A Network Meta-Analysis of Sarcopenia Characteristic Indicators in Different Mouse Models of Muscular Dystrophy

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Abstract

Objective

Through a systematic review, compare the differences in characteristic indicators of muscle atrophy in commonly used mouse models, including muscle mass, muscle strength, muscle fiber cross-sectional area, and indicators of atrophy genes such as Murf-1 and Atrogin-1. Qualitatively and quantitatively explore the characteristics of various mouse models of muscle atrophy.

Methods

A computer search was conducted in databases such as Pubmed, Embase, Cochrane, CNKI, VIP, Wanfang, and Sinomed to collect all literature related to sarcopenia and mouse models, with a search time limit from the establishment of the database to January 17, 2024. The retrieved literature was screened and managed using NoteExpress software, and basic information was summarized using Excel software. Risk of bias assessment was performed using ReviewManange 5.4.1 software, and data analysis was conducted using R software.

Results

A total of 101 studies involving 1930 mice were included. The modeling methods for sarcopenia included obesity-related (8 studies), tumor-related (10 studies), natural aging (21 studies), dexamethasone-induced (10 studies), hindlimb suspension (7 studies), accelerated aging (6 studies), gene knockout (21 studies), chronic kidney disease-related (3 studies), diabetes-related (9 studies), D-galactose-induced (4 studies), and orchidectomy-induced (2 studies) models. The network meta-analysis results showed that, compared to the normal control group, the top three models in terms of skeletal muscle mass reduction were obesity-related, D-galactose-induced, and accelerated aging models. In terms of muscle strength reduction, the top three models were dexamethasone-induced, hindlimb suspension, and gene knockout models. The cross-sectional area of the gastrocnemius muscle fibers, reflecting the degree of muscle cell atrophy, showed that the top three models in atrophy severity were hindlimb suspension, obesity-related, and tumor-related models. Wet weight of the gastrocnemius muscle, representing muscle mass, was significantly lower in the obesity-related, hindlimb suspension, accelerated aging, gene knockout, chronic kidney disease-related, and diabetes-related models compared to the normal control group ($P < 0.05$). Grip strength, representing muscle function, was significantly reduced in the obesity-related, tumor-related, natural aging, dexamethasone-induced, hindlimb suspension, accelerated aging, and gene knockout models compared to the normal control group ($P < 0.05$). HE staining of the gastrocnemius muscle cell cross-sectional area, indicating the degree of muscle cell atrophy, showed significant reductions in the obesity-related, tumor-related, natural aging, dexamethasone-induced, hindlimb suspension, and accelerated aging models compared to the normal control group ($P < 0.05$). In terms of atrophy gene MuRF-1 expression, the tumor-related and

dexamethasone-induced models showed significantly increased expression compared to the normal control group ($P < 0.05$). For atrophy gene Atrogin-1 expression, the dexamethasone model group showed significantly increased expression compared to the normal control group ($P < 0.05$).

Conclusion

Among the 11 sarcopenia models, different models exhibit distinct characteristics in sarcopenia indicators. The obesity-related model is ideal for studying muscle mass reduction, the dexamethasone model is ideal for muscle strength reduction, and the hindlimb suspension model is recommended for skeletal muscle fiber atrophy. The dexamethasone-induced sarcopenia model is recommended for studying the increased expression of atrophy genes MuRF-1 and Atrogin-1. Models showing both skeletal muscle mass and muscle strength reduction include the hindlimb suspension, obesity-related, accelerated aging, and gene knockout models. From the natural aging mouse sarcopenia model, it was found that muscle strength reduction is more sensitive than muscle mass reduction in sarcopenia indicators.

Introduction

Sarcopenia is an age-related disease that is gaining increasing attention as the world progressively enters an era of aging. The pathogenesis of sarcopenia is not yet fully understood [1], and its diagnosis mainly involves the assessment of muscle mass and muscle strength [2]. Mice are commonly used as models for sarcopenia, and there are various ways to create these models. Selecting the appropriate sarcopenia model based on related phenotypes is particularly important for future drug development. Although there are many reviews on animal models of sarcopenia, there has not been a quantitative comparison and analysis through meta-analysis. This paper uses a network meta-analysis approach to assess the quality of the included literature and quantitatively compare 11 types of sarcopenia models based on the results of R software. The aim is to find suitable mouse models for phenotypes such as the decline in skeletal muscle mass and strength in sarcopenia.

Materials and Methods

1.1 **PICOS principle** P is mice in 11 types of sarcopenia models, I is the modeling method of the 11 types of sarcopenia models, C is the comparison, which is mice that have not undergone modeling. O is the outcome indicators, including wet weight of the gastrocnemius muscle, mouse grip strength, cross-sectional area of gastrocnemius muscle fibers stained with HE, and atrophy genes MuRF-1, Atrogin-1 [3]. S is the study design, see inclusion and exclusion criteria for details.

1.2 Search strategy Computer searches of Chinese and English databases such as CNKI, VIP, WanFang, Sinomed, Pubmed, Embase, and Cochrane were conducted to collect all literature related to sarcopenia

and mouse models, with the search time limit from the establishment of the database to January 17, 2024. The search method combined subject terms with free words. The Chinese search terms were sarcopenia, muscle wasting, muscle atrophy, skeletal muscle atrophy, muscle wasting syndrome, senile skeletal muscle atrophy, primary senile muscle atrophy syndrome AND mouse model. The English subject searching strategy was as follows:(((sarcopenia*[MeSH Terms]) OR (sarcopenia [All Fields]) OR (sarcopenias [All Fields])) AND ((mice*[MeSH Terms]) OR (mice [All Fields])) AND ((model [All Fields]) OR (models [All Fields]) OR (modeled [All Fields]) OR (modeler [All Fields]) OR (modelers [All Fields]) OR (modeling [All Fields]) OR (modelings [All Fields]) OR (modelization [All Fields]) OR (modelizations[All Fields]) OR (modelize [All Fields]) OR (modelized [All Fields]) OR (modelled [All Fields]) OR (modeller [All Fields]) OR (modellers [All Fields]) OR (modelling [All Fields]) OR (modellings [All Fields]))).The chinese subject searching strategy was as follows:((myasthenia) OR (hypomyotonia) OR (muscle atrophy) OR (skeletal muscle atrophy) OR (muscle wasting syndrome) OR (age-related skeletal muscle atrophy) OR (primary age-related muscle atrophy syndrome) AND (mouse model)).

1.3 Inclusion and Exclusion Criteria

Inclusion Criteria:

Rigorous experimental design in the literature.

Study subjects. Mice, with no restrictions on breed, age, gender, or modeling method.

Intervention measures. Modeling methods related to sarcopenia.

Sampling site. Muscle.

Outcome indicators. Grip strength, muscle wet weight, protein synthesis and breakdown indicators.

Experimental design includes a normal control group or a group similar to the normal control group.

Exclusion Criteria:

Articles are clinical literature or not based on mouse experiments.

Poor experimental design.

Literature from which data cannot be extracted or that has been published repeatedly.

Reviews or conference papers.

The modeling method is not detailed.

Other diseases related to muscle atrophy, including amyotrophic lateral sclerosis, polymyositis, myasthenia gravis, chronic fatigue syndrome, etc.

Excluding literature on sarcopenia with other diseases.

1.4 Data Extraction

Two researchers independently screened the literature according to the inclusion and exclusion criteria and extracted information from the included studies using Excel software, including the title, first author, publication year, mouse species information, age information of the normal group and model group, mouse weight information, the number of mice in the control group and model group, modeling method, and outcome indicators. Two researchers summarized and checked the data, and when there was disagreement in the literature inclusion and data extraction stages, a third researcher assisted in the judgment.

1.5 Risk of Bias Assessment

We used the SYRCLE (Systematic Review Centre for Laboratory Animal Experimentation) assessment tool to evaluate the effectiveness of animal experiments and research methods. This tool is based on the Cochrane risk assessment and developed to assess the quality of animal research. We used Review Manager 5.4 software to evaluate the quality of the 10 items of the SYRCLE.

1.6 Outcome Indicators

The primary outcome indicators are muscle mass and muscle strength, and the secondary outcome indicators are the cross-sectional area of skeletal muscle stained with HE, and atrophy genes MuRF-1, Atrogin-1.

1.7 Statistical Analysis

Network meta-analysis was conducted on the included studies using software such as Review Manager 5.4, R, and Stata. The two primary outcome indicators and three secondary outcome indicators, all continuous variables, were represented by standardized mean difference (SMD) and 95% confidence interval (CI). Heterogeneity among studies was tested with the I^2 value. A fixed-effects model was used when the I^2 value was < 40%, otherwise, a random-effects model was used. Forest plots and ranking plots were used to compare the effects of the 11 sarcopenia models on various outcome indicators.

Results

2.1 Literature Search and Inclusion Results

A total of 5034 Chinese articles and 1983 English articles were retrieved, totaling 7017 articles. Finally, 101 studies [4–104] were included. The literature screening process is shown in Fig. 1.

2.2 Characteristics and Quality Assessment Results of Included Literature

The studied mice included young mice, aged mice, gene knockout mice, and rapidly aging mice, totaling 1930 mice. Among them, there were 8 articles on obesity-related sarcopenia models, 10 articles on tumor-related sarcopenia models, 21 articles on natural aging sarcopenia models, 10 articles on dexamethasone-induced sarcopenia models, 7 articles on hindlimb suspension sarcopenia models, 6 articles on accelerated aging sarcopenia models, 21 articles on gene knockout sarcopenia models, 3 articles on chronic kidney disease sarcopenia models, 9 articles on diabetes-related sarcopenia models, 4 articles on D-galactose-induced sarcopenia models, and 2 articles on orchiectomy-induced sarcopenia models. The basic characteristics of the included literature are shown in Appendix 1, the risk of bias assessment results are shown in Fig. 2, and the network diagram of the included analysis literature is shown in Fig. 3.

As shown in Fig. 2, there is a risk of bias in the study due to the presence of naturally aging mice, gene knockout mice, and rapidly aging mice, which have inherent age and genetic characteristics. This leads to a higher risk in Item 1: sequence generation (13.9%) and Item 3: allocation concealment (13.9%). Although the articles mention breeding conditions in animal housing randomization, it is not possible to determine whether the breeding conditions or cage placement for all experimental animals are random.

2.3 Meta-Analysis Literature Network Diagram

In the network diagram, each node represents different modeling methods, with A representing the normal control group. All nodes are compared with the normal control group represented by A. The thicker the line between a node and A, the more literature is included for that node. Among them, groups D and H have a larger number of included articles, while groups L and I have fewer included articles.

2.4 Heterogeneity Test of Included Literature

Heterogeneity analysis was conducted on the included literature for 11 types of sarcopenia models based on outcome indicators. For the wet weight of mouse gastrocnemius muscle, 101 articles were included in the analysis, with a heterogeneity of I^2 = 99.43%. For mouse grip strength, 79 articles were included in the analysis, with a heterogeneity of I^2 = 99.51%. For the cross-sectional area of mouse gastrocnemius muscle fibers, 49 articles were included in the analysis, with a heterogeneity of I^2 = 99.43%. For the mouse MuRF-1 atrophy gene, 32 articles were included in the analysis, with a heterogeneity of I^2 = 99.99%. For the mouse Atrogin-1 atrophy gene, 36 articles were included in the analysis, with a heterogeneity of I^2 = 99.3%. Therefore, a random effects model was adopted. The funnel plots of literature bias risk are shown in Figures (4-8).

2.5 Forest Plot Comparing 11 Models

The forest plots analyze outcome indicators such as mouse gastrocnemius muscle wet weight, mouse grip strength, mouse gastrocnemius muscle fiber cross-sectional area, mouse MuRF-1 atrophy gene, and mouse Atrogin-1 atrophy gene, as shown in Figures (9-13).

As shown in Figure 10, the heterogeneity between groups in the comparison of mouse gastrocnemius muscle wet weight among the 11 sarcopenia model groups and the normal control group is I^2 = 4%, allowing for a network meta-analysis. The effect size of group B (obesity-related sarcopenia model group) compared to group A (normal control group) is [MD = -60, 95%CI (-81, -40)], and the effect size of group F (hindlimb suspension sarcopenia model group) compared to group A is [MD = -32, 95%CI (-54, -11)], and so on for other groups, with all p-values < 0.05, indicating a significant decrease in mouse gastrocnemius muscle wet weight compared to the normal control group in groups B, F, G, H, I, J, and K. Groups D and E show effect sizes close to the normal control group.

As shown in Figure 11, the heterogeneity between groups in the comparison of mouse grip strength among the 11 sarcopenia model groups and the normal control group is I^2 = 2%, allowing for a network meta-analysis. The effect sizes of various groups are presented, with all p-values < 0.05, indicating a significant decrease in mouse grip strength compared to the normal control group in groups B, C, D, E, F, G, and H.

As shown in Figure 12, the heterogeneity between groups in the comparison of mouse gastrocnemius muscle fiber cross-sectional area among the 11 sarcopenia model groups and the normal control group is I^2 = 2%, allowing for a network meta-analysis. The effect sizes of various groups are presented, with all p-values < 0.05, indicating a significant decrease in mouse gastrocnemius muscle fiber cross-sectional area compared to the normal control group in groups B, C, D, E, F, G, I, and J.

As shown in Figure 13, the heterogeneity between groups in the comparison of the mouse MuRF-1 atrophy gene among the 11 sarcopenia model groups and the normal control group is I^2 = 2%, allowing for a network meta-analysis. The effect sizes of groups C and E are presented, with both showing a significant increase in the mouse MuRF-1 atrophy gene compared to the normal control group.

As shown in Figure 14, the heterogeneity between groups in the comparison of the mouse Atrogin-1 atrophy gene among the 11 sarcopenia model groups and the normal control group is I^2 = 2%, allowing for a network meta-analysis. The effect size of group E is presented, showing a significant increase in the mouse Atrogin-1 atrophy gene compared to the normal control group.

2.6 Probability Ranking Graph and Table for 11 Sarcopenia Animal Models

Through the probability ranking graph and table, the outcomes of wet weight of mouse gastrocnemius muscle, mouse grip strength, cross-sectional area of mouse gastrocnemius muscle fibers, mouse MuRF-1 atrophy gene, and mouse Atrogin-1 atrophy gene were ranked. The top three models in terms of skeletal muscle mass reduction are obesity-related sarcopenia (0.394095), D-galactose-induced sarcopenia (0.28028), and accelerated aging sarcopenia model (0.11366). In addition, the natural aging

sarcopenia model (0.000005) and dexamethasone-induced sarcopenia model (0.000005) are similar, indicating that naturally aging mice and dexamethasone-treated mice show similar muscle mass decline compared to the normal control group. The top three models in terms of muscle strength decline are dexamethasone-induced sarcopenia model (0.404845), hindlimb suspension sarcopenia model (0.325825), and gene knockout sarcopenia model (0.106415). In HE-stained pathological experiments, the cross-sectional area of mouse gastrocnemius muscle fibers reflects the degree of muscle cell atrophy, with the top three models in atrophy severity being hindlimb suspension sarcopenia model (0.412075), obesity-related sarcopenia (0.28138), and tumor-associated sarcopenia model (0.209365). In terms of the elevation of the MuRF-1 atrophy gene, the smaller the ranking probability, the higher the expression of the skeletal muscle atrophy gene, with the top three being dexamethasone-induced sarcopenia model (0.00116), tumor-associated sarcopenia model (0.00395), and natural aging model (0.04056). In terms of Atrogin-1 atrophy gene expression, the smaller the ranking probability, the higher the expression of the skeletal muscle atrophy gene, with the top three being dexamethasone-induced sarcopenia model (0.00046), tumor-associated sarcopenia model (0.01156), and natural aging model (0.018875).

Compared with the normal control group, the wet weight of the gastrocnemius muscle in the obesity-related sarcopenia model group, hindlimb suspension sarcopenia model group, accelerated aging sarcopenia model group, gene knockout sarcopenia model group, chronic kidney disease sarcopenia model group, diabetes sarcopenia model group, and D-galactose sarcopenia model group was significantly reduced in terms of muscle mass. Compared with the naturally aging sarcopenia model mice, the decrease in muscle mass was more significant in the obesity-related sarcopenia model group, hindlimb suspension sarcopenia model group, accelerated aging sarcopenia model group, gene knockout sarcopenia model group, chronic kidney disease sarcopenia model group, and diabetes sarcopenia model group, while the dexamethasone-induced sarcopenia model was similar to the naturally aging sarcopenia model in terms of muscle mass reduction.

In terms of muscle strength, compared with the normal control group, the grip strength of the obesity-related sarcopenia model group, tumor-associated sarcopenia model group, naturally aging sarcopenia model group, dexamethasone-induced sarcopenia model group, hindlimb suspension sarcopenia model group, accelerated aging sarcopenia model group, and gene knockout sarcopenia model group was significantly reduced. In terms of muscle strength, compared with the naturally aging sarcopenia model, the grip strength reduction was significant in the dexamethasone-induced sarcopenia model group, hindlimb suspension sarcopenia model group, and gene knockout sarcopenia model group. The obesity-related sarcopenia model group, tumor-associated sarcopenia model group, and accelerated aging sarcopenia model group were similar to the naturally aging sarcopenia model in terms of muscle strength reduction.

In terms of cross-sectional area of muscle fibers, compared with the normal control group, the cross-sectional area of gastrocnemius muscle fibers stained with hematoxylin and eosin (HE) in the obesity-related sarcopenia model group, tumor-associated sarcopenia model group, naturally aging sarcopenia

model group, dexamethasone-induced sarcopenia model group, hindlimb suspension sarcopenia model group, accelerated aging sarcopenia model group, chronic kidney disease sarcopenia model group, and diabetes sarcopenia model group was significantly reduced. Compared with the naturally aging sarcopenia model, the cross-sectional area of muscle fibers was significantly reduced in the obesity-related sarcopenia model group, tumor-associated sarcopenia model group, and hindlimb suspension sarcopenia model group. The chronic kidney disease sarcopenia model group and diabetes sarcopenia model group were similar to the naturally aging sarcopenia model in terms of the reduction in the cross-sectional area of muscle fibers.

In terms of MuRF-1 atrophy gene expression, compared with the normal control group, the expression of the MuRF-1 atrophy gene was significantly increased in the tumor-associated sarcopenia model group and dexamethasone-induced sarcopenia model group. Compared with the naturally aging sarcopenia model, the expression of the MuRF-1 atrophy gene was significantly increased in the tumor-associated sarcopenia model group and dexamethasone-induced sarcopenia model group. The hindlimb suspension sarcopenia model group and accelerated aging sarcopenia model group were similar to the naturally aging sarcopenia model in terms of the decrease in MuRF-1 atrophy gene expression.

In terms of Atrogin-1 atrophy gene expression, compared with the normal control group, the expression of the Atrogin-1 atrophy gene was significantly increased in the dexamethasone-induced sarcopenia model group. Compared with the naturally aging sarcopenia model, the expression of the Atrogin-1 atrophy gene was significantly increased in the dexamethasone-induced sarcopenia model group. The hindlimb suspension sarcopenia model group and diabetes sarcopenia model group were similar to the naturally aging sarcopenia model in terms of the decrease in Atrogin-1 atrophy gene expression.

Discussion

4.1 Analysis of Characteristics of Included Studies

Currently, there are various types of sarcopenia models used in animal experiments, but most studies appear in the form of reviews [105], and there are no articles that qualitatively and quantitatively analyze the various models. This paper included 11 sarcopenia modeling methods with characteristic indicators such as muscle mass, muscle strength, and atrophy genes MuRF-1 and Atrogin-1. Among them, the D-galactose sarcopenia model and orchidectomy sarcopenia model have fewer articles meeting the outcome indicators, which may lead to bias in their results. None of the included studies detailed their grouping process, and most animal studies had small sample sizes, which could lead to differences at baseline. There might be a risk of hidden allocation between naturally aging mice, gene knockout mice, and normal young mice. Funnel plots were used to analyze the bias of the five outcome indicators separately, revealing high heterogeneity, indicating that the overall quality of the included studies is not high. Although the control group mice in this paper are non-sarcopenic, their age ranges from several weeks to several months, which may introduce bias. Modeling time may be one of the factors affecting the success of the model. Naturally aging mice are already modeled upon purchase, making it

impossible to standardize the modeling time for each sarcopenia model. Moreover, due to the complexity of multiple intervention factors, it is difficult to systematically integrate and summarize, so subgroup analysis of the age of the control group mice and modeling time cannot be performed. The paper can only use the successful establishment of the model as the criterion for inclusion in the literature. This study only used mice as the research subjects, but currently, the research subjects of sarcopenia models also involve rats, pigs, dogs, zebrafish, and other animals. In the future, cross-species research between humans and animals can be conducted using CERQual and GRADE tools [106], which can improve the clinical translation of animal models.

4.2 Meta-Analysis of Included Studies

The comparison between the 11 sarcopenia models and the normal control group showed that I^2<4%, indicating no heterogeneity between model comparisons, allowing for comparisons between different sarcopenia models. Muscle mass and muscle strength are important diagnostic methods for assessing the occurrence of sarcopenia [107]. In terms of muscle mass, DXA is generally the diagnostic standard, but the machine used for detecting mouse muscle mass is expensive. Currently, a cheaper, simpler, and more accurate method is the D3-creatine (D3-Cr) dilution method, but there are not many articles using the D3-Cr dilution method [108]. Most of the current literature still uses gastrocnemius wet weight to represent mouse muscle mass, so this paper uses gastrocnemius wet weight to represent muscle mass [109]. The cross-sectional area of muscle fibers reflects the degree of fiber atrophy, and muscle wet weight and cross-sectional area are indicators of muscle mass [110]. In the current study of mouse sarcopenia models, the gastrocnemius and soleus muscles are commonly used tissues for HE staining, and this study chose mouse gastrocnemius. Muscle strength reduction is a characteristic indicator of sarcopenia occurrence, and grip strength is mostly used in mouse models [111]. Currently, the indicators for studying mouse grip strength include two forms: forelimb grip strength or four-limb grip strength. Since the hindlimb suspension model mainly involves the loss of gravity in the hindlimbs, and the forelimbs are not affected, this paper chose four-limb grip strength as the outcome indicator. It has been found that muscle atrophy is related to the expression of atrophy genes [112]. The obesity-related sarcopenia model showed significant differences in muscle mass, mouse grip strength, muscle fiber atrophy, and MuRF-1 atrophy gene expression compared to the normal control group, with a greater decrease in muscle mass than other sarcopenia model groups. In terms of muscle mass, the results of the dexamethasone-induced sarcopenia model group were close to those of the naturally aging sarcopenia group, but the dexamethasone-induced sarcopenia model group had significantly increased expression of MuRF-1 and Atrogin-1 atrophy genes. Although other sarcopenia model groups showed an increasing trend in atrophy gene expression, there was no statistical significance. In the outcome indicator of mouse grip strength, the results of the obesity-related sarcopenia model group, tumor-associated sarcopenia model group, and naturally aging sarcopenia model were similar, with the hindlimb suspension sarcopenia model group and dexamethasone-induced sarcopenia model group showing similar decreases in grip strength, and the largest decrease in grip strength. In terms of the cross-sectional area of muscle fibers stained with HE in skeletal muscle, the hindlimb suspension sarcopenia model group had the greatest decrease, indicating that the degree of skeletal muscle atrophy

is higher in the absence of resistance exercise. In terms of MuRF-1 and Atrogin-1 atrophy gene expression, the naturally aging sarcopenia model and the hindlimb suspension sarcopenia model group had similar expressions. Both had increased expression of MuRF-1 and Atrogin-1 atrophy genes, but there was no statistical difference compared to the normal control group. Through the analysis of probability ranking graphs and tables, the models with the greatest changes in each of the five outcome indicators can be identified. In the outcome indicator of skeletal muscle mass reduction, the obesity-related sarcopenia group (0.394095) had the greatest decrease. In the outcome indicator of mouse grip strength reduction, the dexamethasone-induced sarcopenia model (0.404845) had the greatest decrease. In the HE staining pathology experiment, the mouse gastrocnemius muscle fiber cross-sectional area with the greatest atrophy was the hindlimb suspension sarcopenia model (0.412075). In the expression of MuRF-1 and Atrogin-1 atrophy genes, the dexamethasone-induced sarcopenia model group had the greatest increase. From the naturally aging mouse sarcopenia model, it was found that skeletal muscle strength decreased significantly, and although there was a trend of decline in skeletal muscle mass, there was no statistical significance. When the decline in skeletal muscle mass was not different from the normal control group, skeletal muscle strength had already decreased compared to the normal control group, so the decline in skeletal muscle strength is more sensitive to sarcopenia than the decline in skeletal muscle mass.

Conclusion

According to the meta-analysis results of the included research literature, comparisons between 11 models of muscular dystrophy and normal control groups revealed an I^2 < 4%, indicating no heterogeneity among the models, thus allowing for comparison. The obese muscular dystrophy model showed significant differences from the normal control group in terms of muscle mass, mouse grip strength, muscle fiber atrophy, and MuRF-1 atrophy gene expression. It exhibited a greater decrease in muscle mass compared to other dystrophy model groups. In terms of muscle mass performance, the dexamethasone-induced muscular dystrophy model showed results similar to the natural aging dystrophy group, but with significantly elevated expression of MuRF-1 and Atrogin-1 atrophy genes.

Regarding the outcome measure of mouse grip strength, the obese muscular dystrophy model, tumor-related dystrophy model, and natural aging dystrophy model yielded similar results. The hind limb suspension dystrophy model and dexamethasone-induced dystrophy model exhibited similar decreases in mouse grip strength, with the most pronounced decline. In the histological examination of skeletal muscle using HE staining, the hind limb suspension dystrophy model showed the most significant decrease in cross-sectional area of muscle fibers. In terms of MuRF-1 and Atrogin-1 atrophy gene expression, the natural aging dystrophy model exhibited similar expression to the hind limb suspension dystrophy model, with elevated expression levels observed in both.

Through analysis of probability ranking plots and tables, the models with the greatest changes in each outcome measure among the five outcome measures can be identified. Among the models, the obese muscular dystrophy group (0.394095) showed the greatest decrease in skeletal muscle mass. The

dexamethasone-induced dystrophy model (0.404845) exhibited the most significant decline in mouse grip strength. The hind limb suspension dystrophy model (0.412075) showed the most pronounced decrease in cross-sectional area of muscle fibers in the HE staining pathology experiment. Regarding MuRF-1 and Atrogin-1 atrophy gene expression, the dexamethasone-induced dystrophy model group exhibited the most significant elevation. In terms of representing muscle mass with gastrocnemius wet weight, the dexamethasone-induced dystrophy model group showed similar performance to the natural aging mice. In terms of mouse grip strength performance, we found that the hind limb suspension dystrophy model group mice performed similarly to the dexamethasone-induced dystrophy model group mice. In terms of MuRF-1 and Atrogin-1 gene expression, the hind limb suspension dystrophy model group mice exhibited similar expression to the natural aging group mice.

Declarations

Data availability statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request and All data generated or analysed during this study are included in this published article [and its supplementary information files].

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Figures

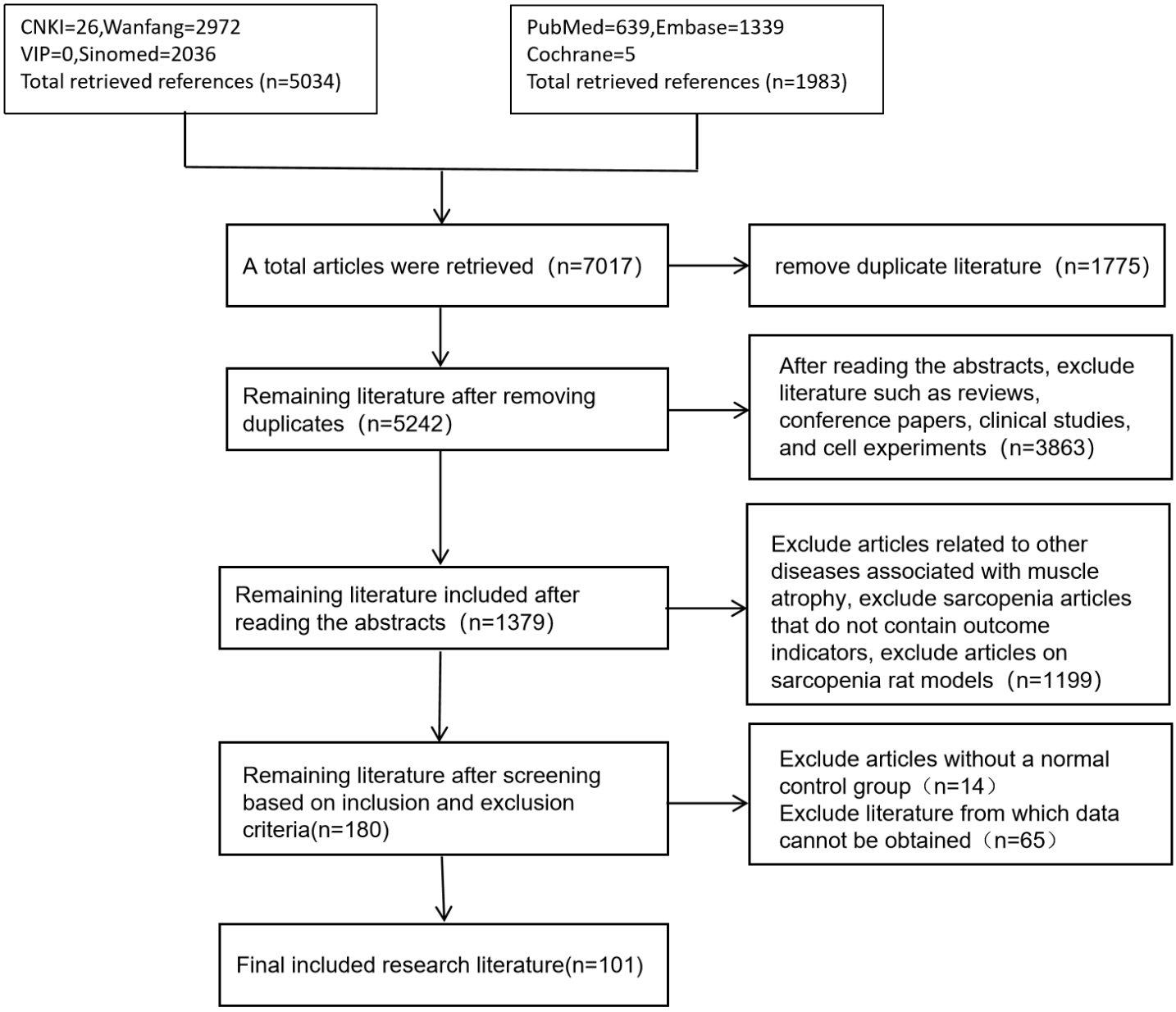
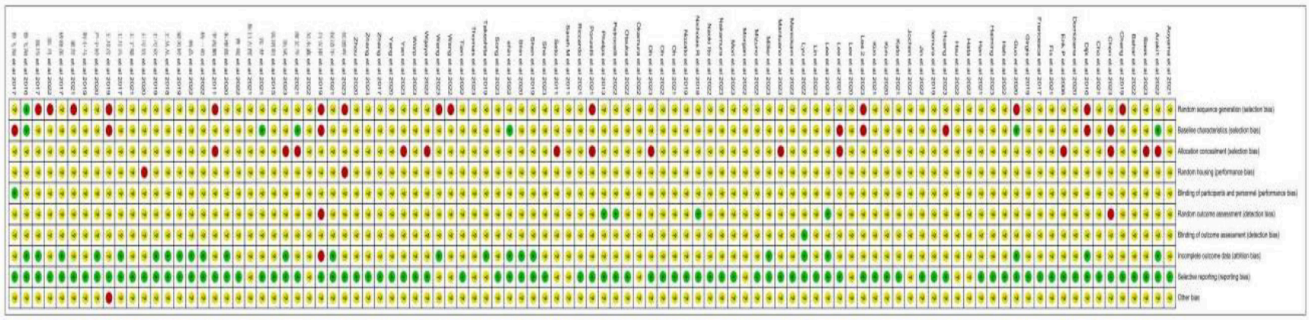


Figure 1

Flowchart of literature screening process



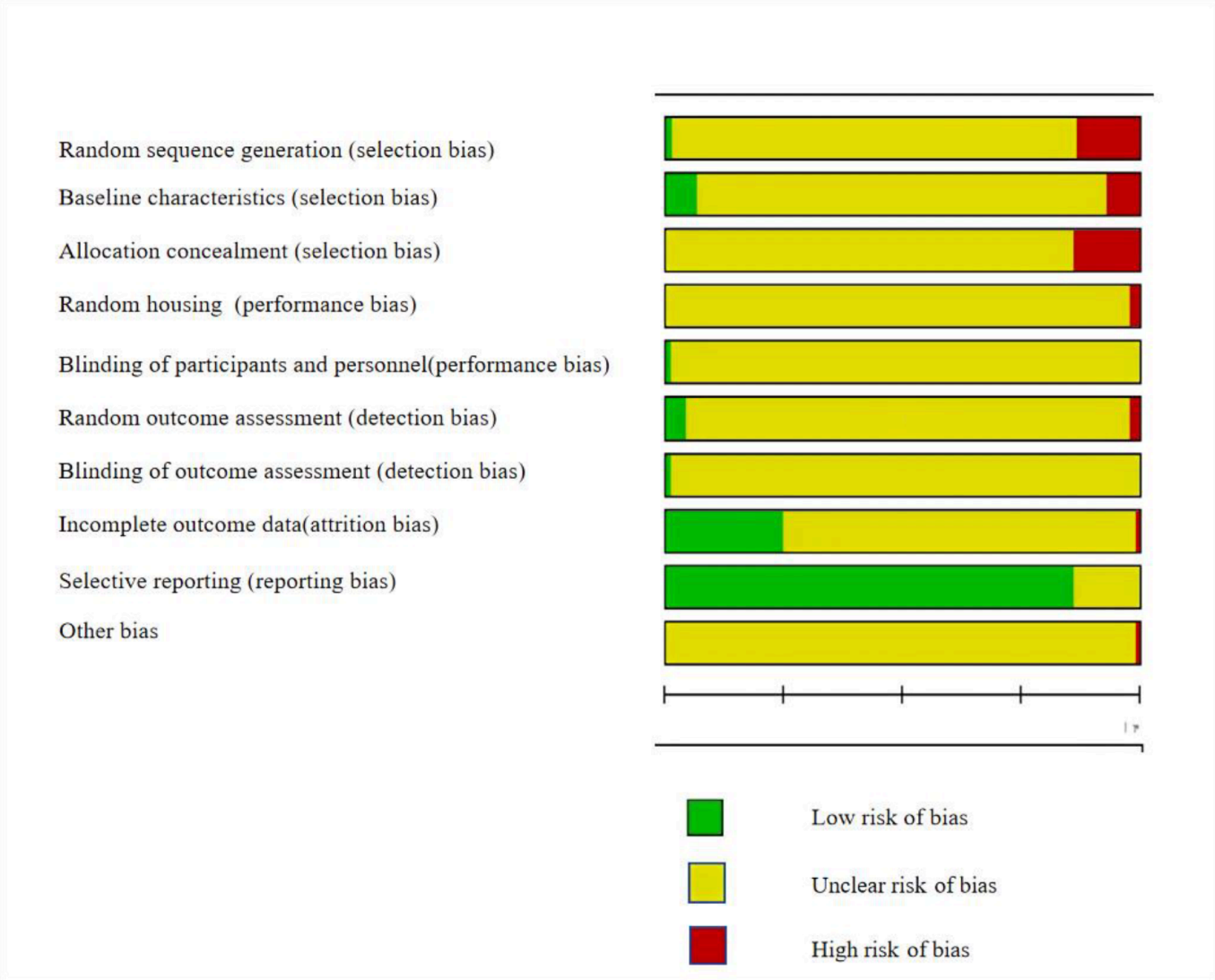


Figure 2. Risk Assessment Results of 101 Articles

Figure 2

Risk Assessment Results of 101 Articles

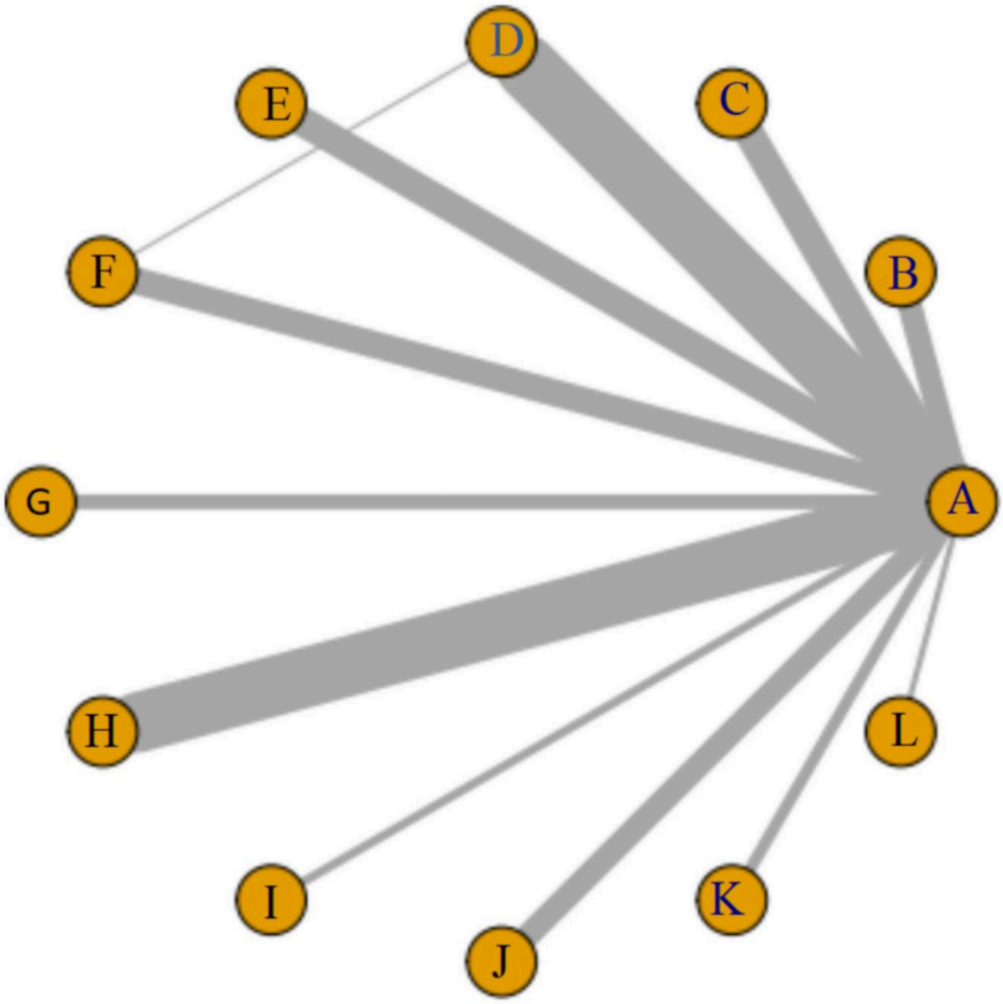


Figure 3

Network Diagram

A: Normal control group

B: Obesity-related sarcopenia group

C: Tumor-related sarcopenia model group

D: Natural aging sarcopenia model group

E: Dexamethasone-induced sarcopenia model group

F: Hindlimb suspension sarcopenia model group

G: Accelerated aging sarcopenia model group

H: Gene knockout sarcopenia model group

I: Chronic kidney disease sarcopenia model group

J: Diabetes-related sarcopenia model group

K: D-galactose-induced sarcopenia model group

L: Orchiectomy-induced sarcopenia model group.

The above letters representing the grouping apply throughout the text.

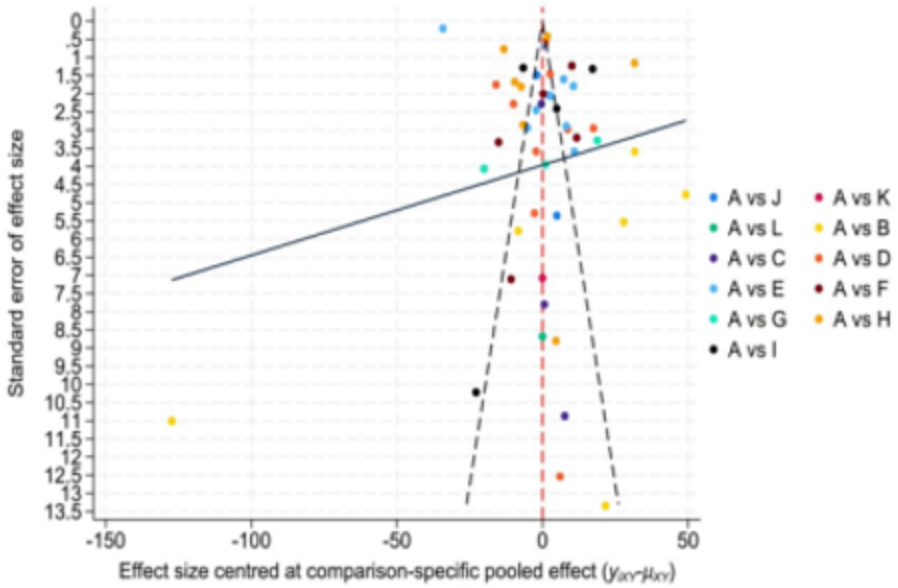


Figure 4. Funnel Plot for Bias Risk Assessment of 101 Included Studies on Mouse Gastrocnemius Muscle Wet Weight

Figure 4

See image above for figure legend

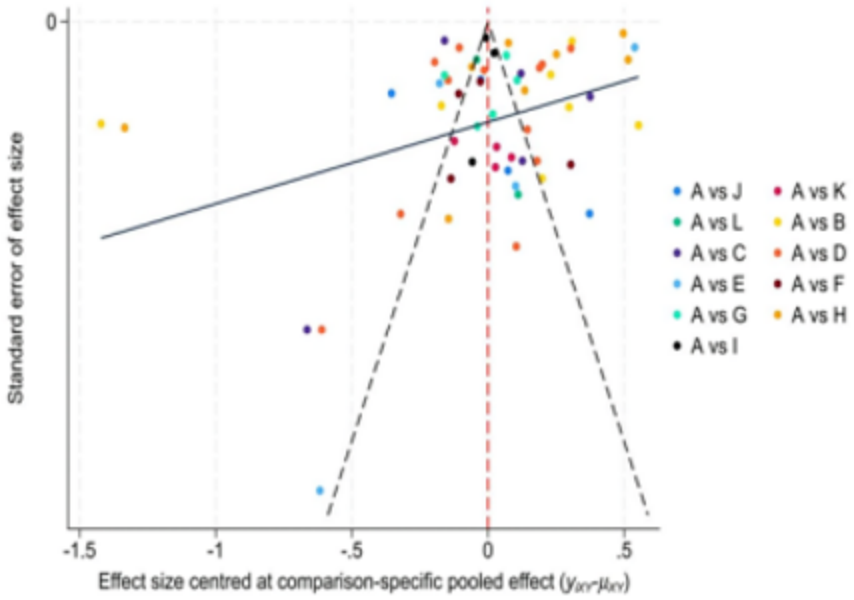


Figure 5. Funnel Plot for Bias Risk Assessment of 101 Included Studies on Mouse Grip Strength

Figure 5

See image above for figure legend

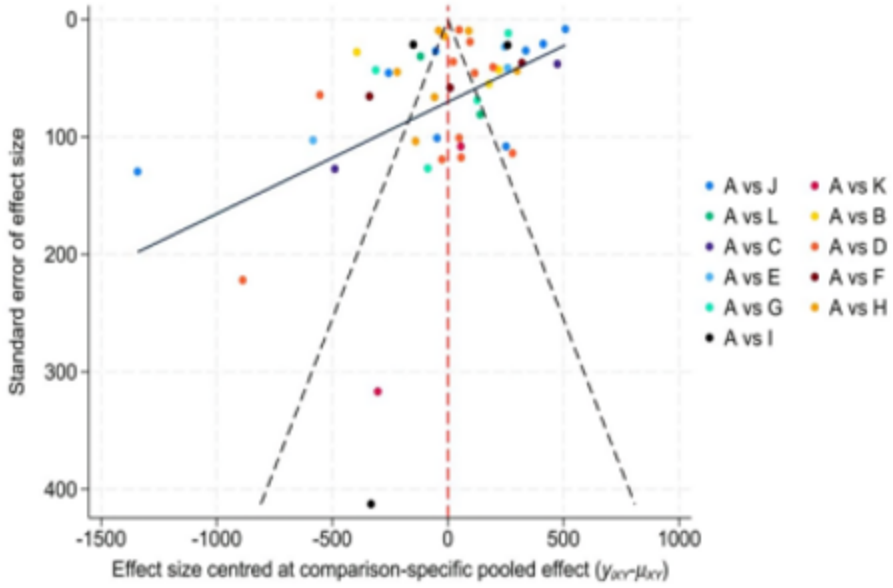


Figure 6. Funnel Plot for Bias Risk Assessment of 96 Included Studies on Mouse Skeletal Muscle Cross-Sectional Area

Figure 6

See image above for figure legend

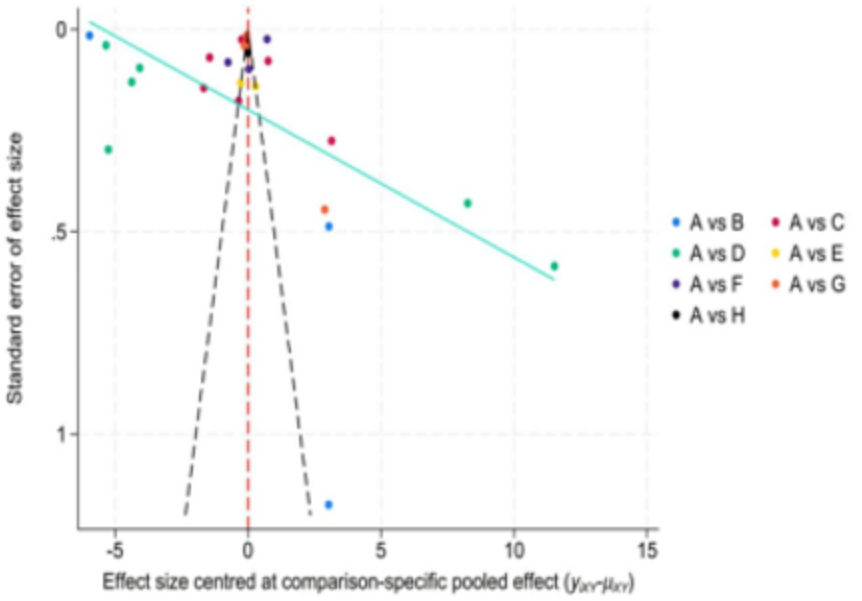


Figure 7. Funnel Plot for Bias Risk Assessment of 50 Included Studies on Mouse MuRF-1 Atrophy Gene

Figure 7

See image above for figure legend

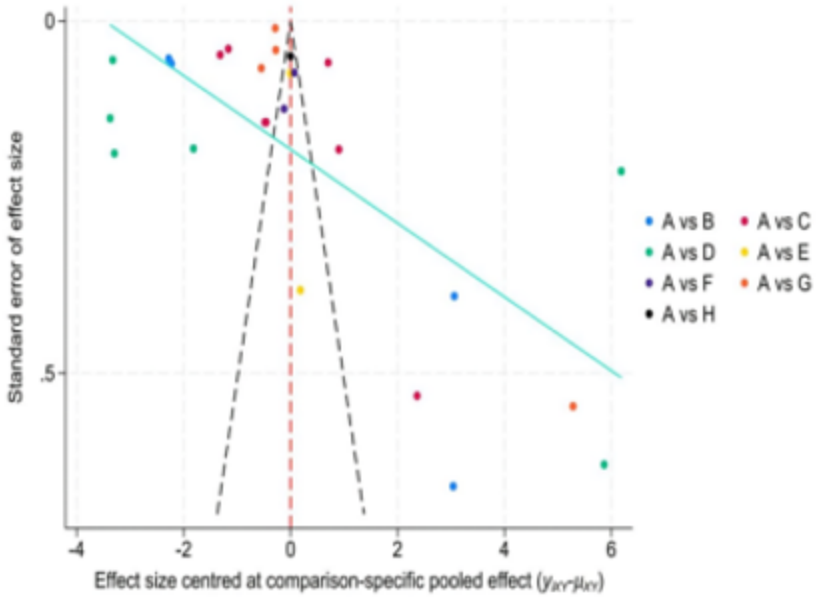


Figure 8. Funnel Plot for Bias Risk Assessment of 52 Included Studies on Mouse Atrogin-1 Atrophy Gene

Figure 8

See image above for figure legend

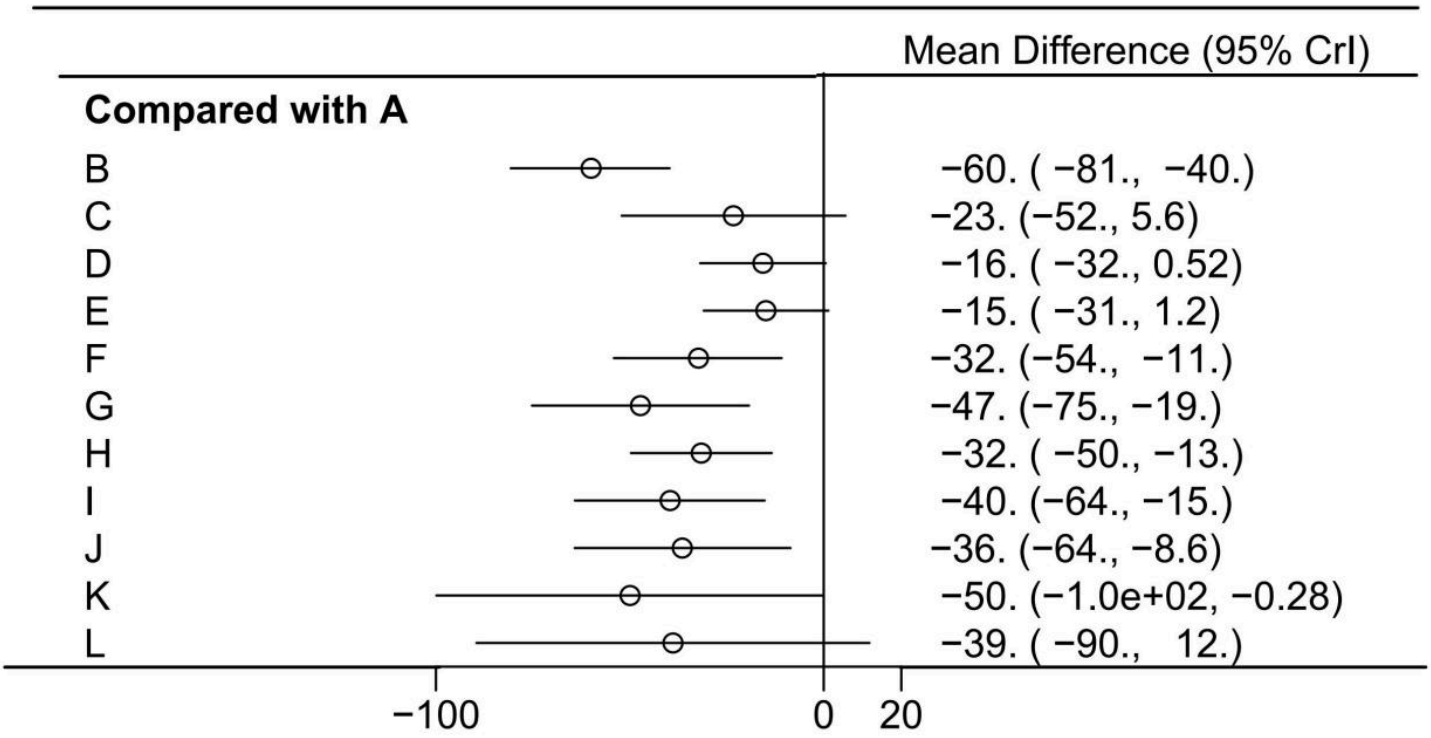


Figure 9

Forest plot comparing the wet weight of gastrocnemius muscle between 11 sarcopenia model groups and the normal control group

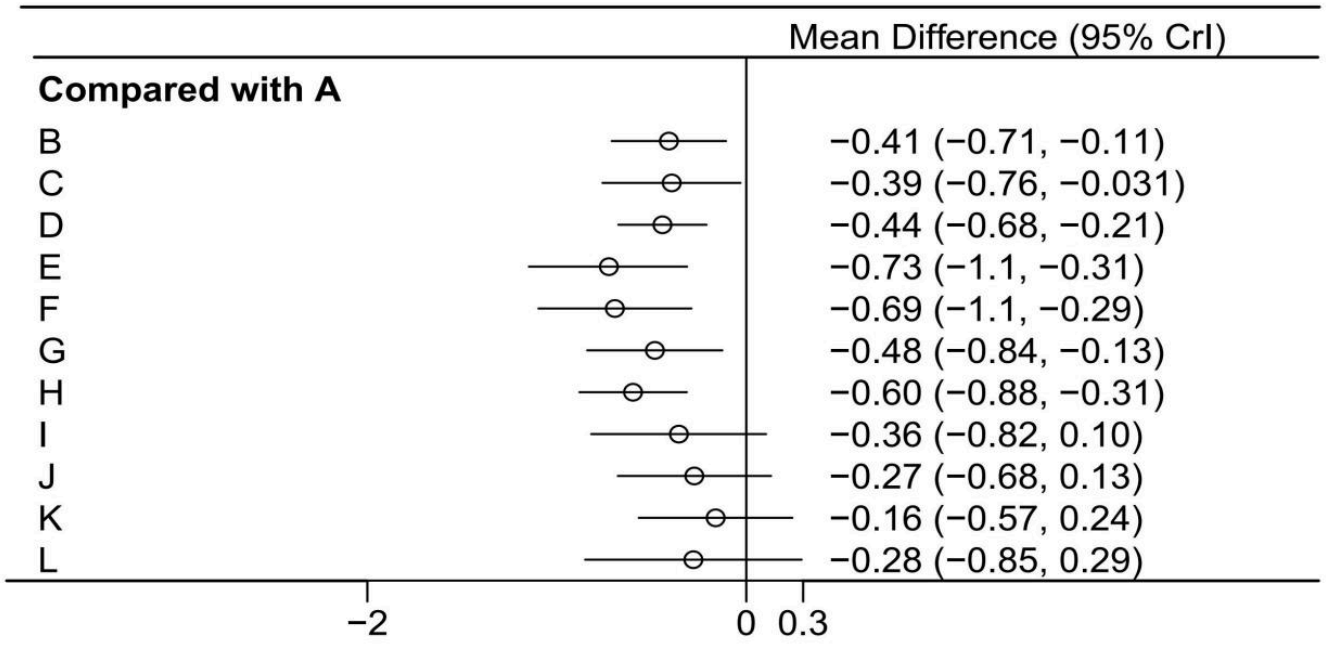


Figure 10

Forest plot of the comparison of grip strength between 11 sarcopenia model groups and normal control group in mice

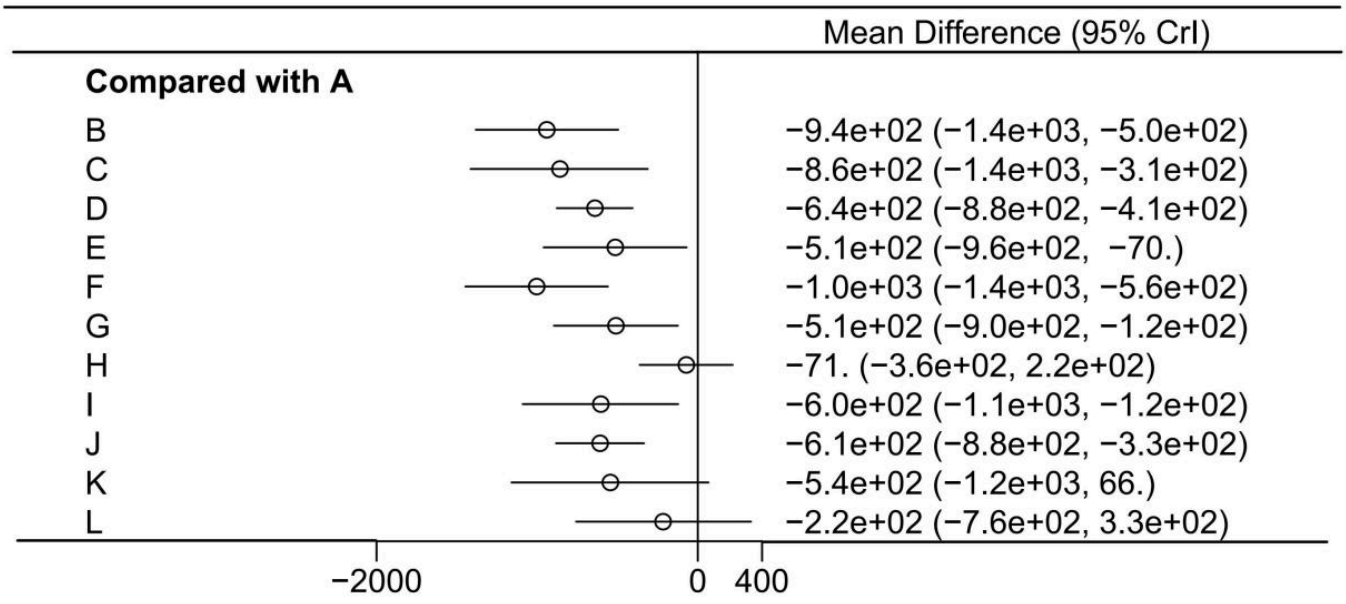


Figure 11

Forest plot of the comparison of cross-sectional area of gastrocnemius muscle fibers stained with hematoxylin and eosin (HE) between 11 sarcopenia model groups and normal control group

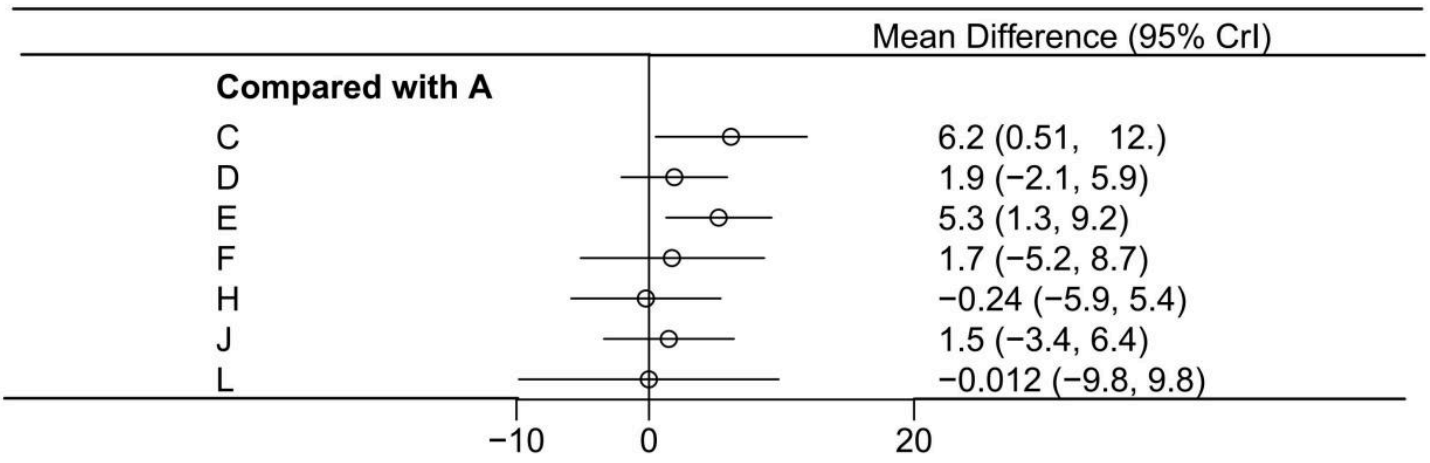


Figure 12

Forest plot of the comparison of MuRF-1 gene expression between 11 sarcopenia model groups and normal control group in mice

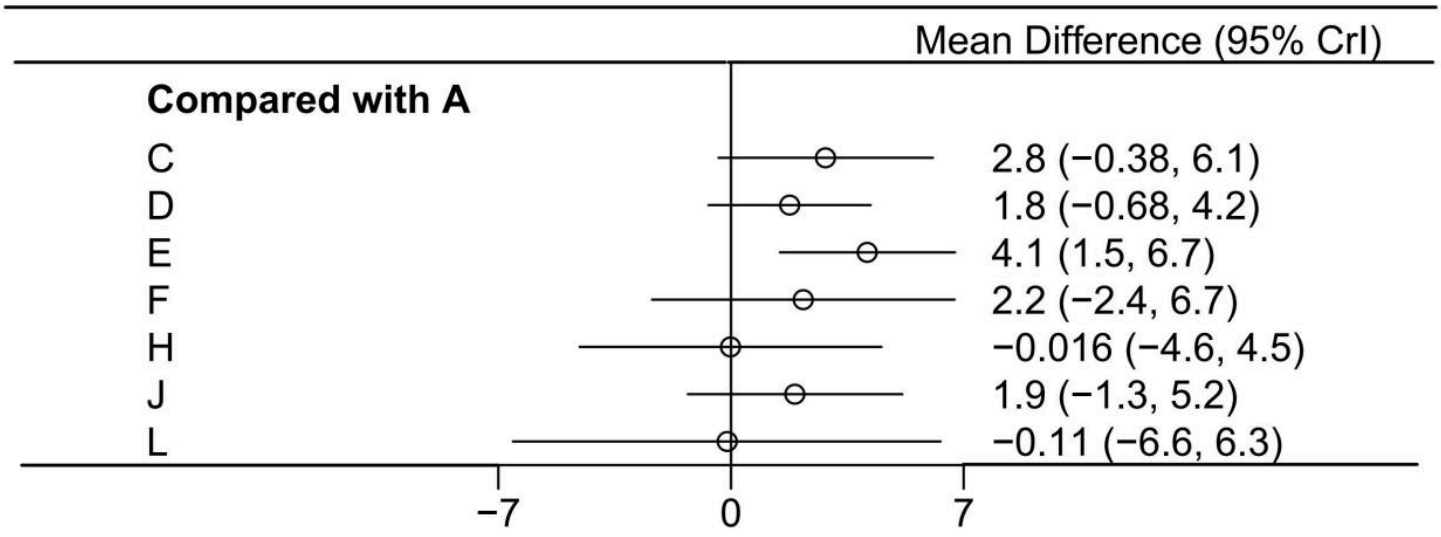
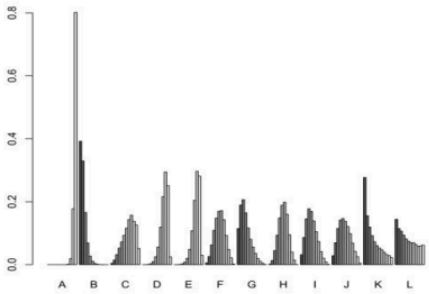
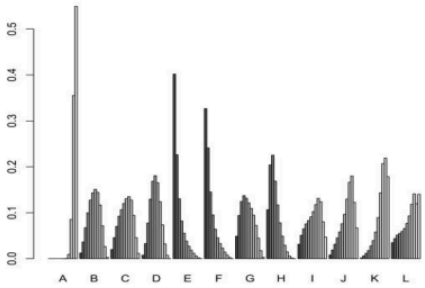


Figure 13

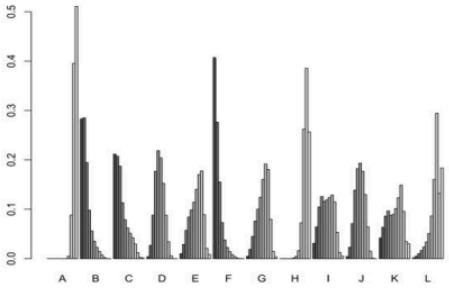
Forest plot of the comparison of Atrogin-1 gene expression between 11 sarcopenia model groups and normal control group in mice



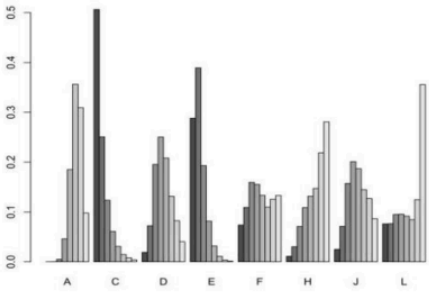
Probability ranking graph for the decline in gastrocnemius muscle wet weight



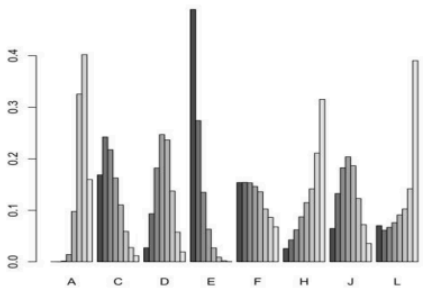
Probability ranking graph for the decline in mouse grip strength



Probability ranking graph for the decline in cross-sectional area of gastrocnemius muscle fibers



Probability ranking graph for the expression of mouse MuRF-1 gene



Probability ranking graph for the expression of mouse Atrogin-1 gene

Figure 14

Probability ranking graph for 11 sarcopenia animal models