Complete Study for Erectile Dysfunction (*CompED*) Improving Diagnosis and Treatment Decision-making.

Julián Chavarriaga[1], Juan Prada[1], Peter Olejua[2], Hugo López-Ramos[1],Maryori Manjarrez[1], José-Miguel Silva[1]

1. Division of Urology, Hospital Universitario San Ignacio. Pontificia Universidad Javeriana. Bogotá, Colombia.
2. Department of Epidemiology and Biostatistics. Hospital Universitario San Ignacio. Pontificia Universidad Javeriana. Bogotá, Colombia.

Corresponding author:

Julián Chavarriaga. M.D. Division of Urology. Hospital Universitario San Ignacio. Pontificia Universidad Javeriana.

Address: Carrera 7 No. 40 – 62. Bogotá. Colombia.

Phone/fax: (57)1 3208320).

Email: chavarriagaj@javeriana.edu.co

ABSTRACT

INTRODUCTION: ED is a condition associated with increasing age and its overall prevalence has been estimated at 18 to 47%. It is associated with numerous comorbidities and lifestyle attributes. Patient evaluation and management should follow a comprehensive, stepwise approach. The aim of this article is to report our experience with a Complete study for ED (*CompED*) including ICI rigidity test, biothesiometry and color duplex doppler ultrasound (CDDUS) after oral therapy failure.

METHODS: One hundred and eighty-seven patients were recruited. Data was collected and analysed prospectively. For descriptive univariate analysis central tendency and dispersion measures were used. For bivariate analysis, p values were calculated, with fisher and a chi-square test. Multivariate analysis was performed using binary decision trees, their respective separating nodes where divided according to the Gini coefficient. Pearson correlation coefficient (PCC) was also used and reported through dispersion diagrams for pairwise correlation to determine the probability of treatment decision-making. R Studio version 4.0.0. was used for statistical calculations.

RESULTS: Between May 2017 and January 2020, 187 patients with ED, underwent the *CompED* test. Mean age was 57 +/- 12.8 years, median follow up was 24 (IQR 12-240) months. Median IIEF-15 Domain A was 6 (IQR 1-30). We divided the patients in subgroups: diabetes, coronary artery disease, prostate cancer treated with radical prostatectomy, radiotherapy or ADT; spinal cord injury, pelvic trauma, HIV. Treatment decision making was eased by the CompED test, 39 (20.6%) of patients were offered a second trial of PD5-I with a daily dose combined with a demand dose. 77 (40.7%) continued with ICI injections and 73 (38.6%) were offered surgery. We found a strong correlation between tumescence and axial rigidity in all treatments decision-making. Multivariate analysis treatment decision tree showed that PSV < 17.5 cm/s, tumescence< 35 %, RI <0.74, age ≥60.5 influenced the decision to offer a penile prosthesis and the best predictor for penile venous surgery was an EDV ≥ 9.25 cm/s with 92% sensitivity, 86% specificity.

CONCLUSION: ED is a high prevalence disease. Specialized testing should be considered in selected patients or patients unresponsive to first line treatment. The *CompED* test stands as a new alternative for the evaluation of patients with ED, improving, being less time consuming and aiding in a more accurate determination of the aetiology and guiding treatment decision-making.

INTRODUCTION

Erectile dysfunction (ED) is the "consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction" according to the Fourth International Consultation on Sexual Medicine.(1) ED is a condition associated with increasing age and its overall prevalence in the USA has been estimated at 18 to 47%, data has shown an increased from 8.2% in men aged 40-49 years to 77.5% in those aged ≥ 75 years.(2–6) Despite as being as prevalent in health surveys it is commonly underdiagnosed and undertreated. In a study that evaluated a 19 million men database it was reported only 6.9% had an ED diagnosis or a phosphodiesterase type 5 inhibitor (PDE5I) prescription.(4,6) This condition is projected to affect more than 320 million men worldwide by 2025 which certainly makes it a public health concern. (4,6,7)

ED is associated with numerous comorbidities and lifestyle attributes such as diabetes mellitus (DM), hypertension, depression, hypothyroidism, human immunodeficiency virus (HIV), lower urinary tract symptoms, smoking, sedentarism and it has shown to be an early warning sign of cardiovascular disease (CVD).(3,6,8–23) Could be a sequela of radical prostatectomy (RP), external beam radiotherapy (EBRT), brachytherapy, androgen deprivation therapy (ADT) for prostate cancer and of pelvic or spinal cord injury (SCI).(8,24–27).

Patient evaluation follows a comprehensive nuanced approach. Evaluation includes a complete sexual, medical and psychosocial history, physical exam and laboratory tests.(2,4,5,7,28) Specialized test could be considered after doing the initial assessment and

should be directed to answer a specific question.(2,4,5,7,28) These tests include vascular testing: colour duplex doppler ultrasonography (CDDUS), dynamic infusion cavernosometry and cavernosography (DICC) and penile angiography, neurological testing as biothesiometry and specialized tests as nocturnal penile tumescence rigidity test (NPTR), Rigidity analysis with intracavernous injection (ICI). (2,4,5,7,28–31)

Management of ED pursue a stepwise strategy. Concurrent lifestyle modification and the use of PDE5I are the first step, oral therapy could be on-demand or daily dosing and the choice should be influenced by timing or frequency of intercourse and interactions with food or alcohol.(2,4,5,28) After oral therapy failure, local therapy (ICI or intraurethral agents) should be offered and should follow a stepwise dosage and drug combination approach.(32) The aforementioned strategies could be use concurrently with vacuum erection device therapy or testosterone replacement therapy in men with documented hypogonadism.(2,5,21,28) The third step in the management of ED would be surgical treatment involving inflatable or malleable penile prosthesis, vascular bypass procedure or venous penile surgery despite not been recommended by most guidelines. (2,5,28)

The aim of this article is to report our experience with the *CompED test* which includes ICI rigidity test, biothesiometry and CDDUS after oral therapy failure to determine the precise etiology of the disease and to decide which management strategy would best fit the-patient.

MATERIALS AND METHODS

Patients

After IRB approval, 187 patients were recruited, all underwent a CompED test (ICI rigidity test, biothesiometry and CDDUS) at our hospital from 2017 to 2020. Data was collected and analysed prospectively. Each patient was invited to participate in our study and a fully signed informed consent was required to participate and became part of the *CompED* database. Eligible patients were patients from 18 to 75 years old with clinical diagnosis of ED who had failed to response to oral therapy with PDE5I and were considered for a subsequent line of treatment. Exclusion criteria were patients with severe neurological or psychological disease who were unable to complete the study.

Treatment and Diagnostic Tests

All patients had failed oral therapy and were willing to undergo the CompED test in the andrology clinic. All patients were screened with the International index of erectile function (IIEF-15) which is a validated multi-dimensional, self-administered questionnaire made of 5 main-domains (Erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction), a score of 0-5 is awarded to each of the 15 questions and the Domain A was related to sexual function, including six questions with a maximum score of 30 and a minimum score of 1. (5,28) We also applied the Male Androgen Deficiency Syndrome (MADS) Screening Questionnaire to predict hypogonadism and designed to collect

information on age, race (African American, white and Hispanic), presence on adult onset diabetes, exercise frequency, overweight status and erectile function.(33) All the patients self-administered both questionnaires before the CompED test.

All the procedures were carried out on the same day. The tests were performed in a quiet and comfortable room, the patient lay on the examination table in a supine position with legs together providing support for the external genitalia. The first test was the biothesiometry evaluating the pallesthetic sensibility of the pudendal afferent pathways. The vibratory sensibility was measured in the glans and base of the penis with a biothesiometer (Bio-Medical instruments Co., Shenzhen, China) The device had a fixed frequency (100 Hz) and variable amplitude. The vibration generated was transmitted to a galvanometer and the amplitude was measured on a reference scale expressed in volts. Results were interpreted using the Breda nomogram for penile biothesiometry; the results were classified as normal or abnormal.(29,34)

The second test was the ultrasound (US) scan, it was performed in a flaccid state with a high-frequency linear array transducer with an ultrasound frequency of 7.5 MHz which allows for high resolution images of the penis and internal vascular structures. Color and spectral Doppler images in addition to B-mode ultrasound were obtained. First a baseline US scan image of the penis was obtained in the longitudinal and transverse planes, including measurement of cavernosal artery diameter, plaques (number, location, size).(30,35,36) After the initial US scan, an intracavernosal injection of alprostadil 20 mcg was delivered and a rigidity test and CDDUS was performed at 5, 10, 15 and 20 minutes after ICI. The rigidity test assessed, axial rigidity using RigiScan® (GoTop Medical, San Diego. Ca, USA)

parameters for penile radial rigidity and tumescense The RigiScan® assessed over 500 patients at San Diego Uro-center., they reported that tumescence at the base should be 3 cm increase over resting tumescence and at the tip of the penis a 2 cm increase over resting tumescence. Ridigidity was: <40% non-rigid, 40-70% buckling will occur, but erection may be stuffable and 70% non-buckling, rigid erection.(37–39) We measured axial rigidity using a scale from 0 to 100% to assessed both tumescence and rigidity according to the aforementioned parameters. Based on clinical observation, 55–60% base rigidity and a 50% tip rigidity has been found to be adequate for vaginal penetration.(37–42) We arbitrarily assigned 50% as the threshold value for axial rigidity and tumescence. The erection angle was also measured with a goniometer and reported from 0 to 90ª. The CDDUS evaluated penile flow velocities including peak systolic velocity (PSV) and end diastolic velocity (EDV). PSV values were considered normal ≥ 35 cm/s and primary criteria for arteriogenic ED included a PSV < 25 cm/s. EDV greater than 5 cm/s in the cavernosal artery demonstrated throughout the study, especially at the most turgid level of erection achieved, was suggestive of a venous leak.(5,31,32,36,43–45)

End Points

The primary end point for the study was to describe patients clinical and sociodemographic characteristics, report and analyse the results of the *CompED* test to determine if treatment decision-making was aided by the study results. Secondary end points included a subgroup analysis of the different groups of patients divided according to the aetiology of ED. Determine which clinical variables prior to the study could impact the results of the *CompED* test, to improve patient selection for the study. Determine which variables of the CompED

test eased the process of treatment decision-making for each subgroup of patients or each type of treatment offered.

We intended to performed a diagnostic accuracy analysis but given that the three tests combined in the *CompED* tests gives different results and made different diagnosis (Vasculogenic, neurogenic ED) the *CompED* could not be compared to a gold standard and we were only able to report its clinical performance characteristics and withdraw our own conclusions.

Statistical Analysis

A diagnostic test should decrease or abolish uncertainty about the presence or absence of ED in one patient by altering the pretest probability. Pretest probability is the probability that a condition is present without input from a diagnostic test.(46–48) The prevalence of a clinical condition in the population is commonly used as an estimate of pretest probability, in this case the prevalence of ED is estimated between 18-47%.(4–6,28)

For descriptive univariate analysis central tendency (median and mean) and dispersion (standard deviation, interquartile range) measures were used. For bivariate analysis, p values were calculated, statistically significance was assumed as $p \leq 0.05$; for continuous variables we used the chi-square test and for categorical variables a fisher test was used. Multivariate analysis was performed using binary decision trees, their respective separating nodes where

divided according to the Gini coefficient, with a minimum of 10 observations to divide each node and a minimum of 5 observations in each sheet with a complexity parameter of 0.025. Pearson correlation coefficient was also used to determine statistical relationship or association between multiple continuous variables, it was reported through dispersion diagrams for pairwise correlation in which we´ll have a positive correlation as the value approaches +1 and a total negative linear correlation as it approaches -1; values below 0.3 are considered to be weak, 0.3-0.7 are moderate and >0.7 are strong correlation. to determine the probability of treatment decision-making; R Studio version 4.0.0. was used for statistical calculations.

RESULTS

Between May 2017 and January 2020, 187 patients with ED, after oral therapy failure underwent the CompED test. Data was collected and analysed prospectively. Mean age of the patients was 57 +/- 12.8 years, median follow up was 24 (IQR 12-240) months. Thirteen patients (6.8%) reported penile curvature before the CompED test and 9 (4.7%) had hypogonadism according to the MADS questionnaire. Median IIEF-15 Domain A was 6 (IQR 1-30) and we found that 73 (38.6%) of our patients answered they were not sexually active when they completed the questionnaire. Twenty-two of our patients had DM, 7 had coronary artery disease (CAD), 109 patients had prostate cancer and 67 were treated with radical prostatectomy (RP), 33 with IMRT and 28 with ADT, of the ADT group 19 had received concurrent ADT and IMRT. 28 patients reported to suffer from hypertension (HTN), 14 have had a pelvic trauma, 5 had SCI, 14 were actively treated for hypotiroidism, 25 of our patients had been diagnosed with HIV, 5 had chronic kidney disease (CKD) and we decided

to include four patients with colorectal cancer who had been treated with abdominoperineal resection. Clinical and sociodemographic characteristics for each group are reported on Table 1.

ICI Rigidity Test

As mentioned before the CompED test includes an ICI rigidity test, CDDUS and biothesiometry. The ICI test was considered positive for ED if the rigidity score was less than 50% at the tip of the penis, 59 patients (31.2%) had a rigidity score below 50%, median axial rigidity was 60% (IQR 30-100), Subgroups with the lowest rigidity percentage were DM median 35% (IQR 22.5-100), CAD median 40% (25-95), CKD median30 (IQR 20-80). Bivariate analysis for axial rigidity showed a statistically significant relation with age p=0.015, time since ED diagnosis P=0.021, DM p=0.027. Decision tree multivariate analysis chose age $\geq$ 44.5 years, time since ED diagnosis $\geq$ 34 months, IIEF <12.5 with 95% sensitivity, 14% specificity, 21% positive predictive value (PPV) and 91% negative predictive value (NPV) to predict an abnormal result (<50%). Tumescence had a statistically significant association with time since ED diagnosis p=0.047 and DM p=0.001. At the decision tree, being diabetic and older than 59.5 were the factors that best predicted an abnormal result; 97% sensibility, 11% specificity, 21% PPV and 94% NPV. (Figure 2.)

Color Doppler Duplex Ultrasound

The CDDUS was performed in all patients at 5, 10 and 15 minutes of ICI, 54 (28.5%) patients had confirmed arterial insufficiency with PSV values below 25 cm/s. Median PSV was 22 (IQR 15-96.4) cm/s, patients with CAD, DM, RP, IMRT, ADT, HTN, hypothyroidism and CKD had a median PSV below 25 cm/s which confirms most of the patients in these

subgroups had artheriogenic ED. EDV was also measured, 25 patients (13.2%) had EDV greater than 5 cm/s which raised the suspicion of venous leakage, of these, 8 patients had venous leak, confirmed with DICC and were offered either dorsal venous ligation or hydraulic penile prosthesis implantation. Median EDV was 4 (IQR 3-16) cm/s, the only subgroup with a median EDV beyond 5 cm/s was the SCI patients, with a mean 6.4 +/- 1.8 cm/s, only one patient in this group had a normal EDV which raise the question if denervation to the smooth muscle of the tunica albuginea could lead to veno-occlusive dysfunction. Resistance Index was calculated, with a mean value of 0.77 +/- 0.176 and taken into consideration for the multivariable analysis.

Bivariate analysis of PSV showed a statistically significant relation with age $p<0.0001$, IIEF-15 $p=0.024$, IMRT $p=0.002$, ADT $p=0.014$, SCI $p=0.020$ and APR $p=0.045$. At the decision tree we found age ≥ 53.5 years and subsequently ≥ 71.5 years with an IIEF < 1.5 and time since ED diagnosis ≥ 22 months predicted an abnormal PSV (<25 cm/s) with 70% sensibility, 56% specificity, 28% PPV and 88% NPV. Regarding the EDV measures we found at the bivariate analysis a statistically significant prediction capability with time since ED diagnosis $p=0.014$ and SCI $p=0.048$. Multivariate analysis and decision trees showed time since diagnosis >78 months, hypothyroidism and IIEF<3 predicted with 16% sensibility, 83% specificity, 19% PPV and 80% NPV an abnormal EDV result ($\geq$ 5cm/s). We should highlight the limited prediction capability of this clinical variables and the test results.

Biothesiometry Test

Pallesthetic sensibility of the pudendal afferent pathways was measured with a biothesiometer, we used the Breda nomogram which proposed to use cut-off values according to age groups. If glans or shaft test results were above the proposed nomogram cut-off values, we suspected the patient could have neurogenic ED. To our surprise 52 patients (27.5%) had abnormal biothesiometry values according to their respective age group. 3 (1.5%) in the 17-30 years old, 6 (3.1%) in the 31-40 years old, 8 (4.2%) in the 41-50 years old, 10 (5.2%) in the 51-60 years old, 16 (8.4%) in the 61-70 years old and 9 (4.7%) in the 71-80 years old. The subgroups with higher biothesiometry results were CAD mean 11,4 +/-7,4, RP mean 8.23 +/- 7.69, IMRT mean 8.0 +/- 6.5 and SCI with the highest mean value 10.2 +/- 8.7. Results are shown on Table 2.

At the bivariate analysis we found statistically significant prediction capability for age $p<0.0001$, penile curvature $p=0.01$, pelvic trauma $p=0.008$, RP $p=0.012$, ADT $o=0.023$, SCI $p=0.027$ and HIV $p=0.0002$. Decision tree showed that at the shaft biothesiometry patients older than 69.5 years had a probability of nearly 100% to have an abnormal result, with 70% sensibility, 35% specificity, 21% PPV, 83% NPV.

All variables multivariate analysis showed that the factors that best predicted to have an abnormal result in any of the three tests were IIEF-15 Domain A < 14 (Same cut-off value as described in other studies), being older than 70 years and to have a past medical history of RP or IMRT; with 89% sensitivity.

Treatment Decision-Making

Treatment decision making was eased by the CompED test, given the good results shown in the test and that neurogenic or vasculogenic ED was discarded, 42 (22.2%) of patients were offered a second trial of PDE5I with a daily dose combined with a demand dose. Eighty-five (44.9%) were recommended to continue with ICI injections and 62 (32.8%) were offered surgery which could include dorsal venous ligation to patients with confirmed venous leak and penile prosthesis if artheriogenic ED was confirmed or if the patient did not accept penile venous surgery (Table 3.). We found that surgical decision making was aid greatly with the *CompED test*, given that all the information necessary to make the decisions was available after the test.

At the Pearson correlation coefficient test for treatment decision-making we found only a strong correlation between axial rigidity and tumescence to decide either for PDE5I, ICI or surgical management (Correlation= 0.72). (Supplementary Figure 1)

Regarding treatment decision-making, multivariate analysis and decision tree for PDE5I determined that a RI $\geq$ 0.8, age $\geq$ 59.5 years predicted well that patients were offered this kind of treatment with 63% sensitivity, 97% specificity, 82% PPV, 91% NPV. ICI therapy decision-making was influenced by a tumescence <59%, IIEF $\geq$ 6.5, age <43 years; with 86% sensitivity, 77% specificity, 76% PPV and 87% NPV. Surgical treatment decision-making had a much branched decision tree; the best predictor for penile venous surgery was an EDV $\geq$ 9.25 cm/s; the decision to offered a penile prosthesis was majorly influenced by a

RI <0.74, age ≥60.5 or tumescence< 35 % but the best predictor was to have a PSV < 17.5 cm/s; with 92% sensitivity, 86% specificity, 92% PPV and 86% NPV. (Figure 3)

The multivariate analysis and decision tree for all offered treatments showed that tumescence <59.5% play an important role in the decision of penile prosthesis implantation; age ≥ 51.5 years and IIEF <6 to preferred ICI therapy and an EDV < 5.85 cm/s to continue with IPD5 (daily and on demand), with 80% sensitivity, 90% specificity, 69% PPV and 91% NPV. (Figure 3.)

Complications

Regarding complications, all patients were routinely checked after the *CompED* test, if they presented a persistent erection for more than one hour, 3 cc of 1% lidocaine, and 1: 100.000 epinephrine, (0.03 mg/ml) were injected intracavernously. None of our patients returned to the ER due to priapism, we had no penile hematomas or injection site infections.

DISCUSSION

ED is an under-reported disease which affects over 70% of men screened for ED on initial questioning, despite these fact physicians surveyed in different countries were found to be reluctant to approach the subject of ED with their patients.(4,7,16,50) Rakovac in her article named “Erectile dysfunction: they don’t talk, we don’t ask” reported 124 men with DM who attended routine outpatient visits and were screened for ED or whether they have been asked

about it. 80% of patients reported they had never been asked about ED by a doctor before and only 58.9% were screened during the study period.(51) Mulhall et al found a decrease in ED diagnosis or treatment in very old age men, they concluded it may reflect the absence of a sexual partner, lack of interest in sexual activity, insufficient bother to seek help or a decreased likelihood that physicians ask very old men about the presence of ED.(4,7)

Many guidelines had proposed similar frameworks for the evaluation and management of ED, all agreed that ED could be an early symptom of occult DM or CVD.(5,28)(10,13–15,20) The first step should be a full medical, phycological, personal and sexual history and thorough clinical examination, self-administered validated questionnaires could be used to assessed the severity of ED (IIEF-5, IEEF-15), all men should undergo a fasting lipid profile, glucose level and testosterone levels.(4,5,7,16,28,50) Specialised testing are reserved for patients who wish to know the aetiology of their ED, history of pelvic, perineal or genital trauma, young patients with lifelong ED, patients unresponsive to medical therapies who may be considered for surgical treatment.(5,28,50) Special tests include the ones mentioned earlier such as NPTR, CDDUS, DICC, ICI, most of these tests are carried out separately and sometimes they could be time consuming and most of the time they could not get a solid conclusion to guide the treatment of ED. The reason after the CompED, was to design a specialised test that includes neurologic, vascular and ICI rigidity testing in a single test and visit to the andrology clinic hoping to improve the assessment and treatment decision-making in patients with ED, time saving and reducing the complication rate of each test separate.

Penile vibratory innervation is positively correlated with sexual response, biothesiometry became increasingly popular in the early 1990s given that it showed promise as a versatile,

office-based, non-invasive evaluating sensory capacity test in patients with erectile dysfunction.(34,52)(29) There is not a standardized method for biothesiometry and due to differences in how biothesiometry is performed, it has been difficult to describe a universal standard of what constitutes a normal biothesiometry.(29,52) Breda et al evaluated 350 men, aged 17 to 80-years-old with normal sexual anamnesis and without neurological pathology with penile and index finger biothesiometry to assessed pallesthetic or vibration sensitivity of the pudendal afferent pathway involved in erectile function. They reported a nomogram of normal penile biothesiometry values in this healthy population in age ranges.(34) A more novel application of biothesiometry were described by Wiggins et al, he presented the penile sensitivity ratio (PSR) which was a ratio between glans/finger (PSR G/F), glans, shaft/finger (PSR GS/F), and PSR glans, shaft/finger, thigh (PSR GS/FT) they concluded the PSR is an standardized biothesiometry parameter and it correlates with diminished reported penile sensitivity.(52) In our study we found that 52 (27.5%) patients, had abnormal biothesiometry values. Subgroups with the highest values were CAD, RP, IMRT and SCI. Bivariate analysis confirmed age $\geq$ 69.5 years, pelvic trauma, RP, ADT, SCI and HIV to have a statistically significant prediction capability to have an abnormal test result.

ICI therapy was considered the first line treatment for ED until the introduction of PDE5I by Pfizer in 1998.(2,16,32,43) It remains as an important second line treatment for ED recommended by all guidelines.(5,28) It is useful not only in the treatment of ED but in the workup and diagnosis of the disease.(32,43) ICI could be used to performed CDDUS and measured the PSV, EDV, and RI and to perform a rigidity and tumescence test.(32) There has been a lot of discussion of whether axial rigidity and tumescence of the penis could be accurately measure or if radial rigidity should be the standard of care when assessing penile

rigidity.(5,28,37–42,53) The RigiScan® device used for the NPTR and daily rigidity measurements works by periodically applying a 113 g traction force to two loops surrounding the penile shaft during a tumescence measurement, and applying a 280 g traction force when the penile circumference increases by 1 cm above the baseline and this displacement in the loops is converted in to a rigidity percentage, if the loops are displace by ≥2.2 cm the patient has 0% rigidity, on the contrary 100% rigidity corresponds to no displacement of the loops.(5,28,37–40) Based on clinical observation, 55–60% base rigidity and a 50% tip rigidity has been found to be adequate for satisfactory vaginal intercourse.(5,28,37–40) Some studies have tried to disprove the efficacy of the devices using radial compression to measure resistance to buckling of the penis arguing that buckling can only be measured by axial loading axial rigidity, not radial penile deformation. (37,38,40) Assuming radial rigidity is dependent not only in penile geometry and erectile tissue properties but in tunical surface wall tension properties.(37,38,40) Timm et al reported that hoop stress and axial stress have a constant relationship independent of the length to diameter ratio rather than as an isotropic beam, they conclude that there is enough data to prove validity and desirability of using radial compression methods to assess penile rigidity(38) In the CompED study 59 patients (31.2%) had an axial rigidity <50%, subgroups with lowest rigidity scores were DM, CAD, CKD. Bivariate analysis, age, time sin ED diagnosis and DM predicted with statistically significance to have an abnormal test. Multivariate analysis showed that age ≥ 44.5 years, times since ED diagnosis ≥ 34 months, IIEF <12.5, were the greatest predictors with 95% sensitivity.

A more refined assessment of penile hemodynamics could be achieved with CDDUS.(4,28,30,35,36,44) The aim is to evaluate the inflow and outflow of blood through

the cavernosal arteries after ICI. Several parameters had been described to distinguish arterial insuffiency and veno-occlusive disfunction.(30,32,35,36,44,54) PSV is the most accurate indicator of arterial disease. Arterial insufficiency is diagnosed when the PSV is less than 25 cm/sec, with 92% accuracy.(30,35,36) Veno-occlusive ED shows a persistent EDV over 5 cm/sec during all phases of erection, and flow in the DDV is visible on Doppler US during all phases. (5,30,35,36,55)

Altinbas et al assessed 88 patients with CDDUS, elastography and the erection hardness score (EHS) and found that 57% of the patients had abnormal CDDUS findings and they classified their patients accordingly as normal (PSV>30, EDV < 5 cm/s), borderline for arterial insufficiency (PSV 25-30 cm/s, EDV < 5 cm/s), arterial insufficiency (PSV < 25 cm/s) and venous insufficiency (EDV > 5 cm/s). They found good correlation between EHS, IIEF-5 scores in patients with arterial failure.(35) Chen et al evaluated diagnostic accuracy of CDDUS parameters for veno-occlusive ED and found the best diagnostic specificity (70.6%), sensitivity (91.7%), and accuracy (84.9%), were achieved with continuous blood flow signals in the deep dorsal vein, PSV > 30 cm/s, EDV > 5 cm/s and peak velocity (PV) of the dorsal vein > 3 cm/s.(45) In our study 54 (28.5%) patients had confirmed arterial insufficiency with PSV values below 25 cm/s. Patients with CAD, DM, RP, IMRT, ADT, HTN, Hypothyroidism and CKD had median PSV values below 25 cm/s. SCI patients had in most cases an EDV value above 5 cm/s, this was confirmed in the bivariate and multivariate analysis.

Xuan et al had compared the Schramek grading system for penile rigidity with CDDUS parameters and found that PSV, EDV and RI of the cavernous artery are significantly

different among different penile rigidity statuses after ICI, the PSV gradually decreased and EDV simultaneously increased, the PSV reflects the function of the cavernous artery and EDV reflects the venous return function. They found that RI of the penile cavernous artery strongly correlates with the penile rigidity status and proposed it should be considered the most valuable hemodynamic parameter to judge penile rigidity status.(44,54) Resistive index (RI) was calculated in our study with a mean RI of 0.77 +/- 0.176 and took into account for multivariate analysis, the model determined that a threshold of <0.8 was better in our study for treatment decision-making, contrary to the universally recommended 0.7.

Limitations of our study are that despite some of our patients had long follow up intervals, some had shorth follow up periods at the time the study was done, which could represent a bias in outcomes report. All patients completed both questionnaires the IIEF-15 and the MADS, some answered they were not sexually active which was assumed as 1 the lowest possible score of the Domain A. The tests were performed on different subset of patients, with distinct clinical features and sociodemographic characteristics, which could represent a bias when looking for statistically significant differences between all the subgroups.

Statistical limitations of our study were that when performing the multivariate analysis and building decision trees to determine which factors could predict positive results at the tests in the *CompED* study; we found that 91.4% of the patients had at least one positive test; this for an statistical model makes it hard to distinguish between groups given that it does not have a good differentiating capability of the statistical technique. Decision trees both to predict the positivity of a test or to aid in treatment decision-making were simple decision trees and it must be taken in to account they could not have a great predictive capacity.

Another possible limitation is that our statistical model may be overfitted which is an statistical model that contains more parameters than can be justified by the data and because the criterion used for selecting the model is not the same as the criterion used to judge the suitability of the model and it could fail to predict future observations reliably. Strategies to lessen the chance of overfitting are cross-validation of the data, which would mean to validate our statistical analysis in a different population but with similar characteristics which was not possible in our study.

CONCLUSION

ED is a high prevalence disease associated with aging, specialized testing should be considered in selected patients or patients unresponsive to first line treatment. The *CompED* test stands as a new alternative for the evaluation of patients with ED, being less time consuming, aiding in a more accurate determination of the aetiology and guiding treatment decision-making. Our findings showed that there are factors that increased the probability to have any of the tests within the CompED study positive, which would help to determine the ideal candidates for the study; amongst thus, age, IIEF, DM, IMRT, RP, ADT, SCI, APR, hypothyroidism, pelvic trauma and HIV. Axial rigidity and tumescence of the ICI rigidity test play an important role in treatment decision making as well as hemodynamic parameters of the CDDUS, without giving much importance to biothesiometry, regardless special subgroups as SCI, pelvic trauma, HIV, RP and IMRT benefit from the biothesiometry and include the results in the decision-making algorithm according to our analysis.

REFERENCES

1. McCabe MP, Sharlip ID, Atalla E, Balon R, Fisher AD, Laumann E, et al. Definitions of Sexual Dysfunctions in Women and Men: A Consensus Statement From the Fourth International Consultation on Sexual Medicine 2015. J Sex Med [Internet]. 2016;13(2):135–43. Available from: http://dx.doi.org/10.1016/j.jsxm.2015.12.019
2. Isidori AM, Giammusso B, Corona G, Verze P. Diagnostic and Therapeutic Workup of Erectile Dysfunction: Results From a Delphi Consensus of Andrology Experts. Sex Med. 2019;7(3):292–302.
3. Kouidrat Y, Pizzol D, Cosco T, Thompson T, Carnaghi M, Bertoldo A, et al. High prevalence of erectile dysfunction in diabetes: a systematic review and meta-analysis of 145 studies. Diabet Med. 2017;34(9):1185–92.
4. Mulhall JP, Giraldi A, Hackett G, Hellstrom WJG, Jannini EA, Rubio-Aurioles E, et al. The 2018 Revision to the Process of Care Model for Evaluation of Erectile Dysfunction. J Sex Med [Internet]. 2018;15(9):1280–92. Available from: https://doi.org/10.1016/j.jsxm.2018.06.005
5. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, et al. Erectile Dysfunction: AUA Guideline. J Urol [Internet]. 2018;200(3):633–41. Available from: https://doi.org/10.1016/j.juro.2018.05.004
6. Mulhall JP, Luo X, Zou KH, Stecher V, Galaznik A. Relationship between age and erectile dysfunction diagnosis or treatment using real-world observational data in the USA. Int J Clin Pract. 2016;70(12):1012–8.
7. Jenkins LC, Hall M, Deveci S, Guhring P, Parker M, Nelson CJ, et al. An Evaluation of a Clinical Care Pathway for the Management of Men With Nonorganic Erectile Dysfunction. J Sex Med [Internet]. 2019;16(10):1541–6. Available from: https://doi.org/10.1016/j.jsxm.2019.07.013
8. Chochina L, Naudet F, Chéhensse C, Manunta A, Damphousse M, Bonan I, et al. Intracavernous Injections in Spinal Cord Injured Men With Erectile Dysfunction, a Systematic Review and Meta-Analysis. Sex Med Rev [Internet]. 2016;4(3):257–69. Available from: http://dx.doi.org/10.1016/j.sxmr.2016.02.005

9. Wong N, Levy M, Stephenson I. Hypogonadism in the HIV-Infected Man. Curr Treat Options Infect Dis. 2017;9(1):104–16.
10. De Ryck I, Van Laeken D, Apers L, Colebunders R. Erectile dysfunction, testosterone deficiency, and risk of coronary heart disease in a cohort of men living with HIV in Belgium. J Sex Med. 2013;10(7):1816–22.
11. Maiorino MI, Bellastella G, Della Volpe E, Casciano O, Scappaticcio L, Cirillo P, et al. Erectile dysfunction in young men with type 1 diabetes. Int J Impot Res [Internet]. 2017;29(1):17–22. Available from: http://dx.doi.org/10.1038/ijir.2016.38
12. Chu N V., Edelman S V. Diabetes and Erectile Dysfunction. Clin Diabetes. 2001;19(1):45–7.
13. Montorsi P, Ravagnani PM, Galli S, Rotatori F, Veglia F, Briganti A, et al. Association between erectile dysfunction and coronary artery disease. Role of coronary clinical presentation and extent of coronary vessels involvement: The COBRA trial. Eur Heart J. 2006;27(22):2632–9.
14. Kurniawan AB, Arso IA, Tau N. Association Between Coronary Artery Lesion Severity and Erectile Dysfunction in Stable Coronary Heart Disease Patients. ACI (Acta Cardiol Indones. 2017;2(1):1–6.
15. Inman BA, St. Sauver JL, Jacobson DJ, Mcgree ME, Nehra A, Lieber MM, et al. A population-based, longitudinal study of erectile dysfunction and future coronary artery disease. Mayo Clin Proc. 2009;84(2):108–13.
16. Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, et al. Erectile dysfunction. Nat Rev Dis Prim. 2016;2:16003.
17. Patel JP, Lee EH, Mena-Hurtado CI, Walker CN. Evaluation and Management of Erectile Dysfunction in the Hypertensive Patient. Curr Cardiol Rep. 2017;19(9).
18. Carrillo-Larco RM, Luza-Dueñas AC, Urdániga-Hung M, Bernabé-Ortiz A. Diagnosis of erectile dysfunction can be used to improve screening for Type 2 diabetes mellitus. Diabet Med. 2018;35(11):1538–43.
19. Jarow JP, Lowe FC. Penile trauma: An etiologic factor in Peyronie's disease and erectile dysfunction. J Urol. 1997;158(4):1388–90.
20. Raheem OA, Su JJ, Wilson JR, Hsieh TC. The Association of Erectile Dysfunction and Cardiovascular Disease: A Systematic Critical Review. Am J Mens Health. 2017;11(3):552–63.
21. Buvat J, Jaoudé GB. Significance of hypogonadism in erectile dysfunction. World J Urol. 2006;24(6):657–67.
22. Asboe D, Catalan J, Mandalia S, Dedes N, Florence E, Schrooten W, et al. Sexual dysfunction in HIV-positive men is multi-factorial: A study of

prevalence and associated factors. AIDS Care - Psychol Socio-Medical Asp AIDS/HIV. 2007;19(8):955–65.
23. Guaraldi G, Luzi K, Murri R, Granata A, De Paola M, Orlando G, et al. Sexual dysfunction in HIV-infected men: Role of antiretroviral therapy, hypogonadism and lipodystrophy. Antivir Ther. 2007;12(7):1059–66.
24. Stanford JL, Feng Z, Hamilton AS, Gilliland FD, Stephenson RA, Eley JW, et al. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: The prostate cancer outcomes study. J Am Med Assoc. 2000;283(3):354–60.
25. Mohamad Al-Ali B, Ponholzer A, Augustin H, Madersbacher S, Pummer K. The Long-Term Effect of Radical Prostatectomy on Erectile Function, Urinary Continence, and Lower Urinary Tract Symptoms: A Comparison to Age-Matched Healthy Controls. Biomed Res Int. 2017;2017.
26. Mandel P, Preisser F, Graefen M, Steuber T, Salomon G, Haese A, et al. High Chance of Late Recovery of Urinary and Erectile Function Beyond 12 Months After Radical Prostatectomy. Eur Urol [Internet]. 2017;71(6):848–50. Available from: http://dx.doi.org/10.1016/j.eururo.2016.09.030
27. Emanu JC, Avildsen IK, Nelson CJ. Erectile dysfunction after radical prostatectomy: Prevalence, medical treatments, and psychosocial interventions. Curr Opin Support Palliat Care. 2016;10(1):102–7.
28. Nickel J. Cua Guideline. Cuaj. 2011;5(5):307.
29. Mulhall JP, Jenkins LC. Atlas of Office Based Andrology Procedures. Atlas Off Based Androl Proced. 2017;9–15.
30. Jung DC, Park SY, Lee JY. Penile doppler ultrasonography revisited. Ultrasonography. 2018;37(1):16–24.
31. Shabsigh R, Fishman IJ, Shotland Y, Karacan I, Dunn JK. Comparison of penile duplex ultrasonography with noctural penile tumescence monitoring for the evaluation of erectile impotence. J Urol. 1990;143(5):924–7.
32. Belew D, Klaassen Z, Lewis RW. Intracavernosal Injection for the Diagnosis, Evaluation, and Treatment of Erectile Dysfunction: A Review. Sex Med Rev. 2015;3(1):11–23.
33. Cumarasamy* S, Razdan S, Winoker J, Poage W, Crawford ED, Stone N. Mp40-06 Assessing the Ability of the Male Androgen Deficiency Syndrome (Mads) Screening Questionnaire To Predict Hypogonadism. J Urol. 2019;201(Supplement 4):9–11.
34. Breda G, Xausa D, Giunta A, Tamai A, Silvestre P, Gherardi L. Nomogram for penile biothesiometry. Eur Urol. 1991;20(1):67–9.

35. Altinbas NK, Hamidi N. Penile doppler ultrasonography and elastography evaluation in patients with erectile dysfunction. Polish J Radiol. 2018;83:e491–9.
36. Gilbert BR. Ultrasound of the male genitalia. Ultrasound of The Male Genitalia. 2015. 1–190 p.
37. Udelson D, Goldstein I. Reply to Editorial Comments on "Axial penile buckling forces vs Rigiscan(TM) radial rigidity as a function of intracavernosal pressure: Why Rigiscan does not predict functional erections in individual patients." Int J Impot Res. 2000;12(1):3–8.
38. Timm GW, Elayaperumal S, Hegrenes J. Biomechanical analysis of penile erections: Penile buckling behaviour under axial loading and radial compression. BJU Int. 2008;102(1):76–84.
39. GIESBERS A, BRUINS J, KRAMER A, JONAS U. New methods in the diagnosis of impotence: Rigiscan. Vol. 5, World journal of urology (Print). 1987. p. 173–7.
40. Udelson D. Biomechanics of male erectile function. J R Soc Interface. 2007;4(17):1031–47.
41. Mulhall JP, Goldstein I, Bushmakin AG, Cappelleri JC, Hvidsten K. Validation of the erection hardness score. J Sex Med. 2007;4(6):1626–34.
42. Goldstein I, Payton TR, Padma-Nathan H, Krane RJ. Characterization of penile erectile states using external computer-based monitoring. Vol. 109, Journal of Biomechanical Engineering. 1987. p. 110–4.
43. Buvat J, Buvat-Herbaut M, Dehaene JL, Lemaire A. Is intracavernous injection of papaverine a reliable screening test for vascular impotence? J Urol. 1986;135(3):476–8.
44. Xuan XJ, Bai G, Zhang CX, Xu C, Lu FD, Peng Y, et al. The application of color Doppler flow imaging in the diagnosis and therapeutic effect evaluation of erectile dysfunction. Asian J Androl. 2016;18(1):118–22.
45. Chen L, Xu L, Wang J, Li H, Zhang D, Zhang C, et al. Diagnostic Accuracy of Different Criteria of Pharmaco-penile Duplex Sonography for Venous Erectile Dysfunction. J Ultrasound Med. 2019;38(10):2739–48.
46. Aliu O, Chung KC. Assessing strength of evidence in diagnostic tests. Plast Reconstr Surg. 2012;129(6):1–20.
47. Cohen JF, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: Explanation and elaboration. BMJ Open. 2016;6(11):1–17.
48. Janes H, Pepe MS, Bossuyt PM, Barlow WE. Research and Reporting Methods Treatment Decisions. Ann Intern Med. 2011;154(4):253–60.

49. Scales CD, Dahm P, Sultan S, Campbell-Scherer D, Devereaux PJ. How to Use an Article About a Diagnostic Test. J Urol. 2008;180(2):469–76.
50. McMahon CG. Current diagnosis and management of erectile dysfunction. Med J Aust. 2019;210(10):469–76.
51. Rakovac Tisdall A, King TFJ, Mahmood WAW, Keat CS, Ali R, Abdin R, et al. Erectile dysfunction: they don't talk, we don't ask. Diabet Med. 2018;35(5):667–8.
52. Wiggins A, Farrell MR, Tsambarlis P, Levine LA. The Penile Sensitivity Ratio: A Novel Application of Biothesiometry to Assess Changes in Penile Sensitivity. J Sex Med [Internet]. 2019;16(3):447–51. Available from: https://doi.org/10.1016/j.jsxm.2019.01.002
53. Bouchelouche K, Nordling J, Hald T, Bouchelouche P. The relationship of penile rigidity and intracavernous vascular resistance in potent men during intracavernous pharmacological testing. J Urol. 2001;166(5):1762–5.
54. Xuan X, Wang D, Sun P, Mei H. Evaluation of penile rigidity with color doppler flow imaging in Chinese patients with erectile dysfunction. Urol Int. 2008;80(3):321–4.
55. Akslan D, Esen AA, Seçil M, Aslan G, Çelebi I, Dicle O. A new method for the evaluation of erectile dysfunction: Sildenafil plus Doppler ultrasonography. J Urol. 2001;166(1):181–4.

TABLES AND FIGURES

Table 1.

Table 1. Clinical and Sociodemographic Characteristics

Comorbidities	n	Age (Years)	Curvature n(%)	Follow up (months)	MADS (+) n(%)	IIEF-15 Domain A
Diabetes	n= 22	59 (54.7-74)	5 (22.7)	24 (12-108)	4 (18.1)	6 (1-25)
Coronary artery disease	n=7	62 (57-75)	1 (14.2)	24 (18-120)	1 (14.2)	1 (1-25)
Prostate Cancer						
1. Radical Prostatectomy	n=67	65 (59.5-75)	2 (2.9)	18 (11-108)	4 (5.8)	1 (1-26)
2. IMRT	n=33	67 (58-78)	1 (3)	24 (12-192)	0	1 (1-30)
3. ADT	n=28	66 (56-78)	2 (7.1)	24 (12-108)	0	1 (1-29)
Hypertension	n=28	60 (55.7-78)	0	24 (!2-120)	3 (10.7)	2.5 (1-30)
Pelvic trauma	n=14	41,5 (32.5-60)	0	24 (12-108)	0	3 (1-26)
Spinal cord injury	n=5	44 (42-50))	0	120 (96-168)	0	9 (1-18)
Hypotiroidism	n=14	65 (52.7-74)	1 (7.1)	24 (12-240)	0	6.5 (1-26)
Abdomino Perineal Resection	n=4	54 (49.7-58)	0	27 (16.5-108)	0	1 (1-26)
HIV	n=25	49 (37-67)	0	24 (12-240)	0	8 (5-24)
Chronic kidney Disease	n=5	54 (51-60)	0	24 (7-48)	1 (20)	1 (1-25)
Total	n=187	58 (50-78)	13 (6.8)	24 (12-240)	9 (4.7)	6 (1-30)

IMRT=Intensity modulated radiotherapy, ADT= Androgen deprivation Therapy, HIV= Human immunodeficiency virus.

***Values are reported as median and (IQR)*

Table 2.

Table 2. Clinical Characteristics of the Complete Study for Erectile Dysfunction

	INTRACAVERNOUS INJECTION TEST			CDDUS		BIOTHESIOMETRY	
	Axial Rigidity	Angle (ª)	Tumescence	PSV	EDV	Shaft	Glans
Diabetes	50 (0-100)	30 (0-80)	40 (10-100)	14 (0-38)	4 (0-9)	5 (3-12)	4 (2-13)
Coronary artery disease	40 (20-95)	30 (20-90)	80 (20-95)	12,5 (9,5-	3,5 (2,5-9,6)	8 (4-25)	4 (2-11)
Prostate Cancer							
1. Radical Prostatectomy	50 (27-100)	40 (27,6-95)	70 (29-100)	20 (15,4-92)	3,5 (2,7-13)	6 (7-36)	7 (7,7-40)
2. IMRT	60 (32-100)	30 (29-95)	60 (32-100)	15 (17,7-92)	3,9 (2,7-	6 (5,9-20)	7 (8,5-36)
3. ADT	50 (0-100)	30 (0-90)	60 (0-100)	17 (9,5-50)	4,2 (1,2-	6 (2-20)	6 (2-36)
Hypertension	50 (0-100)	35 (0-90)	80 (10-100)	19 (5-51)	4,1 (1,4-13)	6 (3-25)	5 (2-19)
Pelvic trauma	70 (0-100)	65 (0-100)	85 (0-100)	28 (0-60)	3,8 (1,4-9,5)	6 (3-8)	5 (3-12)
Spinal cord injury	60 (0-100)	70 (0-80)	80 (30-100)	40 (28-96)	6 (3,6-9,5)	8 (3-25)	9 (3-18)
Hypotiroidism	50 (0-100)	40 (0-90)	50 (30-100)	23,5 (12-50)	5,2 (0-8,7)	5,5 (3-28)	5 (3-19)
Abdomino Perineal Resection	75 (50-100)	65 (30-90)	75 (45-100)	35 (25-50)	2,5 (1,6-5,5)	4,5 (3-5)	5 (2-6)
Chronic kidney Disease	30 (20-80)	30 (30-90)	40 (20-90)	12,5 (9,5-25)	3,5 (2,5-7)	5 (4-15)	5 (4-11)
Total	60 (30-100)	45 (0-100)	80 (0-100)	23 (0-96,4)	4 (3-16)	6 (2-36)	6 (0-40)

CDDUS= Color Doppler Duplex Ultrasound, PSV= Peak systolic velocity, EDV= End diastolic velocity, IMRT=Intensity modulated radiotherapy, ADT= Androgen deprivation Therapy

***Values are reported as median (interquartile range)*

Table 3.

Table 3. Treatment Decision-making					
	n	PD5I	ICI	Penile Prosthesis	Penile Venous Surgery
Diabetes	*n= 22*	4 (9.5)	5 (5.8)	13 (24)	0
Coronary artery disease	*n=7*	1 (2.3)	2 (2.3)	3 (5.5)	0
Prostate Cancer					
1. Radical Prostatectomy	*n=67*	6 (14.2)	37 (43.5)	26 (48.1)	1 (12.5)
2. IMRT	*n=33*	4 (9.5)	16 (18.8)	14 (25.9)	0
3. ADT	*n=28*	2 (4.7)	14 (16.4)	11 (12.9)	1 (12.5)
Hypertension	*n=28*	3 (7.1)	13 (15.2)	9 (10.5)	0
Pelvic trauma	*n=14*	3 (7.1)	7 (8.2)	2 (3.7)	0
Spinal cord injury	*n=5*	2 (4.7)	1 (1.1)	1 (1.85)	0
Hypotiroidism	*n=14*	3 (7.1)	5 (11.9)	6 (11.1)	1 (12.5)
Abdomino Perineal Resection	*n=4*	2 (4.7)	2 (2.3)	0	0
HIV	*n=25*	12	8 (9.4)	2 (3.7)	1 (12.5)
Chronic kidney Disease	*n=5*	1 (2.3)	1 (1.1)	3 (5.5)	0
Idiopathic	*n=4*	0	0	0	4 (50)
Total	*n=187*	42 (22.2)	85 (44.9)	54 (28.5)	8 (4.2)

IMRT=Intensity modulated radiotherapy, ADT= Androgen deprivation Therapy, HIV= Human immunodeficiency virus, PD5I= Phosphodiesterase type 5 inhibitor, ICI= Intracvernous injections.

***Values are reported as n (%)*

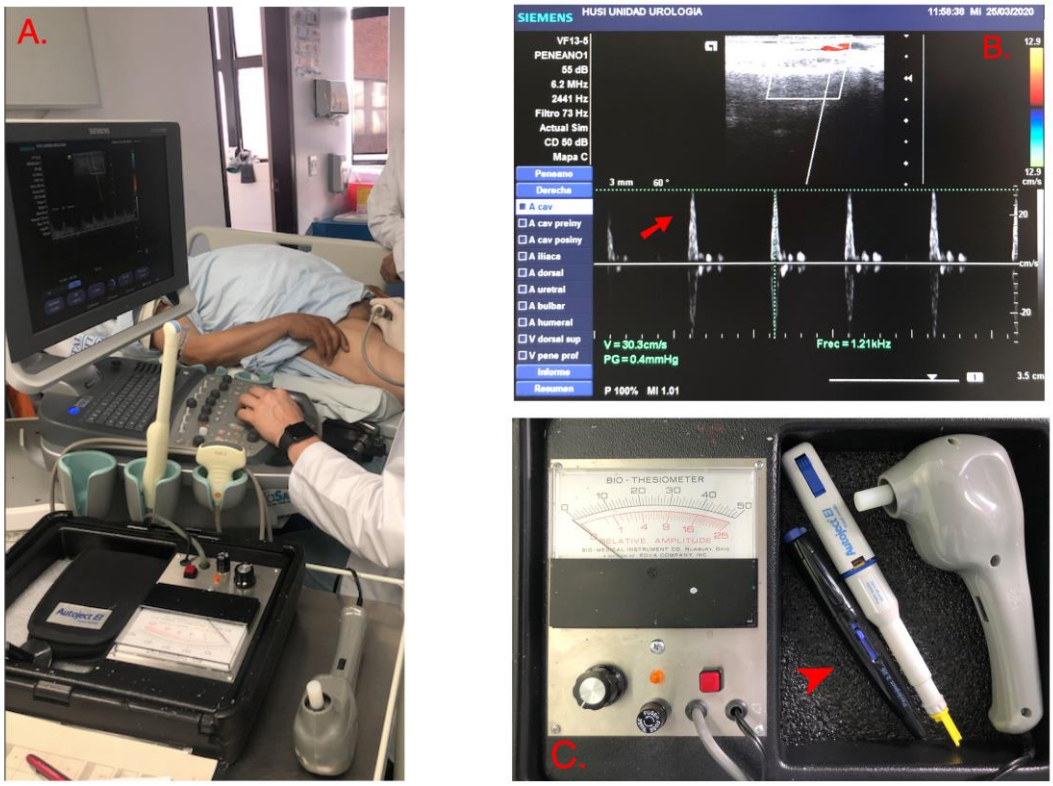

Figure 1. A. Room set up for the *CompED* test. **B.** Colour Duplex Doppler Ultrasound, with high-frequency linear array transducer 7.5 MHz, Penile flow velocities of the cavernosal artery were measured (Arrow) **C.** Biothesiometer manufactured by Bio-Medical instruments, Autoinjectors for the ICI (arrow head).

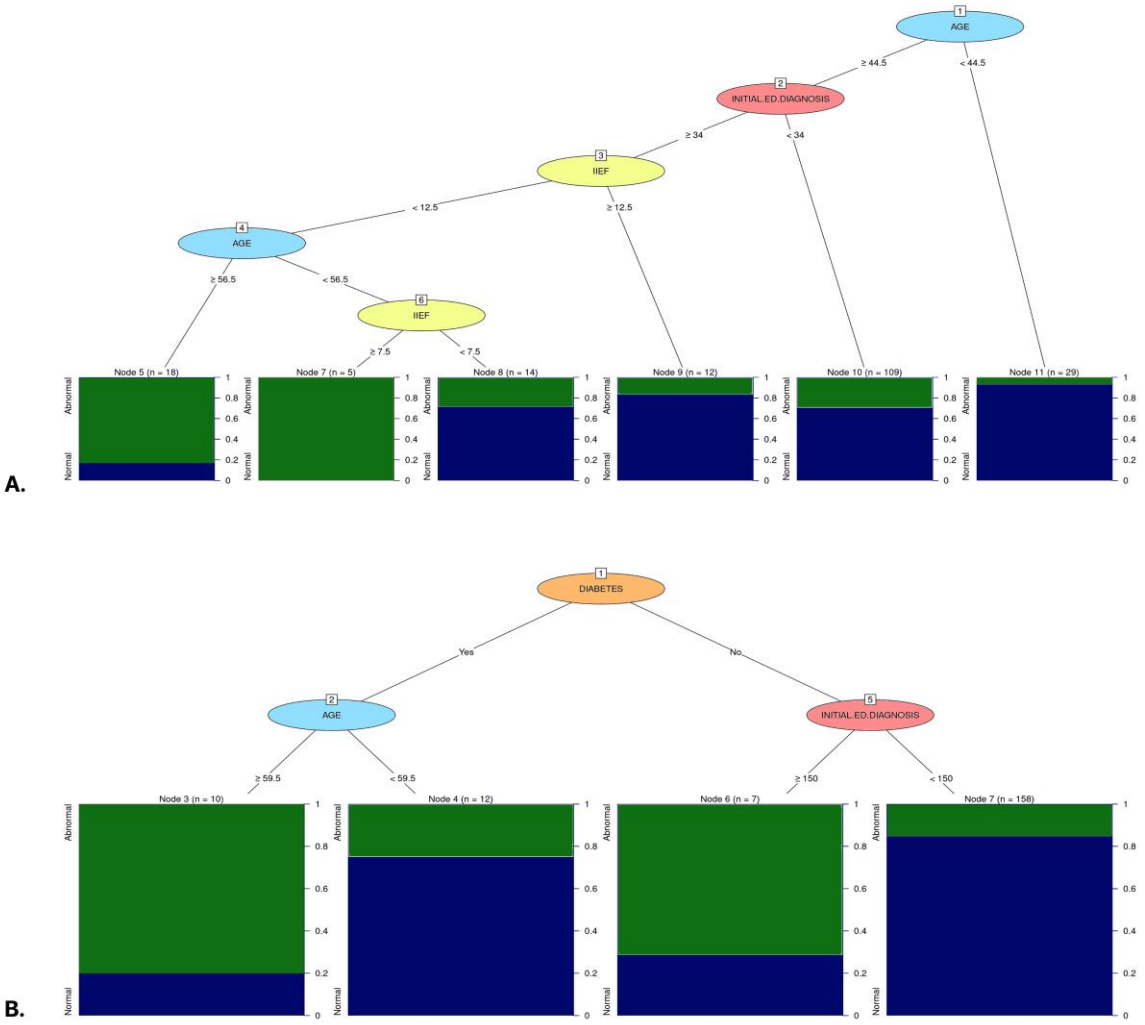

Figure 2. Decision tree of the multivariate analysis to predict a normal (Blue) result or an abnormal (Green) result in the ICI rigidity test, which was defined as abnormal (< 50%) and normal (≥ 50%) **A.** Axial rigidity**. B.** Tumescence.

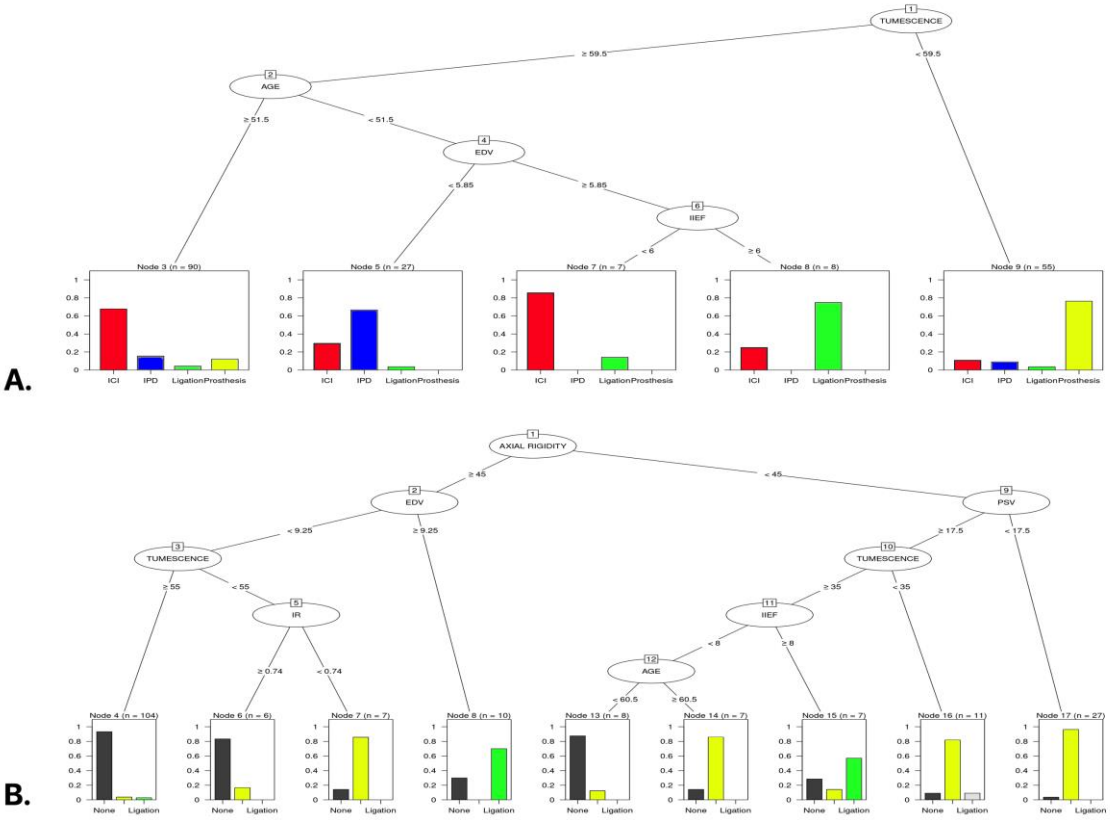

Figure 3. Decision trees of the multivariate analysis to predict treatment decision-making, ICI (Red) PDE5I (Blue) Penile Venous ligation (Green), Penile prosthesis (Yellow), None (Grey) A. Decision tree to predict any kind of treatment (PDE5I, ICI, Penile prosthesis or venous ligation). **B.** Surgical treatment decision tree (Penile prosthesis, Penile venous surgery)

Supplementary Figure 1. Pearson correlation coefficient (PCC) reported through dispersion diagrams for pairwise correlation to determine the probability of treatment decision-making. P=0.719 between axial rigidity and tumescence, P=0.667 between biothesiometry at the shaft and glans and P=0.678 between axial rigidity and angle to predict surgical treatment.