Thermogenic and metabolic response to amino acid solution in brain-dead patients

Beyin ölümü hastalarında aminoasit solüsyonlarına metabolik ve termojenik yanıt

İlkin ÇANKAYALI, Kubilay DEMİRAĞ, Seden KOCABAŞ, Ali Reşat MORAL

BACKGROUND
There is a strong correlation between amino acid infusion and increase in energy expenditure and thermogenesis. In this study, the effects of amino acid solutions on thermogenesis and energy expenditure were investigated in intensive care patients who were diagnosed as brain death.

METHODS
Twenty-six brain-dead patients were included in the study. The patients received a 4 h infusion of standard amino acid solution. Energy expenditure was measured by indirect calorimetric method. ANOVA and Bonferroni tests were used for statistical analysis.

RESULTS
The predicted energy expenditure (PEE) values were higher than the resting energy expenditure (REE) values in 24 patients. The mean REE/PEE value in all patients indicated that there was a 29% decrease in REE when compared to PEE. Body temperature and energy expenditure values were not increased during the parenteral infusion of amino acid solutions. There was no statistically significant difference between mean metabolic measurements and basal values at any time interval during the study period.

CONCLUSION
We conclude that the stimulatory effect of amino acid solution on energy expenditure and thermogenesis is abolished in brain-dead patients. This result may indicate a possible central pathway responsible for the increase in energy expenditure and thermogenesis.

Key Words: Amino acid; brain death; energy expenditure; thermogenesis.

AMAÇ
Aminoasit infüzyonu ile enerji tüketimi ve termojenezdeki artış arasında güçlü bir ilinti vardır. Bu çalışmada, yoğun bakımda beyin ölümü tanısı almış hastalarda termojenez ve enerji tüketimindeki artışa aminoasit solüsyonlarının etkisi araştırıldı.

GEREÇ VE YÖNTEM
Çalışmaya 26 beyin ölümü olgusu dahil edildi. Hastalara dört saat boyunca aminoasit solüsyonu verildi. İstirahat enerji tüketimleri endirekt kalorimetrik yöntemle ölçüldü. İstatistiksel analizler için ANOVA ve Bonferroni testleri kullanıldı.

BULGULAR
Yirmi dört hastada, tahmin edilen (hesaplanan) enerji tüketimi değerleri (TET) ölçülen istirahat enerji tüketimi (İET) değerlerinden daha yüksek bulundu. TET ile karşılaştırıldığında, tüm hastaların ortalama İET/TET değerleri, İET'de %29 değerinde bir azalma olduğunu gösterdi. Vücut ısısı ve enerji tüketimi değerleri parenteral aminoasit infüzyonu sırasında artmadı. Çalışma boyunca herhangi bir zamanda, metabolik ölçümler ve başlangıç değerleri arasında istatistiksel herhangi bir fark bulunmadı.

SONUÇ
Aminoasit solüsyonlarının enerji tüketimi ve termojeneze olan uyarıcı etkilerinin beyin ölümü olgularında görülmediği (yok olduğu) kanısına varıldı. Bu sonuç, enerji tüketimi ve termojenezdeki artıştan merkezi yolların sorumlu olabileceğini göstermektedir.

Anahtar Sözcükler: Amino asit; beyin ölümü; enerji tüketimi; termojenez.

Department of Anesthesiology and Intensive Care Unit, Ege University Faculty of Medicine, Izmir, Turkey.
Ege Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, İzmir.

Correspondence *(İletişim):* İlkin Çankayalı, M.D. Department of Anesthesiology and ICU, Ege University School of Medicine, 35100 Bornova, İzmir, Turkey.
Tel: +090 - 232 - 390 21 42 Fax *(Faks)*: +090 - 232 - 339 76 87 e-mail *(e-posta):* ilkin.cankayali@ege.edu.tr

Possible protein energy malnutrition and related functional disorders may only be prevented by optimal nutritional support and positive nitrogen balance. Amino acid (AA) solutions are one of the components of parenteral nutrition for multidisciplinary intensive care patients. There is a strong correlation between AA infusion and increase in energy expenditure (EE) and thermogenesis.[1-4] It was reported that AA infusion-related EE increase depends on the composition of the AA solution, as well as the clinical condition of the patient.[2,4-6] This hypothesis is also supported by a study indicating that there was an increase in thermogenesis and EE during the parenteral infusion of the AA solutions in unconscious intensive care patients.[4] The mechanism of this increase has not been completely explained. In spite of this knowledge, the effects of AA solutions in brain death, in which there is irreversible destruction of the brain with the resulting total absence of all cortical and brainstem functions, have not been investigated before.

In this study, the effects of AA solutions on thermogenesis and EE were investigated in intensive care patients who were diagnosed as brain death.

MATERIALS AND METHODS

Patients

After obtaining Institutional Ethics Committee approval and written informed consent, the study was carried out at the Department of Anesthesiology and Intensive Care Unit, Ege University Faculty of Medicine. A total of 26 mechanically ventilated patients who were diagnosed as brain death were included in this prospective study. Brain death was determined according to the criteria of the Ministry of Health and the protocol of the university hospital. All patients included in this study were hemodynamically and metabolically stable and had normal laboratory values.

Study design

Predicted energy expenditure (PEE) was calculated using the Harris-Benedict (HB) equation for all patients. PEE was calculated as follows: Male PEE-HB (kcal/day) = 66.473 + (13.7516 * W) + (5.0033 * H) - (6.755 * A); Female PEE-HB (kcal/day) = 655.0955 + (9.5634 * W) + (1.8496 * H) - (4.6756 * A). For both equations, W is body weight in kilograms, H is height in centimeters and A is age in years. PEE was then multiplied by an activity factor of 1.2 (bed rest) and corresponding stress factor according to the diagnosis and clinical stiation of the patient (Table 1). The appropriate exogenous calories were replaced, using a standard enteral nutrition product (Osmolite, Abbott Laboratories, North Chicago, IL, USA) via nasogastric tube. Enteral nutrition was given continuously using an enteral infusion pump (Kangaroo 624 Enteral Feeding Pump, Tyco Healthcare Group LP, Mansfield, MA, USA) before and during the study according to the PEE. Patients were randomly assigned to receive a 4-hour (h) infusion of 0.4 g/kg protein as AA solution. Brain-dead patients received standard AA solution (FreAmine 8.5%, Eczacıbaşı-Baxter, Istanbul, Turkey) using an infusion pump (Life Care Pump - Model 5000, Abbott Laboratories, North Chicago, IL, USA). The composition of the AA solutions infused is presented in Table 2. Enteral nutrition was continued during the 4-h AA infusion period without subtracting the additional energy derived from the AA solution.

Table 1. Etiology of the brain-dead patients

Patient No	Diagnosis
1	1 + 2
2	1 + 2
3	3
4	4
5	5
6	1
7	6
8	1 + 7
9	8
10	9
11	1
12	5
13	1 + 10
14	5
15	1
16	1
17	8
18	11
19	12 + 7
20	11
21	1
22	1
23	1
24	1
25	10 + 12
26	1

Subarachnoid hemorrhage 1; Intracerebral hemorrhage 2; Cranial aneurysm 3; Cardiopulmonary resuscitation, hypoxic encephalopathy 4; Brain tumor 5; Intracerebral hematoma 6; Skull fracture 7; Intraventricular hemorrhage 8; Polytrauma (cerebral infarction) 9; Subdural hematoma 10; Cranial arteriovenous malformations 11; Epidural hematoma 12.

Table 2. The composition of the amino acid solution

FreAmine 8.5%	
Essential AA	
L- Isoleucine	0.59 g
L- Leucine	0.77 g
L- Valine	0.56 g
Total amount of BCAA	1.92 g
L- Lysine	0.62 g
L- Methionine	0.45 g
L- Threonine	0.34 g
L- Tryptophan	0.13 g
L- Phenylalanine	0.48 g
Non-essential AA	
L- Alanine	0.60 g
L- Arginine	0.81 g
L- Histidine	0.24 g
L- Proline	0.95 g
L- Serine	0.50 g
Glycine	1.19 g
L-Cysteine HCl H_2O	<0.02 g
Sodium bisulfide NF	<0.10 g
Phosphoric acid	0115 g
pH	6.5
Osmolarity	810 mOsm/L
Sodium	10 mEq/L
Phosphate	20 mEq/L
Chloride	<3
Acetate	72

BCAA: Branched-chain amino acid.

Table 3. Demographic data of the brain-dead patients

Sex (F/M)	Age (year) Mean±SD	Weight (kg) Mean±SD	Height (cm) Mean±SD
6/20	38.84±17.18	65.26±12.75	167.19±10.27

Ventilation

Mechanical ventilation was instituted via an endotracheal tube or tracheotomy cannula using a volume-cycled ventilator (Horus, Taema Air Liquide, Santé, Antony Cedex, France) and was titrated to maintain blood gases within normal range (PaO_2 >60 mmHg and $PaCO_2$ between 35-45 mmHg). Tidal volumes were between 6-8 ml/kg and respiratory rates between 10-14 breaths/min. Ventilator parameters were not changed throughout the study period. All FiO_2 values were below 60%. All the patients were ventilated in volume-controlled mode.

Measurements

Stabilization of arterial blood gases and hemodynamic parameters was achieved before the start of the study period. Deltatrac II metabolic monitor (Datex-Engstrom Division, Instrumentarium Corp, Finland) was used to measure the resting energy expenditure (REE), oxygen consumption (VO_2) and carbon dioxide production (VCO_2). The Deltatrac II Metabolic Monitor is an open system device that measures VO_2 and VCO_2 in both mechanically and spontaneously breathing patients. This system uses a fast differential paramagnetic oxygen analyzer to measure a different signal between inspired and expired gases, an infrared CO_2 analyzer to measure the CO_2 in the inspired and expired gases, and a gas dilution system to measure flow. This monitor has been previously validated and tested *in vitro* for accuracy and reproducibility.[7]

Before the measurements, the O_2 and CO_2 analyzers were calibrated with a precise mixture containing 95% oxygen and 5% CO_2 (Deltatrac High-Accuracy Calibration Gas, Datex Instrumentation, Helsinki, Finland) according to the manufacturer's guidelines. Basal metabolic data (REE, VO_2, VCO_2 and respiratory quotient [RQ]) were measured during 20 min before the start of AA infusion. Then metabolic data were recorded every 30 min during the 4-h infusion period and at 30, 60, 120 and 180 min after the infusion ended. We recorded the data from the Metabolic Monitor by using the long-trend key, which indicated the mean of all previous measurements. Systolic, diastolic and mean arterial pressure, heart rate and rectal temperature were recorded concomitantly with the metabolic measurements throughout the study.

Statistical methods

The results are presented as mean±SD. Statistical analyses of the patient data were performed by one-way analysis of variance with repeated measures, Wilcoxon test, ANOVA and Bonferroni tests. Values of $p<0.05$ were accepted as statistically significant.

RESULTS

Tables 1 and 3 summarize individual and demographic data.

Predicted energy expenditure and REE values and the calculated REE/PEE ratios are given in Table 4. The PEE values were higher than the REE values in 24 patients. The mean REE/PEE value of all patients indicated that there was a 29% decrease in REE when compared to PEE.

Metabolic measurements are given in Table 5. The body temperature, EE, VCO_2 and VO_2 values

Table 4. Basal PEE, BMR, basal REE, basal REE/basal PEE (%) and basal REE/BMR (%) values in brain-dead patients

Patient Number	BMR (kcal/day)	PEE (kcal/day)	REE (kcal/day)	REE/BMR (%)	REE/PEE (%)
1	1490	1788	820	0.55	0.46
2	1440	1728	610	0.42	0.35
3	1520	2006	730	0.48	0.36
4	1470	1940	1330	0.90	0.69
5	1374	1826	880	0.64	0.48
6	1530	1836	1560	1.02	0.85
7	2440	2928	2400	0.98	0.82
8	1990	2388	2130	1.07	0.89
9	1230	1476	1570	1.28	1.06
10	1750	3465	2130	1.22	0.61
11	1780	2136	1880	1.06	0.88
12	1370	1644	1200	0.88	0.73
13	1584	1660	1460	0.92	0.88
14	1323	1785	790	0.60	0.44
15	1640	1968	1720	1.05	0.87
16	1650	1980	1550	0.94	0.78
17	1534	1840	1010	0.66	0.55
18	1098	1448	760	0.69	0.52
19	1338	1605	1440	1.08	0.90
20	1362	1797	1210	0.89	0.67
21	1924	2308	2450	1.27	1.06
22	1514	1816	1460	0.96	0.80
23	1602	2114	1190	0.74	0.56
24	1788	2145	1710	0.96	0.80
25	1880	2740	2050	1.09	0.75
26	1636	1963	1430	0.87	0.73
Mean±SD	1586.81±276.04	2137.90±584.94	1458.18±632.31	0.89±0.23	0.71±0.20

BMR: Basal metabolic rate; PEE: Predicted energy expenditure; REE: Resting energy expenditure.

did not increase during or after the termination of AA solution infusion. There were no significant differences between mean metabolic measurements and basal values at any time interval.

DISCUSSION

Brain death is a clinical condition in which brain stem reflexes and cerebral functions are irreversibly lost, and diagnosis depends on a series of clinical criteria.

Resting energy expenditure increases significantly after head trauma, as a result of endogenous catecholamine increase. This results in sympathetic nervous system hyperactivity and cerebral metabolism increase.[8-10] The increase in metabolic rate correlates with the increase in intracranial pressure.[11] Acute head trauma is an important cause of AA mobilization from tissues, and patients with serious head trauma have low plasma AA levels.[12] However, these conditions are different in brain death, in which many neuroendocrine changes are seen. The metabolic changes in brain death have not yet been clearly identified, due to the various factors affecting energy input and expenditure. These factors are related to the hypothalamus, which is stimulating the endocrine and the autonomic nervous systems. The stimulation of the ventromedial and paraventricular nuclei of the hypothalamus affects metabolism directly through the autonomic nervous system and the endocrine system. Stimulation of the posterior hypothalamus increases sympathetic activity and basal metabolic rate (BMR), while stimulation of the ventromedial nucleus increases glycogen secretion, glycogenolysis, gluconeogenesis and lipolysis. Lateral hypothalamic stimulation decreases the metabolic rate by increasing insulin secretion.[13,14]

The hypothalamus is located at the base of the third ventricle and is composed of complex nuclei, which are not clearly defined. It is an important part of the central nervous system, which regulates homeostasis by controlling the autonomic nervous system and the endocrine system. Afferent myelinated fibers, which conduct some senses from internal organs, cross the sympathetic ganglions without synapsing and reach the neuron bodies at ganglion spinale, through the rami communicantes albi.

Table 5. Temperature, REE, VCO_2 , VO_2, and RQ values in brain-dead patients

Min	Temperature Mean±SD (n: 26)	REE Mean±SD (n: 26)	VCO_2 Mean±SD (n: 26)	VO_2 Mean±SD (n: 26)	RQ Mean±SD (n: 26)
0	35.00±2.24	1441.15±521.57	170.84±57.06	210.15±79.71	0.81±0.13
30	35.02±2.27	1443.84±512.13	169.26±55.50	212.26±78.04	0.79±0.11
60	35.06±2.17	1465.38±512.28	170.00±56.75	215.00±77.63	0.78±0.10
90	35.07±2.19	1485.00±510.39	171.50±56.52	219.00±78.49	0.78±0.11
120	35.03±2.19	1496.15±507.66	170.46±54.73	220.46±77.61	0.78±0.10
150	35.06±2.23	1510.00±501.46	172.84±53.50	223.07±77.24	0.78±0.10
180	35.09±2.21	1531.53±522.85	175.88±55.85	224.19±80.79	0.78±0.11
210	35.13±2.23	1549.61±544.16	175.34±56.64	227.30±83.45	0.78±0.10
240	35.13±2.29	1561.53±549.69	176.38±55.28	220.23±85.07	0.77±0.10
270	35.16±2.30	1563.46±548.04	176.42±56.67	230.80±85.01	0.77±0.10
300	35.20±2.30	1560.00 ±551.92	177.16±57.71	229.92±85.41	0.78±0.10
360	35.30±2.30	1555.00±554.79	176.15±57.59	228.76±85.26	0.77±0.10
420	35.33±2.28	1545.00±556.13	176.84±58.31	227.65±85.95	0.78±0.10

REE: Resting energy expenditure; VCO_2: Carbon dioxide production; VO_2: Oxygen consumption; RQ: Respiratory quotient.

Afferent myelinated fibers also conduct directly to the hypothalamus.[13,14]

The hypothalamus gathers stimuli from the limbic system and the prefrontal cortex to affect blood hormone levels. It controls hormonal responses by activating the autonomic nervous system and the endocrine system. The hypothalamus is a part of the diencephalon, which lies between the chiasma opticum and corpus mamillare. The numerous afferent and efferent pathways of the hypothalamus have a complex structure. The efferent branches, which lead to the brain stem and medulla spinalis, affect peripheral neurons of the autonomic nervous system. The hypothalamus connects with the parasympathetic nuclei of *n. oculomotorius*, *n. facialis*, *n. glossopharyngeus* and *n. vagus* through a group of neurons at the formatio reticularis. Branches of the tractus reticulospinalis connect with the sympathetic center located between T_1-L_2 segments and the parasympathetic center located between $S_{2\text{-}4}$ segments of the *medulla spinalis*.[13,14]

The hypothalamus has functions such as autonomic and endocrine control, control of neurosecretions, regulation of temperature, food and water intake, and control of mood, behavior and biorhythm. The sympathetic nervous system, which is controlled centrally by the posterior nucleus of the hypothalamus, is a major efferent pathway of EE and substrate use. Thyroid hormones and other parts of the central nervous system, which are related to these hormones, also have an important role in EE.

Excess calory intake increases metabolism and diet-related thermogenesis by directly stimulating the sympathetic nervous system. The fact that beta-blocker therapy decreases REE by depressing the sympathetic nervous system also supports this fact.[15-17] We think our findings support this opinion because the brain stem and autonomic reflexes are irreversibly lost and the sympathetic nervous system is not controlled in damage of brain stem. We observed that body temperature, EE, VCO_2 and VO_2 values did not increase during or after the termination of AA solution infusion. There were no significant differences between mean metabolic measurements and basal values at any time interval. These results may be important findings in brain-dead patients. BMR, REE and thermogenetic activity were also decreased in patients with spinal cord trauma, due to a decrease in physical activity and sympathetic nervous system function.[16]

Pevsner et al.[18] reported the decrease in cerebral metabolic rate to be a reliable prognostic indicator of brain death. Other investigators also confirmed that there is at least a 60-80% decrease in REE, when compared to BMR, in brain death.[19,20]

Bitzani et al.[21] reported the decrease in REE values to be 24.5%, and stated that this finding was in correlation with transcranial ultrasonographic data. Hypothalamic, mesencephalic and bulbar insufficiencies due to decrease or lack of cerebral blood flow are thought to be the cause of the decreases in REE and thermogenetic activity in brain death.

In an experimental model of brain death, blood catecholamine levels showed two peaks, one at the

1st minute and the other at the 120th minute. This biphasic response has been advocated as the cause of hemodynamic instability in brain death.[22] Similarly, Lopau et al.[23] reported that blood levels of norepinephrine, epinephrine, plasma renin, angiotensin 2, endothelin 1, interleukin (IL)-6 and tumor necrosis factor (TNF)-receptor 2 levels decreased significantly during the first hours after diagnosis of brain death and increased afterwards.

Hormonal activities of patients who are in a condition of brain death may vary at different time intervals and blood catecholamine levels may differ, especially during the first stages of brain death. In our study, REE was found to less than BMR in brain death. This finding is parallel to the results of previous metabolic studies. Although there was nearly a 48% decrease in REE in some patients, the measured REE values were more than the PEE values in others. This variance can be explained by the fact that measurements were taken at different periods of the brain death process.

In our study, there was no increase in thermogenetic activity or EE as a result of AA infusions in patients who were diagnosed as brain death. However, it is known that there is a strong correlation between AA infusion and increase in EE and thermogenesis. It was reported that AA infusion-related EE increase depends on the composition of the AA solution, as well as the clinical condition of the patient. In our previous study, we observed increase in EE and thermogenesis during the infusion of both standard and branched-chain AA (BCAA) solutions in unconscious patients.[4] This result can be explained by the fact that neurons at the brain stem, where the hypothalamo-hypophyseal axis and medulla spinalis are related, are not functioning.

We concluded that the thermogenic and EE-increasing effects of AA solutions were induced by central stimulation, rather than being directly related to peripheral metabolism.

REFERENCES

1. Giordano M, Castellino P. Correlation between amino acid induced changes in energy expenditure and protein metabolism in humans. Nutrition 1997;13:309-12.
2. Pitkänen O, Takala J, Pöyhönen M, Kari A. Branched-chain and mixed amino acid solutions and thermogenesis in postoperative patients. Nutrition 1994;10:132-7.
3. Hayashida Y, Kido Y, Tsujinaka T, Abe Y, Kobayashi M, Nishi T, et al. Increased energy expenditure after intravenous administration of amino acids. JPEN J Parenter Enteral Nutr 1992;16:142-8.
4. Cankayali I, Demirag K, Kocabas S, Moral AR. The effects of standard and branched chain amino acid enriched solutions on thermogenesis and energy expenditure in unconscious intensive care patients. Clin Nutr 2004;23:257-63.
5. Selldén E, Lindahl SG. Postoperative nitrogen excretion after amino acid-induced thermogenesis under anesthesia. Anesth Analg 1998;87:641-6.
6. Selldén E. Amino acid administration counteracts hypothermia during anesthesia. [Article in Swedish] Lakartidningen 2001;98:1664-9. [Abstract]
7. Tissot S, Delafosse B, Bertrand O, Bouffard Y, Viale JP, Annat G. Clinical validation of the Deltatrac monitoring system in mechanically ventilated patients. Intensive Care Med 1995;21:149-53.
8. Charlín V, Carrasco F, Ferrer L, Brito A, Poblete R. Protein and energy requirements in patients with severe head injury. [Article in Spanish] Rev Med Chil 1993;121:626-32. [Abst.]
9. Chiolero RL, Thorin D, Schutz Y, Jequier E. Energy metabolism and craniocerebral injury. [Article in French] Ann Fr Anesth Reanim 1990;9:169-75. [Abstract]
10. Raurich JM, Ibáñez J. Metabolic rate in severe head trauma. JPEN J Parenter Enteral Nutr 1994;18:521-4.
11. Bucci MN, Dechert RE, Arnoldi DK, Campbell J, McGillicuddy JE, Bartlett RH. Elevated intracranial pressure associated with hypermetabolism in isolated head trauma. Acta Neurochir (Wien) 1988;93:133-6.
12. Aquilani R, Viglio S, Iadarola P, Guarnaschelli C, Arrigoni N, Fugazza G, et al. Peripheral plasma amino acid abnormalities in rehabilitation patients with severe brain injury. Arch Phys Med Rehabil 2000;81:176-81.
13. Snell RS. Clinical anatomy for medical students. 4th ed. USA: Little, Brown and Company; 1992.
14. Berry M, Bannister LH, Standring SM. Nervous system. In: Williams PL, Bannister LH, Berry MM, Collins P, Dyson M, Dussek JE, et al. editors. Gray's anatomy. 38th ed. New York: Churchill Livingstone; 1995. p. 1286-8.
15. Webber J, Macdonald IA. Signalling in body-weight homeostasis: neuroendocrine efferent signals. Proc Nutr Soc 2000;59:397-404.
16. Monroe MB, Seals DR, Shapiro LF, Bell C, Johnson D, Parker Jones P. Direct evidence for tonic sympathetic support of resting metabolic rate in healthy adult humans. Am J Physiol Endocrinol Metab 2001;280:E740-4.
17. Chioléro RL, Breitenstein E, Thorin D, Christin L, de Tribolet N, Freeman J, et al. Effects of propranolol on resting metabolic rate after severe head injury. Crit Care Med 1989;17:328-34.
18. Pevsner PH, Bhushan C, Ottesen OE, Walker AE. Cerebral blood flow and oxygen consumption. An on-line technique. Johns Hopkins Med J 1971;128:134-40.
19. Langeron O, Couture P, Mateo J, Riou B, Pansard JL, Coriat P. Oxygen consumption and delivery relationship in brain-dead organ donors. Br J Anaesth 1996;76:783-9.
20. Depret J, Teboul JL, Benoit G, Mercat A, Richard C. Global energetic failure in brain-dead patients. Transplantation 1995;60:966-71.
21. Bitzani M, Matamis D, Nalbandi V, Vakalos A, Karasakalides A, Riggos D. Resting energy expenditure in brain death. Intensive Care Med 1999;25:970-6.
22. Chiari P, Hadour G, Michel P, Piriou V, Rodriguez C, Budat C, et al. Biphasic response after brain death induction: prominent part of catecholamines release in this phenomenon. J Heart Lung Transplant. 2000;19:675-82.
23. Lopau K, Mark J, Schramm L, Heidbreder E, Wanner C. Hormonal changes in brain death and immune activation in the donor. Transpl Int 2000;13 Suppl 1:S282-5.