Quality of Reporting in Preclinical Urethral Tissue Engineering Studies: A Systematic Review to Assess Adherence to the ARRIVE Guidelines

Tariq O. Abbas 1,2,3,4,* , Abubakr Elawad 2 , Abdul Kareem Pullattayil S. 5 and Cristian Pablo Pennisi 1

Abstract: Preclinical research within the area of urethral tissue engineering has not yet been successfully translated into an efficient therapeutic option for patients. This gap could be attributed, in part, to inadequate design and reporting of the studies employing laboratory animals. In this study, a systematic review was conducted to investigate the quality of reporting in preclinical studies utilizing tissue engineering approaches for urethral repair. The scope was on studies performed in rabbits, published between January 2014 and March 2020. Quality assessment of the data was conducted according to the Animal Research: Reporting of in Vivo Experiments (ARRIVE) guidelines by the scoring of a 38-item checklist in different categories. A total of 28 articles that fulfilled the eligibility criteria were included in the study. The range of ARRIVE score was from 0 to 100, taking into consideration having reported the item in question or not. The mean checklist score was 53%. The items that attained the highest scores included the number of animals utilized, the size of control and experimental groups, and the definition of experimental outcomes. The least frequently reported items included the data regarding the experimental procedure, housing and husbandry, determination and justification of the number of animals, and reporting of adverse events. Surprisingly, full disclosure about ethical guidelines and animal protocol approval was missing in 54% of the studies. No paper stated the sample size estimation methodology. The quality of reporting improved marginally over the study period. We encourage the utilization of the ARRIVE checklist items when reporting preclinical studies to help the publication of manuscripts that would allow a precise judgment of their scientific merit.

Keywords: urethral strictures; hypospadias; animal experiments; quality assessment; translational research

1 Regenerative Medicine Research Group, Department of Health Science and Technology, Aalborg University, 9220 Aalborg, Denmark; cpennisi@hst.aau.dk
2 Pediatric Urology Section, Sidra Medicine, Doha 26999, Qatar; aelawad@sidra.org
3 College of Medicine, Qatar University, Doha 2713, Qatar
4 Weill Cornell Medicine Qatar, Doha 24144, Qatar
5 Clinical Library, Sidra Medicine, Doha 26999, Qatar; apullattayil@gmail.com

* Correspondence: abbas@hst.aau.dk or tabbas@sidra.org

Citation: Abbas, T.O.; Elawad, A.; Pullattayil S., A.K.; Pennisi, C.P. Quality of Reporting in Preclinical Urethral Tissue Engineering Studies: A Systematic Review to Assess Adherence to the ARRIVE Guidelines. Animals 2021, 11, 2456. https://doi.org/10.3390/ani11082456

Academic Editors: Michael E. Davis and Emrah Yatkin

Received: 7 April 2021 Accepted: 17 August 2021 Published: 21 August 2021

Publisher’s Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).
1. Introduction

Urethral repair is considered a complex task for urologists, where the greatest demand
for clinical needs occurs following urethral strictures in adults and congenital anomalies
(e.g., hypospadias) in children. In adults, it has been estimated that 0.1% of men above
the age of 65 years suffer from urethral strictures, which can occur secondary to different
etiologies, including pelvic trauma, lichen sclerosus, non-specific urethritis, and iatrogenic
injuries [1]. The selection of the surgical management approach is based on the extent and
etiology of the stricture. For distal strictures, the approach includes initial endoscopic ure-
throtomy or dilatation, and subsequent surgical interventions are usually reserved to when
the urethrotomy fails, or the stricture recurs. For short strictures, anastomotic urethroplasty
generally solves the problem. The preferred surgical approach in strictures larger than
1 cm or complicated cases is replacement urethroplasty using an autologous graft that can
be used either as a patch or in full circumference. Although different sources of grafting
material have been tried, buccal mucosa is currently considered the preferred option owing
to its inherent lack of hair, compatibility with a moist environment, and a low rate of donor
site morbidity [2]. In pediatric patients, hypospadias has an incidence of around 1 per
300 male newborns, where the shortage of the urethra is a surgical challenge [3]. The
currently practiced surgical techniques for the management of these diseases have high
complication rates and need specific skills to be applied optimally [3–7]. For both adult and
pediatric patients, there is a wide consensus about the need for further consolidated basic
research, including the use of tissue engineering and regenerative medicine techniques for
urethral reconstruction [8–11].

Among the various animal models used to investigate male urethral repair strategies,
the rabbit model has been by far the most popular choice [10,12,13]. The male rabbit’s
urethra is easily accessible and possesses remarkable histological and functional similarities
to the human urethra, such as a thin epithelial layer supported by the highly vascularized
spongiosum and a urethral smooth muscle layer contributing to the urethral tone [14–18].
In addition, the size of an adult rabbit’s urethra is comparable to that of a male infant,
allowing the use of transurethral instrumentation and procedures employed in pediatric
surgery. Studies using rabbits have, therefore, been instrumental in demonstrating the
feasibility of urethral reconstruction using a variety of synthetic and natural polymeric
matrices [8–10]. Several approaches have been under scrutiny, most of which have shown
the ability to support the recovery of normal urethral architecture and function, with a
similar performance to that of autologous tissue grafts. However, a recent meta-analysis
of 63 preclinical and 13 human studies of tissue engineering for urethral reconstruction
revealed that the efficacy of these approaches could not be defined because of the lack
of well-controlled preclinical investigations. The study also revealed that the promising
preclinical results obtained using cell-laden matrices could surprisingly not be translated
into the clinical studies [10].

Studies in other fields have also shown a number of difficulties in assessing the ef-
cicacy or translating the results from animal research to the clinical context. The issues
include physiological variations among species and strains [19], lack of randomization
and blinding [20], inadequate reporting of methods and materials, and the publication
bias of not describing trials with adverse or indeterminate outcomes, which derive to an
overestimation of the impact of a therapy [21]. In 2009, the National Centre for the Replace-
ment, Refinement, and Reduction of Animals in Research (NC3Rs) examined the nature
of the reporting, experimental design, and statistical analysis in 271 published preclinical
experiments. The survey showed several shortcomings in study design, statistical analysis,
and reporting, and inspired the publication of the Animal Research: Reporting In Vivo
Experiments (ARRIVE) guidelines in 2010 [22–24]. The checklist consists of 20 items that
cover the critical data to be reported in a preclinical scientific paper. Despite increased
awareness in the scientific community, however, which includes the adoption of the guide-
lines by more than 1000 scientific journals, the quality of reporting has not significantly
improved in various research fields [25–27]. In 2018, the NC3Rs formed an international
working group involving journal editors, researchers, and statisticians from a variety of fields with the aim of reviewing and updating the guidelines [28]. As a result, a revised version of the guidelines has recently been published (ARRIVE 2.0) [29].

While the reasons the positive results obtained in preclinical studies for urethral repair have not been reproduced in the subsequent clinical trials are complex, poorly designed experiments and a lack of quality in reporting might be some of the main reasons that hinder clinical translation [30]. However, the quality of reporting in preclinical urethral tissue engineering studies remains unclear. Moreover, it is unknown if the quality of reporting has improved as a consequence of the introduction of the ARRIVE guidelines. This systematic review aims to address these research questions by performing a quality assessment using the ARRIVE guidelines as a checklist. The scope of the review was restricted to studies using rabbits, which are the most employed animal model for preclinical research in urethral reconstruction. The outcome assessment of different tissue engineering approaches is beyond the scope of this review, as has been addressed in other systematic reviews in the literature [12,31,32].

2. Methodology
2.1. Literature Search

Two separate searches were conducted in the databases MEDLINE of PubMed and EMBASE of OVID SP in March 2020. The search terms selected were as follows: rabbit, tissue engineering, stem cell, scaffolds, autologous graft, urethral graft, urethral reconstruction, regenerative medicine, reconstructive surgery, urethra, and animal experimentation. The search fields were controlled by database fields such as MeSH term, Text Word, and All Fields appropriate to the databases. “Publication date: 01/01/2014 to present” and “English language” filters were used. As the ARRIVE guidelines were first released in 2010, we selected to start our search in 2014, assuming that four years would allow the authors of preclinical studies sufficient time to plan, perform, and publish the results according to the guidelines. Details of the search are represented in the PRISMA flow diagram (Figure 1).

2.2. Screening

All retrieved publications were screened at the abstract level initially by the authors T.A. and A.K.P.S. The inclusion criteria were studies that evaluated urethral tissue engineering techniques in rabbits. Exclusion criteria included reviews, studies concerning reconstruction of other parts of the urinary tract, clinical studies, duplicates, and studies using other animal models (flow chart diagram, Figure 1). Group discussions resolved disputes regarding the appropriateness of an article. Eligible articles were included for full-text analysis.

2.3. Data Extraction

Extraction into a standardized data framework derived from the ARRIVE checklist [22] was conducted by two independent reviewers (A.K.P.S. and A.A.). The ARRIVE guideline consists of 20 items, some of which are further divided in subitems. For the purpose of this work, a list of 38 items was elaborated, which includes the items and subitems from the original ARRIVE guideline (Supplementary Table S1). Each of these 38 items was evaluated as “Yes” or “No” to indicate whether it was reported in the study or not. For some of the questions, a third option, “Not Applicable (N/A)”, was included to indicate items that were not relevant for the study (for example, in experiments employing only one experimental group, item 11a concerning allocation becomes N/A). Specific operational instructions (Supplementary Table S1) were provided to both reviewers before they read the selected full-text articles and extracted the data blinded to the analysis from the other reviewer. A training phase through the detailed description and examples of scoring was conducted among the authors before the commencement of the data extraction. Inconsistent data were consequently settled by an additional independent researcher (T.A.).
2.2. Screening
All retrieved publications were screened at the abstract level initially by the authors T.A. and A.K.P.S. The inclusion criteria were studies that evaluated urethral tissue engineering techniques in rabbits. Exclusion criteria included reviews, studies concerning reconstruction of other parts of the urinary tract, clinical studies, duplicates, and studies using other animal models (flow chart diagram, Figure 1). Group discussions resolved disputes regarding the appropriateness of an article. Eligible articles were included for full-text analysis.

2.3. Data Extraction
Extraction into a standardized data framework derived from the ARRIVE checklist [22] was conducted by two independent reviewers (A.K.P.S. and A.A.). The ARRIVE guideline consists of 20 items, some of which are further divided in subitems. For the purpose of this work, a list of 38 items was elaborated, which includes the items and subitems from the original ARRIVE guideline (Supplementary Table S1). Each of these 38 items was evaluated as “Yes” or “No” to indicate whether it was reported in the study or not. For some of the questions, a third option, “Not Applicable (N/A)”, was included to indicate items that were not relevant for the study (for example, in experiments employing only one experimental group, item 11a concerning allocation becomes N/A). Specific operational instructions (Supplementary Table S1) were provided to both reviewers before they read the selected full-text articles and extracted the data blinded to the analysis from the other reviewer. A training phase through the detailed description and examples of scoring was conducted among the authors before the commencement of the data

2.4. Data Analysis
The data were compiled employing a Microsoft Excel spreadsheet and analyzed using IBM SPSS Statistics (version 21). For each of the selected studies, a score was calculated, which represents the percentage of positively reported items. The score was calculated using the following formula:

$$\text{Score} = \left( \frac{N_{\text{yes}}}{38 - N_{\text{na}}} \right) \times 100$$  \hspace{1cm} (1)

where $N_{\text{yes}}$ = number of “Yes” entries, $N_{\text{na}}$ = number of “Not Applicable” entries, and 38 is the total number of items in the ARRIVE guideline. The units of analysis were the individual articles when assessing the scores, and the single ARRIVE item when assessing their adherence across studies. A further analysis was performed to assess the adherence of the studies to several subitems within the ARRIVE checklist. A Mann–Kendall nonparametric test was used to assess whether the scores had a monotonic trend over the years. This is a simple, but robust non-parametric test that does not require the data to be normally distributed or follow a linear trend. The intraclass correlation coefficient (ICC) analysis was utilized to examine the inter-rater agreement between the two reviewers. The ICC was selected because it reflects both degree of correlation and agreement between measurements. ICC values <0.5 are indicative of poor reliability, 0.5–0.75 indicate moderate reliability, 0.75–0.9 indicate good reliability, and >0.90 indicate excellent reliability [33]. Statistical significance was set at $p < 0.05$. 

**Figure 1.** PRISMA flow chart to outline the inclusion process for the articles in this study.
3. Results

As shown in Figure 1, a total of 189 articles were initially screened after the literature search. Following the inclusion and exclusion criteria, a total of 43 studies were selected for full-text reading (Figure 1). Only 28 studies were considered eligible for quality appraisal [34–61]. These studies comprise a range of approaches and scaffolds for urethral repair in rabbits, which are summarized in the Supplementary Table S2. The table provides details about the strain, sex, age, weight, number of animals, graft approach, material, and duration of the implantation. The numbers of rabbits in each experiment was 20 on average and ranged between 7 and 36, and the post-implantation follow-up duration was 5 months on average and varied between two weeks and nine months. All studies used male rabbits, except one study that included male and female animals. The most commonly studied approach was using acellular matrices as a patch (21 studies; length average (15 mm) range (5–20 mm)) versus tubes (7 studies; length average (20 mm) range (10–30 mm)).

After the full analysis was completed by the reviewers, the data were compiled in a spreadsheet (Supplementary File S1), which includes the responses to the 38 items in the operational table based on the ARRIVE guidelines (Supplementary Table S1). The ICC analysis to examine the inter-rater agreement had a value of 0.84 (95% CI 0.802–0.943), which is considered good. The frequencies of the options “Yes”, “No”, and “N/A” following assessment of the selected studies are depicted in Figure 2. It is evident that none of the analyzed articles scored “Yes” for all the items in the checklist or fully complied with the ARRIVE guidelines.

![Figure 2](image-url)

**Figure 2.** Bar chart displaying the frequencies of the options ‘Yes’, ‘No’, and ‘N/A’ among the 28 articles selected for the analysis.

The scores of each individual study, which are based upon the information presented in Figure 2 and compiled in the Supplementary File S1, are presented in Figure 3.
Figure 3. Bar chart displaying the scores of the analyzed articles. Scores represent the percentage adherence to the ARRIVE guidelines on a scale from 0 to 100.

The bar graph displays all the scores assigned to each of the 28 studies, from the lowest (36%) to the highest (65%). The average score was 53%. The general trend of the ARRIVE scores of the included articles over the 5-year study period is shown in Figure 4. The Kendall’s rank correlation coefficient (Tau) was found to be very low (0.102, \( p = 0.479 \)), indicating a weak upward trend in the score values over the analyzed period (2014–2020).

Figure 4. Trend in the score from 2014 to 2020. The trendline presented is from the Mann–Kendall trend analysis on the median of the scores. The stapled lines indicate the 95% confidence interval.
The scores for each of the checklist items are shown in Figure 5. The data were clustered into three groups to evidence the level of adherence to the guidelines of each of the 38 items in the checklist. While 34% of the items (13/38) appeared under the green category (agreement between 80 and 100%), 21% of the studies (8/38) appeared in the orange category (agreement between 50 and 79%), and 45% of the items (17/38) were associated with the red category (agreement between 0 and 49%).

![Figure 5](https://example.com/figure5.png)

**Figure 5.** Bar chart showing the degree of adherence (in %) to the 38 items in the ARRIVE checklist. The data were clustered to display the items in which studies had a high degree of adherence (between 80 and 100%, in green), medium degree of adherence (between 50 and 79%, in yellow), and low degree of adherence (0 to 49%, in red). Items are indicated by their corresponding numbers and a label associated with their content.

The items that attained the highest scores included the number of animals utilized, the size of experimental and control groups, and the definition of experimental outcomes. A description of the study background, including context and rationale, was also adequately provided in all of the studies. However, variables relevant to the reproducibility of the experiments were not often disclosed. The least frequently reported checklist items (only found in ≤10% of the studies) were items 18c (interpretation), 7b (experimental procedures), 17b (adverse events), 6c (experimental unit), 13b (analysis unit), 7d (procedure rational), 11b (animal allocation), 13c (statistical design), and 10b (sample size). These items are related to information on test methods, sample size calculation, statistical approaches, adverse events, and interpretation/scientific outcomes. Although statistical methods were disclosed and described in almost two-thirds of the articles, the statement of statistical methodology was frequently inadequate. Most articles did not include information about data distribution, definition of the unit of analysis, or justification for choosing a specific analytical method.

Surprisingly, none of the articles disclosed the approach to verify that the assumptions for the statistical methods were met. Although every article described the experimental results, some of them failed in specifying the primary and secondary outcomes.
The adherence of the studies to the different parts, rather than the overall item, is shown separately in a table format (Table 1). Concerning the compliance to ethical standards, 92% of the analyzed studies stated that the protocol was approved and 89% referred to national or international guidelines (Table 1a). However, a complete ethical statement, disclosing both the approval of the protocol and guidelines followed, was only present in 46% of the studies. Concerning study design, there were various essential items that were poorly reported. While recording of randomization (6.b) scored 46%, none of the 28 studies reported sample size estimation or steps to reduce assessment bias (Table 1b). Regarding item 7a (experimental procedure), while it scored 96% owing to the majority of studies reporting surgical procedures and anesthesia, very few studies reported postoperative analgesia or euthanasia (Table 1c). Regarding the details of the animals, the most frequently reported information was the weight. However, only 14% of the studies provided the age of the animals (Table 1d). Details concerning the animal’s housing (9a) were infrequently listed (less than 30% of all studies). Only few studies reported the type of facility, cage, bedding material, or number of cage companions (Table 1e). Data about nutritional aspects and environment, such as temperature, humidity, and access to water and food, were also infrequently reported. No environmental enrichment was reported in any of the studies (Table 1f). In relation to the study limitations (18.b), most studies stated general limitations and potential sources of bias. However, only few articles addressed the limitations of the animal model or imprecision of the results (Table 1g).

Table 1. Analysis of adherence of the studies to selected items in the checklist.

| (a) Item 5: Ethical statements | Ratio | %  |
|-------------------------------|-------|----|
| Refers to guidelines          | 25/28 | 89 |
| Approved protocol             | 26/28 | 92 |
| (b) Item 6b: Steps to minimize subjective bias in the study design | | |
| Random allocation             | 13/28 | 46 |
| Blind assessment              | 0/28  | 0  |
| (c) Item 7a: Information about experimental procedures | | |
| Surgical procedure            | 20/28 | 71 |
| Anesthesia                    | 22/28 | 79 |
| Post-operative analgesia      | 4/28  | 14 |
| Method of euthanasia          | 4/28  | 14 |
| (d) Item 8a: Details about animals in the experimental design | | |
| Sex                           | 28/28 | 100|
| Weight and age                | 4/28  | 14 |
| Weight but not age            | 18/28 | 64 |
| Age but not weight            | 0/28  | 0  |
| (e) Item 9a: Information about housing conditions | | |
| Type of facility              | 5/28  | 18 |
| Type of cage                  | 3/28  | 11 |
| Bedding material              | 1/28  | 4  |
| Number of cage companions     | 1/28  | 4  |
4. Discussion

Studies utilizing animal models play a key role in scientific discovery, given that the tests are composed, executed, evaluated, and appropriately communicated following internationally accepted guidelines. A loss of transparency in preclinical research studies has been recognized [62]. Several fundamental components of the experimental design are often overlooked in these published studies, which contributes to irreproducibility of the experiments. Preclinical studies investigating tissue engineering for urethral repair do not seem to be an exception.

Our study determined that the quality of reporting of some key items that influence the interpretation of the study was generally poor in preclinical studies of tissue engineering for urethral repair, and that the quality of reporting improved very slightly over the study period. Noticeably, some details to ensure the reproducibility of preclinical studies, such as animal housing, husbandry, and anesthetics, were infrequently reported, which may significantly affect the study results. For instance, studies have shown that the type of anesthetics may affect the long-term behavior of the animals [63]. Prager et al. stated that housing and husbandry conditions might significantly affect the behavior of rodents and, consequently, influence the results [64]. Confining animals to small cages or keeping several animals per cage after urethroplasty carries a potential risk of higher infection rates [65], and increases the chances of stents’ dislodgement [66] as well as surgical site trauma. There was a low degree of adherence to guidelines in items concerning experimental design, e.g., allocation of the animals to groups and assessor blinding. As studies have shown, these items are fundamental not only to ensure adequate statistical analysis, but also to comply with the ethical principles, as they intend to decrease subjective bias and minimize the number of animals utilized in the study [62,67]. Sample size calculation, randomization, and blinding were also considered to be crucial for transparency and validation of experiments as per the Landis core reporting standards [62]. Our results agree with data from other biomedical areas in which preclinical research has been carried out.

For instance, a study on preclinical research done in the field of rheumatology revealed a lack of reporting of several important items, including the calculation of animal numbers (0%); allocation (0%); randomization (0%); housing and husbandry conditions (5%); and reflection on the replacement, reduction, and refinement principles (3Rs) (0%) [27]. Thus, while a lack of information does not appear to be unique to the field of urethral repair, it is important to stress that proper randomization, allocation, and blinding will be more likely to produce reliable results, which minimize the risk of bias and exaggerated effect sizes [68]. We have found that only three of the articles enrolled in our analysis discussed the “how and why” concerning the animal model utilized and its relevance to human pathology. We believe that this information is of significant importance in tissue engineering for urethral repair experiments, given the fact that no single animal model is considered the best.
representative for human pathology and significant differences exist between the human and animal genital anatomy.

Surprisingly, while most articles presented the essential features of the experimental animals (e.g., strain, sex, age, and weight), no study disclosed the sample size estimation method. While calculation of an accurate sample size might be quite challenging owing to difficulties in the estimation of complication rates and the inherent dispersion of the model, there are some valid alternative approaches to estimate the number of animals needed in an experiment. These approaches include, for instance, performing pilot experiments at a scale that would allow indicating the standard deviation or using Mead’s resource equation when power analysis is not possible. The resource equation approach is useful when there is no available information about standard deviation and/or it is challenging specifying an effect size likely to be clinically meaningful [67].

Another critical finding of our study was related to the lack of discussion about study limitations in the analyzed articles. Moreover, elaboration on the feasibility of translation of the findings into other animal species and human clinical trials was lacking in most of the discussion sections. Efforts should be made to empower the 3Rs principles, making sure to wisely utilize laboratory animals and the available alternative approaches. In addition, to ensure reliable translation of the findings in clinical trials, studies should include a statement indicating measures taken to reduce significant adverse events, as there is a reasonable chance that adverse events may occur as a result of the research procedures.

Our study did not assess whether or not the journals in the analyzed dataset supported the ARRIVE guidelines at the time of submission. While it was not possible to determine how the data might have been biased by publishers, there are several reasons that indicate that their influence has been modest. A recent study demonstrated that a change in the editorial policy of the Nature Publishing group, which requires authors to follow a set of strict guidelines for reporting in vivo research, did not substantially increase the overall compliance [69]. On the other hand, checklist assessments and completion by peer review were not practical, possibly owing to the busy nature of the review process [70]. Various outcomes have been reported in studies evaluating the impact that adherence to the ARRIVE checklist had on the quality of the articles published [71,72]. Interestingly, a randomized controlled trial revealed that mandating the completion of an ARRIVE checklist during paper submission did not help to promote adherence to the guidelines in the articles [73]. As studies have shown, current measures such as endorsement by reviewers and editors to comply with the ARRIVE checklist did not appear to significantly improve the quality of reporting [71,73]. Alternatively, the recently published PREPARE (Planning Research and Experimental Procedures on Animals: Recommendations for Excellence) guidelines [74] might be helpful to enforce more attention to experimental rigor at the earlier phases of the research process.

It is worth noting that the reporting checklists are not strictly universal for experiments related to the different types of interventional studies. Therefore, it is critically important to utilize a suitable type of reporting guidelines accordingly. The EQUATOR (enhancing the quality and transparency of health research) international network [75] enhances the adherence to fulfilling the requirements of adequate reporting in a sensible, transparent, and reproducible manner.

In our assessment of the literature, we employed the ARRIVE guidelines available at the time of the data analysis (version 1.0), which comprise a total of 38 discrete evaluation items. As a means to gain more insight into the quality of the published studies, it has been proposed to arbitrarily operationalize the checklist in more evaluation items. For instance, in a review on preclinical experiments of acute lung injury, Avey et al. have chosen to operationalize the checklist into 109 discrete sub-items [76]. However, this approach might transform the analysis of a large number of articles in a tedious and time-consuming process. To overcome these difficulties, the working group in charge of the revision of the guidelines previously suggested to organize the parts in the ARRIVE checklist into tiers indicating various degrees of priority [28]. This approach would allow prioritizing some of the key
items in the checklist to initially minimize the burden of analysis and provide measures that could be more easily followed by the scientific community. As a conclusion of the work done by the group and concurrently with the completion of this study, ARRIVE version 2.0 has been released [29]. The new version prioritizes the items, adds new information, and provides an accompanying explanation and elaboration (E&E) document to improve the understanding of the application and rationale of each item. The checklist items have been divided into “ARRIVE Essential 10” with the minimum requirements in the manuscripts and “Recommended set” that adds context to the study described. This prioritization scheme is expected to improve adherence to ARRIVE guidelines by paying attention to basic items followed by the gradual fulfillment of the recommended items.

One of the strengths of our study is that it provides an assessment approach that could be utilized to evaluate the reporting quality in several pre-clinical research fields. To value the training effects, there were two independent reviewers who individually scored the different items, and a third reviewer who decided on the discrepant points. Subjectivity of the assessment by the several observers might be considered a limitation in our study. Nevertheless, the great inter-observer agreement confirmed that the analysts had a consistent assessment criterion. Our reviews were performed on studies published between 2014 and 2020, and restricted to experiments on rabbits. When analyzing systematic reviews in the topic of urethral tissue engineering that include studies prior to 2014 and experiments using other animal models, it becomes evident that rabbits represent by far the most frequently used model, comprising 31 studies performed until January 2017. That represents approximately 73% of the total of the studies, versus 24% of studies in dogs and 3% in rats [10,12,31,32]. It is therefore reasonable to assume that our sample (28 studies) would be representative of the general reporting quality in preclinical urethral tissue engineering research. However, further research is required to determine if the results presented here would have been significantly affected by including studies prior to 2014 or studies in other animal species. Although we analyzed the quality of the reporting of animal experiments, we cannot reflect on the overall nature of each research study. Therefore, it would be challenging to judge whether such investigations are flawed owing to a lack of reporting of methodological details. Lastly, one of the limitations of our operationalization table is that it involves several sub items and partial reporting could be considered as “Yes”. For this reason, we have added sub-item analysis to assess the adherence to each single sub item rather than the overall item.

5. Conclusions

Our study recognized that published animal experiments studying tissue engineering approaches for urethral repair display inadequate reporting of fundamental information. The quality of reporting improved only marginally over the study period. Inadequate reporting of the critical points of research experiments could remarkably affect the clarity, reproducibility, and translatability. We encourage the utilization of the ARRIVE checklist items when reporting preclinical studies to help the publication of manuscripts that would allow a precise judgment of their scientific merit. This has the potential to enhance both the translatability of the findings to humans and the fulfilment of the ethical requirements and further supports objective comparison between different studies.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ani11082456/s1, Table S1: Operationalized checklist for the assessment of the quality of reporting in urethral tissue engineering studies. Excerpts from the original ARRIVE guidelines were reformulated as operational questions in the table. The ARRIVE guidelines are published in an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY) [22]. Table S2: Summary of the main aspects of the analyzed studies. File S1: Data collected and analyzed in this study.

Author Contributions: Conceptualization, T.O.A. and A.K.P.S.; Data Collection, T.O.A., A.K.P.S. and A.E.; Analyses of the information, T.O.A., A.K.P.S. and C.P.P.; Writing—original draft preparation,
Animals 2021, 11, 2456

T.O.A.; Writing—review and editing, T.O.A. and C.P.P. All authors have read and agreed to the published version of the manuscript.

Funding: The author(s) received no financial support for the research or authorship.

Institutional Review Board Statement: Not applicable.

Data Availability Statement: The data analyzed in this study are available as supplementary material (Supplementary File S1).

Acknowledgments: We thank the anonymous reviewers for their thoughtful comments that improved the manuscript and Prem Chandra, Biostatistician, Hamad Medical Corporation, Doha, Qatar for his valuable help. We thank Sidra Medicine for providing support to cover the open access fees of this article.

Conflicts of Interest: The authors disclosed no potential conflict of interest concerning the research, authorship, and/or publication of this article.

References

1. Santucci, R.A.; Joyce, G.F.; Wise, M. Male Urethral Stricture Disease. J. Urol. 2007, 177, 1667–1674. [CrossRef]
2. Mangir, N.; Wilson, K.J.; Osman, N.I.; Chapple, C.R. Current state of urethral tissue engineering. Curr. Opin. Urol. 2019, 29, 385–393. [CrossRef]
3. Keays, M.A.; Dave, S. Current hypospadias management: Diagnosis, surgical management, and long-term patient-centred outcomes. Can. Urol. Assoc. J. 2017, 11, S48–S53. [CrossRef]
4. Chapple, C.; Andrich, D.; Atala, A.; Barbagli, G.; Cavalcanti, A.; Kulkarni, S.; Maga, A.; Nakajima, Y. SIU/ICUD Consultation on Urethral Strictures: The Management of Anterior Urethral Stricture Disease Using Substitution Urethroplasty. Urology 2014, 83, S51–S47. [CrossRef]
5. Snodgrass, W.; Bush, N. Primary hypospadias repair techniques: A review of the evidence. Urol. Ann. 2016, 8, 403–408. [CrossRef]
6. Barbagli, G.; Sansalone, S.; Djinovic, R.; Romano, G.; Lazzeri, M. Current controversies in reconstructive surgery of the anterior urethra: A clinical overview. Int. Braz. J. Urol. 2012, 38, 307–316. [CrossRef] [PubMed]
7. Mundy, A.R.; Andrich, D.E. Urethral strictures. BJU Int. 2011, 107, 6–26. [CrossRef] [PubMed]
8. Abbas, T.O.; Mahdi, E.; Hasan, A.; AlAnsari, A.; Pennisi, C.P. Current Status of Tissue Engineering in the Management of Severe Hypospadias. Front. Pediatr. 2018, 5, 283. [CrossRef] [PubMed]
9. Abbas, T.O.; Yalcin, H.C.; Pennisi, C.P. From Acellular Matrices to Smart Polymers: Degradable Scaffolds that are Transforming the Shape of Urethral Tissue Engineering. Int. J. Mol. Sci. 2019, 20, 1763. [CrossRef] [PubMed]
10. Versteegden, L.R.M.; de Jonge, P.K.J.D.; IntHout, J.; van Kuppevelt, T.H.; Oosterwijk, E.; Feitz, W.F.J.; de Vries, R.B.M.; Daamen, W.F. Tissue Engineering of the Urethra: A Systematic Review and Meta-analysis of Preclinical and Clinical Studies. Eur. Urol. 2017, 72, 594–606. [CrossRef]
11. Sievert, K.-D. Tissue Engineering of the Urethra: Solid Basic Research and Farsighted Planning are Required for Clinical Application. Eur. Urol. 2017, 72, 607–609. [CrossRef]
12. Qi, N.; Li, W.; Tian, H. A Systematic Review of Animal and Clinical Studies on the Use of Scaffolds for Urethral Repair. Acta Acad. Med. Wuhu 2016, 36, 111–117. [CrossRef]
13. Rosito, T.E.; Pires, J.A.S.; Delcelo, R.; Ortiz, V.; Macedo Jr, A. Macroscopic and histological evaluation of tunica vaginalis dorsal grafting in the first stage of Bracka’s urethroplasty: An experimental study in rabbits. BJU Int. 2011, 108, E17–E22. [CrossRef] [PubMed]
14. Faydaci, G.; Tarhan, F.; Tuncan, M.; Eryildirim, B.; Celik, O.; Keser, S.H.; Özgül, A. Comparison of Two Experimental Models for Urethral Stricture in the Anterior Urethra of the Male Rabbit. Urology 2012, 80, 225.e7–225.e11. [CrossRef] [PubMed]
15. Zhang, K.; Fu, Q.; Yoo, J.; Chen, X.; Chandra, P.; Mo, X.; Song, L.; Atala, A.; Zhao, W. 3D bioprinting of urethra with PCL/PLCL blend and dual autologous cells in fibrin hydrogel: An in vitro evaluation of biomechanical mechanical property and cell growth environment. Acta Biomater. 2017, 50, 154–164. [CrossRef] [PubMed]
16. Theodorescu, D.; Balcom, A.; Smith, C.; McLorie, G.; Churchill, B.; Khoury, A. Urethral replacement with vascularized tunica vaginalis: Defining the optimal form of use. J. Urol. 1998, 159, 1708–1711. [CrossRef]
17. Kemppainen, E.; Talja, M.; Riihelä, M.; Pohjonen, T.; Törmälä, P.; Alfthan, O. A bioresorbable urethral stent. An experimental study. Urol. Res. 1993, 21, 235–238. Available online: http://www.ncbi.nlm.nih.gov/pubmed/8342257 (accessed on 17 February 2021). [CrossRef]
18. Bradley, J.E.; Anderson, U.A.; Woolsey, S.M.; Thornbury, K.D.; McHale, N.G.; Hollywood, M.A. Characterization of T-type calcium current and its contribution to electrical activity in rabbit urethra. Am. J. Physiol. Cell Physiol. 2004, 286, C1078–C1088. [CrossRef] [PubMed]
19. Festing, M.F.W. The choice of animal model and reduction. Altern. Lab. Anim. 2004, 32 (Suppl. 2), 59–64. Available online: http://www.ncbi.nlm.nih.gov/pubmed/15601228 (accessed on 17 February 2021). [CrossRef] [PubMed]
20. Mignini, L.E.; Khan, K.S. Methodological quality of systematic reviews of animal studies: A survey of reviews of basic research. *BMC Med. Res. Methodol.* 2006, 6, 10. [CrossRef] [PubMed]

21. Korevaar, D.A.; Hoof, L.; Ter Riet, G. Systematic reviews and meta-analyses of preclinical studies: Publication bias in laboratory animal experiments. *Lab. Anim.* 2011, 45, 225–230. [CrossRef]

22. Kilkenny, C.; Browne, W.J.; Cuthill, I.C.; Emerson, M.; Altman, D.G. Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biol.* 2010, 8, e1000412. [CrossRef]

23. Kilkenny, C.; Browne, W.; Cuthill, I.C.; Emerson, M.; Altman, D.G. Animal research: Reporting in vivo experiments: The ARRIVE guidelines. *Br. J. Pharmacol.* 2010, 160, 1577–1579. [CrossRef] [PubMed]

24. van der Worp, H.B.; Howells, D.W.; Sena, E.S.; Porritt, M.J.; Rewell, S.; O’Collins, V.; Macleod, M.R. Can Animal Models of Disease Reliably Inform Human Studies? *PLoS Med.* 2010, 7, e1000245. [CrossRef]

25. Leung, V.; Rousseau-Blasc, F.; Beauchamp, G.; Pang, D.S.J. ARRIVE has not ARRIVED: Support for the ARRIVE (Animal Research: Reporting of In vivo Experiments) guidelines does not improve the reporting quality of papers in animal welfare, analgesia or anesthesia. *PLoS ONE* 2018, 13, e0197882. [CrossRef] [PubMed]

26. Bezdjian, A.; Klis, S.F.L.; Peters, J.P.M.; Grolman, W.; Stegeman, I. Quality of reporting of otorhinolaryngology articles using animal models with the ARRIVE statement. *Lab. Anim.* 2018, 52, 79–87. [CrossRef] [PubMed]

27. Ting, K.H.J.; Hill, C.L.; Whittle, S.L. Quality of reporting of interventional animal studies in rheumatology: A systematic review using the ARRIVE guidelines. *Int. J. Rheum. Dis.* 2015, 18, 488–494. [CrossRef] [PubMed]

28. Percie du Sert, N.; Hurst, V.; Ahluwalia, A.; Alam, S.; Altman, D.G.; Avey, M.T.; Baker, M.; Browne, W.; Clark, A.; Cuthill, I.C.; et al. Revision of the ARRIVE guidelines: Rational and scope. *BMJ Open Sci.* 2018, 2, e000002. [CrossRef] [PubMed]

29. Percie du Sert, N.; Hurst, V.; Ahluwalia, A.; Alam, S.; Avey, M.T.; Baker, M.; Browne, W.J.; Clark, A.; Cuthill, I.C.; Dirnagl, U.; et al. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. *BMC Vet. Res.* 2020, 16, 242. [CrossRef]

30. Collins, F.S.; Tabak, L.A. Policy: NIH plans to enhance reproducibility. *Science* 2018, 505, 612–613. [CrossRef] [PubMed]

31. Žiaran, S.; Galambošová, M.; Daníšovič, Ľ. Tissue engineering of urethra: Systematic review of recent literature. *Exp. Biol. Med.* 2017, 242, 1772–1785. [CrossRef]

32. De Kemp, V.; De Graaf, P.; Flederius, J.O.; Bosch, J.L.H.R.; De Kort, L.M.O. Tissue engineering for human urethral reconstruction: Systematic review of recent literature. *PLoS ONE* 2015, 10, e0118653. [CrossRef]

33. Koo, T.K.; Li, M.Y. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J. Chiropr. Med.* 2016, 15, 155–163. [CrossRef]

34. Huang, J.-W.; Lv, X.-G.; Li, Z.; Song, L.-J.; Feng, C.; Xie, M.-K.; Li, C.; Li, H.-B.; Wang, J.-H.; Zhu, W.-D.; et al. Urethral reconstruction with tissue-engineered human amniotic scaffold in rabbit urethral injury models. *J. Korean Med. Sci.* 2018, 33, 1055005. [CrossRef] [PubMed]

35. Li, H.; Xu, Y.; Xie, H.; Li, C.; Song, L.; Feng, C.; Zhang, Q.; Xie, M.; Wang, Y.; Lv, X. Epithelial-differentiated adipose-derived stem cells seeded bladder acellular matrix grafts for urethral reconstruction: An animal model. *Tissue Eng. Part A* 2014, 20, 774–784. [CrossRef]

36. Wang, F.; Liu, T.; Yang, L.; Zhang, G.; Liu, H.; Yi, X.; Yang, X.; Lin, T.; Qin, W.; Yuan, J. Urethral reconstruction with tissue-engineered human amniotic scaffold in rabbit urethral injury models. *Med. Sci. Monit.* 2014, 20, 2430–2438. [CrossRef] [PubMed]

37. Kajbafzadeh, A.-M.; Sabetkish, S.; Torchii, A.; Amirizadeh, N.; Afshar, K.; Abolghasemi, H.; Elmi, A.; Talab, S.S.; Eshghi, P.; Mohseni, M.J. The application of tissue-engineered preputial matrix and fibrin sealant for urethral leakage in rabbit model. *Int. Urol. Nephrol.* 2014, 46, 1573–1580. [CrossRef]

38. Sun, D.; Yang, Y.; Wei, Z.; Xu, Y.; Zhang, X.; Hong, B. Engineering of pre-vascularized urethral patch with muscle flaps and hypoxia-activated hUCMSCs improves its therapeutic outcome. *J. Cell. Mol. Med.* 2014, 18, 434–443. [CrossRef]

39. Xu, Y.; Sun, D.C.; Wei, Z.T.; Hong, B.F.; Yang, Y. Experimental study on transplantation of autologous minced muscle with human umbilical cord mesenchymal stem cells for urethral reconstruction. *Eur. Rev. Med. Pharmacol. Sci.* 2014, 18, 3412–3419. Available online: http://www.ncbi.nlm.nih.gov/pubmed/25491616 (accessed on 17 February 2021).

40. Arenas da Silva, I.F.; Miclo, L.; Tiemessen, D.; van Kuppevelt, T.H.; Frey, P.; Oosterwijk, E.; Geutjes, P.; Feitz, W.F. Is There a Need for Smooth Muscle Cell Transplantation in Urethral Reconstruction? *Tissue Eng. Part A* 2014, 20, 1542–1549. [CrossRef]

41. Chun, S.Y.; Kim, B.S.; Kwon, S.Y.; Park, S.I.; Song, P.H.; Yoo, E.S.; Kim, B.W.; Kwon, T.G.; Kim, H.T. Urethroplasty using autologous urethral tissue-embedded acellular porcine bladder submucosa matrix grafts for the management of long-segment urethral stricture in a rabbit model. *J. Korean Med. Sci.* 2015, 30, 301–307. [CrossRef]

42. Guo, H.; Sa, Y.; Huang, J.; Wang, Z.; Wang, L.; Xie, M.; Lv, X. Urethral Reconstruction with Small Intestinal Submucosa Seeded with Oral Keratinocytes and TIMP-1 siRNA Transfected Fibroblasts in a Rabbit Model. *Urol. Int.* 2016, 96, 223–230. [CrossRef]

43. Huang, J.-W.; Lv, X.-G.; Li, Z.; Song, L.-J.; Feng, C.; Xie, M.-K.; Li, C.; Li, H.-B.; Wang, J.-H.; Zhu, W.-D.; et al. Urethral reconstruction with a 3D porous bacterial cellulose scaffold seeded with lingual keratinocytes in a rabbit model. *Connect. Tissue Res.* 2015, 56, 434–439. [CrossRef] [PubMed]
Animals 2021, 11, 2456

46. Rogovaya, O.S.; Fayzulin, A.K.; Vasilev, A.V.; Kononov, A.V.; Terskikh, V. V Reconstruction of rabbit urethral epithelium with skin keratinocytes. *Acta Naturae* 2015, 7, 70–77. Available online: http://www.ncbi.nlm.nih.gov/pubmed/25927003 (accessed on 17 February 2021). [CrossRef]

47. Lv, X.; Li, Z.; Chen, S.; Xie, M.; Huang, J.; Peng, X.; Yang, R.; Wang, H.; Xu, Y.; Feng, C. Structural and functional evaluation of oxygenating keratin/silk fibroin scaffold and initial assessment of their potential for urethral tissue engineering. *Biomaterials* 2016, 84, 99–110. [CrossRef] [PubMed]

48. Lv, X.; Guo, Q.; Han, F.; Chen, C.; Ling, C.; Chen, W.; Li, B. Electropun Poly(l-lactide)/Poly(ethylene glycol) Scaffolds Seeded with Human Amniotic Mesenchymal Stem Cells for Urethral Epithelium Repair. *Int. J. Mol. Sci.* 2016, 17, 1262. [CrossRef] [PubMed]

49. Pinnagoda, K.; Larsson, H.M.; Vythilingam, G.; Vardar, E.; Engelhardt, E.-M.; Thambidorai, R.C.; Hubbell, J.A.; Frey, P. Engineered acellular collagen scaffold for endogenous cell guidance, a novel approach in urethral regeneration. *Acta Biomater.* 2016, 43, 208–217. [CrossRef]

50. Güneș, M.; Altok, M.; Güneș, A.; Umul, M.; Özyıldız, Z.; Sönmez, T.T.; Orhan, H.; Özmen, Ö. A Novel Approach to Penile Augmentation Urethroplasty Using Buccal Mucosa and Amniotic Membrane: A Pilot Study in a Rabbit Model. *Urology* 2016, 87, 210–215. [CrossRef]

51. Nikolavsky, D.; Manwaring, J.; Bratslavsky, G.; Caza, T.; Landas, S.; Hryniewicz-Jankowska, A.; Kotula, L. Novel Concept and Method of Endoscopic Urethral Stricture Treatment Using Liquid Buccal Mucosal Graft. *J. Urol.* 2016, 196, 1788–1795. [CrossRef] [PubMed]

52. Liu, Y.; Ma, W.; Liu, B.; Wang, Y.; Chu, J.; Xiong, G.; Shen, L.; Long, C.; Lin, T.; He, D.; et al. Urethral reconstruction with autologous urine-derived stem cells seeded in three-dimensional porous small intestinal submucosa in a rabbit model. *Stem Cell Res. Ther.* 2017, 8, 1943–1949. [CrossRef] [PubMed]

53. Jiang, S.; Xu, Z.; Zhao, Y.; Yan, L.; Zhou, Z.; Gu, G. Urethral Reconstruction Using Mesothelial Cell-Seeded Autogenous Granulation Tissue Tube: An Experimental Study in Male Rats. *Biomed Res. Int.* 2017, 2017, 1–9. [CrossRef]

54. Larsson, H.M.; Vythilingam, G.; Pinnagoda, K.; Vardar, E.; Engelhardt, E.-M.; Sothilingam, S.; Thambidorai, R.C.; Kamarul, T.; Hubbell, J.A.; Frey, P. Fiber density of collagen grafts impacts rabbit urethral regeneration. *Sci. Rep.* 2018, 8, 10057. [CrossRef]

55. Algarrahi, K.; Afias, S.; Sack, B.S.; Yang, X.; Costa, K.; Seager, C.; Estrada, C.R.; Mauney, J.R. Repair of injured urethras with silk fibroin scaffolds in a rabbit model of onlay urethroplasty. *J. Surg. Res.* 2018, 229, 192–199. [CrossRef]

56. Sa, Y.; Wang, L.; Shu, H.; Gu, J. Post-transcriptional suppression of TIMP-1 in epithelial-differentiated adipose-derived stem cells seeded bladder acellular matrix grafts reduces urethral scar formation. *Artif. Cells Nanomed. Biotechnol.* 2018, 46, 306–313. [CrossRef] [PubMed]

57. Sartoneva, R.; Nordback, P.H.; Haimi, S.; Grijpma, D.W.; Lehto, K.; Rooney, N.; Seppänen-Kajiansinkko, R.; Miettinen, S.; Lähdes-Vasama, T. Comparison of Poly(l-lactide-co-ε-caprolactone) and Poly(trimethylene carbonate) Membranes for Urethral Regeneration: An In Vitro and In Vivo Study. *Tissue Eng. Part A* 2018, 24, 117–127. [CrossRef]

58. Pusateri, C.R.; Doudt, A.D.; Gauerke, S.; McCammon, K.; Qin, X.; Ork, B.; Khoury, J.M.; May, A.D.; Zuckerman, J.M. Placental membrane grafts for urethral replacement in a rabbit model: A pilot study. *World J. Urol.* 2019, 38, 2133–2138. [CrossRef] [PubMed]

59. Guo, H.-L.; Jia, Z.-M.; Wang, L.; Bao, X.-Q.; Huang, Y.-C.; Zhou, J.-M.; Xie, H.; Yang, X.-J.; Chen, F. Tubularized urethral reconstruction using a prevascularized capsular tissue prelaminated with buccal mucosa graft in a rabbit model. *Asian J. Androl.* 2019, 21, 381–386. [CrossRef] [PubMed]

60. Hua, X.; Chen, J.; Xu, Y.; Li, B. Combined Dorsal Plus Ventral Double Tunica Vaginalis Graft Urethroplasty: An Experimental Study in Rabs. *Urology* 2019, 126, 209–216. [CrossRef]

61. Li, Y.; Wu, J.; Feng, F.; Men, C.; Yang, D.; Gao, Z.; Zhu, Z.; Cui, Y.; Zhao, H. A Preclinical Study of Cell-seeded Tubularized Scaffolds specially Secreting LL37 for Reconstruction of Long Urethral Defects. *Anticancer Res.* 2017, 37, 4295–4301. [CrossRef] [PubMed]

62. Landis, S.C.; Amara, S.G.; Asadullah, K.; Austin, C.P.; Blumenstein, R.; Bradley, E.W.; Crystal, R.G.; Darnell, R.B.; Ferrante, R.J.; Fillit, H.; et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nat. Cell Biol.* 2012, 490, 187–191. [CrossRef]

63. von der Behrens, W. Animal Models of Tinnitus. *Neural Plast.* 2014, 2014, 1–13. [CrossRef] [PubMed]

64. Prager, E.L.; Bergstrom, H.C.; Grunberg, N.E.; Johnson, L.R. The Importance of Reporting Housing and Husbandry in Rat Research. *Front. Behav. Neurosci.* 2011, 5, 38. [CrossRef] [PubMed]

65. Kirk, R.G.W. Care in the Cage: Materializing Moral Economies of Animal Care in the Biomedical Sciences, c.1945. In *Animal Housing and Human-Animal Relations: Politics, Practices and Infrastructures*; Bjerkdahl, K., Drugli, T., Eds.; Routledge: Oxon, UK, 2018. Available online: http://www.ncbi.nlm.nih.gov/pubmed/30933457 (accessed on 17 February 2021).

66. Abbas, T.O.; Ali, M.; Moog, R. Double-Lumen Valve-Controlled Intra-Operative Pyeloplasty Stent (VIPs): A New Technology for Post-Pyeloplasty Stenting - Proof of Concept Study in a Preclinical Large Animal Model. *Res. Rep. Urol.* 2020, 12, 61–74. [CrossRef]

67. Festing, M.F.W.; Altman, D.G. Guidelines for the Design and Statistical Analysis of Experiments Using Laboratory Animals. *ILAR J.* 2002, 43, 244–258. [CrossRef]
68. Hirst, J.A.; Howick, J.; Aronson, J.K.; Roberts, N.; Perera, R.; Koshtiaris, C.; Heneghan, C. The Need for Randomization in Animal Trials: An Overview of Systematic Reviews. PLoS ONE 2014, 9, e98856. [CrossRef]
69. The NPQIP Collaborative Group. Did a change in Nature journals’ editorial policy for life sciences research improve reporting? BMJ Open Sci. 2019, 3, e000035. [CrossRef]
70. McGrath, J.C.; Lilley, E. Implementing guidelines on reporting research using animals (ARRIVE etc.): New requirements for publication in BJ. Br. J. Pharmacol. 2015, 172, 3189–3193. [CrossRef]
71. Baker, D.; Lidster, K.; Sottomayor, A.; Amor, S. Two Years Later: Journals Are Not Yet Enforcing the ARRIVE Guidelines on Reporting Standards for Pre-Clinical Animal Studies. PLoS Biol. 2014, 12, e1001756. [CrossRef]
72. Flórez-Vargas, O.; Brass, A.; Karystianis, G.; Bramhall, M.; Stevens, R.; Cruickshank, S.; Nenadic, G. Bias in the reporting of sex and age in biomedical research on mouse models. Elife 2016, 5, e13615. [CrossRef]
73. Hair, K.; Macleod, M.R.; Sena, E.S. A randomised controlled trial of an Intervention to Improve Compliance with the ARRIVE guidelines (IICARus). Res. Integr. Peer Rev. 2019, 4, 12. [CrossRef] [PubMed]
74. Smith, A.J.; Clutton, R.E.; Lilley, E.; Hansen, K.E.A.; Brattelid, T. PREPARE: Guidelines for planning animal research and testing. Lab. Anim. 2018, 52, 135–141. [CrossRef] [PubMed]
75. The EQUATOR Network | Enhancing the QUAlity and Transparency Of Health Research. Available online: https://www.equator-network.org/ (accessed on 17 February 2021).
76. Avey, M.T.; Moher, D.; Sullivan, K.J.; Fergusson, D.; Griffin, G.; Grimshaw, J.M.; Hutton, B.; Lalu, M.M.; Macleod, M.; Marshall, J.; et al. The Devil Is in the Details: Incomplete Reporting in Preclinical Animal Research. PLoS ONE 2016, 11, e0166733. [CrossRef]