Original Article

Red cell distribution width and all-cause mortality in patients with atrial fibrillation: A cohort study

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Abstract

Background: Increased red cell distribution width (RDW), a measure of red cell size variability, has been associated with increased mortality in multiple cardiovascular diseases. However, whether RDW is associated with increased mortality in patients with atrial fibrillation remains unknown.

Methods: Using the computerized database of the largest health maintenance organization in Israel, we identified a cohort of adults with atrial fibrillation diagnosed before January 1, 2012. Cardiovascular risk factors and comorbidities were ascertained using an electronic medical record–based algorithm. Mortality was established using the National Death Index through December 31, 2013.

Results: Of 69,412 patients, 12,104 (17.4%) participants died during follow-up. The crude, two-year cumulative all-cause mortality rate increased across RDW quartiles; 9.8%, 13.6%, 18.8%, and 28.5%, respectively. After adjustment for age, sex, anemia, cardiovascular risk factors, comorbidities, and medication use, compared to the lowest RDW quartile, the hazard ratio (HR) for mortality was 1.20 (95% CI, 1.13–1.27) in the second quartile, 1.44 (1.36–1.53) in the third quartile, and 1.90 (1.79–2.00) in the highest RDW quartile. The results were similar after further adjustment for smoking, socioeconomic status, renal function, low and high density lipoprotein cholesterol levels, with HR = 1.82 (1.71–1.93) in the highest RDW quartile compared to the lowest quartile. Changes in RDW over time were strongly associated with mortality; increased RDW was associated with higher risk of mortality and decline in RDW was associated with decreased mortality.

Conclusions: RDW and changes in RDW are independently associated with the risk of all-cause mortality in patients with atrial fibrillation.

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1. Introduction

Red cell distribution width (RDW) is a measure of red cell size variability, with higher RDW values reflecting greater heterogeneity (anisocytosis), and its use in the clinical setting has been confined to the differentiation between several etiologies of anemia [1]. However, in recent years, RDW has emerged as a novel predictor of all-cause mortality in multiple cardiovascular settings including congestive heart failure (CHF), and ischemic heart disease (IHD) [2–8].

Atrial fibrillation is a common cardiac arrhythmia among older adults that is likely to increase 2.5-fold during the next 50 years [9]. Frequent hospitalization, hemodynamic abnormalities, and thromboembolic events related to atrial fibrillation can result in significant morbidity and mortality [10]. Identification of new prognostic risk factors like RDW would be valuable for adverse outcome prediction in patients with atrial fibrillation, especially if obtained routinely and inexpensively. Recently, we showed that RDW is an independent predictor of stroke in patients with atrial fibrillation [11]. However, whether RDW is also associated with increased risk of mortality in patients with atrial fibrillation remains unknown. In this study we aimed to assess the association of RDW and changes in RDW over time with all-cause mortality in patients with atrial fibrillation, using data from a population-based electronic medical registry (EMR) database of the largest health maintenance organization (HMO) in Israel.

2. Materials and methods

2.1. Data source

Clalit Health Services (CHS) is a not-for-profit health care provider covering more than half of the Israeli population [11,12]. The EMR database of the CHS includes data from multiple sources:
primary care physicians, specialty clinics in the community, hospitals, laboratories, and pharmacies. A chronic disease registry is compiled from these data sources. Diagnoses are captured in the registry by diagnosis-specific algorithms, employing code reading (e.g., ICD-9 and ICD) text reading, laboratory test results, and disease-specific drug usage. A record is kept of the sources and dates of diagnosis used to establish the diagnosis, with the earliest recorded date being considered the starting date of the diagnosis.

### Table 1

Baseline distribution of demographic and clinical characteristics of participants according to red blood cell distribution width (RDW) quartiles; CHS cohort, Israel 2012.

| Variable | All \(n=69,412\) | Red cell distribution width (RDW) quartiles |
|----------|-----------------|---------------------------------------------|
|          | \(n=69,412\)    | \(n=19,061\) (≤ 13.6%) | \(n=17,186\) (13.6%–14.3%) | \(n=16,013\) (14.3%–15.2%) | \(n=17,152\) (> 15.2%) |
| **Age** (years) | 74.8 ± 12.0 | 71.8 ± 13.2 | 74.9 ± 11.8 | 76.4 ± 11.0 | 76.6 ± 10.9 |
| **Age** | 65–75 years | 16,178 (23.3%) | 4756 (25.0%) | 4077 (23.8%) | 3538 (22.1%) | 3807 (22.2%) |
| **Gender** | 40,140 (57.8%) | 9085 (47.7%) | 9904 (57.6%) | 10,160 (63.4%) | 10,991 (64.1%) |
| **Ethnicity** | 53,997 (51.9%) | 9252 (48.5%) | 8801 (51.2%) | 8552 (53.4%) | 9392 (54.8%) |
| **Socioeconomic status** | 62,289 (87.9%) | 17,283 (90.7%) | 15,549 (90.5%) | 14,389 (89.9%) | 15,068 (87.8%) |
| **Smoking status** | 34,990 (64.4%) | 12,098 (64.3%) | 10,998 (65.0%) | 10,228 (65.1%) | 10,666 (63.3%) |
| **Comorbidities** | 23,660 (34.2%) | 6194 (32.6%) | 5668 (33.1%) | 5480 (34.4%) | 6318 (37.0%) |
| **Medications use in the prior 120 days** | 29,775 (43.1%) | 8014 (42.2%) | 7253 (42.4%) | 6929 (43.5%) | 7579 (44.4%) |
| **Laboratory tests** | 15,660 (22.7%) | 4781 (25.2%) | 4181 (24.4%) | 3529 (22.1%) | 3169 (18.6%) |
| **Anemia** | 43,990 (64.4%) | 12,098 (64.3%) | 10,998 (65.0%) | 10,228 (65.1%) | 10,666 (63.3%) |
| **Comorbidities** | 24,303 (36.6%) | 6706 (35.7%) | 5932 (35.0%) | 5477 (34.9%) | 6188 (36.7%) |
| **Medications use in the prior 120 days** | 26,047 (37.5%) | 5663 (29.7%) | 6039 (35.1%) | 6394 (39.9%) | 7951 (46.4%) |
| **Laboratory tests** | 56,232 (81.0%) | 13,913 (73.0%) | 13,827 (80.5%) | 13,552 (84.6%) | 14,940 (87.1%) |
| **Medications use in the prior 120 days** | 28,272 (40.7%) | 5696 (29.9%) | 6953 (40.5%) | 7275 (45.4%) | 8348 (48.7%) |
| **Laboratory tests** | 29,775 (43.1%) | 10,163 (53.3%) | 9212 (53.6%) | 8649 (54.0%) | 9149 (53.3%) |
| **Medications use in the prior 120 days** | 37,961 (54.7%) | 8774 (46.0%) | 8997 (52.4%) | 9351 (58.4%) | 10,839 (63.2%) |
| **Laboratory tests** | 5791 (8.3%) | 1134 (5.9%) | 1299 (7.6%) | 1430 (8.9%) | 1928 (11.2%) |
| **Medications use in the prior 120 days** | 41,404 (62.0%) | 3147 (16.5%) | 3301 (19.2%) | 3362 (21.0%) | 4230 (24.7%) |
| **Laboratory tests** | 9930 (14.3%) | 1982 (10.4%) | 2190 (12.7%) | 2404 (15.0%) | 3354 (19.6%) |

**Abbreviations:** CHF—congestive heart failure, IHD—ischemic heart disease, PVD—peripheral vascular disease, TIA—transient ischemic attack, COPD—chronic obstructive pulmonary disease, ACE-inh—angiotensin converting enzyme inhibitor, ARBs—angiotensin receptors blockers, LDL—low density lipoprotein, HDL—high density lipoprotein, RDW—red cell distribution width, eGFR—estimated glomerular filtration rate.

* \( P < 0.05. \)

† Variables with missing data: socioeconomic status 0.5%, smoking status 1.6%, LDL 6.0%, HDL 4.7%, creatinine 0.8%.

2.2. Study population

The CHS computerized database was retrospectively searched for all adult patients (age ≥ 20 years) in whom atrial fibrillation was diagnosed before January 1, 2012 (77,297 subjects). We included only subjects who had at least one complete blood cell count test result performed during the year prior to study entry (69,412 subjects).

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2.3. Follow-up

The cohort of subjects with atrial fibrillation was retrospectively followed for the outcome of all-cause mortality from January 1, 2012 until December 31, 2013. Mortality was established by matching our data with the National Death Index.

2.4. Study variables and definition of terms

The most recent RDW test performed in the year prior to study entry (2011) was used to examine the association of RDW with all-cause mortality. For this purpose, RDW was classified into quartiles (≤13.6%, 13.6–14.3%, 14.3–15.2%, >15.2%). In addition, RDW was classified into two categories based on the upper bound of the normal RDW: normal (RDW ≤14.5%) and elevated (RDW >14.5%). RDW was also tested as a continuous variable. To examine the association of the changes in RDW over time with all-cause mortality, we included subjects with at least two RDW tests performed during the year prior to study entry (n=50,597). The first and last (most recent) tests were selected and each classified into the aforementioned categories. The combinations of the first and second test categories yielded four different combinations: normal-normal (both first and second test were normal), normal-elevated, elevated-normal, and elevated-elevated.

Variables studied as possible confounders were: sociodemographic variables, cardiovascular risk factors and comorbidities reflecting leading causes of death, smoking status, use of selected medications, and selected laboratory tests. Sociodemographic variables included sex, age at the time of study entry, and socioeconomic status (SES) defined based on the SES score of the clinic neighborhood as defined by the Israeli Central Bureau of Statistics and classified into three categories (low, middle, and high). Diagnosis of cardiovascular risk factors and comorbidities included hypertension, diabetes mellitus (DM), CHF, IHD, peripheral vascular disease (PVD), prior stroke or transient ischemic attack (TIA), chronic obstructive pulmonary disease (COPD), and any malignancy not including non-melanoma skin cancer. Medication use was established by searching the pharmacy database, and defined as any prescription filled during the 120 days prior to study entry. The use of the following medications was considered: anticoagulants, antiplatelet, statins, angiotensin converting enzyme inhibitors (ACE-inh), angiotensin receptor blockers (ARBs), and beta-blockers. Smoking status was classified into ever-smoking and never-smoking. In addition to RDW, the following test results were retrieved from the CHS laboratory database: hemoglobin, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and creatinine level. Only blood tests from the year prior to study entry were selected; if more than one test result was available, the blood test conducted nearest to the time of study entry was selected. Anemia was defined as hemoglobin levels <13.0 g/dL in men and <12.0 g/dL in women in accordance with the World Health Organization (WHO) classification criteria [13]. Estimated glomerular filtration rate (eGFR) was calculated based on the formula from the Modification of Diet in Renal Disease Study [14].

2.5. Statistical methods

Continuous variables are summarized with mean ± SD, and categorical variables are presented as numbers and proportions. Analysis of variance (ANOVA) was used to compare continuous variables, and the chi-square test to compare categorical variable between RDW quartiles. Kaplan-Meier method was used to plot the distribution of time to death by RDW quartiles, and the log rank test was used to compare curves. Cox proportional hazard regression models were used to assess the association between time to death and RDW. Two models were tested; Model I included variables with complete data and was adjusted for age, sex, anemia, cardiovascular risk factors and comorbidities (hypertension, DM, CHF, IHD, PVD, stroke or TIA, malignancy, COPD), and selected medication use (anticoagulants, antiplatelet, statins, beta-blockers, ACE-inh and ARBs). In addition to the variables included for Model I, Model II included variables with a missing value (socioeconomic and smoking status, renal function, LDL and HDL levels), with 91.9% of subjects included in Model II overall. Included in both models, all covariates were checked against one another for collinearity. P-values less than 0.05 for the two-tailed tests were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics 21.0, and forest plots were constructed using WinPepi version 11.15.
Table 3
Cox proportional hazard models for the association between red cell distribution width (RDW) quartiles and all-cause mortality in patients with atrial fibrillation; CHS cohort, Israel 2012.

| Variables          | Model I |        |        | Model II |        |        |
|--------------------|---------|--------|--------|----------|--------|--------|
|                    | n=69,412|        |        | n=63,820|        |        |
|                    |         | HR (95% CI) | P value |         | HR (95% CI) | P value |
| RDW Quartiles      |         |        |        |          |        |        |
| Quartile-1 (≤ 13.6%) | Reference |        |        | Reference |        |        |
| Quartile-2 (13.6–14.3%) | 1.20 (1.13–1.27) | < 0.001 |        | 1.16 (1.08–1.24) | < 0.001 |
| Quartile-3 (14.3–15.2%) | 1.44 (1.36–1.53) | < 0.001 |        | 1.40 (1.31–1.49) | < 0.001 |
| Quartile-4 (> 15.2%) | 1.90 (1.79–2.00) | < 0.001 |        | 1.82 (1.71–1.93) | < 0.001 |
| Age                |         |        |        |          |        |        |
| < 65 years         | Reference |        |        | Reference |        |        |
| 65–73 years        | 1.69 (1.54–1.87) | < 0.001 |        | 1.68 (1.52–1.86) | < 0.001 |
| ≥ 75 years         | 3.97 (3.65–4.32) | < 0.001 |        | 3.98 (3.64–4.36) | < 0.001 |
| Gender             |         |        |        |          |        |        |
| Males              | 1.02 (0.99–1.06) | 0.221 |        | 1.10 (1.06–1.15) | < 0.001 |
| Females            |         |        |        |          |        |        |
| Ethnicity          |         |        |        |          |        |        |
| Arabs              | 1.01 (0.95–1.08) | 0.761 |        | 0.98 (0.91–1.06) | 0.646 |
| Jews               | Reference |        |        | Reference |        |        |
| Comorbidities      |         |        |        |          |        |        |
| Hypertension       | 1.27 (1.19–1.35) | < 0.001 |        | 1.19 (1.11–1.28) | < 0.001 |
| Diabetes           | 1.18 (1.14–1.23) | < 0.001 |        | 1.14 (1.10–1.19) | < 0.001 |
| CHF                | 2.14 (2.05–2.22) | < 0.001 |        | 2.11 (2.02–2.20) | < 0.001 |
| IHD                | 1.16 (1.11–1.20) | < 0.001 |        | 1.12 (1.07–1.17) | < 0.001 |
| PVD                | 1.23 (1.17–1.30) | < 0.001 |        | 1.21 (1.14–1.28) | < 0.001 |
| Stroke or TIA      | 1.43 (1.38–1.49) | < 0.001 |        | 1.42 (1.36–1.48) | < 0.001 |
| Malignancy         | 1.28 (1.23–1.33) | < 0.001 |        | 1.33 (1.27–1.39) | < 0.001 |
| COPD               | 1.37 (1.31–1.43) | < 0.001 |        | 1.38 (1.32–1.45) | < 0.001 |
| Medications use in the prior 120 days |        |        |        |          |        |        |
| Anticoagulants     | 0.72 (0.70–0.75) | < 0.001 |        | 0.75 (0.72–0.78) | < 0.001 |
| Antiplatelet       | 0.92 (0.88–0.96) | < 0.001 |        | 0.94 (0.90–0.99) | 0.008 |
| Statins            | 0.60 (0.58–0.62) | < 0.001 |        | 0.63 (0.60–0.66) | < 0.001 |
| ACE-inh & ARBs     | 0.75 (0.72–0.77) | < 0.001 |        | 0.78 (0.75–0.82) | < 0.001 |
| Beta-blockers      | 0.96 (0.92–0.99) | 0.026 |        | 0.94 (0.90–0.98) | 0.003 |
| Laboratory tests   |         |        |        |          |        |        |
| Anemia             | 1.63 (1.57–1.69) | < 0.001 |        | 1.60 (1.54–1.67) | < 0.001 |
| Creatinine         | –       | –       |        | 1.13 (1.11–1.15) | < 0.001 |
| LDL                | –       | –       |        | 1.00 (1.00–1.00) | 0.034 |
| HDL                | –       | –       |        | 0.99 (0.99–0.99) | < 0.001 |
| Socioeconomic status |         |        |        |          |        |        |
| Low                | –       | –       |        | Reference |        |        |
| Middle             | –       | –       |        | 0.99 (0.94–1.03) | 0.499 |
| High               | –       | –       |        | 0.90 (0.86–0.95) | < 0.001 |
| Smoking status     |         |        |        |          |        |        |
| Never              | –       | –       |        | Reference |        |        |
| Ever               | –       | –       |        | 1.01 (0.97–1.06) | 0.646 |

Abbreviations: CHF = congestive heart failure, IHD = ischemic heart disease, PVD = peripheral vascular disease, TIA = transient ischemic attack, COPD = chronic obstructive pulmonary disease, ACE-inh = angiotensin converting enzyme inhibitor, ARBs = angiotensin receptors blockers, LDL = low density lipoprotein, HDL = high density lipoprotein, RDW = red cell distribution width, HR = hazard ratio, CI = confidence interval.

Model I: adjusted for age, gender, ethnicity, cardiovascular risk factors and comorbidities (hypertension, diabetes mellitus, CHF, IHD, PVD, stroke or TIA, malignancy, COPD), anemia, and selected medications use (anticoagulants, antiplatelet, statins, beta-blockers, ACE-inh & ARBs).

Model II: adjusted for socioeconomic status, smoking status, creatinine, LDL and HDL cholesterol levels in addition to covariates in Model I.

1 HR for each 1 mg/dL increase.

3. Results

A total of 69,412 adult subjects with atrial fibrillation were included in the study. The mean age was 74.8 (± 12.0) years, and 35,415 (51.9%) were women. A previous history of stroke or TIA was detected in 16,415 (23.6%) subjects, and overall 28,272 (40.7%) patients with atrial fibrillation were treated with anticoagulants at baseline (Table 1). Compared to those in the lowest quartile, subjects in the highest quartile were older, and were more likely to be women. The proportion of subjects with cardiovascular risk factors, and comorbidities along with the average CHADS2 and CHA2DS2-VASc scores increased across RDW quartiles (Table 1). The baseline socio-demographic, clinical, medication use, and laboratory characteristics of the study participants are presented by RDW quartiles as shown in Table 1.

3.1. Association between RDW and all-cause mortality

Overall, 12,104 (17.4%) of 69,412 participants died during follow up. The distribution of time to death according to RDW quartiles is depicted in Fig. 1. The two-year crude cumulative all-cause
Subjects without anemia (n = 41,480)

Subjects with anemia (n = 27,932)

mortality rate increased across RDW quartiles (9.8%, 13.6%, 18.8%, and 28.5%, respectively) (Table 2).

Multivariate Cox proportional hazard regression analysis showed that RDW was independently associated with all-cause mortality after adjustment for age, sex, anemia, cardiovascular risk factors, comorbidities, and medication use (Model I, Table 3). Compared to subjects in the lowest RDW quartile, the risk of mortality increased with increasing RDW quartiles; adjusted HR was 1.20 (95% CI, 1.13–1.27) for the second RDW quartile, 1.44 (1.36–1.53) for the third quartile, and 1.90 (1.79–2.00) for the highest quartile (P for trend < 0.001) (Model I, Table 3). We reached similar results after further adjusting for smoking, socioeconomic status, renal function, and LDL and HDL levels (Model II, Table 3). Stratified analysis by anemia status of the fully adjusted model showed that the results were similar both for patients with and without anemia (P for interaction = 0.162) (Fig. 2).

The association of RDW with all-cause mortality persisted when tested as a continuous variable: for each 1% increment RDW, the fully adjusted HR = 1.13 (1.12–1.14) (P for trend < 0.001) (Model I, Table 3). When tested as a dichotomous variable, the fully adjusted HR = 1.49 (1.43–1.55) for patients with elevated RDW (≥ 14%) compared to those with normal RDW (< 14.5%) (Model I, Table 3).

3.2. Association between the change in RDW and all-cause mortality

Overall, 50,597 (72.9%) subjects, with at least two RDW tests performed during the year prior to study entry, were included in this analysis. The average time between the first and last RDW tests was 213 ± 88 days. The average difference between the last and first RDW tests was 0.24% ± 1.42. The average RDW difference within each of the four groups is shown in Table 5. Multivariate Cox proportional hazard regression analysis showed that the change in RDW in the year prior to study entry was independently associated with all-cause mortality after adjustment for age, sex, anemia, cardiovascular risk factors, comorbidities, and medication use (Model I, Table 3). Compared to subjects with persistently

| Type of RDW variable | Model I | Model II |
|----------------------|---------|----------|
| RDW Quartiles        |         |          |
| Quartile-1 (≤ 13.6%) | Reference | Reference | < 0.001 | < 0.001 |
| Quartile-2 (13.6–14.3%) | 1.20 (1.13–1.27) | 1.16 (1.08–1.24) | < 0.001 |
| Quartile-3 (14.3–15.2%) | 1.44 (1.36–1.53) | 1.40 (1.31–1.49) | < 0.001 |
| Quartile-4 (≥ 15.2%) | 1.90 (1.79–2.00) | 1.82 (1.71–1.93) | < 0.001 |
| P for trend           | < 0.001 | < 0.001 |
| RDW dichotomous variable |         |          |
| Normal (≤ 14.5%)     | Reference | Reference | < 0.001 | < 0.001 |
| Elevated (≥ 14.5%)   | 1.52 (1.46–1.58) | 1.49 (1.43–1.55) | < 0.001 |
| RDW continuous variable |       |          |
| HR for each 1% increase in RDW | 1.13 (1.12–1.14) | 1.13 (1.12–1.14) | < 0.001 |

Abbreviations: RDW = red cell distribution width, HR = hazard ratio, CI = confidence interval.
Few previous small studies have assessed the association between RDW and all-cause mortality in patients with atrial fibrillation, and these studies have presented conflicting results [18,19]. Wan et al. studied 300 patients with atrial fibrillation and showed that RDW was independently associated with all-cause mortality and major adverse events [18]. Lee et al. studied 567 patients with paroxysmal atrial fibrillation and showed that RDW was significantly associated with composite clinical outcomes of death, hospitalization due to heart failure, and new-onset stroke; however, RDW was not associated with mortality when death was considered as a single outcome [19]. Compared to previous studies, our work more accurately represents everyday real-life scenarios of patients with atrial fibrillation, as it includes a large number of patients from a population-based database. Furthermore, this study was able to examine the association of change in RDW over time and mortality.

The exact biological mechanisms underlying the association of RDW and mortality in patients with atrial fibrillation cannot be gleaned by this cohort study. Furthermore, this cohort study is observational in nature and residual confounding may still exist. Hence, whether RDW has a causal effect in leading to mortality or is simply a marker of other comorbidities or biological mechanisms cannot be proven from this study. In this regard, a potential role may be played by systemic factors that alter erythrocyte hemostasis leading to anisocytosis, such as inflammation and oxidative stress [20,21]. Both decreased serum antioxidant levels (selenium, carotenoids, and vitamin E), and increased inflammation and oxidative stress [20,21]. Both decreased serum antioxidant levels (selenium, carotenoids, and vitamin E), and increased inflammatory biomarkers (IL-6, CRP, soluble TNF receptor I and II) were correlated with increased RDW [22–25]. Although this explanation seems to be plausible, adjustment for CRP and antioxidant levels did not meaningfully attenuate the association between RDW and mortality [25,26].

Our study has other limitations, one of which is that it relies on a computerized database not specifically designed for the present study. In addition, we did not have data on the type of atrial fibrillation (paroxysmal, persistent or permanent). In this study, we included patients who performed a complete blood count test during the year prior to study entry. Hence, one may argue that our study is affected by selection bias because patients with more severe disease tend to perform more tests. However, of the 77,297 patients with atrial fibrillation, 69,412 (~90%) performed the RDW test and were included in the study. Additionally, we did not have data on iron store status and other nutritional deficiencies that may have caused anemia and affected RDW. However, our study shows that RDW is associated with increased risk of all-cause mortality regardless of anemia status.

4. Discussion

This study shows that the risk of all-cause mortality in patients with atrial fibrillation is directly associated with RDW in a dose-response manner. This association was independent of known risk factors of mortality. Notably, RDW is associated with all-cause mortality regardless of anemia status. In addition, this study shows that the dynamic changes in RDW are strongly associated with the risk of all-cause mortality; in patients with elevated RDW, the risk of mortality decreased when RDW declined to normal levels, and in patients with normal RDW, the risk of mortality increased with RDW elevation. Changes in RDW over time were also found to be associated with all-cause mortality in patients with CHF [15].

RDW is well known as a marker associated with increased risk of mortality in multiple cardiovascular settings [2–8]. RDW was also found to be associated with increased mortality and poor clinical outcome in patients with stroke, regardless of atrial fibrillation [16,17]. Furthermore, we recently demonstrated that RDW is an independent risk factor for stroke in patients with atrial fibrillation [11]. Hence, it may be suggested that the increased risk of mortality associated with RDW in patients with atrial fibrillation may be attributed to stroke mortality. Unfortunately, we did not have data related to cause of death; therefore, we were not able to confirm this hypothesis or to assess the relationship of RDW with specific causes of mortality.

5. Conclusion

RDW and change in RDW over time are associated with mortality in patients with atrial fibrillation. Accounting for this widely available inexpensive test may be valuable for the prediction of mortality in patients with atrial fibrillation. Future studies are needed to confirm our findings and to elucidate the underlying mechanism of this association.

Conflicts of interest

The authors report no competing interests.

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