

Penile Doppler Ultrasound Systolic Impairment Predicts Major Cardiovascular Events in poor responders to PDE5-i Therapy

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Abstract

Purpose:

To evaluate the association between penile color Doppler duplex ultrasound (CDDU) parameters and cardiovascular risk (CVR), and whether impaired penile hemodynamics predict future cardiovascular events in men with erectile dysfunction (ED) refractory to phosphodiesterase type 5 inhibitors (PDE5-i).

Materials and Methods:

A total of 285 men who underwent penile CDDU for ED were retrospectively analyzed. Inclusion criteria: age 40–79 years, confirmed ED, inadequate response to ≥ 90 days of PDE5-i therapy. The Charlson Comorbidity Score (CCI) and the 10-year atherosclerotic cardiovascular disease (ASCVD) risk score were calculated. Peak systolic velocity (PSV) and resistive index (RI) were measured at 5 and 20 minutes after intracavernosal injection of prostaglandin E₁. Arteriogenic ED was defined as PSV < 30 cm/s, and veno-occlusive dysfunction as RI < 0.80.

Results:

The median age was 61 years (IQR 55–67). Patients with impaired PSV were older, had higher systolic blood pressure and comorbidity scores. The CCI and the ASCVD 10-year risk score were independent predictors of PSV impairment in univariate linear regression (respectively index $\beta = -1.94$, $p < 0.01$; index $\beta = -0.37$, $p < 0.01$). The multivariate logistic model showed an association between the ASCVD score and the PSV reduction (OR 1.19, 95% CI 1.07–1.32; $p < 0.01$). No significant associations were observed between RI and systemic CVR factors. Patients with impaired PSV experienced a significantly higher incidence of major cardiovascular events during a median follow-up of 53 months compared with those with normal PSV (11.8% vs 3.2%, $p = 0.02$).

Conclusions:

Impaired PSV at penile CDDU is independently associated with higher ASCVD risk and predicts future cardiovascular events in poor responders to PDE5-i. An accurate penile CDDU study might represent a valuable non-invasive tool for CVR stratification and early implementation of prevention strategies in this population.

1. INTRODUCTION

Erectile dysfunction (ED) represents a major men's health issue, affecting approximately 10% of men in their 40s and up to 55% of those in the 60s¹. The condition is being increasingly observed in the general population², a trend that has been partly attributed to neuropsychological disturbances and may also reflect the growing burden of cardiovascular disease (CVDs) and related metabolic disorders in the male population³.

ED can be categorized into psychogenic and organic forms, which often coexist and influence one another⁴. Among organic etiologies, vasculogenic ED is the most prevalent and is characterized by hemodynamic abnormalities that impair penile arterial inflow and/or increase venous outflow during erection⁵. Penile color Doppler duplex ultrasound (CDDU) represents the primary diagnostic tool for evaluating suspected vasculogenic ED⁶. It allows direct assessment of penile vascular function and the diagnosis of arteriogenic ED, which is reflected by a reduced peak systolic velocity (PSV) of the cavernous arteries at the doppler examination⁷.

Over the past decades, substantial evidence has demonstrated a strong association between impaired penile hemodynamic and underlying systemic cardiovascular risk (CVR) factors⁸. The atherosclerotic cardiovascular disease (ASCVD) risk score is a validated tool for estimating the 10-year risk of major cardiovascular events. Males with ED have been shown to carry a higher ASCVD risk, supporting the concept that ED represents an early warning sign for cardiovascular morbidity and mortality⁹.

In this context, abnormalities detected by penile CDDU may reflect the local expression of cumulative CVR affecting systemic vascular function. Furthermore, patients refractory to first-line phosphodiesterase type 5 inhibitors (PDE5-i) therapy seems to exhibit more pronounced systemic vascular dysfunction, suggesting more advanced endothelial impairment¹⁰. However, despite growing interest in this field, few studies have investigated the prognostic value of penile CDDU abnormalities in predicting future major cardiovascular outcomes.

The aim of the present study was to evaluate the association between CVR factors and penile CDDU abnormalities in a cohort of patients poor responders to first-line PDE5-i therapy. Additionally, we sought to determine whether impaired penile CDDU parameters are predictive of future cardiovascular events during cardiovascular follow-up.

2. MATERIALS AND METHODS

2.1. Study design

Data from men who underwent dynamic CDDU as a second-level examination in the diagnostic workflow of ED were retrospectively reviewed. All examinations were performed at a single tertiary academic referral center. Eligible participants met the following criteria: (i) age between 40 and 79 years; (ii) confirmed diagnosis of ED; (iii) inadequate response to PDE5-i, defined as an improvement of fewer than 2 points in the International Index of Erectile Function-5 (IIEF-5) score, after assumption for at least 90 consecutive days.

Patients with a history of major cardiovascular events (myocardial infarction or ischemic stroke) were excluded. Individuals with suspected psychogenic or neurogenic causes of ED were also excluded after evaluation by certified psychosexuologists. Patients with well-known neurological diseases or that had been started a psychotherapeutic path before the second examination were excluded.

Data collection complied with the principles of the Declaration of Helsinki (2024 revision). All participants provided written informed consent to undergo the CDDU and to share anonymized data for research purposes. The study protocol was approved by the University of Trieste Ethics Committee.

2.2. Clinical and Biochemical features

Clinical records were reviewed to identify cardiovascular parameters and to stratify risk factors. All patients underwent serum laboratory prior to CDDU assessment. Health-significant comorbidities were recorded and quantified using the Charlson Comorbidity Index (CCI), referring to the clinical status preceding CDDU. These included arterial hypertension, defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg; body mass index (BMI; kg/m^2); Chronic kidney disease (CKD), assessed on the basis of the estimated glomerular filtration rate (eGFR) according to the Chronic Kidney Disease Epidemiology Collaboration (CKD – EPI) equation; history of Diabetes mellitus (DM), defined according to ESC/EASD guidelines¹¹. The lipid profile included total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Based on these variables, the 10-year ASCVD risk score was calculated according to ESC guidelines¹².

Medication use, including antihypertensive drugs, acetylsalicylic acid (ASA), and statins were recorded.

Personal habits, such as smoking status, alcohol consumption, and physical activity – defined as ≥ 2 self-reported sessions per week of ≥ 30 minutes of moderate exercise – were documented.

2.3. Erectile Function Assessment

All patients completed the International Index of Erectile Function score (IIEF-5) during the first clinical visit. ED severity was classified according to Cappelleri's criteria¹³: scores of 22–25 indicated absence of ED; 17–21 mild ED; 12–16 mild-to-moderate ED; 8–11 moderate ED; and 1–7 severe ED.

All CDDU examinations were performed following intracavernosal injection of 10 μg of prostaglandin E1 (PGE1) (Alprostadil). All evaluations were performed using high-frequency ultrasound probes. PSV and resistive index (RI) were measured bilaterally at the origin of the cavernosal arteries at 5 and 20 minutes after injection. Penile arterial insufficiency was defined as $\text{PSV} < 30$ cm/s, while veno-occlusive dysfunction was defined as $\text{RI} < 0.8$ ¹⁴. For each parameter, the highest value obtained between the two time points was recorded. For analysis, the mean of the right and left cavernosal artery values corresponding to the highest measurement was calculated for both variables (Fig. 1).

2.4. Statistical Analysis

All analyses were performed using the version 4.5.0 of R software (R project – a language for statistic, Wien, <http://www.r-project.org/>). Continuous variables were tested for normality with the Shapiro–Wilk test and are reported as median and interquartile range (IQR). Comparison between patients with impaired PSV and patients with normal parameters were conducted using the Student's *t*-test or Mann–Whitney U test, while categorical variables were compared using the χ^2 or Fisher's exact test, as appropriate.

Univariate and multivariable logistic regression analyses were used to identify predictors of PSV impairment, and results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Model calibration was assessed using the Hosmer–Lemeshow test, and discrimination was evaluated by receiver operating characteristic (ROC) curve analysis, reporting the area under the curve (AUC) with 95% CI. Multicollinearity was checked using the variance inflation factor ($VIF < 5$) and tolerance (> 0.2).

Survival analysis was performed to evaluate the association between PSV impairment and major cardiovascular events, with Kaplan-Meier curves compared using the log-rank test. A two-sided p value < 0.05 was considered statistically significant.

3. RESULTS

3.1. Population characteristics

A total 316 consecutive patients undergoing dynamic CDDU between January 2016 and April 2023 were retrospectively screened. After application of exclusion criteria, 285 patients constituted the final study population. Among them, 34 patients (11.9%) showed impaired PSV at the CDDU exam, while 251 (88.1%) presented normal PSV (**table 1**).

Patients with impaired PSV were older than those with normal CDDU findings (median age 64 vs 60 years, $p = 0.05$) and exhibited a higher comorbidity burden, with $CCI \geq 2$ observed in 38.2% compared with 11.5% in the normal PSV group ($p < 0.01$). Smoking status and alcohol intake did not differ significantly between groups ($p = 0.2$ and $p = 0.8$, respectively). Regular physical activity was significantly more frequent among patients with normal PSV ($p = 0.03$).

Prevalence of AH was numerically higher among patients with impaired PSV (50.0% vs 36.3%, $p = 0.1$). Median systolic blood pressure values were significantly higher in the impaired PSV group (106.7 mmHg vs 98.3 mmHg, $p < 0.01$). Use of single antihypertensive therapy was more common in the PSV impaired cohort (41.2% vs 26.7%), while the assumption of more than one drug was not significantly different ($p = 0.6$).

No significant difference emerged in the prevalence of CKD ($p = 0.9$), DM ($p = 0.4$) or lipid profile parameters, including total cholesterol ($p = 0.4$), HDL ($p = 0.5$) and LDL ($p = 0.2$). Use of cardio-aspirin and statins did not differ significantly between groups ($p = 0.1$ and $p = 0.3$, respectively).

3.2. Erectile function and CDDU parameters

IIEF-5 score distribution differed significantly between groups ($p = 0.01$). Patients with impaired PSV more frequently presented mild-to-moderate (55.9%) and moderate ED (29.4%), compared with 41.4% and 15.5%, respectively, among patients with normal CDDU findings (**table 2**).

Median PSV values were of 28 cm/s and 43 cm/s ($p < 0.01$) for the two groups, respectively. Median RI values also differed significantly between groups ($p < 0.01$), and RI impairment was more frequently

observed among patients with impaired PSV (20.6% vs 7.2%; $p = 0.01$).

3.3. Regression Analysis

In linear regression analysis, regular physical exercise was positively associated with higher PSV at CDDU ($\beta = +2.68 \pm 1.17$; $p = 0.02$), whereas CCI ($\beta = -1.94 \pm 0.67$; $p < 0.01$) and ASCVD risk score ($\beta = -0.37 \pm 0.11$; $p < 0.01$) were inversely correlated with PSV (**Supplementary table 1; Fig. 2**).

No variables were significantly associated with RI values in univariate linear models. At the univariate logistic regression, higher ASCVD risk score (OR 1.23; 95% CI 1.14–1.33; $p < 0.01$), moderate-to-severe ED (OR 2.33; 95% CI 1.11–4.90; $p = 0.03$), and CCI ≥ 2 (OR 4.74; 95% CI 2.14–10.47; $p < 0.01$) were significantly associated with impaired PSV. Regular physical exercise showed a protective effect (OR 0.41; 95% CI 0.18–0.92; $p = 0.03$). In the multivariate model, only the ASCVD risk score remained an independent predictor of impaired PSV (adjusted OR 1.19; 95% CI 1.07–1.32; $p < 0.01$), with no evidence of multicollinearity (VIF = 1.0–1.5, tolerance = 0.5–1.0) (**Table 3**).

Model discrimination analysis demonstrated an AUC of 0.92 (95% CI 0.85–0.99), corresponding to 60% sensitivity and 94% specificity for predicting PSV impairment (**Supplementary Fig. 1**).

3.4. Survival outcomes

During the median follow-up of 53 months (32.5–61), 8 of 243 (3.3%) patients in the normal PSV cohort and 4 of 30 (13.3%) patients in the impaired PSV cohort developed major cardiovascular events.

Patients with impaired PSV experienced a significantly higher rate of major cardiovascular events than those with normal PSV (log-rank $p = 0.02$), with a mean time-to-event of 56.0 ± 20.2 months (Fig. 3).

4. DISCUSSION

The present study suggests that impaired PSV at the penile CDDU is strongly associated with an increased risk of major cardiovascular events in men who are poor responders to first-line PDE5-i for suspected vasculogenic ED. Furthermore, in our cohort, the 10-year ASCVD risk score emerged as an independent predictor of reduced PSV in both linear and logistic regression, reinforcing the concept that penile vascular alterations mirror systemic atherosclerotic disease¹⁵. Notably, the increased CV risk observed in PDE5-i poor responders might be driven by underlying endothelial dysfunction.

The relationship between ED and CVDs has been well established over recent decades. It has been shown that patients with vasculogenic ED carry a higher risk of cardiovascular morbidity and mortality¹⁶. However, clinical decision-making for patients presenting with pathological penile flow parameters at CDDU remain lacking.

The routine use of ultrasound plays a central role in male genital evaluation, representing the gold standard for diagnosing priapism, acute scrotal pain, varicocele, and testicular masses^{17,18}. However, the criteria for selecting patients who may benefit most from PDDU remain debated, leading to variability in

its application and unclear role in the diagnostic workflow of organic ED¹⁹. Furthermore, variability in the hemodynamic parameters should be considered when interpreting results, including probe position, timing of the cavernosal artery sampling, PGE1 administration and redosing protocol, all of which should be standardized and discussed before testing.

Corona et al. demonstrated that when a flaccid PSV threshold of < 13 cm/s correlated with a pathological dynamic PSV after PGE1 injection with an accuracy approaching 85%. This finding suggested that Doppler evaluation in the flaccid state might identify subjects with pathological dynamic PSV. However, based on our findings, dynamic assessment should remain a fundamental step to avoid underdiagnosis of arteriogenic ED, particularly in cases of borderline results.

Penile arterial insufficiency diagnosis at CDDU should be regarded as surrogate marker of systemic microvascular dysfunction. As a matter of fact, reduced PSV has been consistently observed with coronary artery disease and DM, confirming the close relationship between penile hemodynamic impairment and systemic CVDs²⁰. Vasculogenic ED, particularly when arteriogenic dysfunction is documented, may thus represent an independent predictor of future cardiovascular events²¹.

In light of these findings, CDDU may play a crucial role in cardiovascular prevention, prompting more intensive evaluation and management of patients at high risk for major cardiovascular events, which remain associated with substantial mortality.

Endothelial dysfunction represents the key pathophysiological mechanism underlying arteriogenic ED. It disrupts microvascular homeostasis by reducing nitric oxide bioavailability and impairing cavernosal smooth muscle relaxation, leading to reduced arterial inflow and abnormal sinusoidal filling, reflected on CDDU as a reduced PSV, typically below 30 cm/s²². The link between systemic CVDs, endothelial dysfunction, and ED has been recognized for decades. Montorsi et al. were among the first to hypothesize that systematic atherosclerosis affects penile arteries earlier due to their small caliber (≤ 2 mm), identifying ED as a precursor of coronary artery disease²³. In a more recent experience, the pathological morphology identified at the CDDU of the cavernous artery (intima thickness > 0.3 mm) results to be an independent predictor of major cardiovascular events in the future²⁴. Consequently, arteriogenic ED diagnosed by CDDU can be considered an early clinical manifestation of systemic vascular injury. Given the shared pathophysiology and risk factors between ED and CVDs – including DM, obesity, HT, metabolic syndrome, and smoking – risk factors prevention might play a pivotal role in reducing the occurrence of major events in patients with ED²⁵.

In our study, patients with PSV impairment were older, had higher comorbidity scores, and displayed elevated systolic blood pressure, a higher rate of comorbidities, consistent with diffuse vascular compromise. Surprisingly, metabolic markers such as BMI, DM, and lipid fractions did not differ significantly between groups. On one hand the absence of significant differences in biometric, lipid and glycemic profiles further supports the notion that penile vascular impairment may be explained with the

fact that vascular impairment precede CVDs; on the other hand, these data can be biased by the retrospective nature of the study and can be contradicted enrolling more patients in the future.

However, the cumulative burden CVR factors, rather than isolated metabolic abnormalities, appears to better explain penile hemodynamic impairment. This is reflected by the strong inverse correlation between PSV and the 10-year ASCVD risk score observed in linear regression analysis. This latter remained the only significant determinant associated with impaired penile arterial inflow in multivariate logistic regression (OR 1.19; 95% CI 1.07–1.32; $p < 0.01$), corroborating the pathophysiological link between local penile hemodynamics and global cardiovascular status ²⁶.

Notably, our findings align with those reported by Bertini et al., who similarly observed a significant association between ASCVD risk score and PSV reduction in a multivariate logistic model²⁷. Consistent with their results, we did not identify any of the factor predictive of RI impairment, suggesting that this parameter may be less involved in the shared pathophysiological pathway linking arteriogenic ED and systemic atherosclerosis.

Some limitation should be acknowledged. First, the relatively low proportion of patients with severe ED may reflect a selection bias inherent to CDDU evaluation. However, advanced erectile dysfunction is often characterized by poor responsiveness to intracavernosal injection, which may limit the reliability of hemodynamic measurements. Furthermore, the retrospective design carries an inherent risk of selection biases, residual confounding, and lack of standardized protocol control. In addition, the monocentric nature of the study, the intermediate follow-up duration, and the limited number of cardiovascular events restrict the generalizability of the findings.

Despite these limitations, the relationship among the CDDU–detected alterations in hemodynamic and its potential role as a marker of systemic endothelial dysfunction remains of central clinical relevance. Future multicenter prospective studies with longer follow-up are warranted to confirm these findings and to define clinically meaningful PSV thresholds predictive of systemic atherosclerosis and cardiovascular outcomes.

5. CONCLUSIONS

In patients who are poor responders to first-line PDE5-i therapy, impaired PSV was independently associated with a higher ASCVD risk score and correlated with an increased incidence of cardiovascular events during follow-up. The systematic incorporation of penile CDDU as a second-line diagnostic tool in ED may facilitate the early identification of men at increased risk of major cardiovascular events. In this context, CDDU may help identify a subgroup of patients who could benefit from an early cardiovascular screening or aggressive risk factor modification. Further studies are warranted to evaluate the protective impact of early preventive strategies in this population.

DECLARATIONS

Author Contributions:

Conceptualization: G.L., F.Z., A.P.

Methodology: S.B., M.R., T.C.

Data curation: A.S., S.S., G.R., A.B.

Formal analysis: F.Z., S.S., G.R.

Writing – original draft: F.Z., A.P., L.B.

Writing – review & editing: G.R., A.B., T.C., A.Z.

Visualization: L.B., M.R., A.V.

Supervision: G.L., T.C., A.Z.

Project administration: G.L., S.B.

Funding: None

Conflict of Interest Statement: Any to declare.

Data Availability Statement: Patients' data analyzed in the present study are anonymously stored at University of Trieste. They are available upon reasonable request by contacting the corresponding author.

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Ethics Declaration: The present study was approved by the University of Trieste Ethic Committee – protocol n. 186591, rep n. 401/2023.

REFERENCES

1. Nicolosi A., Moreira E. D., Shirai M., Bin Mohd Tambi M. I. & Glasser D. B. Epidemiology of erectile dysfunction in four countries: Cross-national study of the prevalence and correlates of erectile dysfunction. *Urology*. 2003; 201–206.
2. Capogrosso, P. et al. Age at First Presentation for Erectile Dysfunction: Analysis of Changes over a 12-yr Period. *Eur. Urol. Focus*. 2019;899–905.
3. Andersson, C. & Vasan, R. S. Epidemiology of cardiovascular disease in young individuals. *Nat. Rev. Cardiol*. 2018;230–240.
4. Yafi, F. A. et al. Erectile dysfunction. *Nature Reviews Disease Primers*. 2016;2:1,1–20.
5. Stief, C. G., Bahren, W., Scherb, W. & Gall, H. Primary erectile dysfunction. *J. Urol*. 1989;315–318.

6. Bertolotto, M. et al. Sonography of the penis/erectile dysfunction. *Abdom. Radiol. (NY)*. 2020;1973–1989.
7. Lue, T. F. Erectile Dysfunction. *New England Journal of Medicine*. 2000;1802–1813.
8. Woong, J. B. et al. The Correlation between Cardiovascular Risk Factors and Penile Hemodynamic Parameters in Men with Erectile Dysfunction. *Korean J. Urol.* 2009;689–693.
9. Mei, Y. et al. Association between erectile dysfunction and the predicted 10-year risk for atherosclerosis cardiovascular disease among U.S. men: a population-based study from the NHANES 2001–2004. *Front. Endocrinol. (Lausanne)*. 2024;144–2904.
10. Ogreden, E., Oğuz, U., Demirelli, E., Tosun, A. & Yalçın, O. Relationship between Response to PDE5 Inhibitors and Penile Duplex Doppler Ultrasound in Erectile Dysfunction. *Medical Sciences*. 2018;28.
11. Marx, N. et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC). *Eur. Heart J.* 2023;4043–4140.
12. Visseren, F. et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur. Heart J.* 2021;3227–3337.
13. Rosen, R. C., Cappelleri, J. C., Smith, M. D., Lipsky, J. & Peñ, B. M. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int. J. Impot. Res.* 1999;319–326.
14. Sikka, S. C., Hellstrom, W. J. G., Brock, G. & Morales, A. M. Standardization of vascular assessment of erectile dysfunction: standard operating procedures for duplex ultrasound. *J. Sex. Med.* 2013;120–129.
15. McMahon, C. N., Smith, C. J. & Shabsigh, R. Treating erectile dysfunction when PDE5 inhibitors fail. *BMJ: British Medical Journal*. 2006;589.
16. Kessler, A., Sollie, S., Challacombe, B., Briggs, K. & Van Hemelrijck, M. The global prevalence of erectile dysfunction: a review. *BJU Int.* 2019;587–599.
17. Zorzi, F. et al. Scrotal Masses. *Atlas of Ultrasonography in Urology, Andrology, and Nephrology*. 2025;545–554. doi:10.1007/978-3-031-78135-3_49.
18. Bucci, S. et al. The Testicles: Trauma, Inflammation and Testicular Torsion. *Atlas of Ultrasonography in Urology, Andrology, and Nephrology*. 2025;517–531. doi:10.1007/978-3-031-78135-3_47.
19. Cocci, A. et al. The efficacy of penile duplex ultrasound in erectile dysfunction management decision-making: facing the opinion leader. *J. Mens Health*. 2024;8–11.
20. Jin Bae, W. et al. The Correlation between Cardiovascular Risk Factors and Penile Hemodynamic Parameters in Men with Erectile Dysfunction. *Korean J. Urol.* 2009;689–693.
21. Uddin, S. M. I. et al. Erectile Dysfunction as an Independent Predictor of Future Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis. *Circulation*. 2018;540–542.
22. Blick, C., Ritchie, R. W. & Sullivan, M. E. Is Erectile Dysfunction an Example of Abnormal Endothelial Function? *Curr. Vasc. Pharmacol.* 2016;163–167.

23. Montorsi, P. *et al.* The artery size hypothesis: a macrovascular link between erectile dysfunction and coronary artery disease. *Am. J. Cardiol.* 2005;19–23.

24. Caretta, N. *et al.* Penile doppler ultrasound predicts cardiovascular events in men with erectile dysfunction. *Andrology.* 2019;82–87.

25. Kalka, C. *et al.* Men with erectile dysfunction (ED) should be screened for cardiovascular risk factors - Cost-benefit considerations in Swiss men. *Vasa.* 2024;68–76.

26. Imprialos, K., Koutsampasopoulos, K., Manolis, A. & Doumas, M. Erectile Dysfunction as a Cardiovascular Risk Factor: Time to Step Up? *Curr. Vasc. Pharmacol.* 2021;301–312.

27. Bertini, A. *et al.* The atherosclerotic cardiovascular disease risk score is a reliable tool to identify patients with arteriogenic erectile dysfunction. *Andrology.* 2023;1451–1459.

TABLES

Table 1. Baseline demographic, clinical and biochemical features of the study population, overall and stratified by the presence of impaired peak systolic velocity (PSV) at the penile Color doppler duplex ultrasound (CDDU).

	Overall cohort (n = 285, 100%)	Normal CDU (n = 251, 100%)	Impaired PSV at CDU (n=34, 100%)	p-value
Age (years), median (IQR)	61 (55 – 67)	60 (54 – 66.5)	64 (58 – 69)	0.05
BMI (kg/m²), median (IQR)	26.4 (24.0 – 29.4)	25.8 (24.0 – 29.1)	28.3 (26.4 – 30.1)	0.1
CCI < 2, n (%)	243 (85.3%)	222 (88.4%)	21 (61.8%)	<0.01
CCI ≥ 2, n (%)	42 (14.7%)	29 (11.5%)	13 (38.2%)	
Active smoker, n (%)	53 (18.6%)	43 (17.1%)	10 (29.4%)	0.2
Ex-smoker (<10 years), n (%)	38 (13.3%)	32 (12.8%)	6 (17.6%)	
Never or > 10 years quit, n (%)	194 (68.1%)	176 (70.1%)	18 (53.0%)	
Regular exercise, n (%)	126 (44.2%)	117 (46.6%)	9 (26.5%)	0.03
No Regular exercise, n (%)	159 (55.8)	134 (53.4 %)	25 (73.5%)	
Alcohol assumption, n (%)	104 (36.5%)	97 (38.6%)	7 (20.6%)	0.8
No Alcohol assumption, n (%)	181 (63.5%)	176 (70.1%)	27 (79.4%)	
Presence of AH, n (%)	108 (37.9%)	91 (36.3%)	17 (50.0%)	0.1
Absence of AH, No. (%)	177 (62.1%)	160 (63.7%)	17 (50.0%)	
Mean SBP (mmHg), median (IQR)	100 (91 – 106)	98.3 (90 – 106.7)	106.7 (100 – 111.7)	<0.01
Antihypertensive therapy				0.6
No AH therapy, n (%)	108 (37.9%)	91 (36.3%)	17 (50%)	
AH single drug therapy, n (%)	81 (28.4%)	67 (26.7%)	14 (41.2%)	

AH multiple drugs therapy (incl. diuretics), n (%)	27 (9.5%)	24 (9.6%)	3 (8.8%)	
eGFR (ml/min/1.73m²), median (IQR)	89 (74 – 102)	88 (74 – 101)	90 (75 – 102)	0.9
CKD Absent, n (%)	267 (93.7%)	235 (93.6%)	32 (94.1%)	0.9
CKD Any grade, n (%)	18 (6.3 %)	16 (6.4%)	2 (5.9%)	
DM Absent, n (%)	224 (78.6%)	200 (79.7%)	24 (70.6%)	0.4
DM Type I, n (%)	20 (7.0%)	16 (6.4%)	4 (11.8%)	
DM Type II, n (%)	41 (14.4%)	35 (13.9%)	6 (17.6%)	
Total Cholesterol (mg/dl), median (IQR)	200 (163.2 – 229.7)	198 (164.5 – 221)	202 (160.5 – 236)	0.4
HDL (mg/dl), median (IQR)	49 (42 – 58.5)	50 (42 - 59)	47.5 (40.4 – 53.5)	0.5
LDL (mg/dL), median (IQR)	123 (89.6 – 144)	121.5 (85.5 – 149.5)	126 (98 – 137)	0.2
Statin intake, n (%)	97 (34.0%)	83 (33.1%)	14 (41.2%)	0.3
ASA intake, n (%)	55 (19.3%)	52 (20.7%)	3 (8.8%)	0.1

Abbreviations: BMI, Body Mass Index; CCI, Charlson Comorbidity Index; AH, arterial hypertension; SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; DM, diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ASA, acetylSalicylic acid.

Table 2. Erectile function severity according to the International Index of Erectile Function-5 (IIEF-5) and penile color Doppler duplex ultrasound (CDDU) parameters at the time of clinical evaluation.

	Overall cohort (n = 285, 100%)	Normal CDDU (n = 251, 100%)	Impaired PSV at CDDU (n=34, 100%)	p-value
IIEF-5 score, n (%)				0.01
≥ 22 (no ED)	0 (0%)	0 (0%)	0 (0%)	
17 – 21 (mild)	93 (32.6%)	89 (35.5%)	4 (11.8%)	
12 – 16 (mild - to - moderate)	123 (43.2%)	104 (41.4%)	19 (55.9%)	
8 – 11 (moderate)	49 (17.2%)	39 (15.5%)	10 (29.4%)	
1 – 7 (severe)	20 (7.0%)	19 (7.6%)	1 (2.9%)	
CDDU parameters				
Average PSV (cm/s), median (IQR)	52 (42 – 56.7)	43 (41.2 – 52)	28 (27 – 29.3)	<0.01
Average RI, median (IQR)	0.91 (0.85 – 0.99)	0.9 (0.9 – 1)	0.9 (0.85 – 0.9)	<0.01
RI impaired, n (%)	25 (8.8%)	18 (7.2%)	7 (20.6%)	0.01

Abbreviations: IIEF, International Index of Erectile Function; CDDU, color Doppler duplex ultrasound; PSV, peak systolic velocity; RI, resistive index

Table 3. Logistic regression analyses of predictors of impaired peak systolic velocity (PSV) at penile color Doppler duplex ultrasound.

PSV impaired	Univariate	p	Multivariate	p
ASCVD risk score	1.23 (1.14 – 1.33)	<0.01	1.19 (1.07 - 1.32)	<0.01
Regular exercise	0.41 (0.18 – 0.92)	0.03	0.75 (0.12 – 4.8)	0.7
Moderate or severe ED	2.33 (1.11 – 4.9)	0.03	4.57 (0.69 – 30.13)	0.11
Alcohol assumption	0.94 (0.45 – 1.99)	0.88	2.07 (0.36 – 11.84)	0.41
CCI ≥ 2	4.74 (2.14 – 10.47)	<0.01	1.48 (0.16 – 14.03)	0.73
BMI	1.09 (0.96 – 1.23)	0.17	1.21 (0.98 – 1.49)	0.08

Abbreviations: ASCVD, atherosclerotic cardiovascular disease risk score; ED, Erectile Dysfunction; CCI, Charlson Comorbidity Index; BMI, Body Mass Index.

Figures

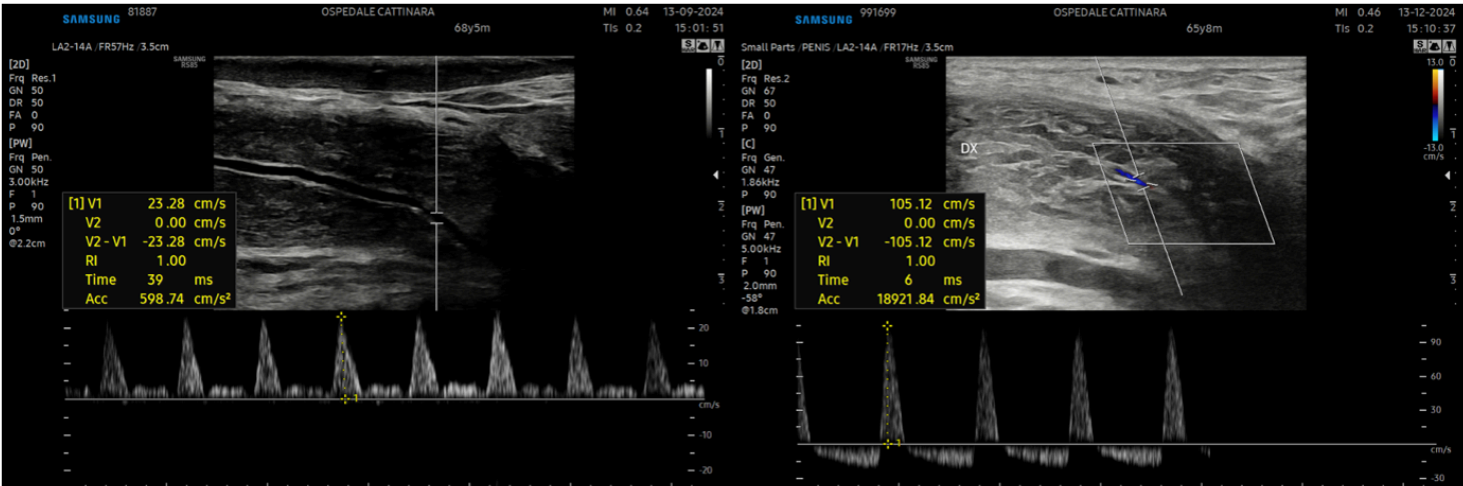


Figure 1

Penile color Doppler ultrasound assessment of the dorsal artery at 20 minutes after PGE1 injection. The left panel shows impaired peak systolic velocity (PSV = 23.28 cm/s) with absent cavernosal tissue distension, consistent with arterial insufficiency. The right panel demonstrates adequate cavernosal distension with preserved arterial inflow (PSV > 105 cm/s). In both scenarios, the resistive index (RI) is preserved, excluding the presence of veno-occlusive dysfunction.

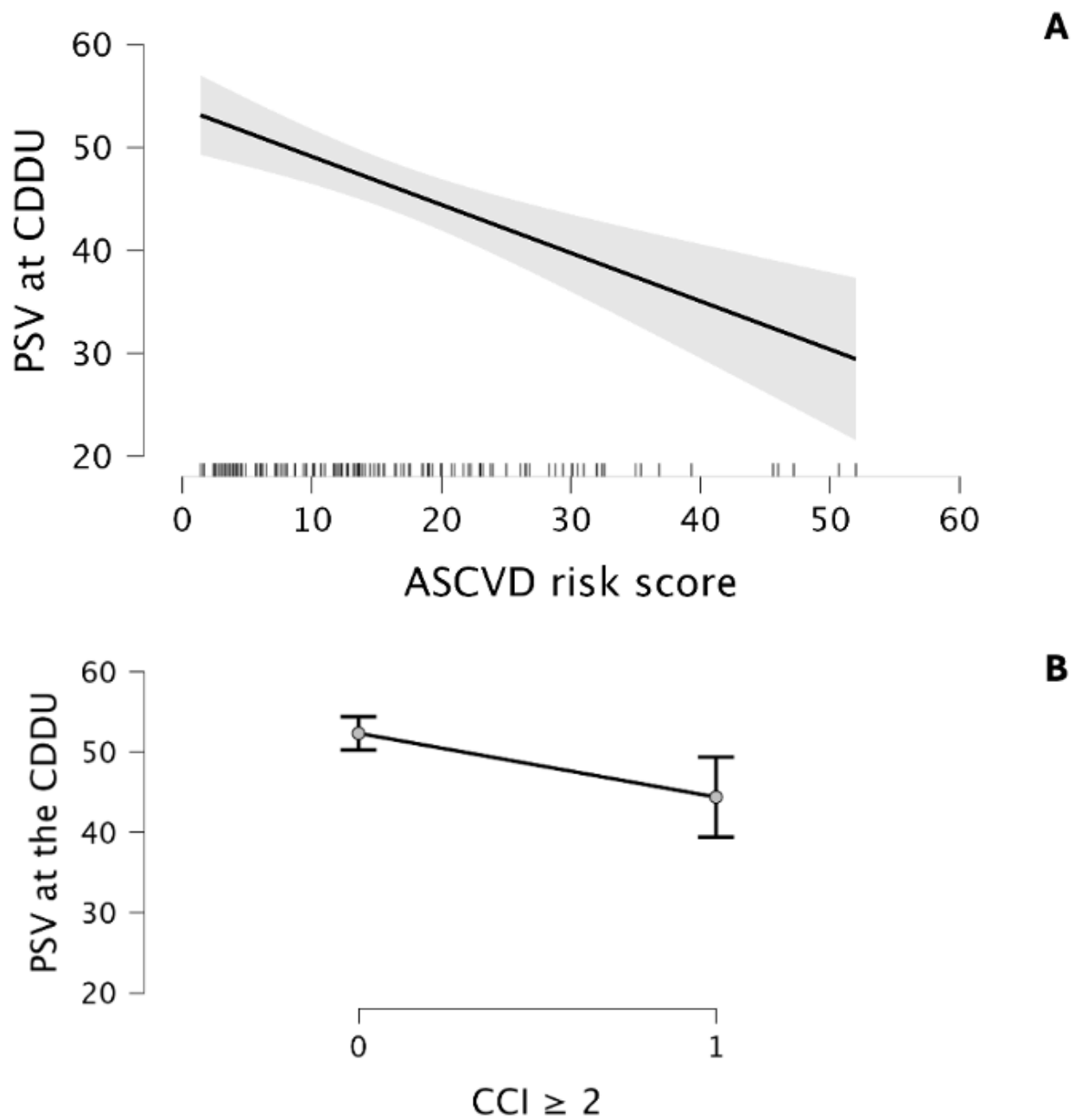


Figure 2

Figure 2. Linear regression displaying inverse correlation between (A) PSV and ASCVD risk score and between (B) PSV and CCI > 2.

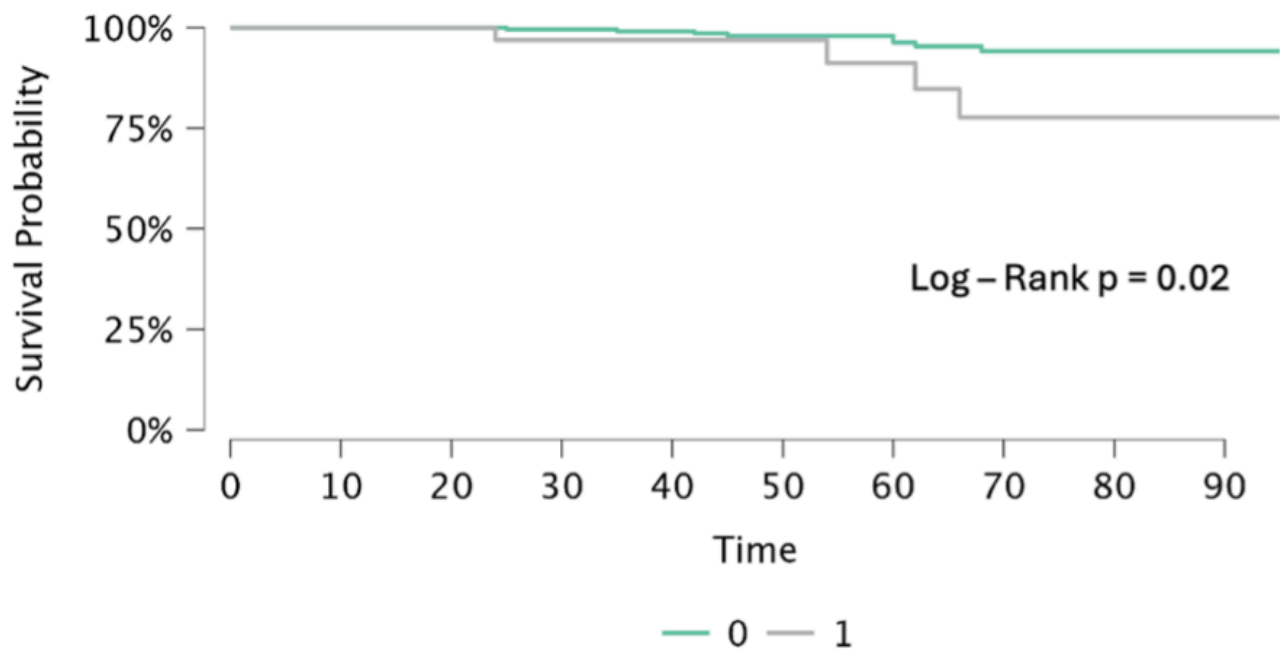


Figure 3

Kaplan–Meier analysis of major cardiovascular event–free survival stratified by penile peak systolic velocity (PSV). Patients with impaired PSV (green line) experienced significantly earlier cardiovascular events compared with those with normal PSV (gray line) during a median follow-up of 53 months (log-rank $p = 0.02$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementarytable1.docx](#)
- [Supplementaryfigure1.png](#)