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European Association of Urology

Review – Benign Prostatic Hyperplasia

Summary Paper on Underactive Bladder from the European Association of Urology Guidelines on Non-neurogenic Male Lower Urinary Tract Symptoms

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Abstract

Background and objective: The European Association of Urology (EAU) Guidelines Panel on non-neurogenic male lower urinary tract symptoms (LUTS) aimed to develop a new subchapter on underactive bladder (UAB) in non-neurogenic men to inform health care providers of current best evidence and practice. Here, we present a summary of the UAB subchapter that is incorporated into the 2024 version of the EAU guidelines on non-neurogenic male LUTS.
Methods: A systematic literature search was conducted from 2002 to 2022, and articles with the highest certainty evidence were selected. A strength rating has been provided for each recommendation according to the EAU Guideline Office methodology.
Key findings and limitations: Detrusor underactivity (DU) is a urodynamic diagnosis defined as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span. UAB is a terminology that should be reserved for describing symptoms and clinical features related to DU. Invasive urodynamics is the only widely accepted method for diagnosing DU. In patients with persistently elevated postvoid residual (ie, >300 ml), intermittent catheterization is indicated and preferred to indwelling catheters. Alpha-adrenergic blockers are recommended before more invasive techniques, but the level

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of evidence is low. In men with DU and concomitant benign prostatic obstruction (BPO), benign prostatic surgery should be considered only after appropriate counseling. In men with DU and no BPO, a test phase of sacral neuromodulation may be considered.
Conclusions and clinical implications: The current text represents a summary of the new subchapter on UAB. For more detailed information, refer to the full-text version available on the EAU website (https://uroweb.org/guidelines/management-of-non-neurogenic-male-luts).
Patient summary: The European Association of Urology guidelines on underactive bladder in non-neurogenic adult men are presented here. Patients must be fully informed of all relevant options and, together with their treating physicians, decide on the most optimal management for them.

1. Introduction

As part of the 2023 European Association of Urology (EAU) guidelines update on non-neurogenic male lower urinary tract symptoms (LUTS), the expert panel aimed to incorporate a wider range of LUTS affecting adult men that were not considered previously in the EAU guidelines compendium. The male LUTS panel undertook a systematic review of the literature, which resulted in a comprehensive new subchapter on underactive bladder (UAB) in non-neurogenic male patients. The EAU Non-neurogenic Male LUTS Guidelines Panel consists of an international group of experts with urological and clinical epidemiological backgrounds. All experts have submitted potential conflict of interest statements, which can be viewed on the EAU website Uroweb: http://uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/. We present here a summarized version, which is now an integral part of the guidelines.

2. Methods

A systematic review (SR) was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [1]. A literature search was conducted in 2023 in PubMed/Medline, EMBASE, and the Cochrane Libraries, covering a time frame between January 1, 2002 and August 29, 2022, to identify reports dealing with any of the following subsections of UAB in adult non-neurogenic male patients: epidemiology, pathophysiology, diagnostic evaluation, treatment, and follow-up. Studies were deemed eligible if these were SRs, meta-analyses, and comparative studies including randomized controlled trials (RCTs) and post hoc studies of RCTs; epidemiological studies were also included. Only English-language articles were considered, and a minimum of ten patients per series was defined for inclusion. A strength rating has been provided for each recommendation according to the EAU Guideline Office methodology [2].

3. Results

3.1. *Epidemiology and pathophysiology*

Various definitions of UAB and detrusor underactivity (DU) can be identified in the current literature. DU appears as the most consistent concept, is based on invasive urodynamic pressure-flow studies, and is defined by the International Continence Society as "a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span" [3]. UAB is a terminology that should be reserved for describing symptoms and clinical features related to DU. A tentative definition has been proposed as "a symptom complex suggestive of detrusor underactivity and usually characterized by prolonged urination time with or without a sensation of incomplete bladder emptying, usually with hesitancy, reduced sensation on filling, and a slow stream" [4].

The prevalence of DU in the general population is unknown. In clinical studies of men with non-neurogenic LUTS referred for videourodynamic studies, the prevalence of DU has been reported to be 10%, ranging up to 48% in the elderly (≥70 yr) [5–7]. DU is a chronic condition, but its natural history in untreated men has shown a plateau-like course with few symptomatic and urodynamic changes over time [8].

Healthy voluntary bladder muscle contraction requires a functional detrusor muscle, intact efferent and afferent innervation, and integrated central neural control mechanisms. Dysfunction of any of these essential components can lead to DU.

3.1.1. *Neurogenic*

Neurogenic DU may be the consequence of peripheral or central nervous system disease. This etiology is covered in the EAU guidelines on neurourology [9].

3.1.2. *Myogenic*

Several conditions can affect the myocytes or their extracellular matrix, resulting in attenuated detrusor contraction. Bladder outflow obstruction (BOO) and diabetic bladder dysfunction are common causes of myogenic DU [10–12].

3.1.3. *Iatrogenic*

Patients may experience DU following pelvic surgery and/or radiotherapy [10]. Pharmacological treatments (eg, drugs with anticholinergic effects or opioids) may also be involved in the impairment of detrusor contractility [10].

3.1.4. Idiopathic

Given the higher prevalence of DU in the elderly, it has been hypothesized that aging would be a major contributor. However, available data do not provide strong evidence to support this assertion [10].

3.2. Diagnostic evaluation

3.2.1. Medical history and physical examination

A review of the medical history can identify potential causes of UAB. The history should also include a thorough evaluation of LUTS, which should be classified into storage, voiding, and postmicturition symptoms. There is no pivotal symptom to identify patients with UAB. The clinical presentation ranges from asymptomatic cases to symptomatic chronic urinary retention. Since UAB is a disorder of the voiding phase, voiding symptoms are to be the predominant ones, but these may be associated with storage symptoms, particularly in case of incomplete bladder emptying or other concomitant bladder dysfunctions [13]. Clinical diagnosis is more difficult when patients have other conditions that may affect the presentation of LUTS, such as known or suspected BOO/benign prostatic obstruction (BPO; Fig. 1). In this setting, there is no validated tool to ascertain the respective roles of DU and BOO on voiding symptoms.

The Bristol Group was the first to attempt to identify systematically which of the LUTS are most closely related to UAB [14]. Several authors have proposed predictive models based on the patient's LUTS to distinguish individuals with a UAB from patients with normal pressure-flow studies or BOO [15,16]. However, there is no conclusive evidence that one prognostic model is more accurate than another.

3.2.2. Questionnaires

There is no specific validated questionnaire for the diagnosis of UAB. Physicians can refer to validated questionnaires for male LUTS, but their clinical benefit to make diagnosis, monitor symptom changes, and suggest treatment in patients with UAB is uncertain [17].

3.2.3. Uroflowmetry

Some authors have proposed to distinguish UAB from BOO based on uroflowmetry parameters, which include not only the maximum urinary flow (Qmax), but also flow patterns and combinations of scores [18,19]. The diagnostic accuracy of the developed models remains to be established.

3.2.4. Ultrasound scan and postvoid residual measurement

Ultrasound findings have been evaluated as noninvasive predictors of DU. In a single-center prospective study including 143 adult males with LUTS, detrusor wall thickness of $\leq$1.23 mm and bladder capacity of >445 ml were associated with urodynamically proven DU, with sensitivity and specificity of 42% and 100%, respectively [20].

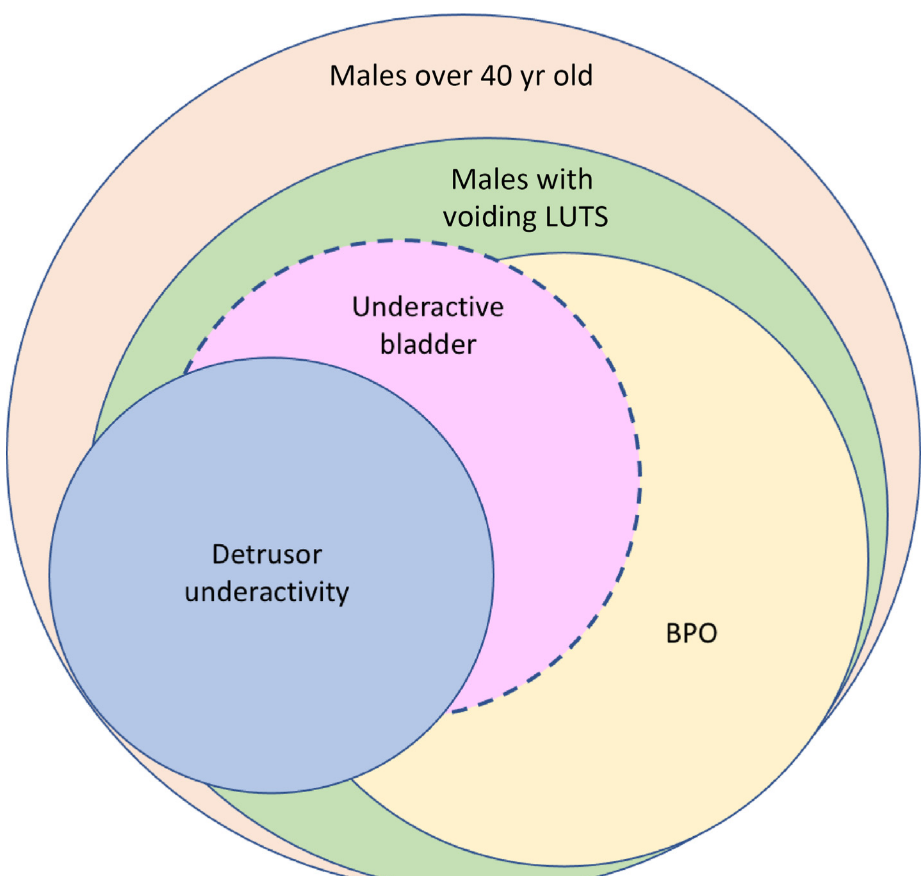

Figure 1 – Schematic representation of overlapping symptoms in adult men with underactive bladder. BPO = benign prostatic obstruction; LUTS = lower urinary tract symptoms.

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DU is often associated with prolonged bladder emptying time and/or postvoid residual (PVR). However, while a high PVR value has been associated with the presence of DU, no consensus cutoff has been identified to diagnose DU and it is unlikely that one will ever exist [21].

3.2.5. Urodynamics

UAB is a clinical diagnosis based on sign and symptoms, and DU is a term that should be reserved for a urodynamic diagnosis [22]. Invasive urodynamics is the only widely accepted method for diagnosing DU [13]. Three indices have been suggested to quantify detrusor power [21]:

1. *Griffiths' Watt factor*: quantification of detrusor power with a formula consisting of detrusor pressure during voiding, contraction speed, and bladder volume at each point of micturition, expressed as W/m^2. Detrusor power varies during voiding; single calculations are usually offered on urodynamic evaluation sheets, for example, maximum detrusor power (Wmax) or detrusor power at maximum flow (WQmax). However, it remains controversial which of the calculations and what threshold value should be used. Expert opinion suggested using a Wmax threshold value of 7.0 W/m^2 [21].
2. *Schafer's detrusor-adjusted mean passive urethral resistance (PURR) factor*: detrusor power can grossly be quantified as very weak, weak, normal, or strong if linearized passive urethral resistance (linPURR) is drawn into the Schafer nomogram. The length of linPURR determines detrusor strength.
3. *Bladder contractility index (BCI)*: quantification of detrusor power/contractility can be derived from Schafer's linPURR lines and calculated using the following formula: BCI = pdetQmax + 5Qmax. A BCI of >150 describes strong contractility, 100–150 normal contractility, and <100 weak contractility. Currently, BCI is the most widely used index in the literature and clinical trials, and is applicable only to men with prostates. It has been suggested that in younger men, a factor of 2.5 instead of 5 should be used.

None of these models are validated, and their concordance for the diagnosis of DU is uncertain [23,24], preventing a consensus to be reached on the optimal method for diagnosing DU. Furthermore, detrusor contraction strength is only one aspect of voiding efficiency, and future models will need to encompass several aspects of assessing detrusor contraction (eg, strength and durability) as well as how the bladder empties.

3.3. Conservative management

In general, the treatment of UAB should focus on symptom relief, avoiding complications and improving, or at least maintaining, quality of life (QoL). It involves a pragmatic approach ensuring timely bladder drainage by trying to improve bladder contraction and/or decrease urethral resistance [21]. An algorithm is proposed in Figure 2.

3.3.1. Behavioral interventions

There are no RCTs or large high-quality studies available investigating the effect of behavioral interventions in male patients with UAB. In patients with sensory impairment, timed or scheduled voiding schemes can be recommended. In patients with bothersome frequency, double or triple voiding as well as Valsalva or the Credé maneuver can reduce PVR and may improve their symptoms; however, no clinical trial has proved the efficacy or harms of these measures in the non-neurogenic male population.

A descriptive cohort investigated male patients with DU started on conservative treatment and the need for clean intermittent catheterization (CIC) after 5 yr [25]. It concluded that male patients with non-neurological DU can remain stable without the need to initiate CIC.

3.3.2. Pelvic floor muscle relaxation training with biofeedback

Successful voiding is initiated by relaxation of the pelvic floor and urinary sphincter [26]. Physiotherapy with pelvic floor muscle relaxation is usually a first-line therapy for voiding dysfunction, but no RCT in male adults investigated its effect on UAB.

3.3.3. Clean intermittent catheterization

In patients with persistently elevated PVR, CIC is the preferred method for complete and timely bladder drainage. No data exist on the maximum accepted PVR, but after 300 ml, the risk of urinary tract infections increases [27].

3.3.4. Indwelling catheters

Indwelling catheters should be avoided (Table 1). If necessary, suprapubic catheters are preferred to urethral catheters due to the risk of traumatic hypospadias.

3.3.5. Intravesical electrical stimulation

Intravesical electrotherapy is an electrical stimulation technique that stimulates the A-delta mechanoreceptor afferents, thereby reinforcing bladder contractions. It consists of daily sessions of stimulation, with ten to 15 sessions considered as a trial period. Afferent circuits should be intact together with a healthy detrusor muscle. In a recently published RCT, intravesical electrotherapy showed significant benefits over a sham procedure, but the study was conducted in a mixed-gender population with neurogenic predominant UAB [28].

3.3.6. Extracorporeal shock wave therapy

Extracorporeal shock wave therapy improves neovascularization and tissue regeneration, and could theoretically improve detrusor contractility. A small placebo-controlled RCT reported significant improvements in PVR and UAB-Q scores at the 4th week but not at the 12th week of follow-up [29,30].

3.4. Pharmacological management

3.4.1. Parasympathomimetics

In an SR and meta-analysis including 12 RCTs, parasympathomimetics showed a small benefit in some patients with (postprocedure) urinary retention with no increase in adverse events, but without improvement of PVR [31,32]. Based upon the available literature, no strong evidence-based conclusions can be drawn (Table 2).

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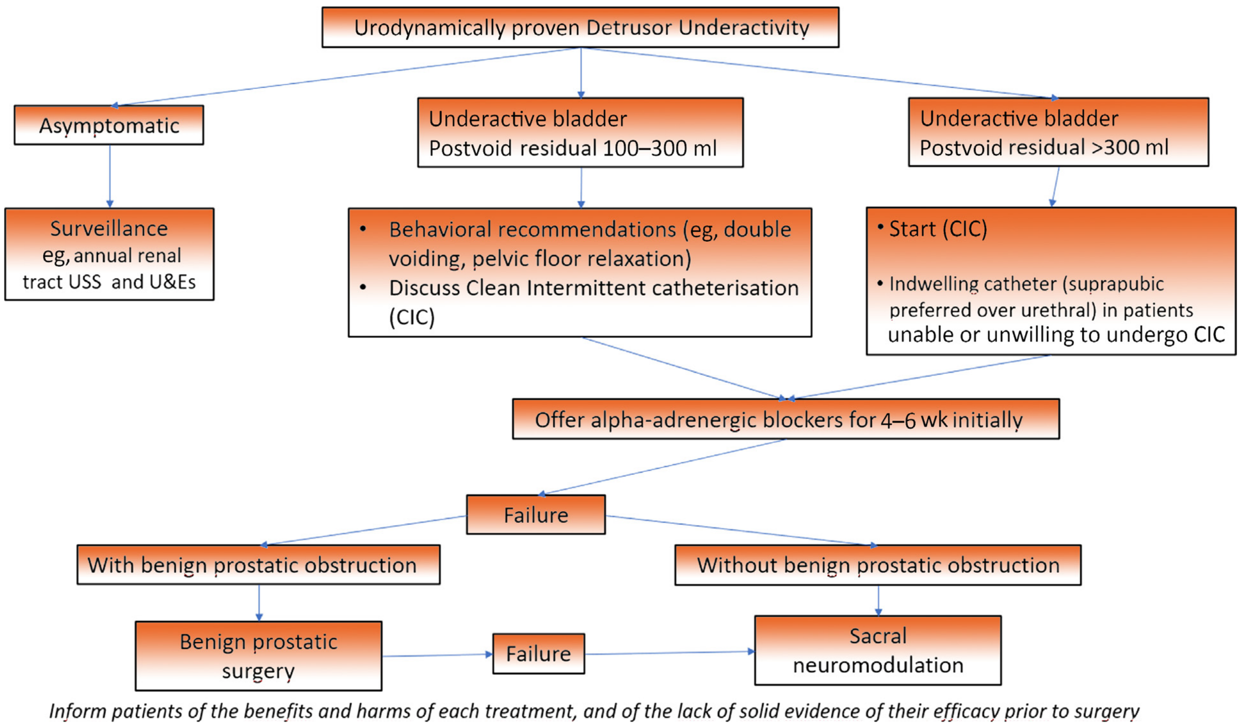

Figure 2 – An algorithm summarizing the diagnosis and treatment of detrusor underactivity and underactive bladder. CIC = clean intermittent catheterization; U&E = urea and electrolyte; USS = ultrasound scan.

Table 1 – Recommendations for conservative management of underactive bladder

Recommendation	Strength rating
Initiate clean intermittent self-catheterization if there is a risk of upper tract damage or postvoid residual is >300 ml.	Weak
Offer indwelling transurethral catheterization or suprapubic cystostomy only when other modalities for urinary drainage have failed or are unsuitable.	Weak

Table 2 – Recommendations for pharmacological management of underactive bladder

Recommendation	Strength rating
Do not routinely recommend parasympathomimetics for the treatment of men with an underactive bladder.	Strong
Offer alpha-adrenergic blockers before more invasive techniques.	Weak

3.4.2. *Alpha-adrenergic blockers*

One alternative to improve bladder emptying and micturition is by reducing outflow resistance in patients with UAB. Although there is a lack of high-quality RCTs, some evidence exists that lowering outflow resistance improves voiding functions and bothersome symptoms in men with UAB. A single-blind prospective RCT investigated 119 patients with UAB, treating them with a cholinergic drug, an alpha-adrenergic blocker, or both. These showed a significant improvement in both symptoms and PVR and flow rate in patients treated with combination therapy compared with those treated with monotherapy [33]. A study evaluated the effects of tadalafil (a phosphodiesterase 5 inhibitor) and silodosin on voiding function in male patients with non-neurogenic DU. After propensity score matching, these drugs showed improvement of QoL, urodynamic parameters, and voiding parameters in both subgroups [15]. Overall, the clinical rigor required to provide evidence-based support for the use of this class of medications in treating UAB is still lacking (Table 2).

3.4.3. *Prostaglandins*

Prostaglandins (PGs) are involved in the modulation of bladder function. There are five subtypes, of which prostaglandins E2 and F2a appear to be predominant in stimulating detrusor contractions. A Cochrane review analyzing three RCTs using intravesical instillation of PGE2 and PGF2a suggests a reduction of postoperative retention after catheter removal [34]. However, due to methodological limitations, the use in clinical practice remains uncertain. One placebo-controlled trial investigated the combination of intravesical PGE2 with bethanechol chloride in 19 patients with UAB [35]. Although they showed a reduction in PVR compared with placebo, clinical relevance is questioned. Overall, the efficacy of the prostaglandin agents in treating UAB is not established.

3.5. *Surgical treatment*

Surgery for men with DU must be evaluated after the failure of conservative and pharmacological treatment. Surgical options for male patients with non-neurogenic UAB/DU

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include benign prostatic surgery and sacral neuromodulation (SNM; Table 3) [36–42].

3.5.1. Surgery for BPO

An SR evaluated the outcomes of surgery for BPO in men with preoperative DU or acontractile detrusor [36]. The mean total International Prostate Symptom Score (IPSS) variation following surgery was reported to range from –3 to –19.5 points. A >3 point improvement in terms of the total IPSS score was evident in 14 studies included in the review. The mean IPSS QoL score variation ranged from –0.9 to –3 points. The mean Qmax improvement ranged from +1.4 to +11.7 ml/s. The mean PVR improvement ranged from –16.5 to –736 ml.

Direct comparisons between patients with DU and those without DU provided conflicting results [36]. A study found that postoperative outcomes 1 mo after photoselective laser vaporization prostatectomy (PVP) had less improvement in patients with DU than in those without [38]. Similarly, another study found that patients with DU had a smaller decrease in the median total IPSS (–6.5 vs –11) and a smaller increase in the Qmax (+3.5 vs +8.2 ml/s) after PVP than those without DU [39].

Other authors found similar outcomes in patients with and without preoperative DU [36]. A retrospective study found that 81% of patients with DU or acontractile detrusor undergoing transurethral resection of the prostate (TURP) achieved a satisfactory treatment outcome defined as improved QoL and voiding efficiency of >50% [41]. A prospective case series found that 78% of patients with DU or acontractile detrusor and concurrent BPO undergoing holmium laser enucleation of the prostate exhibited significant return of bladder contractility, determined by the presence of a sustained, volitional detrusor contraction at 6-mo follow-up [42].

Factors influencing surgical outcomes have been investigated: older age, lack of obstruction, concomitant detrusor overactivity, lower detrusor contractility, and use of TURP or PVP instead of holmium laser enucleation of the prostate were associated with worse outcomes [36]. In total, in men with DU and concomitant BPO, benign prostatic surgery should be considered only after appropriate counseling.

3.5.2. Sacral neuromodulation

SNM has been reported to improve idiopathic urinary retention in women in long-term studies [43]. However, only scarce evidence exists in men with DU or acontractile detrusor. A multicentric, retrospective case series reported the outcomes of SNM in 35 males with DU and symptom duration of >6 mo [38]. A total of 51.4% of patients responded to the first stage, and 72% had favorable responses after the full implantation. Evidence from another retrospective study suggests that residual detrusor contractility is more likely to respond to a trial of SNM than detrusor acontractility [44]. From anecdotal evidence, men with chronic retention and PVR >1.5 l are less likely to respond to SNM.

Table 3 – Recommendations for surgical treatment of underactive bladder

Recommendation	Strength rating
Counsel patients with evidence of detrusor underactivity or acontractile detrusor and concomitant benign prostatic obstruction about the potential subjective and objective benefits of benign prostatic surgery.	Weak
Offer test phase sacral neuromodulation to men with detrusor underactivity and no benign prostatic obstruction if they understand the limited evidence for efficacy.	Weak

3.6. Follow-up

The natural history and clinical evolution at long-term follow-up of men with UAB is not well documented. A small retrospective cohort evaluated the recovery of detrusor contraction 1 yr after (medical or surgical) treatment through videourodynamic studies [45]. In this small cohort, bladder contractility recovery was seen in 44% of patients, and an optimal bladder compliance cutoff value of <80 ml/cmH_2O was predictive of better recovery. The interval between follow-up visits depends on patient characteristics, treatments given, and the frequency of urinary complications.

4. Conclusions

The current text represents a summary of the new subchapter on UAB included in the 2024 EAU guidelines for non-neurogenic male LUTS. For more detailed information, refer to the full-text version available on the EAU website (https://uroweb.org/guidelines/management-of-non-neurogenic-male-luts).

Author contributions: Michael Baboudjian 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: Cornu, Baboudjian, Bhatt, Creta, De Nunzio, Gacci, Hashim, Herrmann, Karavitakis, Malde, Moris, Netsch, Rieken, Sakalis, Tutolo.
Acquisition of data: Cornu, Baboudjian, Bhatt, Creta, De Nunzio, Gacci, Hashim, Herrmann, Karavitakis, Malde, Moris, Netsch, Rieken, Sakalis, Tutolo.
Analysis and interpretation of data: Cornu, Baboudjian, Bhatt, Creta, De Nunzio, Gacci, Hashim, Herrmann, Karavitakis, Malde, Moris, Netsch, Rieken, Sakalis, Tutolo.
Drafting of the manuscript: Baboudjian, Hashim, Cornu.
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