JACC: CASE REPORTS VOL. 4, NO. 23, 2022

CASE REPORT

ADVANCED

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

Heart-Kidney Transplantation in a Transgender Woman

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ABSTRACT

We describe the care of a transgender woman with heart failure who underwent heart-kidney transplantation. Perioperative management of hormone therapy, considerations for future gender-affirming surgeries, and psychosocial aspects of care are discussed. Interdisciplinary collaboration is essential in the treatment of patients with advanced heart failure in the setting of gender-affirming therapies. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:101523) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 55-year-old transgender woman (pronouns: she/her) with advanced heart failure (HF) due to nonischemic cardiomyopathy and chronic kidney disease presented with cardiogenic shock. Briefly, she had received a diagnosis of stage C HF and left ventricular ejection fraction of 25% 10 years prior. Despite subsequent initiation of maximally tolerated guideline-directed medical and device therapy (including carvedilol 25 mg twice daily, spironolactone 50 mg daily, sacubitril-valsartan 49-51 mg twice daily, isosorbide-dinitrate-hydralazine 20.0-37.5 mg 3 times daily, and cardiac resynchronization therapy), her left ventricular function did not improve. Shortly after her HF diagnosis, the patient initiated intramuscular estrogen (in addition to her spironolactone) for gender-affirming hormone

LEARNING OBJECTIVES

- To review the types of gender-affirming hormone therapy and their implications for perioperative management in the setting of advanced heart failure therapies.
- To identify considerations for pursuing gender-affirming surgery after heart-kidney transplantation.
- To recognize the unique psychosocial aspects of care for patients with advanced heart failure who identify as transgender, and the importance of interdisciplinary team collaboration.
- To demonstrate the feasibility of heart-kidney transplantation in patients undergoing gender-affirming therapies.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received April 10, 2022; revised manuscript received June 13, 2022, accepted June 21, 2022.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2022.06.013

ABBREVIATION AND ACRONYM

HF = heart failure

therapy. Two years before presentation, she began to express interest in gender-affirming surgery. Despite her description of stable New York Heart Association functional class II capacity, it was believed that her left ventricular function was not sufficient to safely support major noncardiac surgery, and therefore surgery was deferred. Finally, her history was also notable for a proximal deep vein thrombosis 1 year earlier while she was using hormone therapy. There were no risk factors for thrombus other than her use of estrogen. Given that she wished to continue with hormone therapy, the patient and her clinicians elected to initiate and continue full-dose anticoagulation (apixaban 5 mg twice daily) for a prolonged treatment course after a risk:benefit discussion.

On presentation to the emergency department, she was afebrile, with heart rate of 96 beats/min, blood pressure of 90/68 mm Hg, respiratory rate of 16 breaths/min, and oxygen saturation of 96% on room air. The physical examination was notable for jugular venous distention and lower extremity edema. Laboratory results were notable for lactic acid of 7.0 mmol/L and creatinine of 7.0 mg/dL (baseline 4.0 mg/dL). Right heart catheterization demonstrated right atrial pressure 23 mm Hg, pulmonary artery pressure 82/34 (mean 49) mm Hg, pulmonary capillary wedge pressure 30 mm Hg, and cardiac index 1.8 L/min. An intra-aortic balloon pump was placed, intravenous inotropic agents were started, and continuous renal replacement therapy was initiated. In the coming days, she was unable to be weaned from hemodynamic support. Given her critical state and longstanding history of left ventricular dysfunction, a formal evaluation for suitability for advanced cardiac therapies was initiated by our interdisciplinary team. After considering a left ventricular assist device, heart-kidney transplantation, and supportive/palliative care, the patient and our team elected to pursue dual organ transplantation. Given her pulmonary hypertension, an axillary transaortic axial flow temporary ventricular assist device was placed, which brought her pulmonary pressures to an acceptable range for heart transplantation, and she was subsequently listed as United Network for Organ Sharing status 2 for heart and kidney transplantation.

Regarding the patient's hormone therapy, an interdisciplinary discussion was held among the patient and specialists from the cardiology, endocrinology, hematology, and cardiac behavioral medicine services regarding the risks and benefits of continuing estrogen in the pretransplantation setting. Ultimately, a patient-centered decision was made to continue estrogen therapy but to switch from intramuscular estradiol valerate 10 mg to the lowest weekly transdermal estradiol patch (0.025 mg/day) to mitigate the risk of thromboembolism. Our patient endorsed a desire to minimize the risks of adverse outcomes while awaiting transplantation, even if this meant adjusting her hormone therapy. In the setting of worsening renal function, spironolactone was also held. Regarding anticoagulation, she received maintenance unfractionated heparin in the setting of temporary mechanical circulatory support.

QUESTION 1: WHAT ARE THE TYPES OF GENDER-AFFIRMING HORMONE THERAPY AND THEIR CARDIOMETABOLIC EFFECTS?

Gender-affirming hormone therapy aims to shift the hormone levels so that sex characteristics better align with a patient's gender identity. Dose titration focuses on target hormone levels and individual responses while striving to use the lowest effective dose to minimize adverse side effects and maximize psychosocial benefits. The foundations of therapy for male and female patients who identify as transgender include testosterone and estrogen preparations, respectively (**Table 1**). For transgender women, estradiol alone is often not sufficient to suppress endogenous testosterone, and spironolactone or gonadotropin-releasing hormone agonists are commonly used as adjunctive treatment. The adverse effects of these therapies are well described (**Table 1**) and include an estimated 2- to 4-fold risk of venous thromboembolism for patients using estrogen therapy.[1] Among estrogen preparations, transdermal and injectable estradiol cypionate or valerate may be associated with a lower thromboembolic risk.[2] Data on potential adverse cardiovascular effects of hormone therapy are limited; however, some epidemiologic studies suggest an increased long-term risk for myocardial infarction and death resulting from cardiovascular disease for patients using hormone therapy.[3]

QUESTION 2: HOW DOES THE PATIENT'S HORMONE THERAPY AFFECT PERITRANSPLANTATION MANAGEMENT?

The risks and benefits of continuing or ceasing hormone therapy in the setting of organ transplantation must be discussed with the patient and the interdisciplinary team. In particular, mechanical circulatory support[4] and estrogen therapy[1] are associated with an increased risk of venous thromboembolism. Notably, the majority of available evidence regarding sex hormones and thromboembolism is focused on

TABLE 1 Gender-Affirming Hormone Therapies

Route	Formulation	Frequency	Potential Adverse Effects
Estrogen and antiandrogen regimens for transgender women			
Estrogen			Thromboembolic disease Hyperprolactinemia ?Breast cancer
Oral	Estradiol	Daily	
Parenteral	Estradiol valerate or cypionate	SQ every 2 weeks IM every week	
Transdermal	Estradiol	Twice weekly	
Antiandrogens	GnRH agonist (leuprolide)	Monthly	Dehydration, hyponatremia
	Histrelin implant	Every 12 months	Bone loss (if not combined with estradiol)
	Spironolactone	Daily	Hyperkalemia
Testosterone regimens for transgender men			
Testosterone Oral (not available in the U.S.)	Testosterone undecanoate	Daily	Erythrocytosis Hypertension Obstructive sleep apnea Osteoporosis Hyperlipidemia ?Liver dysfunction
Intranasal	Testosterone nasal gel	3 times daily	
Parenteral	Testosterone enanthate or cypionate	SQ or IM every 2 weeks	
Transdermal	Testosterone gel (1%)	Daily	
	Testosterone patch	Daily	
Implant	Testosterone pellets	Every 3 to 6 months	

Data derived from Tangpricha et al,[2] Connelly et al,[3] and Jurgens et al.[9]
SQ = subcutaneous; IM = intramuscular.

cisgender patients and/or postmenopausal women, with little available data on individuals who identify as transgender. Thus, hormone therapy in the peritransplantation period should be prescribed or withdrawn on an individual basis, taking into account individual risk factors for thrombus and patient preferences. For antiandrogen therapy, the potential harms of stopping spironolactone include associated revirilization and psychological distress.[5] Gonadotropin-releasing hormone agonists may be considered as an alternative regimen if adverse effects arise after antiandrogen therapy is stopped.

There are also important considerations with regard to hormone therapy while a patient is using immunosuppressive agents. Both tacrolimus and estradiol are metabolized through the CYP450 3A4 enzyme complex, such that estradiol can induce lower tacrolimus metabolism with some variability by individual and by estradiol preparation.[6] Thus, in patients receiving estradiol, tacrolimus trough levels and renal function must be monitored closely.

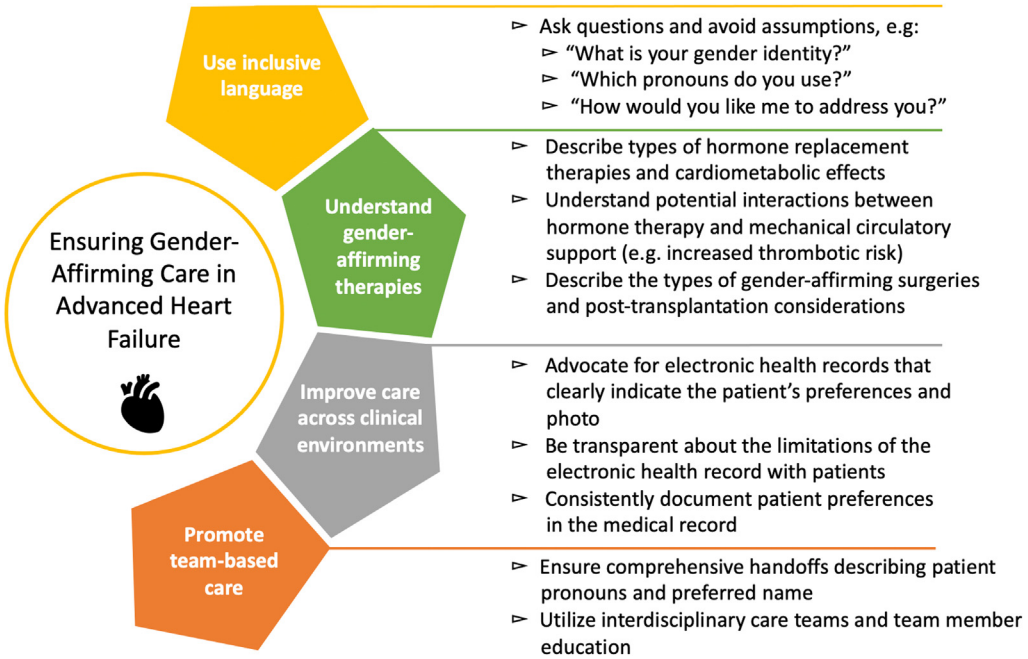
It should be noted that access to gender-affirming medical care has important—even lifesaving—health benefits for patients who desire these services. Patients who identify as transgender and have access to gender-affirming therapies report less psychological distress and suicidal ideation than do adults who are unable to access services.[7] Thus, clinicians should be aware that withdrawal of these therapies in the peritransplantation period may have significant psychological consequences.

QUESTION 3: WHAT CONSIDERATIONS ARE THERE FOR PURSUING GENDER-AFFIRMING SURGERY AFTER HEART TRANSPLANTATION?

For transgender women, common gender-affirming surgeries include feminizing vaginoplasty, augmentation mammoplasty, and facial feminization. For transgender men, common surgeries include masculinizing phalloplasty/scrotoplasty, metoidioplasty, and masculinizing chest surgery.[8] Procedural complications depend on the type of surgery, but in general they include bleeding, infection, wound complications (due to immunosuppressed status), and venous thromboembolism.

Before transplantation, it is important to address the following questions with patients regarding the potential for future gender-affirming surgery: the gender-affirming surgeries desired, and the potential post-transplantation complications that may make it necessary to delay or defer gender-affirming surgery. There are currently no guidelines on the optimal timing for transplantation recipients who identify as transgender pursuing noncardiac surgery. In general, elective surgical procedures are deferred until after the first 6 to 12 months after transplantation until immunosuppression is at a lower and stable dose and when there is a lower risk of graft dysfunction.[9] The benefits of deferring these surgeries should be weighed against the risks of psychological distress that may be experienced by the patient. Additionally, access to essential

FIGURE 1 Strategies for Ensuring Gender-Affirming Care in Advanced Heart Failure



services like gender-affirming surgery can be stymied by a lack of insurance or growing waiting lists in the aftermath of the COVID-19 pandemic.[10] Therefore, interdisciplinary teams should work together to individualize the care plan for each patient, taking into account the medical and psychological risks of pursuing versus delaying surgery. Anesthetic and perioperative management of intercurrent surgery in heart transplantation recipients should follow current guidelines.[11]

QUESTION 4: WHAT DOES PROVIDING PATIENT-CENTERED GENDER-AFFIRMING CARE FOR PATIENTS UNDERGOING HEART TRANSPLANTATION LOOK LIKE?

The transplantation process, in particular heart transplantation, includes lengthy hospitalizations and multiple procedures and can be anxiety provoking, stressful, and psychologically taxing. The stressors and emotions associated with transplantation, such as feelings of lack of autonomy, may be exacerbated in patients who identify as transgender, in particular those who experience stigmatization at the intersection of multiple marginalized identities (ie, Black, transgender, female).[12] Our patient, a woman who identifies as Black and transgender, aptly stated that "people need to know how to take care of Black trans women."

Delivering culturally humble gender-affirming care can support one's sense of identity during the transplantation process. Affirming care involves clinician-level, team-level, and systems-level behaviors (Figure 1). Clinician-level actions include asking questions and avoiding assumptions, particularly related to pronouns, preferred name, and preferences, and team-level changes may involve thoughtful handoffs (eg, reinforcing correct pronoun usage to avoid misgendering the patient) and staff education. As an example of a systems-level barrier to gender-affirming care, during our patient's hospitalization, electronic health record constraints required that her legal name be displayed on the system dashboard and also on any labels for blood draws or diagnostic testing. This resulted in microaggressions and misgendering that exacerbated the patient's distress and symptoms of anxiety and depression. Updating the patient's photo in the electronic health record and posting her pronouns on the door to her hospital room created a more inclusive environment for her recovery and care.

CASE RESOLUTION

The patient underwent successful heart-kidney transplantation on hospital day 102. In the early postoperative period she experienced a deep vein thrombosis. Given that she also had a history of prior

thrombus in the setting of hormone therapy, the patient and her clinicians elected to re-initiate therapeutic anticoagulation in the post-transplantation setting and to defer restarting estrogen until she could safely be given anticoagulation agents again. On postoperative day 8, she experienced a pericardial effusion after her first endomyocardial biopsy and required a pericardiocentesis. In this setting, resumption of therapeutic anticoagulation and hormone therapy were deferred to the outpatient setting, given the need for repeated endomyocardial biopsies for rejection surveillance. She was discharged to rehabilitation on postoperative day 20, with normal function of both grafts. She continues to engage in close follow-up with plans to re-initiate hormone therapy within 3 months.

CLINICAL PERSPECTIVES

This case illustrates the feasibility of, and considerations for, heart-kidney transplantation in a patient who identifies as transgender and is receiving gender-affirming hormone therapy, which to our knowledge has not yet been reported in the published literature. This case demonstrates the importance of understanding the risks and benefits of gender-affirming hormone therapy in the perioperative setting and of providing compassionate patient-centered gender-affirming care to patients undergoing heart transplantation.

ACKNOWLEDGMENTS The authors thank their patient for the privilege of participating in her care and for her invaluable input in the writing of this manuscript.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr. Wilcox has received consultative fees from Amgen, Abbott, Abiomed, and Novartis; and serves on the scientific advisory boards for Abiomed and Cytokinetics. Dr. Pham has received consultative fees from Medtronic, Abbott, and Abiomed. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS awareness, cardiac transplantation, systolic heart failure, thrombosis