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Let's Talk about Sex: Sexual Health in Pulmonary Arterial Hypertension

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Pulmonary arterial hypertension (PAH) is a progressive pulmonary vasculopathy that leads to right ventricular dysfunction and right heart failure. Despite advances in therapy, patients with PAH experience severe impairment in health-related quality of life (HRQOL) (1). Individuals with PAH experience fatigue, shortness of breath, palpitations, and chest pain that limit even usual activity, and these patients are sedentary most of the day (2, 3). Patients with PAH not only manage the physical burden of the disease and complex medical regimens that can include continuous parenteral infusions, but they also experience anxiety and depressive symptoms that can negatively affect social relationships (3, 4).

Sexual health includes a sense of self-esteem, personal attractiveness and competence, and freedom from sexual dysfunction (5). Although an important dimension of quality of life, little is known about sexual health and sexual health–related quality of life (SHRQOL) in PAH. Sexual health may not be adequately discussed during routine follow-up visits. This may be attributable to a lack of confidence or specialized training among healthcare professionals, clinicians' or patients' lack of comfort discussing sensitive topics, patients' reluctance to share intimate details of their relationships and sex lives, cultural sensitivities that make sexual activity taboo, or time constraints. One study showed that nearly all patients with PAH and a majority of their partners (72%) reported that their sex lives were severely affected by the diagnosis of PAH (6). Partners of individuals with PAH also began to view themselves as caregivers rather than intimate partners, especially as the disease progressed (7). Moreover, a small study of women with PAH found that participants had low SHRQOL and endorsed symptoms at degrees comparable to those among individuals with clinically diagnosed sexual dysfunction (8).

In this issue of *AnnalsATS*, Yee and colleagues (pp. 1122–1129) have published their data from semistructured in-depth interviews with 13 self-identified women with PAH who attended the Pulmonary Hypertension Association (PHA) International Pulmonary Hypertension Conference and Scientific Sessions (9). A trained clinical psychologist and a pulmonologist who self-identified as women performed the interviews. Albeit with a small sample size, focused on women, the study was conducted using rigorous qualitative methods. All patients reported experiencing dyspnea during sex and a decrease in the frequency of intimate encounters. Participants distinguished between having unaffected sexual desire and the physical limitations to sexual activity as their symptom burden increased. Patients reported avoiding sexual intercourse for fear of eliciting symptoms. Participants noted that side effects such as vaginal dryness in those on diuretics and heavy and/or prolonged menstrual bleeding in those on anticoagulants negatively affected sexual activity.

Parenteral therapies posed additional challenges in terms of patient (and sexual partner) concerns about catheter dislodgment, treatment interruption, and pump displacement. Participants expressed guilt about the impact of their disease on their sexual partners and their relationships. They also noted that their sexual partners expressed fear of exacerbating patients' symptoms. Finally, participants expressed low self-esteem because of changing body image related to wearing a pump or oxygen tubing or weight gain. A recent study of women with PAH in Italy identified similar themes regarding sexuality and intimate relationships (10).

A clear message from this study is that women (and likely persons of all genders) with PAH need more information, support communities, and counseling from

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healthcare providers regarding sexual health. The American Heart Association and the European Society of Cardiology Council on Cardiovascular Nursing and Allied Professions recommend sexual counseling by healthcare professionals after acute cardiac events to reduce psychological sequelae and address psychosexual needs (6). Perhaps a similar approach should be adopted for patients with PAH after rigorous study of the clinical impact (i.e., a randomized clinical trial). If found to have a positive impact, implementation would require training of healthcare professionals in addressing sexual health as well as adequate resources and time to provide such counseling, which could be delivered in clinics, support groups, or online forums.

The PHA has recognized the impact of a diagnosis of PAH on intimacy and sexuality and has put together an informational guide on intimacy for adult patients (11). This guide addresses "setting the mood," attitudes toward sex, myths about sex and pulmonary hypertension, optimization of the timing of sexual encounters and positions, new partners or being sexual without a partner, props and facilitators, the role of oral sex and masturbation, and creativity and experimentation with the importance of open communication. The PHA has also hosted multiple in-person and online support groups focused on sexuality and intimacy, both at its international conference and locally at pulmonary hypertension care centers.

Healthcare professionals providing care to individuals living with PAH ought to acknowledge that sexual activity is a natural part of life and to assume that their patients are sexually active. Healthcare professionals should feel empowered to approach the topic of sexuality with their patients in a sensitive manner to gauge whether patients have questions or concerns, with or without partners. Unless the medical community taking care of individuals with PAH fosters an open and safe environment to discuss sexuality, sexual practices, and intimacy issues freely and without prejudice, we would be doing our patients a disservice by ignoring a major part of their daily lives that likely has a great impact on their overall quality of life. Simple recommendations such as reminding patients to maintain normal continuous breathing and avoiding holding one's breath during sex (which could trigger a Valsalva maneuver), could have a significant impact on preventing syncopal or near-syncopal events.

Physician–patient gender and racial concordance plays a significant role in some medical conditions (12, 13). The value and impact of clinician–physician concordance need to be explored in the context of sexual health and PAH care overall. Differently gendered and nonbinary patients likely experience different manifestations of sexual dysfunction on the basis of body image and other factors, but these have not been thoroughly explored in PAH, with the few studies so far focused on the experience of cisgender women (8–10). An ongoing study, the PH Life Study at the Rhode Island Hospital Pulmonary Hypertension Center and the Miriam Hospital Center for Behavioral and Preventive Medicine, will provide some much-needed insight into the sexual health of all individuals with PAH (https://redcap.lifespan.org/redcap/surveys/?s=DMLW9KRYNJ).

Clinicians often have a stark view of treatment for PAH. With disease that may not be completely addressed by oral or inhaled therapies, parenteral therapy is warranted. Newer guidelines are driven primarily by patient risk stratification, and combination and escalation therapy is often recommended if low-risk status is not achieved (14, 15). This approach may not account for a patient's perspective or the impact of multiple therapies on HRQOL. Clinicians often focus on life-prolonging interventions and therapies, potentially propagating the myth that patients are not concerned with other important aspects of HRQOL such as sexual function. People can describe "states worse than death" with reduced HRQOL (16). Hence, it is not only important to understand the impact of treatment on patients' exercise capacity and clinical worsening, but it is also imperative to elicit patients' values and perspectives on the impact of therapies on HRQOL.

The authors are to be congratulated on tackling a very sensitive and important topic and advancing the knowledge of sexual health and SHRQOL in PAH. We now need rigorous clinical trials (possibly pragmatic) of targeted interventions for sexual dysfunction in PAH, so that we can improve all facets of the lives of people living with PAH. ■

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Knowledge from the Noise: A Regression Discontinuity Design to Inform Optimal Transfusion Thresholds for Critically Ill Patients

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The landmark TRICC (Transfusion Requirements in Critical Care) trial found no difference in 30-day mortality for critically ill patients treated using a restrictive (hemoglobin <7 g/dl) compared with liberal (hemoglobin <10 g/dl) transfusion threshold (1). After this, the optimal threshold for administering packed red blood cells (pRBCs) has been a topic of great interest for clinicians and researchers. Physiologically, pRBC transfusions improve tissue oxygenation by increasing oxygen-carrying capacity. However, the theoretical benefits of increased oxygen delivery are balanced by potential harms of pRBC transfusion, such as volume overload, transfusion reactions, and infectious disease transmission (2–5). In addition, blood transfusion for those unlikely to benefit is costly, inconsistent with high-value health care, and diminishes the availability of blood products for others (6).

The results of the TRICC trial and other evidence have been broadly incorporated by practice guidelines to support pRBC at a hemoglobin level of <7 g/dl for critically ill but clinically stable intensive care unit (ICU) patients over more liberal transfusion practices (7). Notably, the threshold of 7 g/dl represents the upper bound of conservative strategies used in trials but has itself never been shown to be superior to lower thresholds (or to physiologic triggers without a laboratory-based threshold). There has been little enthusiasm to date to allocate patients to a transfusion threshold <7 g/dl, so randomized controlled trial (RCT) data to guide optimal transfusion thresholds are lacking.

Fortunately, advances in healthcare data richness and analytic techniques for causal estimation have enabled more reliable comparative effectiveness estimates outside of RCTs. A major challenge in generating unbiased effect estimates from such observational data is confounding by indication—when factors influencing a clinician's treatment decision (e.g., severity of illness or likelihood to benefit) also influence outcomes. Common techniques to adjust for these factors may fail to fully account for the differences between patients that clinicians use to make treatment decisions, or data sources may not contain sufficient data to accurately model these factors. The unmeasured confounding that remains violates the assumptions necessary for causal conclusions from many observational study designs. This can mean false or distorted results regarding a treatment's benefits and harms.

Quasi-experimental study designs aim to address this limitation by identifying naturally occurring variation in receipt of a treatment or intervention. Practically, naturally occurring variation is induced by measurement error in in data such as

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