Intensive Care Med (2004) 30:38–44
DOI 10.1007/s00134-003-1923-8

ORIGINAL

Kamel Senouci
Patrice Guerrini
Eloi Diene
Alain Atinault
Jacky Claquin
Francis Bonnet
Philippe Tuppin

A survey on patients admitted in severe coma: implications for brain death identification and organ donation

Received: 17 September 2002
Accepted: 10 June 2003
Published online: 16 August 2003

An editorial regarding this article can be found in the same issue http://dx.doi.org/10.1007/s00134-003-1998-2

K. Senouci · P. Guerrini · E. Diene
A. Atinault · J. Claquin · F. Bonnet
P. Tuppin (✉)
Etablissement français des Greffes,
5 rue Lacuée, 75012 Paris, France
e-mail: ptuppin001@efg.atrium.rss.fr
Tel.: +33-1-44675569
Fax: +33-1-44675930

Abstract *Objective:* To identify factors to improve the identification of brain dead patients in intensive care units (ICUs). *Design and setting:* Prospective study conducted in 79 ICUs in 54 hospitals. *Patients:* All hospitalized patients with a Glasgow Coma Scale (GCS) score less than 8. *Measurements and results:* During the study period hospital staff completed a form for each patient with a GCS less than 8. Hospital information units provided us with statistics from the discharge forms. The characteristics of the hospitals were also recorded. We included a total of 792 patients with a GCS less than 8; 120 of these patients were diagnosed as being clinically brain dead (15.1%). These patients accounted for 11.8% of the comatose patients in ICUs, 11.7% of the deaths occurring in ICUs, and 3.3% of the deaths that occurred in the hospital during the study period. Two multivariate linear regressions were performed to predict the number of clinically brain dead patients in the ICUs. The regression analyses included causes of death or causes of coma, and hospital characteristics. The presence of a coordination team and the number of transplant coordinators were positively associated with the number of brain dead patients in both models. The number of patients carried to the ICU by a mobile emergency unit was also positively associated in the model with causes of coma. *Conclusions:* Increasing the number of hospital coordinators and collaboration with mobile emergency units should lead to the identification of more brain dead patients among comatose patients in ICUs.

Keywords Organ donors · Organ procurement · Brain death · Medical records · Critical illness

Introduction

In European countries, especially France, the number of patients waiting for transplants exceeds the number of transplants performed, and this difference is increasing. In France 9,994 patients were awaiting an organ transplant in 2000. During the same year 1,016 brain dead subjects donated organs, giving a rate of 17 per million population (pmp), and 3,211 transplantations were performed [1]. The donation rate is comparable in other Western countries, except for Spain (34/pmp) and the United States (22/pmp) [2, 3]. Most organ donors are patients who die in hospital due to brain death. Brain death has been estimated to account for 1.2–4.3% of hospital deaths in Europe and the United States [4, 5, 6, 7, 8, 9, 10]. However, it seems more appropriate to estimate the number of potential brain dead donors from the number of patients who die in intensive care units (ICUs). Two studies have reported that brain death represents approximately 13% of all deaths in ICUs [11, 12]. Nevertheless, it would be even better to take patient and ICU characteristics into account to improve the accuracy of these estimates. The aims of this study were therefore to compare several indicators for the estimation of the pool of

Table 1 Rates of patients with suspected or confirmed brain death and those who donated organs in ICUs and hospitals according to patient characteristics (percentages)

	Brain death (*n*=120)	Confirmed brain death (*n*=87)	Organ donors (*n*=25)
Coma in ICU (*n*=1,016)	11.8	8.6	2.5
Coma under controlled ventilation in ICU (*n*=695)	17.2	12.5	3.6
Death after coma under controlled ventilation in ICU (*n*=246)	48.8	35.4	10.2
Death in ICU (*n*=1,027)	11.7	8.5	2.4
Death in hospital (*n*=3,634)	3.3	2.4	0.7

organ donors, to identify factors associated with the number of brain deaths in ICUs, and to build a statistical model to compare the expected and observed numbers of clinical brain deaths.

Materials and methods

Study sample and data collection

The 108 ICUs in Paris and surrounding area (population 12 million) were asked to participate in the survey, and 79 did so. Three of the ICUs that did not participate sent all patients with a GCS score less than 8 to another ICU, 20 reported that they do not admit sufficient numbers of patient with a GCS score less than 8, or that they treat mainly patients with diseases contraindicated for organ donation such as cancer, and 7 would not provide the discharge forms. The 79 ICUs were located in 54 hospitals. All of the hospitals with a transplantation unit in the area were included. All patients admitted to one of these ICUs between 1 May and 30 June 2000 who presented a Glasgow Coma Scale (GCS) score of below 8 while hospitalized were included in the survey. A total of 792 such patients were identified during the study period. Of these 121 had a clinical diagnosis of brainstem death. Brain death was not confirmed in 33 cases; 16 had a medical contraindication for donation (48.5%), 13 had a medical complication during reanimation (39.4%), and the family refused in four cases (12.1%). Organs were not retrieved from 62 of the 87 patients confirmed to be brain dead: 17 due to medical contraindications (18.4%), 14 due to medical complications during reanimation (15.2%), and 31 due to donor refusal reported by the family (33.7%). During this period 3,634 patients died in all of the hospitals, 1,027 of them in ICUs, including 246 who had been in a coma under controlled ventilation. The patients who died from confirmed or unconfirmed brain death accounted for 11.8% of comatose patients admitted to ICUs, 17.2% of those in a coma under controlled ventilation, 48.8% of those who died after being in a coma with ventilation, 11.7% of those who died in all of the ICUs, and 3.3% of those who died in all of the hospitals (Table 1).

An ICU physician completed a standardized form for each patient included with the help of a transplant coordinator. This form contained information concerning the reason for admission, age, gender, clinical status, changes in the GCS score, cause of death, clinical diagnosis of brain death when appropriate and its confirmation, whether organs were extracted, and the reasons. All forms were sent by the member of the hospital staff to the French national agency for organ procurement and organ transplantation (Etablissement français des Greffes) and reviewed for completeness and consistency. Hospital information units provided us with statistics from the discharge forms for all patients hospitalized in the participating ICUs during the survey period. These discharge forms are routinely collected for all patients admitted to French hospitals, but information concerning GCS scores for comatose patients and diagnosis of brain death is not routinely collected. They allowed us to compile data on the number of patients in coma, the number of patients in coma under controlled ventilation, the total number of deaths in both the ICU and the whole hospital during the study period and the reasons for these deaths. This study was approved by a data protection agency (Commission Nationale Informatique et Liberté).

Variable definitions

In France hospitals must be authorized for organ and tissue procurement by the Ministry of Health and the French transplantation agency, and donation is based on a presumed consent scheme. After clinical diagnosis brain death must be confirmed by either two flat electroencephalograms or a cerebral angiography. Mobile emergency teams consist of a staff specialized in intensive care (physician and nurses) using an ambulance equipped with intensive care material. We defined the major groups of diseases that were commonly associated with brain death according to the ICD-10-CM causes of death codes, excluding medical contraindications for organ donation (e.g., cancer with metastasis and severe infection). The groups were: metabolic disorder, drug intoxication, trauma, cerebral accident, shock, anoxia and cardiac arrest, brain infection, primary brain tumor, and epilepsy.

Data analysis

The χ^2 test was used to evaluate differences in proportions between groups. We compared the percentage of patients in whom brain death was confirmed according to diagnosis, type of hospital, existence of a transplantation team, a coordination team, a neurosurgical unit and an emergency department in the hospital, and whether the hospital had a procurement license. The Pearson product-moment correlation coefficient was used to search for significant correlations between the selected indicators in the different hospitals. Simple linear regressions analysis was used to determine factors that are significantly associated with the number of unconfirmed brain deaths in hospitals ICUs. Multiple linear stepwise regression analysis with backwards selection of variables was used to identify significant and independent predictors of the number of brain deaths. Two models including the variables significantly ($p<0.05$) associated with clinical diagnosis of brain death were built: one included the number of comatose patients by groups of disease and the other one the number of deaths by groups of disease. We used two models because more variations between units or hospitals could occur for coma declaration than for deaths in discharge forms. We also want to identify the most useful model including currently available variables. We then compared the number of brain deaths predicted by the model (with 95% confidence interval, CI) with the number of brain deaths actually observed in each hospital. All p values are presented as two-tailed values. Statistical analysis was performed using SAS software (SAS, Cary, N.C., USA).

Table 2 Frequency of brain death in comatose patients and in all of the patients who died in the ICUs according to diagnosis and the characteristics of the hospital

	Coma in ICU		p	Deaths in ICU		p
	n	Brain death (%)		n	Brain death (%)	
Diagnosis						
Drug intoxication	317	0.3	<0.0001	30	3.3	<0.0001
Trauma	152	19.7		79	38.0	
Cerebrovascular accident	211	27.5		169	34.3	
Anoxia/cardiac arrest	170	12.4		40	52.5	
Epilepsy	77	0.0		26	0.0	
Shock	145	1.4		377	0.5	
Primary brain tumor	6	16.7		10	10.0	
Brain infection	44	11.4		24	20.8	
Metabolic disorder	97	1.0		14	7.1	
Type of hospital						
Public teaching	579	14.3	0.008	630	13.2	0.06
Public nonteaching	420	8.8		397	9.3	
Transplantation team						
Yes	418	18.4	<0.0001	473	16.3	<0.0001
No	598	7.2		554	7.8	
Coordination team in the hospital						
Yes	405	20.0	<0.0001	439	18.5	<0.0001
No	611	6.4		588	6.6	
Neurosurgical ICU						
Yes	309	15.9	0.008	275	17.8	0.0002
No	707	10.0		752	9.4	
Emergency department						
Yes	785	10.6	0.37	766	11.0	0.9
No	166	18.1		209	14.4	
Procurement authorization						
Yes	529	16.3	<0.0001	618	14.5	0.0001
No	422	5.5		357	6.4	
Characteristics						
Neurosurgical and transplant units, procurement authorization	230	20.0	<0.0001	236	19.5	<0.0001
Transplant unit, procurement authorization	160	15.0		211	11.4	
Neurosurgical and transplant units	79	12.7		39	25.6	
Procurement authorization	204	9.8		223	9.0	
None	315	6.3		292	5.1	
Total	1016	11.8		1027	11.7	

Results

Significant correlations were found between the number of brain death and patient's characteristics by hospitals, the strongest for brain death after being in a coma with ventilation and for the deaths in the ICUs (r=0.76 for both, p<0.0001). The frequency of clinical brain death was high in patients who fell into a coma following a cerebrovascular accident, trauma, brain primitive tumor, or brain infection and low in patients who fell into a coma due to drug intoxication (Table 2). Brain death was most frequent among patients admitted to teaching hospitals, to hospitals including a transplantation team, an organ procurement coordination team or a neurosurgical unit, and to hospitals with organ procurement authorization. The highest proportions of brain deaths among comatose patients were observed in hospitals with organ procurement authorization, a neurosurgical team and a transplantation team (19.5%), and in hospitals with an organ procurement authorization and a transplantation team (11.4%). This proportion was only 9.0% in hospitals with an organ procurement authorization but neither a neurosurgery team nor a transplantation team and only 5.1% for hospitals with no organ procurement authorization.

Table 3 Univariate and multiple linear regression models predicting the number of brain deaths in ICUs. Model 1 included the significant descriptive variables and those concerning the coma; model 2 included the significant descriptive variables and those concerning death

	Univariate regression		Backward regression (model 1)		Backward regression (model 2)	
	Regression coefficient	*p*	Regression coefficient	*p*	Regression coefficient	*p*
Public teaching hospital	2.3	0.04	–	–	–	–
Procurement authorization	3.3	0.003				
Emergency hospital	1.1	n.s.	–	–	–	–
Coordination team in the hospital	5.1	<0.0001	–	–	1.83	<0.01
Number of coordinators	5.6	<0.0001	3.7	0.0001	–	–
Transplant center	4.2	<0.001	–	–	–	–
Neurosurgical unit	6.5	<0.0001	–		–2.5	<0.01
Number of patients carried by a mobile emergency unit	0.36	<0.0001	0.18	<0.001	–	–
Total number of patients in a coma in the ICUs	0.12	<0.0001	–	–	–	–
Number of patients in a coma due to:						
Drug intoxication	–0.01	n.s.	–	–	–	–
Trauma	0.34	<0.0001	–	–	–	–
Cerebrovascular accident	0.49	<0.0001	–	–	–	–
Anoxia/cardiac arrest	0.55	<0.0001	–	–	–	–
Epilepsy	0.43	n.s.	–	–	–	–
Shock	0.61	<0.0001	–	–	–	–
Primary brain tumor	5.79	<0.0001	–	–	–	–
Brain infection	1.07	<0.0001	–	–	–	–
Metabolic disorder	0.17	n.s.	–	–	–	–
Total number of deaths in the ICUs	0.18	<0.0001				
Number of deaths due to						
Drug intoxication	0.7	n.s.	–	–	–	–
Trauma	0.97	<0.0001	–	–	0.8	<0.0001
Cerebrovascular accident	0.72	<0.0001	–	–	–	–
Anoxia/cardiac arrest	0.34	<0.0001	–	–	–	–
Epilepsy	–0.22	n.s.	–	–	–	–
Shock	0.32	<0.001	–	–	–	–
Primary brain tumor	4.6	<0.0001	–	–	0.56	0.01
Brain infection	1.47	<0.001	–	–	–	–
Metabolic disorder	0.7	n.s.	–	–	–	–

To determine factors that predict the number of clinically brain dead patients declared by hospitals data from six hospitals were merged because they belonged to the same administrative group, meaning that their discharge forms were merged. The first linear regression analysis included the characteristics of the hospitals and the number of comatose patients by groups of disease: only the number of coordinators and the number of patients with a GCS score less than 8 carried by a mobile emergency care unit were significantly predictive of the number of brain deaths (R^2=0.75; Table 3). The second regression analysis included the characteristics of the hospitals and the number of patients who died in the ICUs by groups of disease. The factors predictive of the number of brain deaths were the number of deaths due to trauma, the number of deaths due to a primary brain tumor, and the presence of a coordination team. The presence of a neurosurgical ICU was negatively associated with the number of brain deaths (R^2=0.88; Table 3). We used the second model, including the four significant variables, to predict the number of brain deaths in the ICU of each hospital and to compare these values with the observed number during the study period. The observed number of brain deaths was significantly higher than predicted in one hospital and significantly lower in another; in several hospitals the observed number reached the upper limit of the 95% confidence interval (Fig. 1).

Discussion

Patients with a clinical diagnosis of brain death accounted for 3.3% of hospital deaths in this study, 11.7% of deaths in the ICUs, 11.8% of comatose patients admitted to ICUs, and 15.1% of patients with a GCS less than 8 admitted to ICUs. In other countries brain death has been

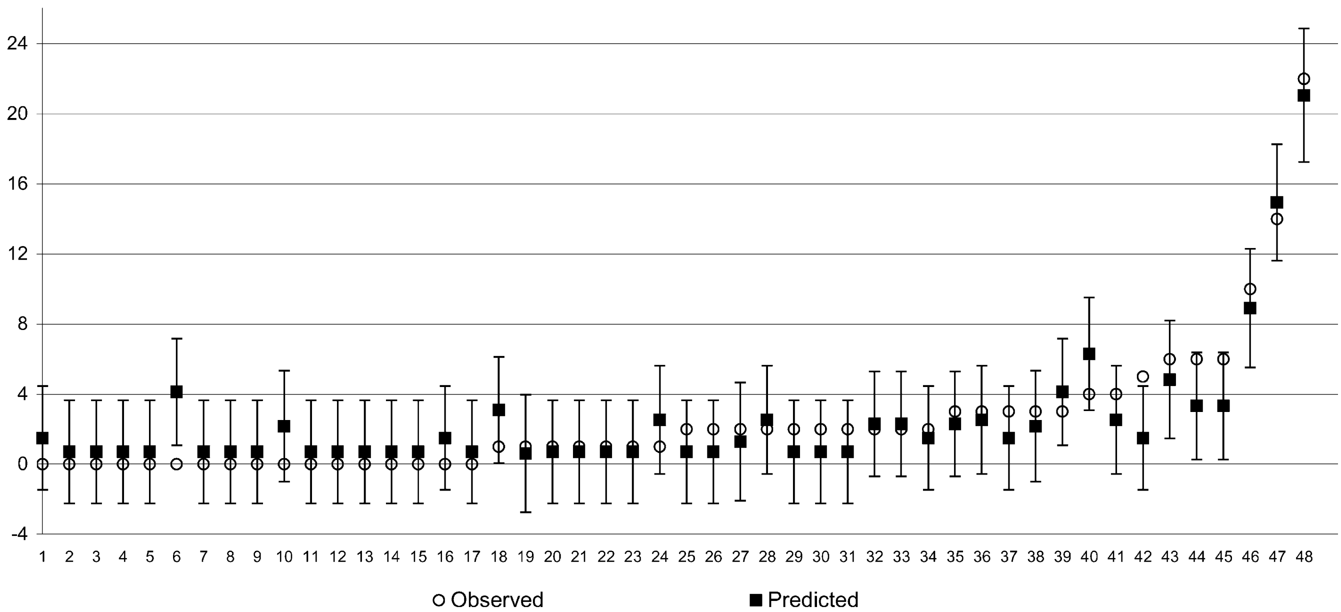

Fig. 1 Observed and predicted number of brain deaths in the hospitals in this study

reported to account for 1.2–4.3% of deaths occurring in hospital [4, 5, 6, 7, 8, 9, 10]. However, a systematic medical review of all deaths revealed that brain death accounted for 13.1% of deaths in Spanish ICUs [12]. If we presume that the rates of the major causes of brain death are comparable in France and Spain, the rate of brain death may have been underestimated in the Paris area. Nevertheless, the Spanish study involved an audit of the medical files of all patients who died in hospital, whereas we obtained the information from clinicians' reports without an audit. Brain death has been shown to account for comparable percentages of deaths in ICUs in the Madrid area (13.4%). An audit of deaths showed that possible brain deaths accounted for 14% of deaths in ICUs, and that confirmed brain deaths accounted for 10% in the United Kingdom [5, 11]. Another explanation for this possible underestimation could be the short study period, which did not make it possible to take monthly variations into account. In the Paris area the donation rates are higher in the winter than in May and June (C. Poinard et al., submitted). Nevertheless, this 2-month period was chosen to make possible comparisons with two similar studies carried out in Paris area. The rate of brain death in our study (11.6/pmp) was similar to the rates in 1988 (11.6/pmp) and 1992 (8.9/pmp), but the rate of retrieved donors was lower in 2000 than in 1988 or 1992 (2.5, 3.5, and 4.5/pmp, respectively [13, 14]). This could be due to an increase in opposition rates during this period (20% in 1988, 19% in 1992, and 33.7% in 2000). Furthermore, the frequency of the two major causes of brain death (trauma and cerebrovascular accident) inversed during this period (43% and 36% in 1992 vs. 26% and 48% in 2000). Differences in rates between studies focusing on deaths in ICUs may also be due to the policy of addressing comatose patients to ICUs from other hospital units. A large number of brain dead patients who were potential donors and were declared in our study were not declared to the regional organ procurement organization; only 68 of the 120 were actually declared. This may reflect self-limitation by the medical teams due to patient characteristics or location in hospitals that are not authorized for organ procurement. We could not compare our data with those of hospital discharge files because data on GCS scores and diagnosis of brain death are not routinely collected, although this should help to identify potential donors.

The expected number of organ donors is usually estimated from specific surveys or from audits of the number of deaths in hospitals or ICUs [11, 12, 15]. These surveys tend to last a long time or to take place retrospectively, such as in the Donor Action program [16]. Although these methods are highly accurate, they are labor intensive. The rates of clinical brain death in function of the total number of deaths in ICUs seem to be more accurate for estimating the potential number of donors in ICUs. In our study a high correlation between hospitals was found for the number of clinically brain dead subjects as a function of the total number of deaths in ICUs, and recent mortality data were available from each unit.

The fact that 15.8% of comatose patients with a GCS less than 8 died due to brain death suggests that the follow-up of these patients in ICUs would be a good way of improving the identification of all potential organ donors. Nevertheless, the number of brain deaths varies according to the diagnosis and hospital characteristics. Attention should focused more specifically on patients with a GCS less than 8 due to a cerebrovascular accident or trauma, as brain death is more frequent in these patients. Furthermore, attention should be paid to patients with a GCS less than 8 following a cardiac arrest or anoxia, because the frequency of brain death is relatively high in these patients. A Spanish study found that 14.9% of deaths were due to clinical brain death in hospitals with neurosurgical and transplantation units, 15.5% in hospitals with only a neurosurgical unit, and 7.6% in hospitals with neither a neurosurgical unit nor a transplant unit. In our study this rate was higher in teaching hospitals with neurosurgical and transplantation units (19.5%), lower in hospitals with at least one transplantation unit (11.4%), and similar in hospitals with procurement authorization but neither a neurosurgical unit nor a transplantation unit (9.0%). In France hospitals can request procurement authorization, and this depends mainly on the hospital's policy. There are fewer authorized hospitals in France than in Spain. Thus the difference in the rate of brain death among all deaths in the ICUs between Spain and France may be due to the fact that our study included hospitals without procurement authorization, in which brain death accounted for 5.1% of deaths in ICUs. Nevertheless, 17% of declared brain deaths in our study occurred in hospitals without procurement authorization, suggesting that the number of potential donors is high as that observed in Spain [17]. This suggests that there is a need to increase the networks between hospitals to help with the management of brain dead patients in hospitals without procurement authorization and in hospitals with low rates of patient admission.

In our models, when coma and coma according to diagnosis were considered, no diagnostic factors were linked to the number of declared cases of brain death. The only factors that were predictive were those that reflected a high number of potential donors and an active search for brain death, such as the number of patients with a GCS score less than 8 carried by an emergency mobile care unit and the presence of hospital coordinators who actively seek potential donors. This confirms that hospital coordinators play a major role, as is the case in a number of countries including Spain [18]. The second model, which included the number of deaths according to their causes, also showed that the presence of coordinators is a predictive factor, as were the numbers of deaths due to trauma and brain tumors. Brain death associated with a brain tumor is not usually declared to the organ procurement organization. However, it was included in our model and may reflect a good knowledge of procurement procedures and the characterization practices performed during organ procurement in ICUs. Trauma is a well known cause of brain death. The presence of a neurosurgical ICU unit was found to be negatively associated with the number of clinical brain deaths in multivariate analysis after adjustment for the presence of a coordination team and for the number of deaths with a diagnosis of trauma or primary brain tumor. These two diagnoses are common in this type of ICU, and this finding could reflect an under declaration by these units, which are usually considered to be a major pool of potential donors. One of the five hospitals with a neurosurgical unit did not have procurement authorization, and one did not have a coordination team, which may not favor the identification of potential donors. Furthermore, neurosurgical units are involved in the diagnosis only of emergency cases. Patients are subsequently referred to other ICUs for continued care. These patients are often sent to other hospitals, where they might be declared. The model including ICU deaths had a better predictive value than the model including ICU comas. This model explained a high proportion of variance, and data for the variables used to calculate the predicted number of brain deaths in an ICU are easy to obtain. It could be used routinely to detect differences between the predicted and observed numbers of brain deaths in ICUs. Nevertheless, this model must be tested in other studies with more patients and over a long time period before it can be validated. It would be useful for local authorities to try to explain these differences and to promote corrective actions in hospitals where the predicted number of brain deaths is significantly higher than the observed number.

Knowledge of the potential number of organ donors, donor recruitment, and donation performance is critical to increase the donor pool. Brain death is frequent in comatose patients with a GCS less than 8 and with specific characteristics at diagnosis, and these patients should be followed-up in ICUs. This could be made possible by the allocation of trained coordination teams. It is also necessary to stress the need for the emergency mobile units to identify suspected potential donors and to refer them to adapted ICUs.

Acknowledgements The authors gratefully acknowledge the participation of the ICUs and medical information units, especially Dr. Louis Brunel (Direction de l'informatique médicale, Assistance Publique des Hôpitaux de Paris) who constructed a special computer program to collect data from the discharge forms for all patients hospitalized in the participating ICUs.

References

1. Etablissement français des Greffes (2001) Rapport d'activité et bilan des activités de prélèvement et de greffe en France en 2000. EfG, Paris
2. Organizacion Nacional de Trasplantes (2001) Memoria de la actividad de donacion y trasplante 2000. ONT, Madrid
3. United Network for Organ Sharing (2000) Annual report of the U.S. scientific registry for transplant recipients and the organ and transplantation network. UNOS, Richmond

4. Salih MA, Harvey I, Frankel S, Coupe DJ, Webb M, Cripps HA (1991) Potential availability of cadaver organs for transplantation. BMJ 302:1053–1055
5. Navarro A (1996) Brain death epidemiology: the Madrid study. Transplant Proc 128:103–104
6. Espinel E (1989) The capacity for organ generation of hospital in Catalonia, Spain: a multicentre study. Transplant Proc 21:1419–1421
7. Siminoff LA, Arnold RM, Caplan AL, Virnig BA, Seltzer DL (1995) Public policy governing organ and tissue procurement in the United States. Ann Intern Med 12:10–17
8. Waller JA, Haisch CE, Skelly JM, Goldberg CG (1993) Potential availability of transplantable organs and tissues in fatalities from injury and nontraumatic intracranial hemorrhage. Transplantation 55:542–546
9. Garrison RN (1991) There is an answer to shortage of organ donors. Surg Obstet Gynecol 173:391–396
10. Nathan HM, Jarrell BE, Broznik B, Kochik R, Hamilton B, Stuart S, Ackroyd T, Nell M (1991) Estimation and characterization of the potential renal organ pool in Pennsylvania. Transplantation 61:142–149
11. Gore SM, Cable DJ, Holland AJ (1992) Organ donation from intensive care units in England and Wales: two year confidential audit of death in intensive care. BMJ 304:349–355
12. Cuende N, Canon JF, Alonso M, Delagebasala CM, Sagredo E, Miranda B (2001) Programa de garantia de calidad en el proceso de donacion y trasplante de la Organizacion Nacional de Trasplantes. Nefrologia 21 [Suppl 4]:65–76
13. Jouan M, Claquin J (1996) Inquiry “INSERM 1992”: opposition to organ harvesting. Transplant Proc 28:390–391
14. Benoit G, Aoun E, Auzepy P (1990) Pour faciliter le don d’organes en Ile-de-France. Presse Med 19:162–165
15. Gortmaker SL, Beasley CL, Brigham LE, Franz HG, Garrison RN, Lucas BA, Patterson RH, Sobol AM, Grenvik NA, Evanisko MJ (1996) Organ donor potential and performance: size and nature of the organ donor shortfall. Crit Care Med 24:432–439
16. Roels L, Wight C (2001) Donor Action: an international initiative to alleviate organ shortage. Prog Transplant 11:90–97
17. Matesanz R, Miranda B, Fernandez Lucas M, Naya MT, Felipe C (1996) Contribution of nontransplant and small hospitals to organ procurement in Spain. Transplant Proc 28:232–233
18. Gubernatis G, Vogelsang F, Kolditz M, Bladtke L, Plessen V, Schafer H, Basse H, Smit H, Zickgraf T, Pichlmayr R, Ketzler K (1997) Professionalization of service for organ donation at peripheral hospitals including total quality management has nearly doubled organ donation in two years. Transplant Proc 29:1489–1492