

Treatment for mixed genesis erectile dysfunction accompanied by chronic pelvic pain or premature ejaculation in men with combat injury

M. Z. Vorobets, D. Z. Vorobets, R. V. Fafula, A. S. Besedina, M. Ye. Kushynska, Z. D. Vorobets, O. M. Chemerys

SNPC “Danylo Halytsky Lviv National Medical University”

Participants in hostilities often face long-term effects of severe injuries, which can markedly impair both quality of life and sexual function.

The objective: to assess the effectiveness of treatment for mixed genesis erectile dysfunction (ED) accompanied by chronic pelvic pain (CPP) or premature ejaculation (PE) in men with combat injury.

Materials and methods. The examination of 60 men aged 20–53, participants in hostilities, with sexual dysfunction was performed. The main complaints were ED accompanied by CPP or PE. According to the form of ED, patients were divided into groups: Group 1 included patients with ED of mixed etiology associated with CPP (n = 32); Group 2 consisted of patients with ED of mixed origin accompanied by PE (n = 28).

Results. It has been demonstrated that lifestyle modification is an effective treatment method for ED, which is accompanied by CPP in men with a combat injury. 62.5% of patients have a significant improvement in erectile function, and 31.2% have a slight improvement. The efficacy of treatment of ED associated with PE is linked to serotonin reuptake inhibitors (SRIs), confirming the key role of the neurotransmitter serotonin in the modulation of ejaculation. Significant improvement in this group was observed in 53.6% of patients, and insignificant in 39.3%.

Conclusions. The most effective method of treatment is lifestyle modification for patients injured as a result of hostilities, with ED of mixed genesis, accompanied by the leading syndrome of CPP. This group demonstrated an improvement in International Index of Erectile Function (IIEF)-5 score from 13.5 ± 2.3 to 21.6 ± 2.1 ($p < 0.05$). Serotonin is a key neurotransmitter involved in the regulation of ejaculation in patients with ED and coexisting PE, as treatment with SRIs prolongs intravaginal ejaculatory latency. This group also demonstrated an improvement in IIEF-5 score from 13.8 ± 2.1 to 22.0 ± 1.9 ($p < 0.05$).

Keywords: erectile dysfunction, combatants, combat trauma, chronic pelvic pain, premature ejaculation, treatment.

Лікування еректильної дисфункції змішаного генезу, що супроводжується хронічним тазовим болем або передчасною еякуляцією, у чоловіків із бойовими травмами

М. З. Воробець, Д. З. Воробець, Р. В. Фафула, А. С. Беседіна, М. Є. Кушинська, З. Д. Воробець, О. М. Чемерис

Учасники бойових дій зазнають довготривалих наслідків тяжких поранень, які суттєво впливають на якість життя та статеву функцію.

Мета дослідження: оцінка ефективності лікування еректильної дисфункції (ЕД) змішаного генезу, що супроводжується хронічним тазовим болем (ХТБ) або передчасною еякуляцією (ПЕ), у чоловіків із бойовими травмами.

Матеріали та методи. У дослідження включено 60 чоловіків віком 20–53 років – учасників бойових дій із сексуальною дисфункцією. Основною скаргою була ЕД, що супроводжувалася ХТБ або ПЕ. Залежно від клінічної форми ЕД пацієнтів розподілено на дві групи: 1-ша група – 32 пацієнти з ЕД змішаного генезу, що супроводжується ХТБ; 2-га група – 28 чоловіків з ЕД змішаного генезу та ПЕ.

Результати. Встановлено, що модифікація способу життя є ефективним методом лікування ЕД, яка супроводжується ХТБ, у чоловіків із бойовими пораненнями: у 62,5% пацієнтів відзначено значне покращення еректильної функції, у 31,2% – незначне покращення. Ефективність лікування ЕД, що супроводжується ПЕ, пов'язана із застосуванням інгібіторів зворотного захоплення серотоніну (ІЗЗС), що підтверджує ключову роль нейромедіатора серотоніну в модуляції еякуляції. У цій групі значне покращення спостерігалось у 53,6% пацієнтів, незначне – у 39,3%.

Висновки. Модифікація способу життя є найефективнішим методом лікування у пацієнтів із бойовими травмами та ЕД змішаного генезу, що супроводжується провідним синдромом ХТБ. У цій групі відзначено покращення показника Міжнародного індексу еректильної функції (МІЕФ)-5 – з $13,5 \pm 2,3$ до $21,6 \pm 2,1$ ($p < 0,05$). Серотонін відіграє провідну роль у модуляції еякуляції у пацієнтів з ЕД та ПЕ, оскільки застосування ІЗЗС сприяє збільшенню інтравагінального латентного часу. У цій групі також зафіксовано покращення показника МІЕФ-5 – з $13,8 \pm 2,1$ до $22,0 \pm 1,9$ ($p < 0,05$).

Ключові слова: еректильна дисфункція, комбатанти, бойова травма, хронічний тазовий біль, передчасна еякуляція, лікування.

Most combat-related injuries are polytraumatic, often involving the lower abdomen and pelvic organs, especially the genitals, which can result in long-term structural dysfunction. Military personnel often face long-term consequences of severe injuries, which can substantially affect their overall quality of life and sexual function [1, 2]. A growing body of evidence indicates that post-traumatic stress disorder (PTSD) caused by trauma leads to increased rates of erectile dysfunction (ED), reduced sexual desire, and premature ejaculation (PE) [2–4]. Men who have participated in combat experience, among other things, have decreased libido, difficulty maintaining arousal, and problems achieving orgasm, and overall sexual health complications [1, 3, 4]. Combat-related injuries can also significantly affect male fertility, as they often occur during the peak reproductive years. Such injuries may impair reproductive function through hormonal disturbances, or psychological stress, potentially leading to long-term fertility challenges [2].

The elucidation of the mechanisms of ED development indicates the predominant secondary nature of sexual disorders. Among the numerous pathological conditions that can precede or worsen sexual dysfunction, neurotic mental disorders, metabolic disturbances, vascular diseases, and partial androgen deficiency are the most prevalent, particularly contributing to ED in combatants [5–10]. Injury should be considered both a physical and a psychological trauma, which is often stretched over time. Libido and erectile function can also be affected by medications prescribed by a doctor, which must be taken into account. PTSD, depressive disorders, chronic post-traumatic pain, and PE may develop as a consequence of combat injuries or even as a result of participation in hostilities and affect sexual function [1–4].

The objective of this study was to assess the effectiveness of treating mixed-etiology ED associated with chronic pelvic pain (CPP) or PE in men who sustained combat injuries.

MATERIALS AND METHODS

The study was based on the results of the examination and treatment of 60 men aged 20–53, participants in hostilities, with sexual dysfunction and the leading complaints of ED.

Members of the commission on ethics in scientific research, experimental development, and scientific works of the SNPC “Danylo Halytsky Lviv National Medical University” did not find any violations of moral and ethical norms (protocol No. 7 dated June 26, 2023). Measures were taken to ensure patient safety, respect for their rights, human dignity, and moral and ethical standards in accordance with the principles of the Helsinki Declaration on Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, and the relevant laws of Ukraine.

Inclusion criteria: patients with ED accompanied by CPP or PE due to combat injuries (shrapnel and bullet wounds, mostly multiple), aged between 20 and 53 years and with minimum chronicity of PE of 3 months. **Exclusion criteria:** clinically significant comorbidity: hepatic, neurological, oncological or endocrine, history of retroperitoneal surgery or radiotherapy, consumption of medications that affect ejaculation, abuse or dependence on psychoactive substances.

All patients underwent a comprehensive laboratory, clinical and instrumental examination at the urology clinic

of the SNPC “Danylo Halytsky Lviv National Medical University” after undergoing treatment and rehabilitation for combat trauma, with complaints of ED persisting for more than 1 month and who consented to participate in the research. All patients underwent a thorough medical history, physical, clinical and psychological examination.

The division of patients into groups was carried out taking into account the data provided in European Association of Urology Guidelines on Sexual and Reproductive Health [11] and in papers [12, 13]. Patients were divided into groups according to the form of ED: Group 1 included patients with combat-related ED of mixed etiology associated with CPP. The group comprised individuals diagnosed with endothelial dysfunction, metabolic syndrome, coronary heart disease, and late-onset hypogonadism (n = 32); Group 2 consisted of patients with combat-related ED of mixed origin accompanied by PE. This group included individuals with endothelial dysfunction, metabolic syndrome, coronary artery disease, and late-onset hypogonadism (n = 28).

A multilevel probabilistic approach was used. Patient outcomes were analyzed based on grouping according to the type of ED. Treatment for all individuals with sexual dysfunction was carried out individually, considering the specifics of their combat injuries, the etiopathogenesis of underlying conditions, and the development and progression of predominant sexological syndromes, in accordance with standardized treatment protocols [11].

The International Index of Erectile Function (IIEF) was used to evaluate the effectiveness of treatment [14, 15]. Question 16 of the questionnaire was based on the patient's subjective overall self-assessment of erectile function and was the first differential criterion for different severity of ED: “Do you consider yourself a man who (a) has no problems with erection; (b) has minimal problems achieving erections; (c) has moderate ED; (d) has severe ED / complete absence of erections?” The assessment system for evaluating sexual, somatic, and mental health in patients with sexual disorders, as well as for measuring treatment effectiveness, is based on a comprehensive, multifaceted approach. It includes: listening to patient complaints, collecting detailed medical and sexological histories, conducting interviews using the IIEF-5 questionnaire and the Erection Hardness Score, administering the Medical Outcomes Study Short Form 36, and performing physical, instrumental, and laboratory examinations. Patient management is carried out according to the established diagnosis and a structured algorithm for the classification and treatment of sexual disorders. The therapeutic process also focuses on the restoration of marital relationships and the adaptation of sexual behavior, achieved through cognitively oriented psychotherapeutic methods.

Treatment of patients with ED of mixed genesis with CPP, standardized, included [16]:

- 1) rational and explanatory psychotherapy, sildenafil (50–100 mg, taken 1 hour before sexual activity), tamsulosin (0.4 mg/day), tizanidine (2 mg 3 times daily), and lornoxicam (4 mg twice daily). Sildenafil was administered on demand, with a minimum of 8 doses per month;
- 2) during the initial assessment, reversible risk factors for ED were identified. Addressing these factors

through lifestyle modifications was implemented either prior to or alongside the treatment of ED. Recommended interventions included weight reduction, regular physical activity, consultation of psychosocial services, review of potential side effects from prescribed or over-the-counter medications, and evaluation for hypogonadism as a reversible factor contributing to ED;

- 3) antibacterial therapy (for a minimum of 14 days) was administered only when patients were diagnosed with prostatitis of category II or category IIIA (CPP syndrome), according to the National Institute of Diabetes and Digestive and Kidney Diseases / National Institutes of Health classification [16, 17]. Antibacterial therapy was tailored to the identified causative pathogen and its antibiotic sensitivity whenever feasible. The treatment regimen included azalides, fluoroquinolones, and tetracyclines.

Treatment of patients with a mixed form of ED and concomitant PE included [16]:

- 1) rational and explanatory psychotherapy, on-demand sildenafil (50–100 mg taken 1 hour before sexual activity), and lifestyle modifications;
- 2) use of serotonin reuptake inhibitors (SRIs);
- 3) antibacterial therapy for a minimum of 14 days was administered only when prostatitis was confirmed as an organic contributor to the development of PE. Whenever possible, treatment was guided by the identified pathogen and its antibiotic sensitivity, using azalides, fluoroquinolones, or tetracyclines.

The improvement criteria were determined according to the data obtained from validated questionnaires. To assess the effectiveness of treatment mixed genesis ED in men with combat injury, the obtained digital data were processed by statistics methods using parametric and non-parametric multiple comparison methods. All data were analyzed using descriptive statistical methods. The normality of the distribution of quantitative variables was assessed using the Shapiro–Wilk test. When the data met

Table 1
Mean pretreatment demographic and clinical values of patients

Variables	Patients with combat-related ED of mixed genesis, accompanied by CPP (Group 1)	Patients with combat-related ED of mixed genesis and PE (Group 2)
Patients, n	32	28
Age, years	39.2 ± 8.5	35.4 ± 6.2
BMI, kg/m ²	25.4 ± 3.2	24.2 ± 3.5
Testosterone, nmol/L	9.5 ± 2.8	9.8 ± 1.8
IIEF-5	13.5 ± 2.3	13.8 ± 2.1

Notes: BMI – body mass index; ED – erectile dysfunction; CPP – chronic pelvic pain; PE – premature ejaculation; IIEF-5 – International Index of Erectile Function.

the assumption of normality, the results were presented as mean ± standard deviation, and group comparisons were performed using Student’s t-test. Correlation analysis was conducted using Pearson’s correlation coefficient. Statistical significance was set at $p < 0.05$. Results are presented as absolute values (n) and relative rates (%). Data processing was performed in Microsoft Excel 365.

RESULTS AND DISCUSSION

The demographic and clinical characteristics of the patients are summarized (Table 1). There was a significant negative correlation between the age and testosterone level ($r = -0.42, p < 0.05$). There were no significant differences in demographic and clinical data between both groups.

The results of treatment of men injured as a result of hostilities, with mixed ED and leading syndrome of CPP, including patients with chronic prostatitis II, IIIa, IIIb categories of Group 1 are presented (Table 2).

The effectiveness of treatment in patients with ED that developed against the background of CPP is presented (Fig. 1). Based on the collected data, lifestyle modification is the most effective method of treatment. At the same

Table 2
Treatment outcomes in Group 1 patients with mixed-origin ED with the leading syndrome of CPP (n = 32)

Treatment method	Patients for whom a therapeutic approach was applied (persons, %)	Significant improvement in erectile and sexual performance (persons, % of all men in the subgroup)*	Significant improvement in erectile and sexual function (persons, % of men treated with this technique)*	Slight improvement in erectile function (persons, %)*	Slight improvement in erectile and sexual function (persons, % of men treated with this technique)*
Rational and explanatory psychotherapy; sildenafil (50–100 mg, 1 hour before sexual activity); tamsulosin 0.4 mg/day; tizanidine 2 mg 3 times daily; and lornoxicam 4 mg twice daily	32 (100)	15 (46.9)	15 (46.9)	8 (25)	8 (25)
Lifestyle modification	21 (65.6)	13 (40.6)	20 (62.5)	6 (18.7)	10 (31.2)
Antibacterial therapy for at least 14 days	14 (43.7)	6 (18.7)	13 (40.1)	4 (12.5)	9 (28.1)

Notes: * – overall effectiveness of the treatment regimen in patients evaluated 1 month after initiation of therapy; ED – erectile dysfunction; CPP – chronic pelvic pain.

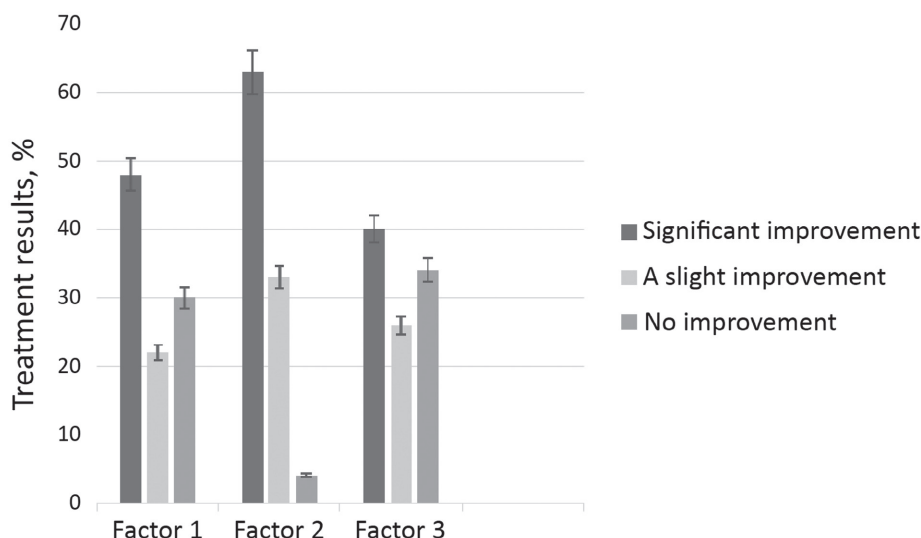


Fig. 1. Treatment outcomes in Group 1 patients with ED of mixed genesis with leading syndrome of CPP (n = 32)

Notes: factor 1 – rational and explanatory psychotherapy, sildenafil, tamsulosin, tizanidine, lornoxicam; factor 2 – lifestyle modification; factor 3 – antibacterial therapy; ED – erectile dysfunction; CPP – chronic pelvic pain.

time, 62.5% of patients experienced a significant improvement in erectile function, and 31.2% experienced a slight improvement. Patients of Group 1 showed an improvement in IIEF-5 from 13.5 ± 2.3 to 21.6 ± 2.1 ($p < 0.05$).

Until now, the absence of an effective standardized method of the gold standard in the treatment of sexual disorders associated with prostatitis of various categories, regardless of pathogenetic therapy, as well as the frequent lack of improvement of sexual function with successful elimination of the inflammatory process and pain in the prostate, once again demonstrates the complex etiology of pathological processes in this group of patients.

The results of treatment of 28 patients with ED and accompanying PE of Group 2 are presented (Table 3).

The effectiveness of ED treatment with concomitant PE is graphically displayed (Fig. 2). Significantly worse indicators of treatment of sexual dysfunction, in particular ED and the organic component of PE caused by chronic prostatitis, are observed. Patients of Group 2

showed an improvement in IIEF-5 from 13.8 ± 2.1 to 22.0 ± 1.9 ($p < 0.05$). These data are consistent with the results of ED treatment for CPP (Group 1).

In men with sexual dysfunction, as a rule, sexual motivation is disturbed: instead of focusing on the process of love play, patients are focused on the fact that sexual intercourse may end prematurely. Instead of positive emotions, they experience tension and anxiety. Taking this into account, patients' ability to learn to clearly navigate their sensations and to apply a functional training option in a timely manner in order to prevent the triggering of the ejaculatory reflex is an important component of the treatment success in all groups of men.

Thus, the results of the study indicate a significant prevalence of neurogenic (psychogenic) PE among men of various ages, which, as a rule, disturbs as a result of received combat injuries. The study demonstrates that the neurotransmitter serotonin is crucial in regulating ejaculation, as the use of SRIs prolongs intravaginal ejaculatory latency.

Table 3

Treatment outcomes in Group 2 patients with ED and accompanying PE (n = 28)

Treatment method	Patients for whom a therapeutic approach was applied (persons, %)	Significant improvement in erectile and sexual performance (persons, % of all men in the subgroup)*	Significant improvement in erectile and sexual function persons, % of men treated with this technique)*	Slight improvement in erectile function (persons, %)*	Slight improvement in erectile and sexual function persons, % of men treated with this technique)*
Rational and explanatory psychotherapy, on-demand sildenafil (50–100 mg taken 1 hour before sexual activity), and lifestyle modifications	28 (100)	16 (57.1)	16 (57.1)	7 (25)	7 (25)
SRI (trazodone)	17 (60.6)	10 (35.6)	15 (53.6)	6 (21.4)	11 (39.3)
Antibacterial therapy for at least 14 days	11 (39.3)	6 (21.4)	15 (53.6)	1 (3.6)	3 (10.7)

Notes: * – overall effectiveness of the treatment regimen in patients evaluated 1 month after initiation of therapy; ED – erectile dysfunction; SRI – serotonin reuptake inhibitor.

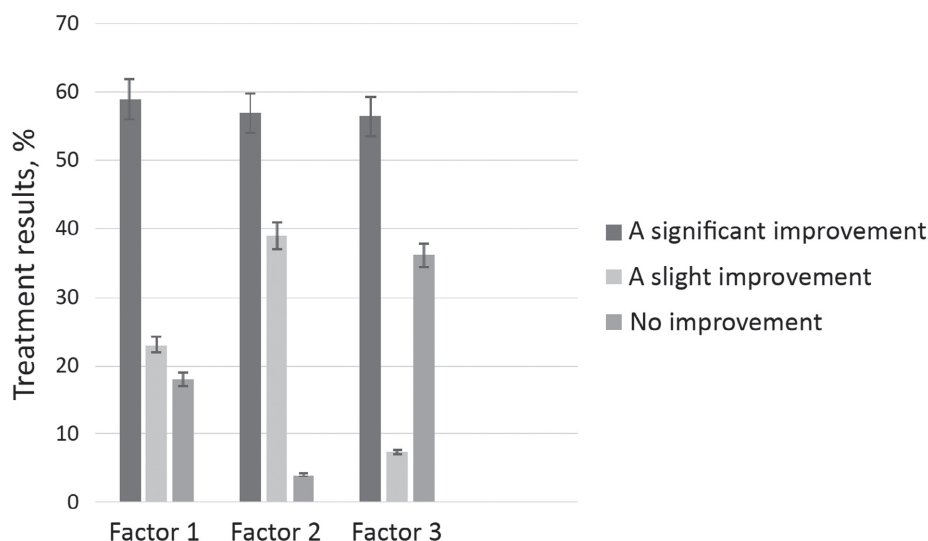


Fig. 2. Treatment outcomes in Group 2 patients with ED and PE (n = 28)

Notes: factor 1 – rational and explanatory psychotherapy, sildenafil (50–100 mg taken 1 hour before sexual activity), and implementation of lifestyle modifications; factor 2 – SRI; factor 3 – antibacterial therapy; ED – erectile dysfunction; PE – premature ejaculation; SRI – serotonin reuptake inhibitor.

Recent research has consistently shown that ED not only impairs sexual function but also reduces overall life satisfaction [4, 18, 19]. Erectile function is increasingly recognized as an indicator of a man's general health [8, 20, 21], as well as an important marker of vascular diseases [5, 22, 23]. The potential success of lifestyle modification is particularly important in individuals with ED and co-morbid cardiovascular or metabolic diseases such as diabetes mellitus, hypertension and, especially, in patients with combat trauma [5, 24–28]. The benefits of lifestyle modifications extend beyond improving erectile function, contributing also to enhanced cardiovascular health, normalized metabolic processes, and better mental well-being. Recent studies highlight the importance of lifestyle normalization for improving both ED and overall well-being [28]. Patients are encouraged to adopt lifestyle changes whether or not they are receiving phosphodiesterase type 5 (PDE-5) inhibitor therapy. Evidence suggests that the effectiveness of PDE-5 inhibitors may be enhanced when other coexisting risk factors are addressed or eliminated [27, 28].

Sildenafil was primarily prescribed in cases of psychogenic ED of various origins to enhance the effects of psychotherapy, helping patients gain confidence in their ability to achieve firm erections, and to prevent the onset of endothelial dysfunction [29–33]. In groups 1 and 2, they tried not to use the PDE-5 inhibitor for more than 1 month, to prevent the patient from becoming psychologically dependent on medication.

Tamsulosin has been used in ED accompanied by CPP since it selectively and competitively blocks postsynaptic α 1-adrenoceptors (α 1A and α 1D) in smooth muscle of the prostate gland, bladder neck, etc. [34]. Tizanidine (α 2-adrenoceptor agonist) was also used for CPP [33]. In the treatment of this pathology, lornoxicam was also used. It is a non-steroidal anti-inflammatory drug with an analgesic, anti-inflammatory and antipyretic effect due to increased inhibition of prostaglandin synthesis [35]. It should be noted that CPP can also occur as a result of prostatic

hyperplasia. Chronic prostatitis / CPP syndrome is a common urological disease that is the most common clinical form of chronic prostatitis. The combination of chronic inflammation of the prostate gland and chronic pain in its pathogenesis creates difficulties in diagnosis and treatment. There is pressure on the urinary tract, urination disorders, constant or periodic pain in the pelvic area, perineum, lower back, and genitals [36–38].

In the treatment of ED accompanied by PE, trazodone (a drug of the class of SRIs) was used. It is used for the treatment of depressive disorders, generalized anxiety disorder, panic states, as well as improving the patient's condition with PTSD, which is characteristic of combatants [39, 40].

CONCLUSIONS

The most effective method of treatment is lifestyle modification for patients injured as a result of hostilities, with ED of mixed genesis, accompanied by the leading syndrome of CPP. Patients with combat-related ED of mixed genesis, accompanied by CPP demonstrated an improvement in IIEF-5 score from 13.5 ± 2.3 to 21.6 ± 2.1 ($p < 0.05$).

The study results reveal a high prevalence of neurogenic (psychogenic) PE across men of different age groups, which, as a rule, is disturbing as a result of received combat injuries. The study confirms that serotonin is a key neurotransmitter in regulating ejaculation among patients with ED and coexisting PE, as treatment with SRIs prolongs intravaginal ejaculatory latency. Patients with combat-related ED of mixed genesis and PE showed an improvement in IIEF-5 score from 13.8 ± 2.1 to 22.0 ± 1.9 ($p < 0.05$).

Funding. The article was published with the support of the National Research Fund grant “Improvement of diagnosis and treatment of disorders of sexual and reproductive functions of men suffered as a result of hostilities” (state registration number 123U105170).

Conflict of interest. The authors declare no conflicts of interest.

Information about the authors

- Vorobets Mykola Z.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: urovorobets@gmail.com*
ORCID: 0000-0002-6104-5769
- Vorobets Dmytro Z.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: dv@ukr.net*
ORCID: 0000-0002-8431-5151
- Fafula Roman V.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: roman_fafula@ukr.net*
ORCID: 0000-0002-0121-9093
- Besedina Anna S.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: annabes@ukr.net*
ORCID: 0000-0001-5152-219X
- Kushynska Mariia Ye.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: kushynskam@ukr.net*
ORCID: 0000-0001-8322-7945
- Vorobets Zinovii D.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: vorobetsz@ukr.net*
ORCID: 0000-0001-6016-0186
- Chemerys Orest M.** – SNPC “Danylo Halytsky Lviv National Medical University”. *E-mail: rector@meduniv.lviv.ua*
ORCID: 0000-0001-8550-6980

Відомості про авторів

- Воробець Микола Зіновійович** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: urovorobets@gmail.com*
ORCID: 0000-0002-6104-5769
- Воробець Дмитро Зіновійович** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: dv@ukr.net*
ORCID: 0000-0002-8431-5151
- Фафула Роман Володимирович** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: roman_fafula@ukr.net*
ORCID: 0000-0002-0121-9093
- Беседіна Анна Сергіївна** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: annabes@ukr.net*
ORCID: 0000-0001-5152-219X
- Кушинська Марія Євгенівна** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: kushynskam@ukr.net*
ORCID: 0000-0001-8322-7945
- Воробець Зіновій Дмитрович** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: vorobetsz@ukr.net*
ORCID: 0000-0001-6016-0186
- Чемерис Орест Мирославович** – ДНТ «Львівський національний медичний університет імені Данила Галицького». *E-mail: rector@meduniv.lviv.ua*
ORCID: 0000-0001-8550-6980

REFERENCES

- Banti M, Walter J, Hudak S, Soderdahl D. Improvised explosive device-related lower genitourinary trauma in current overseas combat operations. *J Trauma Acute Care Surg.* 2016;80(1):131-4. doi: 10.1097/TA.0000000000000864.
- Castillo O, Chen IK, Amini E, Yafi FA, Barham DW. Male sexual health related complications among combat veterans. *Sex Med Rev.* 2022;10(4):691-7. doi: 10.1016/j.sxmr.2022.06.002.
- Bird ER, Piccirillo M, Garcia N, Blais R, Campbell S. Relationship between post-traumatic stress disorder and sexual difficulties: A systematic review of veterans and military personnel. *J Sex Med.* 2021;18(8):1398-426. doi: 10.1016/j.jsxm.2021.05.011.
- Letica-Crepulja M, Stevanović A, Protuder M, Popović B, Salopek-Žiha D, Vondraček S. Predictors of sexual dysfunction in veterans with post-traumatic stress disorder. *J Clin Med.* 2019;8(4):432. doi: 10.3390/jcm8040432.
- Erkan A, Balci M, Tuncel A, Yigit-turk G, Aslan Y, Senel C, et al. The role of androgen receptors in erectile dysfunction due to diabetes mellitus: An experimental study. *Insight Urol.* 2019;40(2):19-28.
- Fan D, Mao W, Wang G, Shi H, Wu Z, Xie J, et al. Study on the relationship between sex hormone changes and erectile dysfunction in patients with chronic prostatitis/chronic pelvic pain syndrome. *Ann Palliat Med.* 2021;10(2):1739-47. doi: 10.21037/apm-20-985.
- Ho JH, Adam S, Azmi S, Ferdousi M, Liu Y, Kalteniece A, et al. Male sexual dysfunction in obesity: The role of sex hormones and small fibre neuropathy. *PLoS One.* 2019;14(9):e0221992. doi: 10.1371/journal.pone.0221992.
- Kumar S, Khurana NK, Lohana S, Khamuani MK, Memon MK, Memon S, et al. Comparison of the prevalence of erectile dysfunction between hypertensive and normotensive participants: A case-control study. *Cureus.* 2020;12(12):e12061. doi: 10.7759/cureus.12061.
- Ma M, Yu B, Qin F, Yuan J. Current approaches to the diagnosis of vascular erectile dysfunction. *Transl Androl Urol.* 2020;9(2):709-21. doi: 10.21037/tau.2020.03.10.
- Salman M, Shehzaadi N, Khan MT, Islam M, Amjad S, Afzal O. Erectile dysfunction: prevalence, risk factors and involvement of antihypertensive drugs intervention. *Trop J Pharm Res.* 2016;15(4):869-76. doi: 10.4314/tjpr.v15i4.29.
- Salonia A, Bettocchi C, Boeri L, Capogrosso P, Carvalho J, Cilesiz NC, et al. European Association of Urology Guidelines on Sexual and Reproductive Health-2021 Update: Male Sexual Dysfunction. *Eur Urol.* 2021;80(3):333-57. doi: 10.1016/j.eururo.2021.06.007.
- Li HJ, Kang DY. Prevalence of sexual dysfunction in men with chronic prostatitis/chronic pelvic pain syndrome: A meta-analysis. *World J Urol.* 2016;34(7):1009-17. doi: 10.1007/s00345-015-1720-3.
- Wu X, Zhang Y, Zhang W, Liu G, Jiang H, Huang H, et al. Erectile Dysfunction in Multiple Sclerosis: A Prevalence Meta-Analysis and Systematic Review. *J Sex Med.* 2022;19(8):1255-68. doi: 10.1016/j.jsxm.2022.05.002.
- Kessler A, Sollie S, Challacombe B, Briggs K, Van Hemelrijck M. The global prevalence of erectile dysfunction: a review. *BJU Int.* 2019;124:587-99. doi: 10.1111/bju.14813.
- Neijenhuijs KI, Holtmaat K, Aaronson NK, Holzner B, Terwee CB, Cuijpers P, et al. The International Index of Erectile Function (IIEF)-A systematic review of measurement properties. *J Sex Med.* 2019;16(7):1078-91. doi: 10.1016/j.jsxm.2019.04.010.
- Vorobets MZ, Vorobets DZ, Melnyk OV, Fafula RV, Chemerys OM. Treatment of men injured in combat operations (combat trauma) with various forms of erectile dysfunction. *Health Man.* 2025;1(92):6-13. doi: 10.30841/2786-7323.1.2025.326324.
- Laksier J, El Bete H, Bellouki O, Boughaleb A. Müllerian cyst: Uncommon etiology of chronic pelvic pain syndrome in men. *Cureus.* 2023;15(11):e49046. doi: 10.7759/cureus.49046.
- Onufrovych OK, Fafula RV, Vorobets MZ, Besedina AS, Melnyk OV, Vorobets DZ, et al. Parameters of oxidative, nitrasive and anti-oxidative status in men with erectile dysfunction due to combat trauma. *Regul Mech Biosys.* 2024;15(1):97-101. doi: 10.15421/022414.
- Reed-Maldonado AB, Lue TF. A syndrome of erectile dysfunction in young

- men? *Transl Androl Urol.* 2016;5(2):228-34. doi: 10.21037/tau.2016.03.02.
20. Carneiro A, Saito OC, Miranda EP. Standardization of penile hemodynamic evaluation through color duplex-doppler ultrasound. *Rev Assoc Med Bras.* 2020;66(9):1180-86. doi: 10.1590/1806-9282.66.9.1180.
21. Leslie SW, Sooriyamoorthy T. Erectile Dysfunction [Internet]. In: StatPearls Treasure Island (FL): StatPearls Publishing; 2025. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK562253/>.
22. Minhas AS, Goerlich E, Corretti MC, Arbab-Zadeh A, Kelle S, Leucker T, et al. Imaging assessment of endothelial function: an index of cardiovascular health. *Front Cardiovasc Med.* 2022;9:778762. doi: 10.3389/fcvm.2022.778762.
23. Wang H, Guo J, Chung E. Metabolic syndrome-associated erectile dysfunction: Multiple vascular endothelial dysfunction mechanisms and potential therapeutic targets. *Int J Biol Sci.* 2025;21(13):5842-58. doi: 10.7150/ijbs.120980.
24. Alkan E, Ugan RA, Basar MM, Halici Z, Karakus E, Balbay MD, et al. Role of endothelin receptors and relationship with nitric oxide synthase in impaired erectile response in diabetic rats. *Andrologia.* 2017;49(2). doi: 10.1111/and.12607.
25. Birowo P, Deswanto IA, Rasyid N. Epidemiology of erectile dysfunction: A cross sectional web-based survey conducted in an Indonesian national referral hospital. *F1000Research.* 2019;8:817. doi: 10.12688/f1000research.18930.1.
26. Elzanaty S, Rezanezhad B, Wilenheimer R, Borgquist R. Association between erectile function and biomarkers of subclinical atherosclerosis: a study based on middle-aged healthy men from the general population. *Curr Urol.* 2016;9(3):119-23. doi: 10.1159/000442865.
27. Gökçe Mİ, Yaman Ö. Erectile dysfunction in the elderly male. *Turk J Urol.* 2017;43:247-251. doi: 10.5152/tud.2017.70482.
28. Rastrelli G, Maggi M. Erectile dysfunction in fit and healthy young men: psychological or pathological? *Transl Androl Urol.* 2016;6(1):9-90. doi: 10.21037/tau.2016.09.06.
29. Andersson KE. PDE5 inhibitors – pharmacology and clinical applications 20 years after sildenafil discovery. *Br J Pharmacol.* 2018;175(13):2554-65. doi: 10.1111/bph.14205.
30. Vorobets DZ, Vorobets MZ, Fafula RV, Chaplyk W. Pathogenetic mechanisms of sexual dysfunction in men with combat trauma and its correction. *Lviv: Novyi Svit;* 2025. 220 p.
31. Kim S, Cho MC, Cho SY, Chung H, Rajasekaran MR. Novel emerging therapies for erectile dysfunction. *World J Mens Health.* 2021;39(1):48-64. doi: 10.5534/wjmh.200007.
32. Ostroff L. Oral PDE5 inhibitors for erectile dysfunction. *US Pharm.* 2018;43(6):29-33.
33. Zhu LL, Wang YH, Zhou Q. Tizanidine: advances in pharmacology & therapeutics and drug formulations. *J Pain Res.* 2024;17:1257-71. doi: 10.2147/jpr.s461032.
34. Gandhi J, Weissbart SJ, Smith NL, Kaplan SA, Dagur G, Zumbo A, et al. The impact and management of sexual dysfunction secondary to pharmacological therapy of benign prostatic hyperplasia. *Transl Androl Urol.* 2017;6(2):295-304. doi: 10.21037/tau.2017.03.57.
35. Najem MM, Mukilan D, Jayakumari S. Safety and efficacy of lornoxicam and diclofenac in patients with post traumatic pain – a review. *J Evolution Med Dent Sci.* 2020;9(24):1827-33. doi: 10.14260/jemds/2020/399.
36. Nurimanov K. Metabolic aspects of chronic prostatitis/chronic pelvic pain syndrome. *Health Man.* 2024;(3):68-72. doi: 10.30841/2786-7323.3.2024.316664.
37. Gorpynchenko II, Nurimanov KR, Poroshina TV, Savchenko VS, Leonenko AM, Drannik GM, et al. Clinical, laboratory and ultrasonographic correlates of prostate calcifications in patients with chronic prostatitis/chronic pelvic pain syndrome. *Cent European J Urol.* 2024;77(2):225-34. doi: 10.5173/ceju.2022.222.
38. Nurimanov K, Nedogonova O, Sherban M. Clinical and laboratory characteristics of chronic prostatitis / chronic pelvic pain syndrome. *Health Man.* 2022;(1-2):42-8. doi: 10.30841/2307-5090.1-2.2022.263906.
39. Ibrahim AE, Elhenawee M, Saleh H, Sebaiby MM. Erectile dysfunction and premature ejaculation drugs: Mode of action and analytical methods literature review. *J Drug Res Dev.* 2021;7(1):1-7. doi: 10.16966/2470-1009.163.
40. Vorobets M, Vorobets D, Chaplyk V, Melnyk O, Onufrovych O, Vorobets Z, et al. Effectiveness of treatment of sexual dysfunction in men with premature ejaculation, injured as a result of hostilities. *Wiad Lek.* 2025;78(2):265-72. doi: 10.36740/WLek/197136.

Стаття надійшла до редакції 08.01.2026. – Дата першого рішення 16.01.2026. – Стаття подана до друку 12.02.2026