Red Cell Distribution Width in Diagnosis of Brain Death

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ABSTRACT

Introduction. Red blood cell distribution (RDW) is a hematologic index automatically calculated by blood cell counters. Research about RDW in traumatic brain injury showed positive correlation between high RDW values and mortality, which inspired us to investigate whether RDW could be used as a supportive diagnostic biomarker for diagnosis of brain death. Our hypothesis is that RDW may be useful as a biomarker that supports the diagnosis of brain death.

Methods. After approval of the ethics committee, 209 patients who had been diagnosed with brain death between January 2012 and July 2018 were retrospectively reviewed. The RDW values of patients on the days of admission, brain death, and cardiac arrest were recorded. Data were collected from hospital database and patient charts.

Results. Statistical analysis revealed that the RDW values on the days of brain death and cardiac arrest were significantly higher than on the day of admission. In addition, the RDW values for the cardiac arrest day were significantly higher than on the day of brain death ($P < .001$).

Conclusions. We can say that the increase in RDW, which is reported to be an indicator of mortality for many diseases, can be a supporting biomarker for brain death diagnosis when evaluated concomitantly with clinical diagnostic criteria.

RED blood cell distribution (RDW) is a hematologic index automatically calculated by blood cell counters. RDW values were investigated in hematologic studies for diagnosis and classification of anemia [1].

Recent studies have found RDW to be significant for both short- and long-term prognosis in pathologies such as vascular, cardiovascular, peripheral artery diseases; traumatic brain injury (TBI); autoimmune and inflammatory diseases; malignancies (cancer and leukemia); and oxidative stress [1].

Brain death is defined as irreversible loss of brain and brainstem functions. Brain death in adults is diagnosed at bedside by clinical examination. However, supporting tests may be needed to diagnose brain death when cranial nerves cannot be evaluated, if the patient is under deep sedation, when apnea testing is inappropriate or cannot be completed, if the patient has multiple organ failure, and when clinical tests are unreliable [2–4].

RDW was used as a prognostic marker for TBI, and high RDW values were correlated with mortality [5]. Research about RDW in TBI inspired us to investigate whether RDW could be used as a supportive diagnostic biomarker for diagnosis of brain death. Our hypothesis is that RDW may be useful as a biomarker that supports the diagnosis of brain death.

METHODS

Collected Data

After ethics committee approval, 210 patients diagnosed with brain death in the intensive care unit of Ankara Numune Education and

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Research Hospital between January 2012 and July 2018 were reviewed retrospectively. Only 1 patient was excluded because of an incomplete medical record. The endpoint of this retrospective study was cardiac arrest following brain death. All data were collected from electronic database records and medical charts and included age, sex, and RDW values on the days of admission, brain death, and cardiac arrest.

Statistical Analysis

Quantitative variables were expressed as mean ± SD, and qualitative variables were expressed as numbers and percentages. The conformity of the numerical data with normal distribution was evaluated by Kolmogorov-Simirnov test. Wilcoxon signed rank test was used to compare numerical data not conforming to normal distribution. We used the box plot to graphically depict the change in RDW data. Statistical analysis was performed with SPSS 23.0 software (IBM, Armonk, New York, United States) for Windows. $P < .05$ was considered to indicate statistical significance.

Power analysis was performed with PASS software (NCSS, Kaysville, Utah, United States). A sample size of 209 achieves 99% power to detect a mean of paired differences of 1 and 0 with an estimated standard deviation of differences of 2 and 3 and with a significance level (α) of 0 and 0.05 using a 2-sided paired t test.

RESULTS

One hundred sixteen (55.2%) male and 94 (44.8%) female patients diagnosed with brain death (age range: 18–92 years; average age: 55.13 years) were enrolled in the study. The mean RDW values on days of hospital admission, brain death, and cardiac arrest were 14.36, 15.37, and 15.76, respectively. Statistical analysis revealed that the RDW values on the days of brain death and cardiac arrest were significantly higher than on the day of admission ($P < .001$). In addition, the RDW value on the day of cardiac arrest was also significantly higher than on the day of brain death ($P < .001$) (Table 1). Patients' RDW values at the time of brain death are higher than RDW values at the time of admission (Fig 1).

DISCUSSION

In the literature, there are studies investigating whether RDW is a diagnostic or prognostic biomarker in anemia [6], cardiovascular diseases [7], acute appendicitis [8], and TBI. However we found no studies concerning the relationship between RDW and brain death or brain death diagnosis.

Table 1. Demographic Characteristics and Comparison of Red Blood Cell Distribution Values

Demographics	Values (N = 209)
Age (y), mean ± SD (range)	55.13 ± 17.5 (18–92)
Sex	
Male	116 (55.2)
Female	94 (44.8)
RDW on admission, mean ± SD (range)	14.36 ± 2.1 (11–26)
RDW on brain death, mean ± SD (range)	15.37 ± 2.4 (12–28)*
RDW on cardiac arrest, mean ± SD (range)	15.76 ± 2.5 (12–29)*,†

Values are given as number (%) unless otherwise specified.
Abbreviation: RDW; red cell distribution width.
*$P < .001$ when compared with the RDW value on admission.
†$P < .001$ when compared with RDW value on the day of brain death.

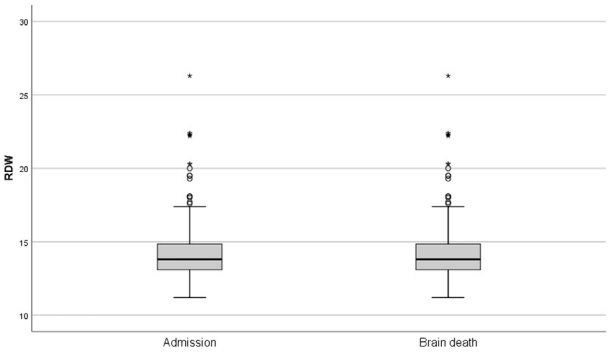

Fig 1. Box plot of red blood cell distribution width (RDW) values in brain death and admission time in patients with brain death.

In one study, an evaluation of RDW in acute heart failure showed an increase in RDW that was independent from nutrition, transfusion, or inflammation status of the patient. It was reported that RDW might predict 1-year mortality in acute heart failure and may contribute to the prognostic value of heart failure biomarkers such as N-terminal pro-brain natriuretic peptide or the interleukin receptor member ST2 [7]. Another study on the prognostic characteristics of RDW was performed in patients with TBI; as a result, RDW increase was predictive of mortality. It was concluded that RDW may be a strong prognostic biomarker for TBI mortality and that more attention should be paid to the RDW level during the evaluation of TBI patients [5]. Increased RDW value is considered as a marker of morphologic or functional (metabolic) imbalance in humans [1]. In our study, we also found that RDW on the day of brain death was significantly higher compared to RDW on admission.

In patients being treated for anemia, after the fifth day of iron replacement, a significant increase in RDW was accepted as an important early finding to confirm iron deficiency and differentiate it from other hypochromic anemias. It was concluded that this could be used in the differential diagnosis of iron deficiency and thalassemia syndromes [6]. Another study investigating RDW for the diagnosis of acute appendicitis found RDW levels to be lower in patients with acute appendicitis than in the control group. However, it was concluded that RDW levels could not be useful for diagnostic purposes because they changed very little [8]. In the evaluation of TBI, protein S100 beta, neuron-specific enolase, glial fibrillary acidic protein, and myelin basic protein are mentioned as promising markers [5]. However, none of them can be studied easily in clinical practice. The fact that RDW is part of a complete blood count, which is a frequently used laboratory test, facilitates its use for diagnostic purposes. In our study, we found that there was a significant increase in RDW on the day of brain death and that it continued to increase until the day of

cardiac arrest. Although it is obvious that brain death is primarily a clinical diagnosis, RDW is an easily studied biomarker to support clinical diagnosis.

CONCLUSIONS

We can say that the increase in RDW, which is reported to be an indicator of mortality for many diseases, can be a supporting biomarker for brain death diagnosis when evaluated concomitantly with clinical diagnostic criteria.

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