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Role of Varicocele Sclerotherapy in the Management of Benign Prostatic Hyperplasia and its Associated Lower Urinary Tract Symptoms

Thesis

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By

Zeinab Aly Moussa Aly
M.B.B.Ch., M.Sc. Radiology

Under the Supervision of

Prof. Dr. Mohamed El Gharib Abou El Ma'aty
Professor of Radiodiagnosis and Interventional Radiology
Faculty of Medicine, Ain Shams University

Prof. Dr. Waleed Mohamed Abd El Hameed Hetta
Professor of Radiodiagnosis and Interventional Radiology
Faculty of Medicine, Ain Shams University

Dr. Khaled Sayed Ahmed Soliman
Lecturer of Radiodiagnosis
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University

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قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

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List of Abbreviations

Abb.	Full term
ADC	Apparent Diffusion Coefficient
AVPs	Amplatz vascular plugs
B-mode	Brightness mode
BOO	Bladder outlet obstruction
BPE	Benign prostatic enlargement
BPH	Benign prostatic hyperplasia
BWT	Bladder wall thickness
CBC	Complete blood picture
cc	Cubic centimetre
cm	Centimetre
(MD) CT	(Multidetector) computed tomography
DHT	Dihydrotestosterone
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
DO	Detrusor over activity
DRE	Digital rectal examination
F	French
FT	Free testosterone
GV	Gonadal vein
(m) g/ml	(Milli) gram/millilitre
Mg/kg	milligram/kilogram
INR	International normalized ratio
IPSS	International prostate symptom score
IQR	Interquartile range
ISV	Internal spermatic vein
IVC	Inferior vena cava
LUTS	Lower urinary tract symptoms
L3 or L4	3^d or 4th lumbar vertebral body
MCi	Millicurie
Mg	Milligram
MHz	Mega hertz
Min	Minutes
ML (/kg)	Millilitre (per kilogram)
ML/sec	Millilitre (per second)

List of Abbreviations cont.

Abb.	Full term
<i>(Mm)²</i>	<i>Millimetre (squared)</i>
<i>MmHg</i>	<i>Millimeter mercury</i>
<i>MR (I)</i>	<i>Magnetic resonance (imaging)</i>
<i>(m) Sec</i>	<i>Millisecond</i>
<i>NBCA (-MS)</i>	<i>N-Butyl 2 Cyanoacrylate (-methacryloxysulfolane)</i>
<i>Ng (/ml)</i>	<i>Nanogram (/millilitre)</i>
<i>OBS</i>	<i>Overactive bladder syndrome</i>
<i>OWVs</i>	<i>One-way valves</i>
<i>P value</i>	<i>Probability value</i>
<i>PSA</i>	<i>Prostate-specific antigen</i>
<i>PVR</i>	<i>Post-void residual</i>
<i>RBCs</i>	<i>Red blood cells</i>
<i>Qmax</i>	<i>Maximum urinary flow rate</i>
<i>QoL</i>	<i>Quality of Life</i>
<i>SBPI</i>	<i>Scrotal blood pool index</i>
<i>SD</i>	<i>Standard deviation</i>
<i>SHBG</i>	<i>Sex hormone binding globulin</i>
<i>SPSS</i>	<i>Statistical Package for the Social Sciences</i>
<i>STDs</i>	<i>Sexually transmitted diseases</i>
<i>STS</i>	<i>Sodium tetradecyl sulfate</i>
<i>Tc</i>	<i>Technetium</i>
<i>TRUS</i>	<i>Transrectal ultrasound</i>
<i>TURP</i>	<i>Transurethral resection prostatectomy</i>
<i>T1WI</i>	<i>T1 weighted images</i>
<i>T2WI</i>	<i>T2 weighted images</i>
<i>UTIs</i>	<i>Urinary tract infections</i>
<i>3D</i>	<i>Three dimensional</i>
<i>°C</i>	<i>Degree Celsius</i>
<i>Π</i>	<i>Pi (=3.14)</i>

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most prevalent ailments of aging men, affecting nearly 50% and 100% of this population by the time they reach 50 and 80 years of age, respectively, with a detrimental impact on their quality of life (QoL) (*Landau & Welliver, 2020*).

The prostate grows at a rate of 2.5% per year in higher age groups and the age-related prostatic enlargement mainly affects the prostatic periurethral zone. Subsequent prostatic urethral compression occurs with resultant urinary outflow obstruction, urinary bladder hypertrophy and reduction of the bladder volume reservoir (*Munsif et al., 2021*).

The lower urinary tract symptoms affect up to 74% of adults above 40 years, 42% of whom report a moderate degree of symptoms. Also, an age-dependent lower urinary symptomatic progression occurs in 5-year increments with a resultant poor sexual life due to erectile & ejaculatory dysfunctions and side effects of antiandrogenic medications (*Lim, 2017*).

To further explore the underlying mechanisms of prostatic enlargement, Gat et al. proposed that the blood flow mechanics of the anatomically connected prostatic and testicular veins follow Pascal's and Bernoulli's laws, which postulate that the fluid hydrostatic pressure equalizes across communicating vessels (*Gat et al., 2008*).

The age-related valvular destruction of the spermatic veins establishes continuous blood columns with elevated hydrostatic pressures that form a pressure gradient diverging the flow carrying free testosterone (dihydrotestosterone or DHT) from the testes to the prostate with subsequent prostatic congestion & androgen-dependent prostatic hyperplasia (*Gat et al., 2008*).

Gat referred to the testicular-prostatic venous backflow as ‘the backdoor phenomenon’, which was used to explain the biologic paradox of testosterone-dependent BPH despite age-dependent serum testosterone decline. Subsequently, Gat considered varicoceles sclerotherapy to be a super-selective intraprostatic androgen deprivation therapy because the occlusion of the refluxing spermatic veins and their vertical bypasses eliminates the testicular-prostatic pressure gradient with backflow cessation and reversal of the prostatic hyperplasia (*Gat et al., 2008*).

Several studies agreed with the Gat theory while others rejected it. The supporting studies included the **Strunk et al. study** that detected an improvement of the urinary symptoms upon sclerotherapy application in patients with prostatomegaly, the **Ur Rehmen et al. study** that found the pressure in the incompetent left ISV to be as postulated by Gat et al. (31 mmHg with Valsalva) using direct measurement, and the **Pejčić et al. study** that detected a fourfold rise in the dihydrotestosterone (DHT) quantity of the BPH specimens using mass spectrometry.

On the other hand, studies that rejected the Gat theory disputed the proposed causal relationship between varicoceles & BPH, and claimed that prostatic enlargement is a multifactorial process caused by androstenedione-dependent DHT, aromatase-dependent estrogen stromal proliferation, androgen & estrogen receptors overexpression, chronic inflammation, and immune dysregulation (***Chen et al., 2020***).

In addition, two prospective studies published different results from those of the Gat studies; **Gaona et al. study** uncovered no statistical significance in varicoceles percentage between patients with prostatic volumes ≥ 40 ml and < 40 ml and **De Caestecker et al. study** detected high periprostatic plexus testosterone in only 2 out of 7 patients undergoing Millin prostatectomy for BPH.