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REFERENCES

1. Tavazzi G, Zanierato M, Via G, Iotti GA, Procaccio F. Are neurogenic stress cardiomyopathy and Takotsubo different syndromes with common pathways? Etiopathological insights on dysfunctional hearts. J Am Coll Cardiol HF 2017;5:940–2.

2. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J 2008;155:408–17.

3. Kantor ED, Rehm CD, Haas JS, Chan AT, Giovannucci EL. Trends in prescription drug use among adults in the United States from 1999-2012. JAMA 2015;314:1818–31.

4. U.S. FDA. Label. December 21, 2017. Available at: https://google2.fda.gov/search?as_sitesearch=https://www.accessdata.fda.gov/drugsatfda_docs/label/2017&q=takotsubo&client=FDAgov&site=FDAgov&lr=&proxystylesheet=FDAgov&requiredfields=-archive:Yes&output=xml_no_dtd&getfields=*&ie=UTF-8&ulang=en&&access=p&sort=date:D:L:d1&entqr=1&entqrm=0&wc=200&wc_mc=1&oe=UTF-8&ud=1. Accessed January 16, 2018.

REPLY: There Should Not Be Much Doubt That Neurogenic Stress Cardiomyopathy in Cardiac Donors Is a Phenotype of Takotsubo Syndrome, and Takotsubo Common Pathways and SNRI Medications

We appreciate Prof. Madias's insightful comments on our paper and strong endorsement of our hypotheses (1). He suggests additional potential solutions for better management of donors with dysfunctional hearts, including sympathetic activity monitoring, donor heart "nursing" with cardiac mechanical support, and ultimately, donor centralization in dedicated "donor ICUs." These approaches, although stimulating and promising, are likely to pose remarkable logistical, organizational, economic, and resource-allocation challenges; however, we will have to accept these challenges if we aim to determine which transiently dysfunctional hearts are suitable for transplantation. Furthermore, as donor management teams do not currently include professionals specifically trained in the complex and evolving field at the boundary between cardiology and critical care, we believe that the development of a new set of medical skills and competences in "donor cardiology and critical care" would now be required. The increasing awareness of the complexity of this field needs to be matched by a growing specialization in a multimodal diagnostic and therapeutic strategy, aiming at a comprehensive, individually tailored donor approach. This is likely to represent an additional task for the expanding domain of acute cardiac care.

The topic discussed by Dr. Woronow and colleagues is extremely interesting and largely underreported. The interaction between neurohormones/catecholamine (both exogenous and endogenous) on the cardiovascular system and other organs is a matter of daily debate in clinical and scientific settings, and especially in intensive care (2,3).

One thought, which has already been discussed elsewhere (4), is that Takotsubo syndrome is likely a well codified clinical entity, part of a wider "family" of cardiomyopathy that can be caused by an incredibly variety of triggers.

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REFERENCES

1. Tavazzi G, Zanierato M, Via G, Iotti GA, Procaccio F. Are neurogenic stress cardiomyopathy and Takotsubo different syndromes with common pathways? Etiopathological insights on dysfunctional hearts. J Am Coll Cardiol HF 2017;5:940–2.

2. Tarvasmäki T, Lassus J, Varpula M, et al., for the CardShock Study Investigators. Current real-life use of vasopressors and inotropes in cardiogenic shock—adrenaline use is associated with excess organ injury and mortality. Crit Care 2016;20:208.

3. Singer M. Catecholamine treatment for shock—equally good or bad? Lancet 2007;370:636–7.

4. Sarapultsev PA, Sarapultsev AP. Stress cardiomyopathy: is it limited to Takotsubo syndrome? Problems of definition. Int J Cardiol 2016;221:698–718.

Solid Organ Transplantation

Recent contributions from the Montreal Heart Institute (Montreal, Quebec, Canada) and Heart Failure and Transplantation Section, Vanderbilt Heart and

Vascular Institute (Nashville, Tennessee) describe gains made in heart transplantation over the last 3 decades (1,2). These analyses underline success in lowering smoking rates in cardiac graft recipients, also recently echoed by liver and lung transplantation groups, but not yet duplicated in modern renal transplantation populations, as smoking cessation is not yet mandated by guideline. Notable also are reductions in use of steroid and increases in platelet inhibition associated with newer immunosuppressive protocols. These newer therapies have had an impact on allograft vasculopathy more likely due to smoking cessation, ubiquitous statin use, and avoidance of transplantation in populations with moderate or severe renal insufficiency than to the newer immunosuppressive regimens. Although focus on avoidance of patients at high risk for adverse prognosis, graft failure and allograft vasculopathy are important, it should be recognized that after solid organ transplantation and its initial rejection phenomena, the greatest hazard to recipient survival relates to the immunocompromised state. Current protocol-driven immunosuppression does not take into account additional comorbidities such as diabetes (either as a primary concern or secondary to immunosuppression) (3) or smoking history (current, prior, or never) (4), which are linked to adverse noncardiovascular outcomes in solid organ transplant patients.

The demonstration of decreased all-cause mortality (and composite, retrospectively defined major adverse cardiac events) over the past decades should now highlight the main issues in improving long-term survival for solid allograft recipients. All-cause mortality will only be reduced when we address the predominant and potentially avoidable causes for nonsurvival: infection and malignancy (5). In this regard, there may be some interest in lowering immunosuppressive doses and in using calcium-channel blockers to assist in treatment of antibiotic-resistant infections including gram negative organisms, tuberculosis, malaria, schistosomiasis, and immunosuppressed transplant recipients (6). Do the authors have any infection-related outcomes with respect to use of calcium-channel blockers?

Additional control of comorbidities such as diabetes (either as a primary problem or secondary to immunosuppression); modified courses of immunosuppression ("personalized immunosuppression") (2,3,5); advanced vaccination protocols; calcium-channel (6) or beta-blockade (7); or smoking cessation efforts to improve the excess risk of infectious death is worth exploring. Our aim to increase the longevity of solid organ transplant recipients requires a concerted effort to combine the skills of cardiologists with those of other specialties currently treating solid organ recipients. An international, easily searchable dataset combining all solid organ transplantations and identifying predefined and centrally adjudicated noncardiovascular and cardiovascular endpoints would be a good start.

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REFERENCES

1. Tremblay-Gravel M, Racine N, de Denus S, et al. Changes in outcomes of cardiac allograft vasculopathy over 30 years following heart transplantation. J Am Coll Cardiol HF 2017;5:891–901.

2. Gupta R, Schlendorf K, Lindenfeld J. Older and wiser: personalized immunosuppression in the current era. J Am Coll Cardiol HF 2017;5:943–5.

3. Weinrauch LA, D'Elia JA, Weir MR, et al. Does diabetes impact therapeutic immunomodulation therapy for kidney transplant recipients? Data from the Folic Acid for Vascular Outcome Reduction In Transplant (FAVORIT) trial. Int J Nephrol Renovasc Dis 2017;10:233–42.

4. Weinrauch LA, Liu J, Claggett B, et al. Smoking and outcomes in kidney transplant recipients: a post hoc survival analysis of the FAVORIT trial. Int J Nephrol Renovasc Dis 2018. In press.

5. Weinrauch LA, D'Elia JA, Weir MR, et al. Infection and malignancy outweigh cardiovascular mortality in kidney transplant recipients: post hoc analysis of the FAVORIT trial. Am J Med 2018;131:165–72.

6. Weinrauch LA, Liu Jiankang, Claggett B, Finn P, Weir MR, D'Elia JA. Calcium channel blockade and survival in recipients of successful renal transplant: an analysis of the FAVORIT trial results. Int J Nephrol Renovasc Dis 2018;11:1–7.

7. Ciarka A, Lund LH, Cleemput JV, Voros G, Droogne W, Van Haeke J. Effect of heart rate and use of beta blockers on mortality after heart transplantation. Am J Cardiol 2016;118:1916–21.

REPLY: Solid Organ Transplantation

We thank Drs. Weinrauch and D'Elia for their interest in our paper (1) and are pleased that they support the concept of personalizing immunosuppression (IS) regimens to account for comorbidities in aging transplant recipients and agree that complications of IS threaten survival.

Regarding calcium-channel blockers, we do not have any evidence that these agents are associated with improved infectious outcomes in the post-transplantation population. With respect to