Prediction of New-Onset and Recurrent Atrial Fibrillation by Complete Blood Count Tests: A Comprehensive Systematic Review with Meta-Analysis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

DE 1 Alexander Weymann
BCDE 2 Sadeq Ali-Hasan-Al-Saegh
DE 3,4 Anton Sabashnikov
E 3,5 Aron-Frederik Popov
AD 6 Seyed Jalil Mirhosseini
F 7 Tong Liu
F 8 Mohammadreza Lotfaliani
D 9,10 Michel Pompeu Barros de Oliveira Sá
B 11 William L. Baker
B 12 Senol Yavuz
B 3,4 Mohamed Zeriouh
B 13 Jae-Sik Jang
C 14 Hamidreza Dehghan
A 7 Lei Meng
D 15 Luca Testa
EF 16 Fabrizio D'Ascenzo
AC 17 Umberto Benedetto
CD 18 Gary Tse
CF 19 Luis Nombela-Franco
EG 1,20 Pascal M. Dohmen
AF 21 Abhishek J. Deshmukh
E 22 Cecilia Linde
AC 23,24 Giuseppe Biondi-Zoccai
DE 25 Gregg W. Stone
ADE 26 Hugh Calkins
Integrated Meta-Analysis of Cardiac Surgery and Cardiology-Group [IMCSC-Group]

1 Department of Cardiac Surgery, University Hospital Oldenburg, European Medical School Oldenburg-Groningen, Carl von Ossietzky University Oldenburg, Oldenburg, Germany
2 Afshar Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
3 Department of Cardiothoracic Transplantation and Mechanical Circulatory Support, Royal Brompton and Harefield NHS Foundation Trust, London, U.K.
4 Department of Thoracic and Cardiovascular Surgery, University Hospital Cologne, Cologne, Germany
5 Department of Thoracic and Cardiovascular Surgery, University Hospital Goethe University Frankfurt, Frankfurt, Germany
6 Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Isfahan, Iran
7 Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular Disease, Department of Cardiology, Second Hospital of Tianjin Medical University, Tianjin, P.R. China
8 Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Isfahan, Iran
9 Division of Cardiovascular Surgery, Pronto Socorro Cardiológico de Pernambuco – PROCAPE, Recife, Brazil
10 University of Pernambuco – UPE, Recife, Brazil
11 Department of Pharmacy, University of Connecticut/Hartford Hospital Evidence-Based Practice Center, Hartford, CT, U.S.A.
12 Department of Cardiovascular Surgery, Bursa Yuksek Ihtisas Training and Research Hospital, Yıldırım/Bursa, Turkey
13 Department of Cardiology, Busan Paik Hospital, Inje University College of Medicine, Jin-gu, Democratic People's Republic of Korea
14 Department of Health Technology Assessment, Shahid Sadoughi University of Medical Sciences and Health Services, Isfahan, Iran
15 Department of Cardiology, IRCCS Pol. S. Donato, San Donato Milanese, Italy
16 Division of Cardiology, Department of Medical Sciences, Città della Salute e della Scienza Hospital, University of Turin, Turin, Italy
17 Bristol Heart Institute, University of Bristol, School of Clinical Sciences, Bristol, U.K.
18 Department of Medicine and Therapeutics, Li Ka Shing Institute of Health Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong
19 Instituto Cardiovascular, Hospital Universitario Clínico San Carlos, Madrid, Spain
20 Department of Cardiothoracic Surgery, Faculty of Health Science, University of the Free State, Bloemfontein, South Africa
21 Mayo Clinic Heart Rhythm Section, Cardiovascular Diseases, Mayo Clinic, Rochester, MN, U.S.A.
22 Department of Cardiology, Karolinska University Hospital, Karolinska Institut, Solna, Sweden
23 Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy
24 Department of AngioCardioNeurology, IRCCS Neuromed, Pozzilli, Italy
25 New York Presbyterian Hospital, Columbia University Medical Center, New York, NY, U.S.A.
26 Department of Cardiology, Johns Hopkins Medical Institutions, Baltimore, MD, U.S.A.

Corresponding Authors: Alexander Weymann, e-mail: weymann.alexander@gmail.com, Seyed Jalil Mirhosseini, e-mail: dr.mirhosseini.imcsc@gmail.com
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Background: Atrial fibrillation (AF) is one of the most critical and frequent arrhythmias precipitating morbidities and mortalities. The complete blood count (CBC) test is an important blood test in clinical practice and is routinely used in the workup of cardiovascular diseases. This systematic review with meta-analysis aimed to determine the strength of evidence for evaluating the association of hematological parameters in the CBC test with new-onset and recurrent AF.

Material/Methods: We conducted a meta-analysis of observational studies evaluating hematologic parameters in patients with new-onset AF and recurrent AF. A comprehensive subgroup analysis was performed to explore potential sources of heterogeneity.

Results: The literature search of all major databases retrieved 2150 studies. After screening, 70 studies were analyzed in the meta-analysis on new-onset AF and 23 studies on recurrent AF. Pooled analysis on new-onset AF showed platelet count (PC) (weighted mean difference (WMD)=WMD of -26.39×10^9/L and $p<0.001$), mean platelet volume (MPV) (WMD=0.42 FL and $p<0.001$), white blood cell (WBC) (WMD=-0.005×10^9/L and $p=0.83$), neutrophil to lymphocyte ratio (NLR) (WMD=0.89 and $p<0.001$), and red blood cell distribution width (RDW) (WMD=0.61% and $p<0.001$) as associated factors. Pooled analysis on recurrent AF revealed PC (WMD=-2.71×10^9/L and $p=0.59$), WBC (WMD=0.20×10^9/L (95% CI: 0.08 to 0.32; $p=0.002$), NLR (WMD=0.37 and $p<0.001$), and RDW (WMD=0.28% and $p<0.001$).

Conclusions: Hematological parameters have significant ability to predict occurrence and recurrence of AF. Therefore, emphasizing the potential predictive role of hematological parameters for new-onset and recurrent AF, we recommend adding the CBC test to the diagnostic modalities of AF in clinical practice.

MeSH Keywords: **Atrial Fibrillation • Blood Platelets • Diagnosis • Meta-Analysis**

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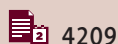
Background

Atrial fibrillation (AF) is one of the most critical and frequent arrhythmias precipitating morbidities and mortalities such as hemodynamic instability, thromboembolism, and stroke, increasing hospital re-admissions and, consequently, health care costs. In general, AF negatively affects patient quality of life [1]. AF alone is associated with 1.5% to 1.9% increase in risk of mortality in a wide spectrum of ages in both genders [2]. Moreover, the situation is likely to worsen since the number of people with AF is expected to double by 2050 [2,3].

The pathophysiological mechanism in AF is highly complex and multifactorial [3]. Prothrombotic state, inflammation, and oxidative stress may play important roles in the occurrence of supraventricular arrhythmia [4]. Introduction of practical and available diagnostic methods and their wider use allows for better identification of patients with new-onset or recurrent AF [3,4]. Traditionally, the major focus in diagnosis and management of AF has been patient medical history, examination, and detection of AF and paroxysmal AF (PAF) using cardiac monitoring.

Complete blood count (CBC) is an important blood test routinely used in clinical practice for workup of cardiovascular diseases

[5]. The relationship between blood parameters in CBC tests and clinical outcomes in patients with ST-segment elevation myocardial infarction has been well documented [5]. However, the diagnostic performance of blood parameters for AF, alone and in combination with other diseases, is still unknown.

Various studies have reported the association of hematological parameters with new-onset and recurrent AF, but the data have been largely inconclusive. This systematic review with meta-analysis sought to determine the strength of evidence in terms of the potential association between a large number of hematologic parameters that can be easily obtained using the CBC test and new-onset and recurrent AF.

Material and Methods

Literature search

A comprehensive literature search was conducted in electronic scientific databases (Medline/PubMed, Embase, Web of Science, and Google Scholar) from their inception through November 30, 2016 to identify relevant studies on the association between blood parameters in CBC tests and new-onset and recurrent AF. Predefined search terms were as follows:

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"white blood cell count", "WBC", "leucocyte", "neutrophil to lymphocyte ratio", "NLR", "platelet count", "mean platelet volume", "MPV", "platelet distribution width" "PDW", "red blood cell count", "RBC count", "red blood cell distribution width", "RDW", and "atrial fibrillation" or "supraventricular arrhythmia". No restrictions were applied regarding sample size of studies, language, and time of publication. To assess additional studies not indexed in common databases, all retrieved references of the enrolled studies, recent published review articles, and meta-analyses were also checked.

Study selection

Studies were included in the analysis when they met the following criteria: 1) human subjects; 2) cohort or case-control studies; 3) comparative studies between AF and non-AF-cohorts in terms of blood parameters; 4) studies comparing patients with recurrent AF (re-occurrence of AF in patients with history of treatment with anti-arrhythmic or electrophysiological interventions for AF) with those with non-recurrent AF focusing on blood parameters. Manuscripts that did not undergo peer-review, abstracts from congress presentations only, and gray literature were not included.

Primary and secondary blood parameters

Platelet count, MPV, PDW, WBC count, NLR, RBC count, and RDW were considered primary blood parameters. MCV, MCHC, HCT, and Hb were defined as secondary parameters.

Data extraction and outcome measures

Six investigators (S.A-H-S, A.S, S.Y, T.L, M-P. S, and J-S. J) independently extracted the data. Discrepancies were resolved by a consensus standardized abstraction checklist used for recording data in each included study. Disagreements were discussed and resolved by senior authors (A.W, A.F-P, G.B.Z, G.D.S and H.C). The following items were extracted from the included studies: author name; publication year; country; study design; sample size; mean age; gender; coexistent cardiovascular diseases, and risk factors, such as diabetes mellitus, hypertension, and history of myocardial infarction; percentage of used anticoagulants; AF type; and details of blood parameters. In order to examine heterogeneity among trials, subgroup analyses of disparities in patients' characteristics were carried out for: (1) the era of publication (pre-2000 vs. post-2000); (2) geographical area (Asia, Europe, Africa, North-America, South-America, and Oceania); (3) study design (case-control vs. cohort); (4) sample size of studies (≤300 vs. >300); (5) mean age (≤60 vs. >60 years); (6) percentage of male patients (≤70% vs. >70%); (7) presence of diabetes (≤30% vs. >30%); (8) presence of hypertension (≤70% vs. >70%); (9) cigarette smoking (≤30% vs. >30%); (10) presence of myocardial infarction (≤20% vs. >20%);

(11) use of cardiovascular drugs, such as diuretics, angiotensin converting enzyme inhibitors, statins and beta-blockers (for each: ≤70% vs. >70%); (12) AF-classification (chronic vs. non-chronic); (13) type of AF (paroxysmal, persistent, permanent); and (12) anticoagulation (code-1: not receiving anticoagulants in both groups; code-2: all participants receiving anticoagulants in both groups; code-3: range of percentages between both groups >50%; code-4: range of percentages between both groups <50%; code-5: no information available about anticoagulation in both groups; and code-6: anticoagulation information not available for 1 group only).

Homogenization of extracted data

Continuous data are expressed as mean ± standard deviation (SD). For studies reporting interquartile ranges, the mean was estimated according to the formula [minimum+maximum+2(median)]/4 and SD was calculated based on the formula (maximum−minimum)/4 for groups with sample sizes of n ≤70 and (maximum−minimum)/6 for sample sizes of >70 [6].

Quality assessment and statistical analysis

The Newcastle-Ottawa scale was independently used by 3 investigators (S.A-H-S, M.G, and L.M) to assess the quality of studies [7]. Total scores ranged from 0 (worst quality) to 9 (best quality) for case-control or cohort studies. Data were analyzed by STATA 11.0 using METAN and METABIAS modules. For non-categorical data, pooled effect size measured was the weighted mean difference (WMD) with 95% CI. P value of <0.1 for Q test or I^2 >50% showed significant heterogeneity among the studies. Heterogeneity among trials was examined by applying a random-effects model when indicated. Publication bias was assessed using the Begg tests. P value of <0.05 was considered statistically significant.

Results

Literature search strategy and included studies

Overall, 2150 studies were retrieved from the literature search and screened databases. We excluded 1179 studies (63.55%) after detailed evaluation during the first review due to unnecessary information (n=750), inadequate report of endpoints of interest (n=370), or report of non-matched data based on mean ±SD or median [minimum-maximum] (n=59). In total, 971 potentially relevant full-text articles were screened, with 70 studies being analyzed in the meta-analysis on new-onset AF and 23 studies on recurrent AF (Supplementary Table 1) [8–77].

Association of hematologic parameters with new-onset AF

Platelet count

A total of 6468 cases were selected from 48 studies, of which 3098 were allocated to the AF group and 3370 to the SR group. Mean platelet count was 236.9×10^9/L in the AF group and 239.9×10^9/L in the SR group (details in Tables 1 and 2). Using a random-effects model, pooled analysis revealed that the mean platelet count was considerably lower in patients with AF than in patients with SR, with a WMD of -26.39×10^9/L (95% CI: -27.80 to -24.99; p<0.001, Figure 1). Significant heterogeneity was observed among the studies (I^2=92.9%; heterogeneity p<0.001).

MPV

A total of 4014 cases were included from 23 studies, of which 1838 were allocated to the AF group and 2176 to the SR group. The mean level of MPV was 9.18 FL in the AF group and 8.48 FL in the SR group (details in Tables 1 and 2). Pooled analysis revealed that MPV level was significantly higher in patients with AF compared to those with SR, with a WMD of 0.42 FL (95% CI: 0.39 to 0.46; p<0.001, Figure 2) using a random-effects model. There was significant heterogeneity among the studies (I^2=95.7%; heterogeneity p<0.001).

PDW

A total of 553 cases were included from 3 studies, of which 275 and 278 were allocated to the AF group and the SR group, respectively. The mean level of PDW was 15.73% in the AF group and 15.60% in the SR group (details in Tables 1 and 2). Using a random-effects model, pooled analysis indicated that PDW was statistically lower in the AF group than in the SR group, with a WMD of -0.24% (95% CI: -0.39 to -0.09; p=0.001). There was significant heterogeneity among the studies (I^2=88.5%; heterogeneity p<0.001)

WBC

A total of 7042 patients were included from 42 studies, of which 3105 were allocated to the AF group and 3937 to the SR group. The mean WBC count was 7.49×10^9/L in patients with AF and 7.16×10^9/L in those with SR (details in Tables 1 and 2). Pooled analysis indicated that the mean count of WBC was similar in AF patients and those with SR, with a WMD of -0.005×10^9/L (95% CI: -0.052 to 0.042; p=0.83, Figure 3), with considerable heterogeneity among the studies (I^2=87.2%; heterogeneity p<0.001).

NLR

A total of 1899 cases were selected from 10 studies, of which 677 were allocated to the AF group and 1222 to the SR group. The mean NLR was 3.56 in the AF group and 2.61 in the SR group (details in Tables 1 and 2). Pooled analysis showed that the NLR was remarkably higher in patients with AF compared to controls, with a WMD of 0.89 (95% CI: 0.79 to 0.99; p<0.001, Figure 4) using a random-effects model. There was significant heterogeneity among the studies (I^2=93.6%; heterogeneity p<0.001).

RBC count

A total of 572 cases were included from 2 studies, of which 251 were allocated to the AF group and 321 to the SR group. The mean RBC count was 4.52×10^{12}/L in the AF group and 4.39×10^{12}/L in the SR group (details in Tables 1 and 2). Using a random-effects model, pooled analysis showed that the mean count of RBC was statistically higher in the AF group compared to the SR group, with a WMD of 0.28×10^{12}/L (95% CI: 0.23 to 0.33; p<0.001). Significant heterogeneity was observed among the studies (I^2=96.8%; heterogeneity p<0.001).

RDW

A total of 1631 cases were included from 8 studies, of which 577 were allocated to the AF group and 1054 to the SR group. The mean of RDW was 14.01% in the AF group and 13.28% in the SR group (details in Tables 1 and 2). Using a random-effects model, pooled analysis revealed that RDW was significantly higher in the AF group than in the SR group, with a WMD of 0.61% (95% CI: 0.56 to 0.66; p<0.001, Figure 5). There was significant heterogeneity among the studies (I^2=94.7%; heterogeneity p<0.001)

Secondary hematological parameters

MCHC was reported in 1 study, which was not included in the meta-analysis. According to pooled assessment analysis, the level of MCV (number of studies=4, WMD of -0.14 FL, 95% CI: -0.51 to 0.23; p=0.46 and I^2=34%; heterogeneity p=0.2) and Hb (number of studies=27, WMD of 0.04 g/dL, 95% CI: -0.02 to 0.10; p=0.23 and I^2=91.1%; heterogeneity p<0.001) were similar in both groups. Pooled analysis showed that HCT (number of studies=11, WMD of 1.79%, 95% CI: 1.43 to 2.15; p<0.001 and I^2=80.6%%; heterogeneity p<0.001) was significantly higher in the AF group compared to the SR group.

Table 1. Characteristics of included studies for meta-analysis of association of hematologic parameters with AF.

First Author	Year	Country	Design	N-AF	N-SR	Age-AF	Age-SR	Male-AF	Male-SR	AC-AF	AC-SR	Type of AF	NOS
Occurrence of AF													
Balci (Male subjects) [8]	2016	Turkey	Case-control	18	17	ND	ND	100	100	ND	ND	ND	8
Balci (Female subjects) [8]	2016	Turkey	Case-control	65	88	ND	ND	0	0	ND	ND	ND	8
Gurses [9]	2016	Turkey	Case-control	86	86	56.6	56.4	51.2	53.5	ND	ND	Combined types	9
Karatas [10]	2016	Turkey	Case-control	40	581	65.7	56.4	70	75	100	100	ND	8
Korantzopoulos [11]	2016	Greece	Case-control	32	69	78	75	47	46	60	0	Combined types	9
Akdag [12]	2015	Turkey	Case-control	96	52	63.6	64.5	64	56	54.16	ND	Combined types	9
Akyuz [13]	2015	Turkey	Case-control	40	50	63	61.5	72.5	72	20	14	Combined types	7
Chavaria [14]	2015	USA	Cohort	40	250	70.6	60.7	65	84	ND	ND	ND	6
Drabik (Persistent AF) [15]	2015	Poland	Case-control	47	50	60.8	59.4	65.95	64	38.3	26	Persistent	9
Drabik (Paroxysmal AF) [15]	2015	Poland	Case-control	41	50	60.6	59.4	46.3	64	51.2	26	Paroxysmal	9
Acet (Paroxysmal AF) [16]	2014	Turkey	Case-control	71	63	63	61.1	42	46	ND	ND	Paroxysmal	9
Acet (Persistent and permanent AF) [16]	2014	Turkey	Case-control	63	63	64.6	61.1	41	46	ND	ND	Combined types	9
Arik (effective INR) [17]	2014	Turkey	Case-control	125	123	70.4	68.9	41.6	39.8	ND	ND	Permanent	8
Arik (ineffective INR) [17]	2014	Turkey	Case-control	125	123	70	68.9	36	39.8	ND	ND	Permanent	8
Distelmaier [18]	2014	USA	Case-control	66	132	73.5	73.5	61	61	ND	ND	ND	7
Erdogan (with normal ventricular rate) [19]	2014	Turkey	Case-control	34	33	70.5	68.6	47.05	51.51	66.6	0	Permanent	10
Erdogan (with high ventricular rate) [19]	2014	Turkey	Case-control	30	33	69	68.6	46.6	51.51	83.3	0	Permanent	10
Zheng [20]	2014	China	Case-control	117	100	64.37	59.1	57.26	60	ND	ND	ND	8
Xu (without thrombotic events) [21]	2014	China	Cohort	57	58	65.19	67	50.9	50	50.9	15.5	ND	7
Xu (with thrombotic events) [21]	2014	China	Cohort	57	58	68.95	67	52.6	50	49.1	15.5	ND	7
Gungor [22]	2014	Turkey	Case-control	117	60	48.3	46.1	60.6	55	75.2	8.3	Combined types	9
Liu [23]	2014	China	Case-control	133	101	ND	ND	ND	ND	ND	ND	Paroxysmal	8

Table 1 continued. Characteristics of included studies for meta-analysis of association of hematologic parameters with AF.

First Author	Year	Country	Design	N-AF	N-SR	Age-AF	Age-SR	Male-AF	Male-SR	AC-AF	AC-SR	Type of AF	NOS
Sarikaya [24]	2014	Turkey	Case-control	63	63	71.09	70.97	47.8	52.2	ND	ND	ND	8
Sonmez [25]	2014	Turkey	Case-control	52	33	70	70	34.61	39.39	59.61	36.36	Persistent	8
Ulu [26]	2014	Turkey	Case-control	25	32	ND	ND	ND	ND	ND	ND	ND	7
Berge [27]	2013	Norway	Cohort	63	126	75	75	71.42	70.63	8	33	Combined types	9
Ertas (without stroke) [28]	2013	Turkey	Case-control	87	24	69	38	44	58	58	0	ND	6
Ertas (with stroke) [28]	2013	Turkey	Case-control	39	24	71	38	36	58	51	0	ND	6
Gungor [29]	2013	Turkey	Case-control	70	70	42.2	42.9	68.5	64.3	ND	ND	Combined types	7
Turgut [30]	2013	Turkey	Case-control	81	81	64	62	51	53	28	20	ND	7
Jaremo (healthy control) [31]	2013	Sweden	Cohort	58	24	69	66	79.3	54.16	12.06	0	ND	8
Jaremo (disease control) [31]	2013	Sweden	Cohort	58	72	69	74	79.3	56.9	12.06	41.66	ND	8
Sahin [32]	2013	Turkey	Case-control	72	72	65.01	64.72	48.2	51.3	ND	ND	Persistent	7
Tekin [33]	2013	Turkey	Case-control	107	112	74	73	31	40	ND	ND	ND	7
Turfan (without stroke) [34]	2013	Turkey	Cohort	77	58	63	56	57.4	51.7	44.3	0	ND	7
Turfan (with stroke) [34]	2013	Turkey	Cohort	63	58	69	56	52.4	51.7	41.3	0	ND	7
Feng [35]	2012	China	Case-control	185	189	65.9	65.7	62.7	60.8	76.8	83.1	Combined types	8
Liu (Paroxysmal AF) [36]	2012	China	Cohort	50	51	64.3	64.4	64	61	100	0	Paroxysmal	8
Liu (Persistent AF) [36]	2012	China	Cohort	56	51	67.2	64.4	61	61	100	0	Persistent	8
Yoshizaki [37]	2012	Japan	Cohort	24	152	74	66	75	77	ND	ND	ND	8
Hayashi (Paroxysmal AF) [38]	2011	Japan	Case-control	14	13	53.1	62.8	93	92	100	100	Paroxysmal	7
Hayashi (Chronic AF) [38]	2011	Japan	Case-control	14	13	60.1	62.8	93	92	100	100	ND	7
Fu [39]	2011	China	Case-control	90	79	54.1	54.8	70	57	22	0	Combined types	8
Liu [40]	2011	China	Case-control	50	401	61.8	54.9	54	48.87	ND	ND	Combined types	8
Letsas (Paroxysmal AF) [41]	2010	Greece	Case-control	45	48	67.4	61.3	62	56	ND	ND	Paroxysmal	9
Letsas (Permanent AF) [41]	2010	Greece	Case-control	41	48	71.9	61.3	63	56	ND	ND	Permanent	9

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Table 1 continued. Characteristics of included studies for meta-analysis of association of hematologic parameters with AF.

First Author	Year	Country	Design	N-AF	N-SR	Age-AF	Age-SR	Male-AF	Male-SR	AC-AF	AC-SR	Type of AF	NOS
Luan (Persistent AF) [42]	2010	China	Case-control	27	26	62.04	44.46	55.56	46.15	ND	ND	Persistent	8
Luan (Paroxysmal AF) [42]	2010	China	Case-control	29	26	57.52	44.46	58.62	46.15	ND	ND	Paroxysmal	8
Alberti [43]	2009	Italy	Case-control	17	34	68.1	60.8	47.05	47.05	0	0	Persistent	7
Dai [44]	2009	China	Case-control	242	280	56.09	50.04	79.8	69.6	ND	ND	Combined types	8
Ichiki [45]	2009	Japan	Case-control	48	24	54	49	81.25	79.16	ND	ND	Paroxysmal	9
Yao (Persistent AF) [46]	2009	China	Case-control	72	78	55.4	52.8	79.2	74.4	15.3	7.7	Persistent	7
Yao (Paroxysmal AF) [46]	2009	China	Case-control	261	78	53.9	52.8	75.5	74.4	12.3	7.7	Paroxysmal	7
Colkesen [47]	2008	Turkey	Case-control	103	87	63	45	55	21	50	14	Paroxysmal	8
Choudhury (disease control) [48]	2008	UK	case-control	121	71	62.58	64.04	76	72	37.2	47.4	ND	6
Choudhury (healthy control) [48]	2008	UK	case-control	121	56	62.58	62.03	76	68	37.2	0	ND	6
Pirat [49]	2007	Turkey	Case-control	18	21	53	46	55	48	ND	ND	ND	7
Yip [50]	2006	Taiwan	Case-control	62	20	66.2	65.3	66.1	60	58.1	0	ND	9
Kamath (Paroxysmal and persistent AF) [51]	2003	UK	Case-control	31	31	61	66	61.3	41.9	0	0	Combined types	6
Kamath (Permanent AF) [51]	2003	UK	Case-control	93	31	66	66	63.4	41.9	0	0	Permanent	6
Kamath (Paroxysmal AF) [52]	2002	UK	Case-control	29	29	61	65	55.17	41.37	37.9	0	Paroxysmal	7
Kamath (Permanent AF) [52]	2002	UK	Case-control	87	29	65	65	63.21	41.37	37.9	0	Permanent	7
Kamath [53]	2002	UK	Case-control	93	50	70	70	62.36	46	0	0	ND	6
Kamath [54]	2002	UK	Case-control	34	23	73	ND	50	ND	0	0	ND	6
Peverill [55]	2001	Australia	Case-control	79	84	63	47	83.5	85.7	ND	ND	ND	8
Kahn (without stroke) [56]	1997	Canada	Case-control	50	31	ND	65	ND	38.7	0	0	ND	7
Kahn (with stroke) [56]	1997	Canada	Case-control	25	11	ND	65	ND	63.6	0	0	ND	7
Lip [57]	1996	UK	Case-control	51	26	70.4	ND	ND	ND	0	0	ND	6

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Table 1 continued. Characteristics of included studies for meta-analysis of association of hematologic parameters with AF.

First Author	Year	Country	Design	N-AF	N-SR	Age-AF	Age-SR	Male-AF	Male-SR	AC-AF	AC-SR	Type of AF	NOS
Gustafsson (without stroke) [58]	1990	Sweden	Case-control	20	20	77	77	ND	ND	0	0	ND	8
Gustafsson (with stroke) [58]	1990	Sweden	Case-control	20	20	77	77	ND	ND	0	0	ND	8
Recurrence of AF													
Gurses [9]	2016	Turkey	Case-control	12	74	57.5	56.1	66.7	48.7	ND	ND	Combined types	9
Hongliang Li [59]	2016	China	Case-control	35	69	62	63	40	47.8	51.4	52.2	Paroxysmal	7
Yanagisawa (without heart failure) [60]	2016	Japan	Cohort	269	409	61.1	61.1	77	75	ND	ND	Combined types	7
Yanagisawa (with heart failure) [60]	2016	Japan	Cohort	42	37	64.2	63	62	87	ND	ND	Combined types	7
Aksu [61]	2015	Turkey	Cohort	7	42	65.01	54.29	57	48	ND	ND	Paroxysmal	9
Gurses [62]	2015	Turkey	Cohort	70	229	56.3	55.1	58.6	43.7	48.57	34.11	Combined types	9
Karavelioglu [63]	2015	Turkey	Cohort	87	131	65.8	63	35.63	46.56	ND	ND	Paroxysmal	7
Wen [64]	2015	China	Cohort	15	60	63.67	63.57	ND	ND	ND	ND	Combined types	9
Guo Xueyuan [65]	2014	China	Cohort	124	255	49.6	49.73	72.9	74.2	ND	ND	ND	9
Aribas [66]	2013	Turkey	Cohort	46	103	61	59	ND	ND	100	100	Persistent	9
Bing Li [67]	2013	China	Cohort	80	208	56	58	72.5	69.7	ND	ND	Paroxysmal	9
Canpolat [68]	2013	Turkey	Cohort	60	191	57.3	53.1	60	49.7	ND	ND	ND	8
Im [69]	2013	South Korea	Cohort	107	392	56.5	56.3	73.8	73.5	ND	ND	Combined types	9
Xiao-nan HE [70]	2013	China	Cohort	106	224	60	59	62.4	70.2	ND	ND	Paroxysmal	6
Ferro [71]	2012	Italy	Cohort	50	94	70.3	71.6	52	61	100	100	Persistent	8
Smit [72]	2012	Netherland	Cohort	30	70	63	65	73.3	74.3	ND	ND	Persistent	7
Wang (Paroxysmal AF) [73]	2012	China	Cohort	41	62	58	57	32.5	37.1	ND	ND	Paroxysmal	7
Wang (Persistent AF) [73]	2012	China	Cohort	30	25	53	52	73.3	76	ND	ND	Persistent	7
Liu (Paroxysmal AF) [74]	2011	China	Cohort	19	58	55	57	84.2	67	100	100	Paroxysmal	8
Liu (Persistent AF) [74]	2011	China	Cohort	17	27	55.2	50.9	88.2	81.5	100	100	Persistent	8
Vizzardi [75]	2009	Italy	Cohort	46	60	69	69	59	63	ND	ND	Persistent	7
Letsas [76]	2009	Germany	Cohort	28	44	53.3	55.8	86	77	ND	ND	Combined types	7
Korantzopoulos [77]	2005	Greece	Cohort	9	21	67	70	44.4	52.38	ND	ND	Persistent	8

Table 2. Information about markers and these levels in each study

First author	Markers	Levels
Occurrence of AF		
Balci (Male subjects) [8]	MPV	MPV [AF: 9.3±0.4 *vs.* SR: 8.65±0.3]
Balci (Female subjects) [8]	MPV	MPV [AF: 8.9±0.3 *vs.* SR: 9±0.2]
Gurses [9]	WBC	WBC [AF: 7.6±3.3 *vs.* SR: 7.1±0.9]
Karatas [10]	PC, MPV, WBC, NLR, RDW, Hb	PC [AF: 230±69.3 *vs.* SR: 240±77.5] MPV [AF: 9.5±1.7 *vs.* SR: 8.7±1] WBC [AF: 12.8±5.6 *vs.* SR: 11.9±4.4] NLR [AF: 6.3±6.3 *vs.* SR: 5.1±4.7] RDW [AF: 13.9±1.7 *vs.* SR: 13.4±1.4] Hb [AF: 13.8±1.7 *vs.* SR: 13.9±1.6]
Korantzopoulos [11]	WBC, RDW, Hb	WBC [AF: 6.46±0.35 *vs.* SR: 7.21±0.8] RDW [AF: 14.6±0.45 *vs.* SR: 13.77±0.22] Hb [AF: 13.05±0.50 *vs.* SR: 13.35±0.60]
Akdag [12]	PC, MPV, WBC, NLR, Hb	PC [AF: 265.6±73.4 *vs.* SR: 248.2±67.2] MPV [AF: 8.9±1.1 *vs.* SR: 7.8±1] WBC [AF: 7.3±1.9 *vs.* SR: 6.9 ±1.8] NLR [AF: 3.6±1.5 *vs.* SR: 2.9±1.3] Hb [AF: 14.3±1.1 *vs.* SR: 14.5±1]
Akyuz [13]	PC, MPV, Hb	PC [AF: 277±79 *vs.* SR: 264±82] MPV [AF: 9.8±0.6 *vs.* SR: 8.4±0.6] Hb [AF: 12.7±1.3 *vs.* SR: 13.1±1.4]
Chavaria [14]	PC, WBC, NLR, Hb	PC [AF: 242.2±54.1 *vs.* SR: 243.2±66.2] WBC [AF: 12.4±3.9 *vs.* SR: 11±3.59] NLR [AF: 3.55±3.15 *vs.* SR: 4.19±3.55] Hb [AF: 14±1.7 *vs.* SR: 14.3±1.7]
Drabik (Persistent AF) [15]	PC, WBC	PC [AF: 202±20.5 *vs.* SR: 219±16.5] WBC [AF: 7.3±0.6 *vs.* SR: 6.45±0.7]
Drabik (Paroxysmal AF) [15]	PC, WBC	PC [AF: 210.25±15.75 *vs.* SR: 219±16.5] WBC [AF: 6.07±0.42 *vs.* SR: 6.45±0.7]
Acet (Paroxysmal AF) [16]	PC, WBC, NLR, Hb	PC [AF: 248.9±59 *vs.* SR: 259.8±95.9] WBC [AF: 11.5±2.5 *vs.* SR: 9.8±2] NLR [AF: 2.5 ±0.6 *vs.* SR: 1.8±0.4] Hb [AF: 13.8±1.7 *vs.* SR: 13.3±1.6]
Acet (Persistent and permanent AF) [16]	PC, WBC, NLR, Hb	PC [AF: 268.6±98 *vs.* SR: 259.8±95.9] WBC [AF: 10.9±2 *vs.* SR: 9.8±2] NLR [AF: 3.4±0.6 *vs.* SR: 1.8±0.4] Hb [AF: 13.9±1.7 *vs.* SR: 13.3±1.6]
Arik (effective INR) [17]	PC, MPV, PDW, WBC, Hb	PC [AF: 258.25±53.83 *vs.* SR: 255.75±41.5] MPV [AF: 7.56±0.63 *vs.* SR: 7.63±0.68] PDW [AF: 17.05±0.86 *vs.* SR: 17.52±0.71] WBC [AF: 7.47±1.23 *vs.* SR: 7.38±1.11] Hb [AF: 12.95±0.96 *vs.* SR: 13.47±0.75]
Arik (ineffective INR) [17]	PC, MPV, PDW, WBC, Hb	PC [AF: 238.75±41.16 *vs.* SR: 255.75±41.5] MPV [AF: 8.26±0.63 *vs.* SR: 7.63±0.68] PDW [AF: 17.50±1.13 *vs.* SR: 17.52±0.71] WBC [AF: 7.49±1.21 *vs.* SR: 7.38±1.11] Hb [AF: 12.95±0.81 *vs.* SR: 13.47±0.75]

Table 2 continued. Information about markers and these levels in each study

First author	Markers	Levels
Distelmaier [18]	PC, WBC, RBC, RDW, MCV, MCHC, HCT, Hb	PC [AF: 202±14.75 *vs.* SR: 215±14.16] WBC [AF: 9.96±1.42 *vs.* SR: 9.18±0.88] RBC [AF: 4.57±0.22 *vs.* SR: 4.23±0.12] RDW [AF: 13.9±0.3 *vs.* SR: 13.62±0.25] MCV [AF: 90.5±1.67 *vs.* SR: 90.78±0.82] MCHC [AF: 33.87±0.35 *vs.* SR: 33.47±0.28] HCT [AF: 41.07±1.92 *vs.* SR: 38.4±1.13] Hb [AF: 13.95±0.65 *vs.* SR: 12.85±0.35]
Erdogan (with normal ventricular rate) [19]	PC, MPV, WBC, HCT, Hb	PC [AF: 245.6±114.9 *vs.* SR: 238.4±66.6] MPV [AF: 7.82±1.2 *vs.* SR: 7.68±0.70] WBC [AF: 7.52±2.06 *vs.* SR: 7.55±1.89] HCT [AF: 39.7±5.2 *vs.* SR: 40.3±3.4] Hb [AF: 14±1.9 *vs.* SR: 13.9±1.3]
Erdogan (with high ventricular rate) [19]	PC, MPV, WBC, HCT, Hb	PC [AF: 225.5±76.3 *vs.* SR: 238.4±66.6] MPV [AF: 8.05±0.6 *vs.* SR: 7.68±0.70] WBC [AF: 7.47±1.47 *vs.* SR: 7.55±1.89] HCT [AF: 40.7±3.8 *vs.* SR: 40.3±3.4] Hb [AF: 14.3±1.3 *vs.* SR: 13.9±1.3]
Zheng [20]	WBC	WBC [AF: 5.6±1.14 *vs.* SR: 5.46±1.21]
Xu (without thrombotic events) [21]	PC, MPV, Hb	PC [AF: 205±31 *vs.* SR: 209±41] MPV [AF: 10.6±1.9 *vs.* SR: 8.7±0.8] Hb [AF: 14.5±1.4 *vs.* SR: 14.6±1.1]
Xu (with thrombotic events) [21]	PC, MPV, Hb	PC [AF: 206±42 *vs.* SR: 209±41] MPV [AF: 11.7±2 *vs.* SR: 8.7±0.8] Hb [AF: 14.6±1.3 *vs.* SR: 14.6±1.1]
Gungor [22]	PC, MPV, WBC, NLR, RDW, MCV, Hb	PC [AF: 249.4±59.4 *vs.* SR: 253.4±61.1] MPV [AF: 8.99±0.65 *vs.* 9.14±0.98] WBC [AF: 7.21±1.62 *vs.* SR: 6.81±1.17] NLR [AF: 2.04±0.94 *vs.* SR: 1.93±0.64] RDW [AF: 13.45±0.2 *vs.* SR: 12.57±0.27] MCV [AF: 90.2±5.4 *vs.* SR: 89.2±3.6] Hb [AF: 14.5±1.4 *vs.* SR: 14.2±1.2]
Liu [23]	RDW	RDW [AF: 12.71±0.9 *vs.* SR: 12.45±0.62]
Sarikaya [24]	RDW, Hb	RDW [AF: 15.13±1.58 *vs.* 14.05±1.15] Hb [AF: 13.74±1.38 *vs.* SR: 13.88±1.62]
Sonmez [25]	PC, NLR, Hb	PC [AF: 231±60 *vs.* 247±67] NLR [AF: 2.7±1.1 *vs.* SR: 2.1±1] Hb [AF: 13.3±1.6 *vs.* SR: 13.1±1.8]
Ulu [26]	PC, PDW, MPV	PC [AF: 236.44±63.92 *vs.* SR: 233.32±86.24] PDW [AF: 12.64±1.43 *vs.* SR: 11.76±1.41] MPV [AF: 11.47±0.93 *vs.* SR: 10.37±1.07]
Berge [27]	PC, Hb	PC [AF: 230±7.5 *vs.* SR: 261.25±4.16] Hb [AF: 14.6±0.2 *vs.* SR: 14.7±0.06]
Ertas (without stroke) [28]	PC, WBC, NLR, RDW, Hb	PC [AF: 232±55 *vs.* SR: 258±54] WBC [AF: 7.8±1.8 *vs.* SR: 7±1.4] NLR [AF: 3.1±2.1 *vs.* SR: 2.05±0.9] RDW [AF: 14.3±1.8 *vs.* SR: 13.2±0.9] Hb [AF: 13±1.4 *vs.* SR: 14±1.7]

Table 2 continued. Information about markers and these levels in each study

First author	Markers	Levels
Ertas (with stroke) [28]	PC, WBC, NLR, RDW, Hb	PC [AF: 240±82 *vs.* SR: 258±54] WBC [AF: 8.6±2.8 *vs.* SR: 7±1.4] NLR [AF: 5.6±3.4 *vs.* SR: 2.05±0.9] RDW [AF: 14.1±1.7 *vs.* SR: 13.2±0.9] Hb [AF: 13±1.6 *vs.* SR: 14±1.7]
Gungor [29]	WBC, Hb	WBC [AF: 6.5±1.5 *vs.* SR: 6.2±1.1] Hb [AF: 14.7±1.5 *vs.* SR: 14.9±1.3]
Turgut [30]	PC, MPV	PC [AF: 274±82 *vs.* SR: 253±83] MPV [AF: 9±0.2 *vs.* SR: 8.4±0.2]
Jaremo (healthy control) [31]	PC	PC [AF: 241±64 *vs.* 260±78]
Jaremo (disease control) [31]	PC	PC [AF: 241±64 *vs.* 265±84]
Sahin [32]	MPV, WBC, NLR	MPV [AF: 8.31±1.12 *vs.* SR: 7.99±1.39] WBC [AF: 7.86±2.04 *vs.* 7.67±2.03] NLR [AF: 2.87±1.3 *vs.* 2.2±1.56]
Tekin [33]	PC, MPV, WBC, HCT	PC [AF: 242±90 *vs.* 243±67] MPV [AF: 9.49±1.08 *vs.* 9.09±1.13] WBC [AF: 7.48±2.15 *vs.* 6.94±1.68] HCT [AF: 40.22±4.8 *vs.* 41.45±4.79]
Turfan (without stroke) [34]	PC, MPV, Hb	PC [AF: 264±94 *vs.* 213±72] MPV [AF: 9.1±1 *vs.* 8.6±1.3] Hb [AF: 12.8±1.1 *vs.* 12.7±1.2]
Turfan (with stroke) [34]	PC, MPV, Hb	PC [AF: 245±73 *vs.* 213±72] MPV [AF: 9.7±0.9 *vs.* 8.6±1.3] Hb [AF: 13±1.4 *vs.* 12.7±1.2]
Feng [35]	PC, MPV, WBC, RBC, MCV	PC [AF: 213.3±82.5 *vs.* SR: 217.6±81.9] MPV [AF: 9.95±1.32 *vs.* SR: 9.02±1.16] WBC [AF: 6.91±3.24 *vs.* SR: 6.88±3.35] RBC [AF: 4.47±0.68 *vs.* 4.56±0.71] MCV [AF: 93.8±5.2 *vs.* 94.1±5.3]
Liu (Paroxysmal AF) [36]	WBC	WBC [AF: 6.76±1.85 *vs.* SR: 6.34±1.89]
Liu (Persistent AF) [36]	WBC	WBC [AF: 6.37±1.66 *vs.* SR: 6.34±1.89]
Yoshizaki [37]	WBC	WBC [AF: 11.1±5.2 *vs.* SR: 10.6±4]
Hayashi (Paroxysmal AF) [38]	PC, WBC	PC [AF: 260±83 *vs.* SR: 190±77] WBC [AF: 5.8±4.2 *vs.* SR: 5.3±3]
Hayashi (Chronic AF) [38]	PC, WBC	PC [AF: 200±14 *vs.* SR: 190±77] WBC [AF: 5.6±3.8 *vs.* SR: 5.3±3]
Fu [39]	PC	PC [AF: 210±55.5 *vs.* SR: 221.1±51.1]
Liu [40]	WBC	WBC [AF: 6.5±1.9 *vs.* SR: 7.2±2.2]
Letsas (Paroxysmal AF) [41]	WBC	WBC [AF: 7.7±2.19 *vs.* SR: 7.15±1.87]
Letsas (Permanent AF) [41]	WBC	WBC [AF: 6.97±1.9 *vs.* SR: 7.15±1.87]
Luan (Persistent AF) [42]	WBC	WBC [AF: 6.13±1.66 *vs.* SR: 6.13±1.95]
Luan (Paroxysmal AF) [42]	WBC	WBC [AF: 6.9±1.28 *vs.* SR: 6.13±1.95]
Alberti [43]	PC, WBC	PC [AF: 185.6±10 *vs.* SR: 243.3±9.4] WBC [AF: 5.6±0.3 *vs.* SR: 6.3±0.3]

Table 2 continued. Information about markers and these levels in each study

First author	Markers	Levels
Dai [44]	WBC	WBC [AF: 7.32±1.89 *vs.* SR: 6.57±1.91]
Ichiki [45]	WBC	WBC [AF: 4.6±0.3 *vs.* SR: 5.3±0.5]
Yao (Persistent AF) [46]	WBC	WBC [AF: 5.76±0.28 *vs.* SR: 5.69±0.35]
Yao (Paroxysmal AF) [46]	WBC	WBC [AF: 5.69±0.31 *vs.* SR: 5.69±0.35]
Colkesen [47]	PC, MPV, WBC	PC [AF: 242±13 *vs.* SR: 236±53] MPV [AF: 10±2 *vs.* SR: 8.3±1.50] WBC [AF: 7.58±2.35 *vs.* SR: 7.47±2.08]
Choudhury (disease control) [48]	PC, MPV, WBC, HCT, Hb	PC [AF: 259.9±66.3 *vs.* SR: 261.1±63.4] MPV [AF: 7.6±1.4 *vs.* SR: 7.8±1.9] WBC [AF: 7.1±1.8 *vs.* SR: 7.1±2.2] HCT [AF: 42.3±4.3 *vs.* SR: 41.6±3.9] Hb [AF: 14.6±1.6 *vs.* SR: 13.9±1.5]
Choudhury (healthy control) [48]	PC, MPV, WBC, HCT, Hb	PC [AF: 259.9±66.3 *vs.* SR: 266.9±56.1] MPV [AF: 7.6±1.4 *vs.* SR: 7.4±0.97] WBC [AF: 7.1±1.8 *vs.* SR: 6.4±1.8] HCT [AF: 42.3±4.3 *vs.* SR: 40.6±33.7] Hb [AF: 14.6±1.6 *vs.* SR: 14.1±1.2]
Pirat [49]	WBC	WBC [AF: 7.45±1.59 *vs.* SR: 6.7±0.98]
Yip [50]	PC, WBC	PC [AF: 204±57 *vs.* SR: 209±49] WBC [AF: 6.7±1.5 *vs.* SR: 6.6±1.7]
Kamath (Paroxysmal and persistent AF) [51]	PC, HCT	PC [AF: 280±81 *vs.* SR: 253±51] HCT [AF: 45±4 *vs.* SR: 42±3]
Kamath (Permanent AF) [51]	PC, HCT	PC [AF: 264±75 *vs.* SR: 253±51] HCT [AF: 43±5 *vs.* SR: 42±3]
Kamath (Paroxysmal AF) [52]	PC, HCT	PC [AF: 279±73 *vs.* SR: 252±53] HCT [AF: 43±5 *vs.* SR: 42±3]
Kamath (Permanent AF) [52]	PC, HCT	PC [AF: 266±76 *vs.* SR: 252±53] HCT [AF: 43±5 *vs.* SR: 42±3]
Kamath [53]	PC	PC [AF: 253±77 *vs.* SR: 261±62]
Kamath [54]	PC	PC [AF: 253±67 *vs.* SR: 270±49]
Peverill [55]	PC, MPV, MCV, HCT	PC [AF: 218±55 *vs.* SR: 241±59] MPV [AF: 9.7±1.4 *vs.* SR: 9.9±1.4] MCV [AF: 89±6 *vs.* SR: 88±7] HCT [AF: 42±5 *vs.* SR: 39±4]
Kahn (without stroke) [56]	PC, Hb	PC [AF: 230±98 *vs.* SR: 233±49] Hb [AF: 14.9±1.3 *vs.* SR: 13.4±1.5]
Kahn (with stroke) [56]	PC, Hb	PC [AF: 253±82 *vs.* SR: 242±77] Hb [AF: 14.1±1.2 *vs.* SR: 14.3±1.7]
Lip [57]	PC	PC [AF: 242±67 *vs.* SR: 224±63]
Gustafsson (without stroke) [58]	PC	PC [AF: 172.25±8.75 *vs.* SR: 234.75±10.75]
Gustafsson (with stroke) [58]	PC	PC [AF: 179±18.5 *vs.* SR: 234.75±10.75]
Recurrence of AF		
Gurses [9]	WBC	WBC [AF: 7.5±3.9 *vs.* SR: 7.6±3.2]
Hongliang Li [59]	PC, WBC, RDW, Hb	PC [AF: 219.77±44.15 *vs.* SR: 199.32±52.58] WBC [AF: 6.51±1.84 *vs.* SR: 7.41±14.65] RDW [AF: 12.81±0.94 *vs.* SR: 12.37±0.56] Hb [AF: 14.11±1.85 *vs.* SR: 13.94±1.21]

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Table 2 continued. Information about markers and these levels in each study

First author	Markers	Levels
Yanagisawa (without heart failure) [60]	WBC, RDW, MCV, Hb	WBC [AF: 5.5±1.4 *vs.* SR: 5.3±1.6] RDW [AF: 13.3±0.8 *vs.* SR: 13.2±0.8] MCV [AF: 92.3±4.4 *vs.* SR: 92±4.2] Hb [AF: 14±1.5 *vs.* SR: 14±1.5]
Yanagisawa (with heart failure) [60]	WBC, RDW, MCV, Hb	WBC [AF: 5.7±1.5 *vs.* SR: 6.1±1.6] RDW [AF: 14.5±2 *vs.* SR: 13.5±0.9] MCV [AF: 91.3±6.4 *vs.* SR: 92.3±4.6] Hb [AF: 13.3±2.3 *vs.* SR: 14.1±1.8]
Aksu [61]		MPV [AF: 8.81±1.4 *vs.* SR: 8.7±1.88] WBC [AF: 6.97±1.6 *vs.* SR: 7.38±1.7] NLR [AF: 2.5±0.78 *vs.* SR: 1.83±0.63] RDW [AF: 16.1±1.44 *vs.* SR: 14.87±0.48] WBC [AF: 13.3±1.34 *vs.* SR: 13.72±1.17]
Gurses [62]	PC, WBC, RDW, Hb	PC [AF: 221.8±56.3 *vs.* SR: 228.4±68.8] WBC [AF: 7.82±2.43 *vs.* SR: 7.44±1.89] RDW [AF: 14.3±0.93 *vs.* SR: 13.52±0.93] Hb [AF: 14.19±1.85 *vs.* SR: 13.92±1.76]
Karavelioglu [63]	PC, WBC, NLR, HCT, Hb	PC [AF: 234±65.1 *vs.* SR: 258.1±93.4] WBC [AF: 7.6±2.64 *vs.* SR: 7.93±2.42] NLR [AF: 2.8±1.59 *vs.* SR: 2.13±1.04] HCT [AF: 40.1±5.1 *vs.* SR: 41.1±5.2] Hb [AF: 13.6±2.9 *vs.* SR: 13.8±2.9]
Wen [64]	PC, WBC, NLR, Hb	PC [AF: 196±59 *vs.* SR: 198±44] WBC [AF: 6.36±1.56 *vs.* SR: 5.63±1.2] NLR [AF: 2.16±1.23 *vs.* SR: 1.94±0.94] Hb [AF: 12.6±1.8 *vs.* SR: 13.1±1.7]
Guo Xueyuan [65]	WBC, NLR, Hb	WBC [AF: 8.17±1.7 *vs.* SR: 7.84±1.6] NLR [AF: 1.9±1.19 *vs.* SR: 1.81±0.1] Hb [AF: 14.84±1.57 *vs.* SR: 14.52±1.82]
Aribas [66]	WBC, NLR	WBC [AF: 7.4±2 *vs.* SR: 7.6±2] NLR [AF: 2.38±2.09 *vs.* SR: 2.23±1.23]
Bing Li [67]	WBC	WBC [AF: 6.7±2.2 *vs.* SR: 6.1±2]
Canpolat [68]	WBC, NLR, Hb	WBC [AF: 8.94±2.08 *vs.* SR: 7.46±2.34] NLR [AF: 3.53±0.95 *vs.* SR: 2.65±0.23] Hb [AF: 13.5±1.8 *vs.* SR: 13.6±1.9]
Im [69]	NLR	NLR [AF: 1.9±1.2 *vs.* SR: 2±2.14]
Xiao-nan HE [70]	WBC	WBC [AF: 6.2±1.8 *vs.* SR: 6.5±1.9]
Ferro [71]	WBC	WBC [AF: 7.44±1.45 *vs.* SR: 7.47±1.71]
Smit [72]	WBC	WBC [AF: 7.7±1.5 *vs.* SR: 7.6±2]
Wang (Paroxysmal AF) [73]	WBC	WBC [AF: 6.1±1.4 *vs.* SR: 6.1±1.4]
Wang (Persistent AF) [73]	WBC	WBC [AF: 6.2±1.9 *vs.* SR: 6.6±1.5]
Liu (Paroxysmal AF) [74]	WBC	WBC [AF: 6.2±2.9 *vs.* SR: 5.9±1.4]
Liu (Persistent AF) [74]	WBC	WBC [AF: 5.6±1.4 *vs.* SR: 6±2.4]
Vizzardi [75]	WBC	WBC [AF: 6.9±1.4 *vs.* SR: 7±5.4]
Letsas [76]	WBC	WBC [AF: 6.86±1.21 *vs.* SR: 5.79±1.39]
Korantzopoulos [77]	WBC	WBC [AF: 7.29±1.84 *vs.* SR: 6.64±1.39]

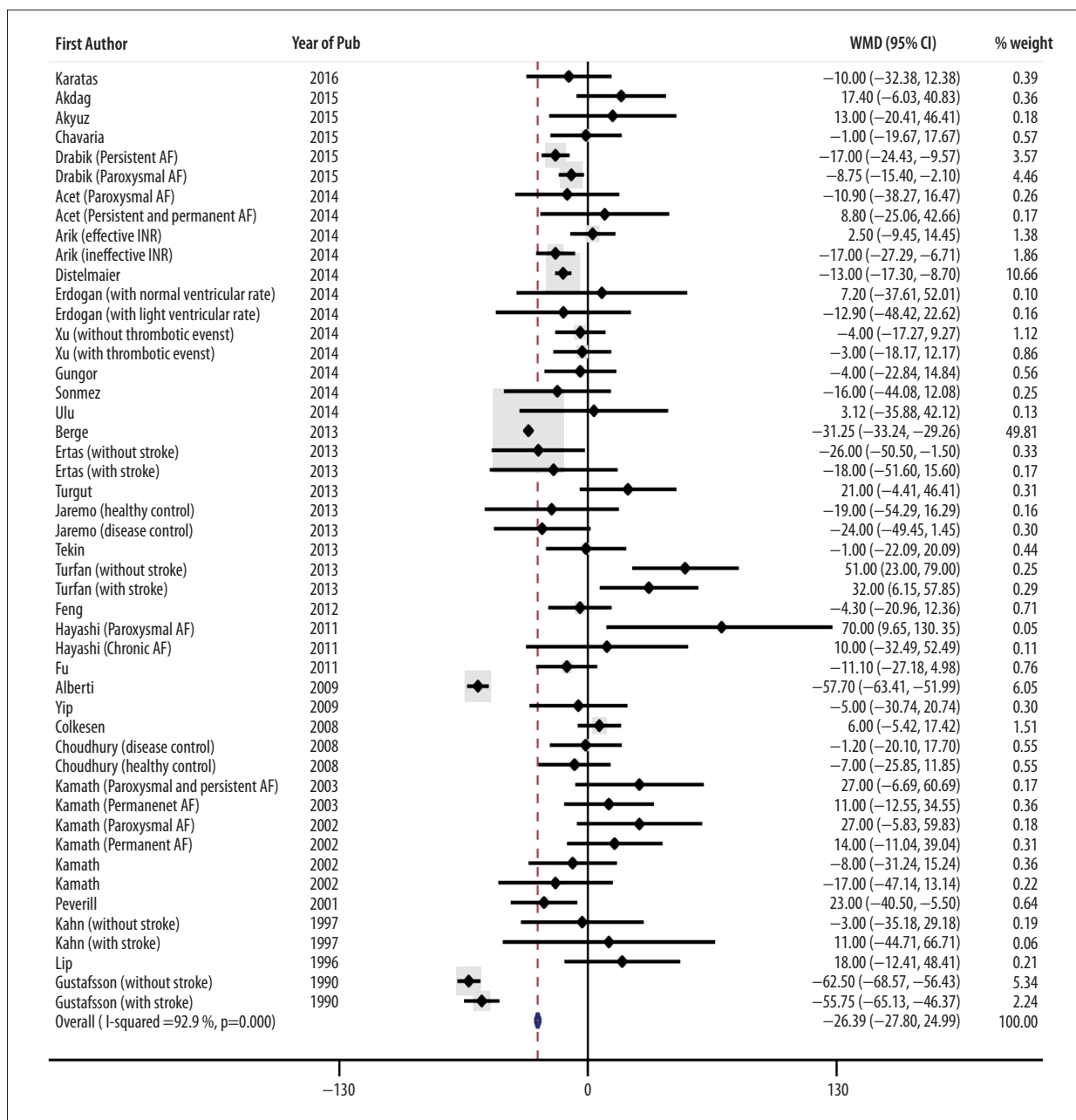| First Author	Year of Pub	WMD (95% CI)	% weight
Karatas	2016	−10.00 (−32.38, 12.38)	0.39
Akdag	2015	17.40 (−6.03, 40.83)	0.36
Akyuz	2015	13.00 (−20.41, 46.41)	0.18
Chavaria	2015	−1.00 (−19.67, 17.67)	0.57
Drabik (Persistent AF)	2015	−17.00 (−24.43, −9.57)	3.57
Drabik (Paroxysmal AF)	2015	−8.75 (−15.40, −2.10)	4.46
Acet (Paroxysmal AF)	2014	−10.90 (−38.27, 16.47)	0.26
Acet (Persistent and permanent AF)	2014	8.80 (−25.06, 42.66)	0.17
Arik (effective INR)	2014	2.50 (−9.45, 14.45)	1.38
Arik (ineffective INR)	2014	−17.00 (−27.29, −6.71)	1.86
Distelmaier	2014	−13.00 (−17.30, −8.70)	10.66
Erdogan (with normal ventricular rate)	2014	7.20 (−37.61, 52.01)	0.10
Erdogan (with light ventricular rate)	2014	−12.90 (−48.42, 22.62)	0.16
Xu (without thrombotic evenst)	2014	−4.00 (−17.27, 9.27)	1.12
Xu (with thrombotic evenst)	2014	−3.00 (−18.17, 12.17)	0.86
Gungor	2014	−4.00 (−22.84, 14.84)	0.56
Sonmez	2014	−16.00 (−44.08, 12.08)	0.25
Ulu	2014	3.12 (−35.88, 42.12)	0.13
Berge	2013	−31.25 (−33.24, −29.26)	49.81
Ertas (without stroke)	2013	−26.00 (−50.50, −1.50)	0.33
Ertas (with stroke)	2013	−18.00 (−51.60, 15.60)	0.17
Turgut	2013	21.00 (−4.41, 46.41)	0.31
Jaremo (healthy control)	2013	−19.00 (−54.29, 16.29)	0.16
Jaremo (disease control)	2013	−24.00 (−49.45, 1.45)	0.30
Tekin	2013	−1.00 (−22.09, 20.09)	0.44
Turfan (without stroke)	2013	51.00 (23.00, 79.00)	0.25
Turfan (with stroke)	2013	32.00 (6.15, 57.85)	0.29
Feng	2012	−4.30 (−20.96, 12.36)	0.71
Hayashi (Paroxysmal AF)	2011	70.00 (9.65, 130. 35)	0.05
Hayashi (Chronic AF)	2011	10.00 (−32.49, 52.49)	0.11
Fu	2011	−11.10 (−27.18, 4.98)	0.76
Alberti	2009	−57.70 (−63.41, −51.99)	6.05
Yip	2009	−5.00 (−30.74, 20.74)	0.30
Colkesen	2008	6.00 (−5.42, 17.42)	1.51
Choudhury (disease control)	2008	−1.20 (−20.10, 17.70)	0.55
Choudhury (healthy control)	2008	−7.00 (−25.85, 11.85)	0.55
Kamath (Paroxysmal and persistent AF)	2003	27.00 (−6.69, 60.69)	0.17
Kamath (Permanenet AF)	2003	11.00 (−12.55, 34.55)	0.36
Kamath (Paroxysmal AF)	2002	27.00 (−5.83, 59.83)	0.18
Kamath (Permanent AF)	2002	14.00 (−11.04, 39.04)	0.31
Kamath	2002	−8.00 (−31.24, 15.24)	0.36
Kamath	2002	−17.00 (−47.14, 13.14)	0.22
Peverill	2001	23.00 (−40.50, −5.50)	0.64
Kahn (without stroke)	1997	−3.00 (−35.18, 29.18)	0.19
Kahn (with stroke)	1997	11.00 (−44.71, 66.71)	0.06
Lip	1996	18.00 (−12.41, 48.41)	0.21
Gustafsson (without stroke)	1990	−62.50 (−68.57, −56.43)	5.34
Gustafsson (with stroke)	1990	−55.75 (−65.13, −46.37)	2.24
Overall (I-squared =92.9 %, p=0.000)		−26.39 (−27.80, 24.99)	100.00

Figure 1. Forest plot of weighted mean difference (WMD) for association between platelet count and occurrence of AF.

Association of hematologic parameters with recurrent AF

Platelet count

A total of 696 cases were selected from 4 studies, of which 207 were allocated to recurrent AF group and 489 to the non-recurrent AF group (details in Tables 1 and 2). Pooled effects analysis showed that the mean platelet count did not differ between groups, with a WMD of -2.71×10^9/L (95% CI: −12.75 to 7.34; p=0.59). Significant heterogeneity was observed among the studies (I^2=69.4%; heterogeneity p=0.02).

WBC

A total of 3716 patients were included from 22 studies, of which 1223 were allocated to the recurrent AF group and 2493 to the non-recurrent AF group (details in Tables 1 and 2). The mean WBC count was 6.89×10^9/L in patients with recurrent AF and 6.79×10^9/L in those with non-recurrent AF. Pooled analysis revealed that the mean count of WBC was statistically higher in the recurrent group compared to the non-recurrent group, with a WMD of 0.20×10^9/L (95% CI: 0.08 to 0.32; p=0.002,

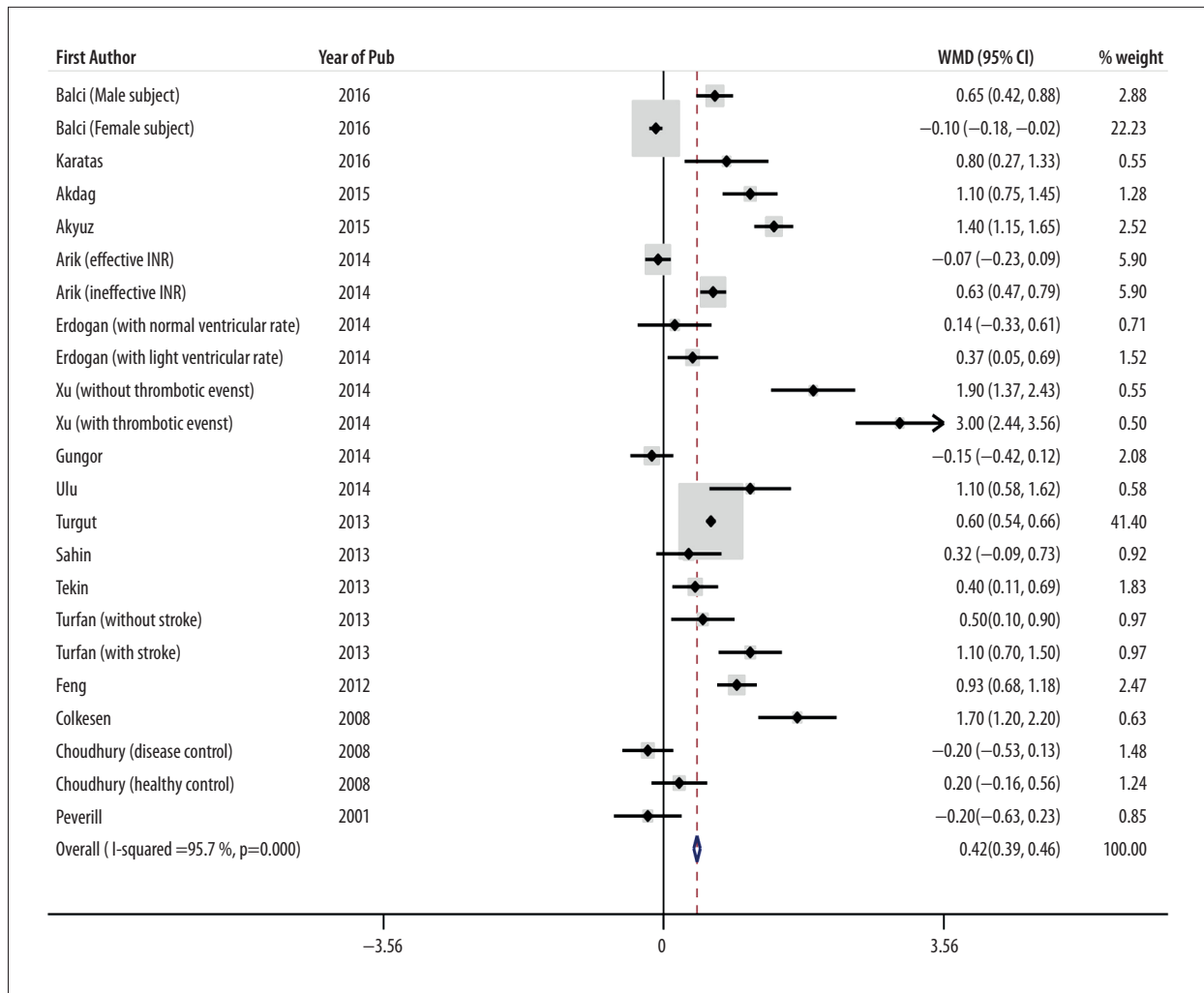| First Author	Year of Pub		WMD (95% CI)	% weight
Balci (Male subject)	2016		0.65 (0.42, 0.88)	2.88
Balci (Female subject)	2016		−0.10 (−0.18, −0.02)	22.23
Karatas	2016		0.80 (0.27, 1.33)	0.55
Akdag	2015		1.10 (0.75, 1.45)	1.28
Akyuz	2015		1.40 (1.15, 1.65)	2.52
Arik (effective INR)	2014		−0.07 (−0.23, 0.09)	5.90
Arik (ineffective INR)	2014		0.63 (0.47, 0.79)	5.90
Erdogan (with normal ventricular rate)	2014		0.14 (−0.33, 0.61)	0.71
Erdogan (with light ventricular rate)	2014		0.37 (0.05, 0.69)	1.52
Xu (without thrombotic evenst)	2014		1.90 (1.37, 2.43)	0.55
Xu (with thrombotic evenst)	2014		3.00 (2.44, 3.56)	0.50
Gungor	2014		−0.15 (−0.42, 0.12)	2.08
Ulu	2014		1.10 (0.58, 1.62)	0.58
Turgut	2013		0.60 (0.54, 0.66)	41.40
Sahin	2013		0.32 (−0.09, 0.73)	0.92
Tekin	2013		0.40 (0.11, 0.69)	1.83
Turfan (without stroke)	2013		0.50 (0.10, 0.90)	0.97
Turfan (with stroke)	2013		1.10 (0.70, 1.50)	0.97
Feng	2012		0.93 (0.68, 1.18)	2.47
Colkesen	2008		1.70 (1.20, 2.20)	0.63
Choudhury (disease control)	2008		−0.20 (−0.53, 0.13)	1.48
Choudhury (healthy control)	2008		0.20 (−0.16, 0.56)	1.24
Peverill	2001		−0.20 (−0.63, 0.23)	0.85
Overall (I-squared =95.7 %, p=0.000)			0.42 (0.39, 0.46)	100.00

−3.56   0   3.56

Figure 2. Forest plot of weighted mean difference (WMD) for association between level of mean platelet volume and occurrence of AF.

Figure 6), with considerable heterogeneity among the studies (I^2=54.7%; heterogeneity p=0.001).

NLR

A total of 1620 cases were selected from 7 studies, of which 446 were allocated to the recurrent AF group and 1174 to the non-recurrent AF group (details in Tables 1 and 2). Pooled assessment analysis indicated that the NLR was significantly higher in patients suffering from recurrent AF compared to the non-recurrent group, with a WMD of 0.37 (95% CI: 0.24 to 0.50; p<0.001, Figure 7). There was significant heterogeneity among the studies (I^2=83.2%; heterogeneity p<0.001).

RDW

A total of 1209 cases were included from 5 studies, of which 423 were allocated to the recurrent AF group and 786 to the non-recurrent AF group (details in Tables 1 and 2). Using a

random-effects model, pooled analysis revealed that RDW was considerably higher in the recurrent AF group than in the non-recurrent group, with a WMD of 0.28% (95% CI: 0.18 to 0.38; p<0.001, Figure 8). There was significant heterogeneity among the studies (I^2=87.5%; heterogeneity p<0.001).

Secondary hematological parameters

MCV and Hb were investigated in at least 2 studies, which were included in the meta-analysis. According to pooled assessment analysis, the levels of MCV (number of studies=2, WMD of 0.21, 95% CI: −0.43 to 0.85; p=0.52 and I^2=1.6%; heterogeneity p=0.31) and Hb (number of studies=9, WMD of 0.04 g/dL, 95% CI: −0.12 to −0.19; p=0.64 and I^2=13.6%; heterogeneity p=0.32) were similar in both groups.

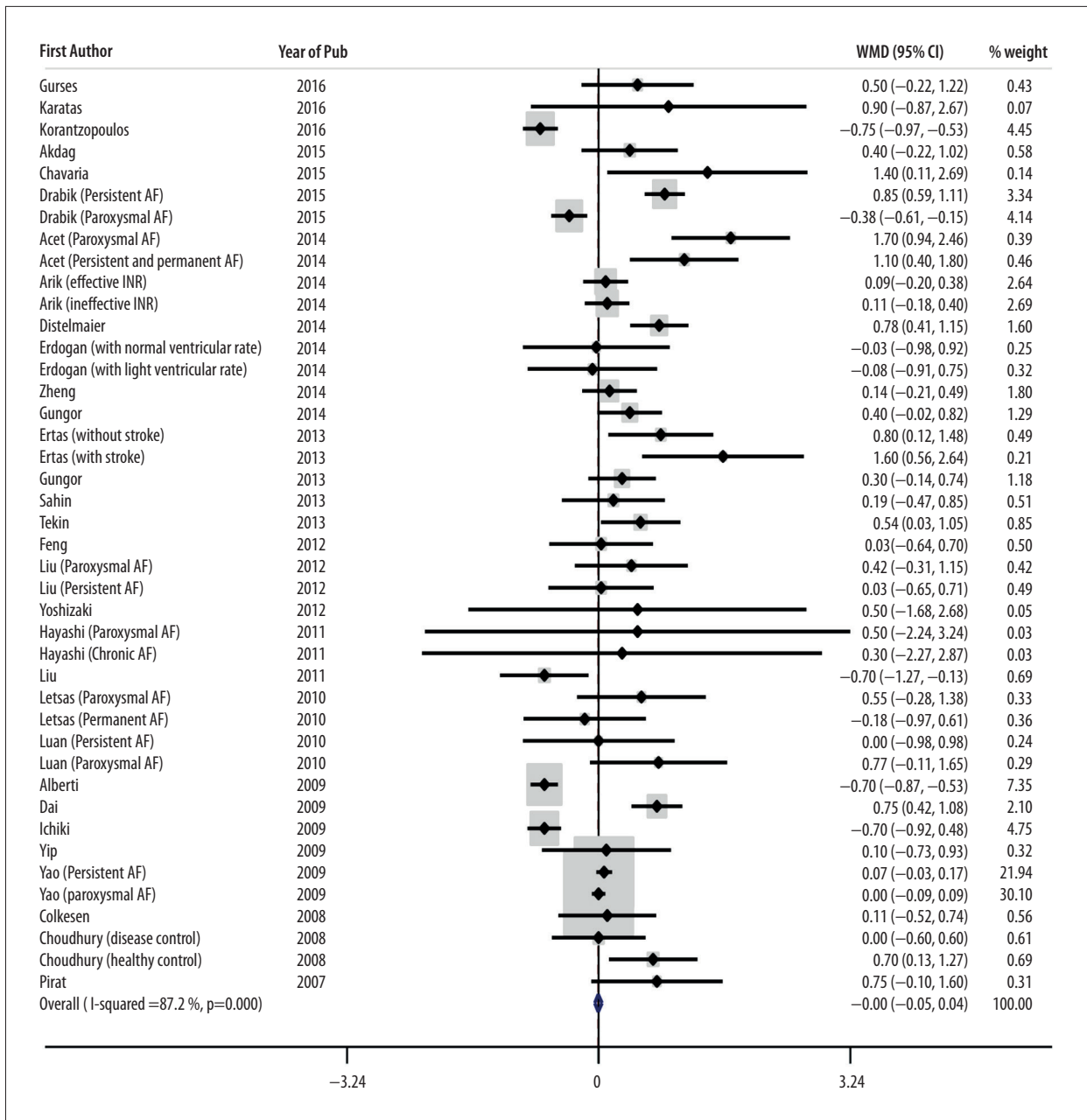| First Author	Year of Pub	WMD (95% CI)	% weight
Gurses	2016	0.50 (−0.22, 1.22)	0.43
Karatas	2016	0.90 (−0.87, 2.67)	0.07
Korantzopoulos	2016	−0.75 (−0.97, −0.53)	4.45
Akdag	2015	0.40 (−0.22, 1.02)	0.58
Chavaria	2015	1.40 (0.11, 2.69)	0.14
Drabik (Persistent AF)	2015	0.85 (0.59, 1.11)	3.34
Drabik (Paroxysmal AF)	2015	−0.38 (−0.61, −0.15)	4.14
Acet (Paroxysmal AF)	2014	1.70 (0.94, 2.46)	0.39
Acet (Persistent and permanent AF)	2014	1.10 (0.40, 1.80)	0.46
Arik (effective INR)	2014	0.09 (−0.20, 0.38)	2.64
Arik (ineffective INR)	2014	0.11 (−0.18, 0.40)	2.69
Distelmaier	2014	0.78 (0.41, 1.15)	1.60
Erdogan (with normal ventricular rate)	2014	−0.03 (−0.98, 0.92)	0.25
Erdogan (with light ventricular rate)	2014	−0.08 (−0.91, 0.75)	0.32
Zheng	2014	0.14 (−0.21, 0.49)	1.80
Gungor	2014	0.40 (−0.02, 0.82)	1.29
Ertas (without stroke)	2013	0.80 (0.12, 1.48)	0.49
Ertas (with stroke)	2013	1.60 (0.56, 2.64)	0.21
Gungor	2013	0.30 (−0.14, 0.74)	1.18
Sahin	2013	0.19 (−0.47, 0.85)	0.51
Tekin	2013	0.54 (0.03, 1.05)	0.85
Feng	2012	0.03 (−0.64, 0.70)	0.50
Liu (Paroxysmal AF)	2012	0.42 (−0.31, 1.15)	0.42
Liu (Persistent AF)	2012	0.03 (−0.65, 0.71)	0.49
Yoshizaki	2012	0.50 (−1.68, 2.68)	0.05
Hayashi (Paroxysmal AF)	2011	0.50 (−2.24, 3.24)	0.03
Hayashi (Chronic AF)	2011	0.30 (−2.27, 2.87)	0.03
Liu	2011	−0.70 (−1.27, −0.13)	0.69
Letsas (Paroxysmal AF)	2010	0.55 (−0.28, 1.38)	0.33
Letsas (Permanent AF)	2010	−0.18 (−0.97, 0.61)	0.36
Luan (Persistent AF)	2010	0.00 (−0.98, 0.98)	0.24
Luan (Paroxysmal AF)	2010	0.77 (−0.11, 1.65)	0.29
Alberti	2009	−0.70 (−0.87, −0.53)	7.35
Dai	2009	0.75 (0.42, 1.08)	2.10
Ichiki	2009	−0.70 (−0.92, 0.48)	4.75
Yip	2009	0.10 (−0.73, 0.93)	0.32
Yao (Persistent AF)	2009	0.07 (−0.03, 0.17)	21.94
Yao (paroxysmal AF)	2009	0.00 (−0.09, 0.09)	30.10
Colkesen	2008	0.11 (−0.52, 0.74)	0.56
Choudhury (disease control)	2008	0.00 (−0.60, 0.60)	0.61
Choudhury (healthy control)	2008	0.70 (0.13, 1.27)	0.69
Pirat	2007	0.75 (−0.10, 1.60)	0.31
Overall (I-squared =87.2 %, p=0.000)		−0.00 (−0.05, 0.04)	100.00

−3.24   0   3.24

Figure 3. Forest plot of weighted mean difference (WMD) for association between white blood cell count and occurrence of AF.

Other parameters

There was an insufficient number of studies for analysis on association between MPV, RBC count, and HCT and recurrent AF.

Publication bias and subgroup analysis

Begg tests suggested that all of the analyses were without publication bias except for association between Hb and recurrent AF. Extra details of characteristics of each study for exploration of heterogeneity factors are presented in Supplementary Table 2. Details of subgroup analysis are reported in detail in Supplementary Table 3.

Discussion

AF is one of the most common cardiac arrhythmias in developing and developed countries, precipitating morbidities and mortalities [78,79]. Various mechanisms are involved in AF, such as inflammation, oxidative stress, and prothrombotic state [79,80]. Therefore, the complications of this arrhythmia
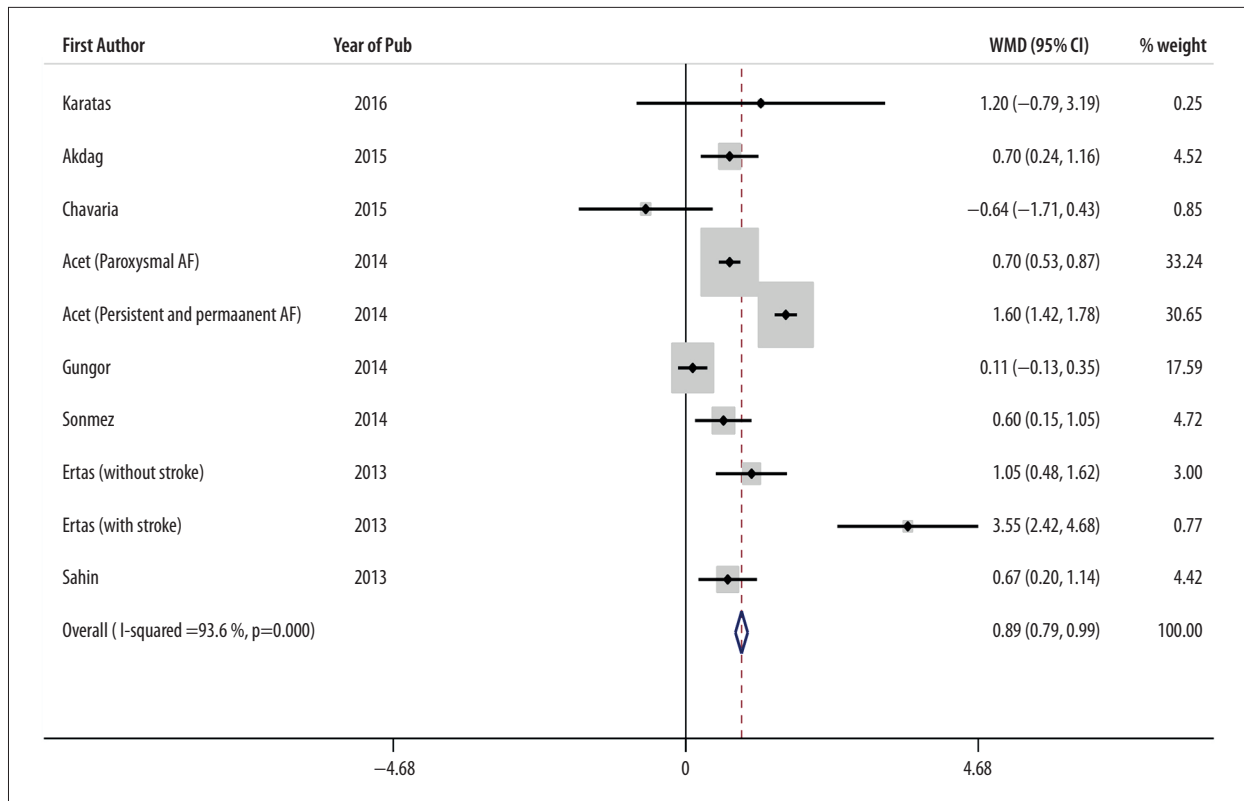
Figure 4. Forest plot of weighted mean difference (WMD) for association between neutrophil to lymphocyte ratio and occurrence of AF.
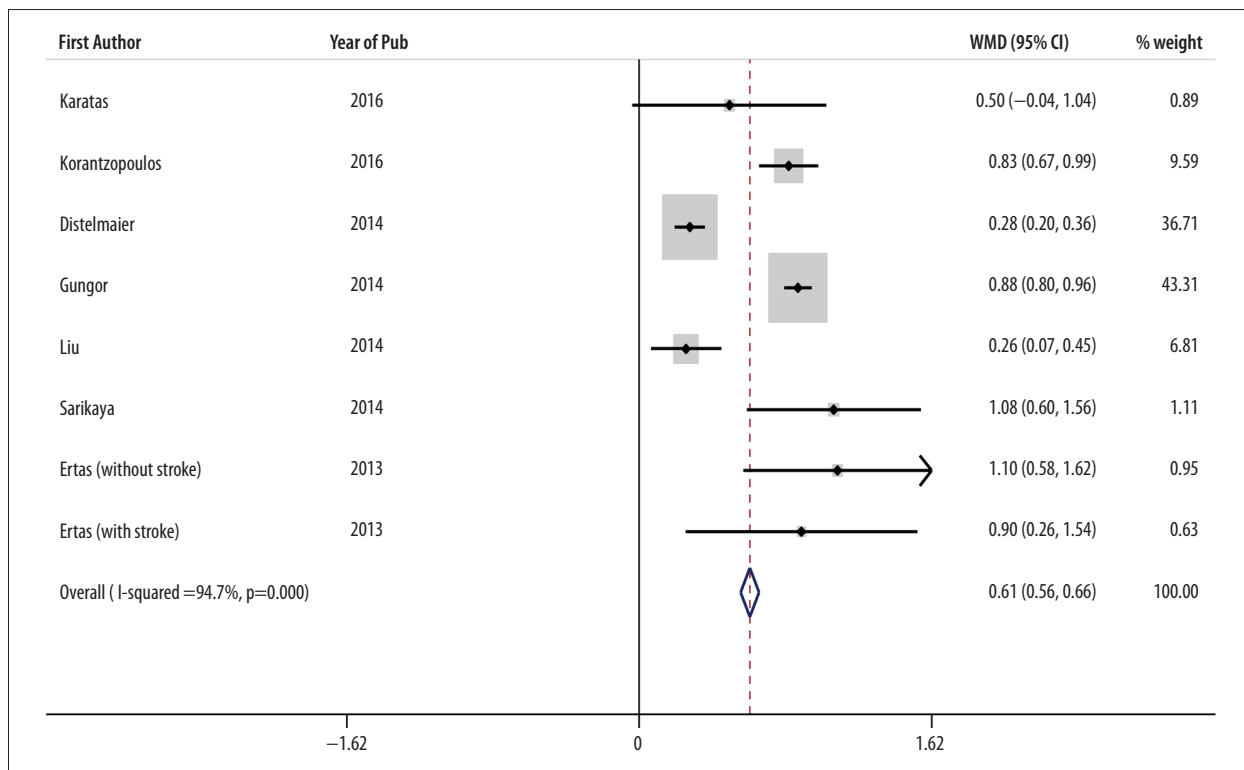

Figure 5. Forest plot of weighted mean difference (WMD) for association between red blood cell distribution width and occurrence of AF.
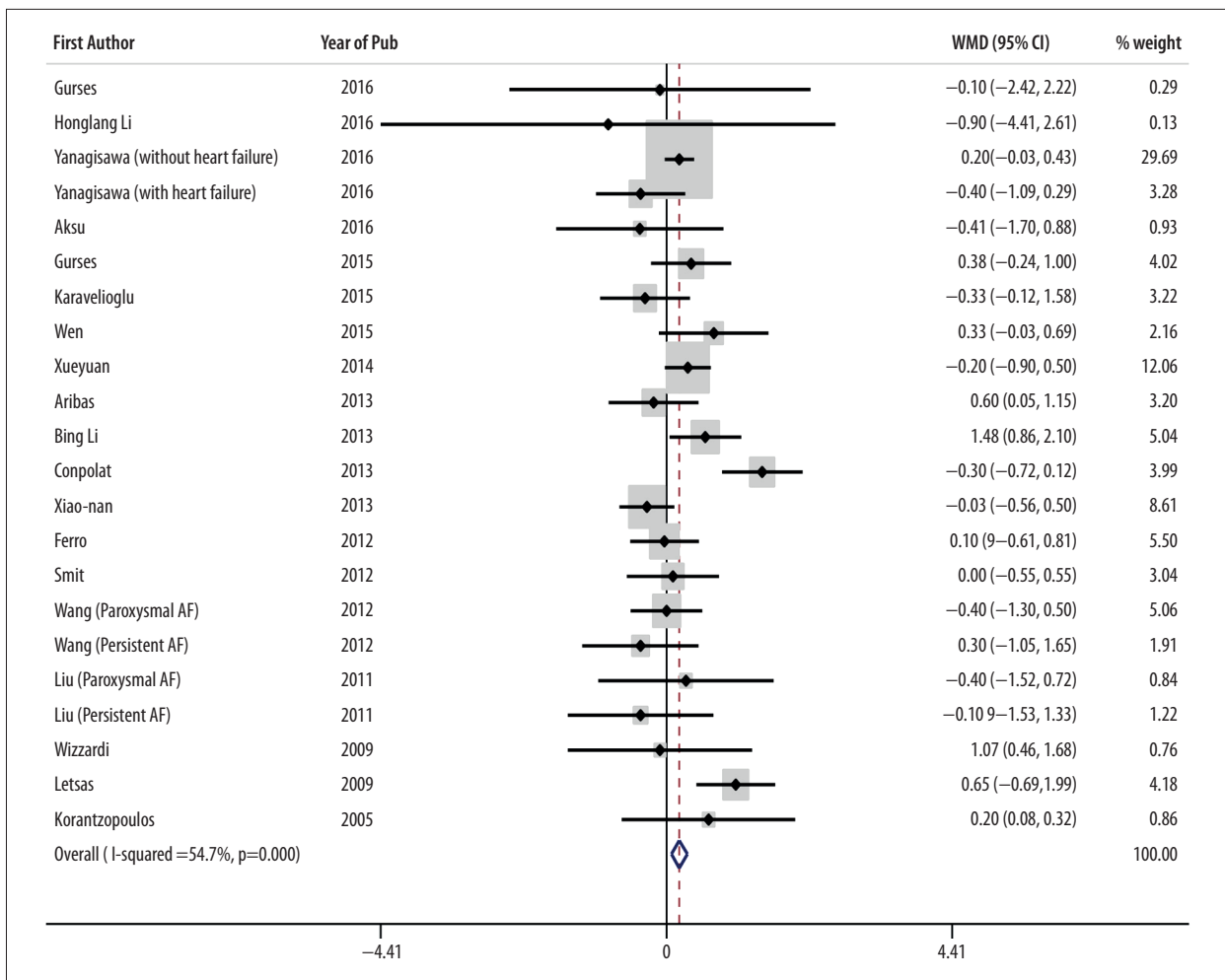
Figure 6. Forest plot of weighted mean difference (WMD) for association between white blood cell count and recurrence of AF.

and their negative effects on quality of life can be decreased by more accurate recognition of mechanisms, timely diagnosis, and appropriate treatment. Although taking patient history, considering the history of cardiac arrhythmia, clinical examinations, ECG, and Holter monitoring can assist in diagnosis and control of AF, some routine diagnostic actions which are performed daily in clinical practice might be of higher value than previously thought [81]. CBC is a routine lab test for most patients, particularly those with cardiovascular diseases hospitalized in cardiology and cardiac surgery wards, as well as CCUs or ICUs [81]. Hematological parameters in CBC tests can indicate hemodynamic status and are appropriate predictors for clinical outcomes of these patients [81]. Varastehravan et al. reported that hematological parameters had considerable ability in prognosis of ST-segment resolution in patients with ST-segment elevation myocardial infarction receiving streptokinase therapy [5].

In the present study, we investigated the association of hematological parameters with new-onset and recurrent AF in order to understand which hematological parameters could be reliable predictors of each type of AF. Although the majority of physicians and researchers have believed that platelet count in cases with new-onset AF is higher than in patients with SR, our findings revealed that the number of platelets was significantly lower in cases with new-onset AF compared to those with SR, resulting in the likelihood of lower platelet count to predict new-onset AF.

Our subgroup analysis showed an inverse relationship between platelet count and new-onset AF in cases of persistent AF, but this relationship was not found in cases of paroxysmal and permanent AF. On the other hand, there was no significant relationship between platelet count and new-onset AF in patients with chronic AF. According to our findings, sample size of the studies, age, diabetes mellitus, differences regarding treatment with anticoagulants, and type of AF are factors of heterogeneity. The present study found no remarkable relationship between platelet count and recurrent AF; therefore, platelet count could be a potential predictor for new-onset
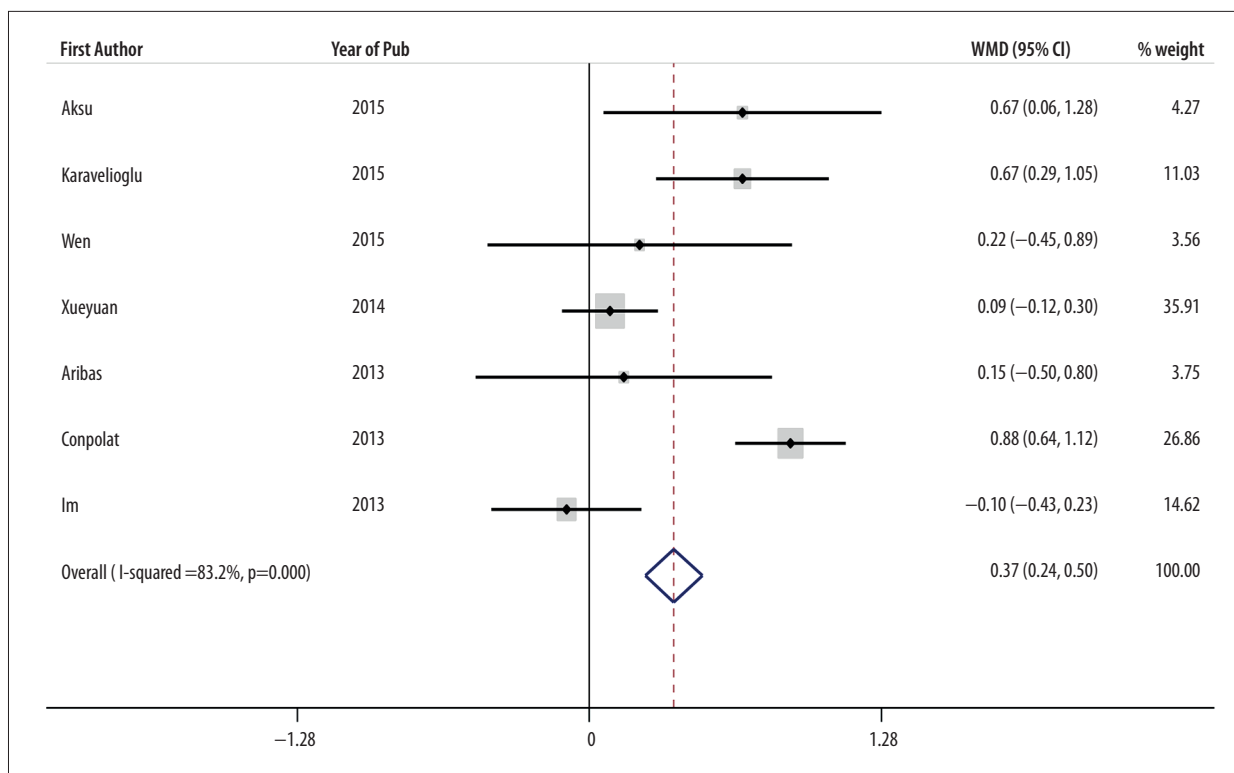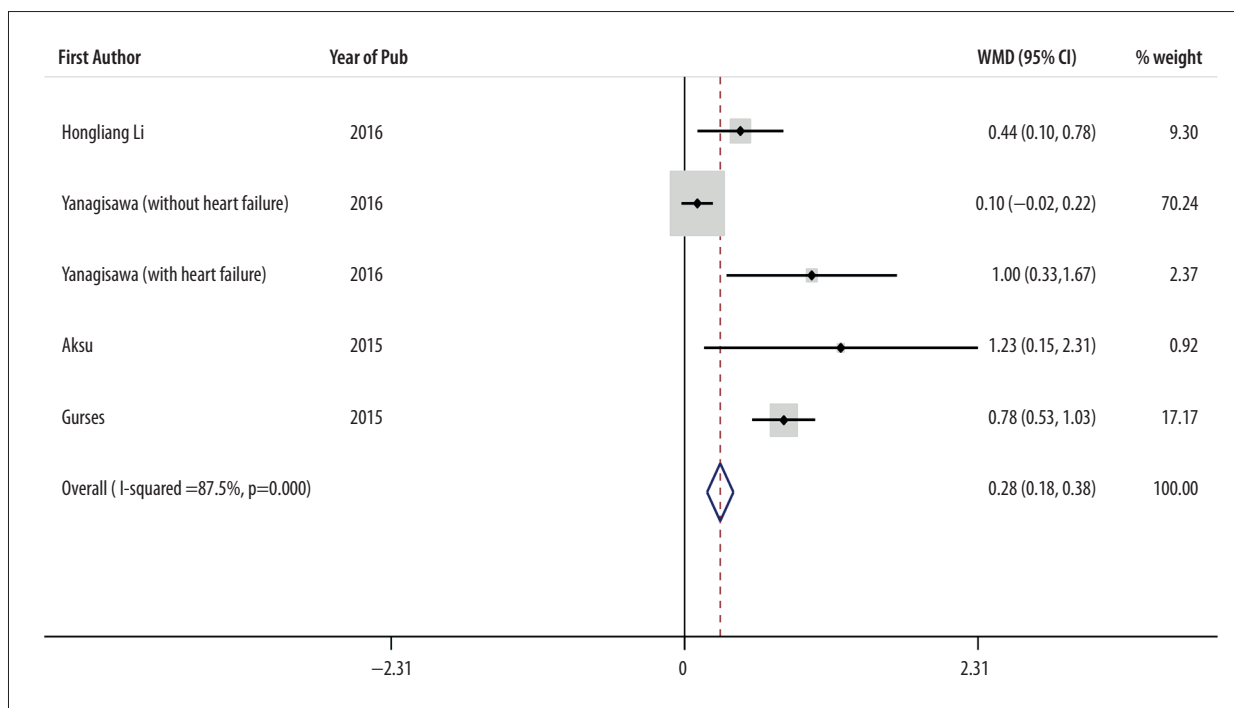
First Author	Year of Pub		WMD (95% CI)	% weight
Aksu	2015		0.67 (0.06, 1.28)	4.27
Karavelioglu	2015		0.67 (0.29, 1.05)	11.03
Wen	2015		0.22 (−0.45, 0.89)	3.56
Xueyuan	2014		0.09 (−0.12, 0.30)	35.91
Aribas	2013		0.15 (−0.50, 0.80)	3.75
Conpolat	2013		0.88 (0.64, 1.12)	26.86
Im	2013		−0.10 (−0.43, 0.23)	14.62
Overall (I-squared =83.2%, p=0.000)			0.37 (0.24, 0.50)	100.00

−1.28　　　　0　　　　1.28

Figure 7. Forest plot of weighted mean difference (WMD) for association between neutrophil to lymphocyte ratio and recurrence of AF.

First Author	Year of Pub		WMD (95% CI)	% weight
Hongliang Li	2016		0.44 (0.10, 0.78)	9.30
Yanagisawa (without heart failure)	2016		0.10 (−0.02, 0.22)	70.24
Yanagisawa (with heart failure)	2016		1.00 (0.33,1.67)	2.37
Aksu	2015		1.23 (0.15, 2.31)	0.92
Gurses	2015		0.78 (0.53, 1.03)	17.17
Overall (I-squared =87.5%, p=0.000)			0.28 (0.18, 0.38)	100.00

−2.31　　　　0　　　　2.31

Figure 8. Forest plot of weighted mean difference (WMD) for association between red blood cell distribution width and recurrence of AF.

AF, but it does not appear to be a significant factor associated with recurrent AF. Regarding the results of this study, PDW was considerably lower in cases with new-onset AF compared to those with SR. Thus, PDW and platelet count both had an inverse relationship with the new-onset AF.

MPV is known as an important biomarker of platelet activity. Large platelets secrete many critical mediators of coagulation, inflammation, thrombosis, and atherosclerosis. Evidence shows a close relationship between MPV and cardiovascular risk factors, such as diabetes mellitus, hypertension, and hypercholesterolemia [82,83]. Interestingly, in a recent study, Sansanayudh et al. reported an association between MPV and coronary artery disease (CAD). Patients with CAD and slow coronary blood flow had larger MPV than in the control group. They concluded that MPV might be used for risk stratification or to raise diagnostic accuracy of the traditional risk stratification markers in CAD patients [84].

The results of our study showed that MPV was also considerably higher in cases with new-onset AF compared to those with SR. According to our subgroup analysis, there was also a direct relationship between MPV and new-onset AF in both chronic and non-chronic AF. Sample sizes of the studies, differences in treatment with anticoagulants, and type of AF appeared to be factors of heterogeneity. Owing to insufficient number of studies on the association between PDW and MPV with recurrent AF, no analysis was performed in this regard.

There is a known relationship between inflammation and development of AF. Activities in hematopoietic tissues producing inflammatory leukocytes are closely associated with systemic inflammation, arterial inflammation, and cardiovascular events; however, their association with AF is unclear [85].

The findings of this study demonstrated that WBC count was not significantly different between cases of new-onset AF compared to those of SR; therefore, WBC is not proposed as a reliable predictor. The present study also confirmed that WBC count was not associated with new-onset AF for chronic and non-chronic AF. Our subgroup analysis indicated that risk factors such as diabetes mellitus, hypertension, and cigarette smoking could be factors of heterogeneity. On the other hand, our results revealed that WBC count was statistically higher in cases of recurrent AF compared to those with non-recurrent AF. Consequently, it can be stated that WBC count might be considered a predictor for recurrent AF, but not for new-onset AF. It also implies that possible inflammatory mechanisms are more active in patients who develop recurrent AF despite antiarrhythmic therapy for AF. As a result, considering inflammatory markers as a valuable tool to detect the risk of recurrent AF after pharmacological interventions and electrophysiology could greatly help in terms of timely diagnosis of AF recurrence.

The neutrophil to lymphocyte ratio is a new systemic inflammatory marker and a prognostic indicator of cardiovascular diseases [86,87]. The results of this study show that NLR is directly associated with new-onset and recurrent AF and generally could be an appropriate and efficient predictor for this disease. In our subgroup analysis, NLR also had this predictive ability for paroxysmal and persistent AF, while the association of NLR with permanent and chronic AF could not be detected due to the lack of relevant studies.

RDW is a parameter used to measure variability in the size of circulatory red blood cells obtained in CBC tests. Higher RDW reflects the presence of anisocytosis, which is associated with impaired erythropoiesis and RBC degradation appearing as chronic inflammation and a high level of oxidative stress [88].

Several studies suggested that RDW can predict poor outcomes in patients with heart failure, stable CAD, and acute myocardial infarction [89–91]. Similarly, our study showed that RDW was clearly higher in cases with new-onset AF compared to cases with SR. However, RDW was significantly increased in patients with recurrent AF versus non-recurrent AF, providing strong evidence that RDW can predicting both new-onset and recurrent AF. Only 2 studies investigated RBC count and its impact on AF, in which pooled analysis showed that RBC count was statistically higher in the AF group than in the SR group. No study was found investigating the relationship between this hematological parameter and recurrent AF.

Anemia increases the risk of cardiovascular complications, such as thromboembolic events, bleeding, and mortality in anticoagulated patients with AF. Patients with anemia and AF are supposed to be closely monitored while under treatment with all types of anticoagulants [92]. In the present study, Hb, HCT, MCV, and MCHC were examined as secondary hematological parameters. Pooled analysis found no significant differences in Hb levels comparing cases of new-onset AF with cases of SR. Notably, our subgroup analysis showed that the status of treatment with anticoagulants was not defined in a significant number of studies. Therefore, we had no information on whether patients enrolled in these studies had been receiving anticoagulant therapy. Concerning general findings, it appears that Hb is not a potential predictor for new-onset AF; however, this might change in the future by defining the therapeutic strategies with anticoagulants as well as the number of patients under treatment. On the other hand, there was an interesting finding about the type of AF. When the studies were sorted in terms of chronic and non-chronic AF, the level of Hb was considerably higher in non-chronic AF and significantly lower in chronic AF. This finding suggests that the type of AF in terms of acute or chronic pattern might have different effects on Hb changes. The merged results rejected any relationship between Hb and new-onset AF; however,

based on our subgroup analysis, we believe that after categorizing the types of AF into chronic and non-chronic, Hb might be a predictor. The results also indicated that the level of Hb was similar in patients with recurrent AF and those with non-chronic AF. Performing subgroup analysis, we found that the lack of association of Hb changes with recurrent AF was not influenced by any factor. Therefore, we strongly corroborate the lack of association between this hematological parameter and recurrent AF.

MCV is a measure of the average red blood cell. Based on our results, the level of MCV did not significantly differ between cases of new-onset AF versus SR cases, thus MCV could not be suggested as a predictor for new-onset AF. Also, our subgroup analysis strongly supported this finding.

Only 2 studies investigated the association of MCV and recurrent AF, and the merged analysis showed that the level of MCV was not significantly related to new-onset AF. HCT is a test for measuring the volume of RBC in relation to the total volume of blood. In the present study, the percentage of HCT was notably higher in cases of new-onset AF versus SR cases. Our subgroup analysis revealed that HCT can predict new-onset AF in non-chronic AF, but this ability was not seen in chronic AF. Due to the insufficient number of studies, we were unable to evaluate the relationship between HCT and recurrent AF.

Lip et al. reported that anticoagulants can reduce the level of hemostatic and hematologic factors in AF patients and, consequently, differences in treatment strategies with anticoagulants in various studies could be considered as a factor of heterogeneity [93–95]. Our subgroup analysis of platelet count, RDW, MCV, HCT, and WBC indicated that differences in using anticoagulants could play a considerable role in the existence of heterogeneity.

It should also be noted that in the meta-analysis on non-experimental studies, more heterogeneity was found, which can be explained by the following: 1) less controlled biases; 2) more confounding factors; and 3) differences in defining outcomes. Millions of CBC tests are performed daily for a large number of hospitalized patients with cardiovascular diseases throughout the world. In the present study, we found that CBC tests, apart from their ability to show a number of various pathologies already well known in clinical practice, might also play a significant role in diagnosis of various types of cardiac arrhythmias. Therefore, in addition to taking patient history, ECG, and Holter monitoring, the information from CBC in terms of AF should also be taken into account as an important diagnostic parameter. Therefore, we should be aware that, despite being one the most routine laboratory tests, the usefulness of CBC should not be underestimated.

Conclusions

Indeed, according to the results of previous research on potential predictive role of various CBC tests on the occurrence of AF that were conglomerated in our meta-analysis, CBC tests are a relatively easy to use and inexpensive tool to provide additional information on potential AF. Although CBC testing cannot replace standard diagnostics, they may be a valuable method to get some additional information in clinical diagnostics. In general, considering the results of this study, we conclude that lower platelet count and PDW, as well as higher MPV, NLR, RBC, RDW, and HTC, could be associated with new-onset AF. We strongly emphasize that MPV, NLR, and RDW have better predictive value in clinical practice for AF. Patients with AF who are under treatment are at high risk of recurrent AF; as a result, CBC is of particular importance for these patients. Our results also indicated that WBC, NLR, and PDW are hematological parameters with significant ability to predict recurrent AF. Therefore, emphasizing the potential predictive role of hematological parameters for new-onset and recurrent AF, we strongly recommend adding CBC testing to the diagnostic modalities of AF in clinical practice.

Supplementary Tables

Supplementary Table 1. Included, and excluded studies according to primary hematological parameters.

Clinical outcomes and biomarkers	Studies were identified and screened [n]	Studies were excluded according to title, abstract or full text (Secondary exclude) [n]	Studies were included [n]	Data for occurrence and recurrence [n]
Platelet count	292	254	38 approved articles with totally 52 enrolled data for meta-analysis (48 studies	**Occurrence:** 48 **Recurrence:** 4
Mean platelet volume	147	129	18 approved articles with totally 24 enrolled data for meta-analysis	**Occurrence:** 23 **Recurrence:** 1
Platelet distribution width	11	9	2 approved articles with totally 3 enrolled data for meta-analysis	**Occurrence:** 3 **Recurrence:** 0
White blood cell	348	299	49 approved articles with totally 64 enrolled data for meta-analysis	**Occurrence:** 42 **Recurrence:** 22
Neutrophil to lymphocyte ratio	41	26	15 approved articles with totally 17 enrolled data for meta-analysis	**Occurrence:** 10 **Recurrence:** 7
Red blood cell	83	81	2 approved articles with totally 2 enrolled data for meta-analysis	**Occurrence:** 2 **Recurrence:** 0
Red blood cell distribution width	49	38	11 approved articles with totally 13 enrolled data for meta-analysis	**Occurrence:** 8 **Recurrence:** 5

Supplementary Table 2. Extra details of characteristics of each study for exploration of heterogeneity factors.

First Author	Geographic Area	Total N	Total age	Total male	Total DM	Total HTN	Total CS	Total Diuretic	Total ACEI	Total. Statin	Total BB	AC-code	Chronic or not
						Occurrence of AF							
Balci (Male subjects) [8]	European	35	ND	100	ND	ND	ND	ND	ND	ND	ND	5	ND
Balci (Female subjects) [8]	European	153	ND	0	ND	ND	ND	ND	ND	ND	ND	5	ND
Gurses [9]	European	172	56.5	52.35	13.95	51.75	ND	ND	ND	ND	ND	5	Non-chronic
Karatas [10]	European	621	61.05	72.5	23	45.5	64	ND	ND	0	ND	2	Non-chronic
Korantzopoulos [11]	European	101	76.5	46.5	27.5	88.5	ND	ND	ND	ND	ND	3	Non-chronic
Akdag [12]	European	148	64.05	60	16.5	22	23.5	ND	ND	ND	ND	6	Combined types
Akyuz [13]	European	90	62.25	72.25	29	42.5	34.25	14.5	20.75	32.5	23	4	Combined types
Chavaria [14]	North America	290	65.65	74.5	29.05	65.65	55.05	ND	ND	ND	ND	5	ND

First Author	Geographic Area	Total N	Total age	Total male	Total DM	Total HTN	Total CS	Total Diuretic	Total ACEI	Total. Statin	Total BB	AC-code	Chronic or not
Drabik (Persistent AF) [15]	European	97	60.1	64.975	20	48.85	22.85	ND	52.25	53.15	60.6	4	Non-chronic
Drabik (Paroxysmal AF) [15]	European	91	60	55.15	16.4	46.05	20	ND	54.05	47.45	57.25	4	Non-chronic
Acet (Paroxysmal AF) [16]	European	134	62.05	44	16.5	18	21.5	ND	ND	ND	ND	5	Non-chronic
Acet (Persistent and permanent AF) [16]	European	126	62.85	43.5	21.5	24	28.5	ND	ND	ND	ND	5	Combined types
Arik (effective INR) [17]	European	248	69.65	40.7	6.05	68.95	13.7	27	59.25	ND	59.7	5	chronic
Arik (ineffective INR) [17]	European	248	69.45	37.9	6.85	65.35	12.1	24.2	55.65	ND	61.3	5	chronic
Distelmaier [18]	North America	198	73.5	61	24	60.5	ND	ND	ND	ND	ND	5	Non-chronic
Erdogan (with normal ventricular rate) [19]	European	67	69.55	49.28	10	65	6	17	53.5	10	43.3	3	chronic
Erdogan (with high ventricular rate) [19]	European	63	68.8	49.055	13.3	56.5	8	25	52	3.5	43.3	3	chronic
Zheng [20]	Asian	217	61.735	58.63	10.84	49.275	32.74	ND	ND	ND	ND	5	ND
Xu (without thrombotic events) [21]	Asian	115	66.095	50.45	37.4	53.1	38.25	ND	42.6	29.55	43.55	4	chronic
Xu (with thrombotic events) [21]	Asian	115	67.975	51.3	36.5	57.5	31.25	ND	40.8	26.05	40.95	4	chronic
Gungor [22]	European	177	47.2	57.8	3.35	14.75	23.15	ND	ND	ND	10.6	3	ND
Liu [23]	Asian	234	ND	ND	ND	ND	ND	ND	ND	ND	ND	5	Non-chronic
Sarikaya [24]	European	126	71.03	50	38	100	ND	ND	ND	ND	ND	5	ND
Sonmez [25]	European	85	70	37	24.21	63.255	ND	14.16	47.17	15.41	35.6	4	Non-chronic
Ulu [26]	European	57	ND	ND	0	0	ND	ND	ND	ND	ND	5	ND
Berge [27]	European	189	75	71.025	8	48	ND	19	21	34.5	28	4	Combined types
Ertas (without stroke) [28]	European	111	53.5	51	8.5	32.5	2	ND	17	ND	30	3	ND
Ertas (with stroke) [28]	European	63	54.5	47	10	47	5	ND	24	ND	16.5	3	ND
Gungor [29]	European	140	42.55	66.4	0	0	31	ND	ND	ND	ND	5	ND
Turgut [30]	European	162	63	52	100	65.5	41.5	6.5	23.5	18	16.5	4	chronic
Jaremo (healthy control) [31]	European	82	67.5	66.73	5.17	21.55	2.585	18.9	13.79	14.655	41.3	4	ND

First Author	Geographic Area	Total N	Total age	Total male	Total DM	Total HTN	Total CS	Total Diuretic	Total ACEI	Total. Statin	Total BB	AC-code	Chronic or not
Jaremo (disease control) [31]	European	130	71.5	68.1	12.75	43.75	9.485	28.65	26.25	25.05	55.92	4	ND
Sahin [32]	European	144	64.865	49.75	100	66.5	44.5	ND	ND	ND	ND	5	Non-chronic
Tekin [33]	European	219	73.5	35.5	13.5	68.5	19	ND	ND	ND	ND	5	chronic
Turfan (without stroke) [34]	European	135	59.5	54.55	15.6	33.1	55.5	ND	ND	ND	ND	4	ND
Turfan (with stroke) [34]	European	121	62.5	52.05	24.6	27	50.6	ND	ND	ND	ND	4	ND
Feng [35]	Asian	374	65.8	61.75	17.65	53.2	25.65	23	41.95	44.85	42.5	4	ND
Liu (Paroxysmal AF) [36]	Asian	101	64.35	62.5	5	32.5	ND	ND	21	15	34	3	Non-chronic
Liu (Persistent AF) [36]	Asian	107	65.8	61	6.5	35	ND	ND	29	13.5	35	3	Non-chronic
Yoshizaki [37]	Asian	176	70	76	32	65	52.5	ND	37.55	38.85	10.6	5	Non-chronic
Hayashi (Paroxysmal AF) [38]	Asian	27	57.95	92.5	14.5	48.5	ND	ND	40.5	26	ND	2	Non-chronic
Hayashi (Chronic AF) [38]	Asian	27	61.45	92.5	11.05	52	ND	ND	37	26	ND	2	chronic
Fu [39]	Asian	169	54.45	63.5	ND	ND	42.45	ND	ND	12.9	6.1	4	Combined types
Liu [40]	Asian	451	58.35	51.435	ND	100	23.7	14.85	71.55	61.15	42.7	5	Combined types
Letsas (Paroxysmal AF) [41]	European	93	64.35	59	6	60.5	ND	ND	43	15.5	34	5	Non-chronic
Letsas (Permanent AF) [41]	European	89	66.6	59.5	11	63	ND	ND	52.5	13.5	35.5	5	chronic
Luan (Persistent AF) [42]	Asian	53	53.25	50.855	0	26.21	30.2	ND	ND	ND	ND	5	Non-chronic
Luan (Paroxysmal AF) [42]	Asian	55	50.99	52.385	0	24.93	30.9	ND	ND	ND	ND	5	Non-chronic
Alberti [43]	European	51	64.45	47.05	ND	ND	ND	ND	ND	ND	ND	1	Non-chronic
Dai [44]	Asian	522	53.065	74.7	6.1	17	ND	ND	ND	ND	ND	5	Non-chronic
Ichiki [45]	Asian	72	51.5	80.205	16	37.5	ND	ND	8	15	ND	5	Non-chronic
Yao (Persistent AF) [46]	Asian	150	54.1	76.8	7.4	0	42.4	ND	ND	8.1	13.2	4	Non-chronic
Yao (Paroxysmal AF) [46]	Asian	339	53.35	74.95	4.25	0	46.55	ND	ND	6.6	7.85	4	Non-chronic
Colkesen [47]	European	190	54	38	18.5	41.5	ND	ND	ND	28	ND	4	Non-chronic

First Author	Geographic Area	Total N	Total age	Total male	Total DM	Total HTN	Total CS	Total Diuretic	Total ACEI	Total. Statin	Total BB	AC-code	Chronic or not
Choudhury (disease control) [48]	European	192	63.31	74	10.5	66.4	ND	33.15	55.7	46.5	43.7	4	ND
Choudhury (healthy control) [48]	European	177	62.305	72	4.1	31.8	ND	17.75	26.85	14.45	21.9	4	ND
Pirat [49]	European	39	49.5	51.5	8	26.5	32	ND	24.5	ND	38	5	Non-chronic
Yip [50]	Asian	82	65.75	63.05	9.7	34.7	5.65	ND	23.4	15.3	ND	3	chronic
Kamath (Paroxysmal and persistent AF) [51]	European	62	63.5	51.6	ND	ND	ND	ND	ND	ND	ND	1	Non-chronic
Kamath (Permanent AF) [51]	European	124	66	52.65	ND	ND	ND	ND	ND	ND	ND	1	chronic
Kamath (Paroxysmal AF) [52]	European	58	63	48.27	6.85	24.135	5.17	ND	ND	ND	ND	4	Non-chronic
Kamath (Permanent AF) [52]	European	116	65	52.29	5.15	30.45	5.17	ND	ND	ND	ND	4	chronic
Kamath [53]	European	143	70	54.18	5.375	29.565	ND	ND	ND	ND	ND	1	ND
Kamath [54]	European	57	ND	ND	ND	ND	ND	ND	ND	ND	ND	1	chronic
Peverill [55]	Oceania	163	55	84.6	ND	ND	ND	ND	ND	ND	ND	5	ND
Kahn (without stroke) [56]	North America	81	ND	ND	ND	ND	ND	ND	ND	ND	ND	1	chronic
Kahn (with stroke) [56]	North America	36	ND	ND	ND	ND	ND	ND	ND	ND	ND	1	chronic
Lip [57]	European	77	ND	ND	ND	ND	ND	ND	ND	ND	ND	1	chronic
Gustafsson (without stroke) [58]	European	40	77	ND	10	25	25	ND	ND	ND	ND	1	ND
Gustafsson (with stroke) [58]	European	40	77	ND	12.5	27.5	30	ND	ND	ND	ND	1	ND
Recurrence of AF													
Gurses [9]	European	86	56.8	57.7	15.8	48.55	ND	ND	21.2	16.5	ND	5	Non-chronic
Hongliang Li [59]	Asian	104	62.5	43.9	24.45	46.1	37.45	ND	41	49.65	42.4	4	Non-chronic
Yanagisawa (without heart failure) [60]	Asian	678	61.1	76	12.5	46	ND	3.5	35	ND	31.5	5	Non-chronic
Yanagisawa (with heart failure) [60]	Asian	79	63.6	74.5	20	38	ND	77.5	58	ND	81.5	5	Non-chronic
Aksu [61]	European	49	59.65	52.5	16.5	48.5	47	ND	ND	ND	ND	5	Non-chronic

First Author	Geographic Area	Total N	Total age	Total male	Total DM	Total HTN	Total CS	Total Diuretic	Total ACEI	Total. Statin	Total BB	AC-code	Chronic or not
Gurses [62]	European	299	55.7	51.15	13.2	42.4	31	ND	ND	ND	ND	4	Non-chronic
Karavelioglu [63]	European	218	64.4	41.095	18	58.5	21	ND	23.5	10.5	67	5	Non-chronic
Wen [64]	Asian	75	63.62	ND	7.5	57.5	20	ND	ND	30	ND	5	Non-chronic
Guo Xueyuan [65]	Asian	379	49.665	73.55	0	0	ND	ND	ND	ND	ND	5	ND
Aribas [66]	European	149	60	ND	29	62.5	18.5	ND	ND	ND	ND	2	Non-chronic
Bing Li [67]	Asian	288	57	71.1	28.65	55.05	38.15	ND	38	14.2	27.7	5	Non-chronic
Canpolat [68]	European	251	55.2	54.85	15.15	44.35	36.55	ND	51.25	18.05	ND	5	Non-chronic
Im [69]	Asian	499	56.4	73.65	15.55	43.9	ND	ND	ND	ND	ND	5	Non-chronic
Xiao-nan HE [70]	Asian	330	59.5	66.3	ND	48.65	ND	ND	50	14	52	5	Non-chronic
Ferro [71]	European	144	70.95	56.5	14	87.5	5	ND	46.5	22.5	ND	2	Non-chronic
Smit [72]	European	100	64	73.8	11.9	65.95	15	41.2	69.05	36.65	89.3	5	Non-chronic
Wang (Paroxysmal AF) [73]	Asian	103	57.5	34.8	ND	41.65	ND	ND	ND	ND	4.24	5	Non-chronic
Wang (Persistent AF) [73]	Asian	55	52.5	74.65	ND	50.35	ND	ND	ND	ND	5.65	5	Non-chronic
Liu (Paroxysmal AF) [74]	Asian	77	56	75.6	ND	37.3	ND	ND	ND	ND	ND	2	Non-chronic
Liu (Persistent AF) [74]	Asian	44	53.05	84.85	ND	51.2	ND	ND	ND	ND	ND	2	Non-chronic
Vizzardi [75]	European	106	69	61	12.05	ND	ND	ND	8	ND	ND	5	Non-chronic
Letsas [76]	European	72	54.55	81.5	21.5	21.5	ND	ND	23	14.5	ND	5	Non-chronic
Korantzopoulos [77]	European	30	68.5	48.39	7.1	64.25	4.75	30.95	35.7	5.55	ND	5	Non-chronic

Supplementary Table 3. Subgroup-analysis.

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Occurrence of AF				
Platelet count				
Year of Publication				No
>2000	43	−23.75 (−25.22 to −22.29)	91% and 0.001 and 0.001	
≤2000	5	−56.50 (−61.45 to −51.55)	90.7% and 0.001 and 0.001	
Geographic area				Yes, probably
Asian	7	−3.88 (−10.98 to 3.22)	13.8% and 0.324 and 0.284	
European	36	−29.41 (−30.95 to −27.88)	93.7% and 0.001 and 0.001	
Africa	–	–	–	
North American	4	−12.11 (−16.25 to −7.96)	0.0% and 0.476 and 0.001	
South American	–	–	–	
Australia	1	−23 (−40.50 to −5.49)	–	
Design of study				No
Cohort	8	−29.09 (−31.01 to −27.16)	92.4% and 0.001 and 0.001	
Case-control	40	−23.30 (−25.36 to −21.25)	93% and 0.001 and 0.001	
Number of population				No
>300	2	−6.33 (−19.68 to 7.03)	0.0% and 0.689 and 0.353	
≤300	46	−26.61 (−28.02 to −25.20)	93.1% and 0.001 and 0.001	
Mean age				No
>60 years	35	−27.69 (−29.13 to −26.25)	94% and 0.001 and 0.001	
≤60 years	8	−2.68 (−9.46 to 4.10)	78.4% and 0.001 and 0.438	
Male				No
>70%	9	−29.76 (−31.69 to −27.83)	83.8% and 0.001 and 0.001	
≤70%	32	−15.69 (−17.94 to −13.43)	90.5% and 0.001 and 0.001	
Diabetes mellitus				Yes, probably
>30%	3	−0.27 (−9.57 to 9.01)	35.9% and 0.210 and 0.953	
≤30%	35	−24.77 (−26.27 to −23.26)	92.2% and 0.001 and 0.001	
Hypertension				No
>70%	–	–	–	
≤70%	39	−24.91 (−26.38 to −23.44)	92.5% and 0.001 and 0.001	
Cigarette smoking				No
>30%	10	−16.36 (−21.68 to −11.04)	92.8% and 0.001 and 0.001	
≤30%	20	−22.62 (−25.67 to −19.56)	92.4% and 0.001 and 0.001	
Medication: Diuretic				No
>70%	–	–	–	
≤70%	13	−28.39 (−30.26 to −26.52)	85.7% and 0.001 and 0.001	
Medication: ACEI				No
>70%	–	–	–	
≤70%	22	−25.47 (−27.18 to −23.76)	86.5% and 0.001 and 0.001	
Medication: Statin				No
>70%	–	–	–	
≤70%	21	−25.33 (−27.06 to −23.61)	88% and 0.001 and 0.001	
Medication: Beta-Blocker				No
>70%	–	–	–	
≤70%	21	−25.36 (−27.06 to −23.66)	86.6% and 0.001 and 0.001	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Anti-coagulant status codes				Yes, probably
1	10	−52.72 (−56.32 to −49.12)	92.3% and 0.001 and 0.001	
2	3	1.69 (−17.11 to 20.53)	67.3% and 0.047 and 0.860	
3	6	−10.36 (−21.43 to 0.69)	0.0% and 0.703 and 0.066	
4	19	−24.85 (−26.58 to −23.13)	91.6% and 0.001 and 0.001	
5	9	−11.38 (−14.88 to −7.88)	36.4% and 0.127 and 0.001	
6	1	17.40 (−6.03 to 40.83)	–	
AF				Yes, probably
Chronic	16	−2.80 (−7.77 to 2.16)	18.1% and 0.246 and 0.268	
Non-chronic	11	−20.88 (−23.55 to −18.20)	95.7% and 0.001 and 0.001	
Type of AF				Yes, probably
Paroxysmal	5	−3.72 (−9.24 to 1.79)	72.1% and 0.006 and 0.186	
Persistent	3	−41.93 (−46.40 to −37.46)	97.4% and 0.001 and 0.001	
Permanent	6	−5.09 (−11.96 to 1.78)	55.3% and 0.048 and 0.147	
Mean platelet volume				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				No
Asian	3	1.37 (1.16 to 1.58)	95.9% and 0.001 and 0.001	
European	19	0.39 (0.35 to 0.43)	95.2% and 0.001 and 0.001	
Africa	–	–	–	
North American	–	–	–	
South American	–	–	–	
Australia	1	−0.20 (−0.63 to 0.23)	–	
Design of study				No
Cohort	4	1.37 (1.14 to 1.60)	94.7% and 0.001 and 0.001	
Case-control	19	0.39 (0.35 to 0.43)	95.4% and 0.001 and 0.001	
Number of population				Yes, probably
>300	2	0.90 (0.67 to 1.13)	0.0% and 0.666 and 0.001	
≤300	21	0.41 (0.36 to 0.45)	96% and 0.001 and 0.001	
Mean age				No
>60 years	16	0.58 (0.54 to 0.63)	94.1and 0.001 and 0.001	
≤60 years	4	0.23 (0.05 to 0.42)	93.5% and 0.001 and 0.012	
Male				No
>70%	6	0.59 (0.46 to 0.71)	93.9% and 0.001 and 0.001	
≤70%	16	0.40 (0.36 to 0.44)	96.4% and 0.001 and 0.001	
Diabetes mellitus				No
>30%	4	0.63 (0.57 to 0.69)	96.8% and 0.001 and 0.001	
≤30%	16	0.49 (0.42 to 0.57)	92.7% and 0.001 and 0.001	
Hypertension				No
>70%	–	–	–	
≤70%	20	0.58 (0.53 to 0.62)	93.8% and 0.001 and 0.001	
Cigarette smoking				No
>30%	8	0.68 (0.62 to 0.74)	94.7% and 0.001 and 0.001	
≤30%	8	0.37 (0.28 to 0.45)	92.1% and 0.001 and 0.001	
Medication: Diuretic				No
>70%	–	–	–	
≤70%	9	0.54 (0.49 to 0.59)	94.3% and 0.001 and 0.001	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Medication: ACEI				No
>70%	–	–	–	
≤70%	11	0.57 (0.52 to 0.62)	95.8% and 0.001 and 0.001	
Medication: Statin				No
>70%	–	–	–	
≤70%	11	0.66 (0.60 to 0.71)	94.7% and 0.001 and 0.001	
Medication: Beta-Blocker				No
>70%	–	–	–	
≤70%	12	0.55 (0.50 to 0.60)	95.8% and 0.001 and 0.001	
Anti-coagulant status codes				Yes, probably
1	–	–	–	
2	1	0.80 (0.26 to 1.33)	–	
3	3	0.081 (−0.109 to 0.272)	66.1% and 0.053 and 0.404	
4	10	0.67 (0.62 to 0.73)	95.1% and 0.001 and 0.001	
5	8	0.108 (0.046 to 0.17)	93.6% and 0.001 and 0.001	
6	1	1.10 (0.75 to 1.45)	–	
AF				No
Chronic	8	0.55 (0.49 to 0.60)	95.7% and 0.001 and 0.001	
Non-chronic	3	0.85 (0.58 to 1.13)	88.6% and 0.001 and 0.001	
Type of AF				No
Paroxysmal	1	1.70 (1.20. to 2.19)	–	
Persistent	1	0.32 (−0.09 to 0.73)	–	
Permanent	4	0.28 (0.17 to 0.38)	91.7% and 0.001 and 0.001	
		WBC		
Year of publication				
>2000				
≤2000		All of studies: after 2000		
Geographic area				No
Asian	15	0.001 (−0.058 to 0.06)	80.8% and 0.001 and 0.973	
European	25	−0.05 (−0.13 to 0.023)	89.3% and 0.001 and 0.159	
Africa	–	–	–	
North American	2	0.828 (0.46 to 1.187)	0.0% and 0.365 and 0.001	
South American	–	–	–	
Australia	–	–	–	
Design of study				Yes, probably
Cohort	4	0.370 (−0.083 to 0.823)	13.2% and 0.326 and 0.109	
Case-control	38	−0.009 (−0.057 to 0.039)	88.2% and 0.001 and 0.708	
Number of population				No
>300	5	0.035 (−0.047 to 0.117)	84.8% and 0.001 and 0.403	
≤300	37	−0.025 (−0.083 to 0.033)	87.7% and 0.001 and 0.398	
Mean age				No
>60 years	27	−0.060 (−0.140 to 0.019)	88.3% and 0.001 and 0.136	
≤60 years	15	0.025 (−0.033 to 0.084)	85.2% and 0.001 and 0.397	
Male				No
>70%	11	0.009 (−0.051 to 0.070)	86.4% and 0.001 and 0.761	
≤70%	31	−0.027 (−0.102 to 0.048)	87.8% and 0.001 and 0.481	
Diabetes mellitus				Yes, probably
>30%	2	0.216 (-0.419 to 0.852)	0.0% and 0.789 and 0.505	
≤30%	38	0.055 (0.005 to 0.104)	85% and 0.001 and 0.030	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Hypertension				Yes, probably
>70%	2	−0.743 (−0.952 to −0.535)	0.0% and 0.873 and 0.001	
≤70%	39	0.097 (0.046 to 0.147)	80.5% and 0.001 and 0.001	
Cigarette smoking				Yes, probably
>30%	11	0.053 (−0.010 to 0.115)	26.4% and 0.193 and 0.102	
≤30%	16	0.231 (0.123 to 0.339)	83.9% and 0.001 and 0.001	
Medication: Diuretic				No
>70%	–	–	–	
≤70%	8	0.061 (−0.102 to 0.224)	41.9% and 0.099 and 0.464	
Medication: ACEI				No
>70%	1	−0.70 (−1.269 to −0.131)	–	
≤70%	21	0.012 (−0.086 to 0.111)	83.2% and 0.001 and 0.804	
Medication: Statin				No
>70%	–	–	–	
≤70%	21	−0.00 (−0.057 to 0.506)	81.8% and 0.001 and 0.990	
Medication: Beta-Blocker				No
>70%	–	–	–	
≤70%	21	0.071 (0.015 to 0.127)	76.2% and 0.001 and 0.012	
Anti-coagulant status codes				Yes, Probably
1	1	−0.70 (−0.875 to −0.525)	–	
2	3	0.661 (−0.627 to 1.949)	0.0% and 0.924 and 0.314	
3	9	−0.232 (−0.397 to −0.067)	85.4% and 0.001 and 0.006	
4	8	0.054 (−0.006 to 0.115)	87.6% and 0.001 and 0.077	
5	20	0.132 (0.030 to 0.233)	85% and 0.001 and 0.011	
6	1	0.400 (−0.220 to 1.020)	–	
AF				Yes, probably
Chronic	8	0.125 (−0.048 to 0.299)	0.0% and 0.833 and 0.156	
Non-chronic	22	−0.050 (−0.102 to 0.001)	92% and 0.001 and 0.056	
Type of AF				Yes, probably
Paroxysmal	9	−0.087 (−0.161 to −0.014)	88.6% and 0.001 and 0.020	
Persistent	6	−0.019 (−0.101 to 0.062)	95.2% and 0.001 and 0.641	
Permanent	5	0.069 (−0.120 to 0.259)	0.0% and 0.958 and 0.473	
NLR				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				No
Asian	–	–	–	
European	9	0.901 (0.802 to 1.000)	94% and 0.001 and 0.001	
Africa	–	–	–	
North American	1	−0.640 (−1.711 to 0.431)	–	
South American	–		–	
Australia	–		–	
Design of study				No
Cohort	1	−0.640 (−1.711 to 0.431)	–	
Case-control	9	0.901 (0.802 to 1.000)	94% and 0.001 and 0.001	
Number of population				No
>300	1	1.200 (−0.789 to 3.189)	–	
≤300	9	0.887 (0.789 to 0.986)	94.3% and 0.001 and 0.001	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Mean age				No
>60 years	7	1.030 (0.919 to 1.141)	91.5% and 0.001 and 0.001	
≤60 years	3	0.365 (0.152 to 0.579)	95.1% and 0.001 and 0.001	
Male				Yes, probably
>70%	2	−0.277 (−1.170 to 0.716)	60.8% and 0.110 and 0.637	
≤70%	8	0.901 (0.801 to 1.00)	94.7% and 0.001 and 0.001	
Diabetes mellitus				No
>30%	1	0.670 (0.201 to 1.139)	–	
≤30%	9	0.898 (0.797 to 0.999)	94.3% and 0.001 and 0.001	
Hypertension				
>70%		All of studies: ≤70%		
≤70%				
Cigarette smoking				No
>30%	3	0.492 (0.072 to 0.912)	62.5% and 0.069 and 0.022	
≤30%	6	0.928 (0.824 to 1.032)	96.2% and 0.001 and 0.001	
Medication: Diuretic				No
>70%	–	–	–	
≤70%	1	0.600 (0.146 to 1.054)	–	
Medication: ACEI				No
>70%	–	–	–	
≤70%	3	1.025 (0.687 to 1.364)	91.2% and 0.001 and 0.001	
Medication: Statin				No
>70%	–	–	–	
≤70%	2	0.630 (0.187 to 1.072)	0.0% and 0.564 and 0.005	
Medication: Beta-Blocker				No
>70%	–	–	–	
≤70%	4	0.408 (0.215 to 0.601)	92.8% and 0.001 and 0.001	
Anti-coagulant status codes				No
1	–	–	–	
2	1	1.200 (−0.789 to 3.189)	–	
3	3	0.365 (0.152 to 0.579)	95.1% and 0.001 and 0.001	
4	1	0.600 (0.146 to 1.054)	–	
5	4	1.081 (0.962 to 1.199)	95.4% and 0.001 and 0.001	
6	1	0.700 (0.236 to 1.164)	–	
AF				No
Chronic	–	–	–	
Non-chronic	4	0.689 (0.538 to 0.840)	0.0% and 0.935 and 0.001	
Type of AF				No
Paroxysmal	1	0.700 (0.529 to 0.871)	–	
Persistent	2	0.634 (0.308 to 0.960)	0.0% and 0.833 and 0.001	
Permanent	–	–	–	
RDW				
Year of publication				
>2000		All of studies: after 2000		
≤2000				

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Geographic area				Yes, probably
Asian	1	0.260 (0.065 to 0.455)	–	
European	6	0.873 (0.806 to 0.941)	0.0% and 0.613 and 0.001	
Africa	-	–	–	
North American	1	0.280 (0.196 to 0.364)	–	
South American	-	–	–	
Australia	-	–	–	
Design of study				
Cohort		All of studies: case-control		
Case-control				
Number of population				No
>300	1	0.500 (–0.039 to 1.039)	–	
≤300	7	0.615 (0.564 to 0.666)	95.5% and 0.001 and 0.001	
Mean age				Yes, probably
>60 years	4	0.412 (0.338 to 0.485)	92.8% and 0.001 and 0.001	
≤60 years	3	0.885 (0.809 to 0.961)	0.0% and 0.716 and 0.001	
Male				No
>70%	1	0.500 (–0.039 to 1.039)	–	
≤70%	6	0.641 (0.588 to 0.694)	95.8% and 0.001 and 0.001	
Diabetes mellitus				No
>30%	-	–	–	
≤30%	7	0.640 (0.587 to 0.692)	95% and 0.001 and 0.001	
Hypertension				Yes, probably
>70%	2	0.856 (0.700 to 1.011)	0.0% and 0.337 and 0.001	
≤70%	5	0.612 (0.556 to 0.668)	96.4% and 0.001 and 0.001	
Cigarette smoking				No
>30%	1	0.500 (–0.039 to 1.039)	–	
≤30%	3	0.885 (0.809 to 0.961)	0.0% and 0.716 and 0.001	
Medication: Diuretic				
>70%			No Data	
≤70%				
Medication: ACEI				No
>70%	-	–	–	
≤70%	2	1.021 (0.615 to 1.426)	0.0% and 0.636 and 0.001	
Medication: Statin				No
>70%	-	–	–	
≤70%	1	0.500 (–0.039 to 1.039)	–	
Medication: Beta-Blocker				No
>70%	-	–	–	
≤70%	3	0.885 (0.809 to 0.961)	0.0% and 0.716 and 0.001	
Anti-coagulant status codes				Yes, probably
1	-	–	–	
2	1	0.500 (–0.039 to 1.039)	–	
3	4	0.875 (0.806 to 0.944)	0.0% and 0.796 and 0.001	
4	-	–	–	
5	3	0.297 (0.221 to 0.373)	80.7% and 0.006 and 0.001	
6	-	–	–	
AF				No
Chronic	-	–	–	
Non-chronic	4	0.379 (0.310 to 0.448)	91.6% and 0.001 and 0.001	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Type of AF				No
Paroxysmal	1	0.260 (0.065 to 0.455)	–	
Persistent	-	–	–	
Permanent	-	–	–	
		MCV		
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				No
Asian	1	–0.300 (–1.364 to 0.764)	–	
European	1	1.000 (–0.337 to 2.337)	–	
Africa	-	–	–	
North American	1	–0.280 (–0.706 to 0.146)	–	
South American	-	–	–	
Australia	1	1.000 (–0.998 to 2.998)	–	
Design of study				
Cohort		All of studies: Case-control		
Case-control				
Number of population				No
>300	1	–0.300 (–1.364 to 0.764)	–	
≤300	3	–0.116 (–0.514 to 0.283)	55% and 0.108 and 0.569	
Mean age				No
>60 years	2	–0.283 (–0.679 to 0.113)	0.0% and 0.162 and 0.973	
≤60 years	2	1.000 (–0.111 to 2.111)	0.0% and 1.000 and 0.078	
Male				No
>70%	1	1.000 (–0.998 to 2.998)	–	
≤70%	3	–0.179 (–0.559 to 0.200)	38.5% and 0.197 and 0.354	
Diabetes mellitus				No
>30%	-	–	–	
≤30%	3	–0.179 (–0.559 to 0.200)	38.5% and 0.197 and 0.354	
Hypertension				No
>70%	-	–	–	
≤70%	3	–0.179 (–0.559 to 0.200)	38.5% and 0.197 and 0.354	
Cigarette smoking				No
>30%	-	–	–	
≤30%	2	0.204 (–0.628 to 1.037)	55% and 0.136 and 0.631	
Medication: Diuretic				No
>70%	-	–	–	
≤70%	1	–0.300 (–1.364 to 0.764)	–	
Medication: ACEI				No
>70%	-	–	–	
≤70%	1	–0.300 (–1.364 to 0.764)	–	
Medication: Statin				No
>70%	-	–	–	
≤70%	1	–0.300 (–1.364 to 0.764)	–	
Medication: Beta-Blocker				No
>70%	-	–	–	
≤70%	2	0.204 (–0.628 to 1.037)	55% and 0.136 and 0.631	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Anti-coagulant status codes				No
1	–	–	–	
2	–	–	–	
3	1	1.000 (–0.337 to 2.337)	–	
4	1	–0.300 (–1.364 to 0.764)	–	
5	2	–0.224 (–0.641 to 0.193)	33.7% and 0.219 and 0.292	
6	–	–	–	
AF				No
Chronic	–	–	–	
Non-chronic	1	–0.280 (–0.706 to 0.146)	–	
Type of AF				No
Paroxysmal	–	–	–	
Persistent	–	–	–	
Permanent	–	–	–	
HCT				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				No
Asian	–	–	–	
European	9	0.552 (0.004 to 1.100)	53.4% and 0.028 and 0.048	
Africa	–	–	–	
North American	1	2.670 (2.168 to 3.172)	–	
South American	–	–	–	
Australia	1	3.000 (1.605 to 4.395)	–	
Design of study				
Cohort		All of studies: Case-control		
Case-control				
Number of population				
>300		All of studies: ≤300		
≤300				
Mean age				No
>60 years	10	1.704 (1.334 to 2.075)	81.4% and 0.001 and 0.001	
≤60 years	1	3.000 (1.605 to 4.395)	–	
Male				No
>70%	3	1.666 (0.767 to 2.566)	67% and 0.048 and 0.001	
≤70%	8	1.813 (1.423 to 2.203)	84.6% and 0.001 and 0.001	
Diabetes mellitus				No
>30%	–	–	–	
≤30%	8	1.691 (1.299 to 2.083)	84.6% and 0.001 and 0.001	
Hypertension				No
>70%	–	–	–	
≤70%	8	1.691 (1.299 to 2.083)	84.6% and 0.001 and 0.001	
Cigarette smoking				No
>30%	–	–	–	
≤30%	5	–0.064 (–0.805 to 0.678)	39.4% and 0.158 and 0.867	
Medication: Diuretic				No
>70%	–	–	–	
≤70%	4	0.402 (–0.488 to 1.292)	0.0% and 0.753 and 0.376	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Medication: ACEI				No
>70%	–	–	–	
≤70%	4	0.402 (−0.488 to 1.292)	0.0% and 0.753 and 0.376	
Medication: Statin				No
>70%	–	–	–	
≤70%	4	0.402 (−0.488 to 1.292)	0.0% and 0.753 and 0.376	
Medication: Beta-Blocker				No
>70%	–	–	–	
≤70%	4	0.402 (−0.488 to 1.292)	0.0% and 0.753 and 0.376	
Anti-coagulant status codes				Yes, probably
1	2	1.819 (0.693 to 2.945)	65.9% and 0.087 and 0.002	
2	–	–	–	
3	2	−0.021 (−1.381 to 1.340)	0.0% and 0.477 and 0.976	
4	4	0.852 (0.001 to 1.704)	0.0% and 0.985 and 0.050	
5	3	2.230 (1.787 to 2.673)	93.9% and 0.001 and 0.001	
6	–	–	–	
AF				No
Chronic	5	0.062 (−0.635 to 0.759)	46.9% and 0.110 and 0.861	
Non-chronic	3	2.611 (2.141 to 3.082)	18.5% and 0.293 and 0.001	
Type of AF				No
Paroxysmal	1	1.000 (−1.122 to 3.122)	–	
Persistent	–	–	–	
Permanent	4	0.617 (−0.215 to 1.450)	0.0% and 0.603 and 0.146	
Hb				
Year of publication				No
>2000	25	0.024 (−0.038 to 0.087)	91.1% and 0.001 and 0.444	
≤2000	2	1.076 (0.522 to 1.630)	85.2% and 0.009 and 0.001	
Geographic area				Yes, probably
Asian	2	−0.048 (−0.366 to 0.271)	0.0% and 0.758 and 0.769	
European	21	−0.150 (−0.219 to −0.081)	76.8% and 0.001 and 0.001	
Africa	–	–	–	
North American	4	0.994 (0.840 to 1.149)	89.4% and 0.001 and 0.001	
South American	–	–	–	
Australia	–	–	–	
Design of study				Yes, probably
Cohort	6	−0.093 (−0.142 to −0.044)	0.0% and 0.488 and 0.001	
Case-control	21	0.102 (0.024 to 0.181)	92.8% and 0.001 and 0.011	
Number of population				No
>300	1	−0.100 (−0.643 to 0.443)	–	
≤300	26	0.039 (−0.023 to 0.102)	91.4% and 0.001 and 0.216	
Mean age				No
>60 years	20	0.033 (−0.032 to 0.098)	92.5% and 0.001 and 0.317	
≤60 years	5	−0.077 (−0.297 to 0.143)	73.5% and 0.005 and 0.494	
Male				No
>70%	6	−0.040 (−0.143 to 0.063)	75.1% and 0.001 and 0.447	
≤70%	19	0.062 (−0.017 to 0.140)	92.7% and 0.001 and 0.123	
Diabetes mellitus				Yes, probably
>30%	2	−0.048 (−0.366 to 0.271)	0.0% and 0.758 and 0.769	
≤30%	23	0.027 (−0.036 to 0.091)	91.8% and 0.001 and 0.401	

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Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Hypertension				Yes, probably
>70%	2	−0.275 (−0.481 to 0.070)	0.0% and 0.583 and 0.009	
≤70%	23	0.055 (−0.011 to 0.120)	91.6% and 0.001 and 0.102	
Cigarette smoking				Yes, probably
>30%	8	−0.054 (−0.223 to 0.114)	0.0% and 0.597 and 0.529	
≤30%	10	−0.308 (−0.422 to −0.193)	80.8% and 0.001 and 0.001	
Medication: Diuretic				No
>70%	–	–	–	
≤70%	9	−0.184 (−0.267 to −0.100)	84.9% and 0.001 and 0.001	
Medication: ACEI				No
>70%	–	–	–	
≤70%	13	−0.192 (−0.272 to −0.112)	80.6% and 0.001 and 0.001	
Medication: Statin				No
>70%	–	–	–	
≤70%	10	−0.017 (−0.114 to 0.079)	58% and 0.011 and 0.729	
Medication: Beta-Blocker				No
>70%	–	–	–	
≤70%	14	−0.172 (−0.251 to −0.094)	80.8% and 0.001 and 0.001	
Anti-coagulant status codes				No
1	2	1.076 (0.522 to 1.630)	85.2% and 0.009 and 0.001	
2	1	−0.100 (−0.643 to 0.443)	–	
3	6	−0.183 (−0.355 to −0.011)	73.3% and 0.002 and 0.037	
4	9	−0.005 (−0.100 to 0.090)	63.2% and 0.005 and 0.913	
5	8	0.148 (0.049 to 0.247)	96.8% and 0.001 and 0.004	
6	1	−0.200 (−0.550 to 0.150)	–	
AF				No
Chronic	8	−0.320 (−0.443 to −0.196)	85.2% and 0.001 and 0.001	
Non-chronic	5	0.543 (0.418 to 0.668)	96.1% and 0.001 and 0.001	
Type of AF				No
Paroxysmal	1	0.500 (−0.059 to 1.059)	–	
Persistent	1	0.200 (−0.553 to 0.953)	–	
Permanent	4	−0.458 (−0.596 to −0.320)	68.5% and 0.023 and 0.001	
Occurrence of AF				
Platelet count				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				Yes, probably
Asian	2	14.48 (−1.95 to 30.91)	28.6% and 0.237 and 0.084	
European	2	−12.96 (−25.66 to −0.272)	40.8% and 0.194 and 0.045	
Africa	–	–	–	
North American	–	–	–	
South American	–	–	–	
Australia	–	–	–	
Design of study				No
Cohort	3	0.217 (−0.188 to 0.622)	50.9% and 0.130 and 0.294	
Case-control	1	20.45 (1.27 to 39.63)	–	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Number of population				
>300			All of studies: ≤300	
≤300				
Mean age				No
>60 years	3	−0.132 (−13.084 to 12.82)	78.8% and 0.009 and 0.984	
≤60 years	1	−6.60 (−22.517 to 9.317)	−	
Male				No
>70%	−	−	−	
≤70%	3	−2.78 (−13.37 to 7.79)	79.6% and 0.007 and 0.606	
Diabetes mellitus				
>30%			All of studies: ≤30%	
≤30%				
Hypertension				
>70%			All of studies: ≤70%	
≤70%				
Cigarette smoking				Yes, probably
>30%	2	4.43 (−7.81 to 16.80)	77.9% and 0.033 and 0.478	
≤30%	2	−17.38 (−34.94 to 0.174)	22.3% and 0.257 and 0.052	
Medication: Diuretic				
>70%			No Data	
≤70%				
Medication: ACEI				No
>70%	−	−	−	
≤70%	2	0.238 (−13.93 to 14.41)	89.4% and 0.002 and 0.974	
Medication: Statin				No
>70%	−	−	−	
≤70%	3	−0.132 (−13.08 to 12.82)	78.8% and 0.009 and 0.984	
Medication: Beta-Blocker				No
>70%	−	−	−	
≤70%	2	0.238 (−13.93 to 14.41)	89.4% and 0.002 and 0.974	
Anti-coagulant status codes				Yes, probably
1	−	−	−	
2	−	−	−	
3	−	−	−	
4	2	4.432 (−7.817 to 16.68)	77.9% and 0.033 and 0.478	
5	2	−17.38 (−34.94 to 0.174)	22.3% and 0.257 and 0.052	
6	−	−	−	
AF				
Chronic			All of studies: non–chronic	
Non-chronic				
Type of AF				No
Paroxysmal	2	0.238 (−13.93 to 14.41)	89.4% and 0.002 and 0.974	
Persistent	−	−	−	
Permanent	−	−	−	
			WBC	
Year of publication				
>2000			All of studies: after 2000	
≤2000				

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Geographic area				Yes, probably
Asian	11	0.136 (–0.013 to 0.284)	34.7% and 0.121 and 0.073	
European	11	0.347 (0.120 to 0.574)	65.1% and 0.001 and 0.003	
Africa	–	–	–	
North American	–	–	–	
South American	–	–	–	
Australia	–	–	–	
Design of study				Yes, probably
Cohort	20	0.202 (0.077 to 0.326)	58.6% and 0.001 and 0.002	
Case-control	2	–0.344 (–2.282 to 1.594)	0.0% and 0.710 and 0.728	
Number of population				No
>300	3	0.146 (–0.030 to 0.321)	63.6% and 0.064 and 0.103	
≤300	19	0.254 (0.077 to 0.430)	55.1% and 0.002 and 0.005	
Mean age				Yes, probably
>60 years	10	0.097 (–0.076 to 0.269)	0.0% and 0.498 and 0.272	
≤60 years	12	0.310 (0.131 to 0.489)	68.7% and 0.001 and 0.001	
Male				No
>70%	9	0.251 (0.093 to 0.410)	49.4% and 0.045 and 0.002	
≤70%	11	0.107 (–0.108 to 0.323)	62.4% and 0.003 and 0.328	
Diabetes mellitus				No
>30%	–	–	–	
≤30%	17	0.286 (0.149 to 0.423)	55.7% and 0.003 and 0.001	
Hypertension				No
>70%	1	–0.030 (–0.560 to 0.50)	–	
≤70%	20	0.215 (0.087 to 0.344)	58.1% and 0.001 and 0.001	
Cigarette smoking				Yes, probably
>30%	5	0.707 (0.376 to 1.037)	63% and 0.029 and 0.001	
≤30%	6	0.032 (–0.261 to 0.325)	0.0% and 0.416 and 0.832	
Medication: Diuretic				No
>70%	1	–0.40 (–1.087 to 0.287)	–	
≤70%	3	0.202 (–0.012 to 0.417)	0.0% and 0.776 and 0.064	
Medication: ACEI				No
>70%	–	–	–	
≤70%	13	0.217 (0.067 to 0.367)	68.8% and 0.001 and 0.005	
Medication: Statin				No
>70%	–	–	–	
≤70%	11	0.321 (0.117 to 0.525)	71.9% and 0.001 and 0.002	
Medication: Beta-Blocker				No
>70%	2	–0.159 (–0.654 to 0.335)	0.0% and 0.322 and 0.528	
≤70%	7	0.083 (–0.087 to 0.252)	42.1% and 0.110 and 0.339	
Anti-coagulant status codes				Yes, probably
1	–	–	–	
2	4	–0.097 (–0.476 to 0.282)	0.0% and 0.860 and 0.617	
3	–	–	–	
4	2	0.341 (–0.269 to 0.952)	0.0% and 0.482 and 0.273	
5	16	0.230 (0.095 to 0.365)	64.5% and 0.001 and 0.001	
6	–	–	–	
AF				No
Chronic	–	–	–	
Non-chronic	21	0.181 (0.049 to 0.314)	56.3% and 0.001 and 0.007	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Type of AF				No
Paroxysmal	7	−0.036 (−0.291 to 0.218)	25.6% and 0.233 and 0.781	
Persistent	7	−0.077 (−0.383 to 0.229)	0.0% and 0.887 and 0.621	
Permanent	–	–	–	
NLR				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				Yes, probably
Asian	3	0.047 (−0.124 to 0.218)	0.0% and 0.552 and 0.588	
European	4	0.750 (0.565 to 0.936)	35.1% and 0.201 and 0.001	
Africa	–	–	–	
North American	–	–	–	
South American	–	–	–	
Australia	–	–	–	
Design of study				
Cohort		All of studies: cohort		
Case-control				
Number of population				No
>300	2	0.035 (−0.142 to 0.212)	0.0% and 0.340 and 0.698	
≤300	5	0.712 (0.533 to 0.891)	41.9% and 0.142 and 0.001	
Mean age				Yes, probably
>60 years	3	0.476 (0.183 to 0.770)	21.4% and 0.280 and 0.001	
≤60 years	4	0.346 (0.207 to 0.485)	90.8% and 0.001 and 0.001	
Male				No
>70%	2	0.035 (−0.142 to 0.212)	0.0% and 0.340 and 0.698	
≤70%	3	0.804 (0.610 to 0.997)	0.0% and 0.593 and 0.001	
Diabetes mellitus				
>30%		All of studies: ≤30%		
≤30%				
Hypertension				
>70%		All of studies: ≤70%		
≤70%				
Cigarette smoking				No
>30%	2	0.851 (0.626 to 1.077)	0.0% and 0.530 and 0.001	
≤30%	3	0.476 (0.183 to 0.770)	21.4% and 0.280 and 0.001	
Medication: Diuretic				
>70%		No data		
≤70%				
Medication: ACEI				No
>70%	–	–	–	
≤70%	2	0.819 (0.615 to 1.023)	0.0% and 0.360 and 0.001	
Medication: Statin				No
>70%	–	–	–	
≤70%	3	0.767 (0.572 to 0.963)	45.6% and 0.159 and 0.001	
Medication: Beta-Blocker				No
>70%	–	0.670 (0.291 to 1.049)	–	
≤70%	1		–	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Anti-coagulant status codes				No
1	–	–	–	
2	1	0.150 (−0.499 to 0.799)	–	
3	–	–	–	
4	–	–	–	
5	6	0.379 (0.250 to 0.507)	–	
6	–	–	–	
AF				No
Chronic	–	–	–	
Non-chronic	6	0.527 (0.370 to 0.684)	80% and 0.001 and 0.001	
Type of AF				No
Paroxysmal	2	0.670 (0.349 to 0.991)	0.0% and 1.000 and 0.001	
Persistent	1	0.150 (−0.499 to 0.799)	–	
Permanent	–	–	–	
RDW				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				Yes, probably
Asian	3	0.165 (0.051 to 0.279)	79.1% and 0.008 and 0.005	
European	2	0.803 (0.560 to 1.045)	0.0% and 0.425 and 0.001	
Africa	–	–	–	
North American	–	–	–	
South American	–	–	–	
Australia	–	–	–	
Design of study				No
Cohort	4	0.264 (0.155 to 0.372)	90.3% and 0.001 and 0.001	
Case-control	1	0.440 (0.102 to 0.778)	–	
Number of population				No
>300	1	0.100 (−0.023 to 0.223)	–	
≤300	4	0.705 (0.516 to 0.894)	31.2% and 0.225 and 0.001	
Mean age				Yes, probably
>60 years	3	0.165 (0.051 to 0.279)	79.1% and 0.008 and 0.005	
≤60 years	2	0.803 (0.560 to 1.045)	0.0% and 0.425 and 0.001	
Male				Yes, probably
>70%	2	0.129 (0.008 to 0.250)	85.1% and 0.010 and 0.036	
≤70%	3	0.680 (0.483 to 0.877)	43.8% and 0.169 and 0.001	
Diabetes mellitus				
>30%		All of studies: ≤30%		
≤30%				
Hypertension				
>70%			≤70%	
≤70%				
Cigarette smoking				No
>30%	3	0.680 (0.483 to 0.877)	43.8% and 0.169 and 0.001	
≤30%	–	–	–	
Medication: Diuretic				No
>70%	1	(0.329 to 1.671)	–	
≤70%	1	0.100 (−0.023 to 0.223)	–	

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Medication: ACEI				No
>70%	–	–	–	
≤70%	3	0.165 (0.051 to 0.279)	79.1% and 0.008 and 0.005	
Medication: Statin				No
>70%	–	–	–	
≤70%	1	0.440 (0.102 to 0.778)	–	
Medication: Beta-Blocker				No
>70%	1	1.000 (0.329 to 1.671)	–	
≤70%	2	0.140 (0.024 to 0.255)	70.8% and 0.064 and 0.018	
Anti-coagulant status codes	–			No
1	–	–	–	
2	–	–	–	
3	2	–	–	
4	3	0.661 (0.460 to 0.861)	60.3% and 0.113 and 0.001	
5	–	0.143 (0.023 to 0.263)	81.2% and 0.005 and 0.020	
6	–	–	–	
AF				
Chronic		All of studies: non–chronic		
Non-chronic				
Type of AF				No
Paroxysmal	2	0.511 (0.188 to 0.834)	46.9% and 0.170 to 0.002	
Persistent	–	–	–	
Permanent	–	–	–	
Hb				
Year of publication				
>2000		All of studies: after 2000		
≤2000				
Geographic area				No
Asian	5	0.046 (–0.133 to 0.226)	43.2% and 0.133 and 0.613	
European	4	0.007 (–0.306 to 0.319)	0.0% and 0.539 and 0.967	
Africa	–	–	–	
North American	–	–	–	
South American	–	–	–	
Australia	–	–	–	
Design of study				No
Cohort	8	0.029 (–0.131 to 0.189)	23.1% and 0.246 and 0.723	
Case-control	1	0.170 (–0.506 to 0.846)	–	
Number of population				No
>300	2	0.095 (–0.099 to 0.288)	54.4% and 0.139 and 0.336	
≤300	7	–0.070 (–0.331 to 0.191)	1.2% and 0.451 and 0.598	
Mean Age				No
>60 years	5	–0.057 (–0.258 to 0.144)	3.0% and 0.390 and 0.576	
≤60 years	4	0.177 (–0.069 to 0.422)	1.5% and 0.385 and 0.159	
Male				No
>70%	3	0.056 (–0.133 to 0.245)	65.4% and 0.056 and 0.563	
≤70%	5	0.035 (–0.248 to 0.319)	0.0% and 0.672 and 0.807	
Diabetes mellitus				
>30%		All of studies: ≤30%		
≤30%				

Subgroup	Studies (N)	WMD (95% CI)	I-squared and Heterogeneity-P-value and Effect-P-value respectively	Is this general item as heterogeneity factor? 1.Yes, probably 2. No
Hypertension				
>70%		All of studies: ≤70%		
≤70%				
Cigarette smoking				No
>30%	4	0.070 (−0.233 to 0.374)	0.0% and 0.582 and 0.650	
≤30%	2	−0.314 (−0.933 to 0.306)	0.0% and 0.645 and 0.321	
Medication: Diuretic				No
>70%	1	−0.800 (−1.706 to 0.106)	–	
≤70%	1	0.00 (−0.231 to 0.231)	–	
Medication: ACEI				No
>70%	–	–	–	
≤70%	5	−0.047 (−0.238 to 0.144)	0.0% and 0.494 and 0.630	
Medication: Statin				No
>70%	–	–	–	
≤70%	4	−0.096 (−0.442 to 0.250)	0.0% and 0.734 and 0.587	
Medication: Beta-Blocker				No
>70%	1	−0.800 (−1.706 to 0.106)	–	
≤70%	3	0.002 (−0.208 to 0.213)	0.0% and 0.782 and 0.984	
Anti-coagulant status codes				No
1	–	–	–	
2	–	–	–	
3	–	–	–	
4	2	0.236 (−0.161 to 0.632)	0.0% and 0.814 and 0.244	
5	7	0.00 (−0.169 to 0.169)	25.5% and 0.234 and 0.998	
6	–	–	–	
AF				No
Chronic	–	–	–	
Non-chronic	8	−0.031 (−0.204 to 0.142)	0.0% and 0.513 and 0.727	
Type of AF				
Paroxysmal	3	−0.070 (−0.531 to 0.391)	0.0% and 0.603 and 0.766	No
Persistent	–	–	–	
Permanent	–	–	–	

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