VIA MEDICA

ORIGINAL AND CLINICAL ARTICLES

Anaesthesiology Intensive Therapy
2018, vol. 50, no 4, 277–282
ISSN 1642–5758
10.5603/AIT.a2018.0037
www.ait.viamedica.pl

Diagnostic accuracy of red blood cell distribution width in predicting in-hospital mortality in patients undergoing high-risk gastrointestinal surgery

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Abstract

Background: The red blood cell distribution width index (RDW) is one of several parameters routinely analysed in peripheral blood counts. The aim of the study was to assess the usefulness of RDW in the prediction of in-hospital mortality in patients undergoing high-risk gastroenterological surgery.

Methods: Prospective observation covered 229 patients who underwent surgery, for whom the risk of cardiovascular complications was high due to the type of procedure. The patient's individual risk was assessed using the criteria of the American Society of Anesthesiologists (ASA-PS). Peripheral blood for morphological examination was collected preoperatively. The following parameters of the red blood cell system were evaluated: red blood cell count (RBC), haemoglobin (Hgb), haematocrit (Hct), mean corpuscular volume (MCV), RDW expressed as a standard deviation (SD) and a coefficient of variation (CV). The occurrence of hospital death was the main endpoint.

Results: Patients who died had had statistically significantly lower RBC, Hgb and Hct values, as well as higher RDW-SD and RDW-CV values. Both the preoperative RDW-SD and RDW-CV values predicted the outcome, respectively: AUC RDW-SD = 0.744 (95% CI: 0.683–0.799; $P < 0.001$), AUC RDW-CV = 0.762 (95% CI: 0.702–0.816; $P < 0.001$). In logistic regression, it was confirmed that RDW predicted mortality (OR RDW-SD = 1.21; $P < 0.001$, OR RDW-CV = 1.62; $P = 0.01$), even after adjustment for individual risk and other erythrocyte parameters.

Conclusion: RDW is a valuable screening predictor of in-hospital mortality in patients undergoing high-risk gastroenterological surgery, regardless of the estimated individual risk and the value of other erythrocyte parameters. Evaluation of the RDW may be helpful in the identification of patients requiring correction of haematological disorders in the pre-operative period, as well as, in particular, surveillance in the perioperative period.

Anaesthesiology Intensive Therapy 2018, vol. 50, no 4, 277–282

Key words: peripheral blood morphology; anaemia; risk; perioperative medicine

The red blood cell distribution width (RDW) is one of the parameters analysed in peripheral blood counts, which reflects the variability of erythrocyte size. Its assessment enables early diagnosis of blood cell structural disorders which, in practice, translates into identification of individuals at risk of anaemia and its clinical sequels. Blood morphological examinations are inexpensive, widely accessible and their results quickly obtained. Additionally, such tests are routinely performed in each patient undergoing high-risk surgery [1].

Therefore, RDW is considered a screening predictive biomarker [2]. Numerous studies have confirmed its usefulness in many non-surgical specialities [3–6] while the available data regarding the use of RDW in perioperative medicine are scarce. Considering the above, the aim of the present study was to evaluate the usefulness of RDW in predicting

in-hospital mortality in patients undergoing high-risk gastroenterological surgeries.

METHODS

The prospective study included 1,089 consecutive patients undergoing surgeries in the Department of Gastroenterological Surgery of the University Hospital; 229 (21%) patients at high risk of cardiovascular complications (> 5%; death or myocardial infarction not leading to death within 30 postoperative days) were selected, taking into account only the specificity of surgery and irrespective of the individual risk. The level of risk was assessed based on the current guidelines of the European Society of Cardiology/European Society of Anaesthesiology (ESC/ESA) [7]. The analysis involved the following surgical procedures: surgeries within the duodenum and pancreas (n = 168); liver resections and biliary tract surgeries (n = 34); procedures for intestinal perforation (n = 20); and oesophageal resections (n = 7).

The clinical and demographical data were collected, i.e. sex, age, BMI, additional diseases and the extent of their control, as well as the type of admission (scheduled, faster-than-scheduled, urgent, emergent). The individual risk was assessed using the criteria of the American Society of Anesthesiologists Physical Status (ASA-PS) [8]. ASA-PS ≥ 3 and/or emergency surgery ("E") were considered a high individual risk [9].

The peripheral blood for tests was collected preoperatively and put in to test tubes containing EDTA (ethylenediaminetetraacetic acid), according to the procedures followed in our centre. The material sent to the laboratory was analysed using an XT-1800i device (Sysmex, Japan). The way to determine RDW by automated blood analysers has been described in detail by Caporal and Comar [10]. The following red blood cell parameters were evaluated: red blood cell count RBC); concentration of haemoglobin (Hgb); haematocrit (Hct); mean corpuscular volume (MCV) and RDW expressed as a standard deviation (SD) and a coefficient of variation (CV).

In-hospital mortality was assumed to be the end point. Additionally, ICU hospitalisation (when required) and length of hospitalisation were analysed.

Since the study was observational, no approval of the bioethics committee was needed [11].

Statistical analysis was performed using MedCalc v.18 (MedCalc Software, Ostend, Belgium). Quantitative variables were presented as means and standard deviations (normal distribution) or as medians and interquartile ranges (IQR) (non-normal distribution). The distribution of quantitative variables was verified using the analysis of variance or the Kruskal-Wallis test. Qualitative variables were presented as absolute values and percentages. The differences in quantitative variables were assessed using the analysis of variance or the Kruskal-Wallis test. The chi-square test was applied for qualitative variables. Correlations were assessed based on the Pearson correlation coefficient or Spearman`s rank correlation coefficient. The statistical relationship for dichotomous variables was evaluated based on odds ratios. The diagnostic accuracy was assessed using the receiver operating characteristic (ROC) curve and the area under the curve (AUC). Finally, a model of logistic regression was constructed, in which in-hospital death was a dependent variable while ASA-PS and red blood cell parameters were independent variables. $P < 0.05$ was considered statistically significant.

RESULTS

CHARACTERISTICS OF PATIENTS

The study group encompassed 229 patients undergoing high-risk surgeries, including 142 (62%) characterised by high individual risk. The median of risk according to ASA-PS was 3 (IQR 2–4). The basic demographic and clinical data are presented in Table 1.

RESULTS OF PERIPHERAL BLOOD MORPHOLOGY REGARDING RED BLOOD CELLS

Medians (IQR) of RBC, Hgb, Hct, MCV, RDW-SD and RDW-CV were as follows: 4.39 T L^{-1} (3.95–4.72); 13.4 g dL^{-1} (12.1–14.2); 39.6% (35.4–41.8); 89.5 fL (87–92.1); 45.9 fL (43–49); and 13.9% (13.2–14.9), respectively. The results of red blood cell morphology in individual risk groups are listed in Table 2. The high-risk group patients had statistically significantly lower values of RBC, Hgb and Hct and higher values of MCV and RDW. There were statistically significant differences in RDW values in the individual ASA-PS classes ($P < 0.001$) (Fig. 1A–B). Moreover, the correlation between RDW-SD and RDW-CV versus the ASA-PS class was also found to be statistically significant (R = 0.3; $P < 0.001$ for both of them).

RESULTS OF PERIPHERAL BLOOD MORPHOLOGY AND THE RISK OF DEATH

The RDW value was significantly higher in the group of non-survivors (Table 3), although it was still within the references limits (norms: RDW-SD 37-54 fL; RDW-CV 11–16%). RDW did not differ between the patients requiring postoperative admission to the ICU and the remaining individuals ($P > 0.05$).

Preoperative RDW-SD and RDW-CV enabled one to predict death: AUC for RDW-SD was 0.744 (95% CI: 0.683–0.799; $P < 0.001$), AUC for RDW-CV was 0.762 (95% CI: 0.702–0.816; $P < 0.001$), respectively. The sensitivity of the model for RDW-SD was 64% while the specificity was 82%, with a cut-off point of > 49.8 fL. The model for RDW-CV was characterised by a sensitivity of 79% and a specificity of 68%, with a cut-off point of > 14.3% (Fig. 2A, B).

The model of multivariate analysis demonstrated that the preoperative RDW value enabled one to predict the risk of early death (Table 4), irrespective of the individual risk and the remaining morphological parameters analysed; thus, the accuracy of this model was found to be very good.

A statistically significant correlation was found between the selected morphological parameters and the length of hospital stay, except for RDW. Otherwise, there was no correlation observed between the morphological parameters and the length of ICU stay (Table 5).

Table 1. Demographic and clinical data

Variable	Value	
Male gender	120	52%
Age [years]	63 (IQR 54–70)	
ASA physical status		
I	4	1.7%
II	83	36.2%
III	118	51.5%
IV	21	9.2%
V	3	1.3%
E	24	10.5%
BMI [kg m^{-2}]	25 (IQR 22.4–28.6)	
Type of admission/procedure		
scheduled/faster	192	83.8%
urgent/emergent	37	16.2%
Individual risk		
high-risk patients	142	62%
low-risk patients	87	38%
Place of transferring the patient from the operating suite		
intensive care unit (ICU)	36	15.7%
surgical department	192	83.8%
Total hospitalisation [days]	12 (IQR 10–19)	
ICU hospitalisation [days]	5 (IQR 2–8)	
Death	14	6.1%
intraoperative	1	0.4%
in the ICU	7	3%
in the surgical department	6	2.6%

DISCUSSION

The usefulness of RDW has recently been evaluated in numerous studies, especially in patients at high risk of cardiac complications. The correlation between RDW and increased risk of thromboembolic complications [3], heart failure [4], myocardial infarction [5] and prognosis in acute pulmonary embolism has been demonstrated. Moreover, RDW has been found likely to be associated with other diseases, including those which are non-cardiological, such as diseases which are internal, and those related to sur-

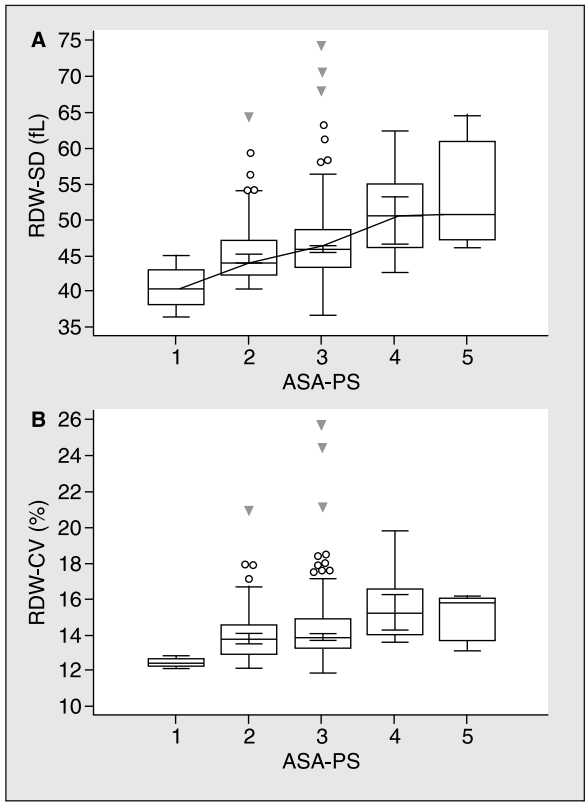

Figure 1. RDW-SD (**A**) and RDW-CV (**B**) in the individual ASA-PS classes

Table 2. Peripheral blood morphology and individual risk

Parameter	Low individual risk	High individual risk	OR (95% CI:)	*P* -value
RBC [T L^{-1}]	4.5 (4.27–4.83)	4.2 (3.85–4.62)	0.13 (0–5847.05)	< 0.001
Hgb [g dL^{-1}]	13.8 (12.53–14.4)	12.8 (11.7–13.9)	0.34 (0.13–0.90)	< 0.001
Hct [%]	40.5 (37.25–42.08)	39.1 (34.6–41.2)	1.7 (0.49–5.90)	0.002
MCV [fL]	88.1 (86–91.2)	90.1 (87.9–93)	1.16 (0.69–1.94)	0.006
RDW-SD [fL]	44 (42.13–47)	46 (44–50.3)	0.82 (0.67–0.99)	< 0.001
RDW-CV [%]	13.7 (13–14.38)	14 (13.4–15.4)	2.30 (1.22–4.36)	0.008

Values of quantitative variables were presented as medians and interquartile ranges; Hgb: concentration of haemoglobin, Hct: haematocrit, MCV: mean corpuscular volume, RBC: red blood cell count, RDW: red blood cell distribution width

Table 3. Peripheral blood morphology and risk of in-hospital death

Parameter	Survival until discharge	In-hospital death	OR (95% CI:)	*P* -value
RBC [T L^{-1}]	4.41 (3.99–4.73)	3.94 (3.29–4.52)	91.22 (0– >1000)	0.02
Hgb [g dL^{-1}]	13.4 (12.2–14.28)	11.85 (9.8–13.6)	1.14 (0.25–5.22)	0.02
Hct [%]	39.7 (35.9–41.88)	35.1 (30.4–40.5)	0.54 (0.15–1.97)	0.02
MCV [fL]	89.5 (87–92.1)	90.2 (87.1–95.9)	1.26 (0.8–1.43)	NS
RDW-SD [fL]	45.4 (43–48.08)	50.5 (43–55)	1.07 (0.86–1.48)	0.002
RDW-CV [%]	13.8 (13.1–14.8)	15.4 (14.4–16.3)	1.01 (0.44–2.36)	0.001

The values of quantitative variables were presented as medians and interquartile ranges; Hgb: concentration of haemoglobin, Hct: haematocrit, MCV: mean corpuscular volume, RBC: red blood cell count, RDW: red blood cell distribution width, NS: not significant ($P > 0.05$)

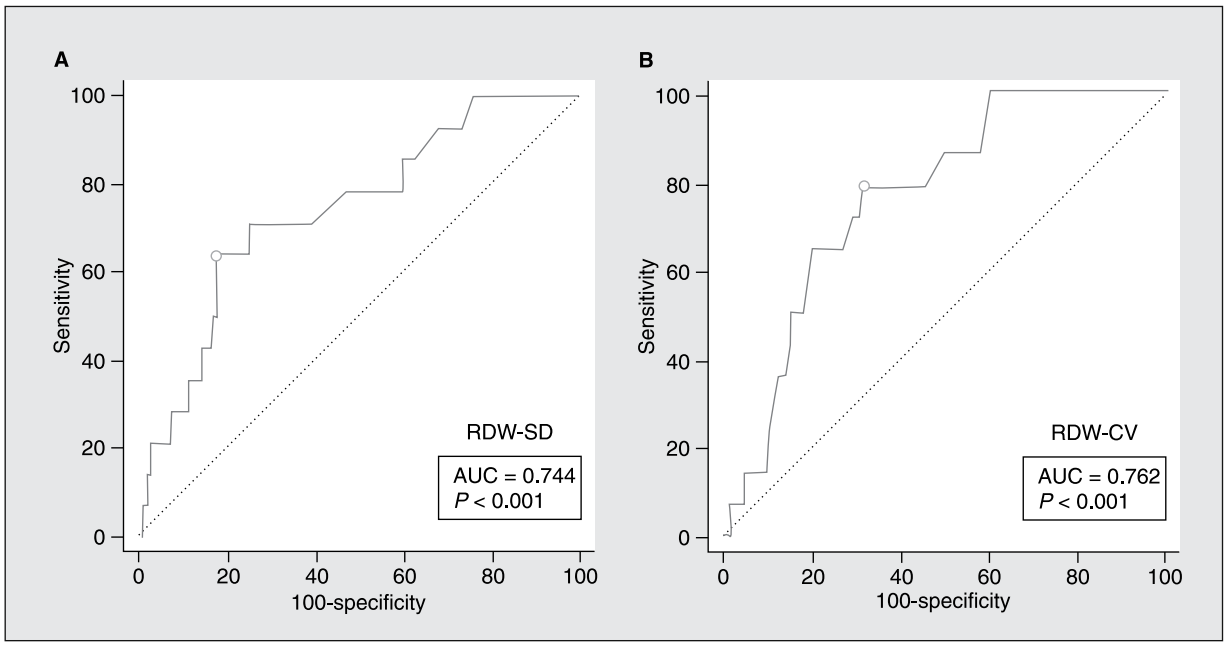

Figure 2. Diagnostic accuracy of RDW-SD (a) and RDW-CV (b) in predicting in-hospital mortality. ASA-PS: physical status class according to the American Society of Anesthesiologists, Hg: concentration of haemoglobin, Hct: haematocrit, MCV: mean corpuscular volume, RBC: red blood cell count, RDW: red blood cell distribution width

Table 4. The relationship between RDW and in-hospital mortality — multivariate analysis

Parameter	RDW-SD		RDW-CV	
	OR (95% CI:)	*P* -value	OR (95% CI:)	*P* -value
ASA-PS class	1.17 (0.35–3.97)	0.8	1.14 (0.32–4.0)	0.8
Emergency surgery	109.52 (10.87–1103.27)	< 0.001	89.13 (9.50–836.60)	< 0.001
RBC	529.78 (0– >1000)	0.4	70.38 (0– >1000)	0.6
Hgb	2.75 (0.41–18.26)	0.3	2.55 (0.40–16.27)	0.3
Hct	0.40 (0.05–2.99)	0.4	0.50 (0.08–3.08)	0.5
MCV	1.26 (0.62–2.56)	0.5	1.27 (0.67–2.40)	0.5
RDW-SD	1.21 (1.05–1.39)	0.007	–	–
RDW-CV	–	–	1.62 (1.12–2.34)	0.01
AUC	**0.933 (95% CI: 0.89–0.96). *P* = 0.03**		**0.908 (95% CI: 0.86–0.94). *P* = 0.04**	

Table 5. Correlation between morphological parameters and length of hospital stay

Correlation coefficient (*P*)	RBC	Hgb	Hct	MCV	RDW-CV	RDW-SD
Length of hospital stay	–0.17 ($P < 0.05$)	–0.24 ($P < 0.05$)	–0.23 ($P < 0.05$)	–0.15 ($P < 0.05$)	0.12 NS	0.07 NS
Length of ICU stay	–0.22 NS	–0.16 NS	–0.10 NS	–0.14 NS	0.18 NS	0.24 NS

Hgb: concentration of haemoglobin, Hct: haematocrit, MCV: mean corpuscular volume, ICU: intensive care unit, RBC: red blood cell count, RDW: red blood cell distribution width, NS: not significant ($P > 0.05$)

gery, intensive care, transplantology, as well as emergency medicine [12–15]. However, it seems that the use of RDW in decision-making regarding perioperative care has not been sufficiently assessed.

Therefore, the aim of the study was to verify the hypothesis that RDW is a valuable prognostic parameter in patients undergoing high-risk gastroenterological surgical procedures. The endpoint analysed was only an early death, which was considered a hard endpoint; the analysis was not focused on strictly cardiac complications. Moreover, the findings confirmed that the relationship observed was independent of the individual risk and the remaining red blood cell parameters determined. A particularly interesting fact was that the risk of death increased proportionally with an increase in RDW and was higher even when RDW was still within the reference values. RDW correlated with an increase in health issues evaluated using ASA-PS.

Our observations are consistent with those reported by other authors, who have concluded that RDW may be considered a general biomarker of basic health status [14]. Sadaka *et al.* [16] evaluated the prognosis in ICU patients by comparing RDW values and scores of widely used prognostic scales, such as APACHE II and SOFA. They have demonstrated that the evaluation of the red blood cell distribution width more accurately predicted the death of patients with sepsis.

The pathophysiological evaluation of the above correlation is not difficult. It is suggested that RDW is a relatively universal marker of pathologies within the red blood cell system. RDW is a good marker of the development of anaemia: in cases of malnutrition, B12, iron or folic acid deficiencies. RDW disorders are usually assessed together with MCV impairments to differentiate the cause of anaemia: low MCV associated with high RDW is characteristic of iron deficiency while low MCV with normal RDW suggests anaemia developing in chronic diseases. The changes in RDW, however, can precede pathologies in haemoglobin concentrations or red blood cell structure, thereby identifying the risk of insufficient supply of oxygen to the tissues at an early stage.

Perioperative anaemia favours the development of oxygen debt, which can be particularly important in patients at risk of cardiovascular complications. Coronary anaemia is likely to lead to acute coronary syndrome while type 2 myocardial infarction is its most common form in surgical patients. The relationship of RDW with myocardial injury in non-cardiac surgery (MINS) requires further studies.

The essential aim of any study is to refer the results to clinical practice. In Poland, according to the directive of the Minister of Health on the organising standard for healthcare in the field of anaesthesiology and intensive care of 2016, the minimal number of intensive care stations should constitute 2% of the total number of 2% of the total numer of beds should constitute the minimum numer of intensive care stations [17]. Due to the increasing number of surgical procedures being performed — in many cases in settings without a postoperative unit equipped with professional intensive care stations and professional personnel — physicians have to choose which patients requiring special surveillance are transferred to the ICU and which to the surgical department they were initially admitted to. The functioning of early warning systems is at least suboptimal in the majority of health care institutions. Hence, the organisation of postoperative care remains some kind of triage in which the demands substantially exceed the available capacities and measures. As the problem is widespread, it is reasonable to search for simple and inexpensive predictive markers, available at all reference levels. Our findings indicate that RDW is one of the parameters which can support the decision-making process.

Our study has some limitations. Since hospitals use different devices to determine morphological parameters, it is impossible to suggest a universal cut-off point in order to estimate the risk of complications. Automated measurements of RDW can be significantly inaccurate, which was perfectly demonstrated by Caporal and Comar [10], who compared the results obtained with the microscopic picture. The accuracy of automated measurements depends on MCV values, the presence of fragments of erythrocytes and haemolysis [10, 18]. Moreover, RDW is also affected by numerous other factors associated with additional diseases or even fat-carbohydrate metabolism [15, 19]. Therefore, RDW should be evaluated in relation to other morphological and clinical parameters. Furthermore, according to Nada [19], patients with arterial hypertension and diabetes treated with indapamide or a combination of a thiazide diuretic and an angiotensin receptor agonist had RDW values similar to those in a healthy population. The above observations show that the

drugs taken can also affect the parameter studied. Moreover, it should be stressed that a pre-laboratory error , namely, the time of sample storage, influences the degradation of erythrocytes, which falsifies the automated analysis of RDW [20].

Nevertheless, the results obtained are encouraging enough to continue research regarding the relationship between RDW and postoperative complications in other non-cardiac surgeries. It seems that RDW should be taken into account as an optimal marker of anaemia. Therefore, our observations should be considered an important voice in the discussion about the role of accurate preparation and optimisation of the patient`s clinical status in anaesthesiological outpatient departments.

CONCLUSIONS

1. RDW is a valuable screening biomarker in predicting in-hospital mortality in patients undergoing high-risk gastroenterological surgical procedures, irrespective of the estimated individual risk and values of red blood cell parameters.
2. The evaluation of RDW can be useful for identifying patients requiring correction of haematological disorders in the preoperative period, as well as special perioperative surveillance and monitoring.

ACKNOWLEDGEMENTS

1. Source of funding: none.
2. Conflict of interest: none.

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Received: 2.03.2018 r.
Accepted: 22.08.2018 r.