

Implications of ICU Stay After Brain Death: The Saudi Experience

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Objective: The interval from brain death (BD) to organ harvesting is critical to the success of transplantation. We evaluated the time from BD onset to harvesting and analyzed sources of delay.

Materials and Methods: This retrospective study was conducted from January 1999 to December 2003. Time intervals analyzed to determine the causes of delay were: time of admission to the intensive care unit (ICU), to the report to the Saudi Center for Organ Transplantation (SCOT), to the documentation of BD, to organ retrieval and/or cardiocirculatory cessation without organ retrieval.

Results: During the 5-year analysis, 1834 people were reported to the SCOT. Of those, more than 1511 (80%) were reported during their first week of treatment in the ICU, and BD was documented in 1099 (59.9%). The mean interval from ICU admission to organ retrieval or cardiac arrest was 10.3 days and that from admission to the report to the SCOT was 5.6 days. In the consensual group, the mean interval from the documentation of BD until harvesting was 2 days, and that from documentation until cardiocirculatory cessation without organ retrieval in the nonconsensual group was 5 days. All subjects demonstrated a significant decrease in systolic blood pressure and a significant increase in plasma sodium and serum creatinine levels. The body temperature, serum plasma levels of sodium, and kidney function (measured by the serum creatinine level) of potential donors were compared, and patients with hypothermia, hypernatremia, or renal failure had a shorter stay in the ICU.

Conclusions: Fewer than 30% of the patients could be maintained on mechanical support for more than 1 week after the declaration BD. It is crucial that we increase hospital-staff awareness about the importance of organ donation and transplantation, improve the identification of BD candidates, and enable the early reporting and documentation of BD.

Key words: Brain death, Duration, Organ donation, ICU, Saudi Arabia

The Kingdom of Saudi Arabia (KSA) has an area of about 2.2 million square kilometers, and in 2003, the population was estimated at about 22 million [1]. The Kingdom has a well-organized healthcare network that includes renal replacement therapy and organ transplantation programs. Initially, renal transplantation was performed with living-related donors. In 1982, the Islamic ulama (scholars) approved organ donation and transplantation and heralded the true era of transplantation programs in the Kingdom [2].

In 1985, the government established the National Kidney Foundation (NKF) as a nonprofit organization. The NKF is the coordinating body of the national deceased organ donation and transplantation network. The NKF was upgraded in 1993 and was renamed the Saudi Center for Organ Transplantation (SCOT) to encompass the transplantation of organs other than kidneys. Since its establishment, the Center has successfully implemented an active deceased organ donation program for numerous organs including the kidney, heart, liver, pancreas, lung, and cornea [3].

In the Kingdom, there are 116 intensive care units (ICUs) with 1418 beds among the hospitals of the Ministry of Health and other healthcare providers [4]. All potential patients with brain death (BD) who were treated in an ICU are reported to the SCOT. Ensuring that the BD protocol is strictly followed is an important objective of the SCOT in any potential BD case.

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Coordinators of the SCOT also supervise the diagnosis and management of BD in all reported cases from medical as well as legal perspectives [3].

It is well known that the dramatic hemodynamic and immunologic changes that occur in an organ donor with BD affect the quality of the potential organ transplant, although the duration of stay in the ICU plays a key role in organ viability [5-8]. Several published studies have shown that valuable donor organs are lost owing to a delay in reporting, documentation, or harvesting [9-11]. This study evaluated the time from the onset of BD to harvesting and analyzed the causes of those delays.

Materials and Methods

This retrospective study was conducted from January 1999 to December 2003. Data pertaining to the duration of BD were recorded daily, beginning at the moment at which a potential BD donor was reported to the SCOT until that patient was pronounced dead and/or the organs were harvested.

The Saudi national protocol regulation followed in all ICUs in the Kingdom specifies that a potential organ donor must have irreversible brain damage and no spontaneous respiration and that the insult (excluding hypothermia [$\leq 35.5^{\circ}\text{C}$]) must have occurred more than 6 hours from the time of admission to the ICU. In addition, the potential donor must not be receiving a sedative, narcotic, or depressant and must not have untreated cardiovascular shock. Metabolic and endocrine causes of coma must also have been ruled out. If a potential donor meets the necessary preconditions and inclusion criteria, 2 clinical examinations for brainstem reflexes must be performed with an observation interval (6 hours for adults) between the 2 examinations. Also required is the confirmation of BD by means of either a flat electroencephalogram of 30 minutes' duration or no circulatory flow as demonstrated by cerebral angiography. An apnea test should be performed as the last test for confirmation of the failure of spontaneous respiration [2]. After the declaration of BD has been made, the patient's family can be approached regarding organ donation, and written consent to proceed with organ procurement (the "opt in" system) must be provided by the donor's next of kin.

The sequence of documented intervals was as follows: from the time of admission to the ICU, to the report to the SCOT, to the documentation of BD, to organ retrieval and/or cardiocirculatory cessation. We sought to evaluate the delays that occurred from the onset of BD to organ harvesting and to analyze the source of those delays. The intervals were analyzed to

determine the underlying causes of delay with regard to the patient's age, sex, and cause of BD (traumatic vs nontraumatic) in relation to body temperature, systolic blood pressure level, and serum plasma levels of sodium, potassium, and creatinine measured on admission to the ICU and at harvesting or cardiocirculatory cessation.

Results

During the 5-year study, 1834 potential cases of BD were reported to the SCOT, with an average annual incidence of potential deceased donors of 18 per million population (pmp). The mean age of reported patients was 28.6 ± 17 years (range, 1 day-90 years). Of all the patients, 398 (21.7%) were 14 years of age or younger, 1307 (71.3%) were between 15 and 55 years, and 129 (7%) were older than 55 years. Seventy-seven percent were men, and 23% were women. The causes of death included head trauma ($n = 1090$; 59.4%), cerebrovascular event or stroke ($n = 396$; 21.6%), and brain anoxia ($n = 218$; 11.9%) (Table 1).

Table 1. Age, sex, and causes of brain death for potential donors

Age	Number	Percentage
< 14 years	398	21.7
15-55 years	1307	71.3
> 55 years	129	7
Total	1834	100.0
Sex		
Male	1413	77.0
Female	421	23.0
Total	1834	100.0
Cause of Death		
Brain anoxia	218	11.9
Cerebrovascular accident	396	21.6
Head trauma	1090	59.4
Primary brain tumor	69	3.8
Other	60	3.3
Total	1834	100.0

The mean systolic blood pressure on admission was 110 mm Hg, which included 469 people (25.4%) with a systolic blood pressure measurement of 90 mm Hg or less. The mean systolic blood pressure before harvesting or cardiac arrest decreased significantly to 97 mm Hg ($P < .001$); this included 681 people (43.1%) whose systolic blood pressure measurement was 90 mm Hg or less.

The mean body temperature on admission was $36.4^{\circ}\text{C} \pm 1.1^{\circ}\text{C}$, which included 338 people (19.2%) who were hypothermic ($< 35.5^{\circ}\text{C}$), 184 (10.4%) who were hyperthermic ($> 37.7^{\circ}\text{C}$), and 1242 (70.4%) whose temperature was between 35.5°C and 37.7°C . There was no significant change in body temperature

before harvesting or cardiac arrest (mean temperature, 36.5°C).

The mean plasma sodium level on admission was 145 ± 12 mmol/L, which included 291 people (16.6%) who were hyponatremic ($\text{Na} < 135$ mmol/L), 699 (40%) who were hypernatremic ($\text{Na} > 145$ mmol/L), and 758 (43.4%) with a plasma sodium level within normal limits. The mean plasma sodium level before harvesting or cardiac arrest increased significantly to 149 mmol/L ($P < .001$), including a significant increase in the hypernatremic subgroups (55.6%).

The mean plasma potassium level on admission and before either harvesting or cardiac arrest was 3.9 or 4.2 mmol/L, respectively. The mean serum creatinine (SCr) level on admission was 120 $\mu\text{mol/L}$. Two hundred ninety-three patients (17%) had an elevated SCr level ($\text{SCr} > 150$ $\mu\text{mol/L}$). The mean SCr level before harvesting or cardiac arrest increased significantly to 180 $\mu\text{mol/L}$ ($P < .001$), which included 542 people (36%) with an elevated level of SCr (Table 2). The duration of ICU stay (from admission to organ retrieval and/or cardiocirculatory cessation) ranged from 24 hours to 101 days (mean, 10.3 days). The interval between admission to the ICU and the report to the SCOT ranged from 8 hours to 101 days (mean, 5.6 days). The time between the report to the

less than 24 hours of that report, and 189 (17.2%) were documented after more than 48 hours (Figure 3). Of 1099 documented cases of BD, 900 families were approached for organ donation, and of those, 229 families (25.4%) consented (Figure 4).

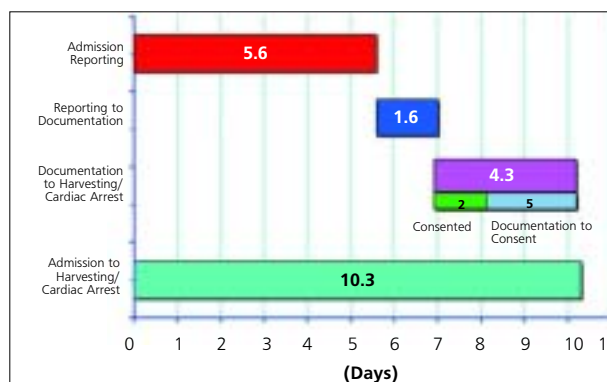


Figure 1. Average time in the intensive care unit for patients with brain death, Saudi Center for Organ Transplantation, 1999-2003.

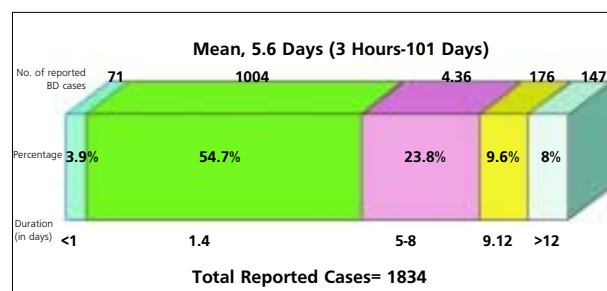


Figure 2. Time in intensive care unit from admission to report for brain death cases, Saudi Center for Organ Transplantation, 1999-2003.

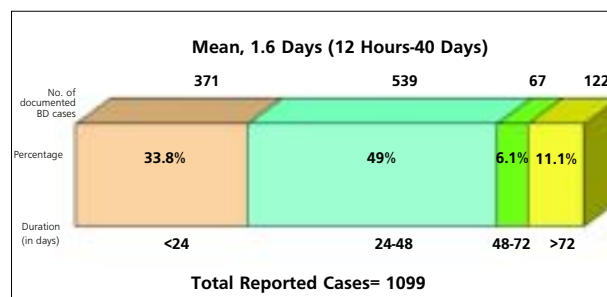


Figure 3. Time in intensive care unit from reporting to documentation of brain death cases, Saudi Center for Organ Transplantation, 1999-2003.

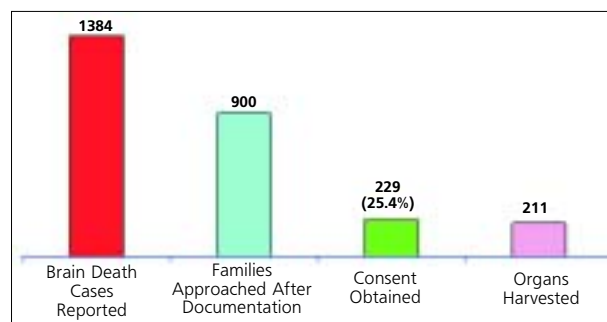


Figure 4. Brain death cases reported, families approached, consent obtained, and organ harvested, 1999-2003.

Table 2. Characteristics of donors during ICU stay

Parameters	Admission	Before harvesting /cardiac arrest	P Value
Systolic BP	110 mm Hg	97 mm Hg	< .001
Temperature	36.4°C	36.5°C	NS
Plasma Na	145 mmol/L	149 mmol/L	< .001
Plasma K	3.9 mmol/L	4.2 mmol/L	< .001 (but within normal range)
Serum Cr	120 $\mu\text{mol/L}$	180 $\mu\text{mol/L}$	< .001

BP, Blood pressure; Na, sodium; K, potassium; Cr, creatinine; NS, not significant.

SCOT and the documentation of BD ranged from 12 hours to 40 days (mean, 1.6 days). In the consensual cases for organ donation, the mean average time from the documentation of BD until harvesting was 2 days, and in the nonconsensual cases, the mean time from the documentation of BD until cardiocirculatory cessation without organ retrieval was 5 days (Figure 1).

Of 1834 total patients, only 71 (3.9%) were reported as "potential BD" within less than 24 hours from admission to the ICU; 759 persons (41.4%) were reported 5 or more days after admission (Figure 2). Of 1834 reported patients, 1099 (60%) were documented as having BD (according to the national protocol regulation). Only 371 (34%) were documented within

Regarding the interval between documentation and organ retrieval, only 49 organs (20%) were retrieved within less than 24 hours after documentation, and 44 (28%) were retrieved after more than 48 hours (Figure 5).

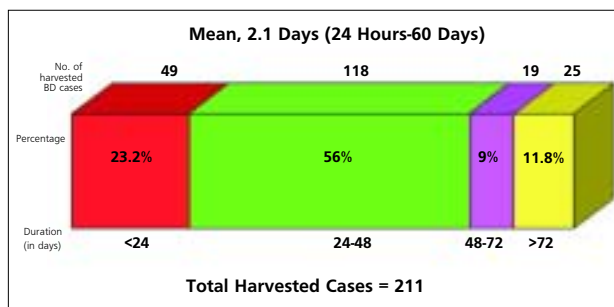


Figure 5. Time from documentation to retrieval of organs, Saudi Center for Organ Transplantation, 1999-2003.

A significant difference was found regarding the mean interval from admission to harvesting or cardiac arrest for men and women (9.9 days vs 11.7 days; $P = .004$). This correlated with the cause of BD as either traumatic (9.3 days) or nontraumatic (11.9 days) ($P = .001$), because 964 (87%) of the traumatic causes and 416 (61.7%) of the nontraumatic causes occurred in men. A significant difference existed regarding the interval from admission to harvesting or cardiac arrest between pediatric patients (11.4 days) and the other age groups (10.3 days; $P = .037$). When the hypothermic subgroup was compared with the other subgroups, a significant difference was found regarding the mean duration of stay in the ICU for temperature on admission (9.4 vs 10.9 days; $P = .018$). A significant difference existed regarding the mean duration of stay in the ICU for plasma sodium levels before harvesting or cardiocirculatory cessation between the hypernatremic subgroup (10 days) and the other plasma sodium level subgroups (11.8 days; $P = .001$). When the hypokalemic subgroup was compared with the other subgroups, a significant difference was found regarding the mean duration of stay in the ICU for plasma potassium levels on admission (9.4 vs 11.1 days; $P = .005$). A significant difference existed regarding the mean duration of stay in the ICU for serum creatinine levels before harvesting or cardiocirculatory cessation between normal SCr and elevated SCr subgroups (11.7 vs 11.1 days; $P = .001$).

Discussion

The retrieval of viable organs for transplantation depends on appropriate medical management both before and after death is declared. Even with inten-

sive care and support, a donor can usually be maintained for only a relatively short time before the pathophysiologic changes induced by BD overwhelm the resuscitative capabilities of the medical team [12].

The actual number of deceased organ donors in the United States (presently about 20 pmp yearly) remains substantially below the estimated maximal volume, which approximates 50 pmp [13]. Donation in Spain has become a commonly used example of success. Organ donation rates there rose from 14 to 34 donors pmp over a 10-year period. This can be attributed to the implementation of the so-called "Spanish Model" [14], which is considered the best organ donation model at the international level [15,16].

Clinicians who care for critically ill or injured patients in the ICU must be able to recognize potential organ donors and must be aware of the criteria for BD and organ donation [17-19]. The Tuscany public hospital network consists of 20 hospitals. In those with a neurosurgery department, 14.7% of the deaths in the ICU are labeled as BDs, compared with 8.6% in those in hospitals without a neurosurgery department [6].

Data published by Van der Hoeven and colleagues confirm the relationship between the duration of BD and hemodynamic instability due to progressive dysfunction and increased immunologic activation of the donor kidney [5].

During our study, we identified 1834 potential BD organ donors (average annual incidence, 18 pmp). Of these, 58.7% were documented as having experienced BD. The percentage of consenting families (the number of families agreeing to donate divided by the number of families asked to donate) was 25.4%, and the overall conversion rate (the number of actual donors divided by the number of potential donors) was 12.4%, compared with 48% in United States [13].

Our study revealed the following data: the young age of potential donors (mean, 28.6 years), a mean duration of 10.2 days spent in the ICU, an interval of 5.5 days to report cases to the SCOT, 1.8 days (mean, 43 hours) to declare BD, 48 hours to procure organs if the family gave consent, and 5 days to cardiocirculatory cessation in nonconsensual cases of organ donation. These data show that there is a delay in recognizing potential organ donors and indicate a lack of recognition of BD by physicians. An additional delay in declaring BD is due mainly to the strict national criteria for declaring BD that must be followed in all ICUs in the Kingdom [2]. Because we follow an opt-in system, the factor that most affects any delay from BD declaration to retrieval is obtaining consent from the next of kin. Other factors include the time required for the logistics of multiorgan harvesting (eg,

waiting for the correction of liver hemodynamics, waiting to determine heart viability, arranging transportation, and waiting for laboratory results).

The entire stay of the patients in our study was characterized by a significant decrease in systolic blood pressure and a significant increase in plasma sodium and serum creatinine levels. Less time was spent in the ICU by those patients with hypothermia, hypernatremia, or renal failure.

Our overall data confirm the need for the early identification of potential candidates for BD, the effective and aggressive maintenance of those patients, and the prevention of complications that can affect the declaration of BD. Our study demonstrates that the most frequent risk factors that affect the viability of donors with BD include older age, a traumatic cause of BD, hypernatremia, acute renal failure, hypothermia, and hypokalemia.

We concluded that despite successful organ transplantation from deceased donors in the Kingdom, we must continue to increase hospital-staff awareness at donating hospitals regarding the importance of organ donation and transplantation, and we must educate ICU staff members about the recognition, early reporting, and documentation of BD cases.

Saudi protocol requires strict criteria for declaring BD and for obtaining consent for harvesting from the patient's next of kin, and these are the major factors that delay organ retrieval. Nevertheless, we believe that when compared with any other modified protocol, the Saudi protocol is far and away the best model, especially for small hospitals in the rural areas.

References

1. Health Statistical Year Book 2003, Ministry of Health, Riyadh, Kingdom of Saudi Arabia
2. Aldress A, Seraj M, Al-Qawi Z, Al-wazna T, Al-Bar M. Diagnosis of brain death and policy on cadaveric organ procurement in K.S.A. *Saudi Kidney Diseases and Transplant Bulletin* 1992; 3: 199-236
3. Shaheen FA, Souqiyeh MZ, Al-Attar B, Al-Khader A. Saudi center for organ transplantation. model of cadaver organ donation and transplantation. *Organs and Tissues* 1999; 1: 43-50
4. Saudi Center for Organ Transplantation, Annual Report 2004. Available at: <http://www.scot.org.sa>. Accessed March 2006
5. van der Hoeven JA, Molema G, Ter Horst GJ, Freund RL, Wiersema J, van Schilfgaarde R, et al. Relationship between duration of brain death and hemodynamic (in)stability on progressive dysfunction and increased immunologic activation of donor kidneys. *Kidney Int* 2003; 64: 1874-1882
6. Kunzendorf U, Hohenstein B, Oberbarnscheid M, Muller E, Renders L, Schott GE, Offermann G. Duration of donor brain death and its influence on kidney graft function. *Am J Transplant* 2002;2(3):292-294
7. Pratschke J, Wilhelm MJ, Kusaka M, Beato F, Milford EL, Hancock WW, Tilney NL. Accelerated rejection of renal allografts from brain-dead donors. *Ann Surg* 2000; 232: 263-271
8. Pratschke J, Wilhelm MJ, Kusaka M, Basker M, Cooper DK, Hancock WW, Tilney NL. Brain death and its influence on donor organ quality and outcome after transplantation. *Transplantation* 1999; 67: 343-348
9. Matesanz R, Miranda B. A decade of continuous improvement in cadaveric organ donation: the Spanish model. *J Nephrol* 2002; 15: 22-8
10. Matesanz R, Bozzi G, Saviozzi AR, Filipponi F, Bozzi G, Chiapparini L, et al. The Tuscany quality improvement programme in organ donation: the first year experience. *Organs and Tissues* 2004; 1: 15-20
11. Nowikowska A, Smietansk M, Pirski MI, Sledzinski Z. Hospital attitude survey-implementing a donor action program in hospitals of Pomerania region, Northern Poland. *Organs and Tissues* 2003; 3: 161-166
12. Shapiro R, Devita MA. Management of potential cadaveric donor. Up-to-date 2006 version 14.1. Available at: <http://www.uptodate.com>. Accessed March 2006
13. Sheehy E, Conrad SL, Brigham LE, Luskin R, Weber P, Eakin M, et al. Estimating the number of potential organ donors in the United States. *N Eng J Med* 2003; 349: 667-674
14. Miranda B, Vilardell J, Grinyo JM. Optimizing cadaveric organ procurement: the catalan and Spanish experience. *Am J Transplant* 2003; 3: 1189-1196
15. Manyalich M, Paredes D, Vilarrodona A, Rodriguez C, Perea M, Trias E. The Spanish Model-TPM can be implemented successfully in Asian countries-yes. 8th Congress of the Asian Society of Transplantation 23-27 September 2003, Kuala Lumpur, Malaysia. S 8-2.
16. Lorber MI. What's new in general surgery: Transplantation. *J Am Coll Surg* 2004; 198: 424-430
17. Karcioğlu O, Ayrik C, Erbil B. The brain-dead patient or a flower in the vase? The emergency department approach to the preservation of the organ donor. *Eur J Emerg Med* 2003; 10: 52-57
18. Rocker G. Organ and tissue donation in the intensive care unit. *CMAJ* 2002; 167: 1248-1249
19. Wang MY, Wallace P, Gruen JP. Brain death documentation: analysis and issues. *Neurosurgery* 2002; 51: 731-735; discussion 735-736