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Fernanda de Andrade

Avaliação Funcional de Pacientes Transplantados Pulmonares Intervivos

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“Aqueles que passam por nós não vão sós, não nos deixam sós. Deixam um pouco de si, levam um pouco de nós. ”

Antoine de Saint-Exupéry

RESUMO

O transplante pulmonar tem sido considerado uma alternativa para melhora da qualidade e expectativa de vida aos pacientes com pneumopatias crônicas avançadas. Uma das formas de transplante pulmonar é o método bilobar intervivos, uma modalidade em que se utilizam os lobos pulmonares de dois doadores vivos em um receptor. Esta técnica tem sido uma alternativa pulmonar, capacidade funcional, força muscular respiratória, nível de dispneia, atividades de vida diária e atividade física além da qualidade de vida. Foi realizada estatística descritiva e na comparação das medidas pré e pós-transplante foi utilizado o teste GEE ($p < 0,05$) e com IC de 95%. A análise foi realizada no programa SPSS versão 21.0. Foram inclusos no estudo 30 pacientes, 17 meninos e 13 meninas. Treze sujeitos vivos foram avaliados pós-transplante e apresentaram melhora na capacidade vital forçada, teste de caminhada de 6 minutos, escala de Borg e saturação de O_2 na comparação pré e pós-transplante ($p < 0,01$). O grau de dispneia apresentado pós-transplante foi leve. Os resultados de qualidade de vida, atividade de vida diária e atividade física foram semelhantes aos previstos na literatura quando comparados aos transplantados pulmonares cadavéricos pós-procedimento. Os valores de pressão inspiratória e expiratória máxima foram avaliados pós e apresentaram valores inferiores aos de crianças e adolescentes saudáveis. Em suma, foi verificada melhora da capacidade funcional e da função pulmonar após o transplante pulmonar intervivos, além de melhora na qualidade de vida. terapêutica para os pacientes pediátricos, proporcionando uma melhora na qualidade de vida destes pacientes. O Brasil é um dos países precursores desta técnica e a sobrevida dos pacientes é variável. Para aumentar as chances de sobrevida é necessário o acompanhamento multidisciplinar permitindo a adesão ao tratamento à longo prazo. Assim, o presente estudo tem como objetivo verificar o perfil da função pulmonar e da capacidade funcional dos pacientes submetidos ao transplante pulmonar intervivos, no período de 1999 a 2015, realizados na Santa Casa de Misericórdia de Porto Alegre. Este trabalho caracteriza-se como um estudo observacional clínico e retrospectivo, transversal, onde pacientes transplantados intervivos que estavam em acompanhamento médico foram avaliados quanto à função.

Palavras-chave: Transplante pulmonar; transplante intervivos; doadores vivos; capacidade funcional; função pulmonar.

ABSTRACT

Lung transplantation has been considered an alternative to improve the quality and life expectancy for patients with advanced chronic lung diseases. One form of lung transplantation is the donor bilobar method, a method in which they use the lung lobes from two living donors in a receiver. This technique has been a therapeutic alternative for pediatric patients, providing an improved quality of life of these patients. Brazil is one of the forerunners countries of this technique and the survival of patients is variable. To increase the chances of survival the multidisciplinary approach is necessary allowing adherence to long-term treatment. Thus, this study aims to determine the profile of lung function and functional capacity of patients undergoing living donor lung transplantation from 1999 to 2015, held at the Santa Casa de Misericordia Hospital. It is characterized as a clinical observational study, retrospective, cross-sectional, where living-donor lobar lung transplantation (LDLLT) patients who were in medical care were assessed for lung function, functional capacity, respiratory muscle strength, level of dyspnea, activities of daily living and physical activity in addition to the quality of life. Descriptive statistics was performed and for the comparison between pre- and post-transplant the GEE test ($p < 0.05$) was used with 95% CI. The analyses were performed using SPSS version 21.0 program. Thirty patients were included in the study, 17 boys and 13 girls. Thirteen alive subjects were evaluated post-transplant and showed improvement in forced vital capacity, 6-minute walk test, Borg scale and O_2 saturation comparing pre and post transplantation conditions ($p < 0.01$). The degree of dyspnea after transplantation was light. The results of quality of life, activities of daily living and physical activity were similar to those provided in the literature when compared to after cadaveric lung transplantation procedure. The values of inspiratory and expiratory pressure were evaluated post LDLLT procedure and showed lower values compared to healthy children and adolescents, as expected. In short, functional capacity, lung function and quality of life were improved after LDLLT in children.

Key Words: Lung transplantation; donor transplantation; living donors; functional capacity; lung function.

SUMÁRIO

1 INTRODUÇÃO

Atualmente o transplante pulmonar tem sido uma alternativa terapêutica aos pacientes em fase terminal de doenças pulmonares, e seu objetivo é proporcionar melhora da qualidade de vida e do prognóstico (1). A indicação para o transplante pulmonar ocorre após uma avaliação minuciosa levando em consideração critérios como: pneumopatia crônica sem resposta a diferentes terapias medicamentosas associadas, avanço progressivo da doença, condição psicológica e social do paciente e da sua família (2,3).

A partir dos dados do último Registro Brasileiro de Transplantes da Associação Brasileira de Transplante de Órgãos (ABTO), foram registrados até 2015 em território nacional, um aumento na evolução do número de transplantes pulmonares, de 67 em 2014 para 73 em 2015, sendo realizados no estado do Rio Grande do Sul 35 transplantes no ano, 4 com doadores vivos. O procedimento de transplante pulmonar é realizado prioritariamente em quatro estados brasileiros: São Paulo, Ceará, Minas Gerais e Rio Grande do Sul. No Brasil, o Rio Grande do Sul é o único estado a realizar o método de transplante intervivos(4).

É visto que o crescimento das listas de espera por doação de órgãos no Brasil, principalmente nos últimos 5 anos, tem como fatores de importância a escassez de órgãos doados tanto adultos como pediátricos e poucas e equipes atuantes na realização do procedimento de transplante pulmonar (5).

No ano de 2015a lista de espera reduziu para 69 receptores no RS, e, nesse período, foram realizados três transplantes pulmonares de doadores vivos (6).

A avaliação inicial do candidato ao transplante envolve provas de função pulmonar, exames laboratoriais, exames de imagem, exames imunológicos, avaliação psicológica e psiquiátrica, avaliação nutricional, avaliação funcional e social do paciente e sua família (2,9). Em seguida, o paciente é encaminhado à lista de transplantes do centro cadastrado (10). Todos os pacientes cadastrados são primeiramente colocados na lista de espera com indicação de substituição pulmonar unilateral ou bilateral (2,11).

Após avaliação minuciosa, ou ainda avanço da doença, tempo de espera na lista de doadores cadavéricos é superior a dois anos e/ou existência de incompatibilidades sanguíneas ou painel imunológico positivo, a equipe médica sugere o método de transplante pulmonar bilobar intervivos (11–15).

Este método apresenta uma maior compatibilidade sanguínea e imunológica, menor risco de rejeição do enxerto além de ser mais rápido por se tratar de um procedimento eletivo que pode ser realizado com doadores familiars (16,17). Como critérios, o paciente deve ter menos de 18 anos, com um diagnósticode doença pulmonar avançada e agravada recentemente; ainda, com tempo de permanência em lista de espera superior a dois anos e com a família engajada no processo de transplante intervivos (18-23).

O transplante intervivos é um método cirúrgico bilobarque é realizado em crianças principalmente em doenças como a fibrose cística (24-25) e a bronquiolite obliterante (26,27), pois apresentam grandes escores de morbi-mortalidade antes da adolescência (28).

Como consequência das patologias os pacientes apresentam dependência de oxigênio e redução da funcionalidade. Estes fatores acarretam má qualidade de vida da criança e gera complicações sistêmicas como alterações hepáticas, cardíacas, nutricionais e respiratórias (27,29).

Mundialmente o transplante pulmonar intervivos é indicado devido ao número de doadores pediátricos ser escasso (29,30). Os Estados Unidos e o Japão são países que realizaram ou realizam o procedimento; o Japão o faz (31), por exemplo, pois não aceita a realização do transplante de órgãos de indivíduos que vieram a óbito; já os EUA realizava o procedimento com sucesso até a criação e uniformização dos transplantes gerenciados pela *United Network for Organ Sharing* (UNOS)(32).

No transplante pulmonar intervivos são realizados seis procedimentos cirúrgicos simultaneamente sendo eles: 2 lobectomias inferiores nos doadores hígidos , 2 pneumonectomias no receptor e seguidas de 2 implantações de lobos inferiores dos doadores no receptor; assim, o risco cirúrgico e as complicações imediatas e tardias são maiores no receptor do que propriamente nos doadores hígidos (2,33–38).

Evitam-se ao máximo os riscos aos doadores, principalmente para a preservação da função dos lobos restantes (39). Os receptores recebem

monitorização especial no período pós-operatório e permanecem em ambiente hospitalar, em geral, durante 3 semanas (40).

As complicações pulmonares do transplante pulmonar intervivos são semelhantes aos demais procedimentos de transplante pulmonar (35,41). Os pacientes podem apresentar rejeição do enxerto (hiperaguda e aguda), sepse, injúrias de reperfusão, infecções, fraqueza muscular respiratória, dentre outros(2,35). Porém, as rejeições agudas podem acontecer no período pós-operatório tardio além das rejeições crônicas do enxerto que tornam necessário o uso de diferentes medicações imunossupressoras, podendo ter o desenvolvimento de bronquiolite obliterante ou ainda necessidade de re–transplante (42–44).

Como fatores que podem influenciar o aparecimento de complicações pós-operatórias, citam-se o tempo da circulação extracorpórea, o tempo de permanência de drenos torácicos, a redução de anestésicos, a retirada da ventilação mecânica invasiva, dor, processo cicatricial, evolução imunológica e o início do uso de imunossupressores (21, 45-46).

No primeiro ano, há maiores índices de mortalidade, devido às afecções peri-operatórias e pós-operatórias imediatas, sendo que a média estimada de sobrevida após o transplante é de aproximadamente 5 anos (47–49). Entretanto, estudos reportam resultados mais positivos no transplante intervivos quando comparados àqueles com doadores cadavéricos (75% *vs.* 50% de sobrevida em 5 anos) (21,50).

Para que os pacientes intervivos restabeleçam a funcionalidade e o condicionamento físico necessário para as atividades de vida diária (AVDs), a reabilitação pulmonar torna-se importante (51-52). A reabilitação pulmonar atua no aumento da força muscular periférica, além de proporcionar a reeducação dos hábitos e afazeres diários, bem como a educação, para prevenir complicações decorrentes do sedentarismo (49,53–57).

O transplante pulmonar intervivos é específico e complexo na técnica cirúrgica, no manejo pós-operatório e na realização da avaliação do candidato, na seleção dos doadores, no procedimento cirúrgico e na reabilitação (58).

Assim o acompanhamento rigoroso e contínuo desses pacientes é fundamental para otmizar os resultados do procedimento do transplante.

O monitoramento das complicações tardias, do nível de atividade física,

das funções pulmonares, do nível de dispneia e da qualidade de vida na alta destes pacientes é necessário e devem ser realizados constantemente, pois após a alta, os pacientes devem realizar 3 meses de reabilitação (56).

Tendo em vista a necessidade do acompanhamento pós-transplante e alta da reabilitação pulmonar desses pacientes, a questão que norteia esse estudo é: Qual o perfil da função pulmonar e da capacidade funcional dos pacientes transplantados pulmonares intervivos realizados na Santa Casa de Misericórdia de Porto Alegre no período de 1999 a 2015?

1.1 OBJETIVOS

1.1.1 Objetivo Principal

Caracterizar o perfil da função pulmonar e da capacidade funcional de pacientes submetidos ao transplante pulmonar intervivos, no período de 1999 a 2015, realizados na Santa Casa de Misericórdia de Porto Alegre.

1.1.2 Objetivos Específicos

a) Identificar os efeitos do procedimento de transplante pulmonar intervivos e seu impacto na saúde geral do paciente;
b) Verificar a qualidade de vida após transplante pulmonar;
c) Identificar o nível de atividade física e atividades de vida diária dos pacientes transplantados pulmonares intervivos após procedimento;
d) Avaliar a força muscular respiratória após procedimento de transplante pulmonar;
e) Avaliar o nível de dispneia dos pacientes transplantados intervivos, após procedimento.

2 REVISÃO DE LITERATURA

2.1 HISTÓRIA DO TRANSPLANTE PULMONAR

O primeiro transplante de pulmonar com humanos foi realizado em 1963, nos Estados Unidos, sendo James Hardy, da Universidade de Missisipi (EUA) o responsável pelos primeiros procedimentos(59). Ao longo do tempo, o método cirúrgico foi aprimorado e mais seletivo conforme a evolução (60).

A evolução dos transplantes na década de 70 foi desencadeada com o avanço da farmacologia e especialmente com a descoberta da ciclosporina. Através deste fármaco a imunossupressão clínica passou a ser mais efetiva e possibilitou a redução de complicações com os órgãos enxertados, menores riscos a infecções tanto pré quanto pós-operatórias bem como proporcionou o manejo precoce das rejeições que acometiam os transplantados (61,62).

Os primeiros relatos de equipe multidisciplinares atuando em transplantes de pulmão foram a partir de 1983, no Canadá (12, 63-64).Na América Latina, o primeiro transplante pulmonar unilateral ocorreu em 1989, no Complexo Hospitalar da Santa Casa de Misericórdia de Porto Alegre, Rio Grande do Sul, Brasil, realizado pelo cirurgião torácico José Camargo e sua equipe. Respectivamente em 1993 e 1999 foram realizados o primeiro transplante bilateral e o primeiro transplante bilobar intervivos (65–67).

A evolução dos transplantes inclue a rigidez dos critérios de seleção dos candidatos (68-70), o avanço da tecnologia e a experiência das equipes, uma vez que, novos elementos passaram a ser utilizados na seleção de procedimentos para cada enfermidade, bem como novos instrumentos a serem utilizados, como por exemplo, a utilização da membrana extracorpórea oxigenada (ECMO)(71-78).

2.2 DOENÇAS PULMONARES AVANÇADAS DA INFÂNCIA E ADOLESCÊNCIA

As indicações mais comuns para a realização do transplante de pulmão podem ser agrupadas em quatro categorias: as pneumopatias obstrutivas que

incluem: DPOC, enfisema por deficiência de alfa-1-antitripsina e bronquiolite obliterante (BO); as pneumopatias restritivas que englobam fibrose pulmonar (FPI), sarcoidose, histiocitose de células de Langerhans, linfangioleiomiomatose e silicose; as pneumopatias supurativas, como a fibrose cística (FC) e bronquiectasias; e por fim, a última categoria são as pneumopatias vasculares, as quais incluem hipertensão da artéria pulmonar primária (HPP) ou secundária (79–82).

Na infância, as apresentações das categorias citadas acima condizem com evidencias de bronquiolite obliterante, em lactentes ou crianças pequenas; fibrose pulmonar, com menor incidência de casos; fibrose cística, responsável pela maioria dos procedimentos de transplante pulmonar em crianças e adolescentes, por ser uma doença de manifestação gênica; e ainda a hipertensão pulmonar, devido àrelação estreita com as cardiopatias congênitas no recem-nascido(28).

A pneumopatia obstrutiva prevalente na infância é a bronquiolite obliterante, que é originada por inflamação das vias aéreas de menor calibre (26). O surgimento da inflamação juntamente com a fibroseperibronquiolar terminal resulta na obstrução total/parcial do lúmen do brônquio, acarretando a obstrução crônica do fluxo aéreo (83).

A bronquiolite obliterante tem incidência maior em lactentes do sexo masculino, e pode estar relacionada à inalação de substâncias tóxicas, fatores imunológicos humorais, síndromes aspirativas, doenças autoimunes, como por exemplo: artrite reumatoide e síndrome de Sjogren, alterações imunológicas, fármacos, fatores genéticos entre outras tantas evidencias ainda em estudo (84-85). Por ser de curso clinico variável, naturalmente infecciosa, é comumente confundida com doenças sibilantes e pós infecciosa (26,86).

A fibrose cística (FC) representa as pneumopatias suporativas da infância com maior expressividade, pois é uma doença hereditária autossômica recessiva, com alteração no cromossomo 7 e tem manifestações clínicas diversas, incluindo: tosse crônica persistente, histórico de bronquiolite de repetição, síndrome do lactente chiador, dentre outros (24,87–89).

Há diferentes mutações gênicas expressas na FC, mas a mutação ΔF508 é responsável pela possibilidade de indicação de transplante pulmonar para a criança, pois fisiopatologicamente há alteração nos canais de cloro (Cl), sódio (Na) e água (H_2O)(88).O resultado é a desidratação das secreções e aumento da viscosidade das mesmas favorecendo a obstrução de ductos além da reação inflamatória e consequentemente resultando no processo de fibrose (90).

Os pacientes com FC apresentam manifestações sistêmicas da doença sendo elas: alterações gastrointestinais, pancreáticas, presença de diabetes *melittus*, mas o acometimento do aparelho respiratório é progressivo e de intensidade variável e tem como determinante a presença de muco viscoso nas vias aéreas de pequeno calibre além do *clearance* mucociliar diminuído (91-92).

As infecções podem ser acompanhadas da colonização bacteriana secundária à retenção de secreção favorece metaplasia do epitélio brônquico, a impactação mucóide periférica e a desorganização da estrutura ciliar com infiltração linfocitária aguda e crônica, o que leva o paciente a maiores exacerbações e maior período e periodicidade das internações hospitalares além da piora clínica e funcional dos mesmos crescentemente, impossibilitando a realização das atividades básicas de vida diária além da dispneia em repouso (79,93).

A Hipertensão Arterial Pulmonar na infância tem como definição, mais adaptável à prática pediátrica, a relação da pressão da artéria pulmonar (PAP) com a pressão arterial sistólica sistêmica (PAS), sendo o critério diagnóstico de HP : PAP > 50% da PAS (94).

A relação da HP vai influenciar no baixo débito cardíaco e esse vai ocasionar uma falha de crescimento, palidez nas extremidades, letargia, irritabilidade, taquipneia e taquicardia, cianose, entre outros (95).

A nível vascular há a diminuição de substancias vasodilatadoras e antiproliferativas prostaciclinas, óxido nítrico (ON) e aumento da produção de substâncias vasoconstritoras e mitógenos (endotelina-1)(96). Por ter um

comportamento diferenciado na infância, há uma maior reatividade dos vasos pulmonares impedindo estabelecer o prognostico correto, mas esse em muitos casos é promissor (97).

Para que o transplante pulmonar seja considerado uma alternativa, são analisados os dados da *International Society for Heart and Lung Transplantation* (ISHLT) que evidenciam a sobrevida de 65% em dois anos além da ineficiente resposta medicamentosa à terapia vasodilatadora ou ainda piora clínica e hemodinâmica. Apesar disso, é um procedimento seleto devido ao risco de mortalidade e a resposta medicamentosa é ineficiente (98).

2.3 PRÉ TRANSPLANTE

O Sistema Único de Saúde (SUS) possui um sistema de cadastro único de transplantes que é regulado pelas Centrais de Transplantes dos Estados e os mesmos enfatizam que para tal procedimento ocorrer como o transplante de qualquer órgão é necessário que o doador esteja diagnosticado com morte encefálica e que a família autorize a doação de órgãos (17,99).

A partir da liberação da família e comprovação do protocolo de morte encefálica é acionada a Central de Transplantes que mantém atualizada a lista de espera de receptores a espera de órgãos, (fígado, rim, pâncreas, coração, osso, pulmão, pele, córneas e multivisceral) e aciona as equipes pertinentes regionais e locais para a avaliação do órgão (7-8,10).

Para a retirada dos órgãos há diferentes tempos, sendo o pulmão, dentre os órgãos sólidos, o mais complicado para a preservação depois da retirada (100). O mesmo é mantido em isquemia fria por um período estimado de quatro a seis horas e isso influencia em longo prazo e ainda os valores de sucesso do procedimento na colocação do receptor permanecem inferiores aos dos demais órgãos (17). Em seguida, é acionada a central para que sejam aproveitados os órgãos nos devidos receptores para os possíveis receptores próximos ao local.

Na espera dessa consequência, da chamada da Central de transplantes para o hospital e para o paciente, já está acontecendo para o receptor a fase pré-transplante, onde o candidato começa realizar consultas médicas, exames, imunizações, cuidados nutricionais bem como a reabilitação pulmonar (68). Essa fase consiste em um período de instabilidades, angústia pela espera por um doador na lista do transplante (75-76). E, em geral, os pacientes tendem a apresentar deterioração rápida de sua condição clínica, tanto do aspecto pulmonar bem como da capacidade funcional, hospitalizações e demais complicações (77).

O receptor pode ser indicado para transplante pulmonar unilateral e bilateral (58). O transplante pulmonar unilateral quando comparado com o transplante pulmonar bilateral é um procedimento cirúrgico mais simples, com menor risco de morbimortalidade e com resultados satisfatórios, além de se poder usar o mesmo doador para dois receptores diferentes, favorecendo mais pacientes da fila de espera (68,78).

Já os pacientes com indicação de um transplante bilateral, apresentam maior duração do procedimento e complexidade, mas tem um ganho funcional melhor e tem-se comprovado ser a melhor alternativa para as doenças hiperinsuflativas, além de permitir maior sobrevida e melhor qualidade de vida (68).

2.4 Procedimento Transplante Bilobar Intervivos

O transplante pulmonar bilobar intervivos é um método cirúrgico de transplante pulmonar proveniente da experiência de Starnes (1994) que tinha como objetivo obter órgãos de um tamanho adequado para receptores pequenos, uma vez que a demanda era crescente de pacientes em estado crítico e doadores pediátricos são raridade (18,22,37,45,101).

Surgiu assim a possibilidade de entre dois doadores familiares, com grupo sanguíneo compatível ao da criança, ofertar um lobo inferior de cada doador para que o receptor pediátrico pudesse sobreviver (16). Foi considerada uma proposta ousada e inteligente, porque além de uma melhor

compatibilidade há a redução da resistência imunológica devido à similitude imunológica decorrente do parentesco entre receptor e doadores, reduzindo o risco de rejeições crônicas após o transplante (18,102).

Porém, esses pacientes apresentam inúmeros episódios de rejeição aguda, uma vez que, o mecanismo imunológico é ativo e também assimétrico em consequência das características diferentes dos dois doadores em questão e devido à competência imunológica infantil (85,103).

Essa tolerância imunológica infantil com os dois doadores familiares permite que sobrevida em 5 anos seja de 75%, e com auxílio da medicação imunossupressora, a evolução e permanência do enxerto não são prejudicados, e o número de rejeições podem ser reduzidas (104).

Como procedimento cirúrgico o transplante bilobar intervivos é demorado e de alto risco, uma vez que, o receptor é seccionado para a retirada dos pulmões, primeiro lado esquerdo depois lado direito e segue com a colocação de um lobo inferior de cada um dos doadores, que são submetidos ao mesmo tempo a uma lobectomia (36).

O tempo de cirurgia é elevado, as medicações de anestesia e sedação precisam ser eficazes para todo esse tempo, e ainda, pode ocorrer a necessidade do uso de circulação extracorpórea para um dos lados ou os dois eletivamente, tornando o aspecto da incisão cirúrgica maior além da permanência de drenos torácicos por alguns dias (98).

Todo o processo pré-transplante, como consultas, reabilitação e exames funcionam igualmente ao dos receptores cadavéricos, pois os mesmos encontram-se ainda ativos em lista até a decisão ser afirmada e a fase pós-transplante desde o tempo de permanência em UTI até a alta hospitalar. Tais procedimentos são similares aos do pós-transplante cadavérico (50,56).

Os doadores não têm apresentado patologias remanescentes ou ainda déficits funcionais relacionados à perda de capacidade pulmonar decorrentes das lobotomias tendo alta assim que possível a capacidade total pulmonar dos doadores deverá ser de 85% do previsto (105).

Esse transplante é favorável ainda ao receptor pediátrico, pois o mesmo ainda está em fase de produção do hormônio do crescimento e demais hormônios, que vem a favorecer positivamente o lobo implantado, a fim de que esse possa evoluir e ter um volume adequado (98).

2.5 Complicações do Transplante Pulmonar

2.5.1 Disfunções Primárias do Enxerto

As disfunções primárias de enxerto (DPE) ainda são responsáveis por um índice de mortalidade dos transplantes pulmonares em torno de 81% (106) e são responsáveis pelo prognóstico do paciente e pelo tempo de permanência em Unidade de Terapia Intensiva (UTI) e consequentemente mais tempo em ambiente hospitalar (106) .

Há incidência elevada de disfunção primária do enxerto (DPE) na recuperação do paciente transplantado que persiste até 72 horas pós, sendo confirmada quando se exclui o quadro de insuficiência respiratória bem como a ausência de alterações radiográficas (68).

A DPE pode ser causada por: infecções, pneumonias por aspiração, complicações vasculares de estenose da veia pulmonar, disfunção cardíaca por sepse ou síndrome da resposta inflamatória sistêmica ou sobrecarga de volume além da rejeição hiperaguda, e são apresentadas pela presença de infiltrados, aumento de resistência vascular e redução da complacência (107).

2.5.2 Infecções

Uma das mais comuns complicações são as infecções devido a contaminação a qual o pulmão do doador foi exposto na UTI; o fato do pulmão ser mantido em isquemia por isso, sem circulação linfática e atividade mucociliar; dor no pós-operatório imediato; o uso de imunossupressores além dos danos causados pela DPE (111).

Antibióticos de largo espectro até o sétimo dia após o transplante são administrados a fim de suprir as necessidades pós-transplante (112).

2.5.3 Insuficiência Renal

A insuficiência renal aguda está associada a maior permanência do paciente em ventilação mecânica, associada ao maior tempo de internação bem como a mortalidade precoce, porém pode ser revertida a função renal e essa pode ser solucionada com o equilíbrio hídrico usando medicações ou ainda usando a diálise de ultra filtração lenta (113).

2.5.4 Rejeições

As rejeições são originarias a partir da resposta dos anticorpos ao órgão enxertado, fazendo com que o sujeito seja exposto a sensibilização em minutos, poucas horas ou tempos depois (114).

As rejeições hiperagudas ocorrem em minutos ou horas após a inserção do enxerto, a aguda ocorre preferencialmente algum tempo após transplante; já a crônica é conhecida pela lesão irreversível crônica da ocorrência da ação dos patógenos (62).

A rejeição hiperaguda é caracterizada em pessoas previamente sensibilizadas ou com incompatibilidade do sistema ABO, sendo as lesões básicas arterite e arteriolite aguda disseminadas, trombose vascular e necrose isquêmica. Assim, no transplante pulmonar é necessário usar provas de reação cruzada que detectam a presença de anticorpos do receptor com os linfócitos do receptor (11,68).

Ainda podem acometer os receptores, as rejeições agudas, que ocorrem depois do transplante e que não são tratadas com os imunossupressores ou ainda, durante a imunoterapia, uma vez que a interferência da imunidade celular, que é caracterizada pela deterioração clínica pode ser tratada com terapia imunossupressora (35).

As rejeições crônicas são caracterizadas pela recorrência de rejeições e as mesmas causam lesões definitivas ao longo do tempo, gerando bronquiolite obliterante. Nesses casos, é cogitada a re-intervenção, se por ventura há sangramento ou ainda sofrimento de anastomoses brônquicas (115-116).

Outras complicações podem ocorrer em menor escala com os pacientes pós-transplante pulmonar, como: doenças abdominais, doenças cardíacas derivadas da sobrecarga além de complicações na caixa torácica, pleurais, hiperinsuflação entre outras. Tais complicações são entendidas como parte do processo minucioso da adaptação pulmonar na nova caixa torácica (117–119).

2.6 Reabilitação Pulmonar

A reabilitação pulmonar é indicada aos pacientes pré e pós-transplante, ou seja, no programa de transplante pulmonar por ser de extrema importância por ser constituído por uma equipe multiprofissional que atua de maneira interdisciplinar com os pacientes com o mesmo objetivo (126-127).

Os pacientes no pós-transplante tem grande aumento de peso devido ao uso de corticoides para evitar a imunorejeição, sendo assim necessário o cuidado na reabilitação pulmonar. Mesmo com possíveis intercorrências e melhores funções gradativas a reabilitação tem como objetivos: promover o recondicionamento, reeducar a postura do paciente devido ao procedimento cirúrgico, readaptar avds, reduzir a toxicidade medicamentosa, evitar rejeições além da melhora da qualidade de vida (124-126).

2.6.1 Capacidade Funcional

Para os pacientes em programa de transplante pulmonar, a reabilitação pulmonar evidencia a avaliação da capacidade funcional, a fim de maximizar a independência funcional do paciente durante as atividades de vida diária por mais tempo possível durante a espera do órgão, o ensinamento de técnicas para eficiente gasto de energia (121).

Indiretamente, haverá o treinamento de exercício físico para aumentar a tolerância ao exercício para fortalecimento dos músculos esqueléticos que auxiliam na realização dos movimentos e produzem energia e evitam a deteriorização dos mesmos. Enfim reduzir e ou amenizar os sintomas para melhorar a qualidade de vida dos pacientes (126).

Os pacientes que realizaram o transplante pulmonar apresentam uma maior perda do percentual de fibras musculares tipo I, uma redução do limiar de lactato, menor função muscular, além de redução de VO_2 max de pico de 40% a 60% pred (122-123). Esses fatores pós-transplante imediato se deve ao tempo prolongado de internação ou ainda pelos efeitos dos imunossupressores.

Porem, em pós-operatório tardio os pacientes já apresentam escores normais de capacidade funcional retornando a funções semelhantes a pacientes com leves patologias pulmonares (124). Os transplantados bilateralmente apresentam escores maiores que os pacientes que transplantaram unilateralmente (122).

2.6.2 Função Pulmonar

Por se tratar de pacientes com pneumopatias crônicas em estado avançado, os mesmos apresentam perda de função pulmonar gradativa e conforme a patologia irão apresentar restrições de capacidade vital bem como redução dos volumes pulmonares, resultando em queixas frequentes de dispneia em repouso e a pequenos esforços das atividades básicas de vida diária (ABVD) como: banhar-se, mover-se de um comodo da casa para outro, para dormir, entre outros esforços que não são mais possíveis a esses pacientes (120).

O fator limitante, a oxigenioterapia, resulta na intoleancia ao exercício associada à progressão da doença, e se agrava conforme o tempo passa na lista de espera para transplante pulmonar, sendo responsáveis pelos impactos negativos na qualidade de vida, pois há restrições para deslocamentos para

atividades ao ar livre, bem como ao convívio social e demais atividades que exijam mais esforço ou capacidade física (121).

Com a grande descompensação dos pacientes dos musculos respiratorios e assim o uso da musculatura acessoria com frequencia devido a fadiga e a perda da força dos musculos respiratorios devido a dependencia do oxigenio, a incapacidade e a deteriorização, o padrao respiratorio torna-se priotitariamente apical, com frequencias respiratorias variadas devido ao esforco (122).

Os pacientes apresentam dores posturais em região cervico- torácica e ainda dores nas costelas, pois dependendo a doença o esforço respiratório causa além da má postura a falta de força muscular respiratória, principalmente diafragmática (123).

Os valores de força respiratoria pos transplante melhoram significativamente dentro do primeiro ano, e sao exames de controle para rejeições ou injurias. Já para a força muscular respiratoria, pouco se sabe quanto tempo é necessário pós o procedimento para que mesma retorne, pois dependendo a cirurgia temos a acão ou dissecação do diafragma, paralisia do mesmo, tempo de tubo ou ventilação mecânica, que influencia no pos operatório do paciente e na força muscular respiratória (124-126).

2.6.2 Qualidade de vida pré-transplante

A qualidade de vida dos pacientes devido às condições antes do procedimento é restrita, os adultos não possuem vida social e o relacionamento com a família e os filhos são limitados. Devido à impossibilidade de deslocamentos, por exemplo, as crianças não brincam por não poderem correr e muitas não têm amigos, pois não frequentam a escola ou ainda faltam muito no ano letivo escolar devido às doenças. (49,124).

A família cria uma espécie de proteção aos pacientes, pois como são sensíveis a qualquer alteração climática, ambiental, comportamental ou ainda estrutural, tornando os passeios raros e, a vitalidade bem como a disposição e bem estar, são prejudicados. (125-127).

Além dos benefícios de qualidade de vida e adaptação ao período pré-transplante, a equipe multidisciplinar, mais especificamente a fisioterapia, tem como objetivo acompanhar o curso, a condições físicas e funcionais do paciente desde o processo de seleção como pós-transplante e alta, tornando assim, essa necessidade com os transplantados pulmonares intervivos, pois os mesmos apresentam além da realização de um procedimento diferenciado, um acompanhamento durante a adolescência e vida adulta.

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4 ARTIGO

FUNCTIONAL CAPACITY AND LUNG FUNCTION OF PATIENTS SUBMITTED TO LIVING DONOR LOBAR LUNG TRANSPLANTATION

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Authors' assignments

Pedro Dal Lago–Research advisor. He was in charge of checking research data, writing the manuscript, and obtaining research clearance and support in all of the decision-making processes and statistics.

Anelise Sonza–Project co-advisor. She was responsible for proofreading and revising the manuscript for grammatical errors, following up of data, and providing support in the adjustment of the data collection instruments and statistical analysis.

José de Jesus Peixoto Camargo - Participant in the research as a medical doctor. He was in charge of the lung transplantation team of the Porto Alegre Santa Casa de Misericordia Hospital, donating his time and contributing with his knowledge and data of lung transplantations.

Spencer Marcantonio Camargo–Participant in the research as a thoracic surgeon medical doctor of the lung transplantation team. He provided support during data collection, searched for patient records, identified past transplantations, analyzed lung transplantation from living donors, and determined the availability of the donors' data for transplantation from living donors.

Juliessa Florian—Participant in the research. She provided support in the contact with patients to schedule evaluations, collected data from medical records, analyzed available data released from the Lung Rehabilitation section of Santa Casa de Misericórdia, provided support for clearance of certain doubts during data collection, and dedicated her time in teaching lung rehabilitation to patients with lung transplantation.

Fernanda de Andrade–M.Sc. student of the rehabilitation sciences program. She executed and designed the study, performed data survey, collected data, searched medical records, drafted the paper by applying data collection instruments, and included a detailed discussion on lung transplantation from living donors.

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LIST OF ABBREVIATIONS

LDLLT–Living Donor Lobar Lung Transplantation

ELA - Everyday Life Activity

QL–Quality of Life

GEE–Generalized Estimating Equations

CI–Confidence interval

ISHLT–International Society Heart Lung Transplantation

ABTO–Brazilian Association of Organ Transplantation

ELAs - Everyday Life Activities

FCF–Free Consent Form

CMV–Cytomegalovirus

SMWT–Six-Minute Walk Test

mMRC–Medical Research Council

Modified Borg Scale - Modified Dyspnea Scale Under Exercise

SF-36–Quality of Life Questionnaire Short Form 36

IPAQ–International Questionnaire on Physical Activity

London–Everyday Life Activity Questionnaire

ATS–ERS–American Thoracic Society–European Respiratory Society

FVC–Forced Vital Capacity

TI–Tiffennau Index

FEV_1–Forced Expiratory Volume at the first second

BMI–Body Mass Index

Pimax–Maximum Inspiratory Pressure

Pemax–Maximum Expiratory Pressure

CF–Cystic Fibrosis

BOS–Bronchiolitis Obliterans Syndrome

ICU - Intensive Care Unit

ABSTRACT

Introduction: Lung transplantation is an alternative for the increased life expectancy of patients with advanced chronic pneumopathies. Among its modalities, the living donor lobar lung transplantation method (LDLLT) is indicated for pediatric patients. This study assessed the lung function profile and functional capacity of the patients submitted to LDLLT, from 1999 to 2015, performed at the Santa Casa de Misericórdia of Porto Alegre, RS, Brazil.

Method: This work is a cross-sectional, clinical, and retrospective observational study, in which living donor transplantation patients under medical follow up were assessed for lung function, functional capacity, respiratory muscle strength, level of dyspnea, everyday life activities (ELAs), and physical activity beyond quality of life (QL). Descriptive statistics was performed, and the GEE test ($p<0.05$) was used at a CI of 95% for comparison of pre- and post-transplantation.

Results: Included in the study were 30 patients, of whom 17 were male and 13 were female. Thirteen living individuals were evaluated in post-transplantation and showed improvement in the forced vital capacity, six-min walking test, dyspnea sensation, and O_2 saturation in the comparison of pre- and post-transplantation ($p < 0.01$). The other variables (QL, ELA, and physical activities) were similar to those predicted in the literature when compared with the post-procedure cadaveric lung transplanted patients.

Conclusion: Improvements in functional capacity and lung function, as well as improved quality of life, could be observed after LDLLT.

INTRODUCTION

Lung transplantation has been a therapeutic alternative to patients with end-stage lung disease, and it aims to provide improved quality of life and the prognostics of these patients (1).

The International Society Heart Lung Transplantation reported a rise in transplantations of pediatric receptors worldwide, with high incidence from ages 11 to 17. Around 550 pediatric transplantations were performed in 2013 alone, and the predominant pathologies were cystic fibrosis followed by lung hypertension and bronchiolitis obliterans (2).

In Brazil, based on the latest Brazilian Transplantation Record of the Brazilian Association of Organ Transplantation until 2015 in the Brazilian territory, a 12.4% increase in the number of lung transplantations performed relative to that in 2014 (3) was recorded. Lung transplantation is performed chiefly in four Brazilian states (São Paulo, Ceará, Minas Gerais, and Rio Grande do Sul), where Rio Grande do Sul is the only state able to perform the living donor transplantation method. Among the 74 lung transplantations performed in 2015 in Rio Grande do Sul, four were from living donors (3).

The implementation of lung transplantation requires an in-depth evaluation (2, 4, 5); from then on, the patient is directed to the transplantation list (6). At first, all patients are registered in the waiting list with indication of unilateral or bilateral lung substitution (5,7). In case of advanced disease, patients with a waiting period higher than two years in the cadaveric donor list and/or existence of blood incompatibilities or positive immune panel are advised by the medical team to undergo living donor lobar lung transplantation (LDLLT) (8).

Based on the ascertainment of possible family donors, of first and second

degree, the ABO system compatibility blood test is chosen. Subsequently, tomography, immune compatibility to assess positive antibodies present besides spirometry, volumetry of the lung lobes, history of respiratory or systemic diseases, and blood pressure level at the lung artery of possible donors (5, 9-11) are determined. Once the compatibilities are checked, the living donor transplantation method shows reduced risk of graft rejection and can be performed with healthy family donors (12).

LDLLT is recommended because of the scarcity of the number of pediatric donors (13, 14). It is a surgical lobar method performed on children in the United States since 1963 (15-17), chiefly for diseases such cystic fibrosis (18, 19) and bronchiolitis obliterans (20, 21). These individuals exhibit high morbidity and mortality levels before adolescence (22). LDLLT is composed of six simultaneous surgical procedures; given the surgical risk, the immediate and long-term complications are more frequent on the receptor than on the healthy donors (7, 23-24). The duration of hospital stay and the complications are similar to the procedure used with cadaveric receptors (25-26). The main complications include graft primary malfunction, graft rejection (hyperacute and acute), sepsis, reperfusion injuries, infections, and respiratory muscle weakness (7, 25).

For living donors to reset the functionality and physical conditioning required for everyday life activities (ELAs), lung rehabilitation is relevant (27-29) because patients present oxygen dependency and shortness of breath following small efforts and functionality reduced to a minimum (30). Thus, lung rehabilitation increases peripheral muscle strength and provides reeducation of

habits and everyday activities, as well as education to prevent further complications resulting from a sedentary lifestyle (31-34).

Monitoring of late complications at the level of physical activity of the lung functions, dyspnea, and quality of life after hospital discharge is required and should be performed continuously. After discharge, patients should perform three months of rehabilitation (13, 21, 35). No studies have assessed the functional capacity and lung function of these patients after living donor transplantation and after the lung rehabilitation period. Thus, the present study aimed to evaluate the profile of lung function and the functional capacity of lung transplantation from living donor patients.

Methods

This work is a clinical and retrospective observational cohort study, in which the patients were submitted to pre- and post-assessment for at least 6 months from the LDLLT occurrence. To this end, data from medical records and assessments performed by the lung transplantation team were also collected related to the pre-transplantation period.

This study was approved by the Ethical Committee for Research of the Federal University of Health Sciences of Porto Alegre, RS, Brazil, under the legal opinion no. 1,283,677. It was performed from November 2015 to May 2016. The survey was performed on living donor lung transplantation patients who underwent the procedure from 1999 through 2015. All the responsible people or patients over 18 signed the free consent form.

Basic procedures were carried out at the hospital complex of Porto Alegre, RS, Brazil, Santa Casa de Misericórdia. Data from the medical records were collected at Porto Alegre, RS, Brazil, Santa Casa de Misericórdia Lung

Transplantation Archive. The following information was collected from the medical records: blood type, age at which the transplantation was performed, level of parenthood of the donors, medical diagnostics, weight and pre-transplantation body mass index (BMI), presence of cytomegalovirus (CMV), complications, period of hospitalization after immediate transplantation, and execution of pre- and posttransplantation rehabilitation program.

At the time of the collection, all patients were in fair cognitive state, which was required for applying tests. Patients scheduled for a medical consultation with the lung transplantation team were submitted to lung function tests (spirometry), functional capacity through the six-minute walk test (SMWT), dyspnea index (mMRC), modified dyspnea scale under exercise (modified Borg scale), quality of life questionnaire (SF-36), inspiratory and expiratory muscle strength (manovacuometry), physical activity questionnaire (IPAQ), and everyday life activities (London).

According to the criteria and directives of the ATS-ERS, spirometry is the standard procedure preceding a patient's medical consultation (36-37). The forced vital capacity (FVC), Tiffennau Index (TI), and forced expiratory volume at the first second (FEV_1) were also measured.

SMWT was initially implemented on the patients from 2008 by the Lung Rehabilitation Department, and it is still performed today. SMWT is performed in a 30 m-long corridor. Oxygen saturation, blood pressure, dyspnea degree, cardiac and respiratory frequencies, and distance traveled are measured before and after the test (38). The percentage of the predicted value and the predicted distance to be traveled were calculated using the formula of Donadio et al. (39). Mass and height were measured based on the BMI.

On the same day of the post-transplantation medical consultation, the quality of life Short Form-36 (SF-36) questionnaire was administered. This questionnaire aimed to assess the scores for functional capacity, physical aspects, pain, general state of health, vitality, social aspects, and mental health (40).

To assess the dyspnea degree and level of physical activity, the Medical Research Council (mMRC) (41) and the short version of the International Questionnaire on Physical Activity (IPAQ) (42-43) questionnaires were applied on the physical activities performed during the last week preceding the questionnaire application. To determine the presence of dyspnea during the basic activities of everyday life, the patients answered the London questionnaire.

Respiratory muscle strength was further determined for all patients who returned to routine consultations via the manovacuometry test with a previously gauged digital manovacuometer (MVD 300, Globalmed, Porto Alegre, RS, Brazil) under a variation of −300 cm H_2O to +300 cm H_2O (44). Maximum inspiratory pressure (Pimax) and maximum expiratory pressure measurements were ascertained (45). Three to 9 tests were performed, and the maximum value obtained was validated based on a lower than 10% variation between the two higher measurements (44). The predicted value formulae by Lanza et al. (2015) were used for patients aged less than 18, whereas the formulae by Kunikoshita et al. (46-47) were used for patients older than 18.

Statistical Analysis

Quantitative variables were stored in electronic worksheets and analyzed using descriptive statistics through percentages, averages, and standard

deviations or medians and interquartile ranges, both together with the variation amplitude.

Categorical variables were described by absolute and relative frequencies. For the simultaneous comparison between intra- and inter-groups, the model of Generalized Estimations Equations (GEE) was employed.

The normal distribution model was applied for the symmetric variables, whereas the Gamma distribution model was used for the asymmetric ones. Associations among changes in the outcomes after intervention were evaluated by the Pearson or Spearman correlation coefficients. The adopted level of significance was 5% ($p<0.05$), and the analyses were performed using SPSS program version 21.0 (IBM Analytics, EUA).

Results

Among the 36 LDLLTs performed at the Santa Casa de Misericórdia de Porto Alegre Hospital from 1999 to 2015, 31 patients were aged below 18 at the time of the transplantation. Among these 31 patients, one patient was excluded because of an encephalopathy after procedure, so 30 patients were analyzed. Among the 30 patients included, 13 were alive and under monitoring by the medical team at the period of the study. Of these 30 patients, the age at which the transplantation was performed was 12.3 ± 3.3 [7–18] years, with 56.7% being males and 43.3% females. Among these 30 patients, 17 died (56.7%) and 13 were kept alive (43.3%). At the moment the transplantation was performed, patients exhibited an average body mass of 30.7 ± 8.4 kg and average BMI of 15.9 ± 1.8 [12.7–19.5] $kg.m^{-2}$. The characterization of the sample is shown in Table 1.

The prevailing medical diagnosis for the living donor transplantation patients was that of cystic fibrosis with 48.1% of the cases (13 patients) followed by bronchiolitis obliterans with 44.4% of the cases (12 patients). Other diagnostics such as lung fibrosis and bronchiectasis were found in 7.4% of the cases, and the medical diagnostics was not present in the medical records for 1% of the patients.

Blood types were identified (ABO system) in the group of living donor transplantation patients. The A+ and O+ types were predominant, as shown in Table 1. The presence of CMV was found in 36.7% of the pre-transplantation receptors, which evidenced the need for immunizations and procedures to prevent pre-transplantation CMV.

Among the donors, 46.7% were both first-degree donors, followed by 20% of one first-degree donor and one second-degree donor, and the remaining, split in lower amounts of second, third-, and fourth-degree donors.

Complications found in patients during and after the surgical procedure were graft primary malfunction (33.3%), acute rejection after transplantation (26.7%), and chronic rejection with indication of re-transplantation (6.7%).

Among the 30 patients, 40% executed the lung rehabilitation program of the Santa Casa de Misericórdia de Porto Alegre Hospital and were in hospital after the transplantation and up to the hospital discharge for an average of 24.6 (±18.3) days in an interval of 1–71 days (Table 1). Nevertheless, 36.6% of the patients died during the procedure or before hospital discharge.

For these patients, pre- and post-transplantation lung function and functional capacity were evaluated (Table 2). Significant improvement in lung

function and functional capacity was found by comparing the findings of pre- and post-transplantation for all the items evaluated ($p<0.01$).

The nutrition state improved, but the ratio of pre- and post-transplantation from living donors was not significantly different, as shown in Table 2.

The quality of life questionnaire SF-36, which represents the patients' quality of life after transplantation, was collected for only 11 patients because one of them refused to execute the tests after transplantation and participate in the study. High averages were obtained from the functional capacity with 92.3 ± 12.1 [60–100] and social aspects 90.9 ± 12.6 [63–100]. Data are presented in Table 3.

In the IPAQ questionnaire of physical activity, 58.3% of the patients were active, whereas the remaining belonged to the categories of irregularly active (33%) or sedentary (8.3%). For the London questionnaire, an interval of 9–18 marks was found, thereby suggesting certain independence in the domestic activities shown by the patients because the questionnaire allows marks from 0 to 75. A low score revealed high independence for everyday activities, as shown in Table 4.

From the application of the dyspnea level (mMRC) questionnaire applied to the late post-LDLLT, the median was 0. This result means that the patients exhibited symptoms of shortness of breath only during intense exercises, as demonstrated in Table 4.

Results for manovacuometry performed in the late post-transplantation, that is, obtained 6 months after lung transplantation, showed Pimax and Pemax values of 69.8 ± 27.5 and 66.0 ± 34.6 cmH_2O, respectively. Such figures are

indicative of weakness in inspiratory and expiratory muscles in the late period after transplantation.

Discussion

The results of the present study show that the procedure was performed mostly in pediatric patients, predominantly males, with BMI lower than that recommended for their age. The procedure was executed most frequently on cystic fibrosis patients, which corroborated the findings reported by Adler et al. (48).

The results of the present study agree with the findings of Donadio et al. (49), who reported that patients with cystic fibrosis entering the lung transplantation list are similar in age, sex, and medical diagnosis. In these patients, several gastric, pancreatic, or respiratory manifestations are also present, thereby making their stay in the waiting list difficult. Hofer et al. (50) stressed that pediatric patients of lung transplantation lists show high recurrence of hospital stay caused by infections and are oxygen dependent for everyday life activities.

Considering that patients have pre-operation weakness and urgency during the procedure, the main intercurrences present in the study are acute rejection, graft primary malfunctions, and the bronchiolitis obliterans syndrome (BOS). Such intercurrences generally develop toward a clinical state of possible re-transplantation. Hayes et al. (51) demonstrated that high BOS levels are present after execution of the procedure, and these levels resulted from sequential chronic graft rejections after the first year of transplantation. Regarding the rejections, Snell et al. (52) found that these events frequently

occurred in patients who underwent living donor transplantation due to the placement of two inflated lobes in the thoracic cage, as well as given the fact that a child's immune system is more active than that of an adult.

The reduced period of hospital stay described in this paper (24.6 days) is probably associated with the use of new technologies such as extracorporeal circulation membrane, assisted mechanical ventilation, early mobilization, and immediate post-surgery immunotherapy; these new techniques reduce the hospital stay period of transplanted patients (53).

In terms of the lung function of the living donor lung transplantation patients, the values obtained for both FVC and forced expiratory volume at the first minute (FEV_1) improved compared with those for the same individuals in the pre-transplantation and post-transplantation periods. However, FEV_1 was lower than the averages predicted by ATS-ERS, and it was also lower than the values reported by Chaves et al. (54), who evaluated pediatric patients with mild cystic fibrosis. According to Costa et al. (55), FEV_1 values lower than normal predict seriousness of illness relative to the lung function and allow the follow up of the post-transplantation disease evolution and current patient condition.

For lung function, the airway obstruction pattern was assessed, with values found for the TI at the pre-transplantation stage as having an obstructive trend resulting from the predominance of patients with cystic fibrosis diagnosis in the sample studied. Although this study did not appoint any statistical significance for this variable, TI values corresponding to post-transplantation are in the average of values for healthy individuals as described by Vilozni et al. (56).

All the factors related to lung function also directly influence the functional capacity of the individuals who underwent transplantation, as stated by Chen et al. (57). In accordance with this study, the values for SMWT were predictive of pre-transplantation mortality and evidenced the patient evolution after the procedure; this result agreed with the findings by Chaikriangkrai et al. (58), who observed that patients of low BMI and SMWT lower than 71.01 m have higher mortality immediately after transplantation.

SMWT as the sub-maximum test of functional capacity represents the sum of different factors, namely, lung function, cardiac function, muscle performance, nutritional state, and peripheral circulation (39). For the values of functional capacity presented in this study, patients increased the values of distance traveled when immediate pre- and post-transplantation and late post-transplantation were compared. Similarly, Yimlamai et al. (59) determined that the best test values are indicative of low Intensive Care Unit periods and under mechanical ventilation after procedure. From the perspective of the traveled distance to serve as mortality predictor, as studied by Kadicar et al. (60), these authors pointed out that the value is close to 400 m. In this way, the average of the distance of the walk by the participants in this study in the pre-transplantation period represents an important mortality predictor factor.

Theoretically, Barr et al. (61) stated that both long-term lung function and functional capacity of patients submitted to living donor transplantation have values similar to those of patients who received lung transplantation from bilateral corpses, thereby indicating that the patients are not harmed if submitted to the lobar transplantation in terms of lung function and functional

capacity, which directly favors the evident improvement in the quality of life in transplanted patients (62).

In terms of quality of life, the results of this study point to values above 50%, stating that the quality of life of patients after transplantation was satisfactory, but the lower scores belonged to pain and general state of health (with averages of 65.8 and 69.3, respectively) with the higher score being related to social aspects. Therefore, living donor receptors could return to a normal life, such as going to school, play, walk, run, and being with friends without depending on oxygen, which corroborated with the studies by Yusen et al. and Smeritschnig et al. (31,62).

In accordance with the results obtained, LDLLT patients of this study should remain active after transplantation to maintain a physical condition not previously possible nor known, as also demonstrated by Downs et al. (27). The study presented in this paper is unique for the use of IPAQ, London, and mMRC questionnaires to assess physical activity, everyday life, and dyspnea of living donor lung transplantation patients. For healthy children and adolescents, values found by Luciano et al. (63) are active and very active, which confirm the findings of the present study and the transplantation success.

In addition to the evaluation of the physical activity level executed, a further relevant factor in the recovery of the lung transplantation patient is respiratory muscle strength. Respiratory muscle strength was evaluated by measuring maximum respiratory pressures (64). In the present study, the values for Pimax and Pemax were below the predicted values for healthy youngsters and children as described by Lanza et al. and Oliveira et al. (46, 65),

thereby demonstrating that the patients under study require respiratory muscle strengthening after the LDLLT procedure.

In conclusion, patients who undergo LDLLT are considered fragile, overprotected, under critical condition at the pre-surgical procedure, and submitted to reduce but not negligible surgical risk. At the post-surgical step, LDLLT general improvement in lung function, functional capacity, and quality of life.

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Table 1–Characterization of the 30 living donor transplantation patients from 1999 to 2015.

Variables	Overall Sample	Descriptive Statistics
Age at the Transplantation (years)	30	12.3 ± 3.3 [7–19]
Sex	30	
Male		17 (56.7)
Female		13 (43.3)
Medical Diagnosis	27*	
Cystic Fibrosis		13 (48.1)
Bronchiolitis Obliterans		12 (44.4)
Other		2 (7.4)
Blood Type	21*	
A+		9 (42.9)
A-		1 (4.8)
B+		2 (9.5)
O+		9 (42.9)
BMI (kg/m²)	24*	15.9 ± 1.8 [12.7–19.5]
Height /Age score-z	24*	−1.91 ± 2.32 [−6.17–3.40]
BMI/ Age score-z	24*	−1.24 ± 1.42 [−3.31–2.32]
Donor	30	
Both first-degree donors		14 (46.7)
One first-degree and another one second-degree donor		6 (20.0)
One first-degree and another one third-degree donor		5 (16.7)
Presence of CMV	30	11 (36.7)
Intercurrences	30	
None		7 (23.3)
Acute Rejection		8 (26.7)
EGF Early Graft Failure		10 (33.3)
Other		3 (10.0)
Re Tx		2 (6.7)
Period of hospital stay (days)	28*	24.6 [1–71]
Executed rehabilitation	30	12 (40)

*Data for a few patients could not be found in view of the loss of medical records following a fire. BMI, body mass index; CMV, cytomegalovirus; EGF, Early Graft Failure; Re Tx, re transplantation.

Table 2–Comparison of living donor pre- and post-transplantation

Variables	Pre (n = 18) * Average ± SD	Post (n = 12) Average ± SD	Difference (CI 95%)	P
Lung Function				
FEV_1 (%)	28.5 ± 2.5	50.3 ± 6.3	21.7 (8.4 a 35.0)	0.001
FVC (%)	38.4 ± 3.1	61.1 ± 5.2	22.6 (11.3 a 34.0)	<0.001
TI (%)	77.4 ± 25.6	83.6 ± 21.5	6.2 (−12.6 a 24.9)	0.009
Functional Capacity (SMWT)				
Distance Traveled (m)	357.2 ± 28.3	522.7 ± 18.3	165.5 (93.8 a 237.3)	<0.001
Distance Traveled (% predicted)	57.1 ± 4.6	78.5 ± 3.8	21.4 (11.3 a 31.5)	<0.001
Sensation of dyspnea (BORG)	3.6 ± 0.6	0.9 ± 0.3	−2.7 (−4.0 a −1.4)	<0.001
O_2 Saturation	82.6 ± 2.1	95.9 ± 1.1	13.4 (8.1 a 18.6)	<0.001
Nutrition State				
<18 years				
H/A- z	−0.65 ± 1.02	−0.78 ± 0.57	−0.13 (−2.66 a 2.41)	0.885
BMI/A z	−0.70 ± 0.29	−1.52 ± 0.50	−0.82 (−2.52 a 0.89)	0.224
≥18 years				
BMI	15.6 ± 1.8	17.4 ± 1.2	1.82 (0.87 a 2.77)	0.003

Groups were compared with pre- and post-late LDLLT using the Bonferroni test, at CI 95%, p≤ 0.01.
*Old results were lost following a fire in the archives of the Lung Transplantation unit of the Santa Casa de Misericórdia Hospital. FEV_1, forced expiratory volume at the first second, FVC, forced vital capacity: TI, Tiffenau Index, BMI, body mass index, H/A- z height by age at the z score; BMI/A-z, body mass index by age at the z-score

Table 3–Data for quality of life (SF-36) after living donor lung transplantation (n =12)

Domains	Average ± SD [min–max]
Functional Capacity	92.3 ± 12.1 [60–100]
Limitation by Physical Aspects	88.6 ± 30.3 [0–100]
Pain	65.8 ± 17.4 [40–80]
General State of Health	69.3 ± 18.1 [37–100]
Vitality	76.8 ± 18.9 [40–100]
Social Aspects	90.9 ± 12.6 [63–100]
Limitation by Emotional Aspects	84.9 ± 22.9 [33–100]
Mental Health	78.3 ± 14.9 [56–96]

Table 4–Data on the level of physical activity, everyday life activities, and level of dyspnea after living donor lung transplantation (n=12)

Variables	Descriptive Statistics *
Level of Physical Activity - IPAC	
Active	7 (58.3)
Irregularly active	4 (33.3)
Sedentary	1 (8.3)
Everyday Life Activities–London	13.1 ± 2.8 [9–18]
Level of dyspnea - mMRC	0 (0–1) [0–4]

* for physical activity level: n (%) and for everyday life activities: average ± standard deviation [minimum–maximum].

5 CONCLUSÃO GERAL

O método de transplante pulmonar do tipo bilobar intervivos é inédito no país, sendo feito somente no Rio Grande do Sul, com grande aceitação e a sua sobrevida de 5 anos em 41% dos casos é satisfatória enquanto procedimento.

Os receptores submetidos ao procedimento, bem como seus doadores são expostos ao risco cirúrgico inevitável, porém a expectativa tanto da família quanto da equipe multidisciplinar supera quando se opta por esse modelo de transplante.

Os mesmos apresentam no período de pós transplante imediato cuidados extremos, principalmente até o primeiro ano, e apresentam progressivamente uma qualidade de vida melhor, um retorno as atividades escolares e de convívio familiar, deixando muitas vezes o autocuidado um pouco aquém do esperado, por considerarem-se com razoável saúde, mesmo que a sobrevida seja limitada. As atividades físicas muitas vezes são esquecidas ou postergadas, bem como as consultas e exames médicos, sendo de responsabilidade dos pais ainda a cobrança pela saúde e a atenção aos cuidados que um transplantado necessita.

Concluiu-se então com este estudo, que os parâmetros de função pulmonar e de capacidade funcional apresentaram melhora após o procedimento de transplante pulmonar intervivos em seus receptores, sendo esse eficaz para a melhora dessas variáveis, porém, com necessidade constante de monitorização e também de acompanhamento.

ANEXO A - NORMAS DE PUBLICAÇÃO DA REVISTA

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Article	**4,000**	**250 structured**	**N/A**	**N/A**
Short Report	3,000	250 structured	30	3
Commentary (invited)	1,000	N/A	10	1
Letter to the Editor	500	N/A	5	1

*includes abstract, introduction, materials and methods, results, discussion
**combined total of figures and tables

Overview: A concise review of a special interest topic in the field of transplantation. Overviews are generally solicited; however, author-initiated proposals will also be considered. Interested authors should submit an outline/abstract of the proposed paper to editorialoffice@journal.tts.org. The proposal will be reviewed with regard to interest, relevance, timeliness and suitability. If suitable, a full version the manuscript will be welcomed. Overviews should adequately encompass the spectrum of the topic and not focus on the particular views and hypotheses of the authors.

Article: A full-length report of completed basic and experimental research, or clinical and translational research.

Short Report: A brief, time-sensitive manuscript reporting item (s) of special significance in the field.

Rigorous Meeting Reports that highlight the aims, scope, and science presented at a conference may be considered for publication.

Commentary: A companion paper highlighting an article of particular note. Commentary provides context to the accompanying submission regarding its significance and potential impact to the field. All commentaries are invited.

Letters to the Editor: There are 2 types of letters.

- *Informational*: A focused submission briefly discussing a significant clinical report or other high interest topic on relevant subject matter.
- *Correspondence*: Comments on articles previously published in *Transplantation*. The authors of the original publication will be given an opportunity to provide a paired response.

Letters are published online only and supplemental Digital Content (SDC) is not considered for this type of submission.

There is no charge to submit to *Transplantation*. If a paper is accepted, authors are responsible for manuscript charges of $80 USD per printed page. (See Accepted Manuscripts and Open Access for more information.) Invited manuscripts and Letters are exempt from these charges.

Where to submit to *Transplantation*

Submissions must be made electronically via www.editorialmanager.com/tpa

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Manuscript preparation, formatting, and policy guidelines are detailed in

- **Manuscript Formatting**
- **Manuscript Processing**
- **Policies**

This information applies to all manuscripts submitted for consideration. Note: Manuscripts not conforming to the required format will be returned to authors for correction.

LANGUAGE: Manuscripts must be written in proper, clear English. Authors needing assistance may consult with outside services providing English Language Assistance.

GENERAL FORMATTING: All manuscripts must be digitally prepared as follows:

- Manuscript text should be double spaced; digital text files should be supplied in Word .doc or .docx format. Image files can be uploaded in .tif, .eps, or .jpg format
- DO NOT upload any file in PDF.

Additionally, manuscripts are encouraged to follow these guidelines to facilitate ease of review:

- 1-inch page margins
- Manuscript pages may be numbered but do NOT in-clude individual line numbers
- Arial or similar san serif typeface, 12-point font size preferred

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Email: editorialoffice@journal.tts.org

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Read the Journal online: www.transplantjournal.com

Manuscript Formatting

Elements: Each submission must be structured as follows:

1. Title Page
2. Authorship Page
3. Abbreviations Page
4. Abstract (if applicable)
5. Main Body Text
6. Acknowledgments (if applicable)
7. References
8. Tables
9. Figure legend (if applicable)
10. Figures
11. Supplemental digital content (to publish) and/or supplemental content (not to publish)

Please refer to the descriptions of the individual items for more detailed information.

Items 1—7 above must be uploaded as the main body document file type. Do not upload separate files for these items.

TITLE PAGE:

INCLUDE the following elements for every submission:

1. *Title:* This should be descriptive of the work; the title should not be a sentence.
2. *Author listing:* Include the full first name, middle initial(s), and family name of each author, each author's highest degree earned, and their affiliations. This should include the academic department(s) and institution(s) to which the work should be attributed.
3. *Correspondence information:* Full name, physical mailing address and current email address for the corresponding author.
4. *Clinical Trial Notation (if applicable):* provide the name of the trial registry and the registration number/ identifier of the trial.

DO NOT INCLUDE Word counts Keywords
Running titles

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1. List each author's specific contributions to the work; list any potential conflict of interest for each author, or make the declaration of no conflict of interest. Please review ICMJE Guidelines for Authorship at http:// www.icmje.org/recommendations for further guidance. **NOTE:** in accordance with the guidelines of the Committee on Publication Ethics (COPE), any change in authorship or contribution AFTER submission MUST BE approved in writing by ALL authors and submitted to the Editorial Office for final consideration.
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3. *Funding:* Disclosure of any funding received for this work, especially details of funding from any of the following organizations: National Institutes of Health (NIH); Wellcome Trust; and Howard Hughes Medical Institute (HHMI). For more information, please visit http://journals.lww.com/transplantjournal/layouts/ oaks.journals/nih.aspx

ABBREVIATIONS PAGE:

1. Authors are required to introduce all utilized acronyms and initialisms likely to be unfamiliar to the reader. These should be listed alphabetically.
2. Acronyms and initialisms should take the form: **[term]**,[meaning] eg: **DNA**, deoxyribonucleic acid.
3. Terms should not be abbreviated unless they are used more than once in the document.

ABSTRACT:

All abstracts are limited to 250 words. This is included in the overall manuscript word count.

Abstracts for Articles and Short Reports must be structured and labeled as follows:

- *Background* - the problem being addressed in the study.
- *Methods* - how the study was performed.

- *Results* - the salient results.
- *Conclusions* - what the authors conclude from the results.

Abstracts for Overviews may be unstructured.

Abstracts are not required for Letters or Commentaries.

MAIN BODY TEXT:

1. *Introduction:* A statement of the purpose of the work, the problem that stimulated it, and a brief summary of any relevant previously published investigations.
2. *Materials and Methods:* Detailed description of how the results were obtained. Avoid lengthy descriptions of well-known and previously published methods, cite the appropriate reference(s) instead. In-depth methods descriptions may be provided as Supplemental Digital Content and will appear in the online version only.
3. *Results*: Raw or minimally reduced findings using the materials and methods described previously. The results should be concise, avoiding redundant tables and figures illustrating the same data.
4. *Discussion:* Interpretation, contextualization, and commentary on the results. Authors should use this section to argue the significance of their work with minimal restating of findings.

Acknowledgments (if applicable):

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2. References must be made using AMA style. See http:// www.amamanualofstyle.com (note: log in or subscription is required)
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3. References in the main body are designated by superscripts.
4. References must be numbered and listed in the order in which they are cited in the text.
5. Examples for formatting reference in journal style is found here http://edmgr.ovid.com/tpa/accounts/ amaguide_21B3.pdf
6. General guidelines:
   - No more than 6 authors should be listed for a citation. If there are 7 or more authors, only the first 3 should be listed followed by ‘‘et al.’’
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- Only published works and manuscripts that have been accepted for publication should be listed in the References.

7. Manuscripts in preparation, unpublished observa-tions, and personal communications should be referred to in parentheses in the text.

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1. Tables may be included in the main body text docu-ment, but do not upload tables more than once (that is, do not upload as a table file type and include in the main document).
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3. Each table must be provided in an editable text file format.
4. Tables should not be embedded in the text sections, but must follow the References section or appear in a separate Word file.
5. DO NOT upload tables as images.
6. Tables should be numbered in sequence as they are referenced in the main text. Tables should have a concise, informative title and data headings must succinctly describe the information in the column or row.
7. Footnotes to tables must be made below the tables to which they refer, using superscript letters to designate.

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Legends must be supplied for all figures at the end of the main text file or in a separate file.

- Supplied on a separate page
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- Numbered to correspond with the appropriate figure

FIGURES

Each figure should be individually uploaded separately as a figure file. These can be .tif, .eps, or .jpg files types. PDFs and PowerPoint files are NOT acceptable. **Do not embed figures into the main body file.**

- Figures should be uploaded in the highest resolution available
- Your manuscript may be returned to you for correction if the images are of insufficient quality
- Authors are encouraged to incorporate other colors in line drawings, graphs and charts
- Axis and labeling of these figures must be in black
- Histology figures: Figures depicting histology will only be published in color and the cost of publishing these figures is borne by the author
- Monochrome images (such as line graphs) should be prepared at a resolution of 1200 dots per inch (DPI).

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SDC files will be available via links placed at the citation points within the article and are not copyedited by the publisher; they will be presented digitally as submitted.

- If providing SDC figure(s), a figure legend should be included on the figure itself.
- For audio and video files, also include the author name, videographer, participants, length (minutes), and size

(MB)

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Authors may submit additional material accessible to Editors and reviewers to further support their submission. This material is provided to enhance the evaluation of the manuscript. It is uploaded as a Supplemental File type and is not published.

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Manuscript Processing

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Policies

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- Participated in research design

- Participated in the writing of the paper
- Participated in the performance of the research
- Contributed new reagents or analytic tools
- Participated in data analysis

An author may list more than one contribution, and more than one author may have contributed to the same aspect of the work. Please review the International Committee of Medical Journal Editors (ICMJE) Guidelines for Authorship at http://www.icmje.org/recommendations for further guidance.

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- Australian & New Zealand Clinical Trials Registry, found at http://www.anzctr.org.au/
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Reports of randomized clinical trials should follow the recommendations given in the Consolidated Standards of Reported Trials (CONSORT) statement http://www.consort-statement. org. In brief, this statement comprises a checklist and flow diagram to help improve the quality of reports of randomized controlled trials and offers a standard way for researchers to report trials. Include both the checklist and the flow diagram in your submission.

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ANEXO B- PARECER CEP UFCSPA

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: PERFIL DA FUNÇÃO PULMONAR E DA CAPACIDADE FUNCIONAL DE PACIENTES TRANSPLANTADOS PULMONARES INTERVIVOS. **Pesquisador:** Pedro Dal Lago **Área Temática:**

Versão: 2

CAAE: 49596315.8.0000.5345

Instituição Proponente: Universidade Federal de Ciências da Saúde de Porto Alegre

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.374.352

Apresentação do Projeto:

O presente estudo trata-se de um estudo observacional clínico, do tipo transversal e retrospectivo, para avaliação de pacientes submetidos ao transplante intervivos de pulmão. Os dados pré transplantes serão obtidos do prontuário, tendo sido realizados pela equipe do transplante pulmonar, e a avaliação após seis meses da realização pela equipe de pesquisa. Serão analisados pacientes submetidos ao transplante no período de 1999 a 2015 no Complexo Hospitalar Irmandade Santa Casa de Misericórdia de Porto Alegre, serão incluídos no estudo 36 pacientes que estão em acompanhamento médico. Estes pacientes serão avaliados quanto à função pulmonar, capacidade funcional, força muscular respiratória, nível de dispneia e qualidade de vida. Serão comparados e correlacionados os dados coletados pré e pós transplante.

Objetivo da Pesquisa:

OBJETIVO GERAL: Caracterizar o perfil da função pulmonar e da capacidade funcional dos pacientes submetidos ao transplante pulmonar intervivos, no período de 1999a 2015, realizados na Santa Casa de Misericórdia de Porto Alegre.

OBJETIVOS SECUNDÁRIOS: Verificar a função pulmonar após o transplante pulmonar intervivos; Verificar a capacidade funcional do paciente transplantado pulmonar intervivos, pré e pós procedimento; Investigar os efeitos do procedimento de transplante pulmonar intervivos e seu impacto na saúde geral do paciente; Verificar a qualidade de vida após transplante pulmonar; Identificar o nível de atividade física e atividades de vida diária dos pacientes transplantados pulmonares intervivos após procedimento; Avaliar a força muscular respiratória após procedimento de transplante pulmonar; Comparar as respostas das variáveis de função pulmonar, capacidade funcional dos pacientes pré e pós transplante; Identificar nível de dispneia dos pacientes transplantados intervivos, após procedimento.

Avaliação dos Riscos e Benefícios:

Apresentados e, assim, descritos no projeto e TCLE. Como benefícios deste estudo, os participantes serão avaliados gratuitamente por uma equipe especializada e os resultados coletados servirão para compreender o estado de saúde do participante naquele momento. Já os eventuais riscos do presente estudo são mínimos, entretanto, o teste de caminhada pode causar cansaço nas pernas, falta de ar ou aumento da frequência cardíaca, mas será orientado a interromper o teste ou descansar. A manovacuometria também poderá gerar um cansaço transitório. Está garantida a plena assistência ao paciente pelos pesquisadores responsáveis, caso haja necessidade.

Comentários e Considerações sobre a Pesquisa: Pesquisa pertinente, objetivos claros, metodologia descrita adequadamente.

Considerações sobre os Termos de apresentação obrigatória: Apresentados adequadamente o termo de anuência do local de realização da pesquisa, termo de consentimento e assentimento e termo de compromisso de entrega de relatório.

Recomendações:

Conclusões ou Pendências e Lista de Inadequações:

Projeto em condições de realização.

Considerações Finais a critério do CEP:

Período de execução dez/2015-julho/2016

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações	PB_INFORMAÇÕES_BÁSICAS_DO_P	04/11/2015		Aceito

Continuação do Parecer: 1.374.352

Básicas do Projeto	ETO_588782.pdf	16:51:43		Aceito
Declaração de Instituição e Infraestrutura	anuencia.docx	04/11/2015 16:51:12	Fernanda de Andrade	Aceito
Outros	relatorio.docx	25/09/2015 14:40:08	Fernanda de Andrade	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	assentimento.docx	25/09/2015 14:37:08	Fernanda de Andrade	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	tcle.docx	25/09/2015 14:35:38	Fernanda de Andrade	Aceito
Projeto Detalhado / Brochura Investigador	projeto.docx	25/09/2015 14:27:58	Fernanda de Andrade	Aceito
Folha de Rosto	201509221433.pdf	24/09/2015 00:10:28	Fernanda de Andrade	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

PORTO ALEGRE, 17 de Dezembro de 2015

Assinado por:
Julia Fernanda Semmelmann Pereira Lima (Coordenador)

ANEXO C- TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE)

Termo de Consentimento Livre e Esclarecido adequado sob nº466/12

O Sr(a) ou seu protegido está sendo convidado(a) a participar de um estudo que tem por objetivo caracterizar o perfil da função pulmonar e capacidade funcional dos pacientes submetidos ao transplante pulmonar intervivos, no período de 1999 a 2015, realizados na Santa Casa de Misericórdia de Porto Alegre. O título do estudo é "PERFIL DA FUNÇÃO PULMONAR E DA CAPACIDADE FUNCIONAL DE PACIENTES TRANSPLANTADOS PULMONARES INTERVIVOS" e será conduzido com o auxílio da Equipe de Transplantes Pulmonares da Santa Casa de Misericórdia.

A coleta dos dados será realizada na Reabilitação Pulmonar do Pavilhão Pereira Filho, na Santa Casa de Misericórdia de Porto Alegre. A sua participação, ou de seu protegido, na pesquisa iniciará após a leitura, o esclarecimento de possíveis dúvidas e do seu consentimento livre e esclarecido por escrito. A assinatura do Termo de Consentimento Livre e Esclarecido será feita em duas vias, permanecendo uma delas com o participante ou seu responsável. Você será informado sobre os procedimentos e resultados da participação na pesquisa e receberá esclarecimento sobre as dúvidas que possam surgir dela.

1. **Dados Coletados:**

As informações coletadas na pesquisa permanecerão no anonimato. Apenas os pesquisadores terão acesso aos dados de identificação, o que torna seus dados confidenciais. Os dados de identificação somente serão utilizados internamente conforme protocolo da pesquisa e para relatar os resultados a você mesmo.

2. **Assistência durante o estudo:**

Durante toda pesquisa os participantes receberão acompanhamento dos pesquisadores para aplicação de questionários de qualidade de vida e atividade física, para o teste de caminhada de seis minutos e para a manovacuometria. Caso houver necessidade de desistência, você poderá fazê-lo no decorrer da pesquisa. Se precisar interromper qualquer parte do estudo por motivos de dor, desconforto, falta de ar, você estará sob cuidados da equipe de pesquisa e será devidamente orientado.

Fases do Estudo:

ENTREVISTA: nesta etapa coletaremos seus dados de identificação e algumas informações referentes aos períodos pré e pós transplante e seu estado de saúde.

AVALIAÇÃO: A avaliação será realizada apenas em um dia. Nesse dia, você ou seu protegido primeiramente irá responder três questionários. O primeiro,

chamado SF-36, é um questionário sobre a qualidade de vida. Os demais questionários abordam as atividades físicas (IPAQ-curto) e atividades de vida diária (questionário London) para sabermos como estão as suas atividades, ou de seu protegido, na sua cidade. Em um segundo momento do mesmo dia, serão verificados massa, estatura e pressão arterial. Na sequência, será realizado um teste de caminhada em um corredor de 30 metros num tempo de seis minutos, sendo que você ou seu protegido pode interromper/sentar quando necessário. Você ou seu protegido deverá caminhar quanto mais rápido conseguir, sendo medido nesse teste quantas voltas você dará, qual o seu batimento do coração, a pressão e grau de falta de ar ou cansaço.

Por fim, você ou seu protegido vai realizar o teste dos músculos respiratórios que é muito parecido com a espirometria. Será colocado um clip nasal, e serão realizadas três inspirações e posteriormente três expirações em um bocal que é conectado a um aparelho que verifica a força os seus músculos inspiratórios e expiratórios. Você ou seu protegido será incentivado a realizar a máxima força inspiratória e expiratória possível. Serão realizadas 3 tentativas, com intervalo de 1 minuto em cada uma para que você ou seu protegido possa descansar e se recuperar. O tempo estimado das avaliações é de em torno de 1 hora e 50 minutos.

3. **Benefícios e Riscos:**

Como benefícios deste estudo, os participantes serão avaliados gratuitamente por uma equipe especializada e os resultados coletados servirão para compreender o estado de saúde do participante naquele momento.

Já os eventuais riscos do presente estudo são mínimos, entretanto, o teste de caminhada pode causar cansaço nas pernas, falta de ar ou aumento da frequência cardíaca, mas será orientado a interromper o teste ou descansar. A manovacuometria também poderá gerar um cansaço transitório. Está garantida a plena assistência ao paciente pelos pesquisadores responsáveis, caso haja necessidade.

4. **Decisão quanto à participação:**

A participação na pesquisa será voluntária. Concordando ou recusando em participar, não serão obtidas vantagens ou desvantagens no atendimento e tratamento no serviço de saúde no qual os pacientes são atendidos. Ninguém será obrigado a responder a todas as perguntas e realizar todas as avaliações e exercícios, podendo interromper ou cancelá-los a qualquer momento sem nenhum constrangimento. A participação em todos os procedimentos da pesquisa não implicará no pagamento de qualquer taxa.

Necessitando quaisquer esclarecimentos sobre a pesquisa ou querendo cancelar a participação nela, o participante poderá entrar em contato direto com a Fisioterapeuta pesquisadora Fernanda de Andrade ou pelo número do seu telefone celular: (54) 9987-7187.

Eu_____ recebi as informações sobre os objetivos da pesquisa de forma clara e concordo em participar do estudo.

Data:____/____/_____

Nome do participante: _____

Nome do responsável: _____

Contato (telefone): (___)_____

Nome da pesquisadora: Fernanda de Andrade

Nome do pesquisador responsável: Dr. Pedro Dal Lago

Comitê de Ética em Pesquisa da UFCSPA: Rua Sarmento Leite, 245–CEP: 90.050-170 Porto Alegre – Rio Grande do Sul
E-mail: CEP@ufcspa.edu.br
Telefone:(51) 3303-8804

_____	_____	_____
Participante ou Responsável	Pesquisador	Pesquisador Responsável