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A multicenter evaluation of external outflow graft obstruction with a fully magnetically levitated left ventricular assist device

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

J Thorac Cardiovasc Surg. 2022 Oct 3:S0022-5223(22)01042-X. doi: 10.1016/j.jtcvs.2022.09.051. Online ahead of print.

ABSTRACT

BACKGROUND: The HeartMate 3 (HM 3; Abbott) left ventricular assist device (LVAD) has improved hemocompatibility-related adverse outcomes. In sporadic cases, external compression of the outflow graft causing obstruction (eOGO) can result from substance accumulation between the outflow graft and its bend relief. We sought to evaluate the prevalence, course, and clinical implications of eOGO in an international study.

METHODS: A multicenter retrospective analysis of HM 3 LVADs implanted between November 2014 and April 2021 (n = 2108) was conducted across 17 cardiac centers in 8 countries. We defined eOGO as obstruction >25% in the cross-sectional area in imaging (percutaneous angiography, computed tomography, or intravascular ultrasound). The prevalence and annual incidence were calculated. Serious adverse events and outcomes (death, transplantation, or device exchange) were analyzed for eOGO cases.

RESULTS: Of 2108 patients, 62 were diagnosed with eOGO at a median LVAD support duration of 953 (interquartile range, 600-1267) days. The prevalence of eOGO was 3.0% and the incidence at 1, 2, 3, 4, and 5 years of support was 0.6%, 2.8%, 4.0%, 5.2%, and 9.1%, respectively. Of 62 patients, 9 were observed, 27 underwent surgical revision, 15 underwent percutaneous stent implantation, 8 received a heart transplant, and 2 died before intervention. One patient underwent surgical revision and later stent implantation. The mortality with therapeutic intervention was 9/53 (17.0%).

CONCLUSIONS: Although uncommon, HM 3 LVAD-supported patients might develop eOGO with an increasing incidence after 1 year of support. Although engineering efforts to reduce this complication are under way, clinicians must maintain a focus on early detection and remain vigilant.

PMID:36562497 | DOI:10.1016/j.jtcvs.2022.09.051

Categorías: Trasplante cardíaco

The potential for Treg-enhancing therapies in transplantation

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Clin Exp Immunol. 2022 Dec 23:uxac118. doi: 10.1093/cei/uxac118. Online ahead of print.

ABSTRACT

Since the discovery of regulatory T cells (Tregs) as crucial regulators of immune tolerance against self-antigens, these cells have become a promising tool for the induction of donor-specific tolerance in transplantation medicine. The therapeutic potential of increasing in vivo Treg numbers for a favorable Treg to Teff cell ratio has already been demonstrated in several sophisticated pre-clinical models and clinical pilot trials. In addition to improving cell quantity, enhancing Treg function utilizing engineering techniques led to encouraging results in models of autoimmunity and

transplantation. Here we aim to discuss the most promising approaches for Treg-enhancing therapies, starting with adoptive transfer approaches and ex vivo expansion cultures (polyclonal vs. antigen-specific), followed by selective in vivo stimulation methods. Furthermore, we address next generation concepts for Treg function enhancement (CARs, TRUCKs, BARs) as well as the advantages and caveats inherit to each approach. Finally, this review will discuss the clinical experience with Treg therapy in ongoing and already published clinical trials, however, data on long-term results and efficacy is still very limited and many questions that might complicate clinical translation remain open. Here, we discuss the hurdles for clinical translation and elaborate on current Treg based therapeutic options as well as their potencies for improving long-term graft survival in transplantation.

PMID:36562079 | DOI:10.1093/cei/uxac118

Categorías: Trasplante cardíaco

Data-independent acquisition proteomics reveals circulating biomarkers of coronary chronic total occlusion in humans

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Front Cardiovasc Med. 2022 Dec 5;9:960105. doi: 10.3389/fcvm.2022.960105. eCollection 2022.

ABSTRACT

INTRODUCTION: The pathophysiology of coronary chronic total occlusion (CTO) has not been fully elucidated.

METHODS: In the present study, we aimed to investigate the potential plasma biomarkers associated with the pathophysiologic progression of CTO and identify protein dynamics in the plasma of CTO vessels immediately after successful revascularization. We quantitatively analyzed the plasma proteome profiles of controls (CON, n = 10) and patients with CTO pre- and post- percutaneous coronary intervention (PCI) (CTO, n = 10) by data-independent acquisition proteomics. We performed enzyme-linked immunosorbent assay (ELISA) to further confirm the common DEPs in the two-group comparisons (CON vs. CTO and CTO vs. CTO-PCI).

RESULTS: A total of 1936 proteins with 69 differentially expressed proteins (DEPs) were detected in the plasma of patients with CTO through quantitative proteomics analysis. For all these DEPs, gene ontology (GO) analysis and protein-protein interaction (PPI) analysis were performed. The results showed that most of the proteins were related to the negative regulation of proteolysis, regulation of peptidase activity, negative regulation of hydrolase activity, humoral immune response, and lipid location. Furthermore, we identified 1927 proteins with 43 DEPs in the plasma of patients with CTO vessels after immediately successful revascularization compared to pre-PCI. GO analysis revealed that the above DEPs were enriched in the biological processes of extracellular structure organization, protein activation cascade, negative regulation of response to external stimulus, plasminogen activation, and fibrinolysis. More importantly, we generated a Venn diagram to identify the common DEPs in the two-group comparisons. Seven proteins, ADH4, CSF1, galectin, LPL, IGF2, IgH, and LGALS1, were found to be dynamically altered in plasma during the pathophysiological progression of CTO vessels and following successful revascularization, moreover, CSF1 and LGALS1 were validated via ELISA.

CONCLUSIONS: The results of this study reveal a dynamic pattern of the molecular response after CTO vessel immediate reperfusion, and identified seven proteins which would be the potential targets for novel therapeutic strategies to prevent coronary CTO.

PMID:36561774 | PMC:PMC9764215 | DOI:10.3389/fcvm.2022.960105

Categorías: Trasplante cardíaco

Condition of the Oral Cavity in Patients After Heart Transplantation: A Preliminary Report

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Ann Transplant. 2022 Dec 23;27:e937734. doi: 10.12659/AOT.937734.

ABSTRACT

BACKGROUND The constant impairment of the immune system caused by lifelong use of immunosuppressive drugs in patients after heart transplantation has a significant impact on oral cavity health. The aim of this study was to analyze the health of the oral cavity in patients after heart transplantation, with particular regard to occurring pathogens. MATERIAL AND METHODS The study included 25 patients after heart transplantation. The research scheme was divided into 2 parts. The first part consisted of a survey on general health and oral hygiene habits. The second part of the examination consisted of an analysis of the health of the oral cavity: the mucosa, periodontium, and hard dental tissues. Particular attention was paid to PET (test for the presence of pathogens causing periodontitis/periimplantitis) and CAT (diagnostic test for the presence of Candida in the oral cavity), which are real-time PCR tests used to detect pathogens causing periodontitis and microorganisms present in oral candidiasis. RESULTS The conducted research and in-depth analysis of the results showed that the oral health condition in patients after heart transplantation is not satisfactory, regardless of the time that has elapsed since the surgery, sex, age, hygiene habits, or the type of immunosuppression used. The oral cavity of patients after heart transplantation is colonized with Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Treponema denticola, and Candida albicans. CONCLUSIONS The cooperation of the dentist with the attending physician at each stage of the treatment should play an unquestionable role.

PMID:36560867 | DOI:10.12659/AOT.937734

Categorías: Trasplante cardíaco

Novel combination of FLNC (c.5707G>A; p. Glu1903Lys) and BAG3 (c.610G>A; p.Gly204Arg) genetic variant expressing restrictive cardiomyopathy phenotype in an adolescent girl

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

J Genet. 2022;101:54.

ABSTRACT

Pediatric restrictive cardiomyopathy (RCM) is the rarest in its group and accounts for only 2.5-5% of all the diagnosed cardiomyopathies in children. It is a relentless disease with poor prognosis, and heart transplantation is the only long-term treatment option. The aetiology of pediatric RCM varies and includes conditions such as endomyocardial fibrosis, storage disorder (Fabry's disease, MPS), drugs, radiation, post-cardiac transplantation and genetic. Genetic causes encompasses mutations in sarcomeric (troponin I and T, actin, myosin and titin) and nonsarcomeric protein-coding genes (Desmin, RSK2, lamin A/C and bcl-2-associated athanogene 3 (*BAG3*)). Inheritance of RCM could be autosomal dominant, autosomal recessive and X-linked. Here, we report a case of RCM in an adolescent girl, who was symptomatic with palpitations and breathlessness on exertion. The patient showed presence of rare variants in *FLNC* (c.5707G>A; p.Glu1903Lys) and *BAG3* genes (c.610G>A; p.Gly204Arg). These two variants were detected individually in asymptomatic father and mother, respectively. *FLNC* gene codes for gamma filamin. These filamin proteins play important role in maintaining the structural integrity of the sarcomere. *BAG3* is the main component of the chaperone-assisted selective autophagy (CASA) pathway. Mutant *FLNC* leads to the formation of protein aggregates which are cleared by an active protein quality control system including CASA pathway. For further verification, *in silico* protein-protein interaction was performed using online software and tools. The results showed evident interaction between *FLNC* and *BAG3* with significant binding score

(-826.6) between them.

PMID:36560844

Categorías: Trasplante cardíaco

Fecal Microbiota Transplantation and Other Gut Microbiota Manipulation Strategies

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Microorganisms. 2022 Dec 7;10(12):2424. doi: 10.3390/microorganisms10122424.

ABSTRACT

The gut microbiota is composed of bacteria, archaea, phages, and protozoa. It is now well known that their mutual interactions and metabolism influence host organism pathophysiology. Over the years, there has been growing interest in the composition of the gut microbiota and intervention strategies in order to modulate it. Characterizing the gut microbial populations represents the first step to clarifying the impact on the health/illness equilibrium, and then developing potential tools suited for each clinical disorder. In this review, we discuss the current gut microbiota manipulation strategies available and their clinical applications in personalized medicine. Among them, FMT represents the most widely explored therapeutic tools as recent guidelines and standardization protocols, not only for intestinal disorders. On the other hand, the use of prebiotics and probiotics has evidence of encouraging findings on their safety, patient compliance, and inter-individual effectiveness. In recent years, avant-garde approaches have emerged, including engineered bacterial strains, phage therapy, and genome editing (CRISPR-Cas9), which require further investigation through clinical trials.

PMID:36557677 | PMC:PMC9781458 | DOI:10.3390/microorganisms10122424

Categorías: Trasplante cardíaco

Assessment of Anti-Human Leukocyte Antigen (HLA)-Antibody-Dependent Humoral Response in Patients before and after Lung Transplantation

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Medicina (Kaunas). 2022 Nov 30;58(12):1771. doi: 10.3390/medicina58121771.

ABSTRACT

Background and Objectives: Testing for anti-human leukocyte antigen (HLA) antibodies both before and after transplantation is of fundamental significance for the success of lung transplantation. The aim of this study was the evaluation of anti-HLA immunization of patients before and after lung transplant who were subjected to qualification and transplantation. *Materials and Methods*: Prior to the transplantation, patients were examined for the presence of IgG class anti-HLA antibodies (anti-human leukocyte antigen), the so-called panel-reactive antibodies (PRA), using the flow cytometry method. After the transplantation, the class and specificity of anti-HLA antibodies (also IgG) were determined using Luminex. *Results*: In the group examined, the PRA results ranged from 0.1% to 66.4%. Low (30%) and average (30-80%) immunization was found in only 9.7% of the group examined. Presence of class I anti-HLA antibodies with MFI (mean fluorescence intensity) greater than 1000 was found in 42.7% of the patients examined, while class II anti-HLA antibodies were found in 38.4%. Immunization levels before and after the transplantation were compared. In 10.87% of patients, DSA antibodies (donor-specific antibodies) with MFI of over 1000 were found. *Conclusions*: It seems that it is possible to confirm the correlation between pre- and post-transplantation immunization with the use of the two presented methods of determining IgG class

anti-HLA antibodies by increasing the size of the group studied and conducting a long-term observation thereof.

PMID:36556973 | PMC:PMC9781897 | DOI:10.3390/medicina58121771

Categorías: Trasplante cardíaco

An Up-to-Date Literature Review on Ventricular Assist Devices Experience in Pediatric Hearts

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Life (Basel). 2022 Nov 30;12(12):2001. doi: 10.3390/life12122001.

ABSTRACT

Ventricular assist devices (VAD) have gained popularity in the pediatric population during recent years, as more and more children require a heart transplant due to improved palliation methods, allowing congenital heart defect patients and children with cardiomyopathies to live longer. Eventually, these children may require heart transplantation, and ventricular assist devices provide a bridge to transplantation in these cases. The FDA has so far approved two types of device: pulsatile and continuous flow (non-pulsatile), which can be axial and centrifugal. Potential eligible studies were searched in three databases: Medline, Embase, and ScienceDirect. Our endeavor retrieved 16 eligible studies focusing on five ventricular assist devices in children. We critically reviewed ventricular assist devices approved for pediatric use in terms of implant indication, main adverse effects, and outcomes. The main adverse effects associated with these devices have been noted to be thromboembolism, infection, bleeding, and hemolysis. However, utilizing left VAD early on, before end-organ dysfunction and deterioration of heart function, may give the patient enough time to recuperate before considering a more long-term solution for ventricular support.

PMID:36556366 | PMC:PMC9788166 | DOI:10.3390/life12122001

Categorías: Trasplante cardíaco

Impact of Left Ventricular Assist Devices on Days Alive and Out of Hospital in Hemodynamically Stable Patients with End-Stage Heart Failure: A Propensity Score Matched Study

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

Life (Basel). 2022 Nov 24;12(12):1966. doi: 10.3390/life12121966.

ABSTRACT

The two main surgical options to treat end-stage heart failure are heart transplantation (HTx) or left ventricular assist device (LVAD) implantation. In hemodynamically stable patients, the decision for HTx listing with or without LVADs is challenging. We analyzed the impact of both options on days alive and out of hospital (DAOH) and survival. This retrospective study screened all patients with HTx or LVAD implantation between 2010 and 2020. The main inclusion criterion was hemodynamic stability defined as independence of intravenous inotropic/vasoactive support at decision. Propensity score matching (PSM) was performed. The primary endpoint was DAOH within one year after the decision. Secondary endpoints included survival, duration until HTx, and hospitalizations. In total, 187 patients received HTx and 227 patients underwent LVAD implantation. There were 21 bridge-to-transplant (BTT)-LVAD patients (implantation less than a month after HTx listing or listing after implantation) and 44 HTx-waiting patients included. PSM identified 17 matched pairs. Median DAOH at one year was not significantly different between the groups (BTT-LVAD: median 281, IQR 89; HTx waiting: median 329, IQR 74; $p = 0.448$). Secondary endpoints did not differ significantly. Our data

suggest that BTT-LVAD implantation may not be favorable in terms of DAOH within one year for hemodynamically stable patients compared to waiting for HTx. Further investigations on quality of life and long-term outcomes are warranted.

PMID:36556331 | PMC:PMC9782187 | DOI:10.3390/life12121966

Categorías: Trasplante cardíaco

Central versus Peripheral Postcardiotomy Veno-Arterial Extracorporeal Membrane Oxygenation: Systematic Review and Individual Patient Data Meta-Analysis

Trasplante cardíaco - Vie, 12/23/2022 - 11:00

J Clin Med. 2022 Dec 14;11(24):7406. doi: 10.3390/jcm11247406.

ABSTRACT

BACKGROUND: It is unclear whether peripheral arterial cannulation is superior to central arterial cannulation for postcardiotomy veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

METHODS: A systematic review was conducted using PubMed, Scopus, and Google Scholar to identify studies on postcardiotomy VA-ECMO for the present individual patient data (IPD) meta-analysis. Analysis was performed according to the intention-to-treat principle.

RESULTS: The investigators of 10 studies agreed to participate in the present IPD meta-analysis. Overall, 1269 patients were included in the analysis. Crude rates of in-hospital mortality after central versus peripheral arterial cannulation for VA-ECMO were 70.7% vs. 63.7%, respectively (adjusted OR 1.38, 95% CI 1.08-1.75). Propensity score matching yielded 538 pairs of patients with balanced baseline characteristics and operative variables. Among these matched cohorts, central arterial cannulation VA-ECMO was associated with significantly higher in-hospital mortality compared to peripheral arterial cannulation VA-ECMO (64.5% vs. 70.8%, $p = 0.027$). These findings were confirmed by aggregate data meta-analysis, which showed that central arterial cannulation was associated with an increased risk of in-hospital mortality compared to peripheral arterial cannulation (OR 1.35, 95% CI 1.04-1.76, I2 21%).

CONCLUSIONS: Among patients requiring postcardiotomy VA-ECMO, central arterial cannulation was associated with an increased risk of in-hospital mortality compared to peripheral arterial cannulation. This increased risk is of limited magnitude, and further studies are needed to confirm the present findings and to identify the mechanisms underlying the potential beneficial effects of peripheral VA-ECMO.

PMID:36556021 | PMC:PMC9785985 | DOI:10.3390/jcm11247406

Categorías: Trasplante cardíaco

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