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ORIGINAL PAPER

Use of oral phosphodiesterase type-5 inhibitors before penile prosthesis implantation: Duration, predictors, and clinical insights

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Summary ***Background: Phosphodiesterase type-5 inhibitors (PDE5i) are the first-line therapy for erectile dysfunction (ED), offering high efficacy and favorable safety profiles. However, data on how long PDE5i remain effective before the need for penile prosthesis (PP) surgery are limited. This study evaluates the duration from PDE5i initiation to PP surgery and identifies predictors of this interval.***
Methods: We conducted a retrospective review of patients with ED who initiated PDE5i therapy and subsequently underwent PP surgery between January 2019 and August 2022. Clinical characteristics, laboratory results, and duration of PDE5i use were extracted from hospital records.
Results: A total of 98 patients were included, with a mean age of 56.1 ± 11.5 years and a mean body mass index (BMI) of 29.8 ± 4.4 kg/m². Comorbidities were present in 88.8 % of patients, including diabetes mellitus (75.5 %), hypertension (54.1 %), and smoking (31.6 %). The mean time from PDE5i initiation to PP surgery was 34.9 ± 24.8 months (≈ 2.9 years). Lower testosterone levels were associated with earlier surgery, while comorbidities were not.
Conclusions: The average duration of PDE5i use prior to PP surgery was approximately three years. Lower testosterone levels may predict earlier surgical intervention, whereas comorbidities did not show a significant association. These findings may assist clinicians in counseling patients and planning treatment strategies.

KEY WORDS: *Erectile dysfunction; Intracavernosal injection; Penile prosthesis surgery; Phosphodiesterase 5 Inhibitors.*

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INTRODUCTION

Erectile dysfunction (ED) refers to the inability to attain and/or sustain an erection adequate for satisfactory sexual intercourse, affecting a large proportion of men worldwide (1-3). Management options include lifestyle modification, medical therapy, and *penile prosthesis* (PP) implantation. Medical therapy primarily relies on *phosphodiesterase type-5 inhibitors* (PDE5i), which are effective and safe but often limited by adherence issues or declining response over time.

PP surgery was traditionally considered a third-line treatment but is now viewed as an appropriate first-line option in suitable patients following thorough counseling (4, 5). Current guidelines recommend tailoring treatment based on patient preference and clinical factors rather than strictly following a stepwise sequence.

Few studies have examined the real-world time interval between initiating PDE5i and proceeding to PP implantation. Understanding this duration and its predictors can improve patient counseling and guide therapeutic decision-making. This study aimed to assess the interval between PDE5i initiation and PP surgery and identify patient-related factors associated with early or delayed surgical intervention.

MATERIALS AND METHODS

After institutional ethics approval (MRC-01-19-429), medical records of patients who underwent PP implantation between January 2019 and August 2022 were retrospectively reviewed (6). Eligible patients were men with ED who initiated and subsequently failed PDE5i therapy. Failure was defined as inadequate response despite appropriate use at maximum doses for at least three months, normal testosterone levels, and proper counseling.

Patients who declined PP implantation or chose alternative second-line therapies such as *intracavernosal injection* (ICI) or *vacuum erection device* (VED) were excluded. All included patients underwent *penile Doppler ultrasound* (PDU) prior to surgery, and only those with controlled diabetes (HbA1c < 8.5%) were eligible.

Demographic and clinical data were collected, including age, BMI, comorbidities, testosterone, lipid profile, and HbA1c. Laboratory tests were performed at a certified laboratory on fasting blood samples within three months before surgery.

Patients were categorized into two groups based on the median interval between PDE5i initiation and PP implantation: less than 29 months (early group) and 29 months or more (late group). Statistical analyses were performed using R software (*version 4.2.3, Vienna, Austria*).

Continuous variables were presented as mean ± SD and compared with Student's t-test. Categorical variables were

Table 1.
Baseline characteristics of included patients.

	Mean ± SD or Number (%)
Demographic and clinical characteristics	
Age (Years)	56.1 ± 11
Weight (Kg)	87.2 ± 14.3
Height (cm)	170.9 ± 6.7
Body mass index (Kg/m^2)	29.8 ± 4.4
Comorbidities	87 (88.8%)
Hypertension	53 (54.1%)
Diabetes Mellitus	74 (75.5%)
Smoking	31 (31.6%)
Laboratory characteristics	
Glucose (mmol/L)	7.6 ± 2.7
HbA1c (%)	6.9 ± 1.3
Cholesterol (mmol/L)	4.3 ± 1.3
HDL Cholesterol (mmol/L)	1.1 ± 0.3
LDL Cholesterol (mmol/L)	2.4 ± 1.1
Triglyceride (mmol/L)	1.6 ± 0.9
Vitamin D (ng/mL)	26.3 ± 11.9
Total Testosterone (nmol/L)	16.5 ± 5.2
Medication history	
Sildenafil	27 (27.6%)
Tadalafil	76 (77.6%)
Vardenafil	13 (13.3%)
Combination of PDE5-i	22 (22.4%)
Penis prosthesis surgery details	
Malleable	11 (11.2%)
Inflatable	87 (88.8%)
Cylinder size (cm)	21.8 ± 1.9
Duration from start of PDE5-I till surgery (months)	34.9 ± 24.8
Median (IQR)	29 (19.8-45.5)

Table 2.
Comparison of patients' characteristics in those who performed PPI < or ≥ 29 months.

	< 29 months	≥ 29 months	p value
Demographic and clinical characteristics			
Age (Years)	58.2 ± 10.8	54.3 ± 11	0.08
Weight (Kg)	87.5 ± 14.5	86.9 ± 14.3	0.84
Height (cm)	169 ± 6.2	172.6 ± 6.7	0.01
Body mass index (Kg/m^2)	30.5 ± 4.3	29.1 ± 4.4	0.11
Multiple comorbidities	23 (53.4%)	23 (40.3%)	0.27
Comorbidities	39 (84.8%)	48 (92.2%)	0.19
HTN	22 (47.8%)	31 (59.6%)	0.14
DM	32 (69.6%)	42 (80.8%)	0.14
Smoking	11 (23.9%)	20 (38.5%)	0.09
Laboratory characteristics			
Glucose (mmol/L)	8 ± 3.3	7.4 ± 2.3	0.34
HbA1c (%)	6.9 ± 1.2	6.9 ± 1.4	0.91
Cholesterol (mmol/L)	4.3 ± 1.4	4.3 ± 1.1	0.82
HDL Cholesterol (mmol/L)	1.1 ± 0.3	1.2 ± 0.4	0.3
LDL Cholesterol (mmol/L)	2.4 ± 1.3	2.4 ± 1	0.99
Triglyceride (mmol/L)	1.7 ± 1	1.6 ± 0.9	0.83
Vitamin D (ng/mL)	24.4 ± 11.1	28 ± 12.5	0.14
Total Testosterone (nmol/L)	14.2 ± 3.7	18.5 ± 6.7	0.004
Medication history			
Sildenafil	11 (23.9%)	16 (30.8%)	0.29
Tadalafil	35 (76.1%)	41 (78.8%)	0.46
Vardenafil	6 (13%)	7 (13.5%)	0.59
Combination of PDE5-is	9 (19.6%)	13 (25%)	0.35
Penis prosthesis surgery details			
Malleable	6 (13%)	5 (9.6%)	0.41
Inflatable	40 (87%)	47 (90.4%)	0.41
Cylinder size (cm)	22 ± 1.8	21.6 ± 2	0.42
Cut-off based on cohort median (29 months)			

compared using the chi-square test, with $p < 0.05$ considered statistically significant.

Results

A total of 98 patients met inclusion criteria. The mean age was 56.1 ± 11.5 years, and mean BMI was 29.8 ± 4.4 kg/m². Diabetes mellitus was the most common comorbidity (75.5%), followed by hypertension (54.1%) and smoking (31.6%) (Table 1). The mean time from PDE5i initiation to PP surgery was 34.9 ± 24.8 months (median 29 months). Most patients (88.8%) received an inflatable PP.

When comparing the early (< 29 months) and late (≥ 29 months) PP groups, testosterone levels were significantly lower in the early group (14.2 ± 3.7 nmol/L) compared with the late group (18.5 ± 6.7 nmol/L; $p = 0.004$) (Table 2). No significant differences were found in comorbidities, lipid profile, or HbA1c between groups.

Discussion

This study analyzed the time interval between PDE5i initiation and PP implantation among men with ED. On average, PP surgery was performed approximately 2.9 years after starting PDE5i. The primary factor associated with earlier surgery was lower testosterone levels, suggesting a potential role for hormonal status in predicting PDE5i responsiveness. ED is a common and multifactorial condition, affecting up to 30 % of men between 40 and 70 years of age (1-3). PDE5i remain the first-line therapy with well-documented efficacy, but up to one-third of men discontinue treatment due to limited efficacy, dissatisfaction, or adverse effects (7, 8). Inadequate education regarding correct medication timing or expectations may also contribute to treatment discontinuation. Previous reports show that side effects account for only a small proportion of discontinuations, whereas psychological factors, comorbidities, or treatment fatigue are more frequent causes (7, 8). Our cohort was not influenced by economic or insurance barriers, ensuring that decisions reflected clinical rather than financial factors.

Among all examined parameters, only testosterone showed a significant difference, being higher among those with longer duration of PDE5i use. Testosterone plays a crucial role in maintaining erectile function and modulating PDE5i response (9, 10). The relationship observed in our study underscores the importance of evaluating and managing testosterone levels in ED patients. Our findings support the notion that adequate testosterone may sustain PDE5i efficacy and delay the

need for surgical intervention. Thus, hormonal assessment should be an integral part of ED management algorithms.

Strengths and limitations

A major strength of this study is the inclusion of patients from a single tertiary center where all individuals were insured for the entire spectrum of ED management, ensuring that treatment decisions were not influenced by financial or insurance constraints. This provides an unbiased evaluation of clinical decision-making in ED management.

However, several limitations should be acknowledged. As this retrospective analysis included only men who eventually underwent PP implantation, we could not compare them with those who continued to respond to PDE5i therapy without requiring surgery. Consequently, the generalizability of our findings to the broader ED population is limited. Additionally, detailed reasons for discontinuing PDE5i were not consistently documented; while treatment failure is presumed, other factors such as partner preference, side effects, or psychological influences may have played a role. Finally, the duration and control of comorbidities were not uniformly recorded. Future prospective studies including both responders and non-responders could better elucidate the transition from medical to surgical management (10).

Conclusions

In this retrospective study, patients underwent PP implantation approximately three years after initiating PDE5i therapy. Lower testosterone levels were associated with earlier surgical intervention, while comorbidities did not significantly influence timing. These findings highlight the importance of hormonal assessment in ED management and may assist clinicians in counseling patients regarding long-term expectations for PDE5i therapy.

Declarations

Ethical approval and consent for participate: *Institutional ethics approval (MRC-01-19-429).*

Availability of data and material: *The data that support the findings of this study are available from the corresponding author upon reasonable request.*

Competing interests: *All the authors declare no conflict of interest.*

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Authors' contributions: *Conceptualization: Onder Canguven. Methodology: Onder Canguven, Ahmad Majzoub Formal analysis: Onder Canguven, Ahmad Majzoub Data Curation: Ahmed Al Saeedi, Yaser M. Ata, and Nadir Fadol Writing— Ahmad Majzoub, and Onder Canguven.Writing—Review & Editing: Onder Canguven, Ahmad Majzoub, Khalid AlKubaisi, Ahmad AlMalki. Supervision: Ahmad Mazjoub, Onder Canguven, Khalid AlKubaisi, Ahmad AlMalki.*

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