UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE

PROGRAMA DE PÓS-GRADUAÇÃO EM PEDIATRIA: ATENÇÃO À SAÚDE DA CRIANÇA E DO ADOLESCENTE

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Força Muscular Periférica em Crianças e Adolescentes com Cardiopatia Congênita: Revisão Sistemática e Metanálise

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RESUMO

INTRODUÇÃO: Pacientes com cardiopatia congênita (CC) são menos ativos quando comparados com indivíduos saudáveis e apresentam limitação da capacidade funcional, relacionada com a presença de fraqueza e fadiga muscular. Em crianças com CC ou algum déficit de desenvolvimento, a força muscular costuma estar diminuída, afetando as habilidades motoras e funcionais na prática das atividades de vida diária, estando relacionada diretamente com a redução da capacidade de exercício. OBJETIVO: O objetivo do presente estudo foi avaliar a força muscular periférica de crianças e adolescentes com CC por meio de uma revisão sistemática com metanálise. MÉTODOS: A revisão sistemática incluiu estudos observacionais que avaliaram a força muscular periférica em crianças e adolescentes menores de 18 anos com CC, bem como controles saudáveis para comparação. A avaliação quantitativa foi realizada por meio de metanálise, comparando-se a dinamometria isocinética e a dinamometria de preensão palmar das crianças e adolescentes com CC e seus respectivos controles. RESULTADOS: Um total de 5.512 artigos identificados na busca preencheram os critérios de elegibilidade e quatro foram incluídos para metanálise nesta revisão. Três estudos avaliaram a força muscular isocinética (FMI) e encontraram redução significativa de 44.63Nm quando comparados com controles saudáveis (95% CI, –75.03 a –14.23; I2 82%, P para heterogeneidade =0.004). Dois estudos avaliaram a força de preensão palmar (FPP) e mostraram que não houve diferença significativa entre pacientes com CC e controles saudáveis, com o valor de 0,08Nm (IC 95%, –6,39 a –6,55; I2 98%, P para heterogeneidade <0,00001). CONCLUSÃO: Crianças e adolescentes com CC apresentaram diminuição da força muscular de membros inferiores, entretanto na força de preensão palmar esse resultado não foi confirmado e os dois grupos foram semelhantes.

PALAVRAS-CHAVE: Defeitos Cardíacos, Congênitos. Força Muscular. Criança. Adolescente. Revisão. Metanálise.

ABSTRACT

INTRODUCTION: Patients with congenital heart disease (CHD) are less active if compared with pairs control and have limited functional capacity, related with muscle weakness and fatigue. Children with CHD or some type of developmental deficit, muscle strength is usually decreased, affecting motor and functional skills in daily life activities, being related with reduction in exercise capacity. OBJECTIVE: The aim of the present study was to evaluate the peripheral muscle strength of children and adolescents with CHD with systematic review and meta-analysis. METHODS: The review included observational studies which evaluated peripheral muscle strength in children and adolescents with CHD under 18 years old and comparison with healthy controls. The quantitative assessment was performed by meta-analysis, comparing isokinetic dynamometry and handgrip dinamometry of children and adolescents with CHD and respective control groups. RESULTS: A total of 5.512 articles identified in the search met the criteria of eligibility and four were included for metanalysis in this review. Three studies evaluated isokinetic muscle strength and found -44.63Nm lower in patients with CHD compared with healthy controls (95% CI, –75.03 to –14.23; I2 82%, P for heterogeneity =0.004). Two studies evaluated handgrip strength and showed that there was no significant difference between patients with CHD and healthy controls, with the value 0,08Nm (95% CI, –6.39 to –6.55; I2 98%, P for heterogeneity<0.00001). CONCLUSION: Children and adolescents with CHD have decrease in muscle strength of the lower limbs and in handgrip strength this result was not confirmed and both groups were similar.

KEYWORDS: Heart Defects, Congenital. Muscle Strength. Child. Adolescent. Review. Meta-Analysis.

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LISTA DE ABREVIATURAS E SIGLAS

AHA	*American Heart Association*
ASHT	*American Society of Hand Therapists*
ATS	*American Thoracic Society*
CC	Cardiopatias Congênitas
CHD	Congenital Heart Disease
CoAo	Coarctação da Aorta/Aortic Coarctation
CSD	Cardiac Septum Defects
DSC	Defeitos do Septo Cardíaco
FM	Força Muscular
FMI	Força Muscular Isocinética
FMP	Força Muscular Periférica
FPP	Força de Preensão Palmar
HS	*Handgrip Strength*
IMS	*Isokinetic Muscle Strength*
MS	*Muscle Strength*
PMS	Peripheral Muscle Strength
TGV	Transposição dos Grandes Vasos/Transposition of Great Vessels
TOF	Tetralogia de Fallot/ Tetralogy of Fallot
UFCSPA	Universidade Federal de Ciências da Saúde de Porto Alegre
VO_2max	Consumo Máximo de Oxigênio/Maximal Oxygen Consumption

SUMÁRIO

1. INTRODUÇÃO

As cardiopatias congênitas (CC) foram descritas no século XVII, sendo consideradas anomalias na estrutura e função cardiocirculatórias. Na maioria dos casos são oriundas de alterações no desenvolvimento embrionário, estando presentes desde o nascimento (CERNACH, 2012; PINTO-JUNIOR, 2015). As anomalias cardíacas estão entre os defeitos mais frequentes ao nascimento, ocorrendo em aproximadamente 1% de todos os nascidos vivos (RUSSEL, 2018), sendo responsáveis por 7% dos óbitos neonatais, 25% destes devido a malformações consideradas graves (CHANGLANI, 2015).

As CC estão relacionadas a alterações em diversos sistemas, tanto antes como após a correção cirúrgica. As alterações nutricionais estão relacionadas ao aumento do sobrepeso e obesidade após a cirurgia, que ocorre na maioria das vezes pelos hábitos alimentares inadequados, associados ao comportamento por parte dos pais em ceder aos desejos alimentares devido ao histórico da doença (COHEN, 2012). Esse comportamento pode ser caracterizado como superproteção e interfere diretamente na prática de atividade física, que na maioria das vezes é prejudicada nessas crianças, levando a uma redução da capacidade de exercício. Essa limitação na capacidade de exercício pode estar relacionada a alterações hemodinâmicas, cardiológicas, musculoesqueléticas e até psicossociais decorrentes do procedimento cirúrgico, o que em alguns casos, interfere no desenvolvimento e predispõe ao sedentarismo (FELTEZ, 2013; MCCRINDLE, 2007).

A força muscular pode ser considerada uma variável relacionada com a aptidão física e o estado de saúde, sendo que a redução da força pode ocasionar limitações funcionais significativas. Em adultos com CC, a força muscular periférica (FMP) pode ser considerada um preditor da força geral, contudo, tais achados não podem ser extrapolados para a população pediátrica (SAVAGE, 2011). A força muscular nas crianças está relacionada diretamente com idade, sexo, altura e peso, apresentando aumento nos valores de acordo com o crescimento e amadurecimento (FELTEZ, 2015).

Em crianças com doenças congênitas ou algum tipo de déficit de desenvolvimento, a força muscular costuma estar diminuída, gerando fraqueza e fadiga muscular que comprometem as habilidades motoras e funcionais nas atividades de vida diárias (WEST, 2019). A redução da força pode estar presente em

diferentes patologias além das cardiopatias, como por exemplo em síndromes genéticas e metabólicas (RUSSEL, 2018), na Distrofia Muscular de Duchenne (POSNER, 2016), doenças reumatológicas (RASHED, 2018), bem como em pacientes submetidos a transplante pulmonar ou cardíaco (DELIVA, 2012).

Para mensuração da força muscular são utilizadas a dinamometria isocinética e manual, sendo a isocinética utilizada para mensuração da força, potência e resistência muscular, considerada o padrão-ouro de mensuração e segura para utilização em população pediátrica (TSIROS, 2011). Já a dinamometria manual é utilizada para mensurar a força muscular dos membros superiores, sendo considerada um preditor de força global em adultos por estar relacionada com a força de braços e costas, entretanto, ainda sem poder ser extrapolado na população pediátrica devido à escassez de estudos que abordem essa relação. (WIND, 2010).

Diante da crescente importância da avaliação e acompanhamento das crianças e adolescentes submetidos a cirurgia cardíaca, torna-se fundamental conhecer os aspectos que estão relacionados diretamente com esse evento, principalmente as alterações na função e capacidade de exercício. Sendo assim, é de fundamental importância realizar a sumarização dos estudos sobre força muscular nos pacientes cardiopatas, bem como identificar a relação dessa variável com a capacidade de exercício e, assim, proporcionar um atendimento de melhor qualidade para essa população.

2. REVISÃO DE LITERATURA

2.1 Cardiopatias Congênitas:

As cardiopatias congênitas começaram a ser identificadas no século XVII através de relatos que correlacionavam sintomas clínicos com achados anatômicos em autópsias. São consideradas anormalidades na estrutura e função cardiocirculatória, presentes desde o nascimento ou algumas vezes, oriundas de alterações no desenvolvimento embrionário (CERNACH, 2012; PINTO-JUNIOR, 2015). A incidência das cardiopatias congênitas atualmente é de 9:1000 nascidos vivos, com uma ocorrência de 3329 casos/ano na Região Sul do Brasil (PINTO-JUNIOR, 2015). Segundo estudo realizado por Van Der Linde *et al.* (2011), as cardiopatias congênitas mais frequentes encontradas foram a comunicação interventricular, comunicação interatrial, persistência do canal arterial, estenose pulmonar, tetralogia de Fallot, coarctação da aorta, transposição das grandes artérias e estenose aórtica.

Entre os defeitos do nascimento, as anomalias cardíacas despontam como as mais frequentes, afetando aproximadamente 1% de todos os nascidos vivos. As principais causas dos defeitos cardíacos congênitos (DCC) são divididas em dois grupos: os agentes ambientais e as causas genéticas. A exposição ambiental a agentes teratogênicos, infecciosos e doenças maternas são responsáveis por 2% de todas as anomalias cardíacas. As causas genéticas para o desenvolvimento de DCC podem ser divididas em 3 categorias: *anomalias cromossômicas*, *doenças monogênicas* e *heranças complexas ou multifatoriais*, sendo estas causas as responsáveis pela maior incidência de malformações congênitas em recém nascidos. Assim, torna-se importante analisar a interação entre agentes ambientais e fatores genéticos para definir a origem das cardiopatias congênitas (CERNACH, 2012).

As cardiopatias congênitas podem ser classificadas em dois grandes grupos: cianóticas e acianóticas, sendo diferenciadas pela presença de cianose na pele e mucosas em virtude da oxigenação insuficiente do sangue e a vascularização pulmonar. Dentro da classificação das cardiopatias, as mais frequentes são as descritas abaixo (BELO, 2016; FELTEZ, 2013):

• *Cianóticas:* Tetralogia de Fallot, Transposição de grandes vasos, Atresia tricúspide, Dupla via de entrada ventricular, Dupla via de saída ventricular, Drenagem venosa anômala total, Drenagem venosa anômala parcial.

• *Acianóticas:* Comunicação interatrial, Comunicação interventricular, Persistência do canal arterial, Defeito do septo atrioventricular, Coartação da aorta, Estenose aórtica, Estenose pulmonar.

São diversos os sinais e sintomas que estão relacionados às cardiopatias congênitas sendo importante a identificação dos mesmos, independentemente da idade em que se manifestam. Sinais e sintomas mais frequentes são sopro, cianose, dificuldade na alimentação, baixo ganho de peso, cansaço, sudorese, taquicardia, cardiomegalia, valores anormais de pressão arterial, alterações de pulso, baqueteamento digital, infecções pulmonares de repetição, dor torácica e síncope (GRAU, 2012).

A maioria das cardiopatias congênitas necessita de correção cirúrgica em algum momento ao longo da vida, sendo o campo da cirurgia cardíaca considerado um dos mais complexos dentro da medicina. A primeira cirurgia cardíaca foi realizada há aproximadamente seis décadas pelo Dr. Robert E. Gross, sendo uma correção da persistência de canal arterial em uma criança que, desde então, tornou-se um procedimento bastante utilizado com baixas taxas de morbidade e mortalidade. (PRATES, 1999). Na Tetralogia de Fallot, a primeira abordagem paliativa foi realizada no ano de 1944 pela Dra. Helen Taussig e Dr. Alfred Blalock. Essas novas descobertas no campo da cirurgia cardíaca levaram a novos estudos com aprimoramento e criação de novas técnicas, bem como uso da hipotermia e circulação extracorpórea (BRAILE, 1996; PRATES, 1999).

O conhecimento adquirido nas últimas décadas sobre cardiopatias congênitas e intervenções cirúrgicas, aliado aos avanços tecnológicos nessa área, tem possibilitado a correção cirúrgica de grande parte das cardiopatias, tanto as de baixa como as de média complexidade, que eram consideradas inoperáveis até algum tempo atrás. Dessa forma, foi possível obter uma redução considerável da morbidade e mortalidade nessa população (RUSSEL, 2018; ATIK, 2004). Apesar dos avanços na cirurgia cardíaca, ainda são frequentes os casos de insucesso devido à grande complexidade desses pacientes, a falha no reconhecimento precoce dos sintomas, às distintas fisiopatologias e a grande variedade de doenças associadas. Sendo assim, muitos são os profissionais envolvidos no cuidado dessas crianças desde a investigação diagnóstica até o tratamento adequado e acompanhamento a longo prazo (ATIK, 2004).

2.2 Complicações das Cardiopatias Congênitas:

As cardiopatias congênitas estão relacionadas com o aparecimento de alterações sistêmicas pré e pós correção cirúrgica, entre as quais se destacam as alterações nutricionais, de peso, altura e também a redução da capacidade de exercício. Essa condição limitada da capacidade de exercício é multifatorial, podendo estar relacionada a alterações hemodinâmicas, cardiológicas, musculoesqueléticas e redução da função pulmonar, geralmente refletindo a complexidade da cardiopatia de base (FELTEZ, 2013; WEST, 2019).

Dentre as alterações relacionadas às cardiopatias congênitas, é importante citar a predisposição à obesidade, tanto na infância quanto ao longo da vida adulta. A ocorrência de obesidade nesses pacientes é multifatorial, podendo estar relacionada com problemas de crescimento desde a primeira infância (PINTO, 2007). O risco de obesidade é maior em cardiopatas do que em crianças saudáveis e isso pode ser explicado pelo fato de que, em alguns casos, a ingesta calórica é aumentada como forma de compensação ao gasto energético demandante da doença, assim como a restrição na prática de atividade física que ocorre nesses pacientes (COHEN, 2012; BAKER, 2007).

Da mesma forma que a obesidade, é importante citar como fator complicador relacionado às CC o impacto psicossocial dessa doença, que pode ser refletido através das dificuldades comportamentais, no baixo desempenho escolar e também na ocorrência de atrasos no desenvolvimento neuropsicomotor. Esses fatores são determinantes para a integração social das crianças e adolescentes cardiopatas tanto antes como após a correção cirúrgica, podendo, se não bem administradas, afetar a qualidade de vida desses pacientes (WERNOVSKY, 2006).

Além disso, os cardiopatas usualmente são criados em um ambiente protegido, principalmente em relação aos possíveis riscos relacionados com o exercício e a prática de atividade física. Isso ocorre em decorrência dos medos e preocupações vindos dos pais, educadores e até equipe médica, sendo que essa superproteção pode influenciar negativamente no desenvolvimento dessas crianças principalmente no pós-operatório, fazendo com que as mesmas se tornem sedentárias (MCCRINDLE, 2007; COHEN, 2012).

2.3 Exercícios nas Cardiopatias Congênitas:

A intolerância ao exercício é comumente encontrada em pacientes cardiopatas, sendo o grau de intolerância relacionado ao tipo de cardiopatia ou malformação, complexidade e gravidade do caso, assim como ao tipo de cirurgia e reparo realizado e as comorbidades associadas no pós-operatório. A redução da capacidade de exercício é considerada multifatorial, entretanto a literatura descreve alguns fatores de maior impacto tais como: alterações hemodinâmicas residuais, incompetência cronotrópica, presença de cianose, hipertensão pulmonar, redução do débito cardíaco, arritmias e limitações ventilatórias, além da inatividade física (PIANOSI, 2009; RHODES, 2005).

Em um estudo realizado por Ray et al. (2011), crianças e adolescentes cardiopatas apresentaram escores de atividade física muito inferiores aos referenciados na literatura para população saudável, sendo que aqueles com defeitos cardíacos menos complexos apresentaram maior nível de atividade física quando comparados aos cardiopatas com defeitos graves. Outro estudo traz que a redução da prática de atividade física em pacientes submetidos a procedimento de Fontan pode ser relacionada à baixa capacidade funcional cardiorrespiratória, a restrição e limitação imposta pelos pais, bem como a fatores psicossociais (MCCRINDLE, 2007).

Mesmo com todos os fatores que interferem na capacidade de exercício, os benefícios e indicações da prática de atividade física nos cardiopatas já se encontram bem estabelecidos. Estudos têm demonstrado que a prática de exercício supervisionado e a inserção em programas de reabilitação cardíaca levam a melhora da capacidade funcional, cardiovascular e musculoesquelética, estando associados também a um aumento na autoestima e qualidade de vida (MOOLA, 2009).

A prática de atividade física nas crianças e adolescentes promove melhora da coordenação motora, autoestima e também do convívio social. Não existem evidências na literatura sobre a necessidade de restrição da prática de atividade física, entretanto deve-se atentar para aqueles pacientes com distúrbios no ritmo cardíaco, sendo indicado o acompanhamento com equipe multiprofissional. Segundo as diretrizes da *American Heart Association* (AHA) a maioria das crianças com cardiopatias congênitas tem menor probabilidade de atender as recomendações de atividade física quando comparadas a indivíduos saudáveis da mesma faixa etária, embora a prática segura de atividade física seja recomendada (LONGMUIR, 2013; PEMBERTON, 2010).

Diferentes tipos de atividade e exercício físico podem ser realizados, entretanto, deve-se seguir algumas recomendações ao avaliar um paciente cardiopata em relação à capacidade ou não de realizar exercícios. As seis etapas recomendadas para avaliação e recomendação da prática de exercício são (BUDTS, 2013):

- História clínica e exame físico
- Avaliação de cinco parâmetros básicos - função ventricular, pressão da artéria pulmonar, dimensão da aorta, arritmias e saturação arterial de oxigênio em repouso e durante o exercício
- Decisão sobre o tipo de exercício
- Teste de exercício cardiopulmonar
- Recomendação da intensidade
- Acompanhamento

2.4 Força Muscular nas Cardiopatias Congênitas:

Nas cardiopatias congênitas, a força muscular está diretamente relacionada com a aptidão física e o estado de saúde e normalmente encontra-se reduzida tanto no pré como no pós operatório, podendo ocasionar limitações funcionais significativas. A força muscular nas crianças pode ser alterada em função de diversos fatores como idade, sexo e altura, de acordo com a curva de crescimento e desenvolvimento, ou ainda decorrente de alterações na massa e fibras musculares (FELTEZ, 2015). Sendo assim, para avaliação em crianças ou adolescentes com alguma patologia, preconiza-se a utilização de valores de referência obtidos em seus pares saudáveis e não os valores advindos da população adulta (WIND, 2010).

A força muscular é reduzida em crianças com diversas patologias, entre elas algumas síndromes genéticas (RUSSEL, 2018), Síndrome de Barth (HORNBY, 2019) e Síndrome de Noonam (CROONEN, 2017), pacientes com Distrofia Muscular de Duchenne (POSNER, 2016) e algumas doenças reumatológicas (RASHED, 2018), além daqueles submetidos a transplante pulmonar ou cardíaco (DELIVA, 2012). Em crianças com doenças congênitas ou algum tipo de déficit de desenvolvimento, a força muscular normalmente encontra-se diminuída, gerando uma fraqueza e fadiga muscular que comprometem o desempenho de habilidades motoras funcionais nas atividades diárias (HOLM, 2008). Sendo assim, torna-se importante a avaliação da força muscular periférica nos cardiopatas por se tratar de uma população com

necessidades e demandas específicas para seu tratamento e acompanhamento clínico.

A força muscular periférica é uma variável que pode ser intimamente relacionada a limitações funcionais, à redução da capacidade de exercício e à qualidade de vida em pacientes com doenças cardíacas. A musculatura periférica está relacionada com a capacidade funcional, sendo que a baixa oferta de oxigênio para os músculos periféricos nos cardiopatas, que ocorre em decorrência das alterações cardiocirculatórias características da doença, pode contribuir para a intolerância ao exercício e, consequentemente para fadiga muscular (MOALLA, 2012; GREUTMANN, 2011).

Em adultos com doença cardíaca, a FMP pode ser considerada um preditor de força global (SAVAGE, 2011), no entanto em crianças ainda são poucos os estudos que trazem essa informação. O estudo realizado por Wind *et al.* (2010) com crianças, adolescentes e jovens adultos saudáveis afirma que existe uma associação entre a força de preensão palmar e a força muscular total, podendo a FPP ser um indicativo da força geral.

A literatura traz que a força muscular isocinética de membros inferiores na população pediátrica se encontra reduzida quando comparada com indivíduos saudáveis (MOALLA, 2006; HOLM, 2007; SANDBERG, 2020). Em relação a força de preensão palmar, alguns estudos mostram uma semelhança dos valores em pacientes cardiopatas e saudáveis (LONGMUIR, 2015), assim como outros estudos mostram uma redução da FPP após cirurgia cardíaca (TURQUETTO, 2018). Entretanto, a maioria dos estudos cita a relação dos valores de força muscular com idade e gênero, sendo que a ampla faixa etária que compreende crianças e adolescentes torna difícil a padronização dessa variável. Assim, tornam-se necessários mais estudos nessa área para melhor embasamento e segurança na abordagem, tanto terapêutica como preventiva.

2.5 Avaliação da Força Muscular:

A força muscular (FM) pode ser considerada um preditor da força global. Os métodos mais utilizados atualmente para avaliação da força muscular são a dinamometria isocinética e manual. A dinamometria isocinética é considerada o padrão-ouro para mensuração da força muscular, sendo realizada através de um dinamômetro isocinético que pode obter medidas como força de pico, resistência,

potência e ângulo de força máxima de diferentes grupos musculares. Entretanto, por ser um método de alto custo, costuma-se utilizar como alternativa à dinamometria de preensão palmar, considerada um método simples e de baixo custo que fornece uma medida quantitativa de força muscular, sendo a mais utilizada na prática clínica. As avaliações da dinamometria isocinética e dinamometria manual são realizadas através da contração máxima da musculatura de membros inferiores e membros superiores (STARK, 2011; TURQUETTO, 2017). A seguir são descritos os métodos de avaliação da força muscular e sua aplicabilidade clínica.

2.5.1 Dinamometria Isocinética:

Os dinamômetros isocinéticos são instrumentos de medida que proporcionam informações quanto à dinâmica e performance dos grupos musculares, assumindo assim que a articulação se move a uma velocidade angular constante (movimento isocinético). Os sistemas isocinéticos são baseados no princípio de que o braço da alavanca se move a uma velocidade angular predeterminada, por maior que seja a força aplicada pelo usuário no giro ou no momento. Ou seja, se o usuário aumentar a força, a máquina aumenta sua resistência de forma a manter a velocidade constante. Além da avaliação da força, também é possível avaliar a fadiga e a resistência muscular através de uma série de contrações repetitivas realizadas a uma velocidade angular preestabelecida (DVIR, 2002).

A dinamometria isocinética é amplamente utilizada em pesquisas e na prática clínica para testar, comparar e também treinar grupos musculares específicos, obtendo assim uma avaliação objetiva da força, potência e resistência muscular (JEE, 2015). A obtenção desses parâmetros é importante para avaliação do impacto do treinamento físico, dos programas de reabilitação, bem como em lesões musculoesqueléticas e algumas condições de saúde, tendo em vista que proporciona avaliação da maturação e envelhecimento muscular. É uma avaliação amplamente descrita no público adulto, e recentemente vem sendo utilizada também em crianças, mostrando-se um método seguro e viável (TSIROS, 2011; JOHNSEN, 2015).

Desde o início das pesquisas na área da isocinética, a articulação do joelho vem sendo priorizada em diversos estudos, podendo ser utilizada tanto na musculatura de membros superiores como inferiores. Os principais grupos musculares avaliados com a dinamometria isocinética são os extensores e os flexores de joelho, bem como flexores plantares do tornozelo (HOLM, 2007; SANDBERG, 2020). Para

avaliação através da dinamometria isocinética, deve-se seguir algumas diretrizes de posicionamento e execução do teste (DVIR, 2002) bem como a comparação com valores de referência para a população pediátrica como os descritos por Wiggin *et al.* (2006) baseados em população saudável.

A execução do teste deve seguir alguns protocolos, sendo realizado com os pacientes sentados em uma cadeira com quadril e joelho a 90º de flexão. O eixo rotacional do braço da alavanca deve ser alinhado com o eixo rotacional da articulação do joelho no côndilo femoral lateral, sendo o ponto de resistência fixado aproximadamente a 3 centímetros acima do maléolo medial. Sempre com uso de feedback visual e auditivo, os pacientes são orientados a realizar os movimentos com força máxima. (BIODEX, 2002; SANTOS, 2013). São consideradas contra indicações para realização do teste as restrições na cicatrização de tecidos moles, presença de dor ou amplitude de movimento limitada, instabilidade articular e distensões musculares (DAVIES, 2012).

Figura 1 - Dinamômetro Isocinético

Fonte: https://www.biodex.com/physical-medicine/products/dynamometers/system-4-pro

2.5.2 Dinamometria Manual:

A dinamometria manual é utilizada para avaliação da força de preensão palmar, sendo considerada um instrumento simples, objetivo, prático e de fácil utilização. Tem sido amplamente utilizada para avaliação da força de preensão em pacientes com

doenças e desordens nas extremidades dos membros superiores como artrite reumatoide, síndrome do túnel do carpo, epicondilite lateral, acidente vascular cerebral, lesões traumáticas, doenças neuromusculares, entre outras. Como em adultos a força de preensão está associada com a força do braço, costas e pernas, podendo ser esta variável considerada indicativa da força muscular generalizada (REIS, 2011; FIGUEIREDO, 2019; WIND, 2010).

Na pediatria, a dinamometria manual vem conquistando espaço e sendo cada vez mais utilizada. Alguns estudos mostram que a mensuração da força muscular através desse instrumento pode ser correlacionada com a força muscular total em crianças e adolescentes (WIND, 2010), já estando disponíveis na literatura valores de normalidade e referência para a população pediátrica saudável, como descrito por McQuiddy *et al.* (2015).

Dentre os aparelhos disponíveis para avaliação, o dinamômetro Jamar tem sido considerado o instrumento mais aceito de acordo com as recomendações da *American Society of Hand Therapists* (ASHT). Seu uso teve início em meados da década de 50, sendo até os dias atuais amplamente utilizado na prática clínica para avaliação e reabilitação (MCQUIDDY, 2015). Este instrumento tem sido considerado padrão-ouro para essa avaliação devido à alta validade e confiabilidade apresentada quando comparado com outros métodos de avaliação da força muscular (REIS, 2011; FIGUEIREDO, 2019).

Figura 2 - Dinamômetro Hidráulico Jamar

Fonte: https://www.jlwinstruments.com/search/?query=isokin

O dinamômetro possui duas alças paralelas, uma fixa e outra móvel com opção de ajuste em 5 posições de acordo com o tamanho da mão do paciente. É composto por um sistema hidráulico fechado que mede a quantidade de força produzida por uma contração isométrica (movimento de preensão) sobre as alças, como demonstrado na figura 2. Para validação do teste é recomendado que sejam realizadas três medidas, considerando a média entre elas para verificação da força máxima de preensão palmar (FIGUEIREDO, 2019).

A execução do teste deve seguir as recomendações propostas pela ASHT. Recomenda-se que o paciente esteja sentado em uma cadeira com os pés apoiados no chão, ombro aduzido e neutramente rodado, cotovelo flexionado a 90°, antebraço em posição neutra e punho posicionado entre 0° e 30° de extensão e entre 0° e 15° de desvio ulnar. Com uso de incentivo verbal, os pacientes são orientados a realizar preensão com força máxima para mensuração da força de membros superiores (FESS e MOORAN, 1981).

3. JUSTIFICATIVA

As cardiopatias congênitas apresentam uma incidência cada vez maior na população, sendo que as alterações cardiovasculares, respiratórias e musculares decorrentes dessas doenças são responsáveis por um declínio funcional mesmo após correção cirúrgica. Em crianças com doenças congênitas, a força muscular normalmente encontra-se diminuída, gerando uma fraqueza e fadiga muscular que compromete seu desempenho das habilidades motoras funcionais nas atividades diárias. Face ao exposto, em virtude da dificuldade na determinação dos melhores métodos para avaliar a força muscular em crianças e adolescentes com cardiopatia congênita e a necessidade de extrapolar estes dados para a prática clínica diária, a maneira mais adequada de avaliar criticamente as informações disponíveis na literatura é através da realização de uma revisão sistemática. A realização desta revisão sistemática e metanálise será de suma importância para auxiliar aos profissionais da saúde na determinação da fraqueza muscular do paciente pediátrico cardiopata bem como estabelecer futuras estratégias de reabilitação.

4. OBJETIVOS

4.1 Objetivo Geral

Revisar sistematicamente a força muscular periférica de crianças e adolescentes com cardiopatia congênita.

4.2 Objetivos Específicos:

- Revisar sistematicamente a força muscular periférica nas diferentes cardiopatias congênitas.

- Revisar sistematicamente a força muscular periférica e sua associação com a capacidade funcional.

- Revisar sistematicamente a força muscular periférica relacionada ao sexo e as diferentes faixas etárias.

5. HIPÓTESES

5.1 Hipótese Nula:

Crianças e adolescentes com cardiopatia congênita não apresentam força muscular periférica reduzida quando comparados a indivíduos saudáveis.

5.2 Hipótese Alternativa:

Crianças e adolescentes com cardiopatia congênita apresentam força muscular periférica reduzida quando comparados a indivíduos saudáveis.

6. MÉTODOS

6.1 Protocolo e Registro

Este estudo segue as recomendações propostas pela *Cochrane* (HIGGINS, 2021)*, sendo* apresentado conforme sugerido pelo PRISMA Statement (PAGE, 2021). O estudo está registrado no PROSPERO – *Internacional Prospective Register of Systematic Reviews* (http://www.crd.york.ac.uk/PROSPERO/), sob número de registro CRD42021225172.

6.2 Critérios de elegibilidade

Foram incluídos estudos observacionais (coorte e transversal) com amostra composta por crianças e adolescentes menores de 18 anos com cardiopatia congênita, entre elas Defeitos do Septo Cardíaco (DSC), Coarctação da Aorta (CoAo), Transposição dos Grandes Vasos (TGV), Tetralogia de Fallot (TOF) e aquelas submetidas a cirurgia de Fontan, além de indivíduos saudáveis para compor o grupo controle. O desfecho primário foi a força muscular periférica (dinamometria de preensão palmar e dinamometria isocinética) e o desfecho secundário a capacidade de exercício, considerando os valores de VO_2máx para a análise. Foram incluídos os estudos que apresentassem os desfechos primários preencheram todos critérios de inclusão, sendo todos em língua inglesa. Foram excluídos os estudos publicados antes de 1990, cartas ou resenhas, teses ou artigos publicados apenas na forma de resumos, incluindo anais de congressos.

6.3 Fontes de informação

Foram realizadas buscas nas bases de dados: MEDLINE acessado via Pubmed, Embase, PEDro e Cochrane, além de referências de estudos publicados na área entre o ano de 1990 e setembro de 2020. Para cada portal de pesquisa, foi elaborada uma estratégia específica de cruzamento dos descritores ou das palavras-chaves para recuperação dos assuntos da literatura científica. Foi realizada uma estratégia de busca utilizando os seguintes descritores em inglês: *Child ou Adolescent* combinadas com *Heart Defects, Congenital, Heart Septal Defects, Aortic Coarctation, Transposition of Great Vessels, Tetralogy of Fallot, Fontan Procedure,* além de *Muscle Strength, Maximal Respiratory Pressures e Exercise*. A estratégia de busca utilizada para o PubMed está descrita como material suplementar.

6.4 Seleção dos estudos

Os títulos e resumos de todos os artigos identificados pela estratégia de busca foram avaliados independentemente por dois autores (CCN e MLYS) em duplicata, sendo utilizada uma lista de verificação de rastreamento padrão com base nos critérios de elegibilidade. Os resumos que não forneciam informações suficientes sobre os critérios de inclusão e exclusão foram selecionados para avaliação do texto completo. Na segunda fase, os mesmos revisores avaliaram de forma independente os textos completos dos artigos e fizeram a seleção de acordo com os critérios de elegibilidade especificados anteriormente. Um terceiro revisor (JLL) resolveu todas as discordâncias relacionadas à elegibilidade do estudo e ajudou na decisão de incluir ou excluir estudos.

6.5 Processo de coleta de dados

A extração dos dados foi realizada pelos mesmos revisores de forma independente, utilizando um formulário de aquisição de dados padronizado contendo informações sobre: desenho do estudo (transversal, caso-controle, coorte), participantes (idade da população e sexo) e desfechos. O desfecho primário avaliado foi a força muscular periférica mensurada por dinamometria isocinética e dinamometria de preensão palmar. O desfecho secundário foi a capacidade de exercício, considerando os valores de consumo máximo de oxigênio (VO_2máx) para a análise.

6.6 Avaliação do risco de viés

A avaliação da qualidade metodológica dos estudos foi realizada de forma independente pelos mesmos dois revisores (CCN e MLYS) através da Escala Newcastle-Ottawa, utilizada para estudos de caso-controle e coorte (WELLS, 2021). Os estudos transversais foram avaliados com uma adaptação da mesma escala (PATRA, 2015). A escala avalia os estudos de acordo com critérios específicos: definição dos grupos expostos e não expostos, seleção e representatividade dos grupos, comparabilidade e variáveis de resultado de interesse. A pontuação da qualidade metodológica dos estudos de coorte e caso-controle foi calculada em três componentes: seleção dos grupos, qualidade de ajuste para confusão e avaliação da exposição após desfecho, sendo a pontuação também adaptada nos casos dos

estudos transversais. Os estudos foram classificados individualmente como “boa”, “razoável” ou “má” qualidade pelos critérios estabelecidos pela escala (MCPHEETERS, 2012). Discordâncias entre os revisores foram resolvidas por consenso.

6.7 Análise dos dados

Para síntese quantitativa, as estimativas de efeito agrupado foram obtidas comparando-se a força isocinética e a força de preensão manual de crianças e adolescentes com DCC e respectivos grupos de controle de saúde. Estimativas combinadas de efeitos foram geradas por meio dos valores máximos obtidos nos estudos revisados e os resultados apresentados como diferença de média ponderada com intervalo de confiança de 95% (IC95%). A heterogeneidade estatística entre os estudos foi avaliada por meio do teste Cochrane Q e do teste de inconsistência (I2), em que valores abaixo de 25% foram considerados indicativos de baixa heterogeneidade, entre 25% e 50% de heterogeneidade moderada e acima de 50% de alta heterogeneidade. Os cálculos foram realizados usando o método de efeitos aleatórios. Um valor de $p \leq 0,05$ foi considerado estatisticamente significativo. Todas as análises foram realizadas com o software Review Manager 5.1 (Cochrane Collaboration).

7. CONCLUSÃO

A presença de cardiopatias congênitas em crianças e adolescentes está relacionada com a diminuição da força muscular de membros inferiores, o que pode ser um preditivo de reduzida capacidade funcional. Entretanto, pode-se perceber com essa revisão que pacientes cardiopatas e saudáveis da mesma faixa etária apresentam força muscular de preensão palmar semelhantes. A literatura ainda é escassa no que se refere à avaliação de força muscular na população pediátrica com cardiopatias congênitas, embora essa população específica venha apresentando demanda crescente por atenção e melhor avaliação clínica e funcional. Diante disso, são necessários mais estudos nesta área, bem como revisões sistemáticas bem estruturadas a fim de reunir as informações disponíveis e, dessa forma, estabelecer uma melhor fundamentação da prática clínica baseada em evidências científicas

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9. ARTIGO CIENTÍFICO

PERIPHERAL MUSCLE STRENGTH IN CHILDREN AND ADOLESCENTS WITH CONGENITAL HEART DISEASE: SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Patients with congenital heart disease (CHD) are less active if compared with pairs control and have limited functional capacity, related with muscle weakness and fatigue. Children with CHD or some type of developmental deficit, muscle strength is usually decreased, affecting motor and functional skills in daily life activities, being related with reduction in exercise capacity. The aim of the present study was to evaluate the peripheral muscle strength of children and adolescents with CHD with systematic review and meta-analysis. The review included observational studies which evaluated peripheral muscle strength in children and adolescents with CHD under 18 years old and comparison with healthy controls. The quantitative assessment was performed by meta-analysis, comparing isokinetic dynamometry and handgrip dinamometry of children and adolescents with CHD and respective control groups. A total of 5.512 articles identified in the search met the criteria of eligibility and four were

included for metanalysis in this review. Three studies evaluated isokinetic muscle strength and found -44.63Nm lower in patients with CHD compared with healthy controls (95% CI, –75.03 to –14.23; I2 82%, P for heterogeneity =0.004). Two studies evaluated handgrip strength and showed that there was no significant difference between patients with CHD and healthy controls, with the value 0,08Nm (95% CI, –6.39 to –6.55; I2 98%, P for heterogeneity<0.00001). Children and adolescents with CHD have decrease in muscle strength of the lower limbs and in handgrip strength this result was not confirmed and both groups were similar.

KEYWORDS: Heart Defects. Congenital. Muscle Strength. Child. Adolescent. Review. Meta-Analysis

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INTRODUCTION

Congenital heart diseases (CHDs) are the most common congenital malformations present from birth, with defects in structure or cardiocirculatory function [1, 2]. Most patients are less active, have a decrease in functional capacity and exercise is limited, as already observed in previous meta-analysis in which patients with CHDs had 9.31 ml/kg/min lower maximal oxygen consumption (VO_2max) compared with healthy control group [3]. These conditions are related to muscle weakness and fatigue [4]. The majority of heart defects require surgical intervention

and some factors remain present even after surgical correction, such as changes in nutritional status, height, and weight [5].

Muscle strength can be considered a variable that is related to physical fitness and health status, and a decrease in this variable can be associated with significant functional limitations. In adults with CHDs, peripheral muscle strength can be considered a predictor of overall strength; however, there are a few reports in pediatric patients [6]. Strength in children is directly related to age, sex, height and weight, with an increase in values according to growth and maturity [5], and can be reduced in different pathologies [7, 8, 9] as well as in patients after lung or heart transplantation [10]. In children with CHDs or some type of developmental deficit, muscle strength is usually decreased, generating muscle weakness and fatigue that compromises motor and functional skills in activities in daily living [11].

Isokinetic dynamometry is used in research and clinical practice to measure strength, power and muscular endurance. Isokinetic tests have been considered safe to use in pediatric populations [12]. Handgrip strength is an adequate instrument with which to measure generalized muscle strength in adults, representing the association of arm, back, and leg strength. There are few studies in the pediatric population, mostly with children with congenital heart disease, so it is difficult to confirm that handgrip can be used as a predictor of general muscle strength [13].

Patients with congenital heart disease (CHD) also have impaired aerobic capacity compared to age and gender-matched healthy controls. These impairments are multifactorial and result from internal and external influences, such as the severity of CHD, number of surgical procedures, hypoactivity, hemodynamic limitations, and pulmonary and musculoskeletal disorders [11]. This reduction in exercise capacity has been widely associated with increased morbidity and mortality in adults [14].

Peripheral muscle strength may be related to exercise capacity and the presence of functional limitations in patients with CHD. Cardiocirculatory changes in cardiac patients are responsible for the low supply of oxygen to muscle groups, which contributes to exercise intolerance and muscle fatigue. The relationship between muscle strength and exercise capacity in children and adolescents with heart disease is still poorly explored in the literature, however, some studies have already shown an association between strength and muscle endurance in training programs [15, 16].

To the best of our knowledge, there have been no systematic reviews of muscle strength in pediatric populations with CHDs. Thus, this systematic review and meta-

analysis aimed to evaluate the peripheral muscle strength of children and adolescents with CHD, and secondly to assess exercise capacity and the relationship with muscular strength.

METHODS

Protocol and Registration

This study was conducted in accordance with the Cochrane Collaboration [17] and is presented as suggested by the Preferred Reporting Items for Systematic Review and Meta-Analyses: The PRISMA Statement [18]. This meta-analysis was registered in the PROSPERO - *International prospective register of systematic reviews*, number CRD42021225172.

Eligibility criteria

We included observational studies (cohort and cross-sectional) that investigated children and adolescents under 18 years with CHD, including cardiac septum defects (CSD), aortic coarctation (CoAo), transposition of the great vessels (TGV), tetralogy of Fallot (TOF), patients submitted to Fontan procedure, and a healthy control group. The primary outcome was peripheral muscle strength (isokinetic dynamometry and handgrip dynamometry). Only studies in English were selected, and those with an analysis of primary outcome were included. We excluded studies that were published before to 1990, letters or reviews, theses or articles published only as abstracts, and conference proceedings.

Strategy of search and selection of studies

We conducted an electronic search in four databases: MEDLINE accessed via PubMed, Embase, PEDro and Cochrane, to obtain all studies published in the area between 1990 and September 2020. For each database, a specific strategy of descriptors and keywords was applied. A search strategy was performed using the following descriptors in English: *Child or Adolescent* combined with *Heart Defects*, *Congenital, Heart Septal Defects*, *Aortic Coarctation*, *Transposition of Great Vessels*, *Tetralogy of Fallot*, *Fontan Procedure*, in addition to *Muscle Strength, Maximal Respiratory Pressures* and *Exercise*. Terms were combined using the Boolean operators “OR” and “AND”. The complete search strategy used for PubMed database is shown in the supplementary material.

Two independent authors (CCN and MYS) screened the titles and abstracts of all articles identified by the search strategy. A standard screening checklist based on the eligibility criteria was used. Abstracts that did not provide enough information on the inclusion and exclusion criteria were selected for evaluation of the full text. In this second phase, the same reviewers independently evaluated the full text articles and made the selection according to the eligibility criteria. A third reviewer (JLL) assessed the studies in cases of disagreement related to the trial eligibility and assisted in the decision to include or exclude studies.

Data extraction

Data extraction was carried out by the same independent reviewers, using a standardized data acquisition form containing information about: study design (cross-sectional, case-control, cohort), participants (population age and gender) and outcomes. The primary outcome was overall muscle strength measured by isokinetic dynamometry and handgrip dynamometry. The secondary outcome evaluated was the exercise capacity considering the values of maximal oxygen consumption (VO_2max) for the analysis.

Risk of bias assessment

The same two reviewers also independently assessed the risk of bias of studies using the Newcastle-Ottawa Scale (NOS) for case-control and cohort studies [19]. Cross-sectional studies were evaluated with an adaptation of the same scale [20]. The NOS evaluates the studies on several design-specific criteria: the definition of the exposed and unexposed groups, selection and representativeness of groups, comparability, and outcome variables of interest. The studies were rated individually as “good,” “fair,” or “poor” quality by the criteria established by NOS [21]. Disagreements between reviewers were resolved by consensus.

Data analysis

For quantitative synthesis, pooled-effect estimates were obtained by comparing the isokinetic strength and handgrip strength of children and adolescents with CHD and respective control health groups. Combined estimates of effects were generated through the maximum values obtained in the studies reviewed and the results were presented as weighted mean differences (WMD) with 95% confidence intervals (95%

CIs). Statistical heterogeneity between the studies was assessed using the Cochrane Q test and the inconsistency test (I^2), in which values below 25% were considered indicative of low heterogeneity, between 25% and 50% moderate heterogeneity and above 50% high heterogeneity. Calculations were performed using the random effects method. A p-value ≤0.05 was considered statistically significant. All analyses were performed using the Review Manager 5.1 software (Cochrane Collaboration).

RESULTS

A total of 5,512 articles identified in the search met the eligibility criteria; 752 were included to full text review and after this stage, four studies were included in this review. Figure 1 shows the flow diagram.

Three cross-sectional studies and one cohort study were included, with a total of 1202 individuals; of these, 238 had CHDs and 964 were healthy controls. The age of participants ranged from 0 to 18 years. The characteristics of the studies are presented in Table 1. The most frequent cardiac diseases in the studies were TOF, TGA, hypoplastic right ventricle (HRV), hypoplastic left ventricle (HLV), tricuspid atresia (TA), pulmonary atresia (PA), atrial septal defect (ASD), ventricular septal defect (VSD) and CoA. Only one study included patients after the Fontan procedure. In methodological analysis, the majority were classified as “fair” by the quality analysis using the NOS scale, representing a medium risk of bias [21] (Table 2).

Peripheral Muscle Strength

The isokinetic muscle strength of the lower limbs was assessed using an isokinetic dynamometer by three studies (n=616). Moalla et al. [4] assessed the strength of the knee extensor muscles using maximal voluntary contraction (MVC) with a gradual increase in strength lasting 2–3s; Holm et al. [22] evaluated knee flexors and extensors muscle strength by using five repetitions at an angular speed of 60° per second; and Sandberg et al. [23] evaluated two muscle groups, namely the knee extensors through the maximum extension with maintenance of contraction for 5s and the plantar flexors of the ankle with the strongest possible flexion for 5s. In the last study, values of isometric muscle strength in knee extensors and ankle plantar flexors were shown; however, for our meta-analysis, we only used the values of knee extensor muscular strength to allow the comparison between the other studies included in this review.

The meta-analysis of isokinetic muscular strength included three studies, showing a reduction of -44.63 Nm in patients with CHDs compared with the control group (95% CI, –75.03 to –14.23; I^2 82%; P for heterogeneity = 0.004) (Figure 2).

Two studies evaluated handgrip strength using manual dynamometry (n=1093). Holm et al. [22] performed an assessment on the dominant and non-dominant hand, using one repetition for each. The study by Zaqout et al. [24] evaluated upper limb strength using the right and left hands. The meta-analysis of the handgrip muscle strength showed no significant difference between patients with CHD and healthy controls, with the value of 0.08 Nm (95% CI, –6.39 to 6.55; I^2 98%; P for heterogeneity <0.00001) (Figure 3).

Exercise test

The exercise capacity was evaluated by one study only. Zaqout et al. [23] assessed the exercise capacity through the progressive 20-m shuttle run test, in which the number of shuttles was converted to stages to calculate maximal oxygen consumption (VO_2max). The VO_2max values of children and adolescents with CHDs and healthy controls were 45.4±3.7 and 46.3±3.4 mL/kg^{-1}/min^{-1} (p = 0.055), respectively, showing that there was no difference in cardiorespiratory fitness between children with repaired CHD and healthy controls.

DISCUSSION

This systematic review with meta-analysis of observational studies showed that children and adolescents with CHDs present a lower isokinetic muscle strength of the lower limbs. However, in handgrip muscle strength, there was no difference between groups.

The evaluation of muscle strength in healthy adults is already well established, as a predictor of global strength and as a parameter related to functional capacity and global health status. In the pediatric population, this evaluation is increasingly used, especially in cardiac patients, patients with genetic and neurological syndromes, and patients with asthma and cystic fibrosis [13, 25].

The main finding of this systematic review with meta-analysis is that children and adolescents with CHD had lower isokinetic strength in comparison with healthy children. This reduction can be related to a lower level of physical activity and a decrease in exercise capacity, which is already known in these patients and may

happen due to a number of factors, including nutritional problems related to obesity, and hemodynamic, musculoskeletal and psychosocial changes resulting from the surgical procedure, as well as overprotection by parents because of the disease [26, 27].

Regarding the isometric strength of the lower limbs, studies included in our analysis [4, 22, 23] showed reduced values in comparison with healthy controls. However, Brassard et al. [28] did not find any difference in the muscular strength of children and adolescents submitted to Fontan procedure and healthy controls. Another study [15] evaluated isokinetic strength in cardiac patients before and after a rehabilitation program and showed that physical training improved the muscle strength in the lower limb, which may be related to the increased oxygenation of peripheral muscles. However, this study evaluates only cardiac patients without any comparison with healthy controls.

A study conducted in 2006 with adolescents with CHDs showed that there was no difference in the strength and endurance of the quadriceps muscles in comparison to healthy patients. Nevertheless, a significant relationship was identified between the maximal voluntary contraction of the quadriceps with VO_2 peak in both groups, demonstrating that muscle weakness is related to exercise tolerance [28]. In our study, it was not possible to analyze VO_2max and its relationship with muscular strength because only one study was included.

Regarding handgrip strength, our meta-analysis did not find any differences between CHD patients and healthy controls, suggesting that these patients perform more activities with their upper limbs and that this variable would not be appropriate to represent global force in this population.

A study carried out by Longmuir in 2015 [29] with Fontan patients of the same age as in our study found that muscle strength and body composition were similar between cardiac patients and healthy controls; this corroborates the data found in our review. On the other hand, Turquetto et al. [30] evaluated patients between 12 and 30 years with a 5-year follow-up after Fontan operation and observed that handgrip strength was reduced in cardiac patients, along with variables related to exercise capacity. This can be explained because the period during which handgrip was evaluated and the age range were both different from those in our study. Moreover, Rego et al. [31] evaluated muscle strength in hospitalized cardiac children before surgery through handgrip dynamometry and revealed that this variable was reduced in

96.6% of cases. When compared with our study, this difference in results can be explained by the fact that most of the studies included in our meta-analysis were conducted in patients after surgery.

To date, little evidence has been found evaluating muscle strength in different types of CHDs, which makes it difficult to extrapolate the data obtained in this study to the entire cardiac population. In addition, we found some studies in the literature using reference values from healthy populations for the evaluation of muscle strength. This can be seen in the study by Fricke et al. [32], with adolescents and young adults with heart disease showing reduced handgrip strength in comparison with the predicted values. The reference values and predictive equations for isokinetic strength and handgrip strength in a healthy pediatric population were described by Wiggin et al. [33] and McQuiddy et al. [34]. However, there have still been few studies that make comparisons between sick and healthy individuals, which is an important and necessary method of assessment to establish a more reliable standard for different populations, requiring more studies to adopt this methodology.

The assessment of exercise capacity in CHD is well established in the literature. A study carried out in 2019 showed that children and adolescents with congenital heart disease have decreased functional capacity and anaerobic thresholds compared to healthy individuals of the same age group [35]. The benefits of training programs are also well established, as is the increase in exercise capacity and muscle strength in pediatric patients with CHD after cardiac rehabilitation [36, 15]. However, the relationship between muscle strength and exercise capacity in this population is still poorly explored in the literature. Our systematic review did not find any data to evaluate this relationship, and further research with larger sample sizes is necessary to confirm this association.

A major strength of this review is that, despite the scarcity in the literature of studies that evaluate muscle strength in children and adolescents with CHD, we found some data about isokinetic muscle strength and handgrip strength in this population that provided significant results in our meta-analysis. This provides greater knowledge about this variable and, consequently, greater safety and reliability to stipulate interventions that are beneficial to this population.

We have some limitations. First, there is a scarcity of articles that assess muscle strength in the pediatric CHDs. Even though this is a predictor of morbidity and mortality in adults, the same cannot be said in the pediatric population. Secondly, in

relation to isometric muscle strength, there are many divergences between the protocols used. Future research is needed to identify potential methodological aspects. Thirdly, the presence of different congenital heart diseases and surgical procedures, which were not stratified by specific type and severity, could explain the results for muscle strength. Fourthly, a publication bias was possibly caused by the exclusion of studies published in other languages (included only studies in English) and grey literature.

CONCLUSION

This systematic review with meta-analysis showed that children and adolescents with congenital heart disease had lower limb muscle strength evaluated by isokinetic dynamometer. Further research with increased methodological quality and larger sample size are still necessary to clarify muscle strength not only in the lower limbs, and the possible relation with exercise capacity.

Potential conflict of interest

I declare that there is no relevant conflict of interest.

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Academic link

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Table 1. Characteristics of the studies included in the systematic review:

Author (date)	Study type	CHD subtype	CHD (n)	CG (n)	Mean age of CHD (SD)	Mean age of CG (SD)	Male/Female CHD	Male/Female CG	Outcomes and Evaluation methods	Muscle strength CHD	Muscle strength CG	VO_2 máx CHD	VO_2 máx CG
Moalla[3]	Cross-sectional	TGA (4), PA (2), TOF (2), ASD (1)	9	14	13.5±1.8	12.8±1.3	6/3	9/5	Isokinetic dynamometer (Dynamometer Cybex Norm II) – Measure of strength of the knee extensors through MVC (Gradual increase in force lasting 2–3s)	101.0±6.2[a]	125.5±7.4[a]	-	-
Holm[21]	Cohort	TOF (29), TGA (32), HRV/HLV (18), TA (3) and others (38)	120	387	10.3±1.7	10.2±1.7	74/46	188/199	Isokinetic dynamometer (Dynamometer Cybex 6000) – Measure of strength of the knee extensors and flexors through 5 repetitions at an angular velocity of 60° per second.	14.8±4.83[a]	18.0±5,22[a]	-	-
									Grip strength (Dynamometer Jamar) – Measure of grip strength of the dominant and nondominant hands with 1 repetition for each hand.	219±106.3[b]	278.8±112.6[b]	-	-

Zaqout[23]	Cross-sectional	VSD (19), COA (10), TOF (22), and TGA (15)	66	520	10.5±1.9	8.3±1.5			Grip strength (Dynamometer TKK 5101 Grip D (Tokio) – Measure of the upper limb through the average of right and left handgrip strength.	16.0±5.9 [b]	12.6±3.0 [b]	45.4 ±3.7	46.3 ±3.4
Sandberg[22]	Cross-sectional	Fontan	43	43	12.2±3.9	12.3±4	24/19	24/19	Isokinetic dynamometer (Dynamometer Anyload VETEK 0-5000 N) – Measure of strength of the knee extensors through the maximum contraction for 5 seconds.	221.8±100.7 [a]	286.2±160.7 [a]	-	-

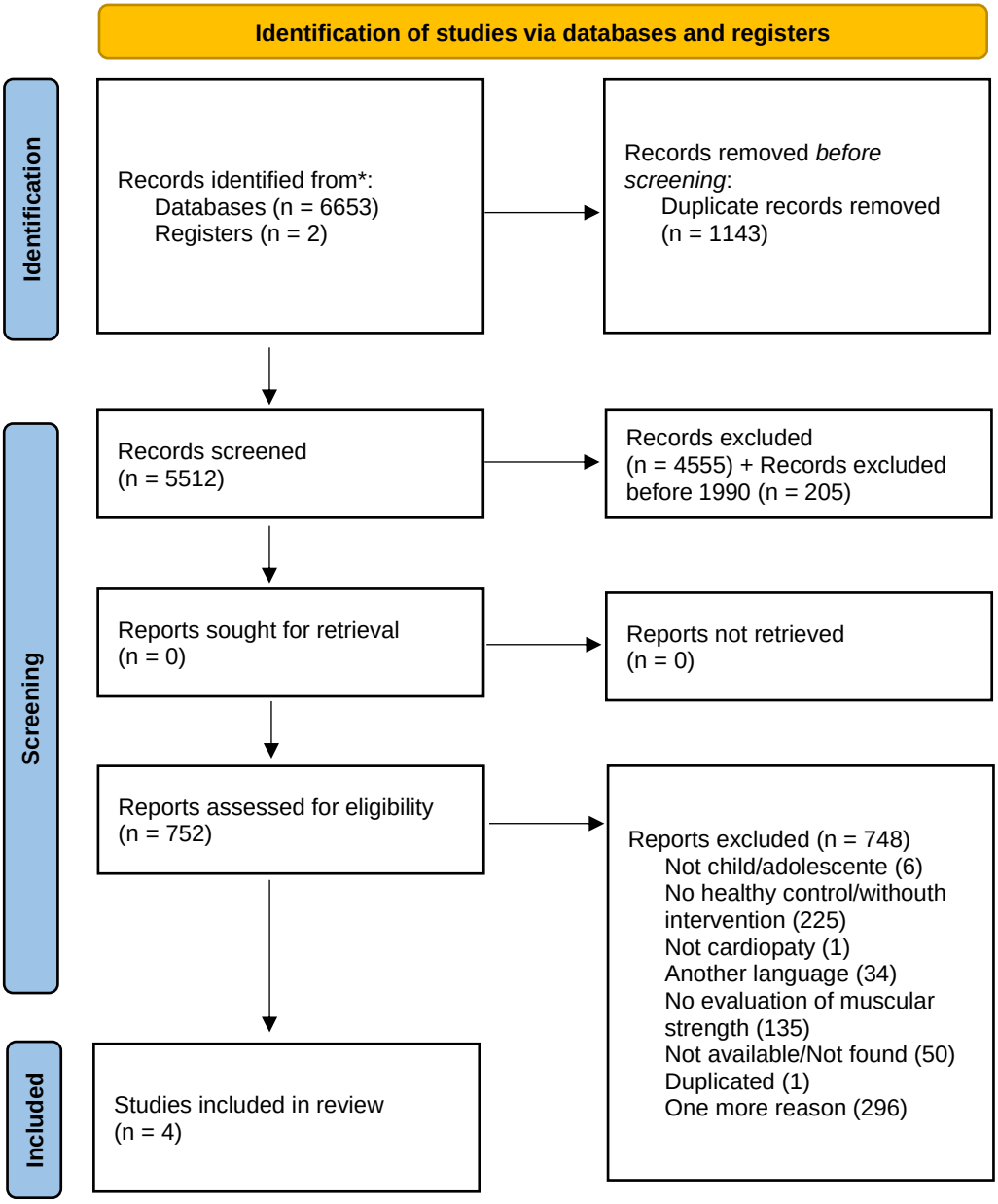
CHD: congenital heart disease; CG: control group; TGA: transposition of the great arteries; PA: pulmonary atresia; TOF: tetralogy of Fallot; ASD: atrial septal defect; VSD: ventricular septal defect; COA: coarctation of aorta; HRV: hypoplastic right ventricle; HLV: hypoplastic left ventricle; TA: tricuspid atresia; MVC: maximal voluntary contraction; VO_2máx: maximal oxygen consumption; [a] Nm: newton meters; [b] N: newton.

Table 2. Evaluation of methodologic quality of studies and risk of bias with Newcastle-Ottawa Scale:

NEWCASTLE-OTTAWA QUALITY ASSESSMENT SCALE				
COHORT STUDIES				
	Selection	**Comparability**	**Outcome**	**Total Stars**
Holm, 2007	**	*	***	6
CROSS-SECTIONAL STUDIES				
	Selection	**Comparability**	**Outcome**	**Total Stars**
Moalla, 2006	**	*	**	5
Zaqout, 2017	***	*	**	6
Sandberg, 2020	***	*	**	6

FIGURES:

Fig 1 Prisma flow diagram of studies evaluated for meta-analysis



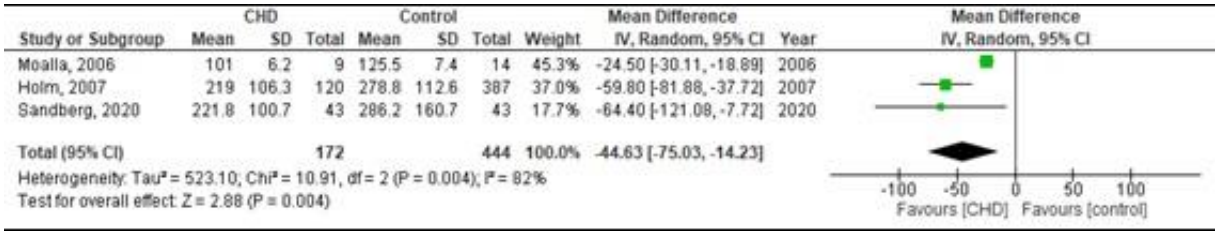


Fig 2 Meta-analysis of isokinetic muscle strength in children and adolescents with CHDs and controls.

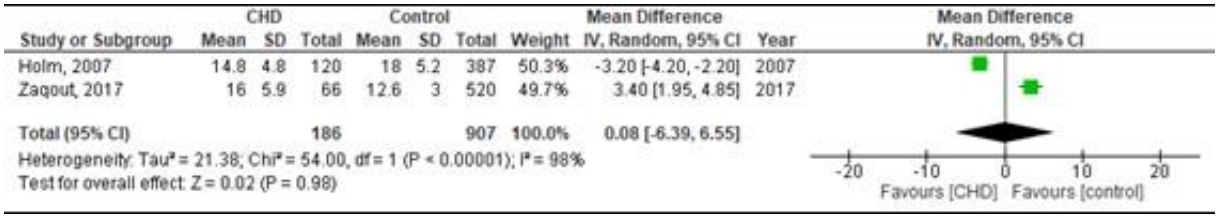


Fig 3 Meta-analysis of handgrip strength in children and adolescents with CHD and controls.

ANEXOS:

ANEXO A – Material Suplementar (Search strategy used for PubMed database):

#1	“Child”[Mesh] OR “Children”
#2	“Adolescent”[Mesh] OR “Adolescents” OR “Adolescence” OR “Teens” OR “Teen” OR “Teenagers” OR “Teenager” OR “Youth” OR “Youths” OR “Adolescents, Female” OR “Adolescent, Female” OR “Female Adolescent” OR “Female Adolescents” OR “Adolescents, Male” OR “Adolescent, Male” OR “Male Adolescent” OR “Male Adolescents”
#3	#1 OR #2
#4	“Heart Defects, Congenital”[Mesh] OR “Congenital Heart Defect” OR “Defect, Congenital Heart” OR “Heart, Malformation Of” OR “Defects, Congenital Heart” OR “Heart Abnormalities” OR “Heart Defect, Congenital” OR “Abnormality, Heart” OR “Abnormalities, Heart” OR “Heart Abnormality” OR “Congenital Heart Defects”
#5	“Heart Septal Defects”[Mesh] OR “Defect, Heart Septal” OR “Defects, Heart Septal” OR “Heart Septal Defect” OR “Septal Defect, Heart” OR “Septal Defects, Heart” OR “Cardiac Septal Defects”
#6	“Aortic Coarctation”[Mesh] OR “Aortic Coarctations” OR “Coarctation, Aortic” OR “Coarctations, Aortic” OR “Coarctation of the Aorta” OR “Coarctation of Aorta” OR “Aorta Coarctation” OR “Aorta Coarctations” OR “Coarctation of Aorta Dominant” OR “Aorta Dominant Coarctation” OR “Aorta Dominant Coarctations”
#7	“Transposition of Great Vessels”[Mesh] OR “Great Vessels Transposition” OR “Great Vessels Transpositions” OR “Dextro-Looped Transposition of the Great Arteries” OR “Dextro Looped Transposition of the Great Arteries” OR “Transposition of Great Arteries” OR “Great Arteries Transposition” OR “Great Arteries Transpositions”
#8	“Tetralogy of Fallot”[Mesh] OR “Tetralogy, Fallot's” OR “Tetralogy, Fallot” OR “Tetralogy, Fallots” OR “Fallot's Tetralogy” OR “Fallot Tetralogy” OR “Fallots Tetralogy”
#9	“Fontan Procedure”[Mesh] OR “Procedure, Fontan” OR “Stage 3 Norwood Procedure” OR “Fontan Palliation” OR “Palliation, Fontan” OR “Norwood Procedure, Stage 3” OR “Norwood Procedure, Stage III” OR

	“Fontan Operation” OR “Operation, Fontan” OR “Stage III Norwood Procedure” OR “Fontan Circulation” OR “Circulation, Fontan” OR “Fontan Circuit” OR “Circuit, Fontan” OR “Hemi-Fontan Procedure” OR “Hemi Fontan Procedure” OR “Procedure, Hemi-Fontan” OR “Norwood Procedure, Stage 2” OR “Bidirectional Glenn Shunt” OR “Bidirectional Glenn Shunts” OR “Glenn Shunt, Bidirectional” OR “Stage II Norwood Procedure” OR “Bidirectional Glenn Procedure” OR “Bidirectional Glenn Procedures” OR “Glenn Procedure, Bidirectional” OR “Procedure, Bidirectional Glenn” OR “Bidirectional Cavopulmonary Shunt” OR “Bidirectional Cavopulmonary Shunts” OR “Cavopulmonary Shunt, Bidirectional” OR “Shunt, Bidirectional Cavopulmonary” OR “Norwood Procedure, Stage II” OR “Stage 2 Norwood Procedure”
#10	#4 OR #5 OR #6 OR #7 OR #8 OR #9
#11	“Muscle Strength”[Mesh] OR “Strength, Muscle” OR “Arthrogenic Muscle Inhibition” OR “Arthrogenic Muscle Inhibitions” OR “Inhibition, Arthrogenic Muscle” OR “Muscle Inhibition, Arthrogenic”
#12	“Maximal Respiratory Pressures”[Mesh] OR “Pressure, Maximal Respiratory” OR “Pressures, Maximal Respiratory” OR “Respiratory Pressure, Maximal” OR “Respiratory Pressures, Maximal” OR “Maximal Respiratory Pressure” OR “Maximum Respiratory Pressure” OR “Maximum Respiratory Pressures” OR “Pressure, Maximum Respiratory” OR “Pressures, Maximum Respiratory” OR “Respiratory Pressure, Maximum” OR “Respiratory Pressures, Maximum” OR “Maximal Inspiratory Pressure” OR “Inspiratory Pressure, Maximal” OR “Inspiratory Pressures, Maximal” OR “Maximal Inspiratory Pressures” OR “Pressure, Maximal Inspiratory” OR “Pressures, Maximal Inspiratory” OR “Maximum Inspiratory Pressure” OR “Inspiratory Pressure, Maximum” OR “Inspiratory Pressures, Maximum” OR “Maximum Inspiratory Pressures” OR “Pressure, Maximum Inspiratory” OR “Pressures, Maximum Inspiratory” OR “Maximal Expiratory Pressure” OR “Expiratory Pressure, Maximal” OR “Expiratory Pressures, Maximal” OR “Maximal Expiratory Pressures” OR “Pressure, Maximal Expiratory” OR “Pressures, Maximal Expiratory” OR “Maximum Expiratory Pressure”

	OR “Expiratory Pressure, Maximum” OR “Expiratory Pressures, Maximum” OR “Maximum Expiratory Pressures” OR “Pressure, Maximum Expiratory” OR “Pressures, Maximum Expiratory”
#13	“Exercise”[Mesh] OR “Exercises” OR “Physical Activity” OR “Activities, Physical” OR “Activity, Physical” OR “Physical Activities” OR “Exercise, Physical” OR “Exercises, Physical” OR “Physical Exercise” OR “Physical Exercises” OR “Acute Exercise” OR “Acute Exercises” OR “Exercise, Acute” OR “Exercises, Acute” OR “Exercise, Isometric” OR “Exercises, Isometric” OR “Isometric Exercises” OR “Isometric Exercise” OR “Exercise, Aerobic” OR “Aerobic Exercise” OR “Aerobic Exercises” OR “Exercises, Aerobic” OR “Exercise Training” OR “Exercise Trainings” OR “Training, Exercise” OR “Trainings, Exercise”
#14	#11 OR #12 OR #13
#15	#3 AND #10 AND #14

ANEXO B – Normas de submissão do periódico Pediatric Cardiology

SUBMISSION GUIDELINES (PEDIATRIC CARDIOLOGY)

Instructions for Authors

Types of Papers

Specific instructions for:

Pediatric Cardiology no longer accepts Case Reports or Images in Pediatric Cardiology for publication, except as noted below.

Original Articles

Original articles must reflect an original study in a field relevant to heart diseases in children (including fetal cardiology) or adult congenital heart diseases. Original articles must include the following components: Title, Key words, List of authors, Abstract, Introduction, Material and methods, Results, Discussion

Study limitations and acknowledgement sections should be provided when relevant. The abstract section must include a hypothesis when indicated, a brief review of material and methods, results and conclusion. There is no specific limitation on number of authors, however, it is expected that authors listed must have all been active participants in the research. There is no specific word count limitation; however, manuscripts must be as concise as possible.

Review Articles

Authors may submit manuscripts reviewing a topic relevant to heart diseases in children. Review articles do not have a specific format, however, in addition to appropriate sections, the manuscript should include a title, list of authors and an abstract.

Letters to the Editor

The editor welcomes letters for publication. These may be 1) comment on or addition to work recently published in the journal; 2) observations or findings too limited for submission as article or case report; or 3) opinion or discussion on matters likely to be of interest to readers. Such letters should not be longer than 400 words, but may be accompanied by a simple table or diagram. The number of authors on the title page should be limited to two authors.

Case Reports

Case reports may be submitted to present a rare finding, novel diagnostic or therapeutic approach or an unusual complication. A limited number of Case Report manuscripts are accepted for publication. The manuscript should be as brief as possible, unnecessary details should not be included and review of literature must be minimized, the emphasis should be on the case presented with brief review of the literature. Images, figures, tables, etc. should be restricted to those which are highly relevant. Case reports should include the following headings: abstract, key words, case report, discussion and references.

Images in Pediatric Cardiology

Interesting images not available in the medical literature may be presented as Images in Pediatric Cardiology manuscript. These manuscripts focus on images of interest with an extremely brief text describing the images, images may include video clips. Images in Pediatric Cardiology should not include review of the literature. A limited number of Images in Pediatric Cardiology manuscripts are accepted for publication. Images in Pediatric Cardiology should include the following headings: abstract, key words, a paragraph or 2 describing the images presented and references.

Manuscript Submission

Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

Permissions

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

Online Submission

Please follow the hyperlink “Submit manuscript” on the right and upload all of your manuscript files following the instructions given on the screen.

Please ensure you provide all relevant editable source files. Failing to submit these source files might cause unnecessary delays in the review and production process.

Title page

Title Page

Please make sure your title page contains the following information.

Title

The title should be concise and informative.

Author information

- The name(s) of the author(s)
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

Abstract

Please provide an abstract of 150 to 250 words. The abstract should not contain any undefined abbreviations or unspecified references.

For life science journals only (when applicable)

Trial registration number and date of registration

Trial registration number, date of registration followed by “retrospectively registered”

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations'. If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

To be used for all articles, including articles with biological applications

Funding (information that explains whether and by whom the research was supported)

Conflicts of interest/Competing interests (include appropriate disclosures)

Availability of data and material (data transparency)

Code availability (software application or custom code)

Authors' contributions (optional: please review the submission guidelines from the journal whether statements are mandatory)

Additional declarations for articles in life science journals that report the results of studies involving humans and/or animals

Ethics approval (include appropriate approvals or waivers)

Consent to participate (include appropriate statements)

Consent for publication (include appropriate statements)

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

Text

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX. LaTeX macro package (Download zip, 188 kB)

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

A note on References

References should be listed in the order they were cited in the text. Please note that we have recently changed the style of reference listing. Pediatric Cardiology no longer requests listing references in alphabetical order.

References

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].
2. This result was later contradicted by Becker and Seligman [5].
3. This effect has been widely studied [1-3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text.

The entries in the list should be numbered consecutively.

If available, please always include DOIs as full DOI links in your reference list (e.g. “https://doi.org/abc”).

- Journal article

  Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. https://doi.org/10.1007/s00421-008-0955-8

  Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329

- Article by DOI

  Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. https://doi.org/10.1007/s001090000086

- Book

  South J, Blass B (2001) The future of modern genomics. Blackwell, London

- Book chapter

  Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257

- Online document

  Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. http://physicsweb.org/articles/news/11/6/16/1. Accessed 26 June 2007

- Dissertation

  Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see ISSN.org LTWA

If you are unsure, please use the full journal title.

Authors preparing their manuscript in LaTeX can use the bibtex file spbasic.bst which is included in Springer's LaTeX macro package.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

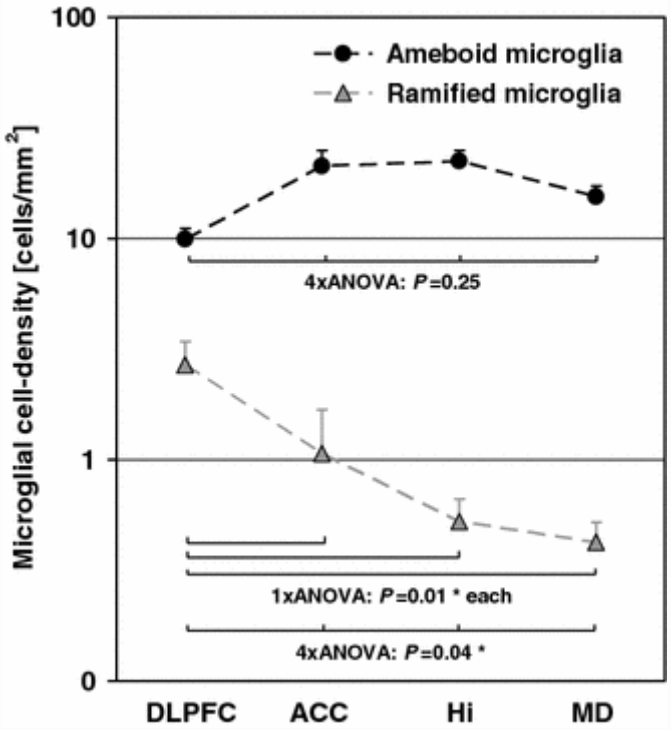
Artwork and Illustrations Guidelines

Electronic Figure Submission

- Supply all figures electronically.

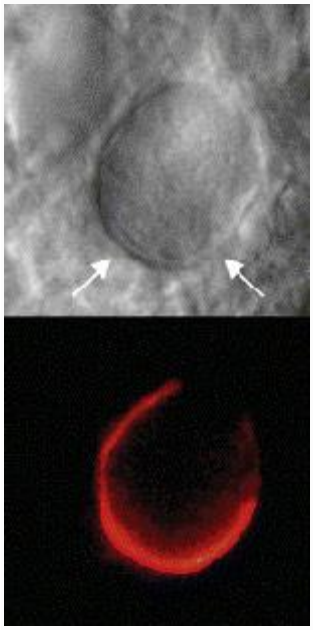
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Line Art



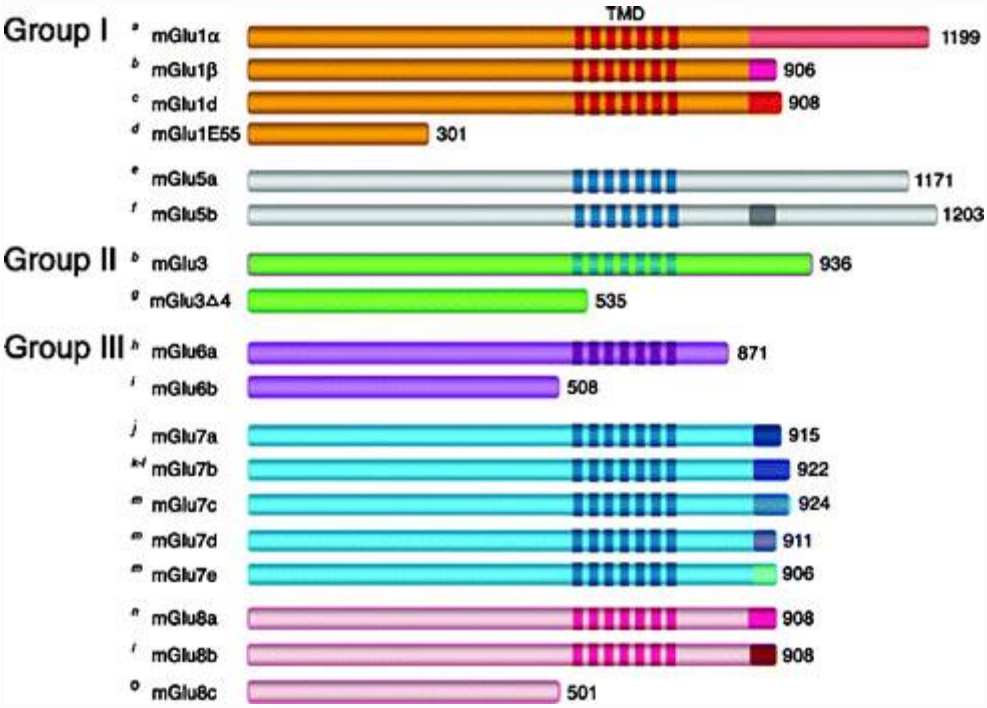
- Definition: Black and white graphic with no shading.
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.
- All lines should be at least 0.1 mm (0.3 pt) wide.
- Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.
- Vector graphics containing fonts must have the fonts embedded in the files.

Halftone Art



- Definition: Photographs, drawings, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi.

Combination Art



- Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.
- Combination artwork should have a minimum resolution of 600 dpi.

Color Art

- Color art is free of charge for online publication.
- If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.
- If the figures will be printed in black and white, do not refer to color in the captions.
- Color illustrations should be submitted as RGB (8 bits per channel).

Figure Lettering

- To add lettering, it is best to use Helvetica or Arial (sans serif fonts).
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions within your illustrations.

Figure Numbering

- All figures are to be numbered using Arabic numerals.
- Figures should always be cited in text in consecutive numerical order.
- Figure parts should be denoted by lowercase letters (a, b, c, etc.).
- If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures,"A1, A2, A3, etc." Figures in online appendices [Supplementary Information (SI)] should, however, be numbered separately.

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When biological material is donated for or data is generated as part of a research project authors should ensure, as part of the informed consent procedure, that the participants are made aware what kind of (personal) data will be processed, how it will be used and for what purpose. In case of data acquired via a biobank/biorepository, it is possible they apply a broad consent which allows research participants to consent to a broad range of uses of their data and samples which is regarded by research ethics committees as specific enough to be considered “informed”. However, authors should always check the specific biobank/biorepository policies or any other type of data provider policies (in case of non-bio research) to be sure that this is the case.

Consent to Participate

For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants (or their parent or legal guardian in the case of children under 16) and a statement to this effect should appear in the manuscript. In the case of articles describing human transplantation studies, authors must include a statement declaring that no organs/tissues were obtained from prisoners and must also name the institution(s)/clinic(s)/department(s) via which organs/tissues were obtained. For manuscripts reporting studies involving vulnerable groups where there is the potential for coercion or where consent may not have been fully informed, extra care will be taken by the editor and may be referred to the Springer Nature Research Integrity Group.

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Summary of requirements

The above should be summarized in a statement and placed in a 'Declarations' section before the reference list under a heading of 'Consent to participate' and/or 'Consent to publish'. Other declarations include Funding, Conflicts of interest/competing interests, Ethics approval, Consent, Data and/or Code availability and Authors' contribution statements.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

Sample statements for **"Consent to participate"**:

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Informed consent was obtained from legal guardians.

Written informed consent was obtained from the parents.

Verbal informed consent was obtained prior to the interview.

Sample statements for **"Consent to publish"**:

The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1a, 1b and 1c.

The participant has consented to the submission of the case report to the journal.

Patients signed informed consent regarding publishing their data and photographs.

Sample statements if identifying information about participants is available in the article:

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