

Cardiac allograft vasculopathy. A disease on the search for therapy



Vasculopatía del injerto cardiaco: una enfermedad en busca de un tratamiento

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To this day, heart transplant is the treatment of choice in patients with heart disease and functional repercussions that is refractory to treatment (both drugs and electrical or mechanical devices) and has no contraindications. The milestone that made heart transplant take the spotlight in the management of these patients was the introduction of calcineurin inhibitors as basic immunosuppressants, which allowed the effective control of acute graft rejection. Immunosuppression patterns based on cyclosporine at the beginning and then on tacrolimus have led to really long survivals with means of up to 12 years.¹ After acute rejection was no longer the main cause of graft failure and occasionally the patient, the long-term survival of the graft is basically limited by the development of coronary vascular disease.

Graft vascular disease represents an accelerated phase of the underlying fibroproliferative process that affects the entire coronary vascular bed diffusely. On the pathological analysis, its appearance is different from classic atherosclerosis of complex and multifactor etiology in that it includes non-immunity factors and, in particular, immunity factors.² As a matter of fact, it is the most conspicuous manifestation of antibody-mediated late rejection, which is why it has sometimes been referred to as "chronic graft rejection". Its incidence based on the angiographic data we have is over 30%-50% from the third to the fifth year after the transplant which has a significant impact on prognosis: it is the leading cause of graft failure and one of the leading causes of death in recipients with long survival rates.³ Also, the management of this process is relatively limited because of its diffuse nature that makes coronary revascularization procedures more difficult.

In the study conducted by Solano-López Morel et al.⁴ and recently published on *REC: Interventional Cardiology*, authors from 2 experienced groups revealed their results with percutaneous revascularization with drug-eluting stents in one of the most severe forms of graft vascular disease: chronic total coronary occlusion. The authors confirmed that the technique was feasible since it used state-of-the-art diagnostic and therapeutic technological means, although they

restricted it to highly selected patients. The findings show that chronic total coronary occlusion has a low but still significant prevalence (12.2% of the patients), late onset (mean, 10 years after the transplant), and even in experienced hands it is barely eligible for percutaneous revascularization (13.5% of the patients with chronic total coronary occlusions). Although the angiographic results are promising (93% of initial success and 2% restenosis only), the prognosis of these patients is still poor (a 21.4% cardiovascular mortality rate with a mean at follow-up of 2.8 years) even compared to graft vascular disease without complete occlusion treated percutaneously (21.4% vs 8.3%). Although the study sample is limited, it would have been interesting to draw a comparison between patients with chronic total coronary occlusions treated percutaneous or medically.

The most important thing of the study conducted by Solano-López Morel et al.⁴ is that it is the first time that the feasibility of the recanalization of chronic total coronary occlusions in graft vascular disease is ever reported. The results are indicative that in these patients, percutaneous procedures are nothing more than palliative care *sensu stricto* whose effectiveness in clinical terms has not been confirmed yet (and probably never will). This comes as no surprise since graft vascular disease is a diffuse and progressive disease that affects both the epicardial coronary arteries and the intramyocardial trajectories and especially the capillary bed. Therefore, same as it happens with other conditions, the most effective management is preventive treatment targeted at well-known etiopathogenic factors including taking good care of the donor, preventing graft primary failure, preventing and treating cytomegalovirus-related infections, the universal use of statins (such as hypolipemiant and immunomodulating statins), and preventing antibody-mediated acute and chronic cell rejection through the use of individual immunosuppression therapies for each patient.⁵

CONFLICTS OF INTEREST

None declared.

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REFERENCES

1. González-Vílchez F, Almenar-Bonet L, Crespo-Leiro MG, et al. Spanish Heart Transplant Teams; collaborators in the Spanish Heart Transplant Registry, 1984-2017. Spanish Heart Transplant Registry. 29th Official Report of the Spanish Society of Cardiology Working Group on Heart Failure. *Rev Esp Cardiol.* 2018;71:952-960.
2. Hernandez JM, de Prada JA, Burgos V, et al. Virtual histology intravascular ultrasound assessment of cardiac allograft vasculopathy from 1 to 20 years after heart transplantation. *J Heart Lung Transplant.* 2009;28:156-162.
3. Chih S, Chong AY, Mielniczuk LM, Bhatt DL, Beanlands RS. Allograft Vasculopathy: The Achilles' Heel of Heart Transplantation. *J Am Coll Cardiol.* 2016;68:80-91.
4. Solano-López Morel J, Fernández-Díaz JA, Martín Yuste V, et al. Outcomes of percutaneous coronary interventions of chronic total occlusions in heart transplant recipients. *REC Interv Cardiol.* 2019;1:152-160.
5. Tremblay-Gravel M, Racine N, de Denuis S, et al. Changes in Outcomes of Cardiac Allograft Vasculopathy Over 30 Years Following Heart Transplantation. *JACC Heart Fail.* 2017;5:891-901.