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«Μεθοδολογία Βιοϊατρικής Έρευνας, Βιοστατιστική
Και Κλινική Βιοπληροφορική»

Analysis of the Quality of Reporting of Randomized Controlled Trials in Anticoagulant versus Antiplatelet Medication in Deep Vein Thrombosis and Pulmonary Embolism as Governed by the CONSORT Statement

Ποιοτική ανάλυση των τυχαιοποιημένων κλινικών μελετών σχετικά με την χρήση αντιπηκτικής αγωγής ή αντιαιμοπεταλιακής αγωγής στην εν τω βάθει φλεβοθρόμβωση και πνευμονική εμβολή σύμφωνα με το CONSORT Statement

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ABSTRACT

BACKGROUND: Randomized controlled trials (RCTs) are the gold standard research in evaluating healthcare interventions. The CONSORT (Consolidated Standards of Reporting Trials) statement is an evidence-based approach to improve the quality of RCTs.

OBJECTIVE: To evaluate the reporting quality of published RCTs concerning the use of anticoagulants versus antiplatelet agents in deep vein thrombosis and pulmonary embolism according to the CONSORT statement.

METHODS: Electronic databases were searched for English-language RCTs involving patients who received either anticoagulant or antiplatelet medication in deep vein thrombosis and pulmonary embolism published from 2000 to 2019. Trials were considered eligible when participants were randomly assigned to at least two treatment arms and included patients who received either anticoagulant or antiplatelet medication in deep vein thrombosis and pulmonary embolism. Quality of reporting was assessed using a 37-item questionnaire based on the CONSORT checklist. Reporting was assessed in 2 publication periods (2000-2013) and (2014-2019). The effect of CONSORT statement in medical journals, according to their impact factor, has also been evaluated.

RESULTS: The search identified 11 eligible articles for analysis. Only 12 of the 37 items of the checklist were addressed in 75% or more of the studies. Most items concerning the methodological issues were reported by fewer than 50% of the studies. Improvements over time were seen for items that assessed the methodological quality with no statistically significant difference. RCTs published in high-ranked journals showed better quality of reporting.

CONCLUSIONS: Quality of reporting in RCTs focusing on the use of anticoagulants versus antiplatelet agents in deep vein thrombosis and pulmonary embolism remains unsatisfactory. Further improvement of reporting is necessary to assess the validity of clinical research.

Keywords: CONSORT, Randomized controlled trials, anticoagulants, antiplatelet medication, pulmonary embolism, deep vein thrombosis.

ΠΕΡΙΛΗΨΗ

ΕΙΣΑΓΩΓΗ: Οι τυχαιοποιημένες κλινικές μελέτες είναι το καλύτερο εργαλείο για την αξιολόγηση των κλινικών παρεμβάσεων. Η χρήση του CONSORT statement είναι μια τεκμηριωμένη προσέγγιση στη βελτίωση της ποιότητας των τυχαιοποιημένων κλινικών μελετών.

ΣΚΟΠΟΣ: Η αξιολόγηση της ποιότητας των δημοσιευμένων τυχαιοποιημένων κλινικών μελετών σχετικά με τη χρήση των αντιπηκτικών ή των αντιαιμοπεταλιακών φαρμάκων στην εν τω βάθει φλεβοθρόμβωση και στην πνευμονική εμβολή σύμφωνα με το CONSORT statement.

ΜΕΘΟΔΟΙ: Οι ηλεκτρονικές βάσεις δεδομένων αναζητήθηκαν για την εύρεση γραμμένων στην αγγλική γλώσσα τυχαιοποιημένων κλινικών μελετών που αφορούσαν ασθενείς που έλαβαν είτε αντιπηκτικά είτε αντιαιμοπεταλιακή φαρμακευτική αγωγή στην εν τω βάθει φλεβοθρόμβωση και στην πνευμονική εμβολή και δημοσιεύθηκαν την περίοδο 2000 έως 2019. Οι κλινικές μελέτες κρίθηκαν κατάλληλες όταν οι ασθενείς τυχαιοποιήθηκαν σε δύο τουλάχιστον ομάδες θεραπείας και περιελάμβαναν ασθενείς που έλαβαν είτε αντιπηκτικά είτε αντιαιμοπεταλιακά φάρμακα στην εν τω βάθει φλεβοθρόμβωση και στην πνευμονική εμβολή. Η αξιολόγηση της ποιότητας των άρθρων έγινε με τη χρήση του ερωτηματολογίου CONSORT με τις 37 ερωτήσεις. Η ποιοτική αξιολόγηση έγινε σε σε 2 περιόδους δημοσίευσης (2000-2013) και (2014-2019). Εκτιμήθηκε επίσης η σχέση μεταξύ του impact factor των ιατρικών περιοδικών και της συμφωνίας των αντίστοιχων άρθρων στο CONSORT statement.

ΑΠΟΤΕΛΕΣΜΑΤΑ: Η αναζήτηση αναγνώρισε 11 κατάλληλα άρθρα για ανάλυση. Μόνο 12 από τις 37 ερωτήσεις του ερωτηματολογίου αναφέρθηκαν σε ποσοστό πάνω από 75% των άρθρων. Οι περισσότερες ερωτήσεις σχετικά με τη μεθοδολογία αναφέρθηκαν σε λιγότερο από το 50% των μελετών. Βελτιώσεις με την πάροδο του χρόνου παρατηρήθηκαν στις ερωτήσεις που αξιολογούσαν τη μεθοδολογία των μελετών χωρίς ωστόσο στατιστικά σημαντική διαφορά. Οι τυχαιοποιημένες κλινικές μελέτες που δημοσιεύτηκαν σε περιοδικά με υψηλό impact factor παρουσίασαν καλύτερα αποτελέσματα ποιοτικής αξιολόγησης.

ΣΥΜΠΕΡΑΣΜΑ: Η ποιότητα των αναφορών των τυχαιοποιημένων κλινικών μελετών σχετικών με τη χρήση αντιπηκτικών ή αντιαιμοπεταλιακών φαρμάκων στην εν τω βάθει φλεβοθρόμβωση και στην πνευμονική εμβολή παραμένει μη ικανοποιητική. Η βελτίωση της ποιότητας της αναφοράς τους κρίνεται αναγκαία για την εκτίμηση της εγκυρότητας της κλινικής έρευνας.

BACKGROUND

Many manuscripts with various methodologies are submitted to biomedical journals annually. Among such manuscripts, Randomized Controlled Trials (RCTs) are at the top level of the evidence hierarchy. Their study design prevents selection and confounding bias and permits blinding of participants and researchers (1). The results of large RCTs have subsequently been translated into guidelines, as transparent and well-designed, conducted and reported RCTs are considered the gold standard research design in evaluating healthcare interventions (2).

However, in various fields of medicine, RCTs suffer from important methodological limitations. Poor reporting of RCTs impedes adequate understanding of the clinical indications and it is responsible for a great deal of avoidable waste in research (3,4). Readers and reviewers of published RCTs need complete, clearly written and transparent information on a study's methodology and findings in order to assess the quality and results of a trial. Because biases can occur in all aspects of studies, poor reporting limits the reader's appreciation of the finding's validity and reliability. This situation may lead to an underestimation or overestimation of the true intervention effect (5).

In response to these concerns about the quality of reporting of RCTs, an international group of clinical trialists, statisticians, epidemiologists, and journal editors, methodologists developed and published the CONsolidated Standards Of Reporting Trials (CONSORT) Statement in 1996 (6). The CONSORT Statement was reviewed in 2001and the most recent version was published in 2010. It contains 37 items (grouped according to the general format of a journal publication; namely, Title and Abstract, Methods, Results, Discussion, and Other Information such as funding) that allow the reader to understand the trial design, how it was conducted, its analysis and interpretation, and the validity of the study results (7).These items are recommended to be incorporated into an RCT. The statement provides guidance for reporting all RCTs with a focus on individually randomized, two groups, parallel trials. It is available as a guide with an explanation and examples for each item and a checklist (8) and it provides authors and editors with the means to write and publish RCTs that are as transparent and as complete as possible, allowing more effective sharing of knowledge and validation of research results by peers. It also consists of a flow diagram that displays the progress of all participants through the trial (7). Unfortunately, according to previous studies, it was observed poor adherence of RCTs to the CONSORT Checklist (9-12).

Venous thromboembolism (VTE), consisting of deep vein thrombosis and pulmonary embolism, is a major and often unrecognized cause of morbidity and mortality in hospitalized and ambulatory patients (13). Although many patients with VTE require extended treatment, it is uncertain whether it is better to use anticoagulant or antiplatelet medication. Randomized controlled trials have been conducted in order to determine whether therapeutic anticoagulation is superior to antiplatelet prophylaxis in the prevention of VTE (14-16).

Although numerous publications have used the CONSORT statement to evaluate the quality of reports of RCTs in various subspecialties of medicine, to our knowledge no publication has evaluated the quality of RCTs focusing on the use of anticoagulant versus antiplatelet medication in deep vein thrombosis and pulmonary embolism. Therefore, the purpose of the present study was to evaluate the compliance of RCTs with the CONSORT Statement, covering a period of the last 19 years in order to assess the quality of reporting of data that are used to inform current treatment guidelines and, hence, influence clinical practice.

Selected Abbreviations and Acronyms

RCT = randomized controlled trial

CONSORT = Consolidated Standards of Reporting Trials

VTE = Venous thromboembolism

IF = impact factor

MATERIALS AND METHODS

Data sources and search strategies

An electronic structured literature search was conducted using databases such as MEDLINE/PubMed, Cochrane library, ScienceDirect to identify possible studies for inclusion. The search strategy identified reports on RCTs involving patients who received either anticoagulants or antiplatelet medications in deep vein thrombosis and pulmonary embolism published within the time period January 2000 to August 2019. As a search criterion we used the combination of the following terms:((antiplatelet OR antiplatelet OR aspirin OR ASA OR acetylsalicylic acid OR dipyridamole OR aggrenox OR ticagrelor OR brilliant OR prasugrel OR clopidogrel OR plavix OR ticlodipine OR ticlid OR anticoagulant OR new oral anticoagulant OR novel oral anticoagulant OR noac OR heparin OR lmwh OR low molecular weight heparin OR vitamin k antagonist OR warfarin OR omnadin OR dalteparin OR fragmin OR enoxaparin OR coreno OR fondaparinux OR arixtra OR rivaroxaban OR xarelto OR pradaxa OR apixaban OR eliquis OR pradaxa OR bendix OR edoxaban OR lixiana OR savaysa)) AND (deep vein thrombosis OR DVT OR venous thromboembolism OR VTE OR pulmonary embolism OR PE).

In PubMed, we used as filters the “Randomized Controlled Trial” type of article, “English” language and “Humans” for species. We did not restrict studies with patients of different age or populations.

Eligibility of studies

In order to determine study eligibility, first, visual inspection of the study title, then the abstract, followed by the full manuscript was conducted. Trials were eligible if they had randomly assigned human subjects to at least two treatment arms and included patients who received either anticoagulant or antiplatelet medication in deep vein thrombosis and pulmonary embolism.

A study was defined as an RCT if the participants were assigned to interventions that were described as random, randomly allocated, randomized, or if randomization was mentioned, and if a control group was included. The control group could receive a placebo or a comparator.

Exclusion criteria were animal studies, reviews, and systematic reviews, meta-analyses, non-randomized studies, follow-up studies of previously published trials, studies with crossover design, economic analyses, safety analyses, dose-comparison studies, small pilot studies, case reports, abstracts, protocols and editorials.

Reporting assessment tool

The assessment of the adequacy of reporting will be evaluated according to the revised CONSORT 2010 checklist which includes a 37-item questionnaire (http://www.consort-statement.org). As guidelines the CONSORT explanation and elaboration document was used (17).

We grouped the reports in two publication periods (2000-2013) and (2014-2019) so as to test for reporting differences over time. Comparing the two time periods, we were able of detecting any improvement of reporting of CONSORT items and obtaining an indication in improvement of validity and quality of RCTs. We used the revised CONSORT version for all extracted articles either or not published before 2010 when the revised CONSORT version was published.

Methodological evaluation

All included articles were read in-depth. During the evaluation the followed procedures were followed:

- All items were investigated in terms of whether they were reported and not if they actually were carried out during the trial. Namely, each item can be characterized as 'yes' if it is clearly and adequately reported, or 'no' if it is partially unclear or not reported at all
- Alternative responses (apart of yes or no) or unclear responses to each question were coded as negative responses
- When an item was reported in a different section of the trial (title, abstract, methods, results, discussion) it was considered as a positive response
- We separated the reported articles into two publication groups: from 2000 to 2013 and from 2014 to 2019

Compliance with the CONSORT items more than 75% was regarded as an adequate cut-off in a number of studies (18-20). The greater than 75% (>75%) compliance with CONSORT statement items was calculated, for example the percentage of the articles (overall and by time period) addressed at least 75% of the 37 checklist items. Comparison among different time periods was made by using the Pearson chi-square test for trend. It was also calculated the percentage of the items per group reported in at least 75% of the articles for the 19-year period and in each time period. We ranked the included articles according to the ISI (Institute for Scientific Information) impact factor (IF) list for 2018 and we searched if high impact factor medical journals presented high compliance with the CONSORT statement. We divided articles into two groups to compare the adherence to the CONSORT statement of the articles in major IF medical journals (IF≥10) with the remaining eligible papers (IF<10). The selection of IF = 10 as the cut-off point was arbitrary. The statistical analysis was made on the IBM SPSS v.21 package. The cutoff point for statistical significance was set at the two-sided 0,05 level.

RESULTS

The process was made in five steps as can be seen in the flow diagram (figure 1). After assessment of title and abstract we excluded animal studies, non-randomized studies, follow-up studies of previously published trials, dose-comparison studies, small pilot studies, case reports, economic analyses, safety analyses, reviews, protocols and editorials. Crossover studies were also excluded. The remaining articles were retrieved in full text, 6 of which were found ineligible for the same reasons explained before and in conclusion 11 articles were included in qualitative analysis,

requiring complete full-text evaluation.

Out of the total 11 eligible trials 4 articles were published in the period 2000-2013 and 7 in 2014-2019.

All CONSORT items and the frequency of adherence to the individual criterion for each of these two periods and for the combined period are shown in Table 1.

In all of the time periods, only 12 items (32,4%) were reported by 75% or more of the studies. These include reporting of structured summary of trial design, methods, results, and conclusions, reporting of scientific background and explanation of rationale, reporting of specific objectives or hypotheses, reporting of description of trial design (such as parallel, factorial) including allocation ratio, reporting of eligibility criteria for participants, reporting of the interventions for each group with sufficient details to allow replication, including how and when they were actually administered, reporting of statistical methods used to compare groups for primary and secondary outcomes, reporting of dates defining the periods of recruitment and follow-up, reporting of a table showing baseline demographic and clinical characteristics for each group, reporting of for each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval), reporting of all important harms or unintended effects in each group and reporting of interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.

It is noticeable that 9 items were reported in all the articles. These include reporting of structured summary of trial design, methods, results, and conclusions, reporting of scientific background and explanation of rationale, reporting of specific objectives or hypotheses, reporting of description of trial design (such as parallel, factorial) including allocation ratio, reporting of the interventions for each group with sufficient details to allow replication, including how and when they were actually administered, reporting of statistical methods used to compare groups for primary and secondary outcomes, reporting of a table showing baseline demographic and clinical characteristics for each group, reporting of all important harms or unintended effects in each group and reporting of interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.

In contrast a number of reports were reported by only a small percentage of the trials in the two periods. For example, only 27% (3 of 11) of reports provided the identification as a randomized trial in the title and 1 only article reported the generalizability of the trial findings if it was applicable. Furthermore, 2 items were not reported at all. These include the reporting of any changes to trial outcomes after the trial commenced, with reasons and the reporting of presentation of both absolute and relative effect sizes for binary outcomes.

The numbers and the percentages of CONSORT items reported by each article are presented in Table 2. The average CONSORT compliance score was 54,9% (35% - 81%). Only one RCT covered more than 75% of the CONSORT items (81%) (21) whereas there were 7 articles with a CONSORT compliance more than 50% .

Period effect

Improvements over time were seen only for 5 of 37 CONSORT items, including the description of eligibility criteria for participants (p=0,17), reporting of who generated the random allocation

sequence, who enrolled participants, and who assigned participants to interventions (p=0,43), description of the similarity of interventions (p=0,24) and the reporting of registration number and name of trial registry (p=0,24) and where the full trial protocol can be assessed, if available (p=0,43). However, the comparison of each item showed no statistically significant differences between the two groups (p-value>0,05).

However, we observed that the reporting of the type of randomization as well as the description of the mechanism used to implement the random allocation sequence were inadequate in both periods.

Impact of CONSORT in High-Ranked Journals

Of the 11 study reports that we analyzed, 4 were published in high-ranked medical journals (IF≥10) and 7 in lower ranked medical journals (IF<10). We noticed that the RCTS of major IF journals performed better compliance with the CONSORT Statement items, as seen in Table 3.

DISCUSSION

In this study we drew upon CONSORT 2010 to evaluate the reporting quality of 11 RCTs with respect to their adherence to all the 37 items of the checklist. To our knowledge, this is the first application of CONSORT analysis to RCTs for anticoagulant versus antiplatelet medication in deep vein thrombosis and pulmonary embolism, covering a period of the last 19 years.

Our study shows that reports of RCTs involving patients prevented with anticoagulant or antiplatelet medication in deep vein thrombosis and pulmonary embolism do not conform absolutely to the guidelines of CONSORT. We found that the evaluated articles could have adhered more to CONSORT 2010 had they been conducted more meticulously. It was found that essential aspects of RCTs are underreported and no article satisfied all criteria evaluated in the study.

However, it was noticed that the RCTs of major IF journals have adhered better to the CONSORT statement and this can be explained by the fact that high-rank journals usually receive and select RCTs with the utmost quality.

Our findings recommend that authors should follow the CONSORT statement during the writing as the journal endorsement of the CONSORT statement might politely influence the completeness of reporting of RCTs. Pandis et al. (22) in their study concluded that the articles published in the period after the implementation of CONSORT reported more items. The CONSORT statement provides authors and editors with the means to write and publish RCTs that are as transparent and as complete as possible, allowing more effective sharing of knowledge and validation of research results by peers. Improving transparency is particularly important in the context of the replication crisis in science.

The study had several strengths. First and foremost among the strengths of the current study is that it included articles published in medical journals that clinicians can find in the PubMed database, in the Cochrane Library and in the ScienceDirect database. Besides, as the above mentioned search engines are open databases and the CONSORT statement is free, the methodology of this study is easily reproducible.

Our study, however, has some limitations. First, as we focused our research on restricting criteria

(specific period of time, written in the English language) the list of research articles found may not be exclusive, contributing to overall bias. Besides, the number of studies is low because RCTs comparing the efficacy and safety of anticoagulants with antiplatelet agents for the prevention of recurrent venous thromboembolism are still being carried out. In addition, the exclusion of specific studies mentioned above contributed to the small number of journals. Hence, generalizability of the findings may be limited.

Furthermore, the limitations of CONSORT must be considered. We used the revised CONSORT 2010 checklist for all the RCTs despite they were published before or after its publication. Besides, another limitation of our study is that it was designed so as to assess the quality of RCTs overall and not the actual performance of the trial procedures. Thus, a method of a trial that is not reported does not mean that it has not been performed. In addition, each item in the CONSORT Checklist carries a significant weight. For example, randomization, blinding, sample size determination, flow diagram, and registration number are important methodological items that can weigh differently in different studies; hence, reporting the whole score may not show the overall quality of the reported RCTs.

CONCLUSION

In conclusion, this study shows that the quality of reporting according to the CONSORT statement of most RCTs is low. It strongly recommends that investigators should be encouraged to adhere to the CONSORT Statement when reporting their RCTs, or even better, to emphasize the need to consider important aspects of interval validity during the planning stage of a trial. Editors of journals should also follow the recommendations. Thereby, RCTs reports based on CONSORT statement criteria can be improved specifically in the areas of methodology, results and discussions of papers and they will provide more valid estimates of treatment effects and serve as a reliable basis for the development of evidence-based guidelines.

Conflicts of interest statement

There are no conflicts of interest.

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Flow diagram

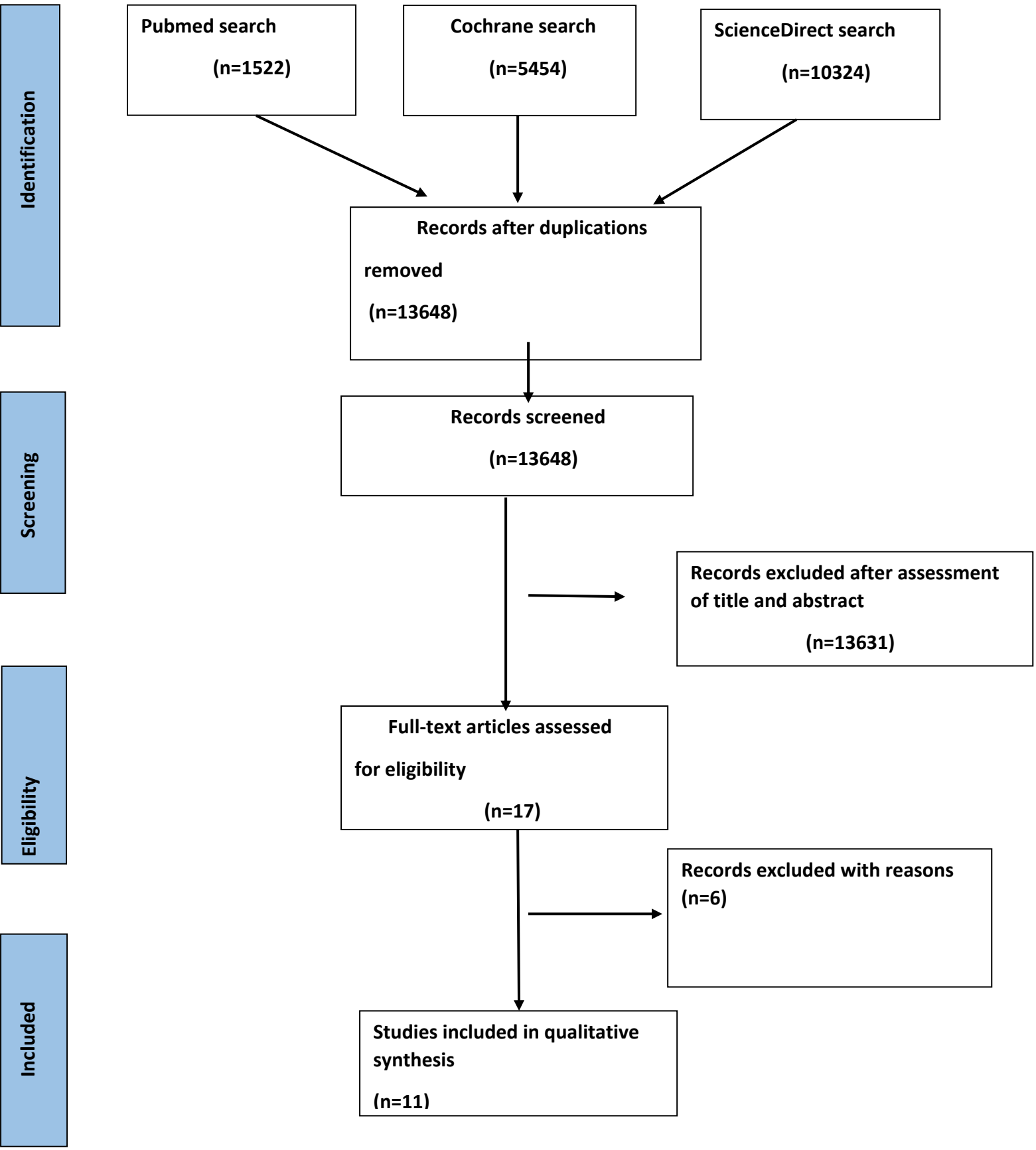

TABLE 1.Proportion of reporting of 37 data items in a total of 11 randomized controlled trials by publication period

Consort Item	Combined (2000-2019) (n=11)	2000-2013 (n=4)	2000-2019 (n=7)	P-value
TITLE AND ABSTRACT				
1a. Identification as a randomised trial in the title	3 (27%)	2 (50%)	1 (14%)	0,20
1b. Structured summary of trial design, methods, results, and conclusions	11 (100%)	4 (100%)	7 (100%)	1
INTRODUCTION				
2a. Scientific background and explanation of rationale	11 (100%)	4 (100%)	7 (100%)	1
2b. Specific objectives or hypotheses	11 (100%)	4 (100%)	7 (100%)	1
METHODS				
3a. Description of trial design (such as parallel, factorial) including allocation ratio	11 (100%)	4 (100%)	7 (100%)	1
3b. Important changes to methods after trial commencement (such as eligibility criteria), with reasons	2 (18%)	2 (50%)	0 (0%)	0,04
4a. Eligibility criteria for participants	10 (91%)	3 (75%)	7 (100%)	0,17
4b. Settings and locations where the data were collected	7 (64%)	4 (100%)	3 (43%)	0,06
5. The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	11 (100%)	4 (100%)	7 (100%)	1
6a. Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	7 (64%)	3 (75%)	4 (57%)	0,55
6b. Any changes to trial outcomes after the trial commenced, with reasons	0 (0%)	0 (0%)	0 (0%)	1
7a. How sample size was determined	7 (64%)	3 (75%)	4 (57%)	0,55
7b. When applicable, explanation of any interim analyses and stopping guidelines	3 (27%)	2 (50%)	1 (14%)	0,20
8a. Method used to generate the random allocation sequence	8 (73%)	3 (75%)	5 (71%)	0,90
8b. Type of randomisation; details of any restriction (such as blocking and block size)	3 (27%)	1 (25%)	2 (23%)	0,90
9. Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	2 (18%)	1 (25%)	1 (14%)	0,66
10. Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	1 (0,09%)	0 (0%)	1 (14%)	0,43
11a. If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	5 (45%)	2 (50%)	3 (43%)	0,82
11b. If relevant, description of the similarity of interventions	2 (18%)	0 (0%)	2 (23%)	0,24
12a Statistical methods used to compare groups for primary and secondary outcomes	11 (100%)	4 (100%)	7 (100%)	1
12b Methods for additional analyses, such as subgroup analyses and adjusted analyses	3 (27%)	3 (75%)	0 (0%)	0,007
RESULTS				
13a. For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	7 (64%)	4 (100%)	4 (57%)	0,12
13b. For each group, losses and exclusions after randomisation, together with reasons	6 (0,55%)	3 (75%)	3 (43%)	0,30
14a. Dates defining the periods of recruitment and follow-up	10 (91%)	4 (100%)	6 (86%)	0,43
14b. Why the trial ended or was stopped	1 (0,09%)	1 (25%)	0 (0%)	0,17
15. A table showing baseline demographic and clinical	11 (100%)	4 (100%)	7 (100%)	1

characteristics for each group				
16. For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	7 (64%)	3 (75%)	4 (57%)	0,55
17a. For each primary and secondary outcome, results for each group, and the estimated effect size and itsprecision (such as 95% confidence interval)	10 (91%)	4 (100%)	6 (86%)	0,43
17b. For binary outcomes, presentation of both absolute and relative effect sizes is recommended	0 (0%)	0 (0%)	0 (0%)	1
18. Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishingpre-specified from exploratory	5 (45%)	3 (75%)	2 (23%)	0,14
19. All important harms or unintended effects in each group	11 (100%)	4 (100%)	7 (100%)	1
DISCUSSION				
20. Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	8 (73%)	3 (75%)	5 (71%)	0,90
21. Generalisability (external validity, applicability) of the trial findings	1 (0,09%)	1 (25%)	0 (0%)	0,17
22. Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	11 (100%)	4 (100%)	7 (100%)	1
OTHER INFORMATION				
23. Registration number and name of trial registry	2 (18%)	0 (0%)	2 (23%)	0,24
24. Where the full trial protocol can be accessed, if available	1 (0,09%)	0 (0%)	1 (14%)	0,43
25. Sources of funding and other support (such as supply of drugs), role of funders	3 (27%)	1 (25%)	2 (23%)	0,90

CONSORT= Consolidated Standards of Reporting Trials
P value were obtained from chi-square tests for trend of associations between proportions for reporting an item and publication period across the two periods.

TABLE 2. List of the analyzed RCTs along with their CONSORT score

Study identification	Year	Journal	Compliance score
Palumbo et al. (26)	2014	Journal of Clinical Oncology	65%
Zou et al. (29)	2014	Blood Coagulation & Fibrinolysis	38%
Anderson et al.(21)	2013	Annals of Internal Medicine	81%
Westrich et al. (27)	2006	The Journal of Arthroplasty	38%

Weitz et al. (12)	2017	The New England Journal of Medicine	68%
Colleoni et al. (11)	2018	Revista Brasileira de Ortopedia	35%
Gelfer et al. (28)	2006	The Journal of Arthroplasty	62%
Yi et al. (25)	2014	Chinese Medical Journal	54%
Anderson et al. (10)	2018	The New England Journal of Medicine	71%
Pessotti et al. (24)	2014	Revista brasileira de cirurgia cardiovascular	41%
Yi et al. (23)	2014	Journal of Stroke and Cerebrovascular Diseases	51%

TABLE 3. Impact Factors 2018 of medical journals and Compliance score of relevant RCTs.

Medical Journal	Impact Factor (IF)	Article	Compliance Score
Annals of Internal Medicine	19.315	Anderson et al. 2013 (21)	81%
The New England Journal of Medicine	70.670	Anderson et al. 2014 (10)	71%
The New England Journal of Medicine	70.670	Weitz et al. 2017 (12)	68%
The Journal of Clinical Oncology	28.245	Palumbo et al. 2014 (26)	65%
The Journal of Arthroplasty	3.524	Gelfer et al. 2006 (28)	62%
Chinese Medical Journal	1.555	Yi et al. 2014 (25)	54%
Journal Stroke and Cerebrovascular Diseases	1.646	Yi et al. 2014 (23)	51%
Revista brasileira de cirurgia cardiovascular	0,796	Pessotti et al. 2014 (24)	41%
Blood Coagulation and Fibrinolysis	1.120	Zou et al. 2014 (29)	38%
The Journal of Arthroplasty	3.524	Westrich et al. 2006 (27)	38%
Revista Brasileira de Ortopedia	0.08	Colleoni et al. 2018 (11)	35%