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Family Refusal to Consent Donation: Retrospective Quantitative Analysis of Its Increasing Tendency and the Associated Factors Over the Last Decade at a Spanish Hospital

José Manuel Viñuela-Prieto[a,b*], Maria Carmen Escarpa Falcón[a], Francisco Javier Candel[a,c], Alonso Mateos Rodríguez, MD[d,e], Juan Ignacio Torres González[d,f], and Francisco del Río Gallegos[a,d]

[a]Transplant Coordination Department, Hospital Clínico San Carlos, Madrid, Spain; [b]Neurosurgery Department, University Hospital La Paz, Madrid, Spain; [c]Health Research Institute, Hospital Clínico San Carlos, Madrid, Spain; [d]Regional Organization for Transplant Coordination (ORCT), Community of Madrid Health Service (SERMAS), Madrid, Spain; [e]School of Medicine, Francisco de Vitoria University, Madrid, Spain; and [f]Nursing, Physiotherapy and Podiatry School, Complutense University, Madrid, Spain

ABSTRACT

Background. Organ and tissue recovery remains limited by several factors. This study retrospectively analyzes the factors associated with family refusal to consent to donation at a high-donor-volume Spanish hospital.

Methods. Data regarding the annual number of potential donors and family refusal rates at hospital and regional levels were retrieved from 2008 to 2017. Descriptive, bivariate, and multivariate analyses were performed to detect those factors independently associated with family refusal. Results were cross-validated using the data from years 2018 and 2019 as the validation group. To explore potential inter-relations between factors a Multiple Correspondence Analysis was performed.

Results. A total of 601 family interviews for petition of consent were conducted between 2008 and 2017, 531 (88.4%) resulted in acceptance and 70 (11.6%) resulted in refusal of the donation. Lesser experience of the interviewers (odds ratio [OR], 2.980; $P = .001$), donation after brain death (OR, 2.485; $P = .013$), number of interviews conducted per family (OR, 1.892; $P < .001$), age of the main decision maker (OR, 1.025; $P = .045$), and high or middle attributed cultural levels (OR, 0.142; $P < .001$ and OR, 0.199; $P < .001$ respectively) were observed to be independently associated with the family final decision. The logistic regression model displayed good predictive power for both derivation and validation cohorts, with an overall predictive accuracy of 80.9% (95% confidence interval, 0.747-0.870; $P < .001$) and 74.4% (95% confidence interval, 0.635-0.854; $P = .001$), respectively.

Conclusions. Transplant coordination team members having a thorough knowledge of the family decision mechanisms may be a key factor in donation process optimization.

FAMILY refusal to consent for the recovery of the deceased's organs is one of the most important factors limiting donation levels [1]. Countries with donor intention registrations and either presumed or informed consent policies are affected by family refusal, because in everyday practice, almost no significant differences exist between them [2,3]. In fact, in most cases in Spain, if there is a contradiction between the wishes of the deceased and the family, the decision of the latter is usually respected. Therefore, family refusal rate represents an important parameter that many national centers for transplant coordination around the world register and analyze [4,5].

*Address correspondence to Dr José Manuel Viñuela-Prieto, Transplant Coordination Department, Hospital Clínico San Carlos, Avda. Profesor Martín Lagos, s/n. 28040, Madrid, Spain. Tel: +34 659 396 490; Fax: +34 91 330 3478. E-mail: jovinuel@ucm.es

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Family refusal rate variations and tendencies through time may not only be influenced by the technological development of medico-surgical procedures, because they also depend on many psychosocial and cultural factors [6]. At the time of the requested interview, the deceased's opinion expressed in life and the family's opinion interact to render a final decision [6,7]. However, during the interview, several other factors might contribute to either favor or disfavor the family's consent. The perceived quality of the medical assistance given to the donor, the correct timing and form of the information given, the type of illness, and the time between the announcement of the death to the family and the request of donation have shown to be related to the rates of family refusal [2,8]. A thorough understanding of these factors will allow transplant coordination team members to better help families in the process of taking donation-related decisions [7].

In Spain, over the last years, refusal rates have progressively decreased, remaining one of the lowest in Europe [4]. The Spanish donation system is structured into 3 levels of coordination—hospital, regional, and national. The Hospital Clínico San Carlos of Madrid, Spain is a tertiary hospital with over 800 inpatient beds that has been working with donors after circulatory death (DCD) since 1989. The Regional Organization for Transplant Coordination (Organización Regional de Coordinación de Transplantes [ORCT]) is the organization in charge of the coordination and supervision of the donation programs of all the hospitals located in the Autonomous Region of Madrid.

Permanent education and training efforts to ensure the availability of highly qualified personnel in the transplant coordination teams are cornerstones of the donation system. In that context, an evidence-based knowledge of the family refusal phenomenon is essential for any coordination team aimed at reaching their highest performance level. This study aims to analyze critical factors associated with family refusal and their tendency over the last decade in the context of a high-donor-volume Spanish hospital.

MATERIALS AND METHODS

Study design

We performed a retrospective study of data records at our center, which is a high-volume, tertiary hospital with one of the highest proportions of DCD in the country. The project was undertaken with institutional and ethics committee approval. The sample consisted on all the potential donors registered in our center during the study period, and the reference population was considered by retrieving data at a regional level. The presence of a contraindication for donation, such as an active neoplasia, a positive drug test, or an infectious disease detected during the evaluation, determined the exclusion from sample. Only lost donors owing to family denial and actual donors were considered to construct the sample.

Regarding donor origin, in the city of Madrid potential donors may be brought to the hospital either by the prehospital emergency service attending patients in the streets and public establishments (SAMUR ["Servicio de Asistencia Municipal de Urgencia y Rescate del Ayuntamiento de Madrid" - Municipal Emergency Assistance and Rescue Service of the City of Madrid]) or by those attending patients in their homes (SUMMA 112 ["Servicio de Urgencias Médicas de Madrid" - Medical Emergency Service of Madrid]).

We considered 2 different types of interviewers based on the years of experience each one had on conducting interviews to request donation. "Expert" interviewers were those who had more than 5 years of experience and "novice" interviewers were those who had less than 5 years of experience.

Data Collection

Data regarding potential donors and percentages of family refusal at a regional level from 2008 to 2017 were obtained from the ORCT database. Data regarding family interviews requesting an organ donation from 2008 to 2017 were collected from the Transplant Coordination Department's records in our center. Data from 2018 and 2019 were retrieved likewise to serve as validation group.

Statistical Analysis

In addition to descriptive statistics for all variables, bivariate analyses between family final decision (donation or refusal) and the different variables were carried out. The Student t test and analysis of variance were used to compare normally distributed continuous variables. In the case of non-normally distributed variables, Mann-Whitney U and Kruskal-Wallis H tests were used. Comparison of proportions for categorical variables was performed either by Fisher exact test or χ^2 test. Odds ratio (OR) and 95% confidence interval (CI) were calculated for all valid associations. Statistically significant association level was considered at a $P \leq .05$.

Multivariate regression analyses were used to produce adjusted results for selected variables associated with family refusal. Logistic regression models (backward stepwise) were performed using the family's final decision as the dependent variable and including those significantly ($P \leq .10$) associated in the bivariate analysis as independent variables. Pairwise correlations between all other covariates were subsequently explored. For significantly correlated covariates ($P \leq .05$), 1 covariate from the pair was excluded from the regression models. To identify the variables independently associated with family refusal, a significance level of $P \leq .05$ was considered. Covariates that were not statistically significant were removed from the models.

The regression model fitted on the 2008 to 2017 group was cross-validated using the data from years 2018 and 2019 as validation group. The predictive power of the logistic regression model to discriminate between family acceptance and refusal of donation when applied to both groups was expressed as the area under the receiver-operating characteristics curve.

Finally, potential inter-relations between the different factors involved in the family decision were explored from a multivariate approach by using Multiple Correspondence Analysis [9-11]. To perform Multiple Correspondence Analysis, by means of the Optimal Scaling algorithm included in the SPSS Version 20 package (IBM, Chicago, Ill, Unites States), final family decision (donation or refusal) and all the variables significantly ($P \leq .05$) associated with it were introduced. Associations between categories suggested by the Multiple Correspondence Analysis (MCA) were subsequently analyzed by χ^2 test.

All statistical analyses were performed using SPSS Version 20.

RESULTS

Regional Reference Data

Results regarding hospital and regional levels, including yearly family refusal rates are summarized in Table 1.

Table 1. Hospital and Regional Level Data Regarding the Total Number of Potential Donors and the Family Refusal Rates Obtained During the 2008 to 2017 Period

	HCSC			ORCT		
	Potential Donors (n)	Family Refusals (n)	Family Refusal rate (%)	Potential Donors (n)	Family Refusals (n)	Family Refusal Rate (%)
2008	59	1	1.7	246	37	15.1
2009	69	6	8.7	262	39	14.9
2010	64	5	7.8	269	38	14.1
2011	56	5	8.9	264	49	18.5
2012	59	6	10.2	275	39	14.2
2013	60	7	11.7	262	37	14.2
2014	64	10	15.6	304	66	21.7
2015	57	10	17.5	279	53	19
2016	64	12	18.8	287	61	21.3
2017	49	8	16.3	277	46	16.6
Total	601	70	11.6	2725	465	17.1

HCSC, Hospital Clínico San Carlos; ORCT, Organización Regional de Coordinación de Transplantes (Regional Organization for Transplant Coordination).

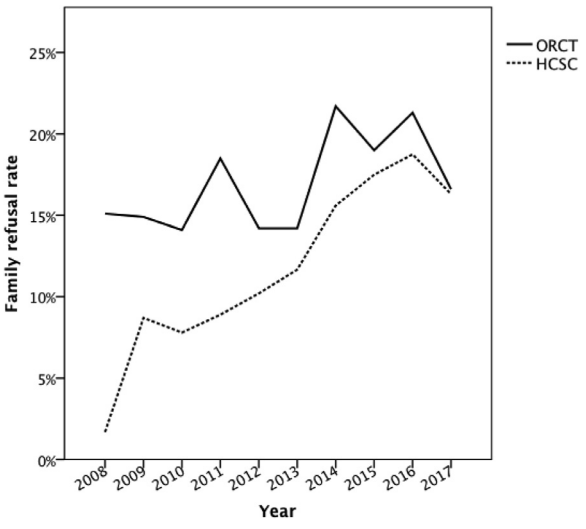

Fig 1. Comparison of the evolution followed by family refusal rates for hospital and regional levels during the 2008 to 2017 period. HCSC, Hospital Clínico San Carlos; ORCT, Organización Regional de Coordinación de Transplantes (Regional Organization for Transplant Coordination).

The increasing trend in the percentage of refusal of donation observed in our hospital over the last decade, along with the family refusal rates registered regionally, are both depicted in Fig 1.

Sample Characteristics and Descriptive Statistics

A total of 621 donor-eligible individuals were registered from 2008 to 2017. Of those, 8 (1.3%) were excluded donors, 3 (0.5%) were excluded owing to the finding of a tumor-related contraindication after initial evaluation in the emergency room, 5 (0.8%) were lost owing to the absence of a decision-making family member, and 4 (0.6%) were lost owing to excessive ischemic times. Thus, the sample included a total of 601 family interviews for petition of consent conducted between 2008 and 2017, 531 (88.4%) resulted in acceptance, and 70 (11.6%) resulted in refusal of the donation.

Complete sample characteristics and interviewers' experience results and its yearly distribution over the 2008 to 2017 period are summarized in Table 2.

Bivariate and Multivariate Analysis of Family Decision

Table 3 shows the level of association between the different variables and the family's final decision (donation or refusal).

Logistic regression was performed to produce adjusted results for selected variables associated with family refusal. Independent variables associated with family refusal selected by the logistic regression model are summarized in Table 4.

The logistic regression model displayed good predictive power as the corresponding receiver operating characteristic curves shown (Fig 2) for both derivation and validation cohorts. A comparison of basic characteristics between derivation and validation cohorts is summarized in Table 5.

Inter-relation Between Factors

Figure 3 summarizes the main results of MCA; to achieve a correct interpretation, it should be noted that those categories close to one another would tend to be associated more frequently and that the categories located closer to the axis intersection would include a greater number of cases. Dimension 1 differentiated both the family's refusal (right/positive side of the axis) and the family's consent to donate (left/negative side of the axis).

The categories potentially associated with family consent would be, between others, donor age <45 years and decision-maker age <35 years or 35 to 45 years. Bivariate analysis showed a significant relationship between these categories ($P < .001$ and $P = .010$, respectively). Correlations were also explored for donor age 45 to 50 years and 51 to 55 years with a decision-maker age 46 to 55 years ($P = .790$ and $P < .001$, respectively). The categories for both donors and decision-making next-of-kin age >55 years were closer to the refusal pole of

Table 2. Sample Characteristics and Descriptive Statistics Including Their Yearly Distribution Over the 2008 to 2017 Period

Variables*	TOTAL	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Test Statistic (Df)	*P* Value†
No. of potential donors	601	59	69	64	56	59	60	64	57	64	49		
Family refusal	70 (11.6)	1 (1.7)	6 (8.7)	5 (7.8)	5 (8.9)	6 (10.2)	7 (11.7)	10 (15.6)	10 (17.5)	12 (18.8)	8 (16.3)	14.795 (9)	.097
Cause of refusal													
Deceased's opposition to donation in life	15 (2.5)	0 (0)	3 (4.3)	2 (3.1)	2 (3.6)	1 (1.7)	0 (0)	2 (3.1)	2 (3.5)	0 (0)	3 (6.1)	11.744 (9)	.228
Family's refusal of consent	55 (9.1)	1 (1.7)	3 (4.3)	3 (4.7)	3 (5.3)	5 (8.5)	7 (11.7)	8 (12.5)	8 (14)	12 (18.8)	5 (10.2)	11.744 (9)	.228
Donor's sex: female	137 (22.8)	17 (28.8)	18 (26.1)	16 (25)	17 (30.4)	7 (11.9)	11 (18.3)	11 (17.2)	13 (22.8)	17 (26.6)	10 (20.4)	10.138 (9)	.339
Donor type: DBD	127 (21.1)	17 (28.8)	18 (26.1)	14 (21.9)	14 (25)	4 (6.8)	8 (13.3)	11 (17.2)	11 (19.3)	14 (21.9)	16 (32.7)	17.747 (9)	.038
Donor's age	48.43 ± 11.61	44.14 ± 11.16	45.19 ± 13.33	47.17 ± 13.25	47.73 ± 9.72	47.69 ± 9.00	49.33 ± 9.58	51.16 ± 10.21	53.84 ± 10.40	48.52 ± 12.44	50.37 ± 13.31	3.734 (9)	<.001
<45 y	207 (34.4)	29 (49.2)	31 (44.9)	25 (39.1)	21 (37.5)	21 (35.6)	18 (30)	15 (23.4)	11 (19.3)	23 (35.9)	13 (26.5)	21.054 (9)	.012
45-50 y	125 (20.8)	17 (28.8)	14 (20.3)	17 (26.6)	18 (32.1)	15 (25.4)	12 (20)	13 (20.3)	7 (12.3)	7 (10.9)	5 (10.2)	18.403 (9)	.031
51-55 y	128 (21.3)	6 (10.2)	13 (18.8)	10 (15.6)	9 (16.1)	12 (20.3)	15 (25)	19 (29.7)	16 (28.1)	14 (21.9)	14 (28.6)	13.078 (9)	.159
>55 y	141 (23.5)	7 (11.9)	11 (15.9)	12 (18.8)	8 (14.3)	11 (18.6)	15 (25)	17 (26.6)	23 (40.4)	20 (31.2)	17 (34.7)	25.852 (9)	.002
Donor's origin													
SAMUR	167 (27.8)	17 (28.8)	21 (30.4)	20 (31.2)	15 (26.8)	19 (32.2)	18 (30)	20 (31.2)	13 (22.8)	17 (26.6)	7 (14.3)	6.989 (9)	.638
SUMMA 112	275 (45.8)	25 (42.4)	28 (40.6)	27 (42.2)	26 (46.4)	36 (61)	30 (50)	31 (48.4)	24 (42.1)	27 (42.2)	21 (42.9)	8.313 (9)	.503
ICU	125 (20.8)	15 (25.4)	16 (23.2)	11 (17.2)	10 (17.9)	4 (6.8)	9 (15)	13 (20.3)	16 (28.1)	14 (21.9)	17 (34.7)	17.687 (9)	.039
Other hospital departments	34 (5.7)	2 (3.4)	4 (5.8)	6 (9.4)	5 (8.9)	0 (0)	3 (5)	0 (0)	4 (7)	6 (9.4)	4 (8.2)	13.207 (9)	.153
Time from hospitalization to last interview													
<75 min	156 (27.6)	14 (26.4)	21 (32.3)	15 (27.3)	11 (21.6)	21 (37.5)	13 (21.7)	20 (33.3)	16 (29.1)	14 (22.2)	11 (22.9)	7.987 (9)	.535
75-120 min	108 (19.1)	11 (20.8)	12 (18.5)	6 (10.9)	8 (15.7)	12 (21.4)	15 (25)	9 (15)	11 (20)	19 (30.2)	5 (10.4)	12.451 (9)	.189
121-780 min	161 (28.4)	15 (28.3)	15 (23.1)	19 (34.5)	19 (37.3)	19 (33.9)	23 (38.3)	18 (30)	12 (21.8)	10 (15.9)	11 (22.9)	14.452 (9)	.107
>780 min	141 (24.9)	13 (24.5)	17 (26.2)	15 (27.3)	13 (25.5)	4 (7.1)	9 (15)	13 (21.7)	16 (29.1)	20 (31.7)	21 (43.8)	24.365 (9)	.004
Interviews conducted per family	2.17 ± 1.38	1.79 ± 1.04	1.98 ± 1.66	2.03 ± 1.22	2.15 ± 1.32	2.32 ± 1.39	2.63 ± 1.35	2.35 ± 1.43	2.23 ± 1.81	2.26 ± 1.27	1.94 ± 0.85	1.856 (9)	.056
1	230 (38.9)	28 (48.3)	35 (53)	25 (39.1)	22 (40.7)	16 (27.1)	14 (23.3)	24 (38.1)	27 (47.4)	23 (37.1)	16 (32.7)	19.965 (9)	.018
2	186 (31.4)	20 (34.5)	18 (27.3)	26 (40.6)	15 (27.8)	25 (42.4)	14 (23.3)	15 (23.8)	15 (26.3)	15 (24.2)	23 (46.9)	18.096 (9)	.034
3 or more	176 (29.7)	10 (17.2)	13 (19.7)	13 (20.3)	17 (31.5)	18 (30.5)	32 (53.3)	24 (38.1)	15 (26.3)	24 (38.7)	10 (20.4)	33.184 (9)	.001
Interviewer: novice	151 (25.1)	0 (0)	0(0)	0(0)	0(0)	8 (13.6)	29 (48.3)	25 (39.1)	29 (50.9)	32 (50)	28 (57.1)	179.048 (9)	<.001
Main decision maker													
Spouse/partner	275 (46.3)	23 (39.7)	26 (39.4)	34 (53.1)	26 (47.3)	34 (57.6)	24 (40.7)	25 (39.1)	31 (54.4)	28 (44.4)	24 (49)	10.387 (9)	.320
Sibling	133 (22.4)	15 (25.9)	16 (24.2)	11 (17.2)	12 (21.8)	11 (18.6)	18 (30.5)	18 (28.1)	10 (17.5)	12 (19)	10 (20.4)	6.752 (9)	.663
Son/daughter	88 (14.8)	9 (15.5)	11 (16.7)	8 (12.5)	8 (14.5)	6 (10.2)	8 (13.6)	13 (20.3)	8 (14)	9 (14.3)	8 (16.3)	3.222 (9)	.955
Parent	88 (14.8)	10 (17.2)	11 (16.7)	11 (17.2)	8 (14.5)	5 (8.5)	9 (15.3)	6 (9.4)	8 (14)	14 (22.2)	6 (12.2)	7.151 (9)	.621
Other	10 (1.7)	1 (1.7)	2 (3)	0 (0)	1 (1.8)	3 (5.1)	0 (0)	2 (3.1)	0 (0)	0 (0)	1 (2)	9.856 (9)	.362
Family members present at the interview	3.55 ± 1.74	3.71 ± 1.79	3.88 ± 1.83	3.66 ± 2.26	3.82 ± 1.61	3.51 ± 1.60	3.55 ± 1.69	3.52 ± 1.57	3.23 ± 1.64	3.29 ± 1.64	3.33 ± 1.53	0.969 (9)	.465
2 or less	183 (30.8)	17 (29.3)	16 (23.9)	29 (45.3)	11 (20)	18 (30.5)	14 (23.3)	18 (29)	21 (36.8)	20 (31.7)	19 (38.8)	15.025 (9)	.090
3	153 (25.8)	15 (25.9)	14 (20.9)	8 (12.5)	15 (27.3)	15 (25.4)	19 (31.7)	17 (27.4)	16 (28.1)	21 (33.3)	13 (26.5)	10.031 (9)	.348
4	130 (21.9)	11 (19)	22 (32.8)	10 (15.6)	11 (20)	14 (23.7)	14 (23.3)	15 (24.2)	11 (19.3)	13 (20.6)	9 (18.4)	7.590 (9)	.576
5 or more	128 (21.5)	15 (25.9)	15 (22.4)	17 (26.6)	18 (32.7)	12 (20.3)	13 (21.7)	12 (19.4)	9 (15.8)	9 (14.3)	8 (16.3)	9.786 (9)	.368
Main decision maker's age	46.41 ± 13.01	44.26 ± 13.60	43.75 ± 11.33	45.95 ± 13.26	45.32 ± 12.62	45.53 ± 10.32	48.81 ± 12.94	45.28 ± 13.61	51.43 ± 13.29	48.68 ± 14.13	45.40 ± 13.69	1.951 (9)	.043
<35 y	117 (20.5)	14 (24.1)	15 (24.6)	10 (16.4)	9 (17)	10 (17.2)	9 (15.3)	15 (24.6)	9 (17)	14 (23.7)	12 (25.5)	5.636 (9)	.776
35-45 y	172 (30.2)	24 (41.4)	24 (39.3)	25 (41)	20 (37.7)	18 (31)	18 (30.5)	15 (24.6)	7 (13.2)	11 (18.6)	10 (21.3)	24.368 (9)	.004
46-55 y	171 (30)	8 (13.8)	15 (24.6)	17 (27.9)	16 (30.2)	22 (37.9)	18 (30.5)	21 (34.4)	20 (37.7)	16 (27.1)	18 (38.3)	13.836 (9)	.128
>55 y	110 (19.3)	12 (20.7)	7 (11.5)	9 (14.8)	8 (15.1)	8 (13.8)	14 (23.7)	10 (16.4)	17 (32.1)	18 (30.5)	7 (14.9)	16.984 (9)	.049
Initial perceived attitude													
Receptive	480 (81.8)	50 (86.2)	52 (77.6)	54 (87.1)	52 (94.5)	42 (72.4)	51 (86.4)	46 (73)	43 (79.6)	47 (75.8)	43 (87.8)	19.077 (9)	.025
Unreceptive	95 (16.2)	7 (12.1)	13 (19.4)	7 (11.3)	3 (5.5)	16 (27.6)	6 (10.2)	13 (20.6)	10 (18.5)	15 (24.2)	5 (10.2)	19.492 (9)	.021
Aggressive	12 (2)	1 (1.7)	2 (3)	1 (1.6)	0 (0)	0 (0)	2 (3.4)	4 (6.3)	1 (1.9)	0 (0)	1 (2)	10.409 (9)	.318
Attributed cultural level													
High	214 (36.5)	25 (43.1)	27 (41.5)	17 (27)	27 (50)	21 (36.2)	16 (27.1)	15 (23.8)	23 (41.8)	19 (30.6)	24 (49)	20.007 (9)	.018
Middle	332 (56.7)	28 (48.3)	34 (52.3)	43 (68.3)	23 (42.6)	33 (56.9)	40 (67.8)	41 (65.1)	30 (54.5)	37 (59.7)	23 (46.9)	16.977 (9)	.049
Low	40 (6.8)	5 (8.6)	4 (6.2)	3 (4.8)	4 (7.4)	4 (6.9)	3 (5.1)	7 (11.1)	2 (3.6)	6 (9.7)	2 (4.1)	5.144 (9)	.822
Relative or friend in the sanitary field	18 (3)	2 (3.4%)	2 (2.9)	1 (1.6)	3 (5.4)	0 (0)	2 (3.3)	1 (1.6)	3 (5.3)	3 (4.7)	1 (2)	5.653 (9)	.774

DBD, donors after brain death; Df, degrees of freedom; ICU, intensive care unit; SAMUR, Servicio de Asistencia Municipal de Urgencia y Rescate del Ayuntamiento de Madrid (Municipal Emergency Assistance and Rescue Service of the City of Madrid); SUMMA 112, Servicio de Urgencias Médicas de Madrid (Medical Emergency Service of Madrid).

* Values are expressed as n (%) or mean ± standard deviation.

† Analysis of variance, Kruskal-Wallis H, or χ^2 test.

Table 3. Bivariate Analysis of Family's Final Decision

Variables*	Actual Donors (n = 531)	Family Refusal (n = 70)	OR (95% CI)	*P* Value†
Donor's sex: female	116 (21.8)	21 (30)	1.533 (0.884-2.660)	.126
Donor type: DBD	105 (19.8)	22 (31.4)	1.860 (1.075-3.216)	.025
Donor's age	48.08 ± 11.70	51.06 ±1 0.59	-	0.044
<45 y	190 (35.8)	17 (24.3)	0.576 (0.324-1.022)	0.057
45-50 y	109 (20.5)	16 (22.9)	1.147 (0.632-2.082)	.652
51-55 y	113 (21.3)	15 (21.4)	1.009 (0.549-1.852)	.977
>55 y	119 (22.4)	22 (31.4)	1.587 (0.921-2.735)	.094
Donor's origin				
SAMUR	145 (27.3)	22 (31.4)	1.220 (0.711-2.093)	.469
SUMMA 112	250 (47.1)	25 (35.7)	0.624 (0.372-1.048)	.073
ICU	108 (20.3)	17 (24.3)	1.256 (0.699-2.257)	.444
Other hospital departments	28 (5.3)	6 (8.6)	1.684 (0.672-4.223)	.262
Time from hospitalization to last interview				
<75 min	148 (29.4)	8 (12.7)	0.349 (0.162-0.751)	.005
75-120 min	97 (19.3)	11 (17.5)	0.885 (0.445-1.760)	.728
121-780 min	141 (28)	20 (31.7)	1.194 (0.679-2.101)	.538
>780 min	117 (23.3)	24 (38.1)	2.030 (1.173-3.515)	.010
Interviews conducted per family	2 ± 1.164	3.5 ± 2.055	-	< .001
One	219 (41.6)	11 (16.7)	0.280 (0.143-0.548)	< .001
Two	175 (33.3)	11 (16.7)	0.401 (0.205-0.786)	.006
Three or more	132 (25.1)	44 (66.7)	5.970 (3.450-10.331)	< .001
Interviewer: novice	125 (23.5)	26 (37.1)	1.919 (1.136-3.243)	.014
Main decision maker				
Spouse/partner	241 (45.7)	34 (50.7)	1.223 (0.735-2.033)	.438
Sibling	121 (23)	12 (17.9)	0.732 (0.380-1.412)	.350
Son/daughter	79 (15)	9 (13.4)	0.880 (0.419-1.848)	.735
Parent	76 (14.4)	12 (17.9)	1.295 (0.662-2.530)	.449
Other	10 (1.9)	0 (0)	-	.255
Family members present at the interview	3.56 ± 1.74	3.51 ± 1.74	-	.817
2 or less	161 (30.6)	22 (32.8)	1.111 (0.646-1.912)	.703
3	135 (25.6)	18 (26.9)	1.067 (0.601-1.895)	.826
4	120 (22.8)	10 (14.9)	0.595 (0.295-1.201)	.144
5 or more	111 (21.1)	17 (25.4)	1.274 (0.707-2.296)	.419
Main decision maker's age	45.86 ± 12.47	51.02 ± 16.23	-	.019
<35 y	106 (20.8)	11 (18)	0.836 (0.421-1.662)	.610
35-45 y	159 (31.2)	13 (21.3)	0.596 (0.314-1.132)	.110
46-55 y	155 (30.5)	16 (26.2)	0.812 (0.445-1.481)	.496
>55 y	89 (17.5)	21 (34.4)	2.478 (1.393-4.405)	.002
Initial perceived attitude				
Receptive	459 (87.8)	21 (32.8)	0.068 (0.038-0.122)	< .001
Unreceptive	63 (12)	32 (50)	7.302 (4.186-12.735)	< .001
Aggressive	1 (0.2)	11 (17.2)	108.340 (13.719-855.593)	< .001
Attributed cultural level				
High	199 (38.2)	15 (23.1)	0.485 (0.265-0.888)	.017
Middle	299 (57.4)	33 (50.8)	0.766 (0.457-1.283)	.310
Low	23 (4.4)	17 (26.2)	7.668 (3.833-15.340)	< .001
Relative or friend in the sanitary field	15 (2.8)	3 (4.3)	1.540 (0.435-5.460)	.500

CI, confidence interval; DBD, donors after brain death; ICU, intensive care unit; OR, odds ratio; SAMUR, Servicio de Asistencia Municipal de Urgencia y Rescate del Ayuntamiento de Madrid (Municipal Emergency Assistance and Rescue Service of the City of Madrid); SUMMA 112, Servicio de Urgencias Médicas de Madrid (Medical Emergency Service of Madrid).

* Values are expressed as n (%) or mean ± standard deviation.

† Analysis of variance, Kruskal-Wallis H, or χ^2 test.

Table 4. Adjusted Variables Associated With Family Refusal Rendered by the Logistic Regression Model (Nagelkerke $R^2 = 0.320$; $P < .001$. Hosmer & Lemeshow: $P = .543$)

Variables	OR (95% CI)	*P* Value
Novice interviewer	2.980 (1.548-5.738)	.001
DBD	2.485 (1.212-5.094)	.013
No. of interviews conducted per family	1.892 (1.544-2.318)	< .001
Main decision maker's age	1.025 (1.001-1.050)	.045
High attributed cultural level	0.142 (0.051-0.398)	< .001
Middle attributed cultural level	0.199 (0.082-0.484)	< .001

CI, confidence interval; DBD, donors after brain death; OR, odds ratio.

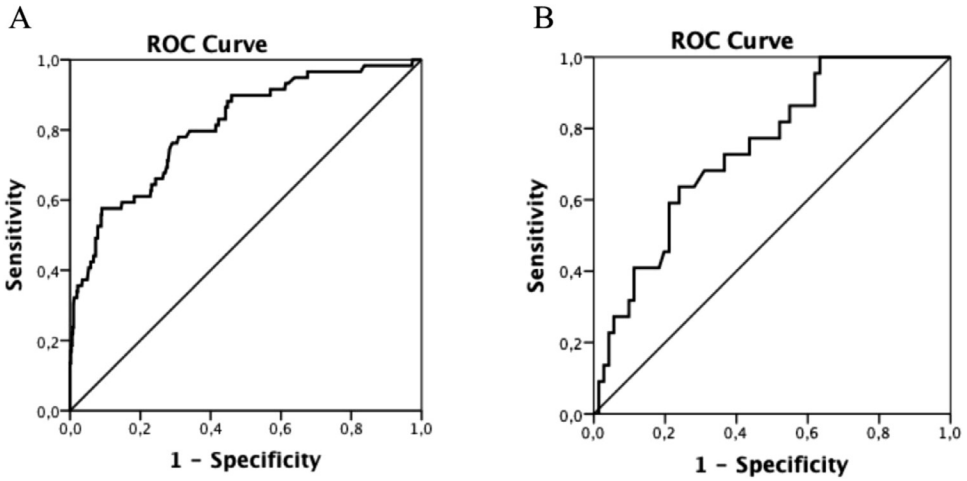

Fig 2. Receiver operator characteristic (ROC) curves obtained for the regression model on the derivation (A) and validation (B) groups. Overall predictive accuracies of 80.9% (95% confidence interval, 0.747-0.870; $P < .001$) and 74.4% (95% confidence interval, 0.635-0.854; $P = .001$) were respectively obtained.

Dimension 1 and the relative closeness between them came to represent a significant correlation level ($P < .001$).

Other categories located in the negative part of Dimension 1 were initial receptiveness to donation, high cultural level, and achievement of a final decision on the first interview. These 3 categories already showed a significant association with the family consent in the bivariate analysis. Additionally, the graphical representation pointed out the statistically significant associations between the 3 categories ($P < .001$ in all cases). Despite the relative closeness of these 3 categories to the category representing a decision-maker age <35 years, no significant associations were observed ($P = .582$, $P = .402$, and $P = .653$, respectively).

The categories depicting the DCD and time <75 minutes and 75 to 120 minutes from hospitalization to last interview fell on to the same positive part of the axis for Dimension 1. The association between the 2 time categories and the DCD were statistically significant ($P < .001$ for both associations). On the opposite side of the axis, donors after brain death (DBD) and time from hospitalization to last interview >780 minutes were located close to one another, thus revealing a significant association between them ($P < .001$).

On the right side of the axis corresponding to Dimension 1, relatively close to family refusal, 3 categories were located closely: low cultural level, unreceptiveness to donation, and ≥3 interviews to reach a final decision. The associations between family refusal and these 3 categories were shown to be significant on the bivariate analysis. Because the graphical representation of the categories suggested, significant associations were observed between them ($P < .001$, $P < .001$, and $P = .001$ for low cultural level vs ≥3 interviews).

Aggressiveness appeared to be such a strong, yet scarce, factor associated with family refusal located by its own on the right upper corner of the graph. Nevertheless, significant associations were observed between aggressiveness, low cultural level, and ≥3 interviews ($P < .001$ in both cases).

DISCUSSION

This study analyzes the increasing trend in family refusal rates over the last decade and its associated factors in a tertiary Spanish hospital. Moreover, we explored the inter-relations existing between the different relevant factors by means of MCA. Family refusal has been identified as one of the most important factors limiting donation rates [1]. Therefore, to address the increasing demand of organs and tissues for transplantation, a comprehensive understanding of the environment in which family decision takes place is of utmost importance.

Table 5. Comparison of Derivation and Validation Cohorts

Variables*	Derivation Cohort	Validation Cohort	*P* Value†
No. of potential donors	601 (86.1)	97 (13.9)	
Family refusal	70 (11.6)	23 (23.7)	.001
Donor's sex: female	137 (22.8)	27 (27.8)	.277
Donor type: DBD	127 (21.1)	25 (25.8)	.304
Donor's age	48.43 ± 11.61	50.86 ± 12.32	.058
Time from hospitalization to last interview			.059
<75 min	156 (27.6)	22 (22.7)	
75-120 min	108 (19.1)	16 (16.5)	
121-780 min	161 (28.4)	22 (22.7)	
>780 min	141 (24.9)	37 (38.1)	
Interviews conducted per family	2.17 ± 1.38	2.03 ± 0.93	.201
Interviewer: novice	151 (25.1)	31 (32)	.155
Main decision maker			.471
Spouse/partner	275 (46.3)	43 (44.8)	
Sibling	133 (22.4)	15 (15.6)	
Son/daughter	88 (14.8)	18 (18.8)	
Parent	88 (14.8)	18 (18.8)	
Other	10 (1.7)	2 (2.1)	
Family members present at the interview	3.55 ± 1.74	3.54 ± 1.58	.925
Main decision maker's age	46.41 ± 13.01	48.82 ± 15.51	.155
Initial perceived attitude			.751
Receptive	480 (81.8)	79 (82.3)	
Unreceptive	95 (16.2)	14 (14.6)	
Aggressive	12 (2)	3 (3.1)	
Attributed cultural level			.326
High	214 (36.5)	27 (28.7)	
Middle	332 (56.7)	59 (62.8)	
Low	40 (6.8)	8 (8.5)	

DBD, donors after brain death.

* Values are expressed as n (%) or mean ± standard deviation.

† Analysis of variance, Kruskal-Wallis H, or χ^2 test.

According to the logistic regression model, those interviewers with <5 years of experience had a significantly higher probability of obtaining a family denial after the request interview. Other authors have already addressed the considerable effects that the interviewer's skills exert on consent rates [1]. The complexity of the emotional framework during the mourning process demands a profound knowledge of the psychological mechanisms involved [7]. That knowledge could be outlined by certain specialized courses that every coordination team member has normally taken before conducting any interview. Nevertheless, the expertise necessary to take the refusal rates to a minimum would, most likely, come from the continuous assessment and understanding of the reasons why a family refuses donation. Apart from mere academic knowledge, interviewers should probably receive more practical information during training. Despite novice interviewers usually accompanying more experienced ones during their first interviews, more objective ways of assessment (eg, analysis of videotaped interviews with simulated families, role playing activities) should be implemented. The arbitrary threshold of 5 years for interviewers to be considered as experts was set owing to the specific distribution of years of experience among our interviewers. In fact, the number of interviews performed per interviewer is usually proportional to the number of years on duty. Nevertheless, further studies should be carried on to create an integrative tool for assessing interviewer expertise.

The margin of improvement of refusal rates at a certain hospital, region, or country is yet unknown. Most likely, it would depend on specific nonmodifiable characteristics of the population. For example, the presence of certain religious beliefs and ethnicities reluctant to donation, the mean cultural level of the population, the confidence on the health and donation system, the transparency of the donation process, and the communication policy of the organization in charge of donation, all may determine, to some extent, the predisposition of a certain family to either donate or refuse before attempting any request interview [6,10,12,13,14].

The regression model also identified the DBD as an independent factor associated with a higher refusal rate. The fact that these donors have spent prolonged hospitalization periods prior to death may predispose families to reduce further surgical manipulation on the deceased's body. The higher age of DBD may also account for the higher probability of refusal as the main decision maker is usually the spouse or partner and their age is also associated with family refusal, as the regression model showed. Furthermore, not understanding or accepting the concept of brain death has been identified as a reason to decline donation by other authors [8,15]. On those particular cases, the information given by the interviewer is crucial.

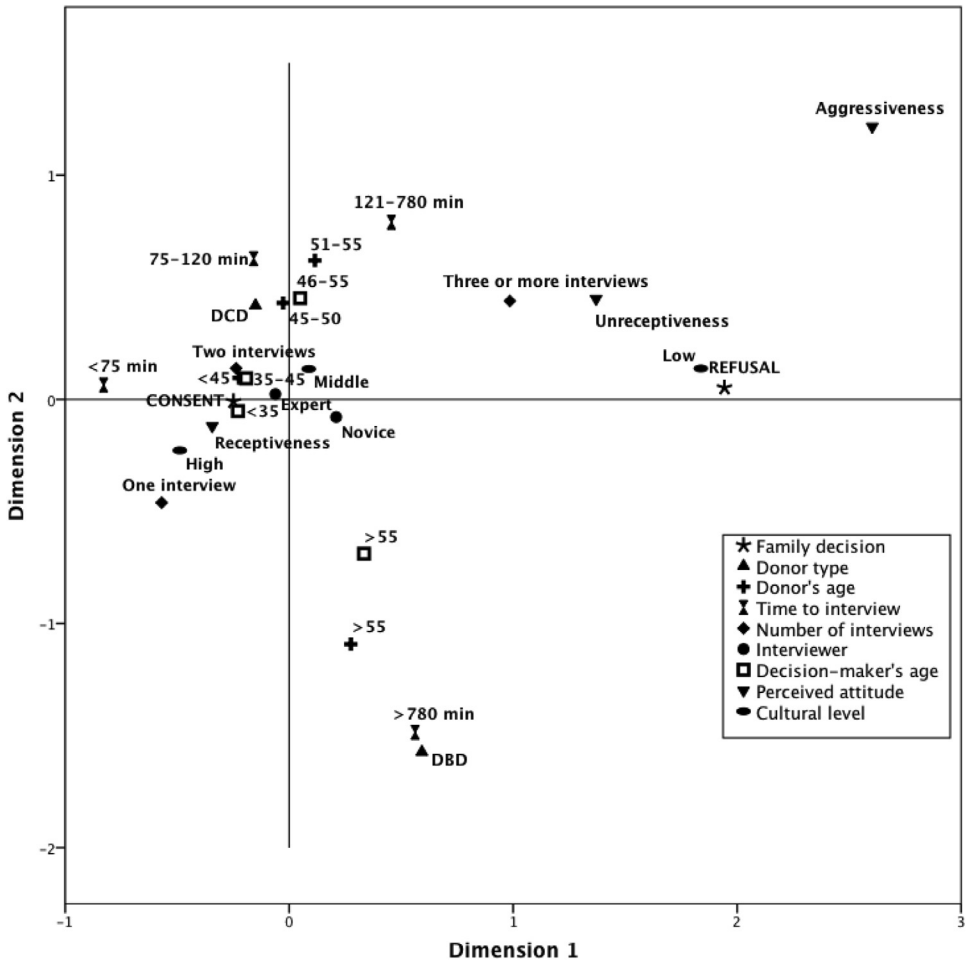

Fig 3. Multiple Correspondence Analysis (MCA) results. DBD, donors after brain death; DCD, donors after circulatory death.

Nevertheless, the grieving families may not be psychologically prepared to receive, comprehend, and process that information at that precise moment. A progressive step-wise way of delivering information regarding brain death and donation could be attempted either at a national scale (focusing on the general population) or at a local scale (focusing on the families visiting patients in the intensive care unit).

The fact that the regression model identified the number of interviews conducted per family as a factor related to family refusal could account for the time lapse that some families needed to cope with the new situation or to fully understand the donation process [2,8]. In that sense, a potential procedural enhancement arises because, when a certain number of interviews are reached, the participation of a more experienced interviewer or a meticulous reinterpretation of the family considerations toward the final decision prior to the next interview, might render a significant effect in refusal rate.

The attributed cultural level of a certain family reflects the interviewer's subjective first impression and might influence the attitude displayed during the whole request process as a self-fulfilling prophecy. In fact, at present time in western countries, donation undoubtedly holds a social aura of solidarity and generosity for most of the population [16]. In that sense, the attributed cultural level as either middle or high could have been influenced by the family's good predisposition to donation and, as a result, the logistic regression model identified both characteristics as associated with lower refusal probability. Nevertheless, the evaluation of the attributed cultural level remains, at least in our case, purely subjective. The development of a validated tool to assess the family's cultural level objectively could help interviewers to produce more reproducible data and, therefore, benefit from other hospitals experiences.

When the evolution patterns of the factors associated with family refusal over the last decade were analyzed, the yearly contribution of each of them could be explored. In fact, the contribution of the novice interviewers was only present from the year 2012 and onwards. Before that date, a higher proportion of DBD could have contributed to the increasing trend in family refusal rates over those years [17]. In addition, the decision maker's mean age has been steadily increasing since 2008, whereas the mean number of interviews conducted per family has remained apparently constant.

Studies on consent for organ donation have classically faced some important limitations. In the major part of the literature, the relationships between the different factors influencing the family's decision making have been explored in an isolated way [2,6,13,14,17]. The present study highlights the potential inter-relations between those factors associated with family decision through an exploratory approach for complex data structures by means of MCA. The graphical bidimensional representation that summarizes the joint relationships among the variables enables an at-a-glance understanding of complex phenomena such as family refusal.

The results showed significant relationships between donor's and the main decision maker's age, although they would cluster into 2 different age groups, each one associated with either the family consent or the family refusal. These results are consistent with the fact that, almost half of the times, the decision maker was the spouse or the partner. Apparently, younger people are slightly more prone to donate than older people [6]. This could be explained by the effect that public information campaigns have exerted over the last years in Spain. Nevertheless, the efficacy and cost efficiency of those campaigns have not recently been explored in terms of reduction of family refusal rates. More studies in this area should be encouraged, because those campaigns are publicly funded.

Regarding the donor type, DCD and DBD were significantly associated with shorter and longer hospitalization times, respectively. As a likely explanation, it must be noted that DCD came from a street environment and hardly spent any time in a hospitalization setting. On the other hand, DBD resulted from long-lasting morbid processes that required prolonged hospitalization periods. Family members may be both physically and mentally exhausted after such long periods of hospitalization. An early approach to those families regarding donation (either by the intensive care unit staff or by the transplant coordinators) could contribute to minimize the burden of decision on an eventual donation.

Another inter-relation highlighted in the MCA was the association between low cultural level, unreceptiveness toward donation, and ≥3 interviews before achieving a final decision. On the opposite side of the axis, significant association between high cultural level, receptiveness, and 1 interview were graphically suggested. The fact that psychosocial and cultural aspects, in addition to preconceived ideas and myths around donation, might effectively contribute to family refusal, could explain the need for a higher number of interviews in the cases of low-cultural level or unreceptive families [18]. An alternative explanation could be related to the time that different families needed to assimilate the death of a beloved one [8]. In addition, unreceptiveness and aggressiveness may reflect a complex emotional state, where anger and wrath predominate and interfere with a proper connection with the interviewer [11]. In turn, aggressiveness could be related to the circumstances in which the death occurred and to the medical assistance provided [7].

On the background, the transparency of sanitary regulations, as well as a strict control of the donation process, is essential to achieve the confidence of the population on the equality and legality of the transplant system. During the request interview, it is of capital importance to consider the way the message is delivered, with exquisite attention to detail and an adequate emotional rapport [19].

As a final consideration, and because of its observational nature, we recommend a careful interpretation of the causality inferences obtained in the present study. Despite the moderately high global discriminative power of the variables included in the logistic regression model, the influence of several other factors not considered in the present work may also be significant. Further study designs should account for this limitation in order to further confirm the hypothesis presented in this article. In that sense, the identification of those factors benefits from qualitative analysis of family decision process [20]. Nevertheless, we consider it remarkable that, despite the significant difference in refusal rates between 2 different years used as validation group, the model's predictive power is barely affected, thus supporting its reliability and robustness. The relative homogeneity of the interviewer training programs and the request protocols in Spain, support the extrapolation of the observations of this study, even though it only provides a single hospital point of view.

In conclusion, results suggest that building expertise of health professionals involved in the first steps of the donation process could be the most suitable strategy to reduce family refusal rates. Nevertheless, continuous assessment of the results obtained should guide the content and methodology of any training program, especially when public funding is involved. More research should focus on the different approaches employed on the team members' training. A corpus of knowledge, both at a national and an international level, integrating the data resulting from this research could help to reduce the family refusal rates.

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