

Prediction of potential organ donation after irreversible brain damage

Luís Torres, Filipe Portela, Manuel Filipe Santos, António Abelha, José Neves and José Machado

Abstract—Identification of patients who will die within, at least, one hour of withdrawal of life-sustaining treatment is the key to successful donation of organs after cardiac death. The accurate prediction of potential organ donation has a great importance, since the limited time window in which occur all the process demands that various tasks must be done quick and effectively. Through a set of known factors/diagnosis, it is possible to determine if a patient who suffers from irreversible brain damage may be a future candidate to organ donation with an associated degree of confidence. So in this work it was developed a prediction system, in terms of its knowledge and representation and reasoning procedures supported by a logic programming based approach to computing an artificial neural network. The factors defined and their relationships were used to identify potential organ donor.

Keywords—Prediction of potential organ donation, Degree of Confidence, Artificial Neural Network.

I. INTRODUCTION

Over the last years, advances in immunosuppressive therapeutics, better patient selection and improved technical expertise (among other factors) have decisively contributed to the success of organ transplantation, which has proven to be a successful treatment for patients with end-stage organ failure[1].

Despite its good results, this treatment has a problem with the lack of resources, i.e. organs, so that the demand far exceeds the number of available donors. The major source of organs is brain (stem) dead patients, but unfortunately (for potential organ recipients) this is not a common form of death. Furthermore, this is an undesirable outcome, since one of the goals of neurocritical care is preventing brain death from occurring [2, 3]. These results in large waiting lists, increasing everyday and considering that transplantation is often the last resort for patients with end-stage organ dysfunction, increasing the potential pool of organ donors become critical [2]. One possible way to expand the donor's group is by the use of organs from donation after cardiac death (DCD), also known as non-heart-beating donors. In general, this kind of donors are patients whose deaths occur in the context of withdrawing life-sustaining treatment (WLST).

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Therapeutic failure, meaningless outcome due to poor prognosis and patient's autonomy/suffering are some of the most common reasons for WLST. The most frequent DCD candidates are patients who suffer from irreversible brain injury but do not meet criteria for brain dead diagnosis [4, 5].

Unfortunately, not all potential DCD became actual donations. The success DCD resides in the period between WLST and death. It is often associated with hypotension and poor organ perfusion that generally result in warm ischemic injury to the organs. According to British Transplantation Society and Intensive Care Society, functional warm ischaemia times vary by organ: [6]

- Liver: 30 minutes;
- Pancreas: 30 minutes;
- Lungs: 60 minutes;
- Kidney: 120 minutes;

Consequently, most DCD protocols discard organ retrieval if the patient is still alive 60 minutes after WSLT. Therefore, it has become clear the need for a model able to identify the patients who are most likely to die within 60 minutes of WLST, because only those can lead to an increase in the absolute number of available donor organs. By the other hand, it is important to clarify that the identification of a potential organ donor does not discharge a physician from treating the patient in his best interest [2, 3].

Among other benefits related to logistics and financial consequences (as reservation of operating theatre and surgical staff), a tool like this would avoid the potential organ recipient and his relatives having false expectations, situation that happens when the one hour deadline is not satisfied [4].

A few tools have been developed to predict this timing, but none is yet established as 'standard'. Between them are those from the University of Wisconsin (UW) and the United Network of Organ Sharing (UNOS). These two consist on having a numerical scale (to assign scores) and perform a trial of spontaneous respiratory rate and oxygenation when the patient is disconnected from mechanical ventilation. However, the lack information about the neurological status of the patient before WLST and the fact that they require temporary disconnection of the patient from the mechanical ventilator can be a problem. In some countries, any intervention during WLST is not directed at improving the palliative care provided is considered medically and ethically inappropriate [5]. In order to overcome this last limitation, new promising models have been developed. Coleman and her team [5] concluded that combining Glasgow Coma Scale (GCS), respiratory and haemodynamic parameters and intensivists opinion, it is possible the time from WLST to death accurately, although their results require validation in a large scale.

In other study, although not proposing any model, Suntharalingam et al [7] identified some factors that may influence the time to death. Cause of neurological injury, low blood pH, and use of inotropes prior to WLST were pointed, but younger age, higher FiO₂ and mode of ventilation were the most important variables associated with shorter time to death.

Rabinstein, Alejandro A., et al [8] build a model based on four clinical variables: absent corneal reflex, absent cough reflex, extensor or absent motor response, and higher oxygenation index. These were established as predictor variables, based on previous findings. After assigning a value to each of the variables, their sum creates a predictive score for cardiac death in patients in neurocritical state (DCD-N score). After an observational study, it was possible to translate that score in terms of probability death within 60 minutes.

By analysing this variety of models and indicators, it is clear that the key to successfully predict death after WLST lies with the identification of the correct clinic variables. Yet, the identification of the set of factors that best can characterize this problem seems something that still needs further analysis. With this article, based on some of the most important variables described, we make a start on the development of a system that can predict the potential organ donation after irreversible brain damage. We will be centred on a logic programming based approach to knowledge representation and reasoning, complemented with a computational framework based on Artificial Neural Networks.

This paper has five sections. Firstly the work and related concepts are introduced then in the second section is studied and analysed the quality of information versus the degree of confidence. In the following two section the knowledge acquired and their reasoning as also the artificial neural network are presented. Finally some conclusions are made and the future work presented.

II. QUALITY-OF-INFORMATION VERSUS DEGREE OF CONFIDENCE

Due to the growing need to offer user support in decision making processes some studies have been presented [9][10], related to the qualitative models and qualitative reasoning in Database Theory and in Artificial Intelligence (AI) research. With respect to the problem of knowledge representation and reasoning in Logic Programming (LP), a measure of the *Quality-of-Information (QoI)* of such programs has been object of some work with promising results [11], [12]. The *QoI* with respect to the extension of a predicate i will be given by a truth-value in the interval $[0,1]$, i.e., if the information is *known (positive)* or *false (negative)* the *QoI* for the extension of *predicate_i* is 1. For situations where the information is unknown, the *QoI* is given by:

$$QoI_i = \lim_{N \rightarrow \infty} \frac{1}{N} = 0 \quad (N \gg 0) \quad (1)$$

where N denotes the cardinality of the set of terms or clauses of the extension of *predicate_i* that stand for the incompleteness under consideration. For situations where the extension of *predicate_i* is unknown but can be taken from a set of values, the *QoI* is given by:

$$QoI_i = 1/Card \quad (2)$$

where $Card$ denotes the cardinality of the *abducibles* set for i , if the *abducibles* set is disjoint. If the *abducibles* set is not disjoint, the *QoI* is given by:

$$QoI_i = \frac{1}{C_1^{Card} + \dots + C_{Card}^{Card}} \quad (3)$$

where C_{Card}^{Card} is a card-combination subset, with $Card$ elements. The next element of the model to be considered is the relative importance that a predicate assigns to each of its attributes under observation, i.e., w_i^k , which stands for the relevance of attribute k in the extension of *predicate_i*. It is also assumed that the weights of all the attribute predicates are normalized, i.e.:

$$\sum_{1 \leq k \leq n} w_i^k = 1, \forall_i \quad (4)$$

where \forall denotes the universal quantifier. It is now possible to define a predicate's scoring function $V_i(x)$ so that, for a value $x = (x_1, \dots, x_n)$, defined in terms of the attributes of *predicate_i*, one may have:

$$V_i(x) = \sum_{1 \leq k \leq n} w_i^k \times QoI_i(x)/n \quad (5)$$

It is now possible to engender all the possible scenarios of the universe of discourse, according to the information given in the logic programs that endorse the information depicted in Fig. 2, i.e., in terms of the extensions of the predicates *General Data*, *Full Outline of UnResponsive (FOUR)*, *Glasgow Coma Scores*, *DCD-N* and *Diagnosis*.

It is now feasible to rewrite the extensions of the predicates referred to above, in terms of a set of possible scenarios according to productions of the type:

$$predicate_i((x_1, \dots, x_n)) :: QoI \quad (6)$$

and evaluate the *Degree of Confidence (DoC)* given by $DoC = V_i(x_1, \dots, x_n)/n$, which denotes one's confidence in a particular term of the extension of *predicate_i*. To be more general, let us suppose that the Universe of Discourse is described by the extension of the predicates:

$$a_1(\dots), a_2(\dots), \dots, a_n(\dots) \quad (n \geq 0) \quad (7)$$

Therefore, for a given *scenario*, one may have (where \perp denotes an argument value of the type unknown; the values of the others arguments stand for themselves):

$$\left\{ \begin{array}{l} \neg a_1(x_1, y_1, z_1) \leftarrow \text{not } a_1(x_1, y_1, z_1) \\ a_1(\perp, [10,20], 15) :: 0.5 \\ \underline{[5, 10] \quad [5,30] \quad [10, 20]} \\ \text{attribute's domains for } x_1, y_1, z_1 \\ \\ \neg a_2(x_2, y_2, z_2) \leftarrow \text{not } a_2(x_2, y_2, z_2) \\ a_2([45,54], [10, 12], \perp) :: 0.65 \\ \underline{[30, 60] \quad [6, 14] \quad [2000, 6000]} \\ \text{attribute's domains for } x_2, y_2, z_2 \\ \\ \vdots \end{array} \right.$$

↓ 1st interaction: transition to continuous intervals

$$\left\{ \begin{array}{l} \neg a_1(x_1, y_1, z_1) \leftarrow \text{not } a_1(x_1, y_1, z_1) \\ a_1([5, 10], [10,20], [15, 15]) :: 0.5 \\ \underline{[5, 10] \quad [5, 30] \quad [10, 20]} \\ \text{attribute's domains for } x_1, y_1, z_1 \\ \\ \neg a_2(x_2, y_2, z_2) \leftarrow \text{not } a_2(x_2, y_2, z_2) \\ a_2([45,54], [10, 12], [2000,6000]) :: 0.65 \\ \underline{[30, 60] \quad [6, 14] \quad [2000, 6000]} \\ \text{attribute's domains for } x_2, y_2, z_2 \\ \\ \vdots \end{array} \right.$$

↓ 2nd interaction: normalization $\frac{Y - Y_{min}}{Y_{max} - Y_{min}}$

$$\left\{ \begin{array}{l} \neg a_1(x_1, y_1, z_1) \leftarrow \text{not } a_1(x_1, y_1, z_1) \\ \\ a_1\left(\left(\frac{5-5}{10-5}, \frac{10-5}{10-5}\right), \left(\frac{10-5}{30-5}, \frac{20-5}{30-5}\right), \left(\frac{15-10}{20-10}, \frac{15-10}{20-10}\right)\right) \equiv \\ \\ a_1([0,1], [0.2, 0.6], [0.5, 0.5]) :: 0.5 \\ \underline{[0, 1] \quad [0, 1] \quad [0, 1]} \\ \text{attribute's domains for } x_1, y_1, z_1 \\ \\ \neg a_2(x_2, y_2, z_2) \leftarrow \text{not } a_2(x_2, y_2, z_2) \\ \\ a_2\left(\left(\frac{45-30}{60-30}, \frac{54-30}{60-30}\right), \left(\frac{10-6}{14-6}, \frac{12-6}{14-6}\right), \left(\frac{2000-2000}{6000-2000}, \frac{6000-2000}{6000-2000}\right)\right) \equiv \\ \\ a_2([0.5, 0.8], [0.5, 0.75], [0, 1]) :: 0.65 \\ \underline{[0, 1] \quad [0, 1] \quad [0, 1]} \\ \text{attribute's domains for } x_2, y_2, z_2 \\ \\ \vdots \end{array} \right.$$

The *Degree of Confidence (DoC)* was evaluated using the equation $DoC = \sqrt{1 - \Delta l^2}$, as it is illustrated in Fig. 1. Here Δl stands for the length of the arguments' intervals, once normalized.

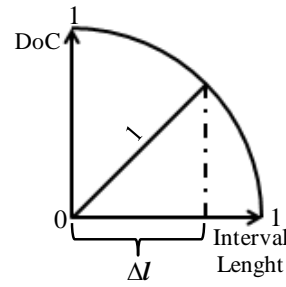


Fig. 1 Evaluation of *Degree of Confidence*

Below, one has the expected representation of the universe of discourse, where all the predicates' arguments are nominal. They speak for one's confidence that the unknown values of the arguments fit into the correspondent intervals referred to above.

$$\left\{ \begin{array}{l} \neg a_1(x_1, y_1, z_1) \leftarrow \text{not } a_1(x_1, y_1, z_1) \\ a_1(0, 0.9, 1) :: 0.5 \\ [0, 1] [0, 1] [0, 1] \\ \\ \neg a_2(x_2, y_2, z_2) \leftarrow \text{not } a_2(x_2, y_2, z_2) \\ a_2(0.9, 0.6, 0) :: 0.65 \\ [0, 1] [0, 1] [0, 1] \\ \\ \vdots \end{array} \right.$$

III. KNOWLEDGE REPRESENTATION AND REASONING

Many approaches for knowledge representation and reasoning have been proposed using the *Logic Programming (LP)* paradigm, namely in the area of Model Theory [13]–[15], and Proof Theory [16], [17]. We follow the proof theoretical approach and an extension to the *LP* language, to knowledge representation and reasoning. An *Extended Logic Program (ELP)* for short) is a finite set of clauses in the form:

$$p \leftarrow p_1, \dots, p_n, \text{not } q_1, \dots, \text{not } q_m \quad (8)$$

$$?(p_1, \dots, p_n, \text{not } q_1, \dots, \text{not } q_m) \quad (n, m \geq 0) \quad (9)$$

Where? There is a domain atom denoting falsity, the p_i , q_j , and p are classical ground literals, i.e., either positive atoms or atoms preceded by the classical negation sign \neg [17]. Under this representation formalism, every program is associated with a set of adducibles [15][18], given here in the form of exceptions to the extensions of the predicates that make the program. Once again, Logic Programming (LP) has emerged as an attractive formalism for knowledge representation and reasoning tasks, introducing an efficient search mechanism for problem solving. Therefore, and in order to exemplify the applicability of our model, we will look at the relational database model, since it provides a basic framework that fits into our expectations [19], and is understood as the genesis of the LP approach to knowledge representation and reasoning.

Consider, for instance, the scenario where a relational database is given in terms of the extensions of the relations or predicates depicted in Fig. 2, which stands for a situation where

one has to manage information about patients in a neurocritical state. Under this scenario some incomplete data is also available. For instance, in relation General Data the use of inotropes in the third patient is unknown, while in relation to Diagnosis values for pH of the first patient range in the interval [7.25, 7.35].

In relation General Data, Ventilation Mode can be: 0 – Pressure Support; Synchronised intermittent mandatory Ventilation-1; or Pressure Control/Volume Control/Pressure regulated Volume Control – 1. In what concerns to use of inotropes: 0 – not use; and 1- used.

The relation FOUR is obtained by the sum of the row, which corresponds to each of its testable components (filled according to this scale). The relation GCS works in the same way, but don't test brain stem reflexes and has a different scale. Despite this, it is still included on this model because it is the most commonly used.

The DCD-N comes from the already mentioned Rabinstein, Alejandro A., et al model, because it provides a simple way to weight some of the most important factors: for the absence of cough reflex it is given 2 points, and for the absence of each of the other 1 point.

Finally, in the relation Diagnosis, causes of neurological injury values correspond to: 3 – intracranial trauma; 2 – intracranial haemorrhage; 1 – hypoxia; 0 – other.

Now, we may consider the extensions of the relations given in Figure 2 to populate the extension of the *potential*_{donor} predicate, given in the form:

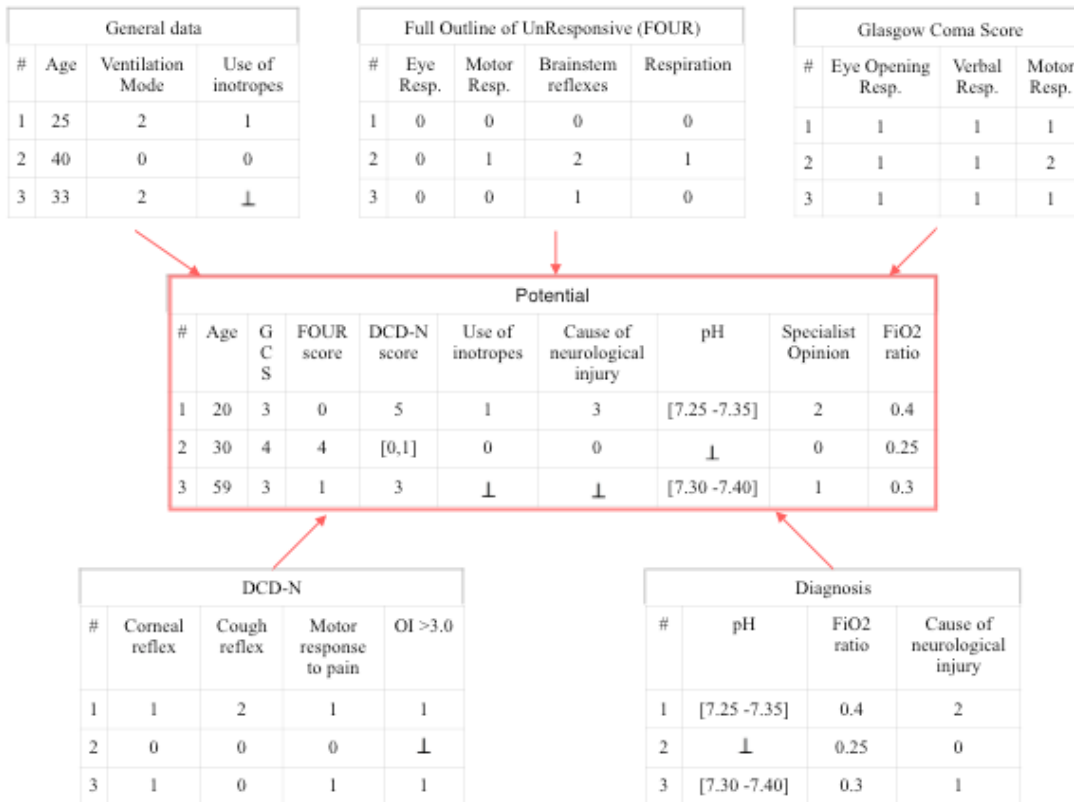


Fig. 2 An extension of the relational database model.

$potential_{donor}: Age, GCS, FOUR_{score}, DCD - N_{score}, Inotropes, Cause, pH, Opinion, FiO_2 \rightarrow \{0,1\}$

where 0 (zero) and 1 (one) denote, respectively, the truth values *false* and *true*. It is now possible to give the extension of the predicate *potential*_{donor}, in the form:

{
 $\neg potential(Age, GCS, FOUR, DCD - N, Ino, C, pH, Op, FiO_2)$
 $\leftarrow not\ potential(Age, GCS, FOUR, DCD - N, Ino, C, pH, Op, FiO_2)$

$potential(20, 3, 0, 5, 1, 3, [7.25 - 7.35], 2, 0.4) :: 1.$
 [3,75] [3,15] [0,16] [0,5] [0,1] [0,3] [7.25,7.40] [0,2] [0.15,0.5]

$potential(30, 4, 4, [0,1], 0, 0, \perp, 0, 0.25) :: 1.$
 [3,75] [3,15] [0,16] [0,5] [0,1] [0,3] [7.25,7.40] [0,2] [0.15,0.5]

In this program, the first clause denotes the closure of predicate *potential*_{donor}. The following clause corresponds to two terms taken from the extension of the *potential*_{donor} relation. It is now possible to have the arguments of the predicates extensions normalized to the interval [0, 1], in order to compute one's confidence that the nominal values of the arguments under considerations fit into the intervals depicted previously. One may have:

{
 $potential([0.24,0.24], [0,0], [0,0], [1,1], [1,1], [1,1], [0,0.67], [1,1]$

```
[0.71,0.71]) :: 1.
    [0,1]    [0,1] [0,1] [0,1] [0,1] [0,1] [0,1] [0,1]
    [0,1]
potential([0.375,0.375], [0.83,0.83], [0.33,0.33], [0,0.2], [0,0], [0,0],
[0,1], [0,0], [0.29,0.29]) :: 1.
    [0,1]    [0,1] [0,1] [0,1] [0,1] [0,1] [0,1] [0,1]
    [0,1]
}
```

The logic program referred to above, is now presented in the form:

```
{
¬potentialDoC(Age, GCS, FOUR, DCD - N, Ino, C, pH, Op, FiO2)
← not potentialDoC(Age, GCS, FOUR, DC - N, Ino, C, pH, Op, FiO2).
potentialDoC(1, 1, 1, 1, 1, 1, 0.74, 1, 1) :: 1.
potentialDoC(1, 1, 1, 0.98, 1, 1, 0, 1, 1) :: 1.
}
```

where its terms make the training and test sets of the following Artificial Neural Network(Figure 3).

IV. ARTIFICIAL NEURAL NETWORKS

The presented model works well to demonstrate how the information comes together to make a prediction, but it was built with the pure objective of demonstration. In order to find more reliable ways to assemble this information Artificial neural Networks (ANNs) and data mining tools can be used. Neves et al [18]–[20] demonstrated how ANNs could be successfully applied to model data and capture complex relationships between inputs and outputs. This kind of tool simulates the structure of the human brain being populated by multiple layers of neurons. As an example, let us consider the case of the third which is given in the form:

```
{
potential: (Age, GCS, FOUR, DCD - N, Ino, C, pH, Op, FiO2)
↓
potential(59, 3, 1, 3, ⊥, ⊥, [7.30 - 7.40], 1, 0.3) :: 1.
[3.75] [3.15] [0.16] [0.5] [0.1] [0.3] [7.25,7.40] [0.2] [0.15,0.5]
↓
potential([59,59], [3,3], [1,1], [ 3,3], [0,1], [0,3], [7.30
- 7.40], [1,1], [0.3, 0.3]) :: 1.
↓
potential([0.78, 0.78], [0,0], [0.06, 0.06], [0.6,0.6], [0,1], [0,1],
[0.33,0.33], [0.5, 0.5] [0.43,0.43]) :: 1.
↓
potentialDoC(1, 1, 1, 1, 0, 0, 1, 1, 1).
}
```

In Figure 3 it is shown how the normalized extremes and theirs DoC values work as inputs to the ANN. The output translates the chance of the patient death within one hour of WLST and DoC the confidence that one has on such a happening. In order to achieve good results, it is imperative to build a database of study cases that can be used to train and test the ANN.

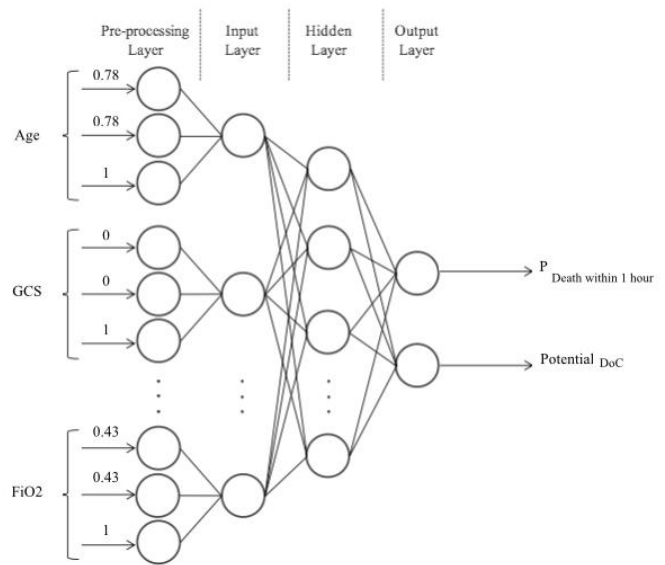


Fig. 3 ANN example for third patient

V. CONCLUSIONS AND FUTURE WORK

Identify the patients who will die in a period of 60 minutes after WLST as potential organ donors is a hard and complex task, which needs to consider many different factors with complex relations among them. All this characteristics highlight the benefits that the aid by AI techniques can bring to this field in order to achieve better prognostics.

In this work, departing from the conclusions of some good existing models, it was presented the founding of a computational framework that uses powerful knowledge representation and reasoning techniques to set the structure of the information and the associate inference mechanisms. This representation is above everything else, very versatile and capable of covering every possible instance by considering incomplete, contradictory, and even unknown data.

Future works, should study the assignment of different weights to different factors when calculating the Degree of Confidence, since the identification of the most important characteristics seems to be in the core of this problem.

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