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(659)

Combined Heart Transplantation and Latissimus Dorsi Myo-Cutaneous Flap as Ultima Ratio Due to Severe Osteomyelitis Following LVAD Implantation and Total Sternectomy

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Introduction: Infections in LVAD-patients are common and may lead to life-threatening complications. Although driveline infections are most commonly detected, development of blood stream infections related to LVAD-implantation can also pilot towards mediastinitis and osteomyelitis, thus resulting in extensive bone destruction of the sternum.

Case Report: A 37-year-old patient was transferred to our heart failure unit following complete sternectomy due to severe osteomyelitis, mediastinitis and a pyopericardium three years after an emergent LVAD implantation. An LVAD weaning was not possible due to immediate compromise of hemodynamics. The patient presented a thorax apertum secured in vacuum therapy and persistent wound infection with 3 MRGN positivity. Through intensified antibiotic therapy, continuous wound dressing and renewal of vacuum therapy, the infection was controlled, and a stable status achieved. After excluding contraindications for heart transplantation (HTx), the patient was accepted for a high-urgency transplantation and successfully transplanted one month later. Thereupon, the thorax was surgically reconstructed using

an extended, right-sided latissimus-dorsi, myo-cutaneous flap. Relevant hemorrhage and partial repositioning of the flap was surgically approached two weeks after the initial procedure. Antibiotic treatment was continued to prevent superinfection and modified due to postoperative pneumonia and coloproctitis. The latissimus plastic showed continuous serous perfusion without inflammation, which was drained once weekly in an external clinic for two months. Echocardiography showed preserved biventricular function. Myocardial biopsies detected no higher-grade rejection as immunosuppression was established. After achieving full recovery, the patient was successfully discharged. Summary: Extended and undetected osteomyelitis can rapidly lead to lifethreatening mediastinitis and sepsis. Whenever inflammation parameters remain elevated, osteomyelitis should always be considered as a focus of infection on patients following LVAD-implantation. A combined heart transplantation and latissimus-dorsi plastic present a viable option for defect coverage and a possible long-term solution after extensive sternal resection in LVAD patients.

(660)

Humoral Response to SARS-CoV-2 mRNA Vaccine in Heart Transplant Recipients up to 4 Months After the Third Vaccine Injection V.M. Ferré,¹ Z. Brouk,² H. Flament,³ C. Kerneis,⁴ C. Charpentier,⁵ C. Verdonk,⁴ E. Vicaut,⁶ L. De Chaisemartin,⁷ D. Descamps,⁵ N. Houhou-Fidouh,⁸ and R. Dorent.⁴ ¹Virology, Université de Paris, IAME, UMR1137, INSERM, F-75018 Paris, France; AP-HP, Hôpital Bichat-Claude Bernard, Virologie, Paris, France; ²Cardiothoracic Surgery, AP-HP, Hôpital Bichat-Claude Bernard, Cadiologie, Paris, France; ³Université de Paris, CRI, INSERM U1149, INSERM, F-75018 Paris, France; AP-HP, Hôpital Bichat-Claude Bernard, Immunologie, Paris, France; ⁴AP-HP, Hôpital Bichat-Claude Bernard, Cardiologie, Paris, France; ⁵Université de Paris, IAME, UMR1137, INSERM, F-75018 Paris, France; AP-HP, Hôpital Bichat-Claude Bernard, Virologie, Paris, France; ⁶Université de Paris, Paris, France; AP-HP, Hôpital Lariboisière, Biostatistics and Clinical Research Department, Paris, France; ⁷Université Paris-Saclay, Inflammation, Microbiota and Immunopathology, INSERM UMR996, Chatenay-Malabry, France; AP-HP, Hôpital Bichat-Claude Bernard, Immunologie, Paris, France; and the ⁸AP-HP, Hôpital Bichat-Claude Bernard, Virologie, Paris, France.

Purpose: Recent studies reported poor to moderate humoral response after 2 vaccine doses in heart transplant recipients (HTR). Currently, French authorities recommend 2 and 3 vaccine injections for transplant recipients with and without prior SARS-CoV-2 infection, respectively. This study aimed to evaluate level and durability of humoral immunity with this vaccination strategy.

Methods: This single-center cohort study included HTR followed at Paris Bichat hospital between January 2020 and September 2021. Analyses were performed using automated immunoassays (Abbot) to quantify antispike IgG (cut-off \geq 7.1 BAU/mL) and anti-nucleocapsid IgG (cut-off index > 0.49). Categorical variables were described as number (%) and continuous variables with median (IQR).

Results: A total of 181 HTR (75.7% males, age 58 y [47-66]) transplanted between June 1990 and June 2021 were included. Median time from transplantation to first vaccine dose was 4.2 y [1.8-6.6]. 143 HTR (79%) had no SARS-CoV-2 infection history (HTRn) and 38 (21%) contracted the infection (HTRi) (56% before and 42% after vaccination initiation). After 2 vaccine doses, anti-S IgG seroconversion was observed for only 16% (n=12/76) of HTRn. Overall, anti-S IgG titers were lower in HTRn than in HTRi (0.5 [0.2-2.6] vs 578 [1.4-4449] BAU/mL, respectively, p=0.0001). The 3rd vaccine dose enabled to obtain 42% (n=33/72) of seroconversion among HTRn with median anti-S titers of 3.2 BAU/mL [0.4-35.0]. Only half seroconverters HTRn reached the 260 BAU/mL cut-off chosen by French authorities to define vaccination efficacy. Interestingly, these patients seem to have a sustained humoral response 4 months after the 3rd dose.

Conclusion: This study gives new insights on the effect of the 3rd vaccine dose in HTR with low rate of seroconversion and low titers of anti-S IgG but sustained humoral response when seroconversion occurs. Studies on vaccine efficacy against SARS-CoV-2 variants and cell-mediated immune response in this cohort are ongoing.



(661)

Long COVID-19 in Heart Transplant Recipients

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Purpose: The goal of this study was to assess the frequency and common symptoms of post-acute COVID-19 syndrome (Long COVID-19) in heart transplant recipients (HTR).

Methods: After obtaining IRB approval, we conducted telephone surveys of HTR (n=30) who had tested positive for SARS-CoV-2 to evaluate their experience with acute COVID-19 illness and assess symptoms of Long COVID-19. Symptoms at onset and also beyond 6, 12, and 24 weeks of the initial diagnosis were recorded. Additionally, medical charts were reviewed for detailed information regarding transplant history, immuno-suppression, COVID-19 management and hospitalization, and COVID-19 vaccination status.

Results: As noted in Table 1, among the 30 participants, 10 (33%) had symptoms consistent with Long COVID-19. Those with Long COVID-19 were more symptomatic during acute illness, with 40% of patients reporting cough, fevers or chills, and headaches, compared with 15%, 25%, and 20% respectively in those without Long COVID-19. Emergency department visits at initial illness (80% vs. 20%) and admission to the intensive care unit were more frequent (60% vs. 5%) in the Long COVID-19. Symptoms of Long COVID-19 lasted for a median of 9 weeks with 30% reporting ongoing symptoms at week 24. The most common persistent symptoms were depression, confusion, and difficulty concentrating.

Conclusion: This study is an early investigation of a complex syndrome of Long COVID-19 in transplant patients. Long COVID-19 is not well described in the transplant setting. HTR at our center with Long COVID-19 were sicker at their initial COVID-19 diagnosis and had more emergency room visits, hospital admissions, and longer hospital stays than those without subsequent Long COVID-19. Although, recall bias could affect participants' ability to remember details and symptoms, this would have impacted both groups similarly as the time since COVID-19 diagnosis to study enrollment was similar between the two groups. These are pre-liminary findings and the study is currently ongoing.

Table I. Demorraphics			COVID-19 variantes history				
	Limited COVID-19 in Heart Transplants (N-20)	Long COVID-19 in Heart Transplants (N-18)	Vaccination status at time of COVID-19	Unraccinated - 16 (80%) Unvaccinated -7 (70%)		Unvaccinated -7 (20%)	
Age, years	Median 56.5 (RQR 48.5-67.3)	Median 35.3 (828.63.5-69.5)	diagnosis	*Breakthrough -2 (20%) Partial vaccination - 1 (19%)		*Broakthrough -2 (20%) Partial vaccination 1 (10%)	
Grader	Male- 18 (90%)	Male- 5 (50%)	Days from COVID-19 diagnosis to subsequent	16 subsequently vaccinated		4 subsequently vacainated	
	Female- 2 (10%)	Femde- 4 (80%)	vaccination	Modian 166 (DQR 82-25	6	Median 167 (JQR 105-229)	
Device	Non-Histopic, 9 (#95)	Non-Westerley, 1 (1975)	Long COVID Parlines (N=14)				
	Hammiry 11 (1995)	Hopenic-4 (49%) Prefer not to identify: 1 (19%)	Paratise of comptone (Molice 8 VM 6-31)		Anade 1		
	Prefer not to identify-0		communication (communication)		3 months-2	3 months- 2	
Race	Diack-2 (10%)	Black-2 (20%)			6 months - 3	6 memba - 3	
	White-8 (40%)	White-3 (50%)	Symptoms at 6 works (Samber of patients reporting)		Shormess of breach -3		
	Parties and to identify & (40%)	Preserves an advantage of Charles			Cough-2		
Transplant History					Headache-3		
Ricard alone	16 (895)	9 (98%)	Serv throat 0				
Eleart hidary	1(20)	1099	Mysigian 3				
Time from transplant to COMD	Moline 1679-1008 ATL 14111	Median 1348 (ESE 664.1718)	Congistion-2				
infection (days)			Loss		Loss of Lots and	all of annual to the	
COVID-29 Area Infertion						Causes romang uns et appente- o	
Symptomatic or Asymptomatic	Symptomatic- 17 (82%)	Symphomatic - 10 (100%)			Confusion- 2		
Down (Down)	Anteplematic 3 (15%)	3.0040			Ek/flewity concentrating: 2		
Service of Frence	a fead	2 (2010)			Anxioy-2		
Cough	203%	4 (40%)			news role . 1		
Fermichills	5 (25%)	4(40%)	Symptoms at 12 works (Number of patients reporting)		Shormon of breath -1		
Finadaches	4 (20%)	4 (40%)		Coupi-1 Econsibilited			
Toticar	8(425)	4(85)	Bodete 1				
Other Could symptomy	(Kathour 2 (18%)	Loss of tasts and annell all (1963)			Sera throat -2		
	Multiser 1(19%)	Medicine: 4 (89%)				Myulgias- 0	
		Veniting or Dianhea = 3 (30%)			Loss of tests mell. 0		
Emergency Department visit	4(20%)	8 (99%)			Nauara'somiting lass of appetite-0		
Hespital Administra	4 (20%)	8 (80%)			Depression -1		
BCU admission	1.0%	61950			Difficulty concentrating- 0		
Elegated deration	57. Ann = 7.(19%)	17.dexx = 5.(50%)			Assisty 0 Shormess of breach -0 Cough-1 Ecumerichilts-0		
	1-2 weeks - 2 (10%)	1-2 weeks = 1 (19%) >2 weeks = 2 (29%)	Symptoms at 24 weeks (Number of patients reporting)				
	>2 weeks = 0						
Symptom duration	< or equal to 4 weeks = 16 (80%)	< or equal to 4 weeks= 5 (50%)			Headache-I		
	4.8 works = 1 (2%)	of made a 1/2000			Sore throat -0 Myulgias- 0		
	Never had comptoms = 3 (22%)						
Days from COVID-19 diagnosis to study	Median 258 days (RQR 258-392)	Median 204 days (8QR 60-296)			Congestion-0	-7.0	
encolment					Napata Vomiting	a been of apporting- 0	
COVID-19 management and outcomes	The second second	I de constante de constant			Depression -1		
Immunosoppression at COVID-19 Eugnosis	s incloands is (60%)		4		Confusion-1		
	Mucohendate 18 (10%)	Messehendate 3 (2012)				Difficulty concentrating-1	
	Similmus -8 (40%)	Similarus-4 (40%)			Assony, a		
	Ciclisporine-2 (19%)		New enset symptoms 4 weeks after COVID-19 (Number of patients		Preume crem part -		
COVID-19 specific treatment	Renderivie 3 (19%)	Rendesivir-7 (70%)	NONLINE)		Brain for.7		
	Management antibactics & (1971)	Manufact (20%) Manufactured antibacture 7 (20%)			Myalgins 1		
*Ersalchrough infuction (fully vaccinated prior to 2 (10%)		5 (505)	Severity (Number of patients reporting)	Severity (Number of patients reporting)		Mid-3	
COVIDI		- ()			Modenne-4		
BioMbcare utilization	Hospital days -1.5 (3QR 0-8)	Hospital days- median 3 (RpR 2.5-8.25)			Severo-1		
	KU days-0	ICU days-modian 1 (IQR 0-5.25)					
Charles and Control of States of States of States	Chipatarei vada-median 1 (KOK 1-125)	Outputent visite-median 1 (304.0-2)					

(662)

Do VAD Infections Predict Post-Heart Transplant Infections or Mortality?

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Purpose: Infections are common after ventricular assist device (VAD) implantation but how these infections impact post-heart transplant (HT) course in patients (pts) supported with short-term (ST) VADs is not fully defined. We investigated whether VAD infections had any impact on post-HT outcomes, such as development of post-HT infections or mortality.

Methods: We performed a retrospective cohort study of 185 HT recipients (HTRs) supported with ST-VADs from 4/2006-10/2020. VAD-specific and -related infections were characterized according to 2011 ISHLT definitions. Statistics were performed using IBM[®] SPSS Statistics version 25.0.

Results: Prior to HT, 41 (22.2%) pts had VAD infections involving the bloodstream (n=17), pump (n=8), pocket (n=2) and driveline (n=22); gram-positive and -negative organisms were responsible for 55.3% and 44.7% of infections, respectively. Pts with VAD infections were predominantly male (68.2%, p=0.19), Caucasian (60.9 %, p=0.59), had non-ischemic cardiomyopathy (61%, p=0.67), and a mean age of 52.6 (p=0.351) at VAD implantation. Those with VAD infections had no significant difference in underlying lung disease (26.8% vs 22.9%, p=0.60), hypertension (41.5% vs 33.3%, p=0.33), diabetes mellitus (29.3% vs 21.5%, p=0.30), or chronic kidney disease (53.7% vs 62.5%, p=0.76). Pts with VAD infections had longer duration of VAD support (513.3 d vs. 290.7 d, p=0.001), but were similar to those without VAD infection in terms of HT hospitalization length of stay (26 d vs 24 d, p=0.28), need for re-operation (19.4% vs 16.7%, p= 0.67), thymoglobulin induction (19.5% v. 21.5%, =0.78), cellular-rejection (12.2% vs 19.4%, p= 0.29), and antibody-mediated rejection (31.7% vs 27.8%, p=0.62). HTRs with prior VAD infections had more post-HT infections, but this did not reach statistical significance (53.6% vs 43.1%, p=0.23), with more bacterial (43.9% v. 30.6%, p=0.11), fungal (14.6% vs 8.3%, p=0.23), and C. difficile (9.8% vs 3.5%, p=0.11) infections. In those with and without pre-HT VAD infections, 1-year all-cause mortality was 14.6% vs 6.9% (p=0.12), and 1-year infection-related mortality was 4.8% vs 3.5% (p=0.65).

Conclusion: In this single center study, there were non-significant increases in post-HT infections and mortality in HTRs with prior VAD infections. Larger studies are needed to further investigate the impact of VAD infections on post-HT outcomes.

(663)

Incidence and Severity of Cytomegalovirus Infection in Seropositive Heart Transplant Recipients

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Purpose: Cytomegalovirus (CMV) infection contributes to morbidity and mortality in heart transplant recipients (HTR). Donor positive, recipient negative (D+/R-) patients are high risk and generally receive antiviral prophylaxis. The burden of CMV infection in recipient seropositive (R+) HTR is less clear, with preventative recommendations mostly extrapolated from other solid organ transplant groups. The aim of this retrospective cohort study was to define the incidence, severity of & risk factors for CMV infection in R+ HTR.

Methods: CMV seropositive HTR were included (2010-2019). Antiviral prophylaxis was not routinely used, with clinical monitoring the local