# Association of standard clinical and laboratory variables with red blood cell distribution width

Patrícia O. Guimarães, MD,[a] Jie-Lena Sun, MS,[a] Kristian Kragholm, MD,[a] Svati H. Shah, MD,[b,c] Karen S. Pieper, MS,[a] William E. Kraus, MD,[b,c] Elizabeth R. Hauser, PhD,[b,c] Christopher B. Granger, MD,[a,c] and L. Kristin Newby, MD, MHS[a,c], for the MURDOCK Horizon 1 Cardiovascular Study Investigators *Durham, NC*

**Background** Red blood cell distribution width (RDW) strongly predicts clinical outcomes among patients with coronary disease and heart failure. The factors underpinning this association are unknown.

**Methods** In 6,447 individuals enrolled in the Measurement to Understand the Reclassification of Disease of Cabarrus/Kannapolis (MURDOCK) Study who had undergone coronary angiography between 2001 and 2007, we used Cox proportional hazards modeling to examine the adjusted association between RDW and death, and death or myocardial infarction (MI). Multiple linear regression using the $R^2$ model selection method was then used to identify clinical factors associated with variation in RDW.

**Results** Median follow-up was 4.2 (interquartile range 2.3-5.9) years, and the median RDW was 13.5% (interquartile range 12.9%-14.3%, clinical laboratory reference range 11.5%-14.5%). Red blood cell distribution width was independently associated with death (adjusted hazard ratio 1.13 per 1% increase in RDW, 95% CI 1.09-1.17), and death or MI (adjusted hazard ratio 1.12, 95% CI 1.08-1.16). Twenty-seven clinical characteristics and laboratory measures were assessed in the multivariable linear regression model; a final model containing 18 variables explained only 21% of the variation in RDW.

**Conclusions** Although strongly associated with death and death or MI, only one-fifth of the variation in RDW was explained by routinely assessed clinical characteristics and laboratory measures. Understanding the latent factors that explain variation in RDW may provide insight into its strong association with risk and identify novel targets to mitigate that risk. (Am Heart J 2016;174:22-28.)

Red blood cell distribution width (RDW) is a measure routinely reported as part of a complete blood count. It represents variability in the size of red blood cells. It is calculated as the standard deviation of mean corpuscular volume divided by mean corpuscular volume × 100, and it is expressed as a percentage.[1] Higher RDW reflects greater heterogeneity in red blood cell size (anisocytosis) in conditions of ineffective erythropoiesis and is traditionally used to differentiate types of anemia.

Beyond this historical diagnostic use, RDW is one of the strongest predictors of outcomes among patients with heart failure[2-6] and coronary artery disease,[7-10] elderly populations,[11] as well as other chronic conditions.[12,13] However, the factors underpinning the association of RDW with clinical outcomes are unknown. Determining these factors may provide novel mechanistic insight into risk for coronary events and death among patients with known or suspected coronary artery disease and in other populations. To this end, we first confirmed the relationship between RDW and clinical outcomes (death and death or myocardial infarction [MI]) in a subset of patients referred to Duke University Medical Center for cardiac catheterization from 2001 through 2007 who comprised the Measurement to Understand the Reclassification of Disease of Cabarrus/Kannapolis (MURDOCK) Horizon 1 Cardiovascular Disease (MURDOCK CV) Study cohort. We then identified clinical and laboratory factors that were independently associated with variation in RDW in an attempt to explain the relationship between RDW and cardiovascular risk.

## Methods

### Study population

Our analyses included 6,447 patients who composed the MURDOCK CV Study population, a subset of patients enrolled in the Duke CATHeterization GENetics (CATHGEN)

*From the [a]Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, [b]Duke Molecular Physiology Institute, Duke University Medical Center, Durham, NC, and [c]Duke Division of Cardiology, Duke University Medical Center, Durham, NC.*

*Larry A. Allen, MD, MHS served as guest editor for this article.*
*Submitted November 25, 2015; accepted January 7, 2016.*

*Reprint requests: L. Kristin Newby, MD, Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715-7969.*
*E-mail: kristin.newby@duke.edu*

*0002-8703*



*http://dx.doi.org/10.1016/j.ahj.2016.01.001*

biorepository.[14] The design and rationale of the MURDOCK CV Study, including cohort selection, were published previously.[15] Briefly, the MURDOCK CV Study cohort included CATHGEN patients who were at least 18 years old and underwent coronary angiography at Duke University Medical Center from December 2001 through November 2007 as part of the workup for possible ischemic heart disease. Patients with severe heart failure (New York Heart Association class IV with left ventricular ejection fraction <35% at catheterization), pulmonary hypertension, and congenital heart disease, and those who underwent catheterization as a part of pre–solid organ or post–solid organ or heart transplant were not eligible for the MURDOCK CV Study cohort.

CATHGEN pairs longitudinal clinical information (symptom histories, clinical characteristics and medical history, angiographic data, and fasting chemistry and lipid profile data from within 1 year preceding catheterization) from the Duke Databank for Cardiovascular Disease with blood samples collected at the time of cardiac catheterization and stored for future use. Longitudinal follow-up for death (via yearly National Death Index and/or Social Security Death Index search) and nonfatal clinical cardiovascular events (from medical record review, and mail or telephone surveys at 6 months after the index catheterization procedure and yearly thereafter) was completed for all MURDOCK CV Study patients. For the MURDOCK CV Study, these data were supplemented by additional laboratory, electrocardiographic, and imaging data for ejection fraction contained within the Duke Decision Support Repository (an enterprise-wide data warehouse containing care-related data from multiple domains) or by direct examination of the medical record.

All patients provided written informed consent to participate in the Duke CATHGEN biorepository. Both CATHGEN and the additional data collection for the MURDOCK CV Study, as well as the current analyses using this data set, were approved by the Duke University Institutional Review Board with a waiver of informed consent and Health Insurance Portability and Accountability Act authorization.

### Statistical analysis

**Association of RDW with clinical outcomes in the MURDOCK Study population.** The associations of RDW with time to death and death or MI over a median follow-up of 4.2 years were determined in multivariable Cox proportional hazards regression models that included RDW as a continuous variable. Thirty-six clinical variables were chosen as candidate predictors based on previous publications or clinical judgment (Appendix 1). For 15 variables with >6% missing values, multiple imputation was used and the resulting values were applied in the multivariable models. Both stepwise and backward variable selections were used as the criteria to select variables with a $P$ value of <.05 for both entering and remaining in the model. The 2 methods produced similar models. The restricted cubic spline transformation method was used to determine the functional form for continuous variables, then piecewise linear splines were applied to those variables whose functional forms were not linear. The assumption of proportional hazards was checked using a score test. The assumption was violated for presentation type with the end point of death or MI. Therefore, this model was stratified on presentation type. Final Cox proportional hazards models were adjusted for all variables identified in Appendix 2.

**Factors associated with variation in RDW.** Descriptive statistics (medians with interquartile ranges [IQRs] for continuous variables and percentages for discrete variables) were used to summarize population characteristics across quartiles of RDW for display purposes.

Univariable and multivariable linear regression were used to assess the association of clinical and laboratory characteristics with RDW. Variables included in these models are listed in Appendix 3. A subset of these variables was retained as the set of key multivariable predictors of RDW using the $R^2$ selection method, which identifies the set of variables that maximizes $R^2$ with the fewest possible variables.

SAS version 8.2 or 9.3 (SAS Institute, Cary, NC) software was used for all statistical analyses.

## Funding sources

This study was supported by funding from the MURDOCK Study through a gift to Duke University from the David H. Murdock Foundation for Business and Culture and Grant No. UL1RR024128-01 from the National Center for Research Resources, a component of the National Institutes of Health, and National Institutes of Health Roadmap for Medical Research. None of the sponsors had a role in study design, data or sample collection, statistical analyses, interpretation of the data, writing of the study manuscript, or the decision to publish.

The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

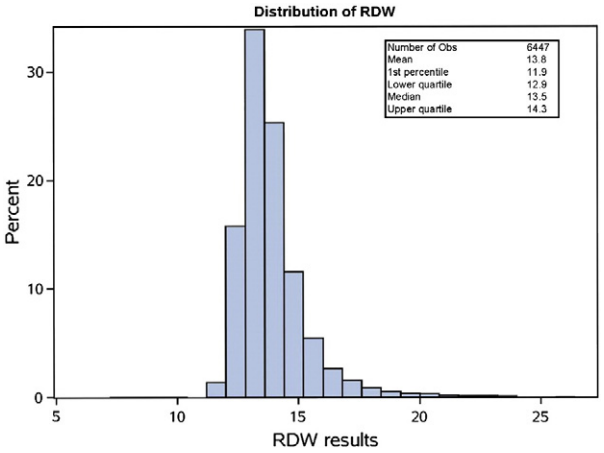
## Results

### Association of RDW with death and death or MI

The distribution of RDW in the study population is shown in Figure. The median RDW was 13.5% (IQR 12.9%-14.3%, clinical laboratory reference range, 11.5%-14.5%).

Of 6,447 patients, 1,037 (16.1%) patients died during a median follow-up of 4.2 (IQR 2.3-5.9) years, and 1,284 (19.9%) experienced the composite end point of death or MI. In adjusted Cox proportional hazards models, RDW was independently associated with death (adjusted hazard ratio 1.13 per 1% absolute increase in RDW, 95% CI 1.09-1.17, $P$ < .0001) and death or MI (adjusted hazard

**Figure**




Distribution of RDW in the MURDOCK CV Study population.

ratio 1.12 per 1% absolute increase in RDW, 95% CI 1.08-1.16, $P < .0001$).

### Relationship of clinical and laboratory characteristics with RDW

**Baseline characteristics according to RDW.** Baseline characteristics according to quartile of RDW are shown in Table I. Patients in the upper quartiles were older, more often women, and less frequently white, and they had lower hemoglobin and higher blood urea nitrogen levels than those in lower quartiles. The prevalence of diabetes, hypertension, congestive heart failure, prior coronary artery bypass graft (CABG), renal disease, and valvular heart disease increased within higher RDW quartiles. Ejection fraction was lower as RDW quartiles increased.

**Association of clinical and laboratory characteristics with variability in RDW.** In univariable linear regression models, 14 variables were significantly associated with RDW: age, race, sex, heart rate, heart failure severity, prior CABG, current or past smoking, valvular disease, modified Charlson index, hemoglobin, blood urea nitrogen, white blood cell count, ejection fraction, and presentation status (outpatient vs other types) (Table II). Hemoglobin explained 14% of the variation in RDW; no other single variable explained more than 5%.

In multivariable linear regression modeling, a model containing 18 variables provided the best balance of $R^2$ and number of model variables (Table III). This model included demographic and clinical characteristics (age, race, sex, heart failure severity, prior CABG, prior MI, history of current or past smoking, valvular disease, modified Charlson index, weight, and systolic and diastolic blood pressure), laboratory tests (hemoglobin, blood urea nitrogen, white blood cell count, and serum sodium), ejection fraction, and whether the patient was an outpatient. In total, this model explained 21% of the variation in RDW.

## Discussion

In our cohort of 6,447 patients undergoing coronary angiography due to concern for ischemic heart disease, we confirmed a strong, independent association of RDW with death and death or MI over a median of 4.2 years of follow-up. To better understand this association, we explored what clinical factors accounted for variation in RDW, but found that only 21% of the variation could be explained by parameters readily available in routine clinical practice. A better understanding of the latent factors that account for the remaining unexplained variation in RDW could lead to novel insight about risk for adverse outcomes associated with RDW.

### Association between RDW and outcomes

It has previously been shown that patients with greater RDW present with higher risk factor burden for coronary heart disease than patients with lower RDW.[7,9,16,17] Several studies have suggested that RDW is a marker of disease progression, as it is higher among sicker patients. Our observations are consistent with these studies; we have shown not only greater prevalence of cardiac risk factors but also greater comorbidity burden as assessed by the Charlson index among patients as quartile of RDW increased.

The first report of RDW as an independent predictor of mortality in cardiovascular cohorts was published in 2007.[5] In this report, among 2679 chronic heart failure patients enrolled in the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program, RDW was one of the variables most strongly associated with cardiovascular death or heart failure hospitalization. The authors also reported that higher RDW was one of the most powerful predictors of all-cause mortality in 2140 heart failure patients from the Duke Databank for Cardiovascular Disease. Higher RDW is also associated with poorer outcomes in populations with other chronic diseases, including diabetes and peripheral artery disease.[12,13] Because RDW is usually part of routine blood examinations, this measure adds no additional cost and could be widely used to improve risk classification of patients with cardiac diseases. Understanding the foundations of the prognostic relationship is important to provide further rationale for its use, as well as provide insight into unknown mechanisms of disease.

It is important to note that RDW values may differ according to the hematologic analyzer used, as the calculation algorithm varies depending on the manufacturer, resulting in excellent within run imprecision for an individual analyzer, but unacceptable bias between analyzers.[18,19] Therefore, establishing a prognostic "cut point" would be challenging. However, in our study, the

**Table I.** Baseline characteristics according to quartile of RDW

| | RDW Quartile 1, 6.5%-12.9% (n = 1617) | RDW Quartile 2, 13.0%-13.4% (n = 1354) | RDW Quartile 3, 13.5%-14.3% (n = 1709) | RDW Quartile 4, 14.4%-27.1% (n = 1490) |
|---|---|---|---|---|
| Age (y) | 58 (51, 67) | 60 (52, 70) | 62 (54, 71) | 62 (54, 71) |
| Female | 473 (29.3) | 457 (33.8) | 632 (37.0) | 692 (46.4) |
| White | 1325 (83.9) | 1072 (80.4) | 1265 (75.4) | 908 (62.0) |
| Cigarette smoking (current/previous) | 857 (53.0) | 683 (50.4) | 857 (50.1) | 740 (49.7) |
| Prior MI | 482 (29.8) | 433 (32) | 502 (29.4) | 450 (30.2) |
| Prior CABG | 267 (16.5) | 253 (18.7) | 365 (21.4) | 338 (22.7) |
| Hypertension | 1032 (63.8) | 894 (66.0) | 1229 (71.9) | 1105 (74.2) |
| Diabetes | 374 (23.1) | 342 (25.3) | 542 (31.7) | 544 (36.5) |
| Congestive heart failure | 239 (15.1) | 273 (20.7) | 442 (26.4) | 541 (36.9) |
| Valvular disease | 55 (3.4) | 46 (3.4) | 63 (3.7) | 101 (6.8) |
| Renal disease | 7 (0.4) | 2 (0.1) | 26 (1.5) | 83 (5.6) |
| NYHA class | | | | |
| 0 | 1342 (89.3) | 1044 (84.5) | 1233 (79.4) | 925 (68.6) |
| 1 | 17 (1.1) | 22 (1.8) | 28 (1.8) | 23 (1.7) |
| 2 | 78 (5.2) | 85 (6.9) | 105 (6.8) | 126 (9.3) |
| 3 | 55 (3.7) | 76 (6.1) | 147 (9.5) | 211 (15.6) |
| 4 | 10 (0.7) | 9 (0.7) | 39 (2.5) | 64 (4.7) |
| Modified Charlson index score | 0.0 (0.0, 0.0) | 0.0 (0.0, 0.0) | 0.0 (0.0, 1.0) | 0.0 (0.0, 1.0) |
| Weight (kg) | 85 (74, 98) | 86 (75, 100) | 88 (75, 102) | 86 (73, 101) |
| Systolic blood pressure (mm Hg) | 143 (129, 159) | 142 (127, 159) | 144 (129, 163) | 144 (126, 163) |
| Diastolic blood pressure (mm Hg) | 81 (72, 89) | 80 (71, 88) | 80 (72, 89) | 79 (69, 89) |
| Carotid bruits | 74 (4.6) | 66 (4.9) | 90 (5.3) | 105 (7.1) |
| Presentation type | | | | |
| Acute MI | 206 (12.7) | 196 (14.5) | 210 (12.3) | 227 (15.2) |
| Outpatient | 877 (54.2) | 731 (54.0) | 914 (53.5) | 711 (47.7) |
| Other | 534 (33.0) | 427 (31.5) | 585 (34.2) | 552 (37.0) |
| Duke CAD severity index | 31 (0, 52) | 31 (0, 52) | 31 (0, 65) | 31 (0, 71) |
| Ejection fraction (%) | 59.3 (52.9, 66.0) | 58.0 (50.4, 65.1) | 57.3 (49.8, 65.0) | 55.0 (45.0, 63.6) |
| Hemoglobin (mg/dL) | 14.2 (13.2, 15.1) | 13.9 (12.8, 14.9) | 13.4 (12.3, 14.6) | 12.4 (11.2, 13.6) |
| White blood cell count ($\times 10^3$/mL) | 6.9 (5.7, 8.5) | 7.3 (6.0, 8.9) | 7.3 (5.9, 8.9) | 7.2 (5.8, 9.1) |
| Sodium (mg/dL) | 140 (138, 141) | 140 (138, 141) | 140 (138, 142) | 139 (138, 141) |
| Blood urea nitrogen (mg/dL) | 15 (12,19) | 16 (13, 20) | 16 (13, 22) | 18 (13, 25) |

Continuous variables are presented as medians (25th, 75th percentiles). All other values are presented as n (%).
Abbreviations: *CAD*, Coronary artery disease; *NYHA*, New York Heart Association.

same analytical technique was used for all patients. Given this and because our analyzes were designed to (1) establish the relationship between RDW as a continuous variable with risk for death and death or MI (rather than to establish a cut point for risk for general use) and (2) to identify factors associated with the variation in RDW across the range of observed values, we do not believe variation by analyzer/analytical technique would affect the main messages from our study: (1) as RDW increases, risk increases, and (2) only a minority of the observed variation in RDW is explained by readily available clinical or laboratory parameters.

## Association between clinical variables and RDW

Although RDW can predict mortality and morbidity among patients with cardiovascular disease and in other populations, the factors responsible for this association are not fully understood. It was previously believed that higher RDW was associated with clinical outcomes due to coexisting anemia. However, several studies have shown that the association of RDW with outcome was independent of whether the patient was anemic.[17,20-22] In the current study, we showed that only 14% of the variation in RDW could be explained by hemoglobin, which strengthens the hypothesis that the mechanism underlying the relationship between RDW and outcomes is not explained by anemia alone. Other possible pathophysiologic mechanisms of this association have been suggested, including inflammation, oxidative stress, impaired iron metabolism, and nutritional deficiencies.[3,23,24] To the extent possible, we included parameters such as hemoglobin, hematocrit, and serum creatinine in our multivariable linear regression analysis examining factors that explained variation in RDW. However, we did not have a nutritional/dietary history, but did account for body mass index, and did not systematically have available a biomarker of inflammation, but accounted for white blood cell count. The Charlson comorbidity index would account to some extent for other major concurrent illnesses, but we did not specifically exclude patients with systemic inflammatory diseases such as rheumatoid arthritis or lupus or chronic viral infections.

Red blood cell distribution width seems to be a chronic disease phase reactant; however, given the small

**Table II.** Variables associated with RDW in univariable analysis

| Variables | Parameter estimate | SE | *t* | *P* | $R^2$ |
|---|---|---|---|---|---|
| Hemoglobin | −0.304 | 0.009 | −32.150 | <.0001 | 0.1382 |
| CHF severity | 0.286 | 0.016 | 17.923 | <.0001 | 0.0475 |
| BUN | 0.034 | 0.002 | 17.092 | <.0001 | 0.0434 |
| White race | −0.559 | 0.041 | −13.790 | <.0001 | 0.0287 |
| Female | 0.380 | 0.036 | 10.474 | <.0001 | 0.0167 |
| Ejection fraction | −0.014 | 0.001 | −10.196 | <.0001 | 0.0159 |
| Modified Charlson index | 0.197 | 0.022 | 9.073 | <.0001 | 0.0126 |
| Heart rate | 0.007 | 0.001 | 6.980 | <.0001 | 0.0075 |
| Valvular disease | 0.561 | 0.088 | 6.371 | <.0001 | 0.0063 |
| Age | 0.008 | 0.001 | 5.679 | <.0001 | 0.0050 |
| Outpatient | −0.145 | 0.035 | −4.092 | <.0001 | 0.0026 |
| WBC | 0.024 | 0.007 | 3.459 | .0005 | 0.0019 |
| Current or previous smoking | −0.110 | 0.035 | −3.114 | .0019 | 0.0015 |
| History of CABG | 0.133 | 0.045 | 2.988 | .0028 | 0.0014 |

Abbreviations: *BUN*, Blood urea nitrogen; *CHF*, chronic heart failure; *WBC*, white blood count.

**Table III.** Final multivariable model for factors associated with RDW (model $R^2 = 0.21$)

| Variables | Parameter estimate | SE | *t* | *P* | Model $R^2$ |
|---|---|---|---|---|---|
| Hemoglobin | −0.274 | 0.011 | −25.362 | <.0001 | 0.2108 |
| White race | −0.359 | 0.040 | −9.072 | <.0001 | |
| CHF severity | 0.016 | 0.002 | 8.121 | <.0001 | |
| BUN | 0.134 | 0.017 | 7.883 | <.0001 | |
| WBC | 0.040 | 0.006 | 6.295 | <.0001 | |
| Ejection fraction | −0.007 | 0.001 | −5.492 | <.0001 | |
| Modified Charlson index | 0.104 | 0.020 | 5.188 | <.0001 | |
| Weight | 0.004 | 0.001 | 5.120 | <.0001 | |
| Systolic blood pressure | −0.005 | 0.001 | −5.064 | <.0001 | |
| Diastolic blood pressure | 0.007 | 0.002 | 4.344 | <.0001 | |
| Valvular disease | 0.330 | 0.082 | 4.029 | <.0001 | |
| Sodium | 0.020 | 0.006 | 3.422 | .0006 | |
| Outpatient | 0.096 | 0.035 | 2.726 | .0064 | |
| History of MI | −0.101 | 0.039 | −2.589 | .0096 | |
| Female | 0.096 | 0.039 | 2.429 | .0152 | |
| History of CABG | 0.098 | 0.043 | 2.311 | .0208 | |
| Age | 0.002 | 0.002 | 1.130 | .2587 | |
| Current or previous smoking | 0.028 | 0.033 | 0.842 | .3997 | |

Abbreviations: *BUN*, Blood urea nitrogen; *CHF*, chronic heart failure; *WBC*, white blood count.

percentage of variation explained by routinely assessed clinical variables and that it remains a strong predictor of outcome even when other biomarkers of risk are considered,[25] the pathophysiological underpinnings of this relationship remain unclear. Further studies are needed to elucidate the pathophysiology underlying variation in RDW, which may provide insight into its broad association with worse outcomes across a variety of disease states, including coronary heart disease.

## Strengths and limitations

This analysis was conducted in a sample of 6,447 patients, all of whom underwent coronary angiography for evaluation of ischemic heart disease at a single center. Therefore, these results may not be generalizable to other populations. However, our confirmation of the association of RDW with poorer outcomes is consistent with results from other cohort studies. Importantly, a strength of our study is that within the same cohort, we attempted to explain this prognostic relationship by identifying clinical and laboratory features that were associated with the variation in RDW. Using access to our institution's electronic data warehouse, we were able to consider a wide range of clinical and laboratory variables for their association with variation in RDW. This by no means represents all of the possible information in the electronic health record, but rather considered variables with possible clinical relevance. Future studies applying machine learning or other "big data" techniques may be able to expand on our work and explain more of the latent variability with information in the medical record. Finally, in a small, nested case-control subset of the cohort used in the current analyses, RDW was independently associated with death and death or MI in elastic net

models that considered 53 candidate protein predictors. Because these models consider variable colinearity simultaneously with variable selection, these results suggest that additional information, even beyond known biomarkers, may also underpin variation in RDW and its association with outcomes. This substudy was too small to be definitive, but larger studies and deeper molecular characterization may provide additional insight.

## Conclusions

Red blood cell distribution width is a powerful independent predictor of death and death or MI among patients referred for coronary angiography. Only one-fifth of the variation in RDW was explained by readily available clinical and laboratory characteristics. Further investigation into the latent factors underpinning variation in RDW may provide novel mechanistic insight into cardiovascular risk and identify novel targets to mitigate that risk.

## Acknowledgements

We would like to thank the patients who participated in CATHGEN and Elaine Dowdy for her study coordination. P.O.G. thanks Conselho Nacional de Desenvolvimento Cientifico e Tecnologico of the Ministry of Science, Technology and Innovation of Brazil for funding support. W.E.K.'s time was funded by the Duke OIAC Pepper Center (P30 AG028716).

## Disclosures

All authors have approved the final manuscript. P.O.G., J-L.S., K.K., S.H.S., W.E.K., and E.R.H. have nothing to disclose. K.S.P. has received funding for consultancy from Bayer, Astra-Zeneca, and GSK. All of Dr Granger's and Dr Newby's relationship disclosures are available at https://www.dcri.org/about-us/conflict-of-interest.

## Appendix. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ahj.2016.01.001.

## References

1. Simel DL, DeLong ER, Feussner JR, et al. Erythrocyte anisocytosis. Visual inspection of blood films vs automated analysis of red blood cell distribution width. Arch Intern Med 1988;148:822-4.
2. Al-Najjar Y, Goode KM, Zhang J, et al. Red cell distribution width: an inexpensive and powerful prognostic marker in heart failure. Eur J Heart Fail 2009;11:1155-62.
3. Allen LA, Felker GM, Mehra MR, et al. Validation and potential mechanisms of red cell distribution width as a prognostic marker in heart failure. J Card Fail 2010;16:230-8.
4. Borne Y, Smith JG, Melander O, et al. Red cell distribution width and risk for first hospitalization due to heart failure: a population-based cohort study. Eur J Heart Fail 2011;13:1355-61.
5. Felker GM, Allen LA, Pocock SJ, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol 2007;50:40-7.
6. Aung N, Ling HZ, Cheng AS, et al. Expansion of the red cell distribution width and evolving iron deficiency as predictors of poor outcome in chronic heart failure. Int J Cardiol 2013;168:1997-2002.
7. Dabbah S, Hammerman H, Markiewicz W, et al. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction. Am J Cardiol 2010;105:312-7.
8. Lappe JM, Horne BD, Shah SH, et al. Red cell distribution width, C-reactive protein, the complete blood count, and mortality in patients with coronary disease and a normal comparison population. Clin Chim Acta 2011;412:2094-9.
9. Tonelli M, Sacks F, Arnold M, et al. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. Circulation 2008;117:163-8.
10. Lee JH, Yang DH, Jang SY, et al. Incremental predictive value of red cell distribution width for 12-month clinical outcome after acute myocardial infarction. Clin Cardiol 2013;36:336-41.
11. Liu XM, Ma CS, Liu XH, et al. Relationship between red blood cell distribution width and intermediate-term mortality in elderly patients after percutaneous coronary intervention. J Geriatr Cardiol 2015;12:17-22.
12. Malandrino N, Wu WC, Taveira TH, et al. Association between red blood cell distribution width and macrovascular and microvascular complications in diabetes. Diabetologia 2012;55:226-35.
13. Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol 2011;107:1241-5.
14. Kraus WE, Granger CB, Sketch Jr MH, et al. A guide for a cardiovascular genomics biorepository: the CATHGEN experience. J Cardiovasc Transl Res 2015;8:449-57.
15. Shah SH, Granger CB, Hauser ER, et al. Reclassification of cardiovascular risk using integrated clinical and molecular biosignatures: design of and rationale for the Measurement to Understand the Reclassification of Disease of Cabarrus and Kannapolis (MURDOCK) Horizon 1 Cardiovascular Disease Study. Am Heart J 2010;160:371-9. [e2].
16. Arbel Y, Birati EY, Finkelstein A, et al. Red blood cell distribution width and 3-year outcome in patients undergoing cardiac catheterization. J Thromb Thrombolysis 2014;37:469-74.
17. Azab B, Torbey E, Hatoum H, et al. Usefulness of red cell distribution width in predicting all-cause long-term mortality after non–ST-elevation myocardial infarction. Cardiology 2011;119:72-80.
18. Buttarello M, Plebani M. Automated blood cell counts: state of the art. Am J Clin Pathol 2008;130:104-16.
19. Lippi G, Pavesi F, Bardi M, et al. Lack of harmonization of red blood cell distribution width (RDW). Evaluation of four hematological analyzers. Clin Biochem 2014;47:1100-3.
20. Cavusoglu E, Chopra V, Gupta A, et al. Relation between red blood cell distribution width (RDW) and all-cause mortality at two years in an unselected population referred for coronary angiography. Int J Cardiol 2010;141:141-6.
21. Poludasu S, Marmur JD, Weedon J, et al. Red cell distribution width (RDW) as a predictor of long-term mortality in patients undergoing percutaneous coronary intervention. Thromb Haemost 2009;102:581-7.
22. Pascual-Figal DA, Bonaque JC, Redondo B, et al. Red blood cell distribution width predicts long-term outcome regardless of anaemia status in acute heart failure patients. Eur J Heart Fail 2009;11:840-6.
23. Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009;133:628-32.

24. Forhecz Z, Gombos T, Borgulya G, et al. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. Am Heart J 2009;158:659-66.

25. Halim SA, Neely ML, Pieper KS, et al. Simultaneous consideration of multiple candidate protein biomarkers for long-term risk for cardiovascular events. Circ Cardiovasc Genet 2015;8:168-77.