Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

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HeartWare Thrombosis After mRNA COVID-19 Vaccination

To the Editor: A woman in her late 50s with end-stage heart failure secondary to nonischemic dilated cardiomyopathy was implanted with a HeartWare left ventricular assist device (LVAD) as bridge to transplant. She was not known to have a hypercoagulable condition and in the 6 years supported on the LVAD before presentation had not experienced power elevations, high watts alarms, or any evidence of hemolysis/thrombosis or hemocompatibility-related adverse event. She was not actively listed for transplant because of personal preference.

She received the initial series of 2 COVID-19 vaccinations with the BNT162b2 (Pfizer-BioNTech COVID mRNA vaccine) and underwent COVID-19 booster 7 months later. She had no immediate reaction and described only arm soreness after the booster. Eight days later, she noted an episode of tea-colored urine but did not notify the LVAD team. Eleven days after the booster, the LVAD team was contacted with concerns of chest pressure and high watts alarms, and the patient reported to the emergency department. There, an episode of hematuria was noted; international normalized ratio was 2.9, and metabolic panel returned hemolyzed. All international normalized ratio readings in the 2 months preceding admission were between 2.4 and 3.9; none were subtherapeutic. She had been compliant with daily aspirin 325 mg daily since implantation.

On admission, powers were noted to be elevated, and initial lactate dehydrogenase (LDH) level was above 3000 U/L. Pump thrombosis was diagnosed, and United Network for Organ Sharing listing status was upgraded appropriately. During the hospitalization course, despite adequate antithrombotic therapy (tirofiban, heparin, and aspirin 325 mg twice daily), powers continued to rise (Figure A, C) and LDH remained markedly elevated (Figure C). HeartWare powers and estimated flows exceeded 20 W and 10 L/min, respectively, and LDH levels peaked at 4458 U/L (Figure C). Given concerns for imminent pump stoppage, she underwent exchange from HeartWare to HeartMate 3 (Thoratec) 10 days after admission, with HeartWare device demonstrating thrombus within the pump housing (Figure B).

COVID mRNA vaccinations are broadly recommended for all patients, including those supported on LVAD therapy, with exceedingly low risk of complications after vaccination.[1] Yet, reports have described increased arterial thromboembolism risk and cerebral venous sinus thrombosis risk after Pfizer-BioNTech vaccine[2] and an increased venous thromboembolism signal after the first Pfizer-BioNTech vaccine dose.[3] These observations highlight the possibility that a proinflammatory milieu after vaccination may increase the risk of thrombosis on rare occasions.

Vaccine-induced thrombotic thrombocytopenia and thrombosis with thrombocytopenia syndrome are phenomena that have been reported after COVID vaccinations with pathophysiologic mechanisms that are presently being studied.[4,5] Our patient received a Pfizer-BioNTech vaccine 8 days before report of tea-colored urine, had a platelet count of less than 150×10^9/L before device exchange, and had confirmed device thrombosis but did not complete all the testing required for the diagnosis to be made before device exchange, raising consideration for potential risk of thrombosis for patients on the thrombosis with thrombocytopenia syndrome spectrum.

Additional reports from other centers with LVAD-supported patients who receive COVID vaccinations may help elucidate a causality and begin to estimate a frequency of what is suspected to be a rare phenomenon. This experience does not represent a contraindication to vaccination; rather, it highlights the importance for LVAD clinicians to remain vigilant and to avoid neglecting an LDH rise or reports of dark urine in the context of recent COVID-19 vaccination among LVAD-supported patients.

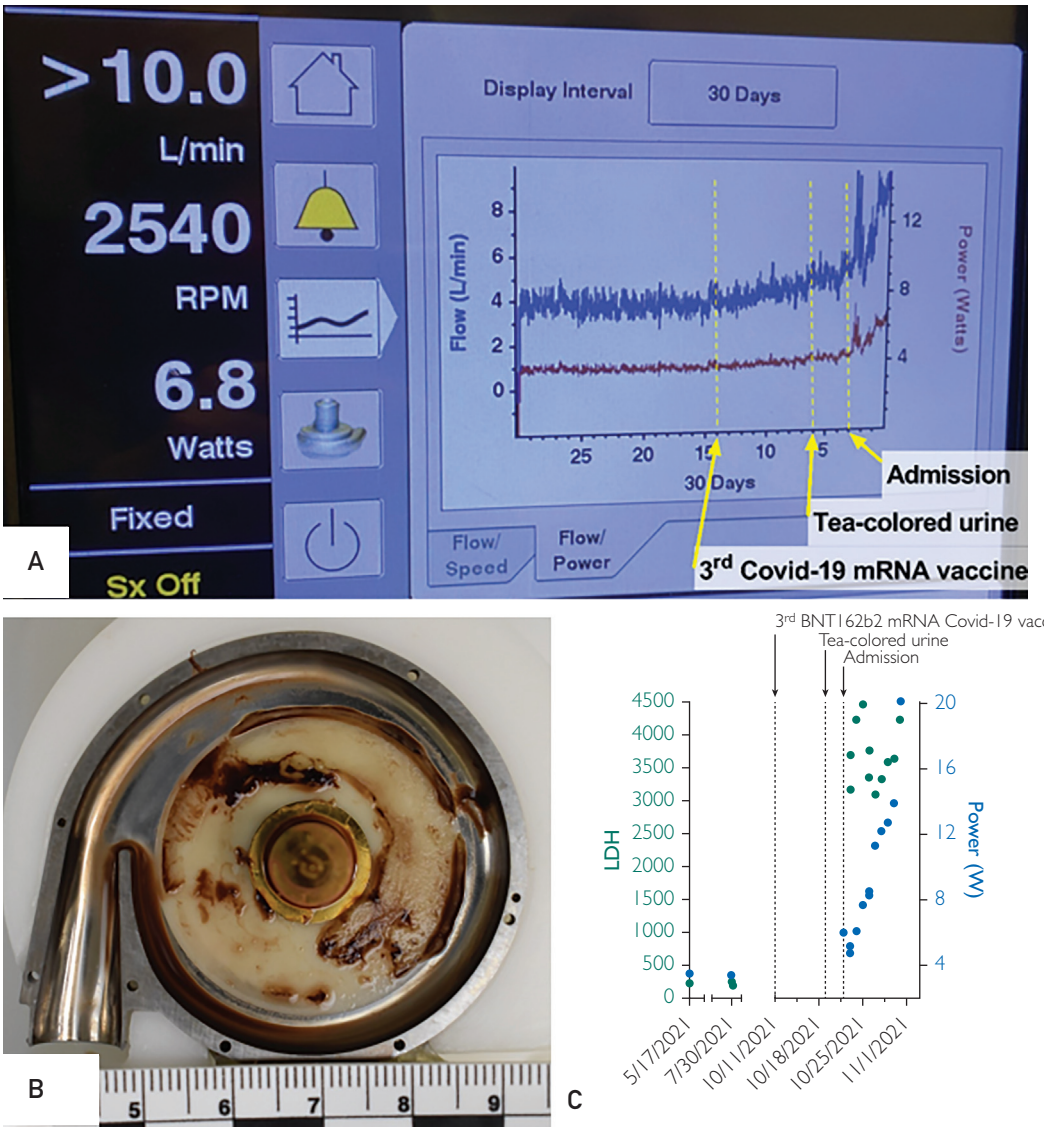

FIGURE. A, HeartWare power and flow waveforms during early hospitalization. Dates of Pfizer-BioNTech COVID-19 booster, symptoms, and admission are superimposed. B, Image from pathology report demonstrating evidence of thrombus within the HeartWare device. C, Timeline of HeartWare power and lactate dehydrogenase (LDH) in the context of thrombosis. Baseline values and dates of vaccination, symptoms, and admission are shown relative to biomarker trends.

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

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Melatonin's Potential Side Effects: It May Be in Your Genes

To the Editor: According to a recent study using data from the 1999-2000 through 2017-2018 cycles of the National Health and Nutrition Examination Survey (NHANES), the prevalence of melatonin supplement consumption, including self-reported use of more than 5 mg/d of melatonin, significantly increased over time.[1] More specifically, the overall reported prevalence of melatonin use increased from 0.4% in 1999-2000 to 2.1% in 2017-2018. Furthermore, the prevalence of melatonin use of more than 5 mg/d rose from 0.08% in 2005-2006 to 0.28% in 2017-2018.[1] These NHANES findings received a great deal of public attention (Altmetric score on March 31, 2022: 1014), including a discussion of possible safety concerns about melatonin. But what are the potential adverse effects of melatonin? According to a recent meta-analysis including data from 79 studies with 3861 participants, melatonin, even when taken in a higher dose (≥10 mg/d) and for 3 months or longer, was not associated with an increased risk of serious adverse effects events. However, a 40% increase in adverse events was found, but these were primarily limited to headache, dizziness, and drowsiness.[2]

Surprisingly, in the discussion of melatonin's safety profile, little attention has been paid to the genetic polymorphism rs10830963 in the melatonin receptor 1B (*MTNR1B*) gene carried by about 30% of the general population.[3] Carriers of the risk G allele of single-nucleotide polymorphism rs10830963 show higher expression of *MTNR1B* in β cells in pancreatic islets compared with noncarriers.[3] Through binding to MTNR1B, melatonin acutely blocks glucose-induced insulin secretion by β cells.[3] Thus, those carrying copies of the G allele where pancreatic expression of *MTNR1B* is increased may show impaired postprandial glucose disposal under the impact of melatonin. In line with this assumption, a randomized crossover study of 845 participants found that an oral glucose tolerance test scheduled 1 hour before habitual bedtime (ie, a time of the day when endogenous melatonin rises in the blood) resulted in lower insulin release and higher plasma glucose concentration. Notably, the effect of late eating impairing glucose tolerance was stronger in carriers of the G allele than in noncarriers.[4] These findings could also explain why the G allele of *MTNR1B* rs10830963 confers an increased risk of type 2 diabetes.[5]

Findings that adverse effects of exogenous melatonin supplements appear to be limited to headache, dizziness, and drowsiness[2] may mislead the patients to believe that melatonin supplements are generally safe. However, as pointed out in this Letter to the Editor, users of melatonin supplements should undergo periodic glycated hemoglobin (HbA1c) monitoring. In this context, physicians and researchers should pay particular attention to those carrying the G allele of *MTNR1B* rs10830963.

POTENTIAL COMPETING INTERESTS

Between 2020 and 2021, Christian Benedict served as a scientific consultant for Repha GmbH, Langenhagen, Germany. No other disclosures related to the content of this commentary were reported.

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Malignant Histiocytosis With PD-L1 Expression—Dramatic Response to Nivolumab

To the Editor: A woman in her 60s was admitted to the hospital for exploration of erythema nodosum, lower limb edema, and asthenia. Clinical examination revealed no other abnormalities, and autoimmune and