

# Fuzzy Logic-Based Model to Stratify Cardiac Surgery Risk

## *Modelo basado en lógica borrosa para estratificar el riesgo de la cirugía cardíaca*

RAÚL A. BORRACCI<sup>MTSAC</sup>, EDUARDO B. ARRIBALZAGA

### ABSTRACT

**Background:** Medical practice is usually performed in a context of uncertainty, where expert knowledge has shown to be efficient in the decision-making process.

**Objective:** The aim of this study was to develop and validate a fuzzy logic-based model to predict cardiac surgery mortality risk.

**Methods:** Four hundred and fifty patients undergoing cardiac surgery were prospectively included in the study and mortality risk was predicted based on five scores: 1) “clinical expert” opinion, 2) fuzzy logic-based system according to expert knowledge, 3) Parsonnet, 4) Ontario and 5) EuroSCORE. The fuzzy logic model was developed in the following stages: expert selection of different mortality predictive variables, tables of influence among variables, construction of a fuzzy cognitive map (FCM) and its implementation in an artificial neuronal network, expert-determined patient risk score, test set risk calculation based on fuzzy predictors, validation set risk using calibrated FCM, and comparison with the other scores according to the level of agreement and precision with ROC curves.

**Results:** The calibrated model was used to predict the outcome of the validation set (360 patients), based on the FCM score and risk predicted by Parsonnet, Ontario and EuroSCORE. The ROC areas showed that FCM had at least the same performance as other scores to predict mortality (ROC=0.793 vs. 0.775, 0.767, 0.741 and 0.701 for EuroSCORE, “expert”, Ontario and Parsonnet, respectively).

**Conclusions:** A fuzzy logic-based system employing expert knowledge and the implementation of an expert system is postulated to predict cardiac surgery mortality risk. The model not only mimicked the outcomes obtained by the “expert”, but had the same performance as others risk scores.

**Key words:** Cardiac Surgical Procedures - Prognosis - Risk Assessment - Fuzzy Logic

### RESUMEN

**Introducción:** La práctica clínica se desarrolla en un contexto de información incierta, en el que el conocimiento “experto” ha demostrado que es muy eficiente para la toma de decisiones.

**Objetivo:** Desarrollar y validar un modelo basado en lógica difusa o borrosa para predecir el riesgo de mortalidad en cirugía cardíaca.

**Material y métodos:** Se incorporaron prospectivamente 450 pacientes sometidos a cirugía cardíaca y se cotejó la predicción de riesgo de mortalidad en base a cinco puntajes: 1) la opinión de un “experto”, 2) el resultado de un sistema basado en lógica difusa según el conocimiento experto, 3) Parsonnet, 4) Ontario y 5) EuroSCORE. El modelo de lógica difusa se desarrolló en las siguientes etapas: selección por un experto de las variables predictivas de mortalidad, confección de tablas de influencia entre variables, construcción de un mapa cognitivo borroso (MCB) e implementación en una red neuronal artificial, determinación por el experto del puntaje de riesgo por paciente, cálculo del riesgo del conjunto de prueba según los predictores borrosos, determinación del riesgo del conjunto de validación usando el MCB ya calibrado y comparación de los resultados con los otros modelos según concordancia y precisión con curvas ROC.

**Resultados:** El modelo calibrado se usó para predecir los resultados del conjunto de validación (360 pacientes), a quienes se les determinó el puntaje del MCB y los riesgos pronosticados por Parsonnet, Ontario y EuroSCORE. Las áreas ROC demostraron que el MCB tuvo por lo menos el mismo desempeño para predecir mortalidad (ROC = 0,793 vs. 0,775, 0,767, 0,741 y 0,701 para el EuroSCORE, “experto”, Ontario y Parsonnet, respectivamente).

**Conclusiones:** Se propone un sistema capaz de aprovechar el conocimiento experto mediante el uso de lógica difusa y la implementación de un sistema experto para predecir la mortalidad en cirugía cardíaca. El modelo no solo imitó los resultados obtenidos por el “experto”, sino que también tuvo el mismo desempeño que otros puntajes.

**Palabras clave:** Procedimientos quirúrgicos cardíacos - Pronóstico - Medición de riesgo - Lógica difusa

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Address for reprints: Raúl A. Borracci - La Pampa 3030, 1.º B - (1428) Buenos Aires, Argentina - e-mail: raborracci@gmail.com

## INTRODUCTION

Risk scores have widely expanded in cardiac surgery and continue to grow (1-6). The usual methodology to build these models is the treatment of a vast amount of data with some kind of multivariate or Bayesian analysis to establish the association of “postoperative death” to a number of independent predictive variables (7-14). The process of decision-making in medical practice is mostly based on interpretation of incomplete data, whose collection implies a margin of error. Medical information is directly obtained from the expert-physician perceptions, or through previous perceptions of similar situations, related in turn to knowledge about the specific disease. But lack of completeness and inaccurate clinical knowledge produces the uncertainty under which decisions have to be adopted. Finally, the impossibility of listing the complete assembly of background or consequences of a particular disease, or the effects arising from its intervention, as well as the impossibility of assessing all the involved variables surrounding many clinical situations determines that expert knowledge is still a relevant valid option for decision-making in medicine.

All risk scores developed up to the present are based on Boolean logic (true/false), which only allows to choose between two or more excluding possibilities: a patient can be or not diabetic, have or not a left main coronary artery lesion, or his ventricular function can be better or worse, conditions that will generate a different weight in the risk score result. Once the true value of each variable is selected, the set of variables is treated with multivariate analysis techniques to obtain a function that can predict with a certain probability margin the surgical result. An initial hypothesis could assume that, in part, the difficulty or deficiency of making a correct prediction with these scores would be due, among other reasons, to an incorrect adjudication of the truth value for each variable. Even if all variables could be defined according to their truth value, there would still remain other non-assessable situations with Boolean logic: age can be calculated in years or in its condition of young, adult or old; but, how could a patient's aspect be measured when he looks younger or older than his chronological age? The problem thus stated points out the limitations of traditional logic to solve the situation of clinical prediction. (15). At the beginning of the XX century, J. Lukasiewicz developed the principles of multi-valued logic, whose formulations may have truth values comprised in a continuous scale ranging from 0 (false) to 1 (true) of classical Boolean logic. For example, the statement “the glass is full” in traditional logic would have the truth value 1 (true) if the glass is full to the brim; conversely, if the glass is filled to 90% its capacity, the statement would be false with truth value of 0. Multi-valued logic allows assigning different degrees of certainty; then, in the latter case, the truth value would be 0.9 (almost true). In 1965, Zadeh (16) introduced the term fuzzy or diffuse logic and developed a

special algebra for the treatment of these fuzzy sets. Fuzzy logic then allows treating inaccurate information, as average height, low temperature or a great force, in terms of fuzzy or imprecise sets. These linguistic descriptions so frequently used in clinical medicine are especially adequate to be treated with this method (17-25). Furthermore, models based on fuzzy logic can be implemented in known systems, such as fuzzy cognitive maps (26-28). This causal map capable of representing the “clinical expert” knowledge can in turn be implemented in an artificial neural network (29).

In conclusion, fuzzy logic is a kind of multi-valued logic that enables to derive conclusions from vague, imprecise or even ambiguous information. In many aspects, fuzzy logic imitates human decision processes in which conducts or decisions must be adopted based on approximate data obtained through the senses.

Based on this theoretical framework, the following objectives were defined:

- To prospectively develop and validate a model to predict post-cardiac surgery mortality risk using fuzzy logic.
- To implement the model in an artificial neural network system based on a fuzzy cognitive map, capable of working as an expert system.
- To compare the predicted results obtained with this model against different internationally validated risk-adjustment systems.
- To analyze the predictive precision of each model based on the observed mortality results.

## METHODS

All patients undergoing cardiac surgery from February 2007 to March 2008 were included in the study. The patients who could not be preoperatively assigned any of the chosen risk scores or be evaluated by the “expert” in order to provide them a risk level, were excluded from the study.

This was a prospective, longitudinal, comparative design study, evaluating different risk scoring models for the prediction of post-cardiac surgery mortality risk. Each surgical patient was assigned five different risk levels according to: “expert” opinion” (R.A.B.), the result of an automated system developed from expert knowledge, and three commonly used internationally validated scores (Parsonnet, Ontario and logistic EuroSCORE) (7-9). Figure 1 shows the study design outline.

### Sequence of study development

**Step 1.** Expert selection of fuzzy variables to predict mortality, expressed as nominal or ordinal variables, with their corresponding categories (see Table in Supplemental material in the web).

**Step 2.** Development of tables of influence among variables and of these with the mortality endpoint. A standard model was used, adjusting and applying the “weights” or “influences” between variables, in a scale between 0 (zero) and 1 (one) (does not affect: 0.0; slightly affects: 0.3; moderately affects: 0.6 and greatly affects: 1.0).

**Step 3.** Construction of a Fuzzy Cognitive Map (FCM) to predict cardiac surgery results based on selected preoperative fuzzy variables. This causal diagram or map was built

assigning relevant system concepts to a series of nodes and a series of connections between nodes showing the causal relationship or influence among variables. The connections between nodes have an associated rank value [0-1] based on the tables of influence.

**Step 4.** The implementation of the fuzzy cognitive map was done in an artificial monolayer neural network similar to the Hopfield network (29) but with self-recurrent connections. The weights associated to the connections matched the weights allocated in the map; the inputs are the values assigned to the selected modality within each variable and the outputs the solutions resulting from the network. The implementation and use of the network was done in three stages: learning, calibration and validation. The network solution was obtained by matrix product [set of values assigned to the modalities times set of weights assigned to the connections] in Microsoft Excel®. The resulting vector was processed within the neuron by means of its hyperbolic tangent activation function to obtain a series of output values in a continuous scale (mortality risk was the only value of interest). The multiple iterations required by the network to give a final value were graphically monitored until a plateau indicated the final result had “stabilized”.

**Step 5.** Patient data collection was prospectively performed with an ad hoc relational database.

**Step 6.** The expert evaluated each patient preoperatively assigning a mortality risk in the low/moderate/high ordinal scale, according to the fuzzy set shown in Figure 2. This was built taking into account international standards of quality accepted at that moment.

**Step 7.** Risk score assessment in a test set of patients using fuzzy predictors. The fuzzy cognitive map built in Step 4 was used to determine surgical risk in a test set of patients, to calibrate these results with those assigned by the expert. Calibration consisted in modifying intra-variable and between variable influence weights initially allocated in the tables of influence.

**Step 8.** Prospective risk score assessment of the validation set using the already calibrated fuzzy cognitive map. The model assigned each patient a risk value in a continuous scale which was also transformed to the same low/moderate/high ordinal scale.

**Step 9.** Patient prospective risk score determined according to Parsonnet, Ontario and logistic EuroSCORE models

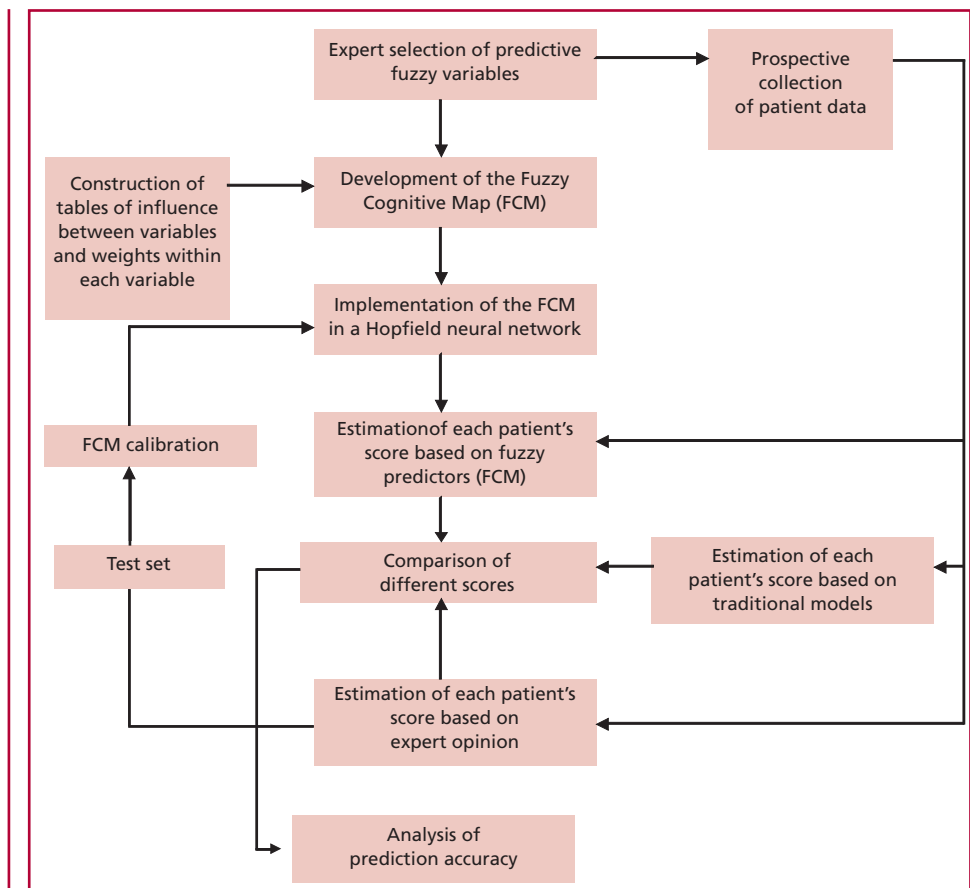
**Step 10.** Comparison of results obtained with the different models. The degree of agreement of the test and validation sets was compared between “expert” and fuzzy cognitive map. Then, as the Parsonnet, Ontario and logistic EuroSCORE are expressed in a continuous scale, linear and non-linear correlation and regression analyses were also performed to relate the fuzzy model with the different scores.

**Step 11.** Finally, the prediction level attained by the “expert” and his derived fuzzy system was compared with that obtained with traditional scores.

**Statistical analysis**

One-way analysis of variance was used to compare initial results between expert opinion expressed in ordinal scale (low/

Fig. 1. Study design.



moderate and high risk groups) and values obtained with fuzzy cognitive map expressed in continuous scale. Cut-off points between groups with low/moderate and moderate/high risk were optimized using ROC curves. Then, values of the fuzzy cognitive map continuous scale were assigned to each fuzzy set to perform the concordance analysis.

The concordance analysis for the three risk categories, low/moderate/high was performed with the C coefficient corrected by grouping; its significance was calculated with the chi-square test. Additionally, Cohen's weighted kappa concordance index was calculated with the corresponding confidence intervals. Weighted kappa was calculated using the quadratic weight method. Linear and non-linear correlation and regression analyses were performed to analyze the type and degree of correlation between continuous values obtained with different classic scores and the fuzzy cognitive map solution. Finally, predictive precision with the different models was estimated comparing ROC areas and their corresponding 95% confidence intervals (CI<sub>95%</sub>) with the Hanley-McNeil method. Epidat 2.1® and SPSS 17® software packages were used for statistical calculations. Sample size for the weighted kappa concordance analysis was performed with the formula considering that the minimal number of observed subjects was greater than  $2c^2$ , where  $c$  is the number of categories (cells of the contingency table). Thus, for a  $3 \times 3$  table there are  $2 \times 9^2 = 162$  subjects. The validation set consisted of a sample size which doubled the calculated one ( $162 \times 2 = 320$  patients) to compensate for possible data loss. As there is yet no consensus on the necessary number of observations to calibrate or test a Hopfield neural network, a test sample of at least one third the originally calculated sample size was used.

### Ethical considerations

Use of medical records was approved by Institutional Ethics Committees and following ANMAT's regulatory requirements for prospective observational clinical trials (Provision 5330/97). In addition, patient consent was obtained to use this information.

### RESULTS

Table 1 summarizes baseline population characteristics according to its preoperative and intraoperative variables, as well as morbidity and mortality associated to the procedures. The expected risks predicted by Ontario and logistic EuroSCORE were near the 4.7% all-cause mortality, and confirmed by ROC areas. Moreover, preoperative risk factor distribution, and postsurgical complications were similar to other published series.

### Model development

The fuzzy cognitive model was developed according to the fuzzy variables selected by the expert and the influence relationships between these variables to predict postoperative cardiac surgery mortality (see Figure in Supplemental material in the web). The fuzzy cognitive model shows preoperative risk factors and their relationships, which the "expert" considers could predict in-hospital mortality for this kind of surgery. The values between nodes correspond to the weight assigned to each connection based on the tables of influence. Values close to 1 (one) indicate that

**Table 1.** Population characteristics. Preoperative and intraoperative variables and immediate postoperative results (n=450)

Variables	n (%)
Preoperative and intraoperative:	
Age, years (mean±SD)	63.7±9.83
Female gender	108 (24.0)
Diabetes	88 (19.6)
Hypertension	284 (63.1)
Obesity	85 (18.9)
Heart failure	51 (11.3)
Stroke	21 (4.7)
Pulmonary disease	47 (10.4)
Renal failure	27 (6.0)
Anemia	12 (2.7)
Unstable angina	223 (49.6)
Recent myocardial infarction	36 (8.0)
Redo	14 (3.1)
Moderate-severe LV dysfunction	149 (33.1)
Calculated risks with: *	
Parsonnet	9.10 (8.29 a 10.5)
Ontario	4.39 (4.02 a 4.80)
EuroSCORE	6.32 (5.62 a 6.87)
Type of surgery:	
Coronary artery	315 (70.0)
Valvular	82 (18.2)
Combined	56 (12.4)
Urgent surgery	80 (17.8)
Off-pump CABG**	161 (51.1)
Postoperative:	
Mortality	21 (4.7)
Extubation in operating room	374 (83.1)
Complications:	
Reoperation for bleeding	8 (1.8)
Infarction (Q type)**	8 (2.5)
Stroke	9 (2.0)
Dialysis	8 (1.8)
Mediastinitis	6 (1.3)

\* calculated on the validation set data (n = 360)

\*\* calculated exclusively for coronary surgery (n = 315)

Risk is expressed as mean ± 95% confidence interval

LV: Left ventricular; SD: standard deviation; CABG: Coronary artery bypass graft surgery

this variable has great influence to predict mortality whereas a value close to 0 (zero) denotes the slight relevance this factor has to predict an adverse event. All variables have a different degree of connection and meet at a central output node, which will predict that particular patient's mortality risk depending on the presence or absence of assigned risk factors. The fuzzy

cognitive model was then implemented in a Hopfield network with auto-recurrent connections. For model learning and calibration stages, data from a sample of 90 patients was incorporated to the network input matrix, and after 12 iterations, its results were expressed by a mortality risk score. This score was compared with the risk predicted by the “expert” for each patient, based on the fuzzy sets for mortality risk adjudication previously defined in Figure 2 (low/moderate/high). Figure 3 shows the comparison between the “expert’s” opinion in an ordinal scale versus the fuzzy cognitive map values in a continuous scale. The transverse lines corresponding to 2.95 and 4.65 scores indicate the cut-off points to transform the continuous scale into an ordinal scale (low, moderate and high risks according to the “expert”), and were obtained by optimization of these limits with ROC curves (ROC area for low-moderate risk limit: 0.89, CI<sub>95%</sub> 0.809-0.978; ROC area for moderate-high risk limit: 0.87, CI<sub>95%</sub> 0.788-0.955). After resolving these limits, the fuzzy cognitive map risks calculated in continuous scale were transformed into an ordinal scale according to the following values: low risk <2.95, moderate risk from 2.95 to 4.65 and high risk >4.65. Finally, to finish the model learning and calibration stage based on the fuzzy cognitive map, its results were correlated with those obtained by the “expert”. The concordance kappa value was 0.672 (CI<sub>95%</sub> 0.553-0.791) and the C contingency coefficient corrected for grouping was 0.81 (p<0.0001).

**Model validation**

The model already calibrated in the development stage was used to predict surgical results in a validation set consisting of 360 patients, whose fuzzy cognitive map score was individually determined. Also, predicted risks for each patient were calculated by three commonly used scores: Parsonnet, Ontario and logistic EuroSCORE. Then, the precision of each model was calculated with ROC curves and compared with the Hanley-McNeil method as shown in Figure 4. The ROC area values show that the fuzzy cognitive map evidenced at least the same performance to predict postoperative cardiac surgery in-hospital mortality in the validation set, although its ROC area was the best. The ROC area for the validation set according to the “expert’s” performance was 0.767 (CI<sub>95%</sub> 0.682-0.850). Using the score range obtained with the fuzzy cognitive map, Figure 5 determines the expected mortality according to the value assigned to each patient or group of patients.

**DISCUSSION**

In this study it was possible to develop and validate a risk adjustment system based on fuzzy logic to predict cardiac surgery in-hospital mortality. This model not only mimicked “expert” results, but had at least the same performance of other risk scores usually used in our setting at the time the study was performed.

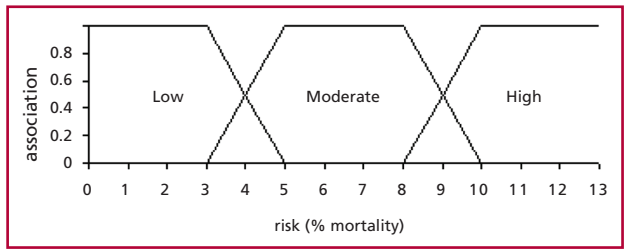


Fig. 2. Fuzzy sets used by the “expert” to assign risks.

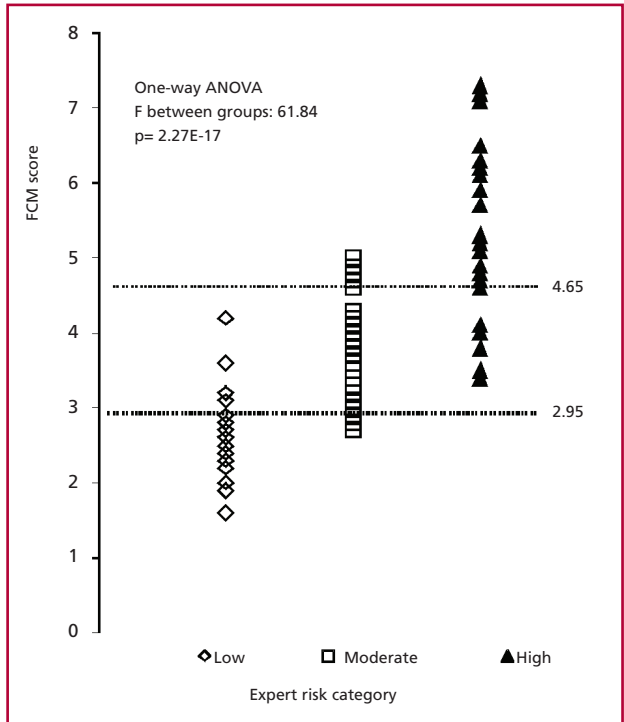
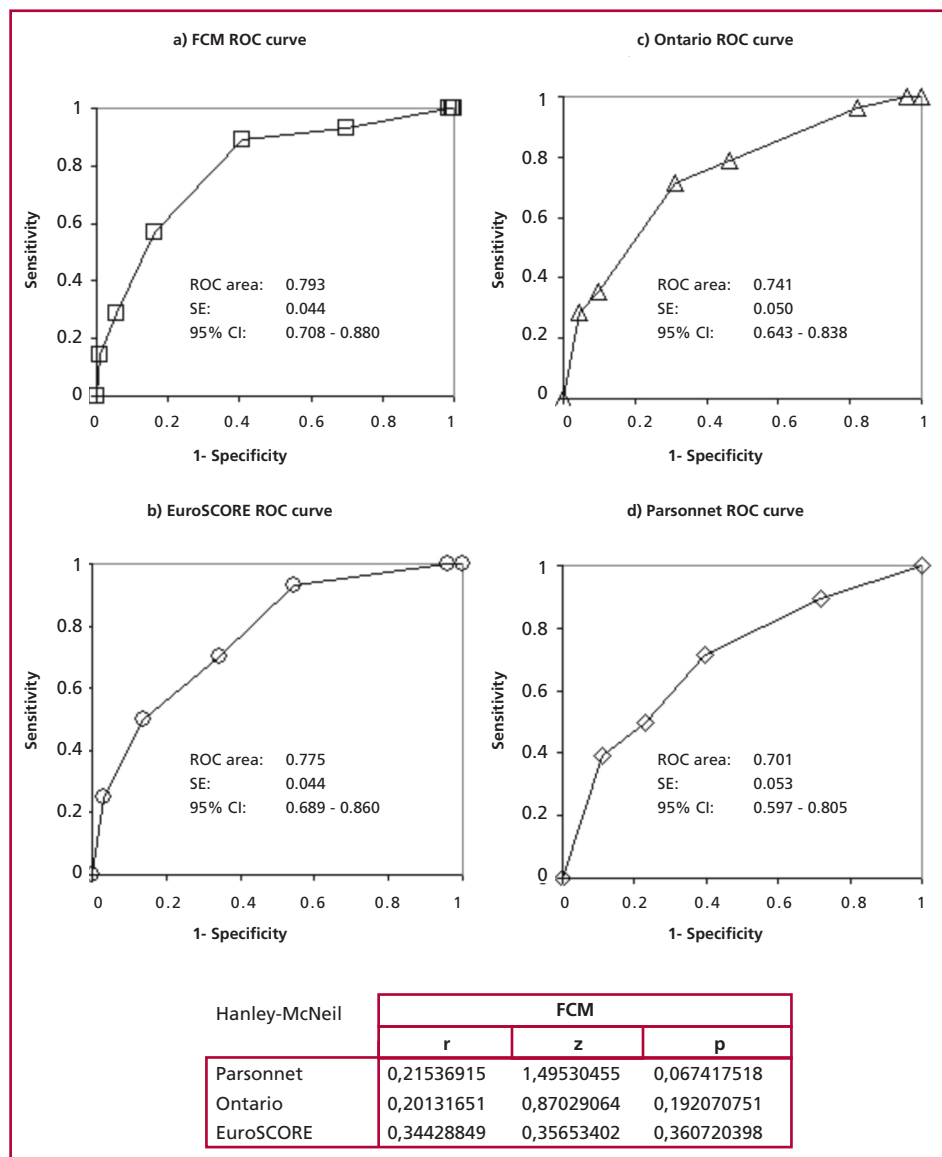


Fig. 3. Initial comparison (test set or learning and calibration set) of “expert” opinion expressed in ordinal scale versus fuzzy cognitive map (FCM) scores represented in a continuous scale. Horizontal lines corresponding to 2.95 and 4.65 scores indicate the cut-off values to transform the continuous scale into an ordinal scale (low, moderate and high risks according to the “expert”). One way analysis of variance was used for statistical analysis.

As the model based on fuzzy logic comparatively gave the best ROC area, it would potentially be possible to obtain an even better performance than that of other scores by adjusting its variables and relationships or by increasing the sample size.

The most important point of the study hypothesis is the characteristic inaccurate management of data collection in medical practice. Medical decisions consider a large volume of information from different sources, as data provided by the patient during anamnesis, physical examination, laboratory and other complementary study results, which can in turn be, incomplete, vague, unknown or even contradictory.



**Fig. 4.** Comparison of ROC curves determined for the fuzzy cognitive map (FCM) and the different risk scores in the validation set. The table at the bottom of the figure shows the correlation (r) and significant (p) values according to the Hanley-McNeil method.

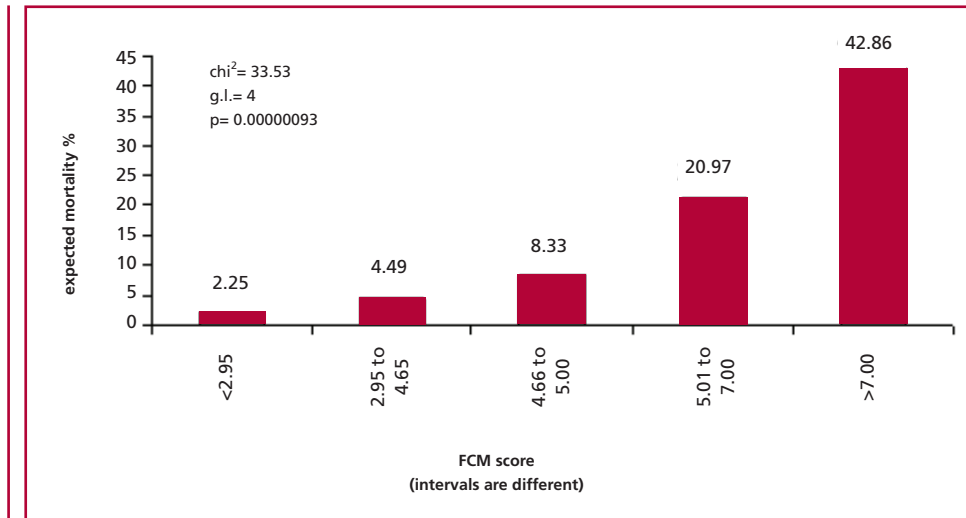
It is evident that in this context, the decision-making process requires tools capable of managing the complexity of the problem, and at the same time infer a result or an opinion.

The possibility of managing expert knowledge as if it were discreet or continuous data that can be algebraically analyzed is the fundamental advantage provided by fuzzy logic and its modeling methods, as the fuzzy cognitive model and the Hopfield artificial neural network. Use of fuzzy logic, which serves as framework for possibilistic models, is able to manage both uncertainty and imprecision in expert systems. In this case, the knowledge-based expert system has a series of rules as well as previously loaded data that must generate an associated conclusion with a certain degree of certainty or probability of occurrence. Conversely the fuzzy cognitive model is built with a series of nodes representing the relevant system concepts or

variables, and a series of connections indicating causal relationships or influences among variables. Each variable is represented by a fuzzy set which can incorporate expert knowledge. Presumably, these models follow a design similar to the human reasoning and decision-making process in its approach to treat complex systems.

The results of this study show that it is possible to use expert knowledge when this is expressed colloquially, establishing the importance of each clinical datum as having low, moderate or high influence on the expected results. Thus, the expert may transmit his knowledge in a diffuse way without being obliged to provide a defined numerical value of strength or association probability between facts. This information was used to model a system that effectively contended with other classical models based on logistic regression or Bayesian analysis. To summarize, clinical data

**Fig. 5.** Expected mortality based on the fuzzy cognitive map (FCM) score.



obtained from the direct observation of the patient entered into an ad hoc form would allow estimation of expected mortality according to a value assigned to each patient or group of patients.

There are some methodological aspects that should be discussed. Firstly, the expert knowledge is not based solely on his clinical experience, but also on all the information collected and learnt from the literature. Thus, his knowledge may probably include, even though partially, the information suggested by a great part of the literature on risk adjustment models he has consulted. Thus, a certain bias could then arise when comparing fuzzy cognitive model performance with that of other scores. A second important point is the way in which weights are assigned to the tables of influence between variables. The “expert” opinion is presented as a fuzzy set; hereafter, the assigned weight has to be adjusted manually (calibration) until the most stable output of the Hopfield network is obtained. This process is performed by “test and error” as there is no alternative method or algorithm to solve it.

The model developed in this work constitutes a true expert system to establish the risk of cardiac surgery, only requiring data or information input provided by the perception of the physician in his usual uncertainty context. It does not aim to replace his clinical judgment, but serve as a support system for decision-making.

Most medical research studies with the application of fuzzy logic are usually associated to the area of artificial intelligence. Fuzzy logic has been used to describe nervous system anatomy (18), as a support system for decision-making in palliative care (19), to predict bleeding risk after amygdlectomy, (20) to monitor mechanical ventilation in children, (30) in the analysis of neurological tremor, (31) for image processing, (30, 32) in cardiovascular research and characterization of different kinds of stroke, (33) and

to monitor and control anesthesia, (34) etc. Moreover, publications using fuzzy cognitive models include models for the treatment of diabetes, (35) diagnosis of urinary disorders and learning difficulties, (36-37) acute abdominal pain expert systems, (38) and medical diagnosis. (39)

#### Limitations

The temporal and possibly regional validity of a score requires constant reevaluation of the risk adjustment system. Thus, an adequate score to evaluate a group of surgical patients at a certain moment could overestimate or underestimate the expected risk of another group in the future, when the standards of quality demand better results. That is why modeling to predict risk must be an iterative process over time to adapt the system to new requirement and quality levels. Another limitation is that the fuzzy cognitive model works as a “black box”, i.e. its functioning is not evident to the user and hence it is not possible to follow the evolution of the process to the final result, which means that the system does not explain or justify its opinion. Finally, modeling of these systems is based on expert knowledge, which may also be incorrect or of lower quality than knowledge acquired by other methods, as the multivariate statistical analysis.

#### CONCLUSIONS

The possibility of having a methodology to take advantage of expert knowledge was investigated using fuzzy logic and the implementation of an expert system. In this study it was possible to develop and validate a risk adjustment system based on fuzzy logic to predict cardiac surgery in-hospital mortality. The model not only mimicked “expert” results, but had at least the same performance as other scores usually employed in our setting. At a larger scale, fuzzy logic and fuzzy cognitive models could be useful to develop distrib-

uted systems capable of combining information from different sources. Finally, models based on fuzzy logic could be part of multiple classification systems that also include a classical statistical approach, diagnostic algorithms and decision trees which might collectively improve the diagnostic precision of the model (40).

#### Conflicts of interest

None declared

(See author's conflicts of interest forms in the web / Supplementary Material)

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