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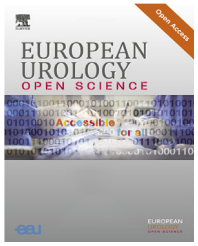

European Association of Urology

Incontinence

Association of Aggression with Lower Urinary Tract Symptoms and Overactive Bladder in Men: Observations from a Large Population-representative Study

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Article info

Article history:
Accepted August 14, 2024

Associate Editor:
Véronique Phé

Keywords:
Aggression
Lower urinary tract symptoms
Overactive bladder

Abstract

Background and objective: Lower urinary tract symptoms (LUTS) and overactive bladder (OAB) intimately affect the psychological wellbeing and mental health of men. However, to date, the association of aggression with LUTS and OAB has not been investigated. To address this knowledge gap, we evaluated the association of aggression with LUTS and OAB in a large representative cohort of men at the population level.
Methods: We used computer-assisted web interviews that included reliable questionnaires for assessment of LUTS, OAB, and aggression. A population-representative group of men was based on the most recent census. For data analysis, we developed univariate and multivariate regression models.
Key findings and limitations: We analyzed data for a cohort of 3001 men that was representative for age and place of residence. Aggression was more prevalent among respondents with LUTS and OAB in comparison to men without these conditions ($p < 0.001$). The scores for aggression were directly proportional to the scores for LUTS and OAB (Spearman's rank correlation coefficients of 0.261 for LUTS and 0.284 for OAB). Univariate linear regression models revealed an association between aggression and LUTS or OAB in all age groups. Finally, multivariable linear

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https://doi.org/10.1016/j.euros.2024.08.009
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regression models confirmed that correlations of aggression with LUTS and OAB were independent of age, sociodemographic parameters, comorbidities, and lifestyle habits (regression coefficients of 0.013 for LUTS and 0.024 for OAB).
Conclusions and clinical implications: Our study is the first to show that aggression among men is consistently associated with LUTS and OAB. Our results open a new research area on the effect of LUTS and OAB or their causes on psychological wellbeing and mental health, and may even support screening for hostile behavior in the clinical setting for individuals who report LUTS and OAB.
Patient summary: We performed the first study to investigate whether aggression is linked to lower urinary tract symptoms (LUTS) and overactive bladder (OAB). Results from our survey in a representative group of men in Poland show that aggression is linked to LUTS and OAB. More research is needed to confirm these results.
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1. Introduction

Lower urinary tract symptoms (LUTS) and overactive bladder (OAB) can be highly bothersome for men [1]. The bother of LUTS and OAB impairs physical and social functioning, work productivity, and overall quality of life. An effect of LUTS and OAB on psychological wellbeing has also been documented, although most studies have focused purely on links to depression and anxiety [2]. Dose-response associations between increasing LUTS and OAB severity and higher risk of clinically relevant depressive symptoms and anxiety have often been observed [2]. However, there has been no investigation of the association between LUTS or OAB and aggression.

Aggression, an overt behavior involving intent to harm another organism or inanimate object [3], is often considered a highly prevalent mental dysfunction [4] and a significant public health burden [5]. Many triggers for aggression have been described for men [6]; thus, there could be a link between aggression and LUTS and OAB because these urology conditions carry significant bother that could theoretically trigger aggressive behavior. Furthermore, testosterone is often considered a critical regulator of aggressive behavior. A recent systematic review by Geniole et al [4] showed that baseline testosterone was significantly associated with aggression (r = 0.054, 95% confidence interval [CI] 0.028–0.080), and that the association was strong and significant for men (r = 0.071, 95% CI 0.041–0.101) but not for women (r = 0.010, 95% CI 0.041–0.044). Notably, no study has been performed on the association between either LUTS or OAB and aggression, even though aggressive behavior has already been linked to multiple conditions and factors, including cancer [7], dementia [8], sleep quality [9], and substance and alcohol abuse [10]. Therefore, the aim of our study was to evaluate for the first time the association of aggression with LUTS and OAB in a large representative cohort of men at the population level. In addition, we analyzed the quality of life of men who had LUTS or OAB and who exhibited aggression.

2. Patients and methods

This study is an extension of ED POLAND, a population-representative survey of men's health in Poland. The extension was designed by the European Association of Urology Young Academic Urologists Working Group on Functional Urology. To obtain high-quality data, we followed all recommendations and standards for performing observational studies [11], and we prespecified all objectives of this extension in the statistical plan before conducting the survey. The research ethics committee of Jagiellonian University Medical College, Krakow, Poland approved our investigation (1072.6120.331.2021) and the study is registered on ClinicalTrials.gov (NCT05462171).

Detailed descriptions of the concepts, aims, design, methodology, and data collection for ED POLAND have already been published [12,13]. In brief, we conducted a computer-assisted web interview because of the personal nature of the topic. A representative adult pool of Polish men was recruited on the basis of the latest census (2021) with quota controls defined according to age and place of residence [14]. Calculations for the sample size estimation also considered the standard deviation for the population, the expected effect size and dropout rate, the power of the study, the hypothesized underlying population-level event rate, and acceptable levels of significance and margins of error. Eventually, our study included men aged at least 18 yr and living in all geographical regions of Poland (all 16 states/voivodships) with adequate proportions of respondents from urban and rural areas. IPSOS, a certified and international research agency with relevant expertise, collected all the data and conducted regular quality control and stratification checks (including calculations of post-stratification weights). Before final data collection, we also conducted pilot web surveys with cognitive debriefing interviews.

2.1. Measures

Data for general sociodemographic parameters were collected.

Lower urinary tract symptoms were evaluated using the International Prostate Symptom Score (IPSS), the questionnaire most widely used for estimating the severity of LUTS in men [15]. An IPSS score was assigned to the specific level of LUTS severity: 0 = no symptoms; 1–7 = mild symptoms; 8–19 = moderate symptoms; and 20–35 = severe symptoms (the greater the score, the greater the severity of symptoms).

OAB was assessed using the Overactive Bladder-Validated 8-item questionnaire (OAB-V8), a screening awareness tool for identifying individuals with bothersome OAB that has been used in large-scale epidemiological studies on LUTS prevalence [16]. A score of ≥8 was the threshold for OAB, with a maximum score of 40 (the higher the score, the greater the severity of symptoms).

Aggression was measured using the aggression module of the Hospital Anxiety and Depression Scale-Modified Version (HADS-M), an instrument widely used in epidemiological studies on aggression [17–21]. Importantly, each HADS-M module, including the aggression module, is an independent scale that is assessed and interpreted separately [22,23]. A score of ≥4 was the threshold for aggression, with a maximum score of 6 (the higher the score, the greater the severity of symptoms).

These three questionnaires have been adapted and translated into Polish and rigorously validated [16,23,24].

Finally, we asked questions on overall quality of life ("If you were to spend the rest of your life in your current condition, how would you describe your overall wellbeing?"), comorbidities (arterial hypertension, myocardial infarction, any cardiac disease, diabetes, overweight, lipid disorders, stroke, any pulmonary disease, depression, any abdominal or pelvic surgeries), and lifestyle habits (smoking, alcohol intake, polypharmacy).

2.2. Statistical analysis

Apart from descriptive statistics for the initial data evaluation, we used nonparametric tests to analyze quantitative variables (Mann-Whitney *U* or Kruskal-Wallis with a post hoc Dunn test, if applicable) and parametric tests for qualitative variables (χ^2 or Fisher's exact test, if low expected counts). We developed linear regression models (univariate and multivariable) to measure the association of LUTS or OAB with aggression and reported results as regression coefficients with a 95% CI; raw scores (raw data) were used for all regression models.

A p value <0.05 was considered to be statistically significant. R version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for data analysis.

3. Results

Our study included 3001 Polish men who were representative for age and place of residence. Detailed demographics of the study participants are provided in Supplementary Table 1.

3.1. Correlations between LUTS or OAB and aggression

We observed significant correlations between LUTS and aggression and between OAB and aggression. For respondents without LUTS or with mild LUTS, aggression was less prevalent, whereas respondents with moderate or severe LUTS had higher prevalence of aggression (p < 0.001; Table 1). Analysis of overall scores revealed that the IPSS score correlated significantly (p < 0.001) and positively (Spearman's rank correlation coefficient r = 0.261) with the HADS-M aggression score: the higher the IPSS score, the higher was the HADS-M aggression score.

Table 1 – Distribution of lower urinary tract symptoms and overactive bladder stratified by aggression status

Parameter	Respondents, *n* (%)		*p* value [a]
	No aggression (*n* = 1912)	Aggression (*n* = 1089)	
Lower urinary tract symptoms			
IPSS 0: no symptoms	226 (11.82)	77 (7.07)	<0.001
IPSS 1–7: mild symptoms	946 (49.48)	408 (37.47)	
IPSS 8–19: moderate symptoms	584 (30.54)	484 (44.44)	
IPSS 20–35: severe symptoms	156 (8.16)	120 (11.02)	
Overactive bladder			
OAB-V8 score <8 points	1417 (74.11)	656 (60.24)	<0.001
OAB-V8 score ≥8 points	495 (25.89)	433 (39.76)	

IPSS = International Prostate Symptom Score; OAB-V8 = Overactive Bladder-Validated 8-item questionnaire.
[a] χ^2 test or Fisher's exact test.

Aggression was less prevalent among respondents without OAB than among respondents with OAB (p < 0.001; Table 1). Analysis of overall scores revealed that the OAB-V8 score correlated significantly (p < 0.001) and positively (Spearman's rank correlation coefficient r = 0.284) with the HADS-M aggression score: the higher the OAB-V8 score, the higher was the HADS-M aggression score.

3.2. Age-specific univariate linear regression

To investigate age-specific associations between LUTS or OAB and aggression, we used univariate linear regression models. The regression coefficients for all age groups were statistically significant for associations between LUTS and aggression, and between OAB and aggression (Table 2). When we combined all age groups, the regression coefficient was 1.027 (95% CI 0.872–1.183; p < 0.001) for correlation between IPSS and HADS-M aggression scores, and 1.418 (95% CI 1.226–1.61; p < 0.001) for correlation between OAB-V8 and HADS-M aggression scores (Table 2).

Table 2 – Univariate regression results for associations between aggression and LUTS and OAB by age group

Age group	Regression coefficient(95% CI)	*p* value
LUTS		
All age groups	1.027 (0.872–1.183)	<0.001
18–24 yr	0.627 (0.139–1.116)	0.012
25–34 yr	1.162 (0.805–1.52)	<0.001
35–44 yr	1.189 (0.89–1.488)	<0.001
45–54 yr	1.004 (0.659–1.349)	<0.001
55–64 yr	1.434 (1.061–1.806)	<0.001
≥65 yr	0.694 (0.098–1.29)	0.023
OAB		
All age groups	1.418 (1.226–1.61)	<0.001
18–24 yr	0.773 (0.177–1.369)	0.012
25–34 yr	1.353 (0.919–1.786)	<0.001
35–44 yr	1.502 (1.109–1.895)	<0.001
45–54 yr	1.678 (1.24–2.115)	<0.001
55–64 yr	1.958 (1.492–2.423)	<0.001
≥65 yr	1.221 (0.569–1.872)	<0.001

CI = confidence interval; LUTS = lower urinary tract symptoms; OAB = overactive bladder.

Table 3 – Multivariable regression results for the association between HADS-M aggression scores and scores for lower urinary tract symptoms by IPSS and overactive bladder by OAB-V8

Instrument	Regression coefficient(95% CI)	*p* value
IPSS	0.013 (0.001–0.024)	0.031
OAB-V8	0.024 (0.015–0.033)	<0.001

CI = confidence interval; HADS-M = Hospital Anxiety and Depression Scale-Modified Version; IPSS = International Prostate Symptom Score; OAB-V8 = Overactive Bladder-Validated 8-item questionnaire.

3.3. *Multivariable linear regression*

Multivariable linear regression revealed that the correlations between LUTS or OAB and aggression were independent of age, sociodemographic parameters, comorbidities, and lifestyle habits (Table 3). For LUTS, the regression coefficient was 0.013, indicating that an average 1-point increase in IPSS was associated with a 0.013-point increase in the HADS-M aggression score. For OAB, the regression coefficient was 0.024, indicating that an average 1-point increase in OAB-V8 score was associated with a 0.024-point increase in the HADS-M aggression score.

3.4. *Item analysis*

Item-specific analysis showed that all the IPSS and OAB-V8 items correlated with aggression ($p < 0.001$, Table 4). IPSS items 5 (hesitancy), 2 (frequency), and 1 (incomplete emptying) had the strongest correlation with aggression (defined as the highest absolute Spearman's rank correlation coefficients). OAB-V8 items 2 (urgency), 7 (urgency), and 8 (urgency urinary incontinence) had the best correlation with aggression, defined again as the highest absolute Spearman's rank correlation coefficients.

3.5. *Effect on quality of life*

The coexistence of LUTS and aggression or of OAB and aggression had negative effects on overall quality of life. Respondents who had LUTS and aggression, or OAB and aggression reported worse overall quality of life in comparison to the other participants ($p < 0.001$; Fig. 1).

Table 4 – Item-specific Spearman's rank correlation results for IPSS and OAB-V8 items in relation to aggression

Item	*r*	*p* value
IPSS item 1	0.206	<0.001
IPSS item 2	0.206	<0.001
IPSS item 3	0.199	<0.001
IPSS item 4	0.185	<0.001
IPSS item 5	0.262	<0.001
IPSS item 6	0.193	<0.001
IPSS item 7	0.18	<0.001
OAB-V8 item 1	0.215	<0.001
OAB-V8 item 2	0.261	<0.001
OAB-V8 item 3	0.227	<0.001
OAB-V8 item 4	0.202	<0.001
OAB-V8 item 5	0.224	<0.001
OAB-V8 item 6	0.209	<0.001
OAB-V8 item 7	0.242	<0.001
OAB-V8 item 8	0.228	<0.001

IPSS = International Prostate Symptom Score; OAB-V8 = Overactive Bladder-Validated 8-item questionnaire.

4. Discussion

To the best of our knowledge, this is the first report of an analysis of associations between aggression and LUTS or OAB. We demonstrated that LUTS and OAB were closely related to aggression. Importantly, the correlations between LUTS and aggression, and between OAB and aggression were independent of age, sociodemographic parameters, comorbidities, and lifestyle habits. We also found that respondents with LUTS and aggression or with OAB and aggression had worse overall quality of life in comparison to the other respondents.

A strength of our findings is the study methodology used. We surveyed a representative pool of men aged ≥18 yr who completed widely accepted questionnaires for assessment of LUTS, OAB, and aggression. In addition, we developed various regression models that incorporated multiple covariates, including sociodemographic parameters, comorbidities, and lifestyle habits.

Many studies have shown that LUTS and OAB have a negative impact on the psychological wellbeing of men [25]. Effects on psychological wellbeing have been identified as a decrease in overall and sex-specific quality of life, sexual dysfunction, distress, embarrassment, social stigma, social isolation, resignation, chronic fatigue, lower self-esteem, and depression and anxiety [25]. Importantly, these effects are independent of culture or ethnic origin [26]. Our study confirms the negative effect of LUTS and OAB on psychological wellbeing among men, and identified aggression as a further negative effect. Because this is the first study to describe associations between aggression and LUTS or OAB, our findings are of important clinical relevance and open a new avenue for research on the effects of LUTS and OAB on mental health among men.

When examining any association between aggression and another parameter, it is important to realize that the construct of aggression is broadly defined. Aggression is typically considered as an intentional act to harm another who is motivated to avoid that harm. Several conceptual frameworks that incorporate the processes relevant to aggressive tendencies and aggression have been described. The most widely used and complex framework is the general aggression model, which provides an integrative view of many more specific theories [27]. The model describes the interplay between multiple personal and situational factors that influence an individual's internal state, encompassing arousal and affective or cognitive aspects, such as anger and hostility, and factors affecting appraisal and decision, such as the level of self-control and attribution bias. When all these factors merge, aggression can eventually occur. Our analysis of the association of aggression with LUTS and OAB further reflects the complexity of the aggression construct, which may even be affected by lower urinary tract functioning. We hypothesize that the bother from LUTS or OAB may add to the negative effect, increase hostile perception, and impair impulse control, finally leading to dysregulation of emotions and to aggression.

Several complex neural mechanisms have been described for aggression [28]. Researchers have postulated that aggressive behaviors are emergent properties of a

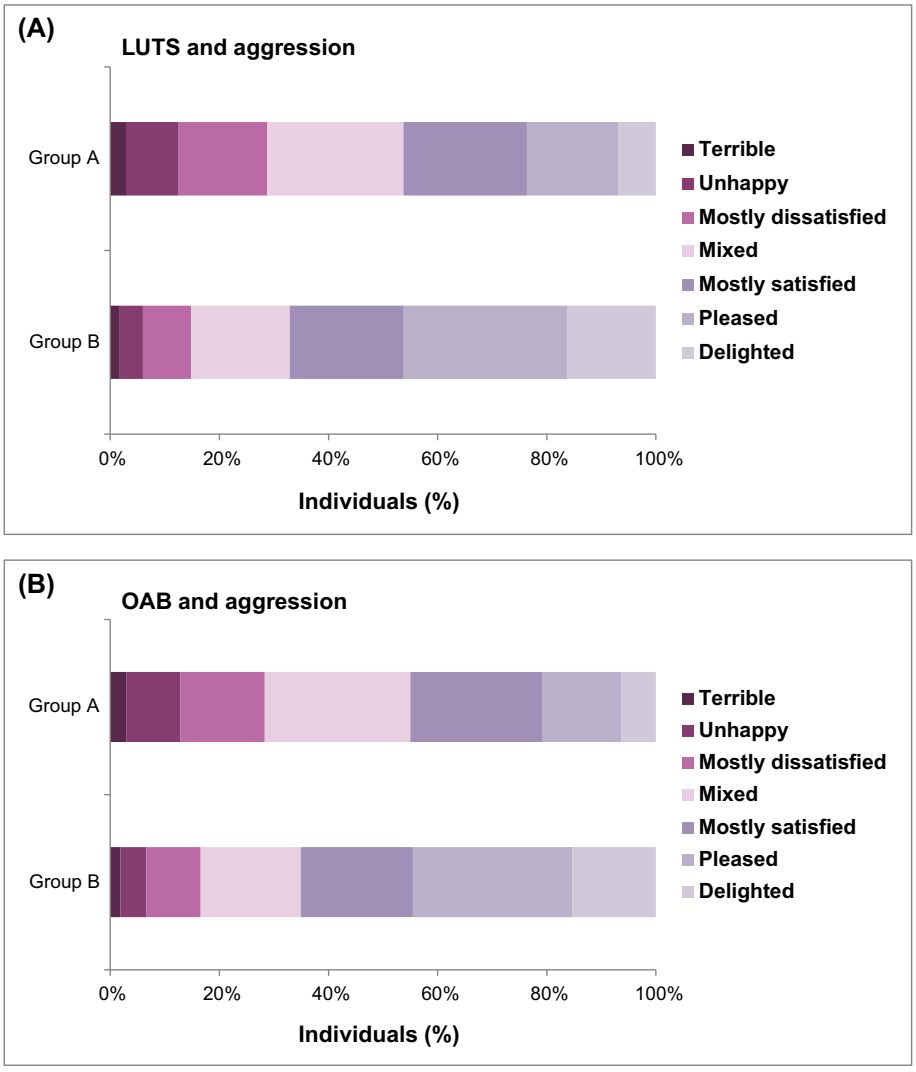

Fig. 1 – (A) Overall quality of life reported by respondents with lower urinary tract symptoms (LUTS) and aggression (group A) and the remaining participants (group B). There was a significant difference ($p < 0.001$; χ^2 test or Fisher's exact test) between the groups. (B) Overall quality of life reported by respondents with overactive bladder (OAB) and aggression (group A) and the remaining participants (group B). There was a significant difference ($p < 0.001$; χ^2 test or Fisher's exact test) between the groups.

social behavior network that includes the medial amygdala, anterior hypothalamus, bed nucleus of the stria terminalis, lateral septum, ventromedial hypothalamus, and periaqueductal gray area [28]. Molecular approaches have revealed biological signals that mediate the components of aggressive behavior. Agents such as 5-hydroxytryptamine, dopamine, γ-aminobutyric acid, noradrenaline, nitric oxide, monoamine oxidase A, and steroid hormones can affect aggressive behaviors [28]. Thus, aggression is undoubtedly a complex social behavior. To make matters more complex, the neural and molecular circuits that control aggression also regulate other social behaviors [28]. Likewise, the physiology of lower urinary tract function is not straightforward. Both central and peripheral nervous systems control the bladder and urethra. Sacral and pontine micturition centers play a special role and are supported by higher centers (cerebral cortex, particularly the anterior cingulated gyrus) [29]. Molecular mechanisms for bladder-urethra function are mainly mediated by acetylcholine, adenosine triphosphate, nitric oxide, cyclic guanosine monophosphate, intracellular calcium, glutamate, γ-aminobutyric acid, 5-hydroxytryptamine, noradrenaline, neuropeptide Y, nerve growth factor, tachykinins (eg, substance P, neurokinin A, and neurokinin B), and sex steroids [30]. Because some elements of neural and molecular mechanisms underlying aggression and lower urinary tract function intersect (eg, the amygdala and the frontal cortex, both of which are brain areas involved in micturition control and emotional regulation), we hypothesized that crosstalk between aggression and impaired bladder-urethra function might even share the same pathophysiology at some point. It is clear that more research is needed to elucidate the neurological and biochemical details of the associations between aggression and LUTS and OAB.

Our multivariable linear regression models that were adjusted for age, sociodemographic parameters, comorbidities, and lifestyle habits identified associations between aggression and LUTS and OAB. We showed that an average 1-point increase in the IPSS or OAB-V8 score was associated with an increase of 0.013 or 0.024 points, respectively, in

the HADS-M aggression score according to the regression coefficients. Therefore, LUTS and OAB were consistently highly associated with aggression, although the consensus in our group is that these associations are of a moderate nature. Although the absolute values for our regression coefficients were low, we need to consider the maximum scale points of the IPSS (35 points), OAB-V8 (40 points), and HADS-M aggression module (6 points). The point ranges for the scales were an important consideration in our careful assessment of the study observations.

Our study has some limitations. The cross-sectional design limited us to longitudinal assessment of correlations between LUTS, OAB, and aggression. For both LUTS and OAB, we used self-reported data; we could not verify any outcomes for lower urinary tract function via clinical diagnosis. However, this lack of verification is a well-known limitation of population-based studies in functional urology [31]. Regarding the aggression module of the HADS-M questionnaire, aggression should be understood as a feeling of aggression or a state of emotional irritation. Therefore, we analyzed aggression in general and did not distinguish various forms of aggressive behavior such as physical and verbal aggression, hostile and instrumental aggression, irritability, anger, hostility, or violence [6]. Furthermore, aggression may be influenced by social, economic, and familial status, as well as personal habits; therefore, reliance on a single self-reported questionnaire may not be sufficient for a careful analysis of aggression. An approach designed to analyze all forms and aspects of aggression would require, apart from a clinical diagnosis, many different measures of aggression that could overwhelm respondents. Finally, the study was performed in one specific cultural setting, and given that aggression is a highly culture-specific issue, the external validity may be limited.

5. Conclusions

In this first study of its kind, we analyzed the association of aggression with LUTS and OAB. Aggression was consistently associated with LUTS or OAB. Notably, the correlations between LUTS, OAB, and aggression were independent of age, sociodemographic parameters, comorbidities, and lifestyle habits. Our findings emphasize the need for awareness of the link between LUTS/OAB and aggression. Further research is needed to confirm the association between LUTS/OAB and aggression, particularly in diverse populations and cultural settings.

Author contributions: Mikolaj Przydacz had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Przydacz, Rajwa, De Cillis, Guillot-Tantay, Herve, Tienza, Tutolo, Gokhan Culha, Geretto, Raison, Werneburg, Miszczyk, Gomez Rivas, Phe, Chlosta, Osman.
Acquisition of data: Przydacz.
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Drafting of the manuscript: Przydacz.
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Statistical analysis: Przydacz.
Obtaining funding: Przydacz, Chlosta.
Administrative, technical, or material support: Przydacz, Chlosta.
Supervision: Przydacz.
Other: None.

Financial disclosures: Mikolaj Przydacz certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: This study was supported by an unrestricted grant from Jagiellonian University Medical College. The funding body had no direct role in the study.

Acknowledgments: The authors thank the study participants for their time.

Ethics considerations: The study was performed in accordance with good clinical practice guidelines and the Declaration of Helsinki. The research ethics committee of Jagiellonian University Medical College, Krakow, Poland approved the study (1072.6120.331.2021). Informed consent was provided by all participants.

Data sharing statement: All the data generated or analyzed during this study are included in this article.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.08.009.

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