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FIXED R-R INTERVALS IN BRAIN DEATH

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SUMMARY

Diagnosis of brain death is one of the most challenging problems in medical practice. Reliable tests must be used in the assessment of brain death because the diagnosis must be 100 percent correct.

The variation of R-R intervals in brain death has not been evaluated systematically. In this study, we attempted to find a correlation between the diagnosis of brain death and the variation of R-R intervals. We observed that R-R intervals in our intensive care unit patients were becoming stationary by the time of brain death diagnosis. In our study, electrocardiogram and Holter recordings were taken for six patients (age: 16-66 years) with the clinical criteria of brain death. No change in heart rate was observed during carotid massage and artificial ventilation. We suggest that this finding, which we have termed "fixation of R-R intervals", might be useful in evaluating brainstem damage and in diagnosing brain death.

Key Words: *Brain Death, R-R Intervals*

ÖZET

R-R İNTERVALLERİ BEYİN ÖLÜMÜNDE SABİTLEŞİR

Beyin ölümü tanısı tıbbi pratikte en karmaşık problemlerden birisidir. Tanının %100 doğru olması gerektiği için beyin ölümünün değerlendirilmesinde güvenilir testlerin kullanılması gereklidir.

Beyin ölümünde R-R intervallerinin değişkenliği henüz sistematik olarak incelenmemiş bulunuyor. Bu çalışmada beyin ölümü tanısı ile R-R intervallerinin değişkenliği arasında korelasyon olup olmadığını incelemeyi planladık. Yoğun bakım ünitemizde beyin ölümü tanısı konduğunda R-R intervallerinin sabitleştiğini gözlemledik. Beyin ölümü klinik kriterlerine sahip 6 beyin zedelenmesi olan hastanın (yaşları 16 ile 66 arasında) elektrokardiogram ve Holter kayıtları alındı. Karotis masajı ve mekanik solunum sırasında kalp hızında değişiklik olmadığını gözlemledik. Bu durumu "R-R intervallerinin sabitleşmesi" olarak adlandırdık. Bu bulgunun beyinsapı hasarının değerlendirilmesi ve beyin ölümü tanısında yararlı olduğunu düşünüyoruz.

Anahtar Kelimeler: *Beyin Ölümü, R-R İntervalleri*

The main findings in brain death are coma, absence of brainstem reflexes and the demonstration of apnea. Persistence of these clinical signs determines the diagnosis of brain death. Clinical examination for the diagnosis of brain death includes investigation of cerebral hemisphere functions and brainstem reflexes as well as laboratory tests.

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The clinical diagnosis of brain death is not generally a difficult problem; however, it carries a great responsibility, because it must be 100 percent correct. Several committees and reviewers have proposed clinical criteria for brain death (1,2,3). Most brain death codes allow for the use of electroencephalography (EEG), which must demonstrate electrocortical silence over a certain period. Cerebral evoked potentials (EP) can also be used to demonstrate the successive loss of activity of various pathways, and other neurophysiological tests demonstrating the loss of cerebral perfusion can also be implemented. Brain scintigraphy can confirm the loss of isotope uptake into the brain, and Doppler sonography can be used to demonstrate cessation of brain perfusion. In essence, brain death is diagnosed when there is no discernible evidence of either cerebral hemisphere or brainstem function for an extended period of time, usually 12 hours or more, and when the loss of brain functions is the result of a structural brain disease and not of a reversible metabolic disease or of depression caused by drugs.

We observed that the R-R intervals of patients in our intensive care unit (ICU) were becoming fixed along with the diagnosis of brain death. As variation of R-R intervals have not been evaluated systematically in brain death, we aimed to focus on this issue using our patient data.

METHOD

Six cases of brain death (ages: 16-66 years) with fixed R-R intervals were observed in our ICU. Brain death was diagnosed according to the existing criteria, based on clinical examination results supported by EEG, EP and cranial computed tomography. After admission to the ICU, patients' pulse rates, blood pressure (by arterial catheter), temperature, saturation of oxygen, etc. were monitored. The patients were all in unresponsive comas, they were not breathing spontaneously, and they had absent cephalic reflexes with non-reactive fixed pupils. Spinal segmental reflexes were occasionally observed.

The etiologies leading to brain death included cerebrovascular event, head injury due to traffic accident, respiratory arrest due to acute respiratory distress syndrome and bullet-induced head injury (Table 1). Patients were ventilated using 10/min inspiration and expiration cycles, generally with a 500 cc volume. The respiratory supply was turned off only in the event of spontaneous cardiac arrest. None of the patients' relatives gave their consent for organ transplantation after the declaration of brain death.

In all cases, 12-lead electrocardiograms (ECG) were obtained at least twice a day, with at least 50 beats per second, and continuous ECG monitoring was carried out for at least two hours with the aid of a Holter system. R-R intervals and heart rate variations were measured from the records in 25 consecutive beats. Heart rates were measured during carotid massage, applied to either carotid for two minutes, with 10 minutes intervals and during artificial ventilation.

Table 1: Age, sex, etiology, tests and follow up distribution of cases.

No	Age	Sex	Cause of the Brain Death	Duration of artificial ventilation (day)	EEG	Cephalic reflexes	BAER	Apnea test	Follow up	R-R Intervals
1	66	Female	Cerebrovascular accident	6	Flat	Negative	No response	No response	Exitus	Fixed
2	45	Male	Cerebrovascular accident	5	Flat	Negative	No response	No response	Exitus	Fixed
3	62	Male	Traffic accident, severe head trauma	5	Flat	Negative	No response	No response	Exitus	Fixed
4	38	Male	Acute respiratory distress syndrome and respiratory arrest	3	Flat	Negative	No response	Not done	Exitus	Fixed
5	22	Male	Bullet injury, head trauma	5	Flat	Negative	No response	No response	Exitus	Fixed
6	16	Female	Traffic accident, severe head trauma	12	Flat	Negative	No response	No response	Exitus	Fixed

RESULTS

R-R intervals were found to be fixed during artificial ventilation over a determined period of time (minimum: 1 minute) (Figure 1). Heart rate was observed to change with increased body temperature and rate of dopamine infusion. However if the vital signs were stable, the R-R intervals were fixed for at least one minute; in other words, there was no change in R-R intervals. We referred to this condition as "fixation of R-R intervals" (Figure 2). No change in heart rate was observed during carotid massage applied to either carotid or during the application of painful stimulus (Figure 3). We also observed by Holter monitoring that the heart rate was fixed if there were no external factors.

DISCUSSION

Cardiac activity is normally under the antagonistic influence of the intracranial parasympathetic (vagal dorsal nucleus) and the extracranial sympathetic systems (4). Three vagal areas participate in cardiac control. The principal parasympathetic afferent input via the nodosa ganglion is to the nucleus of the solitary tract. Cardiac motor efferent sources are the nucleus ambiguus and dorsal vagal nucleus. The principal medullary site of sympathetic cardiac control resides in the rostral ventrolateral medulla. In addition, supramedullary areas such as the parabrachial nucleus in pons, hypothalamus, amygdala, insular cortex, medial medullary region, temporal lobe and cingulate gyrus have important functions in cardiac control mechanisms.

All of the effects of CNS elements on cardiac functions disappear in brain death (5,6). The effects of the parasympathetic system disappear directly. The sympathetic system is affected indirectly with the disappearance of the effects of afferent impulses on the central and cervicothoracal systems. As a result of all these changes, cardiac pacemakers are released from the effects of central regulating systems. They gain autonomy, and start to work with their own rhythms.

Since the variation of R-R intervals are influenced by the respiratory center in the medulla and by parasympathetic nervous system activity associated with the vagal nerve circuit, this variation might be lost in brain death, resulting in fixed R-R intervals.

The coefficient of variation of R-R intervals has been reported to decrease in some conditions such as peripheral neuropathy, barbiturate intoxication and presence of severe brainstem lesions (7,8,9). There are only a few reports examining the relationship between R-R intervals or heart rate variation and brain death. Neru et al reported on four children with brain death among a group of patients, in which they observed an extremely low coefficient of variation of R-R intervals (1.00-1.29%) with brain death (7).

We also observed fixed R-R intervals in our adult patients with brain death. We believe that this is a result of autonomic dysfunction due to severe brain damage. Therefore, we suggest that the investigation of R-R interval variations might be useful in evaluating and diagnosing brain death. We conclude that "R-R interval fixation" is a confirmatory test and could be included in the protocol for assessment of brain death.

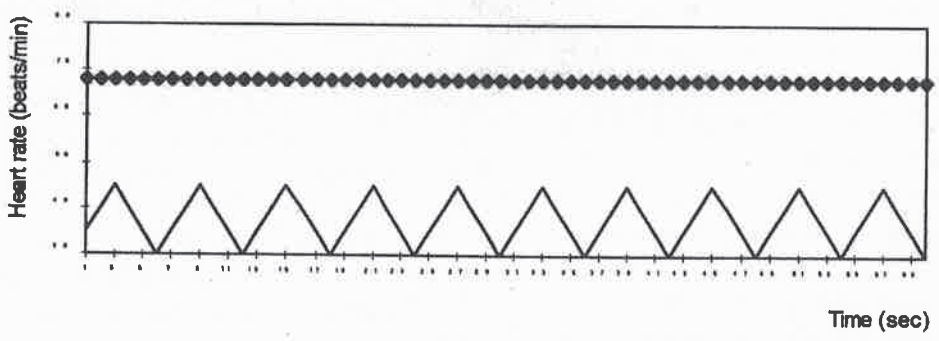

Figure 1: No change in heart rate with artificial ventilation.

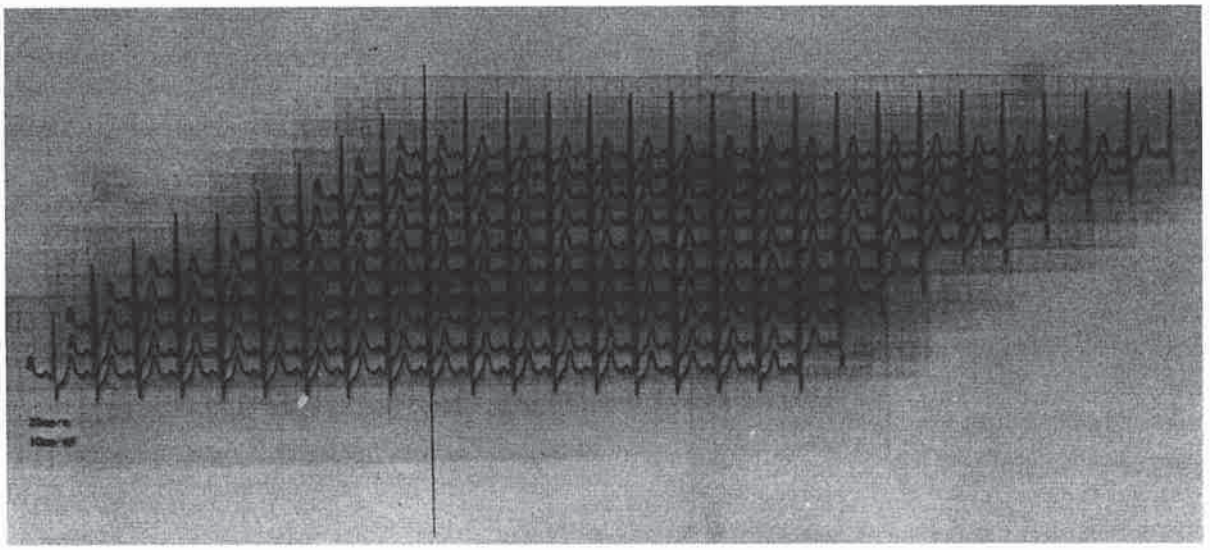

Figure 2: Heart rate stability - "fixation of R-R intervals".

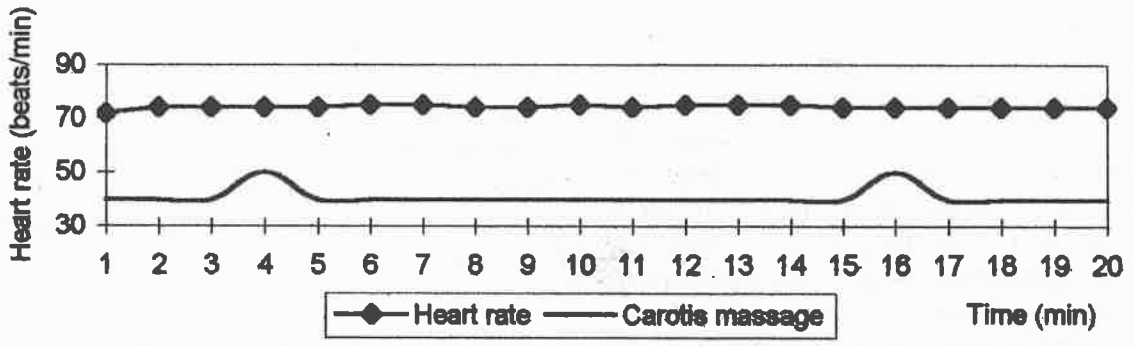

Figure 1: No variation in heart rate during carotis massage

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