Podcast Dr. Lupascu – Part 2

Welcome to this second session of Vascular Stories, the medical podcast on vascular disease. We're here with Dr. Andrea Lupascu, surgeon, angiologist, specialist in internal medicine at the Agostino-Germelli University Polyclinic Foundation, Rome.
In this section of the podcast, we'll explore real data on the appropriateness of phlebology in ge nder medicine in chronic venous disease and deep vein thrombosis.

Good morning, Dr. Lupascu.

Good morning.

Are there any disparities in the access to treatment options?
Yes, there are. Venous thromboembolism incidents and outcomes vary according to race and ethnicity. Lower individual and neighborhood socioeconomic status have been linked to greater venous thromboembolism risk, even in regions with a universal healthcare model such as Denmark, Netherland s and Switzerland.
Although men in the general population have a higher risk of venous thromboembolism recurrence than

women, this risk differs by race, with black and Latina women having a higher recurrence risk of venous thromboembolism than white women in the United States.
In the United States black individuals with venous thromboembolies were five more likely to experience complication of care after hospitalization for venous thromboembolism including readmission bleeding a nd death than white individuals.
Reducing disparities in venous thromboembolism incidents and outcomes will require individual, system -based and societal commitments to equity.

[Jørgensen H, Horváth-Puhó E, Laugesen K, Braekkan S, Hansen JB, Sørensen HT. Socioeconomic status and risk of incident venous thromboembolism. J Thromb Haemost. 2021 Dec;19(12):3051-3061. doi: 10.1111/jth.15523.
Natour AK, Rteil A, Corcoran P, Weaver M, Ahsan S, Kabbani L. Socioeconomic Status and Clinical Stage of Patients Presenting for Treatment of Chronic Venous Disease. Ann Vasc Surg. 2022 Jul;83:305-312. doi: 10.1016/j.avsg.2021.12.010.]

In the case of venous thrombosis, which are the gender-specific risk factors?
Female-specific endocrine disorders like polycystic ovary syndrome,
characterized by hyperandrogenase, appear to increase the risk of thromboembolic events.[1]
Endogenous estradiol and sex hormone binding globulin levels, even in the absence of oral contracepti ves, are linked to a higher thrombotic risk, indicating that female hormonal patterns alone may influence thrombosis.
No evidence was found for an increase in the thrombotic risk in women with primary ovarian insufficienc y based on FSH levels. We can conclude that endogenous sex hormones, particularly estradiol, sex hor mone binding globulin levels and androge excess are important non-exogenous factors influencing the thrombotic risk in young women. These markers may have clinical utility in future individualized

thrombotic risk stratification, especially in women, we like polycystic ovario syndrome or those considering hormonal therapies.[2]

[1][Nassiri Kigloo H, et al. Polycystic Ovary Syndrome, Endometriosis, and Venous Thromboembolism: A Population-Based Study. Gynecol Obstet Invest. 2025. PMID: 40179835. Gariani K, Hugon-Rodin J, Philippe J, Righini M, Blondon M. Association between polycystic ovary syndrome and venous thromboembolism: A systematic review and meta-analysis. Thromb Res. 2020 Jan;185:102-108. doi: 10.1016/j.thromres.2019.11.019.]

[2][Scheres LJJ, van Hylckama Vlieg A, Ballieux BEPB, Fauser BCJM, Rosendaal FR, Middeldorp S, Cannegieter SC; CREW consortium. Endogenous sex hormones and risk of venous thromboembolism in young women. J Thromb Haemost. 2019 Aug;17(8):1297-1304. doi: 10.1111/jth.14474.]

Is there any difference between men and women in the risk of venous thromboembolism?
Men have a consistent higher risk of recurrent thrombosis compared to women. This difference persists even after adjusting for age, comorbidities, thrombosis type and anticoagulant use. The lower recurrence in women is not fully explained by hormone related thrombosis.[3]
Potential explanations include biological differences, higher prevalence of persistent risk factor in men like obesity, elevated D-dimer or thrombin levels, and possible difference in treatment adherence.
We can conclude that sex is an independent predictor of venous thrombosis recurrence. Men may require longer antipobulation therapy after a first thrombotic event, especially if unprovoked. Further research is needed to identify sex-specific resector and improve personalized treatment strategies.

[3][Albertsen IE, Konstantinides SV, Piazza G, Goldhaber SZ, Larsen TB, Søgaard M, Nielsen PB. Risk of Recurrent Venous Thromboembolism in Selected Subgroups of Men: A Danish Nationwide Cohort Study. TH Open. 2022 Nov 18;6(4):e378-e386. doi: 10.1055/a-1949-9404].

What do you think about the thrombotic and hemorrhagic burden in women?
There are gender differences, particularly in women, affect the risk of thrombosis and bleeding and how women respond to antithrombotic therapies. The thrombotic risk in women can vary. Women experience fluctuating pro-
thrombotic activity due to menstrual cycles, oral contraceptives, pregnancy, menopause,
hormone replacement therapy, and plant deflection may be more reactive in women especially premenopausal due to estrogen effect.
Coagulation factors vary with hormonal status, increasing thrombotic risk during pregnancy and postpartum. Also the breeding risk in women can vary. Women have a high risk of bleeding during acute coronary symptoms, percutaneous coronary intervention and this may due to lower body weight and inappropriate dosing of antithrombotic drugs. We can conclude that women have unique thrombotic and bleeding profiles influenced by hormonal and physiological factor.
Antithrombotic therapy should be personalized considering gender specific risks and benefits.

[O'Banion LA, Ozsvath K, Cutler B, Kiguchi M. A review of the current literature of ethnic, gender, and socioeconomic disparities in venous disease. J Vasc Surg Venous Lymphat Disord. 2023 Jul;11(4):682-687. doi: 10.1016/j.jvsv.2023.03.006]

And Dr. Lupascu, what do you think are the future perspectives in phlebology in gender medicine?
Research in gender medicine applied to phlebology is still evolving. We need to work on these points. First, personalized risk stratification.
Sex-
specific risk model should be developed to better predict thrombotic and hemorrhagic events in both women and men. Current tools including gender as a factor, but the more nuanced model could improve accuracy, especially in younger women or those with hormonal influences.
2. Hormonal influence and vascular biology. More research is needed to understand
how estrogens, progesterone, and androgens affect blood infection, coagulation pathways, endothelial health. This could lead to hormone-sensitive therapeutic strategies, especially for women

in reproductive or post-menopausal stages.
3. Sex-based pharmacodynamics and pharmacogenetics Women may metabolize antithrombotic drugs differently due to body composition, hormonal status and liver enzyme activity Future drug trials should include sex-disaggregated data and explore dose optimization for women to reduce bleeding risk without compromising efficacy
4. Improved representation in clinical trials. Women, especially pregnant women, are underrepresented in trials involving antithrombotic therapies. Future studies must include diverse female populations to ensure safety and efficacy across life stages.
5. Digital health and AI integration AI-driven tools could help monitor symptoms, predict complications, and adjust treatments based on sex-specific patterns in chronic venous disease and thrombotic venous disease.
Wearable and mobile apps could track menstrual cycles, pregnancy status, or hormone therapy, integrating this data into personalized care plans.
6. Education and awareness Both patients and healthcare providers need better education on how gender
affects vascular health.
7. Pregnancy-specific guidelines. There is a critical need for clear, evidence-based guidelines on the use of antithrombotic therapies during pregnancies and postpartum.
My final thought is that gender medicine in phlebology is filling its early but essential phase. The integration of biological sex, hormonal status, and gender-specific receptor into clinical practice will not only improve outcomes for women, but also enhance the precision of vascular medicine as a whole.

[Renda G, Patti G, Lang IM, Siller-Matula JM, Hylek EM, Ambrosio G, Haas S, De Caterina R; Working Group on Thrombosis of the Italian Society of Cardiology. Thrombotic and hemorrhagic burden in women: Gender-related issues in the response to antithrombotic therapies. Int J Cardiol. 2019 Jul 1;286:198-207. doi: 10.1016/j.ijcard.2019.02.004].

Thank you, Dr. Lupascu, for dedicating your time and expertise to this podcast. We hope that our discussion provided important insights and reflections.
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