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Association of preoperative red blood cell width and postoperative 30-day mortality in patients undergoing non-cardiac surgery: a retrospective cohort study using propensity-score matching

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Abstract

Background In terms of predicting surgery mortality, it is controversial whether red blood cell width works independently. In non-cardiac surgery patients older than 18 years, we intend to examine the relationship between red blood cell width and postoperative 30-day mortality.

Methods In this retrospective cohort study, 90,785 Singapore General Hospital patients were matched by propensity score between January 1, 2012 and October 31, 2016. It was determined that red blood cell width at baseline and mortality within 30 days after surgery were the independent and dependent variables. We used a non-parametric multivariate logistic regression to balance the confounders among 7807 patients with high RDW and 7807 patients with non-high RDW in the propensity score matching. We investigated the association between RDW and 30-day mortality after surgery using the doubly robust estimation method.

Results Cohorts matched according to propensity score, the risk of 30-day mortality after surgery increased by 114.6.0% among the high RDW group (OR = 2.146, 95% CI 1.645–2.799, $P < 0.00001$). In the crude model, there was a significant association between RDW and 30-day mortality after surgery (OR = 1.877, 95% CI 1.476–2.388, $P < 0.00001$). In the propensity-score adjusted model, the risk of 30-day mortality after surgery in the high RDW group compared to the control group was not as high as in the non-adjusted model (OR = 1.867, 95% CI 1.467–2.376, $P < 0.00001$). Compared to non-high RDW group, the risk of 30-day mortality after surgery increased by 117.0% and 127.7% among high RDW group in the original cohort (OR 2.170, 95% CI 1.754–2.683, $P < 0.00001$) and the weighted cohort (OR 2.272, 95% CI 2.009–2.580, $P < 0.00001$), respectively.

Conclusions According to the results of this observational, propensity score-matched cohort study, uncontrolled high RDW before surgery is associated with an increased risk of death within 30 days after surgery, that is to say, patients over the age of 18 with high preoperative RDW who undergo non-cardiac surgery have a worse postoperative prognosis than those with normal RDW.

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Keywords Red blood cell width, Postoperative mortality, Propensity-score matching, Non-cardiac surgery, Sensitivity analysis

Background

Surgery plays a crucial role in global health care. The perioperative mortality rate is estimated to be as high as 0.8–4% (Boehm et al. 2015). In addition to the major complications induced by anesthesia and surgery, perioperative mortality is mainly negatively affected by individual patient comorbidities. Therefore, whether to find an index that is cost-effective and easily available to help surgeons predict perioperative mortality and provide a reference for the next therapeutic intervention has become an urgent problem to be solved in modern surgery.

The normal range for Red blood cell width (RDW) is 11.0–15.0% (GL Salvagno 2015; Boehm et al. 2015). The larger the value, the greater the difference in red blood cell volume. When the RDW value is significantly increased, it often indicates red blood cell debris, different sizes, red blood cell polymorphism, or increased reticulocytes. Traditionally, RDW is commonly used in the diagnosis or differential diagnosis of hematological diseases (Zvetkova 2017; Piriyakhuntorn et al. 2018), but now it has been shown to be important for predicting the prognosis of some diseases, including cardiovascular disease (Li et al. 2017; Letendre and Goggs 2018), kidney disease (Wang et al. 2018; Yilmaz and Sozel 2021), *and* liver disease (Fan et al. 2018).

Whether RDW is associated with surgical mortality and whether it can be used as an independent predictor of surgery is currently controversial (Lazzeroni et al. 2021; Pluta et al. 2018; Abdullah et al. 2018; Cheung et al. 2016; Shota et al. 2020; Pedrazzani et al. 2020). In non-cardiac surgery patients older than 18 years, we intend to examine the relationship between red blood cell width and postoperative 30-day mortality.

Methods

Study design and data source

This study was based on a secondary analysis of a single-center retrospective study at Singapore General Hospital from January 2012 to October, 2016. One thousand seven hundred beds tertiary academic hospital. We downloaded the raw data for free from the DATADRYAD database (www.datadryad.org). Since Diana Xin Hui Chan et al. transferred the ownership of the original data to the DATADRYAD website, we were able to use these data to perform secondary data analysis based on different scientific assumptions (Dryad data package: Chan, Diana Xin Hui et al. (2018), Data from: Development of the Combined Assessment of Risk Encountered in Surgery (CARES) surgical risk calculator for prediction of post-surgical mortality and need for intensive care unit admission risk—a single-center retrospective study, Dryad, Dataset, https://doi.org/10.5061/dryad.v142481) (Chan et al. 2018). In accordance with all relevant guidelines and regulations, the Singapore Health Institutional Review Board (Singhealth CIRB 2014/651/D) approved the study prior to the start of the experiment. A paper published in the journal described the ethical approval process (McCaffrey et al. 2013).

Study sample

Study participants included 100,873 surgical patients in total. Baseline exclusion criteria for the original study were as follows: (1) in cardiac surgery, burn-related surgery, neurosurgery, and transplantation, patients are categorically more likely to die as a result of intensive blood transfusion requirements, as well as their substantially higher mortality rates; (2) there is no information available about RDW; (3) under 18 years old. A diagram in Fig. 1 shows the process of selecting participants. (4) The collection time of RDW is before surgery, only once. A secondary analysis of 84,547 participants was conducted.

Exposure and outcome

The primary exposure of interest was RDW. In red blood cell volume, RDW is the variance of red blood cell volume compared to a normal reference range. In the laboratory of this hospital, normally, RDW ranges from 10.9 to 15.7%, with levels above 15.7% classified as high (Chan et al. 2018).

After their index operation, patients were followed up for 30 days to determine if any mortality occurred. An electronic health record synchronization with the mortality data was carried out to ensure near-complete follow-up (Chan et al. 2018).

Covariates

As a result of clinical experience and previous research, we identified potential confounders a priori that may affect the relationship between RDW and perioperative prognosis in our study. During the preoperative anesthetic assessment, the following data were included age, gender, race, preoperative estimated glomerular filtration rate (eGFR), presence of cerebrovascular accidents (CVA), diabetes mellitus (DM), ischemic heart disease (IHD), congestive heart failure (CHF), anemia, priority

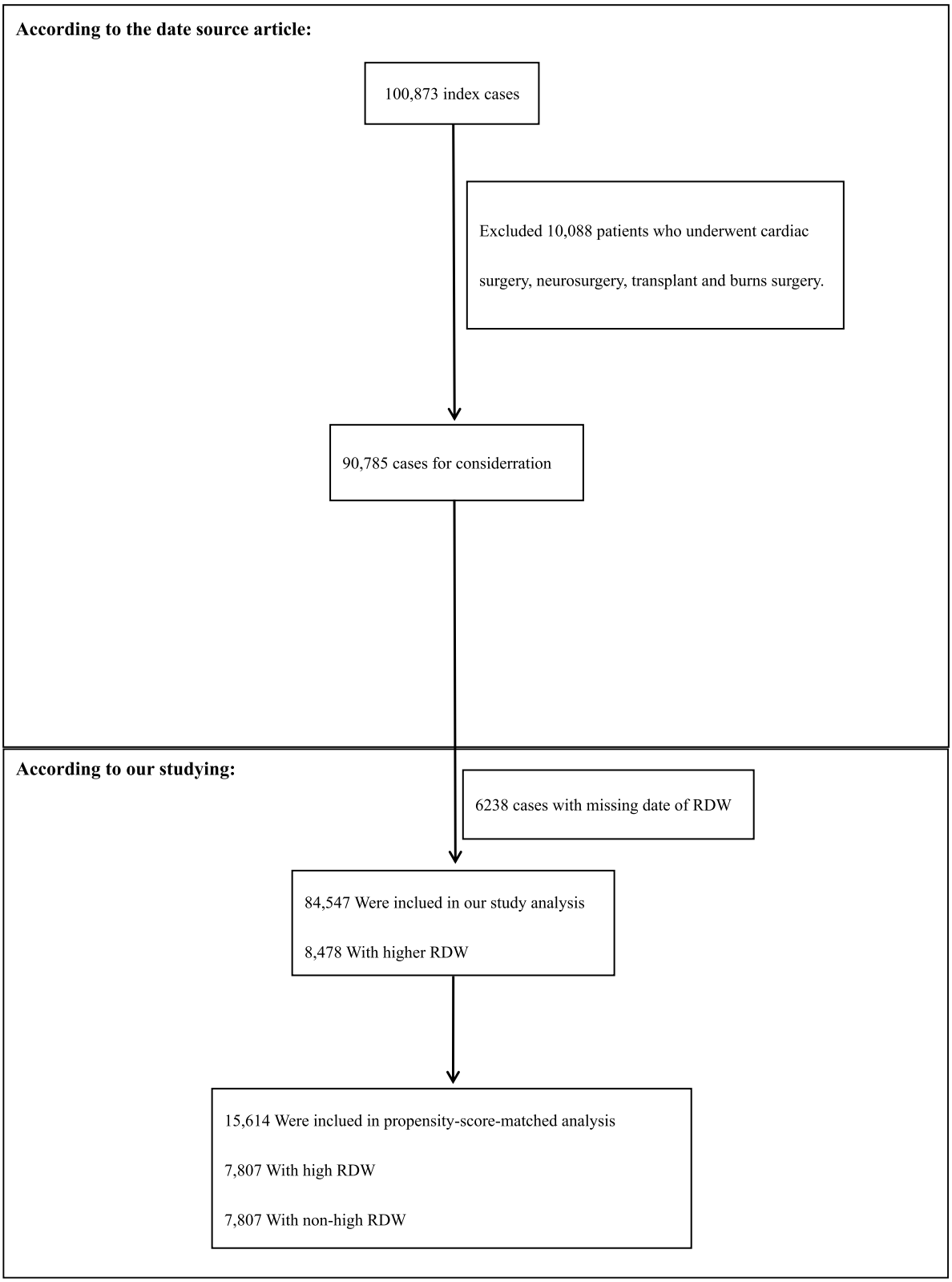

Fig. 1 Study population. Figure 1 showed the inclusion of participants. 100,873 participants were assessed for eligibility in the original study. We excluded patients who underwent cardiac surgery, neurosurgery, transplant and burns surgery, and with missing date of RDW. The final analysis included 84547 subjects in the present study.

of surgery, anesthesia type, surgical risk, preoperative blood transfusion within 30 days, intraoperative blood transfusion data, postoperative blood transfusion data, the Revised Cardiac Risk Index (RCRI) score (Lee et al. 1999), the American Society of Anesthesiologists(ASA) status, admission to ICU for > 24 h (ICUADMGT24H). Preoperative laboratory results including renal group (including eGFR) and full blood count (including hemoglobin concentration) were taken as the latest blood results within 90 days before surgery, and up to the day of surgery. The severity of anemia was defined by WHO's gender-based classification of hemoglobin concentration. Mild anemia was defined as a hemoglobin concentration of 11–12.9 g/dL in males and 11–11.9 g/dL in females; moderate anemia was defined for both genders as hemoglobin concentration between 8–10.9 g/dL and severe anemia was defined as hemoglobin concentration < 8.0 g/dL. Priority of surgery (emergency or elective) and surgical risk classification were based on the 2014 European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA) guidelines (Glance et al. 2012; Kehmeier and Schulze 2014). American Society of Anesthesiologists-Physical Status (ASA-PS) follows that of the ASA-PS definitions (Glance et al. 2012; Kehmeier and Schulze 2014).In accordance with KDIGO guidelines, the preoperative eGFR was calculated from serum creatinine values using the MDRD equation (Levey et al. 2005).

Statistical analyses

A skewed distribution is represented by medians (quartiles) or means (standard deviations) for continuous variables, and a frequency or percentage was used to express categorical variables. Those variables with normal distribution were tested using two-sample-tests, those with non-normal distribution were tested using Wilcoxon rank-sum tests, and those with categorical distributions were tested using chi-square tests (Wu et al. 2020). Data with partial missing values can cause confounding in multivariate regression analysis. In the case of categorical variables, the missing data would be treated as a new independent group; in the case of a continuous variable, the missing data will be replaced with an average or median.

Matching the samples was performed using a greedy algorithm, with a caliper width of 0.01 using a 1:1 protocol without replacement. Based on all baseline covariates, standardized differences (SD) were calculated to assess imbalance and balance pre- and post-matching (Normand et al. 2001). It is indicative of a relatively small imbalance when the standard deviation for a given covariate is less than 10.0% (Normand et al. 2001). RDW and patients' primary and secondary outcomes were also determined using the doubly robust estimation method, which combines multivariate regression with propensity score (McCaffrey et al. 2013; Koch et al. 2018). Using logistic proportional hazards regression, all covariates were adjusted for in the PS-matched cohort.

In addition to the estimated propensity score, the inverse probability of treatment weights (IPTW) was calculated. In this study, IPTW was calculated by taking the inverse of the propensity score for high RDW patients, as well as the inverse of the propensity score for non-high RDW patients (1-propensity score). The weighted cohort was generated using the IPTW model (Koch et al. 2018). This study included a series of sensitivity analyses designed to assess the robustness of its findings and to examine the impact of various association inference models on our results. In the sensitivity analysis, two association inference models were used, one for the original cohort and one for the weighted cohort. There were p values and effect sizes for all these models reported and compared. According to the STROBE statement, all results are reported (Elm et al. 2014; Vandenbroucke et al. 2014). Statistical analysis was performed using R software (http://www.R-project.org, The R Foundation) and Empower-Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). Statistical significance was defined as $P < 0.05$ for two-tailed tests.

The propensity score (PS) indicates the probability that each observation result is assigned to the treatment group if all variables observed in the clinical study exist. Observational clinical studies can synthesize all known observed variables through propensity score values, and then balance treatment and control group observations by propensity score matching, stratification, regression adjustment, weighting, etc. The distribution of variables, thereby reducing bias and increasing the comparability of the two groups. The use of propensity scores by researchers can allow observational clinical studies to achieve post-hoc randomization without over-stratification and over-matching, so that the research results are closer to the "real world" actual intervention effects. As a new method of balancing observed variables, the propensity score method is widely used in the study of observational and clinical non-randomized data. This method treats each propensity score as an independent variable whose distribution is randomized to achieve a study effect similar to that of a randomized controlled trial (RCT) with minimal bias. Therefore, this study employed the propensity score method (PSM) analysis to explore whether there is an association between RDW and perioperative mortality.

Results

Study population

We identified 84,547 participants (46.14% men and 53.86% women) who met our inclusion criteria (Fig. 1) of whom 8,478 (10.1%) with high RDW(> 15.7%) and 76,069 (89.9%) with non-high RDW (≤ 15.7%). Population average age was 52.91 ± 16.88 years. Participants in high RDW and non-high RDW groups (Table 1) have different baseline characteristics, based on propensity-score matching (PS), we identified a cohort of patients who shared similar baseline characteristics. An unparsimonious multivariable logistic regression model was used to estimate the propensity score (Ahmed et al. 2006), all baseline characteristics highlighted in Table 1 serve as covariates with RDW as the independent variable. In order to match variables, the following were used: age, gender, race, eGFR, CVA, DM, IHD, CHF, ASA status, RCRI score, ICUADMGT24H, anemia, priority of surgery, anesthesia type, surgical risk, preoperative blood transfusion within 30 days, intraoperative blood transfusion data, postoperative blood transfusion data.

Several baseline characteristics differed between high RDW and non-high RDW groups until propensity-score matching was applied (Table 1). In general, higher RDW was associated with higher risk among patients, such as RCRI score, Anemia, CV, IHD, CHF, DM, ASA, and ICU admission rate. One-to-one matching based on the propensity score, 7807 non-high RDW patients matched with 7807 high subjects. It is evident from Table 2 that the propensity score was well-matched for almost all variables (standard deviations less than 10.0%). As a result, there was only a slight difference in baseline characteristics between non-high RDW and high RDW groups, which characteristics the two groups were still slightly statistically, but likely not clinically, significantly different, namely the rate of anemia, postoperative transfusion and ASA classification.

Association between RDW and 30-day mortality after surgery

In the propensity-score-matched cohort, we examined the association between RDW and 30-day mortality after surgery using a logistic proportional-hazards regression model. In Table 3, the results of the unadjusted, minimally adjusted, fully adjusted, and propensity score-adjusted analyses are shown simultaneously. In the crude model, there was a significant association between RDW and 30-day mortality after surgery (OR = 1.877, 95% confidence interval (CI) 1.476–2.388, $P < 0.00001$). Namely, the risk of 30-day mortality after surgery increased by 87.7.0% among the high RDW group than the non-high RDW group. In the minimally adjusted model (adjusted age, gender, race), the association still existed (OR 2.077, 95% CI 1.628–2.649, $P < 0.00001$). After adjusting for the full covariates (age, gender, race, eGFR, CVA, DM, IHD, CHF, ASA status, RCRI score, ICUADMGT24H, anemia, priority of surgery, anesthesia type, surgical risk, preoperative blood transfusion with in 30 days, intraoperative blood transfusion data, postoperative blood transfusion data), furthermore, we were able to detect a significant statistical connection herewith (OR = 2.146, 95% CI 1.645–2.799, $P < 0.00001$). In the propensity-score adjusted model, the risk of mortality in the high RDW group did not drop after the propensity score matching, but the increased risk of mortality compared to the control group was not as high as in the non-adjusted model.

Sensitivity analysis

We used inverse probability of treatment weights (IPTW) to generate a weighted cohort. Based on the original cohort and the weighted cohort, we performed the logistic proportional-hazards regression model to assess the relationship between RDW and 30-day mortality after surgery. A simultaneous comparison of the unadjusted, minimally adjusted, and fully adjusted models was shown in Table 4. In both the original and weighted cohorts, the higher RDW was associated with a higher death rate after surgery at 30 days. As compared to non-high RDW group in the full model, the risk of 30-day mortality after surgery in high RDW group increased by 117.0% in the original cohort (OR = 2.277, 95%CI 1.754–2.683, $P < 0.0001$) and 122.7% in the weighted cohort (OR = 2.227, 95% CI 2.009–2.580, $P < 0.00001$), respectively.

Subgroup analysis

We used a subgroup analysis to detect the effect of potential confounders which may affect the relationship between RDW and postoperative 30-day mortality. Table 5 showed after conducting subgroup analysis on stratified variables such as age, gender, and different types of surgery priority, we found a positive correlation between RDW and the risk of postoperative 30-day mortality.

Discussion

This study showed that high RDW was significantly associated with higher risks of postoperative 30-day mortality in non-cardiac surgery patients over 18 years of age compared to the non-high group. A number of statistical analyses confirmed this finding, including the doubly robust estimation method, the propensity score-based IPW model, the propensity score-based patient-matching model, the logistic regression based multivariate analysis model and the sensitivity analysis model. According to the study, an uncontrolled high RDW before surgery

Table 1 Baseline characteristics before propensity-score matching in the original cohort

Category	Low RDW	High RDW	Standardize diff	*P* value
N	76069	8478		
Age (years)	52.84 ± 16.89	53.62 ± 16.84	4.7%	< 0.001
PREOP-EGFR	96.22 ± 31.10	98.29 ± 46.30	5.3%	< 0.001
PS	0.08 ± 0.11	0.32 ± 0.22	135.5%	< 0.001
GENDER			26.6%	< 0.001
Male	36092 (47.45%)	2922 (34.47%)		
Female	39977 (52.55%)	5556 (65.53%)		
Preop-transfusion with in 30days*n*(%)			28.5%	< 0.001
0 units	74881 (98.44%)	7850 (92.59%)		
1 units	652 (0.86%)	329 (3.88%)		
2 or more units	536 (0.71%)	299 (3.53%)		
Intraop-transfusion			47%	< 0.001
0 units	72806 (95.71%)	6870 (81.03%)		
1 units	3263 (4.29%)	1608 (18.97%)		
Postop-transfusion with in 30days			35%	< 0.001
0 units	75720 (99.54%)	7885 (93.01%)		
1 units	228 (0.30%)	379 (4.47%)		
2 units	121 (0.16%)	214 (2.52%)		
Anesthesia type *n*(%)			4.2%	< 0.001
ga	63240 (83.14%)	7178 (84.67%)		
ra	12829 (16.87%)	1300 (15.33%)		
Priority of surgery *n*(%)			7.9%	< 0.001
Elective	60188 (79.12%)	6430 (75.84%)		
Emergency	15881 (20.88%)	2048 (24.16%)		
Surgical risk			25%	< 0.001
Low	39961 (52.53%)	3553 (41.91%)		
Moderate	33446 (43.97%)	4298 (50.70%)		
High	2662 (3.50%)	627 (7.40%)		
RACE			13.6%	< 0.001
Chinese	54987 (72.29%)	5692 (67.14%)		
Indian	6681 (8.78%)	844 (9.96%)		
Malay	7324 (9.63%)	1146 (13.52%)		
Others	7077 (9.30%)	796 (9.39%)		
ANEMIA			149.2%	< 0.001
None	59399 (78.09%)	1750 (20.64%)		
Mild	10637 (13.98%)	2053 (24.22%)		
Moderate/severe	6033 (7.93%)	4675 (55.14%)		
ICUADMGT24H			14.4%	< 0.001
No	75165 (98.81%)	8196 (96.67%)		
Yes	904 (1.19%)	282 (3.33%)		
RCRI.SCORE			33.3%	< 0.001
Level 1	40539 (53.29%)	3432 (40.48%)		
Level 2	10226 (13.44%)	1778 (20.97%)		
Level 3	1923 (2.53%)	462 (5.45%)		
Level 4	648 (0.85%)	223 (2.63%)		
NA	22733 (29.89%)	2583 (30.47%)		
CVA CATEGORY			5.3%	< 0.001
No	51180 (67.28%)	5600 (66.05%)		
Yes	1299 (1.71%)	205 (2.42%)		

Table 1 (continued)

Category	Low RDW	High RDW	Standardize diff	*P* value
NA	23590 (31.01%)	2673 (31.53%)		
IHD CATEGORY			11%	< 0.001
No	48760 (64.10%)	5173 (61.02%)		
Yes	3522 (4.63%)	602 (7.10%)		
NA	23787 (31.27%)	2703 (31.88%)		
CHF CATEGORY			13.2%	< 0.001
No	53750 (70.66%)	5779 (68.17%)		
Yes	577 (0.76%)	198 (2.34%)		
NA	21742 (28.58%)	2501 (29.50%)		
DM CATEGORY			9.3%	< 0.001
No	52167 (68.58%)	5625 (66.35%)		
Yes	1636 (2.15%)	309 (3.65%)		
NA	22266 (29.27%)	2544 (30.01%)		
ASA CATEGORY			41.5%	< 0.001
Level I	18383 (24.17%)	1327 (15.65%)		
Level II	42568 (55.96%)	4074 (48.05%)		
Level III	10677 (14.04%)	2271 (26.79%)		
Level IV–VI	730 (0.96%)	335 (3.95%)		
NA	3711 (4.88%)	471 (5.56%)		

Values are n (%) or mean ± SD

Abbreviations: *GA* General anesthesia, *RA* Regional anesthesia, *SD* Standardized diffffferences

PREOP-eGFR preoperative estimated glomerular filtration rate (mL/min/1.73m2), PS Propensity score, NA not available, CVA cerebrovascular accidents, IHD ischemic heart disease, CHF congestive heart failure, DM diabetes mellitus requiring insulin therapy; creatinine>2.0mg/dl, Preop preoperative, Intraop intraoperative, Postop postoperative, RCRI Revised Cardiac Risk Index, ASA American Society of Anesthesiologists, ICU Intensive Care Unit, ICUADMGT24H admission to ICU for >24 hours

increased the risk of death rather than critical complications within 30 days of the surgery.

RDW is a well-known independent predictor of mortality and incidence rate in patients undergoing cardiac surgery (Balta et al. 2013; Polat et al. 2014; Collas et al. 2016). However, in non-cardiac surgery, the impact of RDW on postoperative mortality is still controversial. In a prospective observation of 229 patients undergoing high-risk gastrointestinal surgery, it was confirmed that RDW can predict postoperative mortality (OR RDW-SD = 1.21; $P < 0.001$, OR RDW-CV = 1.62; $P = 0.01$ (Pluta et al. 2018). An analysis of non-cardiac surgery patients at the Icelandic National University Hospital was carried out in a retrospective cohort study, in accordance with the preoperative RDW (≤ 13.3%, 13.4–14.0%, 14.1–14.7%, 14.8–15.8%, and > 15.8%), patients were grouped into five predefined groups. All-cause long-term mortality was the primary outcome, with secondary outcomes including 30-day mortality, length of stay, and readmissions within 30 days compared with propensity score matching (PSM) cohort from patients with RDW ≤ 13.3%. Patients with RDW between 14.8% and 15.8% (HR = 1.33; 95% CI, 1.15–1.59; $P < 0.001$) and above 15.8% (HR = 1.66; 95% CI, 1.4–1.95; $P < 0.001$) had a higher hazard of mortality, compared with matched controls with RDW ≤ 13.3%. This is basically consistent with our research results. Domestic scholars's study also supports the above conclusion. A propensity matching analysis conducted by Kung-Chuan Cheng et al. (Cheng et al. 2022) on 5315 patients with stage I-II colorectal cancer who underwent inpatient surgery at Chang Gung Memorial Hospital from 2001 to 2018 showed that high RDW remained a negative predictor of overall survival (OS) (HR = 1.49, 95% CI 1.25–1.78) and disease-free survival (DFS) and cancer-specific survival (CSS) after early colorectal cancer radical surgery. In another study on gastric cancer patients undergoing radical surgery (Yazici et al. 2017), it was found that a high preoperative RDW value was an important predictor of 60 day mortality (17.9 ± 4.3 vs 16.0 ± 3.2; $P = 0.015$). In patients with RDW ≥ 16%, the disease-free and overall survival rates of advanced gastric cancer decreased ($P = 0.04$). We found a significant association between RDW and postoperative mortality using the doubly robust estimation method in the propensity-score matched cohort. High RDW increased the risk of 30-day mortality after surgery by 114.6.0%. And the figure dropped to 86.7% after adjusting the propensity score. Thus the results better showed the relationship between RDW and he risk of 30-day mortality after surgery in the real world. Furthermore, we adjusted for

Table 2 Baseline characteristics after propensity-score matching in the original cohort

RDW	≤ 15.7%	> 15.7%	Standardize diff	*P* value
N	7807	7807		
Age (years)	54.96 ± 18.56	54.03 ± 16.84	5.2%	0.001
PREOP-EGFR	94.11 ± 45.03	95.33 ± 43.71	2.7%	0.087
PS	0.29 ± 0.21	0.29 ± 0.21	1.5%	0.353
GENDER			13.1%	< 0.001
Male	3294 (42.19%)	2795 (35.80%)		
Female	4513 (57.81%)	5012 (64.20%)		
Preop-transfusion with in 30 days *n*(%)			1.6%	0.624
0 units	7275 (93.19%)	7291 (93.39%)		
1 units	295 (3.78%)	273 (3.50%)		
2 or more units	237 (3.04%)	243 (3.11%)		
Intraop-transfusion			1.2%	0.546
0 units	6503 (83.30%)	6531 (83.66%)		
1 units	1304 (16.70%)	1276 (16.34%)		
Postop-transfusion with in 30 days			4.2%	0.033
0 units	7494 (95.99%)	7443 (95.34%)		
1 units	202 (2.59%)	257 (3.29%)		
2 units	111 (1.42%)	107 (1.37%)		
Anesthesia type *n*(%)			1.2%	0.460
ga	6560 (84.03%)	6526 (83.59%)		
ra	1247 (15.97%)	1281 (16.41%)		
Priority of surgery *n*(%)			9.9%	< 0.001
Elective	5531 (70.85%)	5872 (75.21%)		
Emergency	2276 (29.15%)	1935 (24.79%)		
Surgical risk			3.9%	0.050
Low	3346 (42.86%)	3379 (43.28%)		
Moderate	3843 (49.23%)	3890 (49.83%)		
High	618 (7.92%)	538 (6.89%)		
RACE			28.3%	< 0.001
Chinese	4953 (63.44%)	5273 (67.54%)		
Indian	757 (9.70%)	785 (10.06%)		
Malay	700 (8.97%)	1045 (13.39%)		
Others	1397 (17.89%)	704 (9.02%)		
ANEMIA			9.0%	< 0.001
None	1862 (23.85%)	1750 (22.42%)		
Mild	1753 (22.45%)	2053 (26.30%)		
Moderate/severe	4192 (53.70%)	4004 (51.29%)		
ICUADMGT24H			0.8%	0.619
No	7548 (96.68%)	7559 (96.82%)		
Yes	259 (3.32%)	248 (3.18%)		
RCRI.Score			3.9%	0.196
Level 1	3291 (42.15%)	3205 (41.05%)		
Level 2	1501 (19.23%)	1570 (20.11%)		
Level 3	475 (6.08%)	437 (5.60%)		
Level 4	226 (2.89%)	209 (2.68%)		
NA	2314 (29.64%)	2386 (30.56%)		
CVA Category			4.7%	0.013
No	5235 (67.06%)	5145 (65.90%)		
Yes	230 (2.95%)	188 (2.41%)		

Table 2 (continued)

RDW	≤ 15.7%	> 15.7%	Standardize diff	*P* value
NA	2342 (30.00%)	2474 (31.69%)		
IHD Category			5.8%	0.002
No	4783 (61.27%)	4734 (60.64%)		
Yes	669 (8.57%)	569 (7.29%)		
NA	2355 (30.17%)	2504 (32.07%)		
CHF Category			3.1%	0.160
No	5405 (69.23%)	5324 (68.20%)		
Yes	193 (2.47%)	175 (2.24%)		
NA	2209 (28.30%)	2308 (29.56%)		
DM Category			3.1%	0.149
No	5265 (67.44%)	5150 (65.97%)		
Yes	291 (3.73%)	304 (3.89%)		
NA	2251 (28.83%)	2353 (30.14%)		
ASA Category			16.5%	< 0.001
Level I	1626 (20.83%)	1241 (15.90%)		
Level II	3327 (42.62%)	3756 (48.11%)		
Level III	2096 (26.85%)	2081 (26.66%)		
Level IV–VI	216 (2.77%)	301 (3.86%)		
NA	542 (6.94%)	428 (5.48%)		

Values are n (%) or mean ± SD

Abbreviations: *GA* General anesthesia, *RA* Regional anesthesia, *SD* Standardized diffffferences

PREOP-eGFR preoperative estimated glomerular filtration rate (mL/min/1.73m2), PS Propensity score, NA not available, CVA cerebrovascular accidents, IHD ischemic heart disease, CHF congestive heart failure, DM diabetes mellitus requiring insulin therapy; creatinine>2.0mg/dl, Preop preoperative, Intraop intraoperative, Postop postoperative, RCRI Revised Cardiac Risk Index, ASA American Society of Anesthesiologists, ICU Intensive Care Unit, ICUADMGT24H admission to ICU for >24 hours

Table 3 The results of multivariate analyses in propensity score matched cohort

Exposure	Non-adjusted (OR, 95% CI, *P*)	Adjust I (OR, 95% CI, *P*)	Adjust II (OR, 95% CI, *P*)	Adjust III (OR, 95% CI, *P*)
30-day mortality				
RDW ≤ 15.7%	Ref	Ref	Ref	Ref
RDW > 15.7%	1.877 (1.476, 2.388) < 0.00001	2.077 (1.628, 2.649) < 0.00001	2.146 (1.645, 2.799) < 0.00001	1.867(1.467, 2.376) < 0.00001

The results were expressed as odds ratio (95%confidence interval) *P*-value

Non-adjusted model adjust for: None

Adjust I model adjust for: age, gender, race

Adjust II model adjust for: age, gender,race,perioperative blood transfusion with in 30days, intraoperative blood transfusion,postoperative blood transfusion with in 30days,preoperative eGFR, presence of CVA,DM, IHD, CHF, priority of surgery, anesthesia type, surgical risk, the RCRI score, the ASA status.anemia, ICU

Adjust III model adjust for: Propensity score

different covariates. Several biochemical parameters were adjusted, including eGFR, CVA, DM, IHD, CHF, the RCRI score, ASA status, and hemoglobin. Additionally, our sample size is larger (90,785), and the participants represent four races in Singapore, making it a more representative sample of Asians. The results of our study indicates association between high RDW and a higher risk of 30-day mortality after surgery. Understanding high RDW as a potential risk factor for perioperative period will allow us to communicate risk better with patients and provide more personalized prevention approach and management protocols. The findings of our study are helpful for promoting propensity score methods in correlation studies.

Nevertheless, some people opposed the above view. Xingchen Li et al. (Li et al. 2021) retrospectively analyzed 157 patients who underwent radical resection of the liver and found that low preoperative RDW levels were associated with lower survival rates after radical resection of cholangiocarcinoma (ICC), meaning that patients

Table 4 Association between RDW and thirty-day mortality in different models of the original and the weighted cohort

	Exposure	Non-adjusted(OR,95% CI, P)	Adjust I(OR,95% CI, P)	Adjust II(OR,95% CI, P)
A	RDW≤15.7	Ref	Ref	Ref
	RDW > 15.7	6.831 (5.738, 8.133) <0.00001	6.382 (5.345, 7.622) <0.00001	2.170 (1.754, 2.683) <0.00001
B	RDW≤15.7	Ref	Ref	Ref
	RDW > 15.7	3.079 (2.760, 3.434) <0.00001	2.751 (2.465, 3.071) <0.00001	2.277 (2.009, 2.580) <0.00001

A In the original cohort; B In the weighted cohort

Non-adjusted model adjust for: None

Adjust I model adjust for: age, gender, race

Adjust II model adjust for: age, gender, race, perioperative blood transfusion with in 30days, intraoperative blood transfusion, postoperative blood transfusion with in 30days, preoperative eGFR, presence of CVA,DM, IHD, CHF, priority of surgery, anesthesia type, surgical risk, the RCRI score, the ASA status.anemia, ICU

with higher RDW values had better prognosis. Not come singly but in pairs, a retrospective study involving 380 patients with colorectal cancer liver metastasis (CRLM) who underwent liver resection revealed a significant association between preoperative, red blood cell distribution width- coefficient of variation *(*RDW-CV*)* elevation and better postoperative progression free survival (PFS) through univariate and multivariate Cox regression analysis (mPFS: 5.0 vs. 8.9 months, $P=0.007$; mOS 59.0 vs. 42.0 months, $P=0.041$) (Chen et al. 2021). Pedrazzani C et al. (Pedrazzani et al. 2020) analyzed 591 patients who underwent colorectal cancer surgery and found that patients with a value higher than 14.1% (H-RDW) did not show a shorter cancer-related survival period. Meanwhile, according to *tumor node metastasis* (TNM) staging, H-RDW is only associated with a decrease in postoperative survival rate in stage I ($p=0.001$), but H-RDW does not seem to affect survival rates in stages II–IV.

Inconsistent findings may be caused by the following factors: (1) study participants are diverse in terms of their racial, gender, nationality, age, and other characteristics. (2) The sample size of different studies varies greatly. (3) There were various confounding variables taken into account in these studies to adjust for the relationship between RDW and postoperative mortality. (4) Results vary greatly depending on the time between follow-ups. (5) There are different ways to handle confounding factors. As a result of our findings, the existing literature supports the hypothesis that high RDW increases 30-day mortality after surgery, highlighting the importance of reducing RDW before surgery.

RDW value is a widely used diagnostic indicator in clinical practice and is one of the blood routine tests. This indicator detection has the advantages of simplicity, low cost, easy access, and wide applicability, making it highly practical in clinical practice. RDW values are often used for differential diagnosis of anemia, and in recent years, increasing evidence suggests that RDW values are associated with various human diseases and their complications, and more importantly, with overall mortality rates in the general population. Researchers have generally realized that traditional applications of RDW limited to early detection of anemia are far from sufficient, and the clinical application scope of RDW should be expanded.

The increase of RDW reflects the changes of erythrocyte homeostasis, including erythropoiesis disorder, abnormal erythrocyte metabolism and survival, which may be caused by various abnormal conditions in the body, including inflammation, oxidative stress, malnutrition, erythrocyte fragmentation, hypertension, dyslipidemia and erythropoietin abnormality (Imai et al. 2017; Roumeliotis et al. 2020; Ma et al. 2018; Xu et al. 2018). Patients with high RDW often have more significant inflammatory reactions and malnutrition before surgery, inhibiting the proliferation of bone marrow primitive cells, allowing immature red blood cells to enter the bloodstream. At the same time, aging red

Table 5 Effect size of RDW on 30-day mortality in prespecified and exploratory subgroups

Characteristic	No. of participants	OR (95% CI)	*P* value
AGE (years)			
< 50	3149	1.5000 (0.250,8.989)	0.65717
≥ 50	6173	2.097(1.538,2.860)	< 0.00001
Gender			
Male	2726	1.562 (0.948, 2.574)	0.08025
Female	6159	1.687 (1.119, 2.542)	0.01250
Priority of surgery *n*(%)			
Elective	8488	1.432 (0.882,2.325)	0.14660
Emergency	1308	2.633(1.549,4.475)	0.00035

Note 1: Above models adjusted for age, gender, and priority of surgery

Note 2: In each case, the model is not adjusted for the stratification variable

blood cells in the bloodstream are reduced, resulting in smaller or larger red blood cells present in the bloodstream, ultimately leading to an increase in RDW (Patel et al. 2015). Another explanation for the relationship between chronic inflammation and elevated RDW may be the increased fragility of red blood cells (Maurya et al. 2015) and oxidation of hemoglobin (Mohanty et al. 2014) due to exposure to free radicals in an inflammatory state secondary to increased lipid oxidation, indicating that red blood cells are cleared, thereby increasing RDW. Other mechanisms, such as increased release of free histones and increased binding of free histones to red blood cells, Kordbacheh F et al. (Kordbacheh et al. 2017) could also explain the observed association.

A series of inflammatory factors inhibit the maturation of red blood cells, leading to obstacles and ineffective generation of mature red blood cells, increased heterogeneity of red blood cells, and an increase in RDW (Pierce and Larson 2005). Therefore, RDW can reflect the general health status, subclinical and clinical disease status, and provide valuable information for predicting the prognosis of patients with various common acute and chronic diseases, such as diabetes (Khalil et al. 2019), traumatic brain injury (TBI) (Mutlu et al. 2019), and oxidative stress (Burns et al. 2019) association.

Study strengths and limitations

Strengths of this study include the following. As far as we know, patients undergoing non-cardiac surgery have fewer cohort studies using propensity score matching to explore the relationship between preoperative RDW and postoperative 30-day mortality. First, a cross-sectional study was conducted to investigate the relationship between RDW and postoperative prognosis using the PSM. Observational studies have increasingly used PSM methods in recent years. With the PSM method, a wide range of data requirements can be satisfied, including reducing inter-group differences, balancing confounding variables, and achieving the effect of "similar randomization". Second, to reduce treatment selection bias inherent in retrospective studies, in order to minimize baseline differences between groups, we employ the doubly robust estimation method. Third, using a sensitivity analysis, we validated the data's reliability. As part of this study, IPTW was primarily used to establish a weighted cohort and further investigate the relationship between RDW and postoperative 30-day mortality rate. Fourth, unlike previous retrospective cohort studies, this study included a larger sample size of participants. Additionally, this clinical database contained detailed information about demographics, preexisting comorbidities, and risk assessment methods that can affect morbidity and mortality independently.

However, there are several limitations to the present stud. First, the study population consisted of only Asian patients. In order to enhance the reliability of the data, multicenter research can be conducted to expand the study population. The collection time of RDW is before surgery, only once, and the raw data did not provide information on surgical intervention during patient follow-up. This limits the exploration of this study, in the future, we can consider designing our studies or collaborating with other researchers to collect as many variables as possible, including information on surgical intervention during patient follow-up, the investigators must have homogenous groups. Second, this study is a secondary analysis of a single center retrospective study, no further analysis was made about other risk tool or markers, or laboratory testing. It was not possible to eliminate residual and/or unmeasured confounding factors from the evaluated associations (e.g., inflammatory markers and socioeconomic factors) and investigate the long-term relationship between RDW and health outcomes. Third, although the PSM tried to balance known confounding variables to the best of its ability, it did not ensure that all measures of baseline characteristics matched, nor did it account for the influence of unknown variables. As a measure of reducing interference from variables, we set the calliper width to 0.01. Fourth, in addition, other diseases, as well as fat and carbohydrate metabolism, can also affect RDW (Engstrom et al. 2014; Nada 2015). These variables or measured quantities are dependent. Therefore, at the moment, no causal relationship should be described for mortality, but maybe the co-existence of some other mechanism (inflammation, aging, hypoxia and so on). Fifth, it discharged patients with high-risk injuries, such as nerve injuries, burns, and serious infections, despite the fact that it was originally aimed at non-cardiac surgery populations. Sixth, our research objective is to explore the impact of baseline RDW on mortality occurring within 90 days, the time span in the raw data is indeed very large. This might lead to selection bias.

According to the study, an uncontrolled high RDW before surgery increased the risk of death rather than critical complications within 30 days of the surgery.

Conclusion

According to the results of this observational, propensity score-matched cohort study, uncontrolled high RDW before surgery is associated with an increased risk of death within 30 days after surgery, that is to say, patients over the age of 18 with high preoperative RDW who undergo non-cardiac surgery have a worse postoperative prognosis than those with normal RDW.

Abbreviations

RDW	Red Blood cell width
H-RDW	High RDW
PS	Propensity score
CI	Confidence interval
OR	Oddsratio
NA	Not Available
CVA	Cerebrovascular accidents
eGFR	Estimated glomerular filtration rate
IHD	Ischemic Heart disease
CHF	Congestive Heart failure
DM	Diabetes Mellitus
Preop	Preoperative
Intraop	Intraoperative
Postop	Postoperative
RCRI	Revised Cardiac Risk Index
ASA	American Society of Anesthesiologists
ICU	Intensive care unit
ICUADMGT24H	Admission To ICU for > 24 h
GA	General Anesthesia
RA	Regional Anesthesia
SD	Standard deviation

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Authors' Contribution
W conceived the research, drafted the manuscript, F did the statistical analysis. X revised the manuscript and designed the study. C and L took part in the discussion. All authors read and approved the final manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all Participants. This study has been approved by the SingHealth Centralised Institutional Review Board (CIRB). (Singhealth CIRB 2014/651/D).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

Abdullah HR, Sim YE, Sim YT, Ang AL, Chan YH, Richards T, Ong BC. Preoperative red cell distribution width and 30-day mortality in older patients undergoing non-cardiac surgery: a retrospective cohort observational study. Sci Rep. 2018;8(1):6226.
Ahmed A, Husain A, Love TE, Gambassi G, Dell'Italia LJ, Francis GS, Gheorghiade M, Allman RM, Meleth S, Bourge RC. Heart failure, chronic diuretic use, and increase in mortality and hospitalization: an observational study using propensity score methods. Eur Heart J. 2006;27(12):1431–9.
Balta S, Demirkol S, Aydogan M, Unlu M. Red cell distribution width is a predictor of mortality in patients undergoing coronary artery bypass surgery. Eur J Cardiothorac Surg. 2013;44(2):396–7.
Boehm O, Pfeiffer MK, Baumgarten G, Hoeft A. Perioperative risk and mortality after major surgery. ANAESTHESIST. 2015;64(11):814–27.
Burns CD, Brown JP, Corwin HL, Gross I, Ozawa SJ, Shander A. Special report from the society for the advancement of blood management: the choosing wisely campaign. Anesth Analg. 2019;129(5):1381–6.
Chan D, Sim YE, Chan YH, Poopalalingam R, Abdullah HR. Development of the Combined Assessment of Risk Encountered in Surgery (CARES) surgical risk calculator for prediction of postsurgical mortality and need for intensive care unit admission risk: a single-center retrospective study. BMJ Open. 2018;8(3):e19427.
Chen Q, Mao R, Zhao J, Bi X, Li Z, Huang Z, Zhang Y, Zhou J, Zhao H, Cai J. Nomograms incorporating preoperative RDW level for the prediction of postoperative complications and survival in colorectal liver metastases after resection. Ann Palliat Med. 2021;10(4):4143–58.
Cheng KC, Lin YM, Liu CC, Wu KL, Lee KC. High red cell distribution width is associated with worse prognosis in early colorectal cancer after curative resection: a propensity-matched analysis. Cancers (Basel). 2022;14(4):945.
Cheung YN, Shum HP, Chan KC, Yan WW. Preoperative red cell distribution width: Not a useful prognostic indicator for 30-day mortality in patients who undergo major- or ultra-major noncardiac surgery. Indian J Crit Care Med. 2016;20(11):647–52.
Collas VM, Paelinck BP, Rodrigus IE, Vrints CJ, Van Craenenbroeck EM, Bosmans JM. Red cell distribution width improves the prediction of prognosis after transcatheter aortic valve implantation. Eur J Cardiothorac Surg. 2016;49(2):471–7.
Engstrom G, Smith JG, Persson M, Nilsson PM, Melander O, Hedblad B. Red cell distribution width, haemoglobin A1c and incidence of diabetes mellitus. J Intern Med. 2014;276(2):174–83.
Fan X, Deng H, Wang X, Fu S, Liu Z, Sang J, Zhang X, Li N, Han Q, Liu Z. Association of red blood cell distribution width with severity of hepatitis B virus-related liver diseases. CLIN CHIM ACTA. 2018;482:155–60.
Glance LG, Lustik SJ, Hannan EL, Osler TM, Mukamel DB, Qian F, Dick AW. The Surgical Mortality Probability Model: derivation and validation of a simple risk prediction rule for noncardiac surgery. Ann Surg. 2012;255(4):696–702.
Imai R, Uemura Y, Okumura T, Takemoto K, Uchikawa T, Koyasu M, Ishikawa S, Iwamiya S, Ozaki Y, Shibata R, et al. Impact of red blood cell distribution width on non-cardiac mortality in patients with acute decompensated heart failure with preserved ejection fraction. J Cardiol. 2017;70(6):591–7.
Kehmeier ES, Schulze VT. Cardiovascular assessment and management prior to non-cardiac surgery. Comment on the new 2014 ESC/ESA guidelines. HERZ. 2015;40(8):1043–7.
Khalil A, Shehata M, Abdeltawab A, Onsy A. Red blood cell distribution width and coronary artery disease severity in diabetic patients. Future Cardiol. 2019;15(5):355–66.
Koch B, Vock DM, Wolfson J. Covariate selection with group lasso and doubly robust estimation of causal effects. Biometrics. 2018;74(1):8–17.
Kordbacheh F, O'Meara CH, Coupland LA, Lelliott PM, Parish CR. Extracellular histones induce erythrocyte fragility and anemia. Blood. 2017;130(26):2884–8.
Lazzeroni D, Moderato L, Marazzi PL, Pellegrino C, Musiari E, Castiglioni P, Camaiora U, Bini M, Geroldi S, Brambilla L, et al. Red blood cell distribution width as a novel prognostic marker after myocardial revascularization or cardiac valve surgery. Sci Rep. 2021;11(1):7889.

Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100(10):1043–9.
Letendre JA, Goggs R. Determining prognosis in canine sepsis by bedside measurement of cell-free DNA and nucleosomes. J Vet Emerg Crit Care (San Antonio). 2018;28(6):503–11.
Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, De Zeeuw D, Hostetter TH, Lameire N, Eknoyan G. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2005;67(6):2089–100.
Li N, Zhou H, Tang Q. Red blood cell distribution width: a novel predictive indicator for cardiovascular and cerebrovascular diseases. DIS MARKERS. 2017;2017:7089493.
Li X, Chen Q, Bi X, Zhao J, Li Z, Zhou J, Huang Z, Zhang Y, Mao R, Zhao H, et al. Preoperatively elevated RDW-SD and RDW-CV predict favorable survival in intrahepatic cholangiocarcinoma patients after curative resection. BMC Surg. 2021;21(1):105.
Ma Y, Jin Z, Zhou S, Ye H, Jiang S, Yu K. Prognostic significance of the red blood cell distribution width that maintain at high level following completion of first line therapy in mutiple myeloma patients. Oncotarget. 2018;9(11):10118–27.
Maurya PK, Kumar P, Chandra P. Biomarkers of oxidative stress in erythrocytes as a function of human age. World J Methodol. 2015;5(4):216–22.
McCaffrey DF, Griffin BA, Almirall D, Slaughter ME, Ramchand R, Burgette LF. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med. 2013;32(19):3388–414.
Mohanty JG, Nagababu E, Rifkind JM. Red blood cell oxidative stress impairs oxygen delivery and induces red blood cell aging. Front Physiol. 2014;5:84.
Mutlu NM, Peker TT, Soyal OB, Akcaboy ZN, Akcaboy EY, Titiz AP, Ciftci A, Gogus N. Red cell distribution width in diagnosis of brain death. Transplant Proc. 2019;51(7):2189–91.
Nada AM. Red cell distribution width in type 2 diabetic patients. Diabetes Metab Syndr Obes. 2015;8:525–33.
Normand ST, Landrum MB, Guadagnoli E, Ayanian JZ, Ryan TJ, Cleary PD, McNeil BJ. Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: a matched analysis using propensity scores. J Clin Epidemiol 2001;54(4):387–98.
Patel HH, Patel HR, Higgins JM. Modulation of red blood cell population dynamics is a fundamental homeostatic response to disease. Am J Hematol. 2015;90(5):422–8.
Pedrazzani C, Tripepi M, Turri G, Fernandes E, Scotton G, Conci S, Campagnaro T, Ruzzenente A, Guglielmi A. Prognostic value of red cell distribution width (RDW) in colorectal cancer. Results from a single-center cohort on 591 patients. Sci Rep. 2020;10(1):1072.
Pierce CN, Larson DF. Inflammatory cytokine inhibition of erythropoiesis in patients implanted with a mechanical circulatory assist device. Perfusion. 2005;20(2):83–90.
Piriyakhuntorn P, Tantiworawit A, Rattanathammethee T, Chai-Adisaksopha C, Rattarittamrong E, Norasetthada L. The role of red cell distribution width in the differential diagnosis of iron deficiency anemia and non-transfusiondependent thalassemia patients. Hematol Rep. 2018;10(3):7605.
Pluta M, Klocek T, Krzych LJ. Diagnostic accuracy of red blood cell distribution width in predicting in-hospital mortality in patients undergoing high-risk gastrointestinal surgery. Anaesthesiol Intensive Ther. 2018;50(4):277–82.
Polat V, Iscan S, Etli M, El KH, Gursu O, Eker E, Ozdemir F. Red cell distribution width as a prognostic indicator in pediatric heart disease and after surgery. Biomed Res Int. 2014;2014: 681679.
Roumeliotis S, Stamou A, Roumeliotis A, Theodoridis M, Leivaditis K, Panagoutsos S, Liakopoulos V. Red blood cell distribution width is associated with deterioration of renal function and cardiovascular morbidity and mortality in patients with diabetic kidney disease. Life (Basel). 2020;10(11):301.
Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: a simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci. 2015;52(2):86–105.
Shota S, Saito H, Kono Y, Murakami Y, Shishido Y, Miyatani K, Matsunaga T, Fukumoto Y, Fujiwara Y. Prognostic significance of pre- and post-operative red-cell distribution width in patients with gastric cancer. J Gastrointest Surg. 2020;24(5):1010–7.
Vandenbroucke JP, von Elm E, Altman DG, Gotzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Int J Surg. 2014;12(12):1500–24.
von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014;12(12):1495–9.
Wang B, Lu H, Gong Y, Ying B, Cheng B. The association between red blood cell distribution width and mortality in critically ill patients with acute kidney injury. BIOMED RES INT. 2018;2018:9658216.
Wu Y, Hu H, Cai J, Chen R, Zuo X, Cheng H, Yan D. A prediction nomogram for the 3-year risk of incident diabetes among Chinese adults. Sci Rep. 2020;10(1):21716.
Xu WY, Yang XB, Wang WQ, Bai Y, Long JY, Lin JZ, Xiong JP, Zheng YC, He XD, Zhao HT, et al. Prognostic impact of the red cell distribution width in esophageal cancer patients: A systematic review and meta-analysis. World J Gastroenterol. 2018;24(19):2120–9.
Yazici P, Demir U, Bozkurt E, Isil GR, Mihmanli M. The role of red cell distribution width in the prognosis of patients with gastric cancer. Cancer Biomark. 2017;18(1):19–25.
Yilmaz F, Sozel H. Red blood cell distribution width is a predictor of chronic kidney disease progression and all-cause mortality. Bratisl Lek Listy. 2021;122(1):49–55.
Zvetkova EDF. Medical significance of simultaneous application of red blood cell distribution width (RDW) and neopterin as diagnostic/ prognostic biomarkers in clinical practice. Pteridines. 2017;2017(28):133e–40e.

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