same parameter is included, should be analyzed in more detail.

In this study, the use of MTARNs enabled a broader graphical analysis of the content of the explored data generating hypotheses that were proven correct, as well as the elaboration of new hypotheses that could be studied in future works. The raised hypotheses can be studied through new observations in patients undergoing myocardial revascularization surgery, seeking the patterns detected in the results of this research. The results demonstrate the feasibility of recommending association rule mining practices using multi-target networks for studies of patients’ parameters undergoing myocardial revascularization surgery. This technique may be applied to another clinical studies.

We can highlight some essential medical observations about risk factors in patients undergoing coronary artery bypass grafting: (i) confirmation of risk in patients of advanced age; (ii) observation that smoking is not a predominant factor; and (iii) female patients are a group that needs more care. This latter hypothesis was generated in health scientific research and we demonstrated this influence in this work.

For future works, it is possible to apply the multi-target approach with MTARN in data from patients with other types of pathology and to compare them with existing knowledge in the specialized literature. In addition to being able to generate an alert intelligent system for preventive monitoring of patients, indicating which parameter should be regulated in order to avoid complications and deaths with the use of Explicable Artificial Intelligence.

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