

Reporting quality of animal studies published in journals listed in ULAKBIM TR index: a systematic review on compliance to the ARRIVE guidelines

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ABSTRACT: Transparent reporting of animal studies is key to ensure reproducibility. The primary guideline for reporting animal studies is the ARRIVE (Animal Research: Reporting of In Vivo Experiments). We aimed to evaluate the compliance to the updated ARRIVE guidelines (version 2.0, date 2020) in animal studies published in journals indexed by the Turkish Academic Network and Information Centre (ULAKBIM TR Index). This was a retrospective analysis of reporting quality of animal studies published in journals listed in ULAKBIM TR Index between January 2010 and August 2021. The percentage of articles that fully reported each " of the ARRIVE Essential 10: Compliance Questionnaire was calculated, and effects of journal- and article-related factors were evaluated. Totally, 235 articles published in 89 journals were included into the analysis. The mean percentage of fully reported items was 59.1%±10.9%, the least reported items being those related with bias – “blinding”, “allocation to study groups”, “assessment of statistical assumptions”, “excluded animals”, and “sample size calculation” (0.9%-10.6%). The journal’s publisher, frequency, language, being indexed in the Science Citation Index Expanded, and the ratio of animal studies had no significant effect on this percentage ($p>0.05$). However, journals supporting the ARRIVE guidelines had significantly higher compliance (62.1%±10.1% vs. 58.2%±11.0% for supporters and non-supporters, respectively; $p=0.017$, 95%CI -7.0 to -0.7). Articles published after 2015 had higher compliance to the ARRIVE guidelines than those published previously (60.9%±10.4% vs. 57.9%±11.1%, respectively; $p=0.037$, 95%CI -5.8 to -0.2). Although progress has been made, compliance to the ARRIVE guidelines is still low in animal studies published in journals listed in ULAKBIM TR Index – Turkey’s scientific journal database that covers over 800 peer-review journals. In order to increase the reporting quality and reproducibility of animal studies, it is imperative to raise awareness among researchers and journals, and to enforce the ARRIVE guidelines in editorial policy of journals.

KEYWORDS: Bibliographic database; experimental animal model; ethics; guideline adherence; journal article

1. INTRODUCTION

The reproducibility of animal experiments is critical to scientific knowledge and progress [1]. There has been increasing concern regarding challenges in reproducing preclinical experiments in animal models and translating them to clinical studies [2,3]. In order to maximise the quality and reliability of published animal research, and to enable others to better scrutinise, evaluate and reproduce it, the ARRIVE guidelines (Animal Research: Reporting of *In Vivo* Experiments) were first released in 2010 by an international group of researchers, journal editors, and related stakeholders [4]. The guidelines have since been revised and recently updated in 2020 as the ARRIVE guidelines version 2.0 [5]. The ARRIVE guidelines are a checklist of recommendations to ensure the transparent and thorough reporting of all types of research involving animals [5].

Although it has been more than 10 years since it was first published and supported by many journals and scientific organizations, compliance to the ARRIVE guideline is still not at the desired level [6,7]. It is also questioned whether compliance to the guidelines improves the quality of reporting animal studies [7,8]. Nevertheless, reporting quality of the literature should be continuously monitored in order to take effective measures to ensure transparency of animal research [9]. The studies evaluating the reporting quality of animal studies have been published on the basis of country, discipline, or animal model [10-14].

Turkey is a country that has experienced a rapid development in scientific publishing with growing number of peer-reviewed journals. The Turkish Academic Network and Information Centre (ULAKBIM), founded in 1996, has been indexing these journals (TR Index) according to the international standards in order

to increase their accessibility and quality [15]. The journals indexed in ULAKBIM TR Index covers a wide range of natural and social science disciplines and selected by the experts according to the predefined criteria [16]. In this system, where over 800 scientific journals are currently indexed, publications originating from animal studies have an important place and increasing impact on international literature. However, there is no study evaluating the quality of reporting and adherence to the ARRIVE guidelines in experimental animal studies published in journals indexed in ULAKBIM TR Index.

This study aims to evaluate the level of compliance to the ARRIVE guidelines 2.0, which was updated in 2020, and to determine the factors affecting this compliance in the experimental animal studies published in journals indexed in ULAKBIM TR Index.

2. RESULTS

2.1. Characteristics of the articles and journals

Totally, 235 articles published in 89 journals were included into the analysis. Of these 235 articles, 139 (59.1%) were published between 2010-2015 and the remaining 96 (40.9%) between 2016-2020. The number of authors was 6 or less in 162 (68.9%), and language of the article was English in 174 (74.0%).

The characteristics of the journals in which the selected articles were published are summarized in Table 1. The journals are published by either a scientific society (51.2%) or a university (48.8%) with a frequency of 4 (52.4%) or 6 (20.2%) times a year, fully (53.6%) or partly (39.3%) in English. Total number of articles per journal since 2010 ranges from 53 to 2184 (mean 598.9±408.2), of which 1% to 28.3% (mean 4.7%±4.3%) based on experimental animal studies. Besides ULAKBIM TR Index, 20.2% of the journals is also indexed in Science Citation Index Expanded (SCI-Exp), and 57.1% in other indexes including Scopus, Google Scholar, EMBASE, or Emerging Science Citation Index (SCI) (Table 1). Of the 84 journals in which selected 235 articles were published, only 21 (25%) supported ARRIVE, while the rest did not mention the need for ARRIVE compliance for animal studies in their instruction for authors section (Table 1).

Table 1. Characteristics of the journals (n=84) in which 235 articles were published

		Number of journals	%
Publisher	Society	43	51.2%
	University	41	48.8%
Frequency	≤4/year	63	75.0%
	>4/year	21	25.0%
Language	English	45	53.6%
	English/Turkish or Turkish	39	46.4%
International index (in addition to "ULAKBIM TR Index")	None	19	22.6%
	SCI-Exp	17	20.2%
	Indexes other than SCI-Exp	48	57.1%
ARRIVE support	Non-supporting	63	75.0%
	Supporting	21	25.0%
Total number of articles since 2010	≤500	43	51.2%
	>500	41	48.8%
Number of articles on animal studies since 2010	≤20	55	65.5%
	>20	29	34.5%
Ratio of number articles on animal studies to all articles in journal	≤5%	62	73.8%
	>5%	22	26.2%
Total		84	100%

Table 2. Compliance of 235 articles to the essential 10 items of ARRIVE guidelines 2.0

Item	Question(s)	Fully reported		Partially reported		Not reported		Not applicable	
		# of articles	%	# of articles	%	# of articles	%	# of articles	%
1. Study design	1.1. Are all experimental and control groups clearly identified?	228	97.0	5	2.1	1	0.4	1	0.4
	1.2. Is the experimental unit (e.g., an animal, litter or cage of animals) clearly identified?	227	96.6	7	3.0	0	0.0	1	0.4
2. Sample size	2.1. Is the exact number of experimental units in each group at the start of the study provided (e.g., in the format 'n=')?	203	86.4	6	2.6	26	11.1	0	0.0
	2.2. Is the method by which the sample size was chosen explained?	5	2.1	0	0.0	230	97.9	0	0.0
3. Inclusion & exclusion criteria	3.1. Are the criteria used for including and excluding animals, experimental units or data points provided?	8	3.4	2	0.9	225	95.7	0	0.0
	3.2. Are any exclusions of animals, experimental units, or data points reported, or is there a statement indicating that there were no exclusions?	11	4.7	0	0.0	224	95.3	0	0.0
4. Randomisation	4. Is the method by which experimental units were allocated to control and treatment groups described?	115	48.9	2	0.9	117	49.8	1	0.4
5. Blinding	5. Is it clear whether researchers were aware of, or blinded to, the group allocation at any stage of the experiment or data analysis?	25	10.6	1	0.4	209	88.9	0	0.0
6. Outcome measures	6. For all experimental outcomes presented, are details provided of exactly what parameter was measured?	228	97.0	4	1.7	3	1.3	0	0.0
7. Statistical methods	7.1. Is the statistical approach used to analyse each outcome detailed?	193	82.1	25	10.6	16	6.8	1	0.4
	7.2. Is there a description of any methods used to assess whether data met statistical assumptions?	56	23.8	1	0.4	177	75.3	1	0.4
8. Experimental animals	8.1. Are all species of animal used specified?	230	97.9	0	0.0	5	2.1	0	0.0
	8.2. Is the sex of the animals specified?	213	90.6	0	0.0	22	9.4	0	0.0
	8.3. Is at least one of age, weight or developmental stage of the animals specified?	226	96.2	0	0.0	9	3.8	0	0.0
9. Experimental procedures	9.1. Are both the timing and frequency with which procedures took place specified?	231	98.3	4	1.7	0	0.0	0	0.0
	9.2. Are details of acclimatisation periods to experimental locations provided?	146	62.1	21	8.9	64	27.2	3	1.3
10. Results	10.1. Are descriptive statistics for each experimental group provided, with a measure of variability (e.g., mean and SD, or median and range)?	155	66.0	4	1.7	74	31.5	1	0.4
	10.2. Is the effect size and confidence interval provided?	2	0.9	2	0.9	230	97.9	1	0.4

ARRIVE: Animal Research: Reporting of In Vivo Experiments

2.2. Compliance to the ARRIVE Guidelines 2.0

For each item of the guideline, the percentage of articles that “fully comply” with the ARRIVE Essential 10 ranged between 0.9% and 98.3% as those “partially comply” ranged between 0% to 10.6% (Table 2 and 3). Based on the percentage of fully reported items, compliance level to the ARRIVE guidelines was considered as moderate (50-80%) in 206 (87.7%), poor (<50%) in 27 (11.5%), and excellent (>80%) only in 2 (0.9%) articles.

While the highest compliance was recorded for the items related to the identification of animals and experimental procedure, the compliance was remarkably lower for the items on statistical analysis and sample size calculation (Table 3).

Table 3. Percentage of articles fully reporting individual essential items of the ARRIVE guidelines 2.0.

Item of the ARRIVE guidelines 2.0	Number of articles	%	Compliance level to ARRIVE 2.0
9.1. Are both the timing and frequency with which procedures took place specified?	231	98.3%	Excellent
8.1. Are all species of animal used specified?	230	97.9%	Excellent
1.1. Are all experimental and control groups clearly identified?	228	97.0%	Excellent
6. For all experimental outcomes presented. are details provided of exactly what parameter was measured?	228	97.0%	Excellent
1.2. Is the experimental unit (e.g. an animal. litter or cage of animals) clearly identified?	227	96.6%	Excellent
8.3. Is at least one of age. weight or developmental stage of the animals specified?	226	96.2%	Excellent
8.2. Is the sex of the animals specified?	213	90.6%	Excellent
2.1. Is the exact number of experimental units in each group at the start of the study provided (e.g. in the format ‘n=’)?	203	86.4%	Excellent
7.1. Is the statistical approach used to analyse each outcome detailed?	193	82.1%	Excellent
10.1. Are descriptive statistics for each experimental group provided. with a measure of variability (e.g. mean and SD. or median and range)?	155	66.0%	Moderate
9.2. Are details of acclimatisation periods to experimental locations provided?	146	62.1%	Moderate
4. Is the method by which experimental units were allocated to control and treatment groups described?	115	48.9%	Poor
7.2. Is there a description of any methods used to assess whether data met statistical assumptions?	56	23.8%	Poor
5. Is it clear whether researchers were aware of. or blinded to. the group allocation at any stage of the experiment or data analysis?	25	10.6%	Poor
3.2. Are any exclusions of animals. experimental units. or data points reported. or is there a statement indicating that there were no exclusions?	11	4.7%	Poor
3.1. Are the criteria used for including and excluding animals. experimental units. or data points provided?	8	3.4%	Poor
2.2. Is the method by which the sample size was chosen explained?	5	2.1%	Poor
10.2. Is the effect size and confidence interval provided?	2	0.9%	Poor

ARRIVE: Animal Research: Reporting of In Vivo Experiments

The mean percentage of fully reported items was 59.1%±10.9% for all articles (n=235). Among parameters of the journal in which the article was published; the publisher, frequency, language, being indexed in SCI-Exp, the total number of articles published, and the ratio of animal studies did not have a significant effect on this percentage ($p>0.05$ for all, Table 4). However, journal's support for the ARRIVE guidelines significantly increased the percentage of fully reported items (58.2%±11.0% vs. 62.1%±10.1%, for non-supporters and supporters, respectively; $p=0.017$, 95%CI -7.0 to -0.7; Table 4).

Considering the article-related parameters, the year of publication and the number of authors had a significant effect on compliance to the ARRIVE guidelines. The percentage of fully reported items was significantly higher in articles published in 2016 and later than those published previously (60.9%±10.4% vs. 57.9%±11.1%, respectively; $p=0.037$, 95%CI -5.8 to -0.2; Table 4). Articles with 7 or more authors also had a significantly higher percentage of fully reported items than those with 6 or fewer authors (62.4%±9.7% vs. 57.7%±11.1%, respectively; $p=0.002$, 95%CI -7.7 to -1.8; Table 4). Although percentage of fully reported items was higher in articles published in English (60.0%±10.5%) than in Turkish (56.8%±11.8%), the difference was not statistically significant ($p=0.053$, 95%CI -0.03 to 6.3; Table 4).

Table 4. Effect of journal- and article-related parameters on compliance to the ARRIVE guidelines

Journal-related parameters		Number of articles	% of fully reported items of ARRIVE guidelines	<i>p</i> value* [95% CI]
Publisher	Society	142	59.7%±10.5%	0.335 [-1.4 to 4.2]
	University	93	58.3%±11.5%	
Frequency	≤4/year	138	58.8%±11.4%	0.579 [-3.6 to 2.0]
	>4/year	97	59.6%±10.2%	
Language	English	140	59.7%±10.6%	0.364 [-1.5 to 4.1]
	English/Turkish or Turkish	95	58.4%±11.3%	
Indexed in SCI-Exp	Yes	91	60.1%±9.7%	0.271 [-4.5 to 1.3]
	No	144	58.5%±11.6%	
ARRIVE support	Non-supporting	175	58.2%±11.0%	0.017 [-7.0 to -0.7]
	Supporting	60	62.1%±10.1%	
Total number of articles since 2010	≤500	78	58.3%±11.1%	0.4225 [-4.2 to 1.7]
	>500	157	59.6%±10.8%	
Number of articles on animal studies since 2010	≤20	94	59.3%±11.0%	0.8822 [-2.6 to 3.1]
	>20	141	59.1%±10.9%	
Ratio of articles on animal studies to all articles in journal	≤5%	126	59.9%±11.1%	0.246 [-1.1 to 4.4]
	>5%	109	58.3%±10.7%	
Article-related parameters				
Number of authors	≤6	162	57.7%±11.1%	0.002 [-7.7 to -1.8]
	>6	73	62.4%±9.7%	
Publication year	2010-2015	139	57.9%±11.1%	0.037 [-5.8 to -0.2]
	2016-2020	96	60.9%±10.4%	
Language of article	English	174	60.0%±10.5%	0.053 [-0.03 to 6.3]
	Turkish	61	56.8%±11.8%	
Total		235	59.1%±10.9%	

*Equal variance t-test.

ULAKBIM TR Index: Journal Index of The Turkish Academic Network and Information Centre, ARRIVE: Animal Research: Reporting of In Vivo Experiments, SCI-Exp: Science Citation Index-Expanded (Web of Science) CI: Confidence interval

3. DISCUSSION

The reporting quality of animal studies has been a topic of interest, as the reproducibility and transparency of these studies have been heavily questioned in recent years [9,17,18]. While awareness on scientific, ethical and financial cost of irreproducible animal research is increasing, intensive efforts are being made to improve the reporting quality of animal studies. This is primarily achieved by a large-scale support of the guidelines by biomedical journals and the scientific community, and also by monitoring the reporting quality of animal studies. Despite all these efforts, recent reports stating that the reporting quality of animal studies continue to be low are noteworthy [4,7,9,19,20]. Due to the limited compliance to the ARRIVE guidelines, ARRIVE was updated in 2020 providing more practical usage by scientists, journal editors, reviewers and authors [5]. It is necessary to continue supporting the ARRIVE guidelines and monitor reporting quality of animal studies to increase reproducibility of experiments and animal welfare. While there are underlying reasons common to all animal studies for limited compliance to the guidelines, country-, animal model-, or disease-specific factors should also be considered. For this reason, there are many studies in the literature in which publications from different countries and on various animal models were evaluated for compliance to the ARRIVE guidelines [10,12-14,21]. Turkey has made a significant progress in scientific publishing in recent years and has become the source of an increasing number of biomedical journals and publications. In this study, we evaluated the reporting quality of articles based on animal studies published in ULAKBIM TR indexed journals, the Turkish database indexing over 800 biomedical journals, according to their compliance with the updated ARRIVE guidelines.

The results of our study showed that similar to the other reports [7,9], reporting quality of animal studies is low as indicated by mean percentage of fully reported items of the ARRIVE guidelines being only 59.1%±10.9% among 235 articles. Overall compliance to the ARRIVE guidelines was considered as “low to moderate” in 233 out of 235 articles. Leung *et al.* [7] reported that the percentage of fully reported items of the ARRIVE guidelines ranges between 51.8% and 60.5% of 236 articles depending on the year of publication and support of the journal for the ARRIVE guidelines. Other studies evaluating the compliance to the ARRIVE guidelines for articles from different journal databases, countries, and animal models also revealed this figure as 50%-60% [4,10,13,21,22].

It is remarkable that the least reported items are those related with bias such as “blinding”, “allocation to study groups”, “assessment of statistical assumptions”, “excluded animals”, “sample size calculation” (items “9.2”, “4”, “7.2”, “5”, “3.2”, “3.1”, “2.2”, “10.2”). This is in line with the previous analysis of experimental animal models [4,7,10,13,21-23]. Among these items, “sample size calculation” is of particular concern, as it is the least reported (0%-5%) and the most critical parameter for animal use and interpretation of findings.

In the present study, it was noted that the journal's support of the ARRIVE guideline significantly increased the reporting quality of the article. This is in contrary to the findings of Leung *et al.* [7] who reported that journal support for the ARRIVE guidelines has not resulted in an improvement in reporting quality. This difference between the two studies is likely to be due to the difference in time-frame and article sampling. As the present study covers 10 years after introduction of the ARRIVE guidelines analyzing all the experimental animal studies, Leung *et al.* [7] study covers 5 years reporting a selected sample of anesthesia, analgesia, and animal welfare papers. It was also noteworthy that as the time after the introduction of the ARRIVE guideline increases, compliance level of articles increases significantly. This finding is in line with previous studies [7] and indicates that awareness of the importance of reporting animal studies and the ARRIVE guidelines has increased in recent years. Although it was observed that the compliance to the ARRIVE guidelines was higher in the articles published in journals whose publication language was only in English and those indexed by SCI-Exp, this increase was not statistically significant. Similarly, it was seen that the compliance of the articles published in English to the ARRIVE guidelines was significantly higher, although not statistically significant, compared to the Turkish ones. A surprising finding was that the compliance to the ARRIVE guidelines was significantly higher in articles with 7 or more authors. This finding, which has not been reported in the literature before, suggests that the quality of reporting increases with increasing number of authors, which is the case for multidisciplinary studies.

The main limitations of the present study are subjective assessment of articles by two investigators, and evaluation of articles published in journals indexed only in ULAKBIM TR Index. We overcame the subjective

assessment by providing a consensus for the data evaluated differently by investigators. The present study only covers the journals listed in a national index, not allowing generalization of findings to other indexes or to other publications originating from Turkey.

On the basis of findings of the present study, our suggestions to improve the reporting quality of experimental animal studies are as follows:

- increasing awareness of importance of reporting quality, transparency, and reproducibility of animal studies among scientific societies, ethics committee members, journal editors, and researchers at the national level
- endorsement of the ARRIVE guidelines by journals through mandatory submission of completed ARRIVE Compliance Questionnaire at the article submission stage
- requirement of referring to the ARRIVE guideline in the ethics committee application files

4. CONCLUSION

In conclusion, although progress has been made in recent years, compliance to the ARRIVE guidelines is still low in experimental animal studies published in journals listed in ULAKBIM TR Index. This compliance is lowest for the items of the ARRIVE that are critical for animal welfare and interpretation of findings, such as blinding, allocation to study groups, assessment of statistical assumptions, excluded animals, and sample size calculation. In order to increase the reporting quality and reproducibility of animal studies, it is imperative to raise awareness among researchers and journals, and to enforce the ARRIVE guidelines in editorial policy.

5. MATERIALS AND METHODS

5.1. Study design and article sampling

This study was a retrospective analysis of reporting quality of published literature, performed between June-October 2021. For article sampling, "science database" in ULAKBIM TR Index source was systematically searched [15]. The subject categories were selected as "Medicine", "Dentistry", and "Pharmacy", and subject area were set to "all". The research terms were either of "rat", "mouse", "rabbit", or "guinea pig" (both in English and Turkish) in the abstract section. Articles reporting the results of animal-based experimental studies published between January 2010 and August 2021 were included. Articles published in journals that published 2 or less animal studies since 2010; review articles; only clinical; meta-analysis; unusual journal issue (e.g., supplement, meeting papers); duplications were excluded from the analysis.

In order to avoid article selection bias, "the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement" was taken as a basis during the selection of the articles included in the analysis [24]. This study does not involve any experimentation or data collection on humans or animals, thus does not require ethics committee approval [25].

Among 1090 preselected articles that were determined according to the article selection criteria, 230 to 285 are needed to have a confidence level of 95% that percentage of "fully reported" items is 25%-50%, predefined ratio of compliance to ARRIVE guidelines according to the literature, within margin error of 5% [7]. A total of 285 articles were selected by random sampling by using GraphPad random number generator to avoid sampling bias. After exclusion of 50 articles not complying to the selection criteria, the final sample size for analysis was 235 articles. The flow-chart showing the process of article selection and sampling was presented in Figure 1.

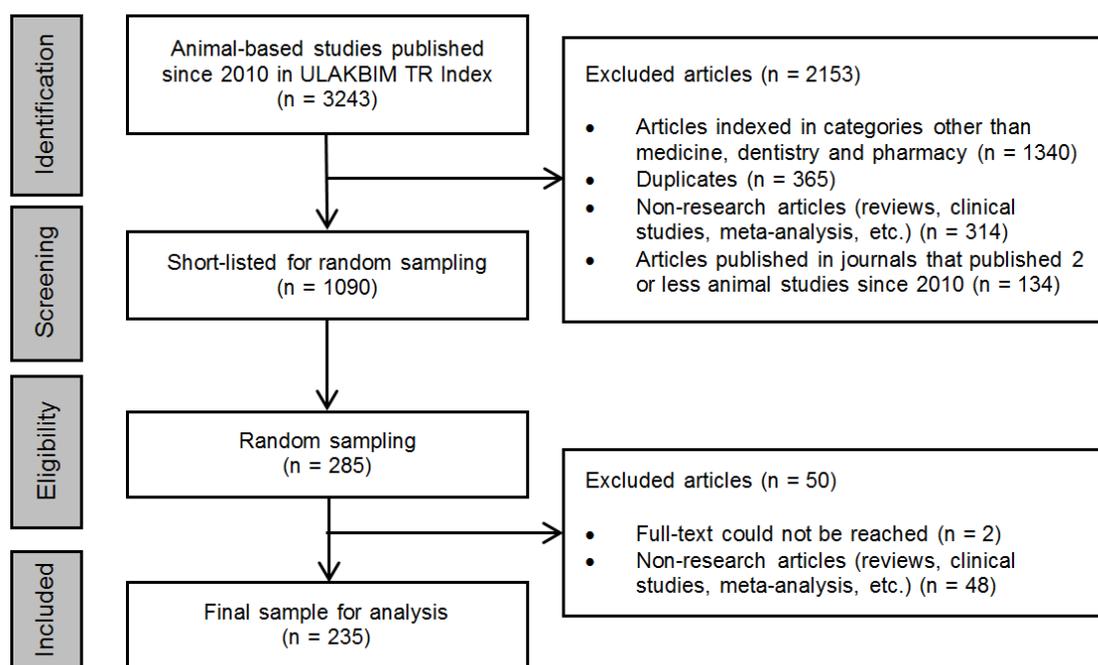


Figure 1. Prisma flow chart for the process of article selection and sampling

5.2. The ARRIVE Essential 10: Compliance Questionnaire

The ARRIVE guidelines contain a total of 21 items, 10 of which are determined to be “Essential 10” and the rest are “Recommended Set”, which complement the Essential 10 [5]. The guidelines are a useful resource for both authors preparing manuscripts describing animal research, and those assessing the quality of reporting and transparency of the manuscripts [5]. In order to increase the compliance of articles to the ARRIVE guidelines, a compliance questionnaire was prepared by the ARRIVE working group for use of those assessing the reporting quality of the manuscripts such as journal editors, peer reviewers, and researchers [5]. In our study, we used the items of ARRIVE Essential 10: Compliance Questionnaire to evaluate the compliance of the selected articles to the ARRIVE guidelines 2.0 [5]. For the assessment of risk of bias, we used the ARRIVE 2.0 items related with “blinding”, “allocation to study groups”, “assessment of statistical assumptions”, “excluded animals”, and “sample size calculation” (items “9.2”, “4”, “7.2”, “5”, “3.2”, “3.1”, “2.2”, “10.2”).

5.3. Outcomes

In order to estimate the level of adherence of the articles to the ARRIVE Essential 10: Compliance Questionnaire items, percentages of articles that “fully reported”, “partially reported” and “not reported” for each item were calculated. Additionally, ratio of articles classified according to the predefined quality thresholds (percentage of “fully reported” items) as excellent (>80%), average (50-80%), and poor (<50%) were also reported [6].

Effects of journal- and article-related factors on the compliance of articles to the ARRIVE guidelines were also evaluated. Journal-related factors were the support of the ARRIVE guidelines (supporting vs. non-supporting journals), publication language (English vs. Turkish or Turkish/English), frequency (quarterly vs. less), ratio of animal studies in all published articles in the last year, SCI-Exp indexing status (indexed vs. not-indexed), and publisher (university vs. scientific society). Article-related factors were the number of authors and date and language of the article.

Article selection and data extraction were performed independently by two authors (OEE and GÇ), and inconsistencies were resolved with consensus.

5.4. Statistical analysis

Data extracted from articles were entered into Microsoft Excel, and descriptive and comparative analysis were performed by using GraphPad Prism 5 for Windows (Version 5.01, GraphPad Software Inc., San Diego, California, USA). An equal variance t-test was used to compare the mean percentages of “fully reported” items of the ARRIVE guidelines between articles grouped according to the journal- and article-related parameters. Statistical level of significance was set to $p < 0.05$, and given together with 95% confidence interval (CI).

Author contributions: Concept – S.E.A., O.E.E., G.Ç.; Design – S.E.A., O.E.E., G.Ç.; Supervision – S.E.A.; Data Collection and/or Processing – S.E.A., O.E.E., G.Ç.; Analysis and/or Interpretation – S.E.A.; Literature Search – S.E.A., O.E.E., G.Ç.; Writing – S.E.A.; Critical Reviews – S.E.A., O.E.E., G.Ç.

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