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ANÁLISE DA SOBREVIDA EM TRANSPLANTE CARDÍACO: EXPERIÊNCIA DE CENTRO ÚNICO BRASILEIRO

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Dissertação apresentada ao Programa de Pós-Graduação *Stricto Sensu* do Instituto de Medicina Integral Prof. Fernando Figueira – IMIP, como requisito parcial à obtenção do título de Mestre em Cuidados Intensivos.

Linha de pesquisa: Estudos clínicos, translacionais, epidemiológicos e prevenção de agravos.

Orientador: Prof. Dr. Cristiano Berardo Carneiro da Cunha

Coorientador: Prof. Dr. Rodrigo Melo Gallindo

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Instituto de Medicina Integral Professor Fernando Figueira – IMIP
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RESUMO

Introdução: As doenças cardiovasculares são a principal causa de mortes no mundo e a sua progressão que leva à disfunção cardíaca, determina a insuficiência cardíaca. O transplante cardíaco continua sendo o tratamento padrão ouro para insuficiência cardíaca avançada, apresentando melhora na curva de sobrevida destes pacientes. **Objetivo:** Determinar a sobrevida e os fatores de risco para mortalidade precoce em nos pacientes adultos receptores de transplante cardíaco em um centro brasileiro. **Métodos:** Este estudo de coorte retrospectivo envolveu 255 pacientes adultos transplantados cardíacos de único centro no Brasil. Os dados foram coletados em prontuários e bancos de dados, com três períodos definidos (2012-2015, 2016-2019 e 2020-2022). A análise estatística utilizou curvas de sobrevivência de Kaplan-Meier, análise de riscos proporcionais de Cox para fatores de risco de mortalidade em 30 dias e testes Log-rank. **Resultados:** No total de 255 pacientes, 75 realizaram o transplante no 1º período, 124 no 2º e 56 no 3º (marcado pela pandemia COVID-19). Os receptores eram maioritariamente do sexo masculino (74,9%), a média de idade foi de 46,6 anos. As principais causas de insuficiência cardíaca foram cardiomiopatia dilatada idiopática (33,9%), cardiomiopatia chagásica (18%) e cardiomiopatia isquêmica (14,3%). A probabilidade de sobrevida global de 68,1% em 1 ano, 58% em 5 anos e 40,8% em 10 anos após o transplante cardíaco. A sobrevivência melhorou significativamente ao longo do tempo de acordo com os períodos analisados. Combinando os períodos mais recentes (2016 a 2022), a sobrevida foi de 73,2% no 1º ano e 63% em 5 anos. Os principais fatores de risco para mortalidade em 30 dias foram: maior tempo de circulação extracorpórea, período inicial dos transplantes (2012 a 2015), maior idade do doador e estado nutricional do doador (sobrepeso ou obesidade). As principais causas de morte em até 30 dias pós-transplante foram infecção e disfunção primária do enxerto. O presente trabalho resultou em 3 publicações: um artigo completo, publicado no *Brazilizan Journal of Cardiovascular Surgery* e dois resumos publicados no *Journal of Heart and Lung Transplantation* e no *European Heart Journal*, ambos apresentados como poster em congressos internacionais. O produto técnico relacionado à pesquisa foi o Simpósio Brasileiro de Transplante Cardíaco 2022, evento que reuniu palestrantes locais e nacionais, reunindo os principais centros de transplante cardíaco do Brasil. **Conclusão:** O transplante cardíaco neste centro apresentou redução significativa da letalidade precoce e as curvas de sobrevida apresentaram melhora nos períodos mais recentes. principal causa de morte foi infecção, seguida pela disfunção primária do enxerto.

Palavras-chave: Transplante cardíaco. Mortalidade. Disfunção primária do enxerto. COVID-19. Análise de sobrevida.

ABSTRACT

Introduction: Cardiovascular diseases are the leading cause of death worldwide, and their progression leading to heart dysfunction determines heart failure. Heart transplantation remains the gold standard treatment for advanced heart failure, improving the survival curve of these patients. **Objective:** To determine survival rates and the risk factors for early mortality in adult heart transplant recipients at a Brazilian center. **Methods:** This retrospective cohort study included 255 adult heart transplant patients from a single center in Brazil. Data were collected from medical records and databases, with three defined periods (2012–2015, 2016–2019, and 2020–2022). Statistical analysis used Kaplan-Meier survival curves, Cox proportional hazards analysis for 30-day mortality risk factors, and Log-rank tests. **Results:** Of the 255 patients, 75 underwent transplant in the 1st period, 124 in the 2nd, and 56 in the 3rd (marked by the COVID-19 pandemic). Most recipients were male (74.9%), with a mean age of 46.6 years. The main causes of heart failure were idiopathic dilated cardiomyopathy (33.9%), Chagas cardiomyopathy (18%), and ischemic cardiomyopathy (14.3%). The overall survival probabilities were 68.1% at 1 year, 58% at 5 years, and 40.8% at 10 years after heart transplantation. Survival improved significantly over time, according to the periods analyzed. Combining the most recent periods (2016–2022), survival was 73.2% at 1 year and 63% at 5 years. The main risk factors for 30-day mortality were longer extracorporeal circulation time, earlier transplant periods (2012–2015), older donor age, and the donor's nutritional status (overweight or obesity). The main causes of death within 30 days post-transplant were infection and primary graft dysfunction. This research resulted in three publications: a full article published in the Brazilian Journal of Cardiovascular Surgery and two abstracts published in the Journal of Heart and Lung Transplantation and the European Heart Journal, both presented as posters at international conferences. The technical product related to this research was the 2022 Brazilian Heart Transplant Symposium, an event that gathered local and national speakers, bringing together the leading heart transplant centers in Brazil. **Conclusion:** Heart transplantation at this center showed a significant reduction in early mortality, and survival curves improved in more recent periods. The leading cause of death was infection, followed by primary graft dysfunction.

Keywords: Heart transplantation, Mortality, Primary graft dysfunction, COVID-19, Survival analysis.

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LISTA DE ABREVIATURAS E SIGLAS

ABTO	Associação Brasileira de Transplante de Órgãos
AVC	Acidente vascular cerebral
BIA	Balão intra-aórtico
BJCVS	*Brazillian Journal of Cardiovascular Surgery* (Revista Brasileira de Cirurgia Cardiovascular)
CEC	Circulação extracorpórea
CEP	Comitê de Ética em Pesquisa
DCV	Doença Cardiovascular
DM	Diabetes Mellitus
DVA	Droga vasoativa
ECG	Eletrocardiograma
ECMO	*Extracorporeal Membrane Oxigenation* (Membrana de Oxigenação Extracorpórea)
FE	Fração de ejeção do ventrículo esquerdo
HAS	Hipertensão arterial sistêmica
IC	Insuficiência Cardíaca
IHTSA	*International Heart Transplant Score Algorithm* (Algoritmo Internacional de Pontuação de Transplante Cardíaco)
IMC	Índice de massa corpórea
IMIP	Instituto de Medicina Integral Prof. Fernando Figueira
IMPACT	*Index for Mortality Prediction After Cardiac Transplantation* (Índice para Predição de Mortalidade Após Transplante Cardíaco)
IRA	Insuficiência renal aguda
IRC	Insuficiência renal crônica
ME	Morte encefálica
MS	Ministério da Saúde
Na	Sódio
NYHA	*New York Heart Association* (Associação do Coração de Nova York)
PCR	Parada cardiorrespiratória
PRA	Painel de reatividade de anticorpos
SAME	Serviço de arquivo médico
SIM	Sistema de Informação de Mortalidade

STROBE	*Strengthening the Reporting of Observational Studies in Epidemiology* (Fortalecimento do Relatório de Estudos Observacionais em Epidemiologia)
SUS	Sistema Único de Saúde
TCE	Traumatismo cranioencefálico
TCLE	Termo de Consentimento Livre e Esclarecido
Tx	Transplante Cardíaco
UTI	Unidade de Terapia Intensiva
VD	Ventrículo Direito
VE	Ventrículo Esquerdo
VO_2 max	Volume de oxigênio máximo consumido

SUMÁRIO

1 INTRODUÇÃO

As Doenças Cardiovasculares (DCV) são a principal causa de mortes no mundo. Estima-se que 17,9 milhões de pessoas morreram de DCV em 2019, representando 32% de todas as mortes. Destas mortes, 85% foram devido a doença cardíaca e acidente vascular cerebral (AVC). Mais de três quartos das mortes por DCV ocorrem em países de baixa e média renda. Das 17 milhões de mortes prematuras (em pessoas com menos de 70 anos) estimadas no mundo devido a doenças não transmissíveis em 2019, 38% foram causadas por doenças cardiovasculares.[1]

Dentre as DCV, a hipertensão arterial sistêmica (HAS), infarto do miocárdio, fibrilação atrial e insuficiência cardíaca (IC) afetam aproximadamente 45,7 milhões de pessoas no Brasil, o que representa 32% da população adulta. As doenças cardíacas resultaram em um custo financeiro de 17,3 bilhões de dólares em 2015 e cerca de 5,5% do total nacional das despesas com assistência à saúde no Brasil. Cerca de 62,9% desse custo recaiu sobre o Sistema Único de Saúde (SUS).[2]

A progressão da doença cardiovascular determina a IC, que resulta no comprometimento estrutural ou funcional do enchimento ventricular ou da ejeção de sangue, manifestada por dispneia e fadiga. O diagnóstico desta condição dá-se baseado em uma história clínica cuidadosa e exame físico minucioso, não havendo um único teste diagnóstico para o diagnóstico de IC, tratando-se, portanto, de um diagnóstico clínico.[3]

A síndrome clínica de IC pode resultar de doenças do pericárdio, miocárdio, endocárdio, válvulas cardíacas ou grandes vasos, mas a maioria dos pacientes com IC têm sintomas devidos à função miocárdica prejudicada do ventrículo esquerdo (VE). Um estudo brasileiro mostrou que as etiologias da IC foram: isquêmica em 29,7%; hipertensiva em 20,8%; valvar em 15%; chagásica em 14,7%; idiopática em 8% e outras em 11,8%.[4]

Atualmente, 5,7 milhões de pessoas nos Estados Unidos da América têm IC. Até 2030, mais de 8 milhões de pessoas terão essa condição, o que representa um aumento de 46% na prevalência. Os dados indicam que a IC é um problema de saúde pública mundial importante. Embora a incidência de IC seja estável, a prevalência vai aumentar devido ao envelhecimento da população e melhorias no tratamento cardiovascular, aumentando a sobrevida. Isso causará novos incrementos nas taxas de hospitalização e, consequentemente, nos custos com a saúde. A mudança para um estilo de vida ocidental nos países em desenvolvimento pode estar contribuindo para uma verdadeira pandemia de IC.[5] Classicamente, a IC é classificada

conforme proposto pela *New York Heart Association* (NYHA), de acordo com os sintomas apresentados no Quadro 1. [6]

Quadro 1. Classificação da Insuficiência Cardíaca pela *New York Heart Association*

Classe	Definição
I	Ausência de sintomas
II	Atividades físicas habituais causam sintomas. Limitação leve
III	Atividades físicas menos intensas que as habituais causam sintomas. Limitação importante, porém, confortável no repouso
IV	Incapacidade para realizar qualquer atividade sem apresentar desconforto. Sintomas no repouso

Fonte: Adaptado de *"The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th Ed. Boston: Little, Brown, 1994".*

A estratificação de pacientes com IC é uma medida simples, baseada em dados de história, e que permite ao profissional de saúde avaliar o momento evolutivo da doença em que o paciente se encontra, avaliar qualidade de vida e prognóstico e estabelecer prioridades e linhas terapêuticas. Esta forma de categorização permite uma compreensão evolutiva da doença e, ainda, serve de base para a identificação de pacientes com indicação de intervenções predominantemente preventivas (estágios A e B), terapêuticas (estágios C) ou seleção de pacientes para procedimentos especializados e cuidados paliativos (estágio D), conforme Quadro 2.[6]

Quadro 2. Estágios da IC, *American College of Cardiology/American Heart Association*

Estágio	Descrição
A	Risco de desenvolver IC. Sem doença estrutural ou sintomas de IC
B	Doença estrutural cardíaca presente. Sem sintomas de IC
C	Doença estrutural cardíaca presente. Sintomas prévios ou atuais de IC
D	IC refratária ao tratamento clínico. Requer intervenção especializada

IC, insuficiência cardíaca.

Fonte: Adaptado de *"Hunt as et al.,8 2009 focused update incorporated into the ACC/AHA 2005 guidelines. J Am Coll Cardiol. 2009;53:e1–90".*

Embora a sobrevida dos pacientes portadores de IC tenha melhorado nos últimos anos, as taxas de mortalidade por IC permanecem próximo a 50% dentro de 5 anos do diagnóstico.[7,8] No estudo *Atherosclerosis Risk in Communities*, a letalidade de 30 dias, 1 ano e 5 anos após hospitalização por IC foram de 10,4, 22,0 e 42,3%, respectivamente.[9] Em outro estudo de coorte populacional, as sobrevidas em 5 anos para os estágios A, B, C e D da IC foram de 97%, 96%, 75% e 20%, respectivamente.[10] A letalidade global nos pacientes após 30 dias do internamento por IC diminuiu de 12,6% para 10,8% de 1993 a 2006; no entanto, isso foi devido a menor mortalidade hospitalar. A letalidade pós-alta aumentou de 4,3% para 6,4% durante o mesmo período.[11] Essas tendências temporais observadas na sobrevida dos pacientes com IC são principalmente restritas aos pacientes com Fração de Ejeção (FE) reduzida e não são vistas naqueles com FE preservada.[12]

Pacientes progridem para uma condição mais grave quando os tratamentos tradicionais medicamentosos otimizados não são mais efetivos, requerendo terapias mais avançadas como suporte circulatório mecânico, transplante cardíaco (Tx) e/ou cuidados paliativos são necessários. Esta condição é chamada insuficiência cardíaca crônica avançada.[13]

Os critérios diagnósticos da IC avançada incluem: sintomas graves de IC (NYHA III ou IV), disfunção cardíaca grave (FE $\leq$ 30%), disfunção isolada do ventrículo direito (VD), disfunções valvares inoperáveis ou anormalidades congênitas.[13]

Apesar dos avanços notáveis no tratamento clínico e de dispositivos no tratamento da IC crônica, aproximadamente 5–7% da população com IC evoluirá para IC avançada.[14] O Tx continua sendo o padrão-ouro para o tratamento da IC avançada na ausência de contraindicações.[15]

Embora ensaios controlados nunca tenham sido realizados, há um consenso de que o transplante adequadamente selecionado (respeitando as indicações e contraindicações das diretrizes) proporciona aumento significativo da sobrevida, capacidade de exercício, qualidade de vida, em comparação com o tratamento convencional, entretanto a percentagem de pacientes que retornam ao trabalho seja menor que a esperada.[15,16]

A complexidade da avaliação do receptor exige uma abordagem de equipe multidisciplinar. A avaliação inicial envolve a história clínica e exames físicos, Eletrocardiograma (ECG) de 12 derivações, monitorização de Holter e ecocardiograma, com avaliação da função cardíaca, além de teste de exercício cardiopulmonar, que mensura o volume de oxigênio máximo consumido (VO_2 max). Além disso, é necessária uma relação de troca respiratória > 1,0 ou um limiar anaeróbico entre 50 e 60% do VO_2 max, para evitar subestimação da capacidade funcional.[17]

Uma avaliação neuropsiquiátrica deve ser realizada para que o candidato possa compreender as dificuldades vivenciadas durante o período de espera, recuperação e período pós-operatório; compreender a lógica dos medicamentos antirrejeição; e entender as regras para viver com um novo coração. Um assistente social experiente deve explicar a necessidade de apoio social e financeiro adequado. Todos os pacientes são orientados parar de fumar, cessar o uso de álcool e de outras drogas recreativas.[17]

Na indicação do Tx, deve-se contemplar a relação risco-benefício individual e, idealmente, populacional. A alocação de órgãos para transplante possui implicações éticas, pois são recursos escassos que devem ser preferencialmente ofertados para aqueles com maior probabilidade de sobrevida no longo prazo. O Quadro 3 descreve as indicações para o Tx, segundo a 3ª Diretriz Brasileira de Transplante Cardíaco, publicada em 2018.[18]

Quadro 3. Indicações de transplante cardíaco

Classe de Recomendação	**Indicação**
I	IC avançada na dependência de drogas inotrópicas e/ou suporte circulatório mecânico
	IC avançada classe funcional III persistente e IV com tratamento otimizado na presença de outros fatores de mau prognóstico
	IC avançada e VO_2 de pico ≤ 12mL/kg/minuto em pacientes em uso de betabloqueadores
	IC avançada e VO_2 de pico ≤ 14 mL/kg/minuto em pacientes intolerantes a betabloqueadores
	Arritmias ventriculares sintomáticas e refratárias ao manejo com fármacos, dispositivos elétricos e procedimentos de ablação
IIa	IC refratária e VO_2 de pico ≤ 50% do previsto em pacientes com < 50 anos e mulheres
	Doença isquêmica com angina refratária sem possibilidade de revascularização
IIb	IC refratária e VO_2 de pico ajustado para massa magra ≤ 19 mL/kg/minuto em pacientes com índice de massa corporal > 30
	IC refratária e equivalente ventilatório de gás carbônico (relação VE/VCO_2) > 35 particularmente se VO_2 de pico ≤ 14 mL/kg/minuto e/ou teste cardiopulmonar submáximo (RER < 1,05)
III	Disfunção sistólica isolada
	Prognóstico adverso estimado apenas por escores prognósticos ou VO_2 de pico isoladamente
	IC classe funcional NYHA III-IV sem otimização terapêutica

IC: insuficiência cardíaca; VO_2: consumo de oxigênio; VE/VCO_2: equivalente ventilatório de gás carbônico; RER: coeficiente respiratório: NYHA: *New York Heart Association.*

Fonte: adaptado de "3ª Diretriz Brasileira de transplante cardíaco. Arq Bras Cardiol. 2018; 111(2):230-289."

O primeiro Tx entre seres humanos foi realizado em dezembro de 1967, na África do Sul, por Christiaan Barnard no Groote Schuur Hospital. O paciente sobreviveu por 18 dias e faleceu em decorrência de infecção.[19] Houve grande entusiasmo na época; devido às complicações como rejeição e infecção, a maioria das equipes interrompeu temporariamente seus programas de transplante.[20]

No Brasil, o primeiro Tx foi realizado no dia 26 de maio de 1968 e o paciente faleceu 28 dias após o procedimento, devido rejeição ao enxerto. Após os 3 primeiros casos realizados pela equipe chefiada pelos Drs. Zerbini e Décourt, entre 1968 e 1969, houve um lapso de tempo de 17 anos e, a partir de 1984, teve início o programa de transplantes em vários centros. Nos anos 80, com a introdução da ciclosporina, houve uma retomada dos programas de transplante, com o crescimento de procedimentos e número de centros envolvidos.[20]

A superioridade da sobrevida do transplante cardíaco em relação aos pacientes com IC avançada é evidente quando comparado ao tratamento clínico e assistência circulatória. Em alguns estudos realizados nos Estados Unidos, a mortalidade em 30 dias é entre 5% a 10% geralmente causado por falência do enxerto, disfunção orgânica múltipla e infecção, e a sobrevida em 1 ano de aproximadamente 85% e existe uma diminuição na sobrevivência de aproximadamente 3,4% por ano pós-transplante.[17]

Atualmente, o Tx ortotópico é o tratamento padrão-ouro para pacientes com insuficiência cardíaca congestiva refratária de doenças cardíacas em estágio terminal. Muitas técnicas de transplante de coração foram descritas. A técnica biatrial, refinada e popularizada por Lower e Shumway em 1960, foi utilizada para a realização do primeiro Tx e foi amplamente utilizada por sua relativa simplicidade.[21]

No entanto, a técnica biatrial, quando comparada com a técnica bicaval, apresenta várias desvantagens, incluindo grandes átrios direito e esquerdo (doador e receptor combinado), com geometria distorcida que pode levar a maior incidência de incompetência das valvas mitral e tricúspide, distúrbios do ritmo e tendência de formação de trombo e aneurisma septal. Devido a essas desvantagens, a técnica biatrial foi substituída principalmente pela técnica bicaval, que tem sido a técnica preferida na maioria dos centros de transplante.[22,23]

A técnica de Tx heterotópico, descrita por Barnard em 1975, foi desenvolvida para tratar pacientes com hipertensão pulmonar irreversível, e como forma de suporte caso o coração doador falhe por disfunção primária do enxerto ou rejeição grave. No entanto, ainda é uma técnica útil como assistência biológica do ventrículo esquerdo (um novo método de dois estágios) para o tratamento da insuficiência cardíaca em algumas circunstâncias específicas.[24,25]

As técnicas de Tx em pacientes com cardiopatias congênitas em estágio terminal são complexas e dependem das anormalidades anatômicas. São desafiadoras, particularmente

naqueles que tiveram cirurgia prévia de reparo ou paliação. Em pacientes com *situs inversus*, onde o átrio "esquerdo" está na linha média ou desviado para a direita e o átrio "direito" está à esquerda, a técnica cirúrgica se modifica: as veias pulmonares esquerdas do coração do doador são suturadas, o átrio esquerdo é aberto entre as veias pulmonares direitas e, em seguida, anastomosado ao átrio esquerdo do receptor.[21]

De acordo com o registo da Associação Brasileira de Transplante de Órgãos (ABTO), no Brasil, de 2011 a 2021, foram realizados 3.435 transplantes de coração. A partir de 2014 o Brasil mantém um volume cirúrgico acima de 300 transplantes de coração por ano, sendo o recorde em 2017 quando foram realizados 380 procedimentos. Devido a pandemia da COVID-19 houve uma queda expressiva no número de transplantes em 2020 e 2021, sendo realizados respectivamente 307 e 332 transplantes cardíacos no Brasil.[26]

Pernambuco, a partir de 2012, com o início do serviço de Tx do IMIP, apresentou um incremento importante na quantidade de transplantes por ano, sendo destaque no cenário nacional a partir de 2015 desde quando se mantém entre 2º e 3º estado que mais realiza transplante cardíaco em números absolutos, atrás de São Paulo e alternando 2º lugar com Minas Gerais.[26–35]

2 MODELO TEÓRICO

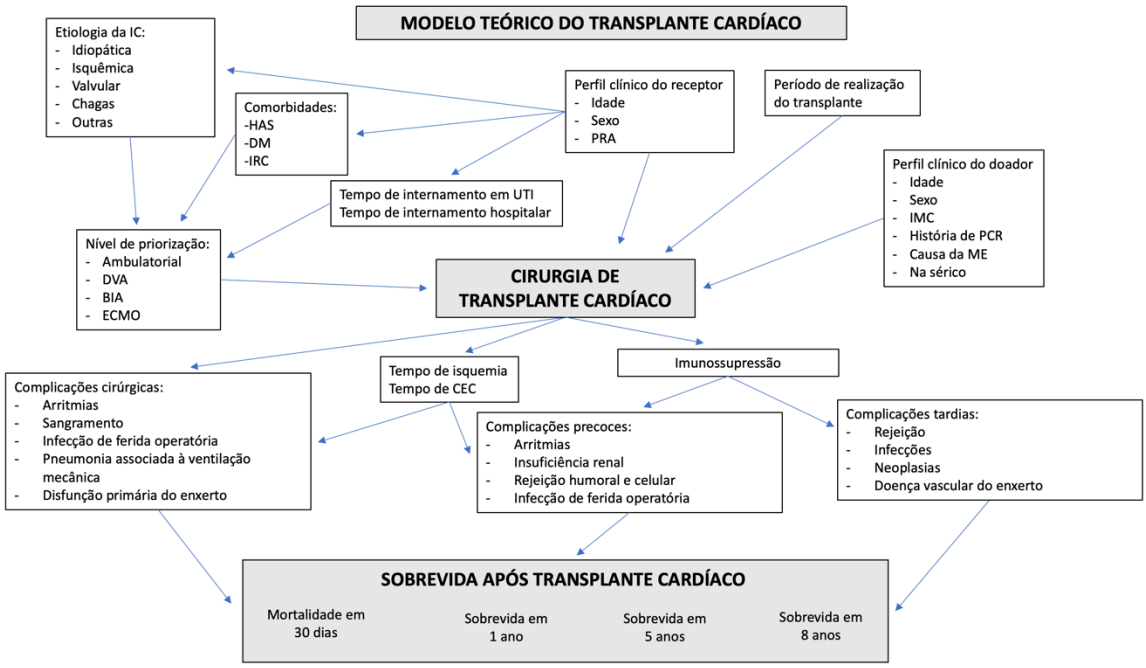


Figura 1: Modelo teórico. BIA: Balão intra-aórtico; DM: Diabetes Mellitus; DVA: Droga vasoativa; ECMO: *Extracorporeal membrane oxigenation;* HAS: Hipertensão arterial sistêmica; IC: Insuficiência cardíaca; IMC: índice de massa corpórea; IRC: Insuficiência renal crônica; ME: Morte encefálica; Na: Sódio; PCR parada cardiorrespiratória; PRA: Painel de reatividade de anticorpos; UTI: Unidade de terapia intensiva.

Fonte: Do autor

3 OBJETIVOS

3.1 Objetivo geral

Determinar a sobrevida global de pacientes submetidos ao transplante cardíaco e identificar os fatores de risco para óbito em até 30 dias pós transplante.

3.2 Objetivos específicos

Descrever e comparar as características sociodemográficas e clínicas dos doadores de coração e dos pacientes submetidos a Tx no IMIP entre os sobreviventes e os que foram a óbito;

Descrever e comparar as variáveis referentes ao procedimento de transplante incluindo os tempos cirúrgicos de isquemia do órgão e de circulação extracorpórea (CEC) entre os sobreviventes e os que foram a óbito;

Determinar a letalidade e identificar os fatores de risco para o óbito em até 30 dias após o transplante cardíaco.

Estabelecer a distribuição das causas dos óbitos nessa população de acordo com o tempo de seguimento após o Tx;

Determinar a probabilidade de sobrevida global e comparar os subgrupos de acordo com diferentes fatores.

4 MÉTODOS

4.1 Tipo de estudo

O estudo é uma coorte retrospectiva.

4.2 Local do estudo

O estudo foi realizado em Recife/PE, no Instituto de Medicina Integral Prof. Fernando Figueira (IMIP), importante centro de referência em transplante cardíaco na região nordeste do Brasil.

4.3 Período do estudo

O estudo foi realizado no período de setembro de 2021 a outubro de 2023, envolvendo os pacientes que foram transplantados no IMIP de julho de 2012 a dezembro de 2022.

4.4 População do estudo

Todos os pacientes adultos que se submeteram a Tx no IMIP durante os anos de 2012 a 2022.

4.5 Critérios e procedimentos para seleção dos participantes

4.5.1 Critérios de inclusão

Foram incluídos os pacientes submetidos a Tx no IMIP que tinham 18 anos de idade ou mais na época do Tx.

4.5.2 Critérios de exclusão

- Pacientes submetidos a re-transplante cardíaco;

- Pacientes que não utilizaram a técnica ortotópica bicaval padrão (paciente *situs inversus*);

- Pacientes com indicação de transplante cardíaco devido cardiopatia congênita.

4.5.3 Procedimentos para captação e acompanhamento dos participantes

A lista com a identificação do número do prontuário dos pacientes submetidos a Tx no IMIP no período do estudo foi feita a partir do banco de dados do serviço de Tx do IMIP e os prontuários foram solicitados ao Serviço de Arquivo Médico (SAME) do IMIP.

Os dados secundários foram complementados a partir de bancos de dados existentes no Departamento de Cardiologia e Cirurgia Cardiovascular do IMIP e do Serviço de Transplante Cardíaco do IMIP, das fichas de perfusão cirúrgicas e do Sistema Nacional de Transplantes.

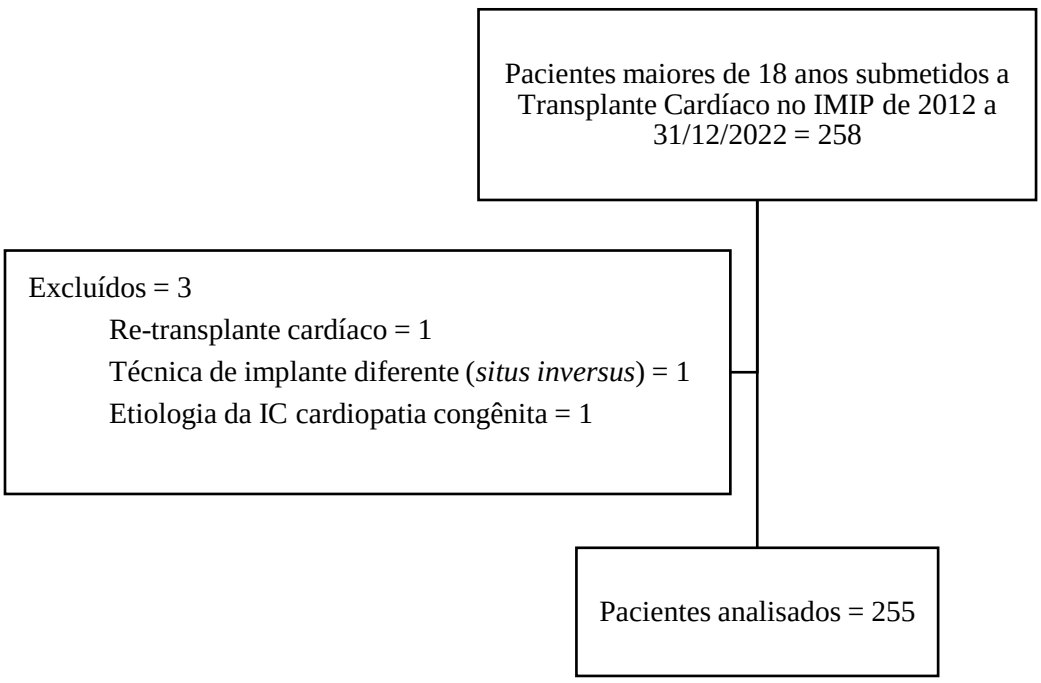
Foi utilizada uma lista de checagem (Apêndice 1) para verificar os critérios de elegibilidade e inclusão no estudo.

No caso de não constar nas bases de dados locais, a data do óbito foi obtida utilizando-se o Sistema de Informação sobre Mortalidade.

Os dados foram coletados pelos pesquisadores preenchendo o formulário específico elaborado para esta pesquisa (Apêndice 4).

4.6 Fluxograma para captação e acompanhamento dos participantes

Figura 2. Fluxograma de captação dos participantes, de acordo com o *guideline Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE)[36].



Fonte: Do autor.

4.7 Variáveis de análise

4.7.1 Variáveis independentes (preditoras)

Receptor: idade, sexo, altura, peso, índice de massa corpórea, comorbidades (HAS, Diabetes Mellitus (DM), Insuficiência Renal Aguda (IRA), Insuficiência Renal Crônica (IRC) e tabagismo), nível de priorização, classificação sanguínea ABO, Painel de Reatividade de Anticorpos (PRA);

Cirurgia: Tempo de isquemia, tempo de isquemia longo, tempo de CEC;

Doador: idade, sexo, grupo sanguíneo ABO, peso, altura, IMC, causa da morte encefálica (ME), tempo de internamento, história de parada cardiorrespiratória (PCR), uso de droga vasoativa (DVA), Sódio (Na) sérico;

4.7.2 Variáveis dependentes (desfechos)

Óbito: Variável categórica (sim ou não);

Óbito em 30 dias: Variável categórica (sim ou não);

4.8 Definição e operacionalização dos termos, critérios e variáveis

Idade doador: Variável discreta (anos);

Idade receptor: Variável discreta (anos na data do transplante);

Sexo doador: Variável categórica (masculino e feminino);

Sexo receptor: Variável categórica (masculino e feminino);

Altura doador: Variável contínua (metros);

Altura receptor: Variável contínua (metros);

IMC doador: Variável contínua (kg/m2);

IMC receptor: Variável contínua (kg/m2);

Peso doador: Variável contínua (kg);

Peso receptor: Variável contínua (kg);

HAS: Variável categórica (Sim ou Não) – pressão arterial sistólica ≥ 140mmHg ou PAD ≥ 90mmHg. Definido como “Sim” se estiver relatado em prontuário médico.

DM: Variável categórica (Sim ou Não) – Definido diagnóstico segundo os critérios da Sociedade Brasileira de Diabetes. Classificado como “Sim” se estiver relatado em prontuário médico.

Tabagismo: Categóricas (Sim ou Não) – Definido como tabagismo ativo ou histórico relatado em prontuário médico.

Priorização: variável categórica (Sim ou Não) – Paciente em lista para transplante cardíaco em internação hospitalar e uso de DVA ou assistência circulatória mecânica, em uso de balão intra-aórtico (BIA) ou membrana de oxigenação extracorpórea (ECMO). Classificado como "Sim" se estiver relatado no Sistema Nacional de Transplantes.

Assistência circulatória mecânica: variável categórica (Sim ou Não) – Paciente em lista para transplante em priorização e uso de qualquer tipo de assistência circulatória mecânica (BIA ou ECMO). Classificado como "Sim" se estiver relatado no Sistema Nacional de Transplantes.

Tempo de isquemia: variável discreta (minutos), que compreende o tempo entre o pinçamento da aorta na captação do órgão e do restabelecimento do fluxo sanguíneo coronariano no implante do coração.

ABO receptor: categórica nominal (A, B, O, AB), corresponde à classificação sanguínea;

ABO doador: categórica nominal (A, B, O, AB);

Tempo de isquemia longo: variável categórica (Sim > 240min, Não ≤ 240min)

Tempo de CEC: variável discreta (minutos), que compreende o tempo utilizado em CEC durante a realização da cirurgia;

Causa da ME: categórica nominal – Traumatismo cranioencefálico (TCE), AVC e outras;

Tempo de internamento doador: discreta (dias), compreende o tempo em dias desde o internamento no hospital até a cirurgia de captação de múltiplos órgãos;

Óbito: categóricas (sim ou não);

Períodos do estudo: 1º de 2012 a 2015 experiência inicial; 2º de 2016 a 2019 após mudança de protocolo de imunossupressão; 3º de 2020 a 2022 pandemia de COVID-19;

Data final do seguimento: categórica ordinal (dia/mês/ano), data do evento óbito ou data limite do acompanhamento da coorte no caso de não evento ou perda de acompanhamento (censura);

Dias de seguimento: Discreta (dias), diferença entre a data do transplante e a data final do seguimento;

Tempo de sobrevida meses: Variável contínua (meses) – Definido pela variável "Dias de seguimento" dividido por 30 dias.

4.9 Procedimentos, testes, técnicas e exames

Os pacientes foram submetidos a cirurgia de transplante cardíaco ortotópico bicaval, utilizando as mesmas técnicas em todo período do estudo.

As captações dos órgãos foram realizadas após a autorização familiar em doadores com diagnóstico de ME, através de esternotomia mediana. Para a coleta do coração, a proteção miocárdica utilizada foi a solução cristaloide gelada composta por histidina-triptofano-cetoglutarato – Custodiol® - dose de 20ml/kg, infundida entre 8 e 10 minutos, na raiz da aorta após o clampeamento da aorta ascendente;

Após a retirada, os órgãos foram embalados em 3 sacos plásticos estéreis, acondicionados em caixa térmica e transportados até o IMIP, onde foram realizadas as cirurgias de implante nos pacientes receptores.

A lista de transplante cardíaco no Sistema Nacional de Transplantes determina a ordem em que os pacientes serão transplantados e se baseia na data em que o paciente foi listado, na compatibilidade da tipagem sanguínea e nos níveis de priorização em que se encontra. Existem para transplante de coração os pacientes que aguardam o órgão de forma ambulatorial e aqueles em ambiente hospitalar apresentam 2 níveis de priorização: os pacientes em uso de drogas vasoativas e os pacientes em uso de assistência circulatória mecânica, sendo estes últimos de maior prioridade.

Os implantes dos corações doados foram realizados através de esternotomia mediana, pela técnica ortotópica bicaval, com utilização de CEC.

Após o término das cirurgias, os pacientes foram encaminhados ao pós-operatório na Unidade de Terapia Intensiva (UTI) de Transplantes do IMIP. Quando em condições de alta da UTI foram para uma das Enfermarias de Cardiologia ou da Unidade Geral de Transplantes do IMIP.

A terapia de imunossupressão para Tx no IMIP consistiu na terapia tríplice: corticoide, inibidor da calcineurina e antiproliferativo. O protocolo de corticoide precoce utilizado até meados de 2015 no IMIP consistiu em metilprednisolona 10mg/kg via endovenosa durante a cirurgia (5mg/kg na indução anestésica e 5mg/kg após a reperfusão do órgão), nos 3 primeiros dias de pós-operatório também 10mg/kg, seguido por um desmame de diário de 100mg até a dose de 100mg/dia. A partir dessa dose, o corticoide venoso era modificado para via oral com prednisona 1mg/kg/dia, o desmame gradual até descontinuação após a biópsia do 6º mês pós-transplante nos pacientes com baixo risco de rejeição (transplante não-duplo, pacientes não-sensibilizados e sem história de rejeição prévia). Os demais imunossupressores: ciclosporina (inibidor de calcineurina) e micofenolato (antiproliferativo), eram iniciados assim que a via oral estivesse disponível, habitualmente no 1º dia pós-operatório após a extubação.

A partir de meados de 2015, o protocolo do corticoide venoso foi baseado à época no protocolo da Cleveland Clinic, que consistia na mesma dose inicial de metilprednisolona 10mg/kg durante a cirurgia, porém no 1º dia pós-operatório a manutenção era realizada com

metilprednisolona 125mg a cada 8h, seguido de 20mg de prednisona a partir do 2º dia até 3 meses de pós-operatório, com redução para descontinuação no 6º mês, nos pacientes com baixo risco de rejeição. Neste mesmo período, houve uma atualização também para os outros imunossupressores orais, sendo a ciclosporina substituída pelo tacrolimus, devido este ter um menor tempo para receber o resultado da dosagem sanguínea, permitindo um melhor ajuste da imunossupressão.

4.10 Coleta de dados

Foram levantados todos os pacientes submetidos a transplante de coração no IMIP, no período de julho de 2012 até dezembro de 2022. Em seguida, os prontuários foram resgatados junto ao SAME, onde foram verificados os dados para preenchimento do Instrumento de Coleta.

Os dados foram coletados pelos pesquisadores integrantes do estudo, utilizando formulários padronizados (Apêndice 3), pré-codificados para entrada em computador.

Esses formulários foram devidamente armazenados em pastas de arquivo específicas, antes e depois da digitação e análise, sob responsabilidade do próprio pesquisador.

4.11 Processamento e análise dos dados

4.11.1 Processamento dos dados

Os formulários preenchidos foram revisados rigorosamente pelo pesquisador para a checagem das informações coletadas com informações constantes em prontuários. Os dados foram digitados em planilha eletrônica no software Microsoft Excel.

O tempo de sobrevida foi calculado em dias a partir da data do transplante até a data do óbito ou até a censura, sendo considerada a data da última consulta para os pacientes com perda de acompanhamento.

4.11.2 Análise dos dados

A partir da planilha completa no Microsoft Excel, os dados foram avaliados estatisticamente através do Software STATA versão 18.0 (Stata Corp).

Os dados categóricos foram apresentados através de frequências absolutas e relativas. Os dados contínuos foram resumidos através das medidas de tendência central e de dispersão

Um modelo univariado e multivariado de risco proporcional de Cox foi utilizado para estimar o HR e identificar os fatores preditores para ocorrência de óbito em 30 dias. Foram

incluídas no modelo univariado as variáveis que apresentaram um valor de p <0,30.

A probabilidade de sobrevida global foi estimada pelo método de Kaplan-Meier, considerando o número de dias a partir da data do transplante renal até a data do óbito e como dia de censura a data do último acompanhamento do estudo. As curvasb de SG dos pacientes em diferentes periódos foram comparadas utilizando o teste Log rank.

4.12 Aspectos éticos

A pesquisa obedeceu às normas da Declaração de Helsinki, foi submetida ao Comitê de Ética em Pesquisa da instituição e aprovada pelo número CAAE: 40888620.4.0000.5201.

Os pacientes foram abordados ambulatorialmente em consultório no IMIP para participar da pesquisa e assinar o Termo de Consentimento Livre e Esclarecido (TCLE);

Foi solicitada dispensa do TCLE (Apêndice 3) em alguns casos, pois houve pacientes que perderam de acompanhamento no IMIP ou que evoluíram para óbito.

Os pesquisadores se comprometeram em manter o sigilo e confidencialidade dos participantes do estudo.

Os pesquisadores negam a existência e conflitos de interesse no estudo.

5 RESULTADOS

Artigo 1

Trabalho publicado como artigo original pela revista ***Brazillian Journal of Cardiovascular Surgery*, Fator de Impacto – 1.1 (2023), Qualis CAPES A4**, com a carta de aceite e as instruções aos autores da revista disponíveis respectivamente nos Anexos B e C.

1. Ferraz DLM, Cunha CBCD, Figueira FAMDS, Silva ITC, Monteiro VS, Carneiro RMD, Castro BG, Requião MB, Oliveira VF, Silva PJXD, Tchaick RM, Furtado AFP, Silva MFOD Filha, Souza RCF, Mello MJG, Gallindo RM. Survival Analysis in Adult Heart Transplantation: Experience from a Brazilian Single Center. Braz J Cardiovasc Surg. 2024 Sep 6;39(5):e20230394. doi: 10.21470/1678-9741-2023-0394. PMID: 39241193; PMCID: PMC11379139.

Artigo 2

Trabalho aceito e apresentado como poster no 44º congresso anual da *International Society for Heart and Lung Transplantation* em Praga, República Tcheca e seu resumo publicado na revista ***Journal of Heart and Lung Transplantation*, Fator de Impacto – 6.4 (2023), Qualis CAPES A1,** com a carta de aceite para apresentação disponível no Anexo D.

2. Ferraz DL, Monteiro V, Cunha C, Figueira F, Silva I, Carneiro R, et al. Heart Transplantation Learning Curve at a High-Volume Center in Northeast Brazil. The Journal of Heart and Lung Transplantation. 2024 Apr 1;43(4):S562–3.

Artigo 3

Trabalho aceito e apresentado como poster no congresso anual da *European Society of Cardiology (ESC Congress 2024)* em Londres, Inglaterra e seu resumo publicado na revista ***European Heart Journal*, Fator de Impacto – 37.6 (2023), Qualis CAPES A1.**

3. V Monteiro, D Ferraz, C Cunha, F Figueira, I Silva, R Tchaick, B Castro, R Carneiro, M Oliveira Filha, A Lapa, M Lira, P Xavier, V Borba, J Freitas Filho, C Costa, Influence of donor and harvesting protocol on 30 day mortality after heart transplantation, *European Heart Journal*, Volume 45, Issue Supplement_1, October 2024, ehae666.2507, https://doi.org/10.1093/eurheartj/ehae666.2507

Produto Técnico

O produto técnico desta pesquisa foi a criação do evento **Simpósio Brasileiro de Transplante Cardíaco 2022**, realizado em Recife-PE nos dias 8 e 9 de julho de 2022, no Hotel Beach Class Convention By HOM. Houve aulas e discussões multidisciplinares com palestrantes locais e nacionais. Existe um relatório específico deste produto técnico com os detalhes do projeto e de sua execução.

O Simpósio Brasileiro de Transplante Cardíaco foi realizado em mais duas edições: 2023 em Recife-PE e 2024 em Brasília-DF.

Artigo 1

ORIGINAL ARTICLE

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Survival Analysis in Adult Heart Transplantation: Experience from a Brazilian Single Center

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This study was carried out at the Cardiology, Instituto de Medicina Integral Professor Fernando Figueira (IMIP), Recife, Pernambuco, Brazil.

ABSTRACT

Introduction: Heart transplantation is the gold standard for advanced heart failure treatment. This study examines the survival rates and risk factors for early mortality in adult heart transplant recipients at a Brazilian center.

Methods: This retrospective cohort study involved 255 adult heart transplant patients from a single center in Brazil. Data were collected from medical records and databases including three defined periods (2012-2015, 2016-2019, and 2020-2022). Statistical analysis employed Kaplan-Meier survival curves, Cox proportional hazards analysis for 30-day mortality risk factors, and Log-rank tests.

Results: The recipients were mostly male (74.9%), and the mean age was 46.6 years. Main causes of heart failure were idiopathic dilated cardiomyopathy (33.9%), Chagas cardiomyopathy (18%), and ischemic cardiomyopathy (14.3%). The study revealed an overall survival of 68.1% at one year, 58% at five years, and 40.8% at 10 years after heart transplantation. Survival improved significantly over time, combining the most recent periods (2016 to 2022) it was 73.2% in the first year and 63% in five years. The main risk factors for 30-day mortality were longer time on cardiopulmonary bypass, the initial period of transplants (2012 to 2015), older age of the donor, and nutritional status of the donor (overweight or obese). The main causes of death within 30 days post-transplant were infection and primary graft dysfunction.

Conclusion: The survival analysis by period demonstrated that the increased surgical volume, coupled with the team's experience and modifications to the immunosuppression protocol, contributed to the improved early and mid-term outcomes.

Keywords: Survival Rate. Chagas Cardiomyopathy. Overweight. Dilated Cardiomyopathy. Cardiopulmonar Bypass. Caude of Death. Heart Transplantation. Risk Factors.

Abbreviations, Acronyms & Symbols

BD	= Brain death	ICU	= Intensive care unit
BMI	= Body mass index	IQR	= Interquartile range
CI	= Confidence interval	MCS	= Mechanical circulatory support
COVID-19	= Coronavirus disease 2019	Na	= Serum sodium
CPB	= Cardiopulmonary bypass	PRA	= Panel reactive antibody
CPR	= Cardiopulmonary resuscitation	SARS-CoV-2	= Severe acute respiratory syndrome coronavirus 2
HF	= Heart failure	SD	= Standard deviation
HR	= Hazard ratio	TBI	= Traumatic brain injury
HTx	= Heart transplantation		

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INTRODUCTION

The progression of cardiovascular disease leads to heart failure (HF), resulting in structural or functional impairment of ventricular filling or blood ejection[1]. Advanced chronic HF is defined when traditional treatments are no longer effective. Heart transplantation (HTx) remains the gold standard for the treatment of advanced HF in the absence of contraindications[2,3].

The first human heart transplant was performed in December 1967 in South Africa by Christiaan Barnard at Groote Schuur Hospital[4]. There was great enthusiasm at the time; however, due to complications such as rejection and infection, most teams interrupted their transplant programs. In Brazil, after the first three cases carried out by the team led by Drs. Zerbini and Décourt between 1968 and 1969, there was a lapse of 17 years, and from 1984, several centers started their heart transplant programs[5].

According to the registry of the Associação Brasileira de Transplante de Órgãos, a total of 6,108 heart transplants were performed in Brazil until December 2022. Since 2014, the country consistently maintained a surgical volume exceeding 300 heart transplants per year, reaching a peak in 2017 with 380 procedures. However, the coronavirus disease 2019 (COVID-19) pandemic led to a noteworthy decline in transplants in 2020, with only 308 heart transplants performed in Brazil[6].

By analyzing survival curves, the most critical post-transplant periods can be defined in the short, medium, and long terms. Understanding the distribution of causes of death over time can optimize survival, and the identification of risk factors for early death is essential to improve patient care and outcomes in HTx. The objectives of this study are to determine the survival rate of patients undergoing HTx in different periods of the center's experience and to identify the risk factors for early death.

METHODS

Patients

This study is a retrospective cohort; 258 consecutive adult patients who underwent HTx from 2012 to 12/31/2022 at a single center in Brazil were included. Three patients were excluded: one who underwent heart re-transplantation, one due to the etiology of complex congenital heart disease, and one due to a surgical technique other than standard bicaval orthotopic surgery (*situs inversus* patient). The study followed the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (or STROBE) guideline[7]. The research followed the standards of the Declaration of Helsinki, was submitted to the institution's Research Ethics Committee, and was approved by CAAE number 40888620.4.0000.5201.

The patients underwent bicaval orthotopic heart transplant surgery, using the same techniques throughout the study period. Organ harvesting was carried out after family authorization in donors diagnosed with brain death (BD), through median sternotomy. To collect the heart, the myocardial protection used was the ice-cold crystalloid solution histidine-tryptophan-ketoglutarate at a dose of 20 ml/kg, infused between eight and 10 minutes, into the aortic root after clamping the ascending aorta. After removal, the organs were packed in three sterile plastic bags, placed in a thermal box, and transported to the transplant center, where implant surgeries were performed on recipient patients. The harvesting surgery was performed locally, in hospitals in the same city as the transplant center, or regionally, in cities up to 846 km away, using land and air transport.

Implant surgeries were performed through median sternotomy, using the bicaval orthotopic technique, and cardiopulmonary bypass (CPB). The patients were sent to the immediate postoperative period in the intensive care unit (ICU) and then sent to the ward when in clinical condition until hospital discharge.

Immunosuppression

Immunosuppression for HTx consisted of triple therapy: corticosteroids, calcineurin inhibitors, and antiproliferatives. The early corticosteroid protocol used until mid-2015 was methylprednisolone (10 mg/kg) intravenously during surgery (5 mg/kg during anesthetic induction and 5 mg/kg after organ reperfusion), and in the first three postoperative days, 10 mg/kg of methylprednisolone, followed by weaning from 100 mg daily to a dose of 100 mg/day. From this dose onwards, the intravenous corticosteroid was changed to oral with prednisone 1 mg/kg/day, gradually weaning until discontinuation after the biopsy in the sixth month post-transplant in patients with a low risk of rejection (non-double transplant, non-sensitized patients and without a history of previous rejection). In highly sensitized patients, induction therapy with thymoglobulin was performed. The other immunosuppressants, cyclosporine (calcineurin inhibitor) and mycophenolate (antiproliferative), were started as soon as the oral route was available, usually on the first postoperative day after extubation.

As of mid-2015, the intravenous corticosteroid protocol was based on the Cleveland Clinic protocol, which consisted of the same initial dose of methylprednisolone (10 mg/kg) during surgery. On the first postoperative day, maintenance was performed with methylprednisolone (125 mg) every eight hours, followed by 20 mg of prednisone on the second day for up to three months, reduced to discontinuation on the sixth month, in patients with a low risk of rejection. During the same period, there was also an update for other oral immunosuppressants, with cyclosporine being replaced by tacrolimus, due to the latter having a faster blood dosage result, allowing better adjustment of immunosuppression.

Data Collection

Recipient data were obtained from medical records and the database of cardiology, cardiovascular surgery, and heart transplant services. Donor data was obtained through the National Transplant System.

The variables collected were recipient and donor age, sex, weight, and height; recipient comorbidities (diabetes and hypertension), panel reactive antibody, priority status, use of mechanical circulatory support before transplantation, graft ischemic time, city of retrieval operation; date of transplant, final date (death or censored), death, cause of death; donor history of cardiorespiratory resuscitation, use of vasoactive drugs, use of antibiotics, serum sodium, and hospital length of stay. The calculated variables were recipient and donor body mass index.

Three periods of transplantation were defined: period 1 (2012 to 2015), related to the initial experience; period 2 (2016 to 2019), after changing the early corticosteroid protocol; and period 3 (2020 to 2022), which occurred during the COVID-19 pandemic.

Death within 30 days after transplantation was defined as early mortality. Death occurring after 30 days of HTx was considered as late mortality.

Statistical Analysis

Survival time was calculated from the date of transplantation to the date of death or until censoring, considering the date of the last consultation for patients lost to follow-up. Missing data were excluded depending on the variable under analysis.
To identify risk factors for 30-day mortality, the population was categorized into two groups, survivors and non-survivors at 30 days, and the analysis was conducted using Cox proportional hazards modeling.
The Kaplan-Meier method was used to obtain survival curves. Based on these analyses, comparisons were made between groups: HTx periods, donors and recipients of the opposite sex, transplantation with ABO-heterogeneous group compatible, and age groups (< 60 and ≥ 60 years old). The differences were assessed using the Log-rank test. A value of $P<0.05$ was considered statistically significant. All statistical analyses were performed using Stata software, version 18.0 (Stata Corp).

RESULTS

Study Population

In this cohort, data from 255 adult patients who underwent HTx between 2012 and 2022 were analyzed. The mean age of the recipients was 46.6 years, with 74.9% being male. The clinical characteristics of the studied population are shown in Table 1. Most patients undergoing HTx had blood group O (48.2%), followed by groups A (38.0%), B (8.2%), and AB (5.5%). Donors had the following proportions: O (63.1%), A (31.4%), B (5.1%), and AB (0.4%). There was a non-identical ABO (only compatible) group-matched transplant rate of 20% (51 patients).
The etiologies of HF that led to the indication for HTx are listed in Figure 1. Idiopathic dilated cardiomyopathy was the main cause of indication for HTx, followed by chagasic and ischemic cardiomyopathy. Causes classified as "other" in Figure 1 included storage diseases such as amyloidosis or hemochromatosis, arrhythmogenic right ventricular dysplasia, leptospirosis, tachycardiomyopathy, and hyperthyroidism. No data were found in the medical records regarding the etiology of HF in 10 patients, who are not included in this analysis.
The general characteristics of heart donors are described in Table 2. The main cause of BD in donors was traumatic brain injury (TBI), followed by stroke as seen in Figure 2. Data classified as "other" include cerebral hypoxia, intracranial hypertension, exogenous intoxication, meningoencephalitis, brain abscess, and brain tumor.

Early Results

In total, 34 patients (13.3%) died within 30 days postoperatively. There was a significant reduction in 30-day lethality in the analysis by periods: period 1 (2012 to 2015) 22.7%, period 2 (2016 to 2019) 10.4%, and period 3 (2020 to 2022) 7.14%, with $P=0.011$. When compared to period 1, a lower risk of early death was founded for both period 2 (hazard ratio [HR] 0.43; 95% confidence interval [CI] 0.19-0.95) and period 3 (HR 0.29; 95% CI 0.49-0.74).

The distribution of heart transplants performed over the years and their relationship with 30-day mortality, which highlights the service's learning curve, is shown in Figure 3. Regarding the factors that increase the risk of mortality in 30 days, longer time on CPB, the initial period (2012-2015) of transplants, older age of the donor, and nutritional status of the donor (overweight or obese) were founded in the univariable analysis, as shown in Tables 1 and 2.
In multivariable analysis using Cox regression, the first model included all variables with a P-value < 0.300. In this analysis, it was found that CPB time (HR 1.01; 95% CI 1.002-1.014; $P=0.011$) and donor age (HR 1.08; 95% CI 1.023-1.139; $P=0.005$) presented statistical significance. However, as CPB time had 27% missing data, only 186 patients were included in this analysis. The second multivariable analysis model included variables with a P-value < 0.300, excluding CPB time. At the end of this analysis, 255 study patients were included, and statistical significance was reached for the donor's age and for the most recent transplant periods, as shown in Table 3.

Survival Analysis

The mean and median follow-up times were 3.1 and 2.4 years, respectively. The longest follow-up time was 10.5 years, and 108 deaths occurred during this period. Overall survival for one, five, and 10 years was 68.1%, 58.0%, and 40.8%, respectively. The median survival time was 8.8 years (Figure 4A).
Analyzing survival by transplant periods, a difference was found between periods 1 and 2 with statistical significance ($P=0.009$). When compared to period 1, we found HR 0.55 and 95% CI 0.36-0.85 for period 2 and HR 0.64 and 95% CI 0.36-1.12 for period 3 (Figure 4B). Survival in the most recent periods (from 2016 to 2022) was 73.2% in the first year and 63% in five years (Figure 4C).
In other subgroup analyses, there was no difference in survival in transplants with donors and recipients of the opposite sex, as well as patients who received transplant ABO-heterogeneous group compatible. However, there was a difference in the analysis by age group, with patients aged 60 years or older having a median survival of 1.14 year, while younger patients had a median of 8.8 years ($P=0.0045$).

Causes of Death

In this cohort of 255 individuals, 108 deaths occurred in 10.5 years of follow-up. The main cause of death was infection (including bloodstream, lung, sepsis, etc.) in 47 patients. The second most frequent cause was COVID-19, with 15 patients, and the third cause was primary graft dysfunction, with seven patients. The following were classified as "other": stroke, sudden death, neoplasia, hemorrhagic shock, diabetic ketoacidosis, recurrence of Chagas disease, aneurysm rupture, or undetermined cause.
In the first 30 postoperative days, 56% of deaths occurred due to infectious causes, 21% due to primary graft dysfunction, 6% due to rejection, and 3% due to COVID-19. Between 31 days and one year after transplant, 54% died from infection, 13% from rejection, and 13% from COVID-19. Patients older than one year died from infection in 11%, from rejection in 14%, from COVID-19 in 29%, and from other causes in 46% (Figure 5).

Table 1. Characteristics of heart transplant recipients and comparison between survivors and non-survivors in 30-day mortality.

Recipient's variables	All cohort (N = 255)	HTx survivors (N = 221)	HTx non-survivors (N = 34)	HR	95% CI	*P*-value
Age (years)				1.02	1.00-1.05	0.090
Mean ± SD	46.6 ± 12.9	46.1 ± 13.0	50.3 ± 11.5			
Median (IQR)	49 (39-56)	48 (37-56)	51 (44-59)			
Age group ≥ 60 years	45 (17.6%)	37 (16.7%)	8 (23.5%)	1.44	0.65-3.18	0.366
Sex						
Male	191 (74.9%)	168 (76.0%)	23 (67.6%)	1.00		
Female	64 (25.1%)	53 (24.0%)	11 (32.4%)	1.47	0.72-3.01	0.294
BMI (kg/m^2)				1.03	0.95-1.11	0.437
Mean ± SD	23.5 ± 4.0	23.4 ± 4.1	24.1 ± 4.1			
Median (IQR)	23.0 (20.8-25.9)	22.9 (20.8-25.8)	24.1 (21.0-27.1)			
Nutritional status						
BMI (kg/m^2)						
BMI < 18.5	23 (9.0%)	20 (9.1%)	3 (8.8%)	1.22	0.36-4.18	0.753
BMI = 18.5-24.9	146 (57.3%)	130 (58.8%)	16 (47.1%)	1.00		
BMI ≥ 25	86 (86.7%)	71 (32.1%)	15 (44.1%)	1.61	0.80-3.26	0.184
Diabetes (N=243)	37 (15.2%)	33 (15.1%)	4 (16.0%)	1.05	0.36-3.07	0.923
Hypertension (N=243)	83 (34.2%)	77 (35.3%)	6 (24.0%)	0.60	0.23-1.50	0.277
PRA > 0% (N=216)	33 (15.3%)	27 (14.0%)	6 (26.1%)	2.09	0.82-5.31	0.120
Priority status	105 (41.2%)	87 (39.4%)	18 (52.9%)	1.70	0.87-3.33	0.123
MCS	12 (4.7%)	9 (4.1%)	3 (8.8%)	2.24	0.68-7.33	0.183
Ischemic time (min.) (N=192)				1.00	0.99-1.00	0.392
Mean ± SD	177.0 ± 70.1	175.6 ± 69.8	190.1 ± 73.6			
Median (IQR)	187.5 (110-240)	185 (108-240)	235 (20-250)			
Prolonged ischemic time > 240 min. (N=192)	45 (23.4%)	39 (22.5%)	6 (31.6%)	1.54	0.59-4.07	0.377
Retrieval operation						
Local	131 (51.4%)	115 (52.0%)	16 (47.1%)	1.00		
Regional	124 (48.6%)	106 (48.0%)	18 (52.9%)	1.21	0.62-2.37	0.581
CPB time (min.) (N=186)				1.01	1.00-1.02	0.001
Mean ± SD	126.5 ± 41.4	123.2 ± 34.5	156.7 ± 74.9			
Median (IQR)	117 (100-138)	116 (100-135)	120 (105-193)			
HTx period						
2012-2015	75 (29.4%)	58 (26.3%)	17 (50.0%)	1.00		
2016-2019	124 (48.6%)	111 (50.2%)	13 (38.2%)	0.43	0.21-0.88	0.021
2020-2022	56 (22.0%)	52 (23.5%)	4 (11.8%)	0.29	0.10-0.85	0.024

BMI=body mass index; CI=confidence interval; CPB=cardiopulmonary bypass; HR=hazard ratio; HTx=heart transplantation; IQR=interquartile range; MCS=mechanical circulatory support; PRA=panel reactive antibody; SD=standard deviation

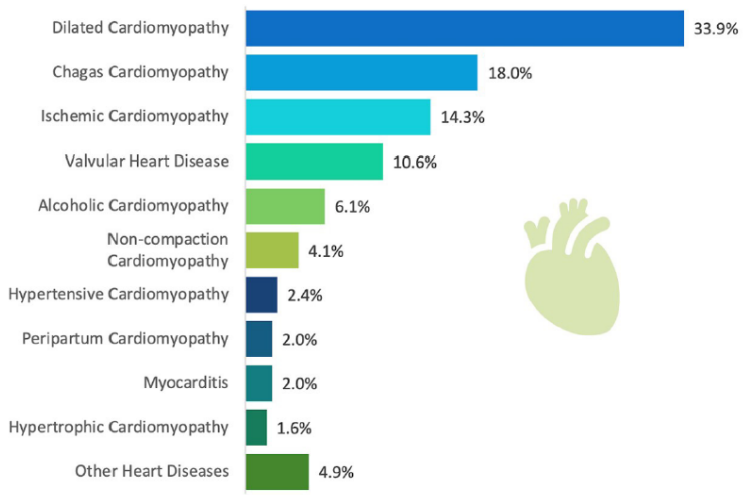

Fig. 1 - *Heart failure etiology among heart transplant recipients from 2012 to 2022.*

DISCUSSION

Post-heart transplant survival analysis involves a series of factors: the experience of the transplant center, the profile of recipient patients with their different levels of severity, the profile of organ donors, postoperative management in the ICU, adjustments of immunosuppressants, postoperative complications of infection, rejection, vascular graft disease, and neoplasms.

When comparing the recipient's basic characteristics with other published Brazilian studies, Chagas disease was the second most common etiology of heart transplant recipients in this study, while in other centers, after idiopathic dilated heart disease, the second most common etiology is ischemic.

In a study of a center in São Paulo, the etiologies of HF were dilated cardiomyopathy (45.6%), ischemic (25%), and chagasic (22.8%) in a series of patients until 1998[5]. A study in the city of Fortaleza presented the following causes of cardiomyopathy: idiopathic (32.2%), ischemic (25.5%), and chagasic (17.5%)[8]. While in this study carried out in Recife, the main etiologies were idiopathic (33.9%), chagasic (18%), and ischemic (14%).

In an epidemiological study published in 2011, the state of Pernambuco ranked second in Brazil in acute cases of Chagas disease with 274 cases (2001 to 2006), behind Bahia with 441 cases[9]. A study of the prevalence of Chagas disease in Brazil, published in 2014, presented Bahia with 2.4% and Pernambuco with 9.1%[10]. In addition to the high prevalence of Chagas disease in Pernambuco, the hospital also receives patients from Bahia for HTx, justifying this emphasis on chagasic heart disease among heart recipients in this population.

Regarding the characteristics of heart donors, we see a difference when comparing with international data. According to the International Society for Heart and Lung Transplantation (or ISHLT) registry, with more than 90% of the data coming from transplants performed in the United States of America and Europe, the mean age of donors is 35 years old, and the causes of BD were TBI (45%), stroke (24%), and others (30%)[11]. In our study, the mean age was 29 years old, and the causes were TBI (77%), stroke (18%), and others (5%).

This higher rate of TBI in Brazil reflects the consequences of reckless driving, with high rates of automobile accidents and in addition to those caused by firearms, bladed weapons, and blunt trauma due to urban violence.

The main cause of early mortality in this study in post-heart transplant patients was infections, which caused 56% of deaths in the first 30 days. We can compare this data with a European study, which showed 10% of deaths due to infection within 30 days[12].

Given immunosuppression and the need for hospitalization while on the waiting list, heart transplant recipients are at high risk of contracting hospital-acquired infections. Bloodstream infections, related to catheters and circulatory assistance devices, urinary tract infections, and pneumonia associated with mechanical ventilation can progress to sepsis in the context of post-transplant immunosuppression and lead to death.

Deaths due to acute rejection in the present study showed a lower percentage, 6% within 30 days and 13% from 31 days to one year, when compared to the same European study with 28% and 32%, respectively[12].

Primary graft dysfunction was the second cause of early death in this study (21%). It is a multifactorial condition with its pathophysiology not yet well understood, but it presents some known risk factors such as recipient patients using vasoactive drugs or mechanical circulatory assistance, elderly donors, and prolonged ischemia time.

Table 2. Characteristics of heart transplant donors and comparison between groups of surviving and non-surviving recipients in 30-day mortality.

Donor variables	All cohort (N = 255)	HTx survivors (N = 221)	HTx non-survivors (N = 34)	HR	95% CI	*P*-value
Age (years)				1.06	1.03-1.10	0.001
Mean ± SD	29.6 ± 9.8	28.8 ± 9.5	35.1 ± 9.8			
Median (IQR)	28 (21-38)	27 (21-37)	37 (28-44)			
Sex						
Male	217 (85.1%)	188 (85.1%)	29 (85.3%)	1.00		
Female	38 (14.9%)	33 (14.9%)	5 (14.7%)	0.99	0.39-2.57	0.993
BMI (kg/m²) (N = 254)				1.07	0.98-1.17	0.145
Mean ± SD	25.7 ± 3.3	25.6 ± 3.4	26.5 ± 2.6			
Median (IQR)	25.3 (23.6-27.7)	25.1 (23.4-27.7)	26.2 (24.7-28.3)			
Nutritional status						
BMI (kg/m²) (N = 254)						
BMI < 18.5	0 (0%)	0 (0%)	0 (0%)			
BMI = 18.5-24.9	119 (46.9%)	109 (49.5%)	10 (29.4%)	1.00		
BMI ≥ 25	135 (53.1%)	111 (50.5%)	24 (70.6%)	2.19	1.05-4.58	0.037
History of CPR (N=254)	36 (14.5%)	31 (14.1%)	5 (14.7%)	1.04	0.41-2.71	0.923
Use of vasoactive drugs (N=254)	222 (87.4%)	193 (87.7%)	29 (85.3%)	0.83	0.32-2.1	0.699
Use of antibiotics (N=254)	153 (60.2%)	135 (61.4%)	18 (52.9%)	0.71	0.36-1.40	0.328
Na > 164 mEq/L (N=254)	69 (27.2%)	62 (28.2%)	7 (20.6%)	0.67	0.29-1.54	0.347
Na (mEq/L) (N=254)				0.99	0.97-1.01	0.386
Mean ± SD	157.2 ± 13.9	157.5 ± 13.9	155.4 ± 14.0			
Median (IQR)	157 (147-166)	158 (147-166.5)	154.5 (147-163)			
Hospital length of stay (days) (N=254)				1.06	1.00-1.13	0.053
Mean ± SD	4.8 ± 4.2	4.6 ± 3.2	5.8 ± 8.1			
Median (IQR)	4 (3-6)	4 (3-6)	3.5 (3-6)			

BMI=body mass index; CI=confidence interval; CPR=cardiopulmonary resuscitation; HR=hazard ratio; HTx=heart transplantation; IQR=interquartile range; Na=serum sodium; SD=standard deviation

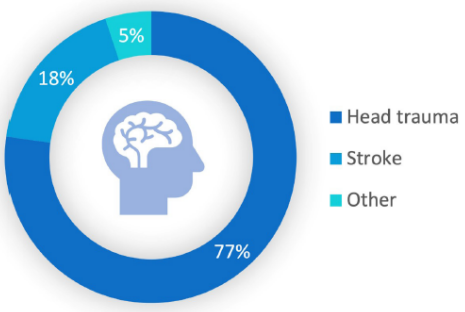

Fig. 2 - *Causes of brain death in heart donors between 2012 and 2022.*

In the univariable analysis, one of the factors that presented statistical significance was the CPB time. However, there is a bias in this variable, considering that a longer CPB time depends on several factors such as: the difficulty in cardiectomy of the recipient (mainly in cases of previous median sternotomy), the heart implantation technique following the anastomoses, as well as the reperfusion time of the organ necessary to restore the biventricular cardiac function of the graft. It is necessary to maintain the patient on CPB until adequate hemodynamic stability is achieved, with an adjustment of vasoactive drugs and an assessment of the need for circulatory assistance in case of primary graft dysfunction.

Therefore, the prolonged CPB time reflects a technically more difficult procedure, and the patient is also subject to the consequences of the CPB itself, with a greater risk of presenting systemic inflammatory response syndrome, platelet dysfunction, and hemolysis.

Fig. 3 - *Distribution of heart transplants performed between 2012 and 2022, showing the prioritization status and the 30-day mortality curve per year.*

Table 3. Multivariable analysis of risk factors for mortality within 30 days after heart transplantation.

Variables	All cohort (N = 255)	HTx survivors (N = 221)	HTx non-survivors (N = 34)	HR	95% CI	*P*-value
Donor age (years)				1.06	1.02-1.10	0.001
Mean ± SD	29.6 ± 9.8	28.8 ± 9.5	35.1 ± 9.8			
Median (IQR)	28 (21-38)	27 (21-37)	37 (28-44)			
HTx period						
2012-2015	75 (29.4%)	58 (26.3%)	17 (50.0%)	1.00		
2016-2019	124 (48.6%)	111 (50.2%)	13 (38.2%)	0.41	0.20-0.85	0.016
2020-2022	56 (22.0%)	52 (23.5%)	4 (11.8%)	0.32	0.11-0.96	0.042

CI=confidence interval; HR=hazard ratio; HTx=heart transplantation; IQR=interquartile range; SD=standard deviation

Patients who received hearts from donors with a BMI ≥ 25 kg/m^2 and who were older had worse 30-day survival results in the univariable analysis. Overweight may be related to other comorbidities not listed, such as hypertension and diabetes mellitus in the donor, which may favor more primary graft dysfunction.

Analysis between study periods demonstrated that initial 30-day mortality was higher, and a progressive and significant reduction in subsequent periods, reaching a rate < 10% as of 2018. The success of the learning curve is due to constant updating of the team, together with training and gaining experience from professionals in different sectors of the hospital, which improves the clinical evaluation of both donor and recipient and the exchange of experiences between transplant centers in Brazil.

The institution that developed this study has become a high-volume heart transplant center, performing more than 20 transplants per year, and this has resulted in a significant improvement in outcomes. An important point to be highlighted was the change in the immunosuppression protocol carried out in mid-2015, with lower doses of corticosteroids, which drastically reduced complications of infection and early mortality, also reflecting survival in the mid-term.

The third period of the study (2020 to 2022) was marked by the COVID-19 pandemic, with airway disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Due to the large number of infected people, there was a significant drop in the number of heart transplants performed.

In addition to there being restrictions on the care of patients with HF in hospitals with the closure of outpatient care and emergency rooms full of patients with severe acute respiratory syndrome, the low circulation of people in cities also led to a significant drop in organ donations.

In 2020, transplants were only performed in patients non-prioritized in this cohort, which highlighted the difficulty in accessing the evaluating and listing of more critical patients. The

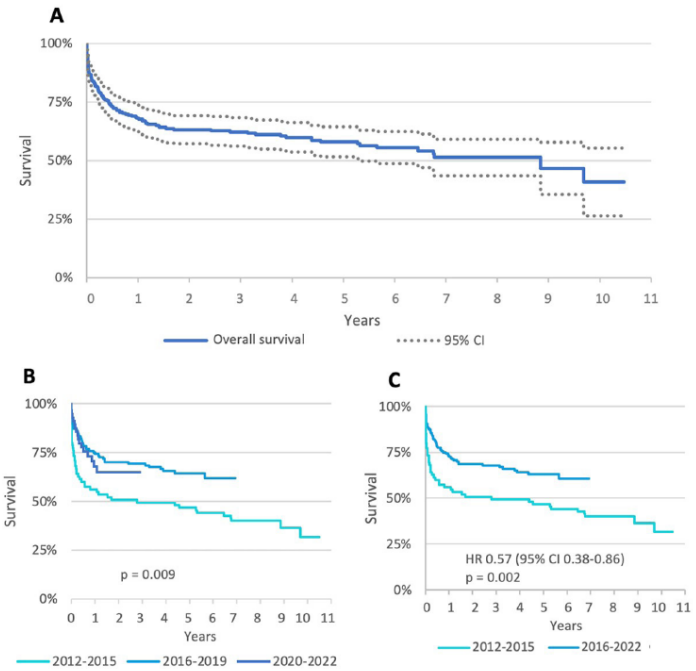

Fig. 4 - *Kaplan-Meier survival curves of heart transplant recipients between 2012 and 2022. A) Overall survival; B) survival curves comparing the three study periods; C) survival curves comparing two periods (union of the most recent periods). CI=confidence interval; HR=hazard ratio.*

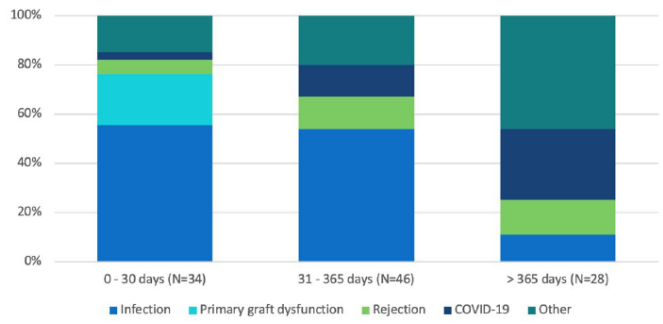

Fig. 5 - *Causes of death in adult heart transplant recipients between 2012 and 2022. COVID-19=coronavirus disease 2019.*

longer time to obtain donors also led to a greater possibility of death on the waiting list. Associated with this, there was a change in the downward trend in the 30-day mortality rate that year.

In 2021, with the start of vaccination against SARS-CoV-2 in Brazil and the institution of specific protocols for testing donors and recipients, there was a drop in the number of COVID-19 cases and an increase in the number of heart transplants performed in our service, due to increasing safety when carrying out the procedure.

In 2022, with the pandemic still ongoing but stable, there was the arrival of rapid SARS-CoV-2 antigen tests and the advancement of vaccination. This improves the access of patients with HF to the hospital. Considering the worsening of these patients' conditions due to a lack of follow-up, the vast majority (77.8%) of transplants performed at the institution in 2022 were performed on priority recipients. However, the mark of 0% mortality in 30 days was reached this year.

The analysis of medium-term survival published with Brazilian data shows similarities between regions. In a study published in 2021 with 2,197 patients from Brazil, survival was 70.9% in one year, 59.5% in five years, and 45.1% in 10 years, with a median survival time of 8.3 years[13].

Two studies in hospitals in São Paulo showed survival rates at one and five years of 70.4% and 59.9% at the Instituto Dante Pazzanese de Cardiologia[14] and 71% and 54.4% with the team from the Universidade Federal de São Paulo. A published study from Hospital de Messejana in Ceará showed overall survival rates of 73% and 60% at one and five years, respectively. Our study revealed overall survival rates at one and five years of 68% and 58%. These data were negatively impacted by the initial results of the learning curve but were also strongly affected by the pandemic. COVID-19 was responsible for early postoperative mortality, accounting for 13% of deaths between 30 days and one year, but primarily for late postoperative mortality, being the cause in 29% of deaths in patients beyond one year after transplant.

Patients in the age group of 60 years or older did not have a difference in 30-day mortality. However, the result of the overall survival curve was significantly worse compared to younger individuals. One of the factors that may contribute to this group of patients is frailty. In a study conducted in Australia, pre-transplant frailty status was an independent risk factor for increased mortality and length of stay after cardiac transplantation[15].

Limitations

The limitations of the study are related to its retrospective nature, being from a single center, and having a relatively small sample. We will continue collecting data for an analysis with more participants and longer follow-up.

CONCLUSION

Adult HTx has shown a significant decrease in early mortality over the years. The third period of the study (2020 to 2022) was marked by the COVID-19 pandemic, which adversely affected the annual transplant numbers. The survival analysis by period demonstrated that the increased surgical volume, coupled with the team's experience and modifications to the immunosuppression protocol, contributed to the improved early and mid-term outcomes.

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No conflict of interest.

Authors' Roles & Responsibilities

DLMF	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
CBCC	Drafting the work or revising it critically for important intellectual content; final approval of the version to be published
FAMSF	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
ITCS	Drafting the work or revising it critically for important intellectual content; final approval of the version to be published
VSM	Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
RMDC	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
BGC	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
MBR	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
VFO	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
PJXS	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
RMT	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
AFPF	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
MFOSF	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published
RCFS	Drafting the work or revising it critically for important intellectual content; final approval of the version to be published
MJGM	Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
RMG	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

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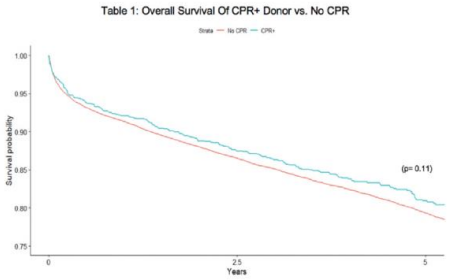
Artigo 2



(1215)

Impact of Initial Hematocrit Levels During Direct Procurement and Perfusion on the Likelihood of Primary Graft Dysfunction in Donation After Circulatory Death Heart Transplant Patients

E. Odekunle,[1] A. Makarem,[2] G. Olverson,[3] K. Drezek,[2] E. Michel,[2] D. D'Alessandro,[2] A. Osho,[2] and S. Rabi.[2] [1]Rutgers New Jersey Medical School, Newark, NJ; [2]Cardiac Surgery Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA; [3]University of Rochester School of Medicine and Dentistry, Rochester, NY

Purpose: In heart transplantation following donation after circulatory death (DCD) using the direct procurement and perfusion (DPP) method, there is limited data regarding the impact of the ex-vivo circuit hematocrit level on recipient outcomes, such as the incidence of primary graft dysfunction, post-transplantation.

Methods: This single-center retrospective cohort study of consecutive DCD heart transplant recipients between December 2019 and January 2023 utilized univariable and multivariable regression models to assess the association between initial hematocrit (HCT) levels of the perfusate (HCT < 15 % packed cell volume (PCV) vs. HCT ≥ 15 %PCV) and the occurrence of primary graft dysfunction (PGD) following heart transplantation from DCD donors. Secondary outcomes such as pre-and post-transplant lactate levels, inotrope score, intensive care length of stay, and overall survival were explored.

Results: A total of 74 DCD heart recipients were included in the study. 25 recipients had a HCT < 15%PCV and 49 recipients had a HCT ≥15%PCV. The odds of experiencing moderate and severe PGD and ECMO were not significantly different between recipients with HCT ≥15% PCV and those with HCT < 15% PCV (PGD: OR = 0.90 [0.266 - 3.042]; P = 0.8654) (EMCO: OR = 1.181 [0.325 - 4.295]; P = 0.8003). The mean inotrope score 48 hours post-admission was significantly higher in DCD recipients with a higher perfusate HCT (5.79 vs. 10.64; P = 0.0090) but was similar at admission for both groups (12.77 vs. 15.16; P = 0.1734). There was a trend toward longer hospital and intensive care unit length of stay for the higher HCT group although this did not achieve statistical significance post-transplant hospital LOS in days (14 [11 - 20] vs. 19 [14 - 26]; P = 0.3719), post-transplant ICU LOS in days (6 [5 - 7] vs. 8[6 - 12]; P = 0.1042)). Recipient survival to discharge was similar between both groups (HCT < 15 %PCV 100% vs. HCT ≥15 %PCV 91.7%; P = 0.2918).

Conclusion: Higher HCT during ex-vivo perfusion of DCD hearts does not protect against PGD post-transplant and may be associated with higher inotrope requirements and longer ICU stays. Findings raise important questions about optimal HCT levels for ex-vivo perfusion and may contribute to decreasing warm ischemia time during DCD donor blood extraction.

(1216)

Heart Transplantation Learning Curve at a High-Volume Center in Northeast Brazil

D.L. Ferraz,[1] V. Monteiro,[2] C. Cunha,[2] F. Figueira,[2] I. Silva,[2] R. Carneiro,[2] M. Oliveira Filha,[2] A. Lapa,[2] P. Xavier,[2] M. Lira,[2] and B. Castro.[2] [1]Cardiovascular Surgery, Instituto de Medicina Integral Professor Fernando Figueira, Recife, Brazil; [2]Instituto de Medicina Integral Professor Fernando Figueira, Recife, Brazil

Purpose: The treatment of heart failure (HF) has advanced significantly in recent years. The outcomes of heart transplantation (HTx) must follow this trend to remain the gold standard for advanced HF treatment. The experience of transplant centers leads to improved results over time, both in terms of early mortality and medium to long-term survival.

Methods: This retrospective cohort study included 255 adult patients who underwent heart transplantation at a Northeast Brazilian center that transitioned to a high-volume facility between 2012 and 2022. The patients were categorized into three periods: Initial (2012-2015), Intermediate (2016-2019), and Recent (2020-2022). Cox regression was used to evaluate factors impacting 30-day mortality, and Kaplan-Meier curves were analyzed survival in these periods.

Results: The mean age was 46.6 years, 74.9% was male. 30-day mortality rates in the Initial, Intermediate, and Recent periods were 22.7%, 10.4%, and 7.14%, respectively. Significant differences were observed, with HR 0.43 (95% CI 0.19-0.95) for the Intermediate period and HR 0.29 (95% CI 0.49-0.74) for the Recent period when compared to the Initial period (Table 1). Medium-term survival also exhibited statistical significance when comparing the Initial period with the Intermediate/Recent periods (Figure 1).

Conclusion: The center's experience plays a pivotal role in improving outcomes. Maintaining a high volume of annual heart transplantations keeps the team closely connected to patients, streamlines routines, and enhances processes. Continuous training and education are essential for sustaining service quality.

Table 1. Characteristics of heart transplant recipients and comparison between survivors and non-survivors in 30-day mortality.

Recipients variables	All cohort N = 255	HTx Survivors N = 221	HTx Non-survivors N = 34	HR	95% CI	p
Age (years)				1.02	1.00-1.05	0.090
Mean ± SD	46.6 ± 12.9	46.1 ± 13.0	50.3 ±11.5			
Median (IQR)	49 (39-56)	48 (37-56)	51 (44-59)			
Age group ≥ 60 years	45 (17.6%)	37 (16.7%)	8 (23.5%)	1.44	0.65-3.18	0.366
Gender						
Male	191 (74.9%)	168 (76.0%)	23 (67.6%)	1.00		
Female	64 (25.1%)	53 (24.0%)	11 (32.4%)	1.47	0.72-3.01	0.294
PRA >0% (N=216)	33 (15.3%)	27 (14.0%)	6 (26.1%)	2.09	0.82-5.31	0.120
Priority status	105 (41.2%)	87 (39.4%)	18 (52.9%)	1.70	0.87-3.33	0.123
HTx period						
2012-2015	75 (29.4%)	58 (26.3%)	17 (50.0%)	1.00		
2016-2019	124 (48.6%)	111 (50.2%)	13 (38.2%)	0.43	0.21-0.88	0.021
2020-2022	56 (22.0%)	52 (23.5%)	4 (11.8%)	0.29	0.10-0.85	0.024

CI, confidence interval; HR, hazard ratio; HTx, heart transplantation; IQR, interquartile range; PRA, panel reactive antibody; SD, standard deviation.

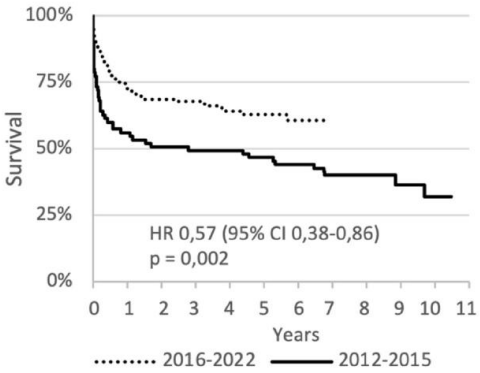


Fig. 1 - Kaplan-Meier survival curves of heart transplant recipients between 2012 and 2022. Survival curves comparing 2 periods (Initial vs Intermediate/Recent). CI, confidence interval; HR, hazard ratio.

(1217)

Surgeon Years of Experience and Survival After Heart Transplantation

A.F. Akbar,[1] A.L. Zhou,[1] J.M. Ruck,[2] D. Paneitz,[2] S. Rokui,[2] B.L. Shou,[3] R.A. Riojas,[2] A. Polanco,[2] and A. Kilic.[2] [1]Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD; [2]Department of Surgery, Johns Hopkins Hospital, Baltimore, MD; [3]Johns Hopkins University School of Medicine, Baltimore, MD

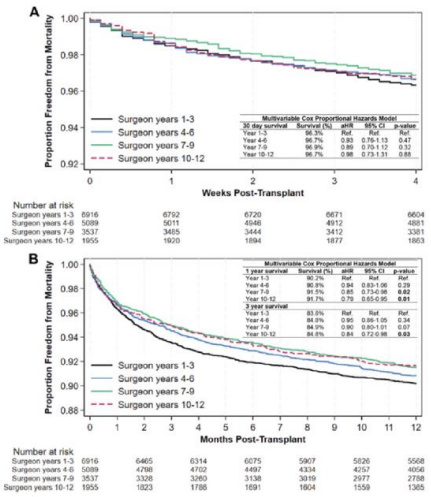
Purpose: It is unknown whether surgeon experience level impacts heart transplant (HT) outcomes. We investigated the effect of HT surgeon experience within the first 12 years of practice on post-transplant survival.

Methods: Adult isolated HT recipients 2008-2022 in the United Network for Organ Sharing database were stratified based on their surgeon's years of experience at time of transplant (Y1-3 vs. Y4-6 vs. Y7-9 vs. Y10-12) using encrypted National Provider Identifier data. We excluded all transplants by surgeons in practice before 2008, as those surgeon's experience data was not completely available. We compared post-transplant survival by surgeon experience using multivariable Cox regression adjusted for transplant year, center volume, and baseline characteristics with $p < 0.2$ on univariate analysis.

Results: Of 36,317 HT during the study period, 17,497 (48.2%) met criteria. For those 17,497 HT, surgeon experience was Y1-3 for 39.5%, Y4-6 for 29.1%, Y7-9 for 20.2%, and Y10-12 for 11.1%. Y10-12 surgeon recipients had the shortest waitlist time (days: 43 vs. 60 [Y7-9] vs. 70 [Y4-6] vs. 70 [Y1-3]) and highest likelihood of pre-transplant ECMO (5.0% vs. 3.3% [Y7-9] vs. 3.2% [Y4-6] vs. 2.4% [Y1-3]) and intra-aortic balloon pump (19.4% vs. 17.9% [Y7-9] vs. 15.2% [Y4-6] vs. 13.6% [Y1-3], all $p < 0.001$). Compared with Y1-3 HT, 30 day mortality was similar for Y4-6, Y7-9, and Y10-12 (**Fig. 1A**). Compared with Y1-3 HT, 1 year mortality was similar for Y4-6 (9.2% vs. 9.8%; aHR 0.94 [95%CI: 0.83-1.06], p=0.29, **Fig. 1B**), 15% lower for Y7-9 (8.5% vs. 9.8%; aHR 0.85 [95%CI: 0.73-0.98], p=0.02), and 21% lower for Y10-12 (8.3% vs. 9.8%; aHR 0.79 [95%CI: 0.65-0.95], p=0.01). Compared with Y1-3 HT, 3 year mortality was similar for Y4-6 and Y7-9, but 16% lower for Y10-12 (15.2% vs. 16.2%; aHR 0.84 [95%CI: 0.72-0.98], p=0.03).

Conclusion: Post-transplant mortality was similar at 30 days regardless of surgeon experience, but lower at 1 year for transplants by surgeons with ≥ 7 years of experience and 3 years for transplants by surgeons with ≥ 10 years of experience.

Figure 1. Kaplan Meier curves comparing (**A**) 30 day and (**B**) 1 year post-transplant survival by surgeon years of experience at the time of heart transplant



(1218)

Across Borders: Outcomes of Heart Transplant from Non-Mainland Donors

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Purpose: Donation of organs from non-mainland geographies can help expand the donor pool but may pose logistical challenges. The aim of this study was to evaluate outcomes of heart transplant from non-mainland donors.

Methods: Adults (≥18 years) undergoing heart-only transplant in the United States from 2008-2022 were identified using the UNOS/OPTN database. Recipients were stratified by receipt of hearts from non-mainland (Alaska, Hawaii, Bermuda, and Puerto Rico) vs. mainland donors, by donor hospital. Mortality risk was compared using Kaplan-Meier survival curves and multivariable Cox regression.

Results: Of 31048 heart transplant recipients identified, 262 (0.8%) received hearts from non-mainland donors. Of the non-mainland group, 65 (25%) of donors were from AK, 5 (2%) were from Bermuda, 5 (2%) were from HI, and 187 (71%) were from PR. Median ischemic time (5.3 [3.9-6.1] vs. 3.2 [2.5-3.8] hours, $p < 0.001$) and geographic distance traveled (916 [702.8-1241] vs. 106 [16-305], $p < 0.001$) were both increased in the non-mainland group (Table 1). Post-transplant outcomes, including LOS, dialysis, acute rejection, pacemaker, and stroke rates were similar. Survival was also similar between recipients of hearts from non-mainland and mainland donors (log-rank p=0.81, Figure 1), even after adjusting for baseline characteristics (aHR = 1.12 [95% CI 0.90-1.38], p=0.32).

Conclusion: We found similar outcomes for recipients of heart transplant from non-mainland and mainland donors, despite increased ischemic time and distance traveled for non-mainland donors, supporting donation from non-mainland donors in heart transplant.

Artigo 3

European Heart Journal (2024) 45 (Suppl 1)
Cardiovascular Surgery – Transplantation

Influence of donor and harvesting protocol on 30 day mortality after heart transplantation

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Funding Acknowledgements: None.

Purpose: Heart transplantation continues to be the gold standard for the treatment of advanced HF, as it promotes increased survival, exercise capacity and quality of life. The choice of the potential donor, as well as the safety of the harvesting process, graft preservation and transportation are fundamental to the success of the procedure. With the territorial extension of Brazil and a large number of donations in other states and regions, evaluating donors remotely, as well as structuring an adequate fundraising plan are fundamental. Therefore, the study of these variables and their influence on the outcome at 30 days was the objective of this study.

Methods: A retrospective cohort was conducted involving patients aged 18 or over, who underwent heart transplantation from July 2012 to July 2022 at our center. Patients who underwent re-transplantation and those who not used the bicaval technique were excluded. Statistical analysis was performed using STATA Software version 18. The Kaplan-Meier method was used to obtain the overall survival curve and, to identify risk factors for death, Cox proportional hazards. The Log test -rank was used for comparisons between groups.

Results: 255 cases of heart transplantation were studied, with a 30-day survival rate of 86.6%. The average age of donors was 29 years old and the main cause of death was traumatic brain injury.Regarding the factors that increase the risk of mortality in 30 days, the longest CPB time (HR 1.01; 95% CI 1.002-1.014; p = 0.011) and the donor's age (HR 1.08; 95% CI 1.023-1.139; p = 0.005) were statistically significant. In the univariate analysis, the donor's nutritional status (overweight or obese) was also significant (p = 0.03).The donor's length of hospital stay, use of vasoactive drugs or antimicrobials, serum sodium level or history of previous PCR did not influence the recipient's 30-day survival. Distance organ retrival surgery did not influence the outcome as long as the ischemia time of less than 240 minutes was respected.

Conclusion: The distance harvesting protocol used in our institution proved to be safe and effective. Adequate evaluation of the donor through echocardiography as well as management of vasoactive drugs and electrolytes may have influenced the non-relevance of classic factors that affect the outcomes of patients after heart transplantation.

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6 CONCLUSÕES

O transplante cardíaco neste centro apresentou redução significativa da letalidade precoce, com diminuição da mortalidade em 30 dias ao longo dos anos. Da mesma forma as curvas de sobrevida apresentaram melhora nos períodos mais recentes. O terceiro período do estudo (2020 a 2022) foi marcado pela pandemia de COVID-19, que impactou as taxas de transplantes. A infecção foi a principal causa de morte desde a fase precoce e até o primeiro ano pós-transplante, seguida pela disfunção primária do enxerto, nos primeiros 30 dias e pela rejeição entre 31 dias e 1 ano.

7 CONSIDERAÇÕES FINAIS

O presente estudo traz contribuições para a pesquisa clínica do IMIP pela confecção de um banco de dados robusto dos pacientes adultos submetidos a transplante cardíaco nesta instituição. Isto permite uma complementação das análises ao longo do tempo, de forma a observar o passado e promover a história de um programa importante no cenário nacional.

A análise por períodos mostra que o aumento do volume cirúrgico e a experiência da equipe, aliados às mudanças no protocolo de imunossupressão, contribuíram para a melhora dos resultados ao longo do tempo.

Novas ações podem ser consideradas para a prática clínica, focando nas principais causas de óbito por fase do período pós-operatório, a fim de melhorar os resultados da sobrevida em curto, médio e longo prazos, por exemplo no combate às infecções e nas estratégias para minimizar a incidência de falência primária do enxerto.

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APÊNDICE A: LISTA DE CHECAGEM

LISTA DE CHECAGEM

PESQUISA: Análise da sobrevida em transplante cardíaco: experiência de centro único brasileiro

Data: _____/_____/_____

Pesquisador Responsável:
Diogo Ferraz

Nome do Paciente:_____
Registro IMIP: _____

CRITÉRIOS DE INCLUSÃO

Paciente realizou transplante cardíaco no IMIP	1. ☐ Sim	2. ☐ Não
Idade ≥ 18 anos	1. ☐ Sim	2. ☐ Não

CRITÉRIOS DE EXCLUSÃO

Paciente já tinha transplante cardíaco prévio?	1. ☐ Sim	2. ☐ Não
Paciente realizou outra técnica que não ortotópica bicaval?	1. ☐ Sim	2. ☐ Não

☐ **EXCLUÍDO**

☐ **INCLUÍDO**
Formulário nº.: ☐

Responsável pelo Preenchimento: _____

APÊNDICE B: TCLE

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Análise da sobrevida em transplante cardíaco: experiência de centro único brasileiro

Você está sendo convidado(a) a participar de uma pesquisa porque foi atendido ou está sendo atendida nesta instituição. Para que você possa decidir se quer participar ou não, precisa conhecer os benefícios, os riscos e as consequências pela sua participação.

Este documento é chamado de Termo de Consentimento Livre e Esclarecido (TCLE) e tem esse nome porque você só deve aceitar participar desta pesquisa depois de ter lido e entendido este documento. Leia as informações com atenção e converse com o pesquisador responsável e com a equipe da pesquisa sobre quaisquer dúvidas que você tenha. Caso haja alguma palavra ou frase que você não entenda, converse com a pessoa responsável por obter este consentimento, para maiores esclarecimentos. Caso prefira, converse com os seus familiares, amigos e com a equipe médica antes de tomar uma decisão. Se você tiver dúvidas depois de ler estas informações, entre em contato com o pesquisador responsável.

Após receber todas as informações, e todas as dúvidas forem esclarecidas, você poderá fornecer seu consentimento, rubricando e/ou assinando em todas as páginas deste Termo, em duas vias (uma do pesquisador responsável e outra do participante da pesquisa), caso queira participar.

PROPÓSITO DA PESQUISA

Identificar as taxas de sobrevida dos pacientes submetidos ao transplante cardíaco do Instituto de Medicina Integral Professor Fernando Figueira (IMIP).

PROCEDIMENTOS DA PESQUISA

Fazer uma revisão trabalhos científicos sobre o tema.
Coletar dados de prontuário médico. Utilizar banco de dados do Serviço de Cirurgia Cardiovascular do IMIP e do Transplante Cardíaco.
Submeter os resultados da pesquisa para posterior publicação em revista científica nacional ou internacional.

Se você concordar, os pesquisadores responsáveis por esta pesquisa consultarão seus dados clínicos e laboratoriais que se encontram no seu prontuário. Todos os dados coletados serão mantidos em sigilo e confidencialidade.

BENEFÍCIOS:

Este estudo contribuirá no desenvolvimento de estratégias que visem melhorar a expectativa de vida dos pacientes transplantados cardíacos.

RISCOS:

Os riscos deste estudo estariam relacionados com a quebra de confidencialidade mediante a divulgação de dados e identificação não autorizada pelos pacientes, a qual resultaria em danos psicológicos, morais e/ou materiais aos pacientes ou a terceiros. Porém, todos os cuidados serão tomados para que as identidades dos pacientes não sejam reveladas.

CUSTOS

O participante não pagará por qualquer procedimento, medicação ou exames exigidos como parte desta pesquisa.

CONFIDENCIALIDADE

Se você optar por participar desta pesquisa, as informações sobre a sua saúde e seus dados pessoais serão mantidas de maneira confidencial e sigilosa. Seus dados somente serão utilizados depois de anonimizados (ou seja, sem sua identificação). Apenas os pesquisadores autorizados terão acesso aos dados individuais, resultados de exames e testes bem como às informações do seu registro médico. Mesmo que estes dados sejam utilizados para propósitos de divulgação e/ou publicação científica, sua identidade permanecerá em segredo.

PARTICIPAÇÃO VOLUNTÁRIA

A sua participação é voluntária e a recusa em autorizar a sua participação não acarretará quaisquer penalidades ou perda de benefícios aos quais você tem direito, ou mudança no seu tratamento e acompanhamento médico nesta instituição. Você poderá retirar seu consentimento a qualquer momento sem qualquer prejuízo. Em caso de você decidir interromper sua participação na pesquisa, a equipe de pesquisadores deve ser comunicada e a coleta de dados relativos à pesquisa será imediatamente interrompida.

ACESSO AOS RESULTADOS DE EXAMES

Você pode ter acesso a qualquer resultado relacionado à esta pesquisa. Estes resultados serão enviados ao seu médico e ele os discutirá com você. Se você tiver interesse, você poderá receber uma cópia dos mesmos.

GARANTIA DE ESCLARECIMENTOS

A pessoa responsável pela obtenção deste Termo de Consentimento Livre e Esclarecido lhe explicou claramente o conteúdo destas informações e se colocou à disposição para responder às suas perguntas sempre que tiver novas dúvidas. Você terá garantia de acesso, em qualquer etapa da pesquisa, sobre qualquer esclarecimento de eventuais dúvidas e inclusive para tomar conhecimento dos resultados desta pesquisa. **Neste caso, por favor, ligue para o Dr. Diogo Ferraz no telefone (81) 99882-7582 e diogoferraz_@hotmail.com de 08 às 17h.**

Se você tiver alguma consideração ou dúvida sobre esta pesquisa, entre em contato com o comitê de Ética em Pesquisa Envolvendo Seres Humanos do IMIP (CEP-IMIP) que objetiva defender os interesses dos participantes, respeitando seus direitos e contribuir para o desenvolvimento da pesquisa desde que atenda às condutas éticas.

O CEP-IMIP está situado à Rua dos Coelhos, nº 300, Boa Vista. Diretoria de Pesquisa do IMIP, Prédio Administrativo Orlando Onofre, 1º Andar tel: (81) 2122-4756 – E-mail: comitedeetica@imip.org.br O CEP/IMIP funciona de 2ª a 6ª feira, nos seguintes horários: 07:00 às 11:30 h e 13:30 às 16:00h.

Este termo está sendo elaborado em duas vias, sendo que uma via ficará com você e outra será arquivada com os pesquisadores responsáveis.

CONSENTIMENTO

Li as informações acima e entendi o propósito do estudo. Ficaram claros para mim quais são procedimentos a serem realizados, riscos, benefícios e a garantia de esclarecimentos permanentes.

Ficou claro também que a minha participação é isenta de despesas e que tenho garantia do acesso aos dados e de esclarecer minhas dúvidas a qualquer tempo.
Entendo que meu nome não será publicado e toda tentativa será feita para assegurar o meu anonimato.

Concordo voluntariamente em participar desta pesquisa e poderei retirar o meu consentimento a qualquer momento, sem penalidade ou prejuízo ou perda de qualquer benefício que eu possa ter adquirido.

Eu, por intermédio deste, dou livremente meu consentimento para participar nesta pesquisa.

Participante da pesquisa	/ / **Data**
Testemunha	/ / **Data**

Eu, abaixo assinado, expliquei completamente os detalhes relevantes desta pesquisa ao paciente indicado acima e/ou pessoa autorizada para consentir pelo mesmo.

Pesquisador	/ / **Data**

Rubrica do Participante da Pesquisa	**Rubrica do Pesquisador**

APÊNDICE C: SOLICITAÇÃO DE DISPENSA DO TCLE

SOLICITAÇÃO DE DISPENSA DO TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE)

Solicito a dispensa da aplicação do Termo de Consentimento Livre e Esclarecido do projeto de pesquisa intitulado: **Análise da sobrevida em transplante cardíaco: experiência de centro único brasileiro.**

O nosso projeto se propõe a identificar as taxas de sobrevida de pacientes submetidos ao Transplante Cardíaco do Instituto de Medicina Integral Professor Fernando Figueira (IMIP) utilizando o banco de dados do Serviço de Cardiologia e Cirurgia Cardiovascular do IMIP, pesquisa em prontuário e do Sistema de Informação sobre Mortalidade em caso de não obtenção da data do óbito. Os dados serão avaliados estatisticamente através do Software SPSS versão 19.

Para os pacientes em acompanhamento no IMIP será solicitada a assinatura do TCLE, porém em alguns casos tornam-se inviáveis essas assinaturas devido falecimento ou perda de acompanhamento ao longo do tempo no IMIP, pois pacientes podem retornar aos estados de origem

Este estudo contribuirá no desenvolvimento de estratégias que visem melhorar a expectativa de vida dos pacientes transplantados cardíacos. Há importância epidemiológica no contexto brasileiro para divulgação desses dados mostrando o aumento da expectativa de vida dos pacientes portadores de insuficiência cardíaca.

Os pesquisadores declaram:

a) Que o acesso aos dados registrados em prontuário de pacientes ou em bases de dados para fins da pesquisa cientifica será feito somente após aprovação do projeto de pesquisa pelo Comitê de Ética;

b) O acesso aos dados será supervisionado por uma pessoa que esteja plenamente informada sobre as exigências de confiabilidade;

c) Assegurar o compromisso com a privacidade e a confidencialidade dos dados utilizados preservando integralmente o anonimato e a imagem do participante bem como a sua não estigmatização.

d) Assegurar a não utilização as informações em prejuízo das pessoas e/ou das comunidades, inclusive em termos de autoestima, de prestígio e/ou econômico-financeiro;

e) O pesquisador responsável estabeleceu salvaguardas seguras para confidencialidades dos dados de pesquisa;

Nestes termos, me comprometo a cumprir todas as diretrizes e normas regulamentadoras descritas na Resolução (citar qual Resolução 466/2012 ou 510/2016) do CNS/CONEP e suas complementares no que diz respeito ao sigilo e confidencialidade dos dados utilizados.

Recife, 25 de setembro de 2022.

_____

Pesquisador Responsável / Orientador

APÊNDICE D: FORMULÁRIO PARA CAPTAÇÃO DE DADOS

FORMULÁRIO DE AVALIAÇÃO

Projeto de Pesquisa: ANÁLISE DA SOBREVIDA EM TRANSPLANTE CARDÍACO: EXPERIÊNCIA DE CENTRO ÚNICO BRASILEIRO

Mestrado em Cuidados Intensivos Pesquisador Responsável: Diogo Ferraz

Nome: _____
Data de Nascimento:____/____/_____ Data de Tx:____/____/_____ Idade ao Tx:____
Sexo: Masculino☐ Feminino☐ Altura: _____cm Peso: _____Kg
Óbito: Sim ☐ Não ☐ Data: ___/____/____ Causa:_____

Receptor:		
Diagnóstico:	Sim	Não
Miocardiopatia isquêmica		
Miocardiopatia Valvar		
Miocardiopatia dilatada idiopática		
Congênita		
Outra?_____		
DM:		
HAS:		
Insuficiência renal aguda ou crônica		
Tabagismo		
Tipo de sangue	A ☐ A ☐ B ☐ AB ☐ O	
PRA (%)		
Cirurgia Cardíaca Prévia		
Nível priorização:	☐ ECMO ☐ BIA ☐ DVA ☐ Ambulatorial	
Tempo de Isquemia (minutos):		
Tempo de CEC (minutos):		
Tempo de UTI (dias)		
Data da Alta Hospitalar	/ /	
Doador:		
Idade:		
Sexo:		
Altura (cm):		
Peso (kg):		
Tempo de Isquemia (minutos):		
Tipo de sangue	☐ A ☐ B ☐ AB ☐ O	
Causa da Morte:	☐ TCE ☐ Evento Cerebrovascular ☐ Outras	
Tempo de internamento:		
História de PCR?		
Uso de DVA?		
Na sérico:		

Responsável pelo Preenchimento: _____

ANEXO A: APROVAÇÃO DO PROJETO PELO CEP DO IMIP

INSTITUTO DE MEDICINA INTEGRAL PROFESSOR FERNANDO FIGUEIRA - IMIP/PE

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Análise da sobrevida em transplante cardíaco: experiência de centro único brasileiro

Pesquisador: DIOGO FERRAZ
Área Temática:
Versão: 2
CAAE: 40888620.4.0000.5201
Instituição Proponente: Instituto de Medicina Integral Professor Fernando Figueira - IMIP/PE
Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.556.249

Apresentação do Projeto:
INTRODUÇÃO
Com o envelhecimento da população, tem-se uma substituição das doenças infecto parasitarias para as doenças crônicas não transmissíveis como as doenças cardiovasculares, elevando os casos de Insuficiência Cardíaca (IC). O Transplante Cardíaco é opção terapêutica considerada em pacientes com IC avançada e refratária ao tratamento otimizado, de acordo com diretrizes nacionais e internacionais (SBC, 2018).
A IC é uma síndrome clínica complexa, na qual o coração é incapaz de bombear sangue de forma a atender às necessidades metabólicas tissulares, ou pode fazê-lo somente com elevadas pressões de enchimento (SBC, 2018). Atualmente, é a opção que apresenta melhor sobrevida para pacientes com IC grave refratária ao tratamento clínico, chegando a ter mortalidade imediata muito baixa (BACAL et al., 2018). Sabe-se que vários fatores influenciam na sobrevida dos receptores no período pós-transplante cardíacos e que uns dos mais importantes são as alterações do sistema imunológico, causadas pelas terapias imunossupressoras obrigatórias após o procedimento cirúrgico. Além disso, existem outras variáveis do doador e do receptor que pode influenciar negativamente na sobrevida como: idade, a causa da morte, sexo, reoperação e prioridade para transplante (ASSEF et al.,2001).
O uso de dispositivos temporário como suporte circulatório mecânico vem sendo utilizado como

Endereço: Rua dos Coelhos, 300
Bairro: Boa Vista **CEP:** 50.070-902
UF: PE **Município:** RECIFE
Telefone: (81)2122-4756 **Fax:** (81)2122-4782 **E-mail:** comitedeetica@imip.org.br

alternativa de resgate hemodinâmico: como ponte para decisão, ponte para recuperação e ponte para transplante para transplante. Já atinge melhoras nas taxas de sobrevivência quando usados para obter estabilidade clínica (BACAL et al., 2018). Entretanto, só se tem na literatura dados confiáveis de curto prazo.

Vários estudos têm mostrado um excelente resultado de sobrevivência após transplante cardíaco, principalmente quando se compara com o curso natural da IC em estágio final. Segundo a ABTO, o Brasil consegue dados de sobrevida dos doentes muito semelhantes aos de outros países, indica uma sobrevida de 73% no primeiro ano após a intervenção e uma sobrevida em 7 anos de 60% estatísticas muito próximas de países de primeiro mundo (ABTO, 2018).

Quando comparado com a década de 1980, ocorreu uma melhora significativa em comparação com a sobrevivência de 76,9% em 1 ano e 62,7% em 5 anos (ABTO, 2018). Através do desenvolvimento de novas técnicas cirúrgicas, drogas imunossupressoras, métodos de diagnóstico e abordagens da equipe multidisciplinar (CUSTODIO et al., 2013).

JUSTIFICATIVA

É importante ter o conhecimento dos resultados de sobrevida após o transplante cardíaco tanto para melhora do serviço quanto da assistência aos pacientes transplantados.

Levantar dados sobre os principais fatores que interferem na sobrevida dos pacientes transplantados cardíacos pode auxiliar no desenvolvimento de estratégias que visam melhorar a qualidade de vida dos transplantados.

Objetivo da Pesquisa:

OBJETIVOS

Objetivo Geral

Identificar as taxas de sobrevida de pacientes submetidos ao transplante cardíaco do Instituto de Medicina Integral Professor Fernando Figueira (IMIP).

Objetivos Específicos

Avaliar o perfil dos pacientes submetidos a transplante cardíaco no IMIP (idade, gênero, peso, altura, etiologia da insuficiência cardíaca, comorbidades, priorização por droga vasoativa ou assistência circulatória mecânica etc);

Avaliar o perfil dos doadores (idade, gênero, causa da morte encefálica etc);

Quantificar os tempos cirúrgicos, principalmente circulação extracorpórea e tempo de isquemia do

órgão, se a captação foi fora de Recife;
Avaliar as taxas de rejeição após transplante;
Avaliar os resultados cirúrgicos através da ecocardiografia levando em consideração função biventricular;
Identificar os índices tempo de UTI e internamento hospitalar, e das complicações, acidente vascular encefálico, insuficiência renal, síndrome do baixo débito cardíaco e de mortalidade hospitalar dos pacientes submetidos a transplante cardíaco no IMIP.

Avallação dos RIscos e Benefícios:
Riscos:
Os riscos deste relato estariam relacionados com a quebra de confidencialidade mediante a divulgacao de dados e identificacao nao autorizada pelos pacientes, a qual resultaria em danos psicologicos, morais e/ou materiais aos pacientes ou a terceiros. Porem, todos os cuidados serao tomados para que as identidades dos pacientes nao sejam reveladas.
Beneficios:
Este estudo contribuirá no desenvolvimento de estratégias que visem melhorar a expectativa de vida dos pacientes transplantados cardíacos.

Comentários e Considerações sobre a Pesquisa:
Trata-se de uma pesquisa do serviço de cardiologia do IMIP para identificar a taxa de sobrevida de pacientes submetidos ao transplante cardíaco. Os pesquisadores informam que para coletar as informações irão utilizar prontuários, dados dos bancos de dados do Departamento de Cirurgia Cardiovascular do IMIP e do Serviço de Transplante Cardíaco do IMIP e das fichas de perfusão.

Considerações sobre os Termos de apresentação obrigatória:
Vide campo "Conclusões ou Pendências e Lista de Inadequações".

Recomendações:
Vide campo "Conclusões ou Pendências e Lista de Inadequações".

Conclusões ou Pendências e Lista de Inadequações:
Pendência 1: Incluir TCLE para os pacientes - Pendência resolvida;

Pendência 2: Incluir termo de confidencialidade assinado - Pendência resolvida;

Pendência 3 – Realizar adequação do cronograma de atividades - Pendência resolvida;

Pendência 4 – Realizar melhor detalhamento dos tópicos: justificativa, objetivos, coleta de dados e desfechos - Pendência resolvida.

Situação do protocolo: aprovado.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇOES_BASICAS_DO_PROJETO_1642210.pdf	10/02/2021 14:59:23		Aceito
Outros	CARTA_DE_ENCAMINHAMENTO_SOBREVIDA.pdf	10/02/2021 14:59:00	DIOGO FERRAZ	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_CEP_SOBREVIDA_2.doc	21/12/2020 15:42:00	DIOGO FERRAZ	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_SOBREVIDA.docx	21/12/2020 15:39:33	DIOGO FERRAZ	Aceito
Outros	Lattes_Cristiano.pdf	01/12/2020 18:08:20	DIOGO FERRAZ	Aceito
Outros	Lattes_Ana_Flavia.pdf	01/12/2020 18:06:07	DIOGO FERRAZ	Aceito
Outros	Lattes_Camila.pdf	01/12/2020 18:04:22	DIOGO FERRAZ	Aceito
Outros	Lattes_Raphaely.pdf	01/12/2020 18:03:59	DIOGO FERRAZ	Aceito
Outros	Lattes_Maria_Thereza.pdf	01/12/2020 18:03:28	DIOGO FERRAZ	Aceito
Outros	Lattes_Valeria.pdf	01/12/2020 18:02:57	DIOGO FERRAZ	Aceito
Outros	Lattes_Anna.pdf	01/12/2020 17:55:32	DIOGO FERRAZ	Aceito
Outros	Lattes_Rodrigo.pdf	01/12/2020 17:55:05	DIOGO FERRAZ	Aceito
Outros	Lattes_Diogo.pdf	01/12/2020 17:54:34	DIOGO FERRAZ	Aceito

Outros	Termo_de_Confidencialidade_SOBREVIDA.pdf	01/12/2020 17:53:31	DIOGO FERRAZ	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Solicitacao_de_dispensa_TCLE_SOBREVIDA.pdf	01/12/2020 17:52:39	DIOGO FERRAZ	Aceito
Outros	Carta_de_Anuencia_SOBREVIDA.pdf	01/12/2020 17:51:07	DIOGO FERRAZ	Aceito
Outros	Email_SIGAP_SOBREVIDA.pdf	01/12/2020 17:47:01	DIOGO FERRAZ	Aceito
Folha de Rosto	Folha_de_Rosto_assinada_SOBREVIDA.pdf	01/12/2020 17:30:07	DIOGO FERRAZ	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

RECIFE, 24 de Fevereiro de 2021

Assinado por:
Lygia Carmen de Moraes Vanderlei
(Coordenador(a))

ANEXO B: CARTA DE ACEITE DA REVISTA CIENTÍFICA

Brazilian Journal of Cardiovascular Surgery

Decision Letter (RBCCV-2023-0394.R1)

From: prbevora@fmrp.usp.br

To: diogoferraz_@hotmail.com

CC:

Subject: Brazilian Journal of Cardiovascular Surgery - Decision on Manuscript ID RBCCV-2023-0394.R1

Body: January 23, 2024]

Dear Dr. Ferraz:

It is a pleasure to accept your manuscript entitled "Survival Analysis in Adult Heart Transplantation: Experience from a Brazilian Single-Center" in its current form for publication in the Brazilian Journal of Cardiovascular Surgery. The comments of the reviewer(s) who reviewed your manuscript are included at the foot of this letter.

Thank you for your fine contribution. On behalf of the Editors of the Brazilian Journal of Cardiovascular Surgery, we look forward to your continued contributions to the Journal.

Sincerely,
Dr. Paulo Roberto Evora
Editor-in-Chief, Brazilian Journal of Cardiovascular Surgery
prbevora@fmrp.usp.br

==========

Reviewer: 1
Comments:
The authors responded to the previous comments and I don't have further comments

==========

Date Sent: 23-Jan-2024

Close Window

ANEXO C: INSTRUÇÕES PARA AUTORES – BJCVS

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INSTRUCTIONS FOR AUTHORS

Brazilian Journal of Cardiovascular Surgery

1. Purpose and Editorial Policy

The Brazilian Journal of Cardiovascular Surgery (BJCVS) is the official publication of the Sociedade Brasileira de Cirurgia Cardiovascular (SBCCV). It is a peer-reviewed scientific journal, published on a rolling basis and with regular circulation since 1986.

BJCVS aims to register the scientific production and innovation in cardiovascular surgery and encourage continuous education, professional improvement, and the ongoing development of specialty professionals. With its commitment to these goals, BJCVS has a significant impact on cardiovascular surgery practice and related fields.

BJCVS follows the recommendations set by the International Committee of Medical Journal Editors (ICMJE - www.icmje. org), the Committee on Publication Ethics (COPE - https:// publicationethics.org/), the Council of Science Editors (CSE - https://www.councilscienceeditors.org/) and the World Association Medical Editors (WAME - http://www.wame.org/).

BJCVS welcomes the submission of papers focusing on topics related to cardiovascular surgery and its associated areas. BJCVS also accepts preprints, which are preliminary versions of a work shared publicly before going through the formal peer review process and publication in a journal. The journal publishes the following categories of articles: Original Articles, Review Articles, Brief Communications, How I Do It, Multimedia, Letter to the Editor, Editorial and Guidelines.

The acceptance of articles will be based on their originality, significance, and scientific contribution to the field. Articles with purely propagandistic or commercial purposes will not be accepted.

Articles should be submitted only in English, using clear and precise language while avoiding colloquial (informal) writing. Only manuscripts whose data are not being evaluated by other journals and/or which have not been previously published will be considered for evaluation. Once approved, reproduction of the manuscripts, whether in whole or in part, requires explicit consent from the BJCVS editor. Keep your registration updated, as communication with the authors is conducted exclusively by email..

The journal will be published in its entirety on the website www.bjcvs.org and on SciELO at www.scielo.br/rbccv, with specific links on the website of SBCCV (www.sbccv.org.br) and CTSNET (www.ctsnet.org).

Recognizing the importance of disseminating the published articles, BJCVS is indexed in the main international databases: Web of Science (Clarivate Analytics), PubMed Central, PubMed/ Medline, SCOPUS (SCImago), Proquest, LATINDEX, Redalyc, EBSCO, and Google Scholar. Moreover, it is also indexed in national databases: LILACS and SciELO.

BJCVS does not charge any Article Processing Charge (APC) for the submission, evaluation, review, publication, distribution, or downloading of manuscripts. Publication is completely free and open access.

2. Research with Human Subjects and Experimental Studies

Research involving human subjects must be submitted to the Ethics Committee of the institution, in accordance with the Declaration of Helsinki of 1975, revised in 2013 (available at Research involving human subjects must be submitted to the Ethics Committee of the institution, in accordance with the Declaration of Helsinki of 1975, revised in 2013 (available at https://www.wma.net/policies-post/wma-declaration-of helsinki-ethical-principles-for-medical-research-involving human-subjects/#:~:text=The%20World%20Medical%20 Association%20(WMA,identifiable%20human%20material%20 and%20data.) and Resolution 466/2012 of the Brazilian National Health Council (available at http://bvsms.saude.gov.br/bvs/saudelegis/cns/2013/res0466_12_12_2012.html).) and Resolution 466/2012 of the Brazilian National Health Council (available at http://bvsms.saude.gov.br/bvs/ saudelegis/cns/2013/res0466_12_12_2012.html).

Manuscripts must be accompanied by a statement confirming that the research was carried out with the informed and appropriate consent of everyone involved. Written consent must be obtained from the patient (or their legal guardian or executor, if applicable) for publication of any details or photographs that could identify an individual.

Experimental work involving animals must comply with the **ARRIVE** (Animal Research: Reporting of In Vivo Experiments) and **PREPARE** (Planning Research and Experimental Procedures on Animals: Recommendations for Excellence) guidelines, which must be applied in addition to the Brazilian Guideline for Animal Care and the Use of Animals in Teaching or Scientific Research Activities (DBCA), from the Brazilian National Council for the Control of Animal Experimentation (CONCEA).

- The **PREPARE** guidelines can be found at https://norecopa. no/prepare.
- The **ARRIVE** guidelines can be found at https:// arriveguidelines.org/.
- The **CONCEA Normative Resolution No. 55** guidelines can be found at https://www.in.gov.br/web/dou/-/resolucao-n-55-de-5-de-outubro-de-2022-434869177
- CONCEA: https://www.gov.br/mcti/concea

3. Ethical Considerations

BJCVS supports the recommendations of the Committee on Publication Ethics (COPE), the Council of Science Editors (CSE) and the World Association Medical Editors (WAME) regarding ethical standards of publication, addressing plagiarism, self-plagiarism, redundant publication, data fabrication, and corrections and retractions. Any cases of misconduct will be dealt with the appropriate sanctions established by the Editorial Board.

- **Plagiarism** is the appropriation of someone else's ideas, processes, results, or words without proper acknowledgment. Authors hold full responsibility for the content and information presented in their manuscripts. BJCVS uses the Similarity Check software, which allows to detect similarities in the submitted materials. **Manuscripts found to contain plagiarism will be rejected, and authors may incur sanctions determined by the Editorial Board.**
- **Text Recycling**, also known as self-plagiarism, is the practice of reusing some or all the content of a previous work without proper attribution or proper citation in a new work. This can include reusing entire sections from a previous publication or mixing excerpts from different previous works. In other words, text recycling occurs when an author incorporates excerpts from their own previously published work into a new work, without indicating that these excerpts have been published before. This practice is considered unethical because it can be seen as an attempt to deceive the reader by presenting

information as new and original when it has already been previously published. **Manuscripts that present text recycling will be rejected, and authors may incur sanctions determined by the Editorial Board.**

- **Duplicate Submission and Redundant Publication:** The BJCVS is committed to publishing only original material that has not been previously published or is under review by other journals, including in languages other than English. Articles submitted to the BJCVS should not be submitted to any other journal while under evaluation. Duplicate submission refers to the practice of submitting the same study to multiple journals, while redundant publication involves the inappropriate division of study results into multiple articles (also known as salami publication), which may result in the rejection or retraction of the article, and authors may face sanctions established by the BJCVS Editorial Board.
- **Data Fabrication and Falsification:** If any fraud in the manipulation of images, data fabrication or falsification is identified in a manuscript, **it will be promptly excluded from the evaluation process and authors may face sanctions determined by the Editorial Board.**
- **Corrections and Retractions:** Errors or failures, regardless of their nature or origin, that do not constitute misconduct will be corrected by erratum. In articles already published in which misconduct has been identified, retraction will be made stating the reason for the retraction properly referenced. All authors will be asked to agree to the content.
- **Conflict of Interest Statement:** BJCVS requests that all authors declare any financial, personal, or organizational relationships that may inappropriately influence (bias) their work. Authors must disclose a possible conflict of interest, in addition to the liability of any violation. For more information on conflict of interest, BJCVS recommends consulting the ICMJE (http://www.icmje.org/conflicts-of-interest/) and WAME (http://wame.org/wame-editorial-on-conflict-of-interest) guidelines.
  Conflicts include:
- **Financial** - funding and other payments, goods or services received or expected by the authors related to the subject of the work, or from organizations with an interest in the result of the work.
- **Affiliations** – being employed, serving on the advisory board, or being a member of an organization with an interest in the outcome of the work.
- **Intellectual property** – ownership of patents or trademarks by the authors or their organization
- **Personal** - Friends, family, relationships, and other close personal connections.
- **Ideological** – beliefs or activism, such as political or religious affiliations, relevant to the work
- **Academic** - Competitors or someone whose work is criticized.
  If there is no conflict, the authors must declare no conflict of interest.
  that they have no conflicts to declare. **Any conflicts of interest must be disclosed at the time of manuscript submission by the ScholarOne system.**
- **Use of chatbots in manuscripts submitted to BJCVS:**in order to ensure the integrity and reliability of the results and conclusions presented in scientific manuscripts that use chatbots such as ChatGPT, and to maintain public confidence in the findings and advances presented, BJCVS supports WAME recommendations (https://wame.org/ page3.php?id=106) on the ethical considerations related to these technologies in scientific manuscripts, namely
- **Transparency:**Authors should be transparent about the use of chatbots in the manuscript writing process, including detailed information (name, version, model and source of the technology used), as well as explaining the role of chatbots in the development of the text.
- **Responsibility:**Authors are responsible for the work performed by chatbots in their manuscripts, including the accuracy of the information presented and the absence of plagiarism. Authors should also be able to state that there is no plagiarism in their article, including in the text produced by chatbots.
- **Attribution:** Authors must ensure proper attribution of all sources, including material produced by chatbots. Authors should also seek out and cite sources that support statements made by chatbots.
- **Limitations:**Authors should discuss the limitations and potential biases associated with using chatbots in the production of scientific texts. Authors should disclose the use of generative artificial intelligence (AI) and AI-assisted technologies in the writing process by including a statement in the main manuscript file before the **References** section. The statement should be presented in a new section titled **"Declaration of Generative AI and AI-Assisted Technologies in the Writing Process".**
- **Statement:** "During the preparation of this work, the author(s) used [NAME OF THE TOOL/SERVICE] for the purpose of [REASON]. After using this tool/service, the author(s) have reviewed and edited the content as necessary and assume full

responsibility for the content of the publication". This statement does not apply to the use of basic tools for grammar and spelling checking and reference management, among others. If there is nothing to reveal, there is no need to add a statement.

- **Originality and Copyright Statement:** Authors retain the copyright to their articles and agree to grant BJCVS the license to publish, provided that the authorship is properly credited and that the original article is quoted correctly. By submitting the manuscript, the authors declare that the work is original and does not contain fabrication, fraud, or plagiarism; does not infringe any copyright or property rights of third parties; is not under consideration for publication in another journal; and has not been previously published. In addition, authors must ensure that they meet the authorship requirements as recommended by the ICMJE (please refer to the **Manuscript Preparation** section) and understand that, if the article or part of it is found to be flawed or fraudulent, each author bear shared responsibility
- **Sanctions:** Practices that harm scientific integrity such as Plagiarism, Self-Plagiarism, Duplicate Publication and Redundant Publication will be taken for evaluation by the Editorial Board for decision on penalties such as suspension for a period determined by the Editorial Board. Authors will be immediately notified of all steps of this process.

4.Use of Inclusive Language

Inclusive language is sensitive to differences and promotes equal opportunities, respecting individual differences, and avoiding any implication of superiority based on age, gender, race, ethnicity, culture, sexual orientation, disability, or health status. BJCVS advises authors to ensure that their manuscripts are free of prejudice, stereotypes, slang, and references to dominant cultures, in addition to avoid using descriptors that refer to irrelevant personal attributes. To strive for gender neutrality and to avoid using offensive or exclusionary terms in coding terminology, BJCVS recommends the use of plural nouns. For more information, authors are encouraged to refer to chapter 11 of the AMA Manual of Style, 11th edition, at https://academic.oup.com/amamanualofstyle/book/27941/ chapter/207567296?login=true#362714659.

5.Preprints

BJCVS recognizes the value of new scientific media and enables readers and researchers to have faster access to the results of recent research prior to its publication. Therefore, BJCVS accepts manuscripts that have been deposited on non-commercial preprint servers.

Preprints are preliminary versions of scientific works that are publicly shared in online repositories prior to its peer review and publication in a scientific journal. It is a way to accelerate the process of scientific communication, allowing researchers to promptly share their findings with the academic community. Preprints can be found in public repositories such as bioRxiv and medRxiv, which are platforms dedicated to biology and medicine publications, respectively. These repositories are maintained by non-profit organizations and offer free access to the public for reading and downloading.

To ensure transparency and integrity in the handling of preprints submitted to the BJCVS, authors are encouraged to provide the following information:

- **Preprint identification:** Authors must provide detailed information about the preprint, including title, authors, name of the repository where it was published, date of publication and Digital Object Identifier (DOI) if available
- **Relationship with the submitted work:** Authors should clearly explain the relationship between the preprint and the work submitted to the journal, e.g., if the preprint is an earlier version of the submitted work or if it contains supplementary information.
- **Conflict of interest:** Authors must disclose any conflicts of interest related to the preprint, such as funding from a company or institution with an interest in the work.

BJCVS recommends completing the Open Science Compliance Form, that must be submitted as a **Supplementary File** together with the manuscript. This information is important for the BJCVS editors to evaluate the originality and relevance of the submitted work, as well as to avoid duplication or redundant information in subsequent publications.

6.Quality Standards

BJCVS requires all submitted articles to meet the quality standards set by the guidelines for producing health research reports - Enhancing the Quality and Transparency of Health Research (EQUATOR) Network (https://www.equator-network.org/):

- AGREE or RIGHT for clinical practice guidelines - http://www.equator-network.org/reporting-guidelines/theagree-reporting-checklist-a-tool-to-improve-reportingof-clinical-practice-guidelines/
- https://www.equator-network.org/reporting-guidelines/right-statement/
- ARRIVE for animal experiments - https://www.nc3rs.org.uk/arrive-guidelines
- CARE for case reports - https://www.care-statement.org/
- CHEERS for economic evaluations - http://www.equator-network.org/wp-content/uploads/2013/04/Revised-CHEERS-Checklist-Oct13.pdf
- CONSORT for randomized trials - http://www.consortstatement.org/
- PRISMA for systematic reviews - http://www.equatornetwork.org/reporting-guidelines/prisma/
- SPIRIT or PRISMA-P for study protocols - http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinicaltrials/
- http://www.equator-network.org/reporting-guidelines/prisma-protocols/
- SQUIRE for quality improvement studies - http://squire-statement.org/index.cfm?fuseaction=Page.ViewPage&PageID=471
- STARD for diagnostic accuracy studies - http://www.equator-network.org/reporting-guidelines/stard/
- STROBE for observational studies - https://www.strobe-statement.org/index.php?id=strobe-home
- TREND for non-randomized trials - https://www.cdc.gov/trendstatement/index.html

6.1 Clinical Trials

Clinical trial registration: BJCVS supports the World Health Organization (WHO) and ICMJE clinical trial registration policies, recognizing the importance of these initiatives for the registration and international dissemination of open access clinical trial data. Therefore, only clinical research articles that have received an identification number in one of the Clinical Trials Registries recognized by WHO and ICMJE (Brazilian Clinical Trial Registry - REBEC - http://www.ensaiosclinicos.gov.br/ or http://apps.who.int/trialsearch/default.aspx) will be accepted for publication. The registration identification number must be given in the "Methods" section.

Randomized trials should follow the **CONSORT** guidelines (http://www.consort-statement.org). This statement provides an evidence-based approach to improving the quality of clinical trial reports. All manuscripts describing a clinical study should include the **CONSORT Flow Diagram** showing the number of participants in each intervention group, as well as a detailed description of how many patients were excluded at each step from the data analysis. All clinical trials must be registered and made available on an open access website. The trial protocol (including the complete statistical analysis plan) should be submitted with the manuscript.

6.2 Data Sharing Statement

As recommended by the ICMJE and the BJCVS, clinical trials must include a data sharing statement. This statement should specify: the individual patient data, a data dictionary that defines each field in the dataset and supporting documentation (e.g., statistical/analytical code), that will be shared; details on when, where, and how the data is available (informing the access link to the data repository); types of analyses that are allowed; and if there are restrictions on the use of the data. If there any reasons why the data cannot be shared, an explanation should be provided. Examples of data sharing statements that meet ICMJE requirements are available at http://www.icmje.org/ news-and-editorials/data_sharing_june_2017.pdf.

7. Types of Manuscript

- **Original Article:** Articles reporting new and/or innovative results for cardiovascular surgery. This category includes clinical trials, cohort studies, case-control, prevalence, incidence, accuracy and cost-benefit studies, cross-sectional studies, epidemiological and experimental assessments, among other observational studies, and should contain:

Maximum Title length (words)	40

Running title (words)	12
Maximum Abstract length (words)	250
Maximum length excluding abstract, tables, figures and references (words)	5,000
Maximum number of figures and tables	08
Maximum number of references	25

- **Review Article:** Studies that use systematic methods and explicit criteria to identify, select and critically evaluate relevant research. This category includes systematic review with and without meta-analyzes

Maximum Title length (words)	40
Running title (words)	12
Maximum Abstract length (words)	250
Maximum length excluding abstract, tables, figures and references (words)	6500
Maximum number of figures and tables	08
Maximum number of references	75

The BJCVS requests that authors register their systematic reviews on platforms such as Prospero (https://www.crd.york.ac.uk/prospero/) and include the registration number in the Methods section. Prospero is an international database of systematic reviews and meta-analyses, which aims to enhance the transparency and quality of these studies. Registering a systematic review in Prospero helps ensure that the research is planned and conducted in an appropriate and transparent manner

- **Brief Communication:** Articles intended to promptly share newly obtained results on topics of great interest. This type of article primarily focuses on innovative hypotheses that are likely to establish new paradigms in the field of cardiovascular surgery. Authors should adhere to the following guidelines:

Maximum Title length (words)	40
Running title (words)	12
Maximum Abstract length	100
Maximum length excluding Abstract, tables, figures and references (words)	1,500
Maximum number of figures and tables	02
Maximum number of references	20

- **How I Do It:** Articles that address procedures with distinct or innovative characteristics in the field of cardiovascular surgery.

Maximum Title length (words)	40
Running title (words)	12
Maximum Abstract length (words)	100
Maximum length excluding abstract, tables, figures and references (words)	1,500
Maximum number of figures and tables	08
Maximum number of references	10

- **Multimedia:** Modality that allows the submission of videos (MP3 or MP4 format) or images that provide valuable insights into significant disease states or their treatments. The multimedia submission should adhere to the following requirements:

Maximum Title length (words)	40
Running title (words)	12
Maximum length excluding abstract, tables, figures and references (words)	1,500
Maximum number of videos	02
Maximum number of figures	04
Maximum number of references	08

- **Letters to the Editor:** Letters to the editor provide an opportunity for readers to express their comments, discuss or criticize articles published in the BJCVS, as well as address other topics of general interest.

Maximum Title length (words)	40
Running title (words)	12
Maximum length excluding abstract and references (words)	1,000
Maximum number of references	06

- **Editorial:** By invitation only.
- **Guidelines:** Only at the discretion of the Department Boards of the Sociedade Brasileira de Cirurgia Cardiovascular..

8. Manuscript Preparation

Manuscripts must be submitted in Microsoft Office Word file, with mandatory configuration of A4 paper pages (210x297 mm) and 2 cm margins on all sides. The recommended font is Times New Roman size 12 and the text should have a line spacing of 1.5 pt.

The **Letter to the Editor** should be sent separately from the manuscript and should inform the reasons why the BJCVS was selected for submission, including mentioning the scientific contributions of the manuscript to the subject matter.

The BJCVS follows a double-anonymous peer review process, which is performed by three or more reviewers assigned to evaluate the articles. Throughout the evaluation process, the identities of reviewers and authors are hidden from each other. To facilitate the submission process, the BJCVS recommends that authors prepare their manuscripts in separate files, as described below:

Title Page:

1. Title and Authorship:

- The title of the paper should be concise, informative, and in English. For clinical trials, systematic reviews, and meta-analysis, it is recommended to include the type of study as a subtitle, for example: "Noninvasive ventilation during immediate postoperative period in cardiac surgery patients: systematic review and meta-analysis".
- A running title must be provided, following the specified limit for each type of manuscript.
- If a title requires more extensive wording, it should be submitted for approval by the Editor-in-Chief.
- The full names of all authors, as well as the responsibilities of each author, should follow the authorship criteria of ICMJE (information below). Each author's affiliation should include university, department, city, zip code, country, email address and ORCID (all authors must be registered in ORCID – Open Researcher and Contributor ID – https:// orcid.org/signin).
- A corresponding author must be indicated.

Types of Manuscripts and Word Limits (Checklist)					
Type	**Manuscript (words)**	**Abstract**	**Abstract Type**	**Tables/Figures (No.)**	**References (No.)**
Original Article	5	250	Structured	8	25
Review Article	6,5	250	Structured	8	75
Brief Communication	1,5	100	Unstructured	2	20
How I Do It	1,5	100	Unstructured	8	10
Multimedia	1,5	N/A	N/A	04 (02 videos)	8
Letter to the Editor	1	N/A	N/A	N/A	6

- **Authors' Responsibility:** It is mandatory for each author to confirm their substantial contributions to the work and assume responsibility for a significant portion of the manuscript's content. Each author should specify their contributions to the work. The corresponding author or the author who submitted the work will indicate, during the submission process, their guarantee and accuracy regarding the integrity of all the reported data in the manuscript. Except for new technology articles, statements regarding scientific responsibility are not included in the published manuscript.
  The BJCVS recommends that authorship be based on the following four criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis or interpretation of data for the work; and
2. Drafting the work or revising it critically for important intellectual content;
3. Final approval of the version to be published; and
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

- For individuals who do not meet the authorship criteria but have contributed to the study, they must be listed in the Acknowledgments section, as well as financial support from funding agencies.

2.Manuscript Structure

- The articles should be divided according to the study design and follow the recommendations of the EQUATOR Network (https://www.equator-network.org/):
  - **Original Articles and Rapid Research Communications:** Introduction, Methods, Results, Discussion, Conclusion, Acknowledgments, and References.
  - **Review Articles and Cutting-edge Reviews:** Can be structured in sections at the discretion of the author.
  - **Case Reports:** Introduction, Case Report and Conclusion.
  - **Multimedia:** Patient Characterization and Description of the Technique Employed.
  - **Special Articles (New Techniques, Letter to the Editor, Editorial and Guidelines):** Can be structured in sections at the discretion of the author.

Manuscript Structure (Checklist)		
	Abstract Structure	**Manuscript Structure**
Original Article Review Article	Introduction Methods Results Conclusion	Introduction Methods Results Discussion Conclusion Funding (if any) Acknowledgments References
Brief Communication	Unstructured	Introduction Comments References
How I Do It	Unstructured	Introduction Technique or Procedure Discussion Conclusion References
Multimedia	Unstructured	Case Presentation Description of the Technique Employed Comment References
Letter to the Editor, Editorial and Guidelines	N/A	N/A

- **Abstract:** it should be structured into four sections: Introduction, Methods, Results, and Conclusion. It is important to avoid the use of abbreviations. The maximum number of words in the abstract should follow the recommendations for each type of manuscript. In Case Reports, the abstract should be structured into three sections: Background, Case Presentation, and Conclusion. In the New Techniques type, the abstract must be unstructured. The Multimedia type does not require an abstract.
- **Keywords:** Three to five English descriptors should also be included. Descriptors can be found at the following electronic addresses: https://decsfinder.bvsalud.org/ dmfs (DeCS/MeSH Finder) or https://meshb.nlm.nih.gov/MeSHonDemand (MeSH on Demand).
- **Abbreviations and Terminology:** The use of abbreviations should be kept to a minimum. When long expressions need to be repeated, it is recommended to use capitalized initials as replacements after the first mention, followed by the initials in parentheses. All abbreviations in tables and figures must be defined in the respective captions. The BJCVS adopts the Universal Official Anatomical Terminology, approved by the International Federation of Associations of Anatomists (IFAA).
- **Units of Measurement:** values of physical quantities must be reported according to the standards of the International System of Units.
- **Funding:** Any sources of research assistance, including project numbers and responsible institutions, must be declared. The role of funding agencies in study design, data collection, analysis and interpretation, and manuscript writing should be also stated in the Acknowledgments section.
- **Acknowledgments:** All contributors who have made substantial contributions to the manuscript (e.g., data collection, analysis, and writing or editing assistance), but do not meet the criteria for authorship, should be mentioned, as well as their specific contributions, in the Acknowledgments section.
- **References:** References should be standardized according to the Vancouver style, as specified by the International Committee of Medical Journal Editors (examples of references are available at https://www.nlm.nih.gov/bsd/uniform_requirements.html).
  References must be identified, in the body of the text, with Arabic numerals, placed in superscript, and in square brackets, obeying the order of their appearance in the text. The accuracy of the references is the responsibility of the author.
  - If more than two references are cited in sequence, only the first and last references should be typed, separated by a dash (Example: [6-9]). In cases of non-sequential citation, all references must be typed and separated by commas (Example: [6,7,9]).
  - Avoid citing theses, dissertations, books and chapters, newspapers or non-scientific journals (magazines), and articles "in press", except when it is a theoretical reference (e.g., Cochrane Handbook).
  - The BJCVS encourages the use of DOI, as it provides a permanent access link to the electronic article.
  - For articles or texts published on the Internet that do not have a DOI, provide the complete URL address, as well as the date of access when it was consulted.
- **Preprint** When a manuscript that has been published in a preprint repository is later published as a peer-reviewed article, the official publication should be referenced. Preprints that are fundamental to the development of the manuscript or have significant advances in the field, but have not yet been properly published, can be cited. Preprints should be explicitly identified as such, for example:
  - Li X, Lidsky P, Xiao Y, Wu CT, Garcia-Knight M, Yang J, Nakayama T, Nayak JV, Jackson PK, Andino R, Shu X. Ethacridine inhibits SARS-CoV-2 by inactivating viral particles in cellular models. bioRxiv [Preprint]. 2020 Nov 2:2020.10.28.359042. doi: 10.1101/2020.10.28.359042
- **Data Reference:**The BJCVS encourages citation of underlying or relevant datasets in the manuscript by mentioning them in the text and including them in the References section. Data references should include the following elements: author(s) name(s), dataset title, data repository, version (if available), year, and a global persistent identifier. Examples:
  - **Research Data:**Coin L. Genomics of development and disease [dataset]. 2014 Jun 1 [cited 2017 Jun 9]. The University of Queensland. Available from: http://dx.doi. org/10.14264/uql.2016.583

- **Repository Data:** Dryad Digital Repository [Internet]. Durham (NC): Dryad. 2008 Jan - [cited 2014 Oct 3]. Available from: https://datadryad.org/stash/
- **Data Deposited in Repositories:** Kraemer MUG, Sinka ME, Duda KA, Mylne A, Shearer FM, Brady OJ, Messina JP, Barker CM, Moore CG, Carvalho RG, Coelho GE, Van Bortel W, Hendrickx G, Schaffner F, Wint GRW, Elyazar IRF, Teng H, Hay SI. The global compendium of Aedes aegypti and Ae. albopictus occurrence [dataset]. 2015 Jun 30 [cited 2015 Oct 23]. In: Dryad Digital Repository [Internet]. Durham (NC): Dryad. 2008 Jan - . 3 files: 3.406 MB; 1.549 MB; 1.815 MB. Available from: https://datadryad. org/stash/dataset/doi:10.5061/dryad.47v3c. Referenced in doi: 10.7554/eLife.08347
- **Data Described in Articles:** Kraemer MUG, Sinka ME, Duda KA, Mylne A, Shearer FM, Brady OJ, Messina JP, Barker CM, Moore CG, Carvalho RG, Coelho GE, Van Bortel W, Hendrickx G, Schaffner F, Wint GRW, Elyazar IRF, Teng H, Hay SI. The global compendium of Aedes aegypti and Ae. albopictus occurrence [dataset]. Sci Data. 2015 Jul 7 [cited 2015 Oct 23];2:150035. Available from: http:// www.nature.com/articles/sdata201535. doi: 10.1038/ sdata.2015.35

- **Tables and Figures:** : Tables and Figures must be numbered in the order of their appearance in the text, have a title and be submitted as separate files. Tables should not contain redundant data already mentioned in the text. They must have an open format with an all-white background. The abbreviations used in tables must be mentioned in alphabetical order in the footer, with their respective full forms. Likewise, the abbreviations used in figures must be explained in the figure captions. Figures will be published in color only if the author agrees to bear the costs of printing. Only images in TIFF or JPEG formats will be accepted, with minimum resolutions according to the image type: 1200 dpi for simple black and white graphics, 300 dpi for black and white photographs and 600 dpi for color photographs. Authors are requested to archive the original images they possess in case there are any issues with the submitted images, in which case the original images may be requested.
- **Videos:** Videos can be uploaded as Supplemental Files along with the manuscript via ScholarOne. The accepted digital formats are MPEG-4 and MP. Contributors must be succinct, and editors reserve the right to require a shorter video duration. The video must be of high quality (both in content and visibility) and must demonstrate the description provided in the manuscript. In addition, the content of the video should directly correspond to the video caption. Videos should not display explicit advertising of any products. Educational presentations are encouraged.
- **Patient Consent:** The corresponding author must confirm in the Copyright Transfer Agreement (CTA) that they have obtained a signed release form from each recorded video authorizing its offline and/or online distribution. The BJCVS suggests that patients should not be identified in the video. Editors may request additional video editing from authors prior to publication.

9. Manuscript Evaluation Process

The BJCVS follows a double-anonymous peer review process, where three or more reviewers are assigned to evaluate the articles. Throughout the evaluation process, the identities of reviewers and authors are hidden from each other.

The Editor reviews the manuscript to determine its suitability for the peer review process. If the manuscript is deemed to be of insufficient quality or outside the scope of the journal, it should be rejected without any further processing.

All scientific contributions are assessed by the Editor, Area Associate Editors, Editorial Board Members and/or Guest Reviewers, with the following processes:

Adequacy to standards	The initial analysis is conducted by the Editorial Assistant, to ensure compliance with the Author Instructions. If the manuscript does not meet the established standards, it will be returned to the authors for correction. Once the manuscript is deemed appropriate to the Journal's

	standards, it is directed to the Editor-in-Chief.
Evaluation Process	The Editor-in-Chief assesses the quality and interest of the manuscript and forwards it to the Associate Area Editor. The Associate Area Editor evaluates the manuscript and refers it to three Reviewers.
Opinions	The Reviewers submit their opinions directly in the ScholarOne system. The Associate Editor, based on the opinions, makes the editorial decision: · accept, · revise, · or reject and the decision is forwarded to the Editor-in-Chief
Approval or Rejection	The Editor-in-Chief decides on the approval for publication or rejection of the manuscript, and the decision is communicated to the authors. If the manuscript is accepted, it enters the publishing process for publication.

9.1 Preprints Evaluation Process

Although the BJCVS follows the double anonymization peer review process for manuscripts submitted to the journal, this process cannot be implemented for preprints, since authors and reviewers are known. However, the BJCVS adopts the single anonymous process for preprints, in which reviewers are known to the authors of the preprint, but not the other way around. This ensures a critical and impartial evaluation of the preprints before potential publication in the BJCVS

Whenever necessary, the BJCVS will ask the authors of the preprints to provide detailed information on the methodology used in the research, results obtained, and conclusions reached, so that the reviewers can assess the quality of the work appropriately

The BJCVS may also ask authors for information about any peer review that the preprint has already undergone in another repository, if applicable, to help reviewers in conducting a more comprehensive evaluation of the preprint's quality.

10. Electronic Submission

To submit a manuscript to the BJCVS, authors are required to use the online submission system provided by ScholarOne, at https://mc04.manuscriptcentral.com/rbccv-scielo. The submission must include the following:

- Letter of Presentation, explaining why the BJCVS was chosen for submission. It should also highlight the scientific contributions of the manuscript to the relevant subject matter.
- Conflict of interest statement of each author (the statement must be completed via ScholarOne platform).
- Title and Authorship Page.
- Manuscript.
- **After manuscript accepted:** Authors' Declaration duly signed by all authors.

Each document must be attached separately in the designated field within the ScholarOne system. Before initiating the process, the person responsible for the submission must previously register in the system as an author and create/associate their ORCID registration – https://orcid.org/signin. All authors must have the registration associated with an updated ORCID

11. Proofs

The corresponding author will receive a proof of the manuscript in a text file (.doc and .docx), which includes observations and changes made by the technical reading team. The author will have four days to review the proof. If there are still questions regarding the proof, the editorial team will contact the author to address them, until a final version of the text is reached

Upon acceptance of the manuscript, the corresponding authors will receive the finalized version of the article in PDF format for approval. To open these files, Acrobat Reader needs to be installed (available as a free download at http://get.adobe.com/reader/). Corrections requested at this stage of the process should be limited to typographical errors and should not involve changes to the content of the study or the list of authors. Once the proof is approved, authors must return the approved version via email within 48 hours of receiving the message. After the completion of the PDF production process, the article will be sent for publication.

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ANEXO D: CARTA DE ACEITE - APRESENTAÇÃO EM CONGRESSO

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INVITATION SUMMARY

Control Number: **5656**
Abstract Title: ***Heart Transplantation Learning Curve at a High-Volume Center in Northeast Brazil***

Dear Diogo Ferraz,

You are confirmed to give a presentation of your research **IN PERSON** in a **Poster Session** during the **ISHLT 44th Annual Meeting and Scientific Sessions** to be held 10-13 April, 2024 at the Prague Congress Center in Prague, Czech Republic.

For over four decades, the ISHLT Annual Meetings have convened the world's most influential researchers and most innovative practitioners to share their science, ideas and passion around advanced heart and lung disease, and work like yours is instrumental to the ongoing success of the conference. We are pleased to include your research in the 2024 scientific program.

Below is a copy of the invitation. ***Please print or bookmark this page for future reference***. You will receive more information soon about preparing your presentation for the conference.

We look forward to your contribution to this year's exciting annual meeting scientific program. If you have any questions, please do not hesitate to contact Susie Newton (susie.newton@ishlt.org) at the Society office.

See You In Prague!

Sincerely,

Goran Dellgren, MD, PhD
ISHLT2024 Scientific Program Chair
Sahlgrenska University Hospital
Gotenburg, Sweden