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Recent trends in the management of undescended testes in Hungary

Ph.D. Thesis

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3. LIST OF ABBREVIATIONS

AHPCP	Association of Hungarian Primary Care Paediatricians
AHRQ	Agency for Healthcare Research and Quality
AUA	American Urological Association
BAPS	British Association of Paediatric Surgeons
BAUS	British Association of Urologic Surgeons
CGRP	Calcitonin gene-related peptide
CPG	Clinical practice guideline
CT	Computed tomography
CUA	Canadian Urological Association
DSD	Disorders of sex development
EAU	European Association of Urology
ESPU	European Society for Paediatric Urology
EUPSA	European Paediatric Surgeons' Association
FSO	Fowler-Stephens orchiopexy
GnRH	Gonadotropin-releasing hormone
GR	Grade of recommendation
HAPS	Hungarian Association of Paediatric Surgeons
hCG	Human chorionic gonadotropin
HIT	High intra-abdominal testis
IAT	Intra-abdominal testis
INSL3	Insulin-like hormone 3
ITGCN	Intratubular germ cell neoplasia
LE	Level of evidence
LIT	Low intra-abdominal testis
MHR	Ministry of Human Resources
MRI	Magnetic resonance imaging
NPT	Non-palpable testis
PCP	Primary care paediatrician
RT	Retractile testis
SLTO	Staged laparoscopic traction orchiopexy
UDT	Undescended testis
US	Ultrasound

4. INTRODUCTION

4.1. Background

Undescended testis (UDT) or cryptorchidism is one of the most common disorders in boys concerning approximately 3.5% of male newborns [1, 2]. Incidence depends on gestational age and varies between 1.0% and 4.6% in full-term, with rates as high as 45% in preterm neonates [3]. Despite spontaneous descent during the first months of life, approximately 1.0% of male infants still have persistent UDT at the end of their first year [2]. Cryptorchidism may be unilateral or bilateral, with right-sided predominance (70-80%) [2].

Testicular descent is thought to occur during two hormonally controlled phases [4, 5]. The first phase occurs between 8 and15 weeks when insulin-like hormone 3 (INSL3) from the Leydig cells causes swelling reaction in the gubernaculum, thereby anchoring the testis near the future inguinal canal as the foetus grows [4]. Testosterone stimulates regression of the cranial suspensory ligament to enhance the transabdominal phase [4]. In the second (inguinoscrotal) phase – between 25 and 35 weeks – the gubernaculum bulges out of the external ring and migrates to the scrotum, all under control of testosterone [4]. However, androgen acts mostly indirectly through the genitofemoral nerve, which produces calcitonin gene-related peptide (CGRP) to control gubernacular development [4]. Although it is clear that a failure of testicular descend is likely due to a failure of one or both phases, the cause(s) and mechanism(s) of this disruptions are still unclear and key exposures in the occurrence of cryptorchidism remain elusive [5].

Aetiology and pathogenesis seem to be multifactorial with potential contribution of several mechanisms, including genetic, hormonal, and mechanical factors such as growth parameters of the newborn (birth weight, gestational age, size for gestational age), maternal smoking during pregnancy, familial aggregation of cryptorchidism and rare genetic variants e.g., INSL3 gene mutation [5, 6]. However, the relative importance of each risk factor may vary considerably between mother-son pairs depending on numerous genetic, maternal, placental, and foetal factors, which all could vary between regions [5].

Most cases of UDT are isolated without other innate malformations; few are associated with comorbidities such as cardiac or genitourinary anomalies, as well congenital syndromes (e.g., Down, Noonan, prune belly or partial androgen insensitivity syndrome) [2, 7, 8]. In addition, intra-abdominal testes (IATs) may be associated with an abnormal differentiation of the midline

developmental field [7]. Cryptorchidism is also one component of theorized testicular dysgenesis syndrome, in which four individual conditions (cryptorchidism, testicular cancer, hypospadias, and impaired spermatogenesis) possibly share the same prenatal aetiology [5, 9]. Hypospadias is comparatively more common among those with cryptorchidism; however, in absolute terms only a small proportion of boys born with cryptorchidism – approx. 2% – will also have hypospadias [5]. In rare instances, the testis will disappear due to torsion or some other cause; this condition called testicular regression syndrome as well as "vanishing testis" [5, 10].

4.2. Classification

Clinical classification of non-scrotal testes basically distinguishes retractile and truly UDT [11]. Retractile testis (RT) is defined as a testis that has completed its descent into the scrotum but due to an overactive cremasteric reflex can may move in and out of the scrotum [12]. Truly UDT can further categorized into congenital and acquired forms [11]. Congenital forms – causes by failure of testicular descent into the scrotum – can be into divided intra-abdominal, intra-canalicular, supra-scrotal and ectopic testes [11]. Acquired forms – a previously intra-scrotal testis can no longer be manipulated into a stable position in the scrotum – include primary and secondary types [11]. Primary acquired forms are described as either ascending testes, i.e., those which cannot be brought down into the scrotum, or high scrotal testes, i.e., those which can be still manipulated into a high scrotal (unstable) position [11]. Retractile testes can become into acquired forms over time [12]. Secondary acquired forms are the result of ipsilateral groin surgery and are termed "trapped testes" or iatrogenic cryptorchidism [11].

In terms of surgical management, the most useful classification is to categorize UDTs into palpable and non-palpable testes (NPT) [3]. Generally, 20% of UDTs are non-palpable [3]. Most of NPTs (35-82%) are non-viable (testicular nubbin or vanished testis), 3-39% are extra-abdominal, and 15-34.1% of them falling into intra-abdominal category [3, 8].

Updated Ain Shams Laparoscopic Classification of Impalpable Testes based on laparoscopic findings [13]. Five main types are distinguished: type I: no testis is visualized; type II: the testis is peeping (trans-inguinal); type III: testis situated ≤2 cm proximal to the ipsilateral internal inguinal ring [low intra-abdominal testis (LIT)]; type IV: testis situated >2 cm proximal to the ipsilateral internal inguinal ring [high intra-abdominal testis (HIT)], type 5: syndromic NPT [13].

4.3. Diagnostic evaluation

History taking and physical examination are key in evaluating children with UDTs [3]. Localization studies using different imaging techniques are usually without any additional benefit [3].

4.3.1. History

In the anamnesis, perinatal history should be considered, including prematurity, maternal and paternal hormonal exposure, tobacco smoking, and genetic or hormonal disorders [3, 14]. History of previously descended testes might be indicative of testicular ascent, while prior inguinal surgery is suggestive of secondary UDT caused by entrapment [3, 15].

4.3.2. Physical examination

Examination should be performed in warm environment when the child is relaxed [14]. After general physical examination and inspection of the corresponding region, an UDT is searched by carefully advancing the examining fingers along the inguinal canal towards the pubis region [3]. A possible inguinal testis can be felt to bounce under the examiner's fingers [16]. Examination usually occurs in supine position, however, in some cases, it should be considered that abduction of both hips as well as standing position can facilitate the pursue of the testis [14, 17]. If no testis can be identified along the normal path of descent, possible ectopic locations must be taken in consideration [3]. During the examination, UDT should be determined into non-palpable or palpable category, because this will guide the surgical intervention [18]. Furthermore, in newborn cases with NPT or UDTs on both sides and any sign of disorders of sex development (DSD), such as concomitant hypospadias or scrotal hyperpigmentation, urgent endocrinological and genetic evaluation is necessary [3].

4.3.3. Imaging studies

Imaging studies cannot determine with certainty whether a testis is present or absent: all English language considered high quality clinical practice guidelines (CPGs) – CPGs from Agency for Healthcare Research and Quality (AHRQ), American Urological Association (AUA), British Association of Paediatric Surgeons/British Association of Urologic Surgeons (BAPS/BAUS), Canadian Urological Association (CUA), and European Association of Urology/European Society for Paediatric Urology (EAU/ESPU) – recommend against the routine use of ultrasound (US) and other diagnostic imaging since it does not change management and does not add diagnostic accuracy [3, 17, 19-22].

Although US is a non-invasive tool, it is costly, and in case of a NPT, lacks the diagnostic accuracy to prove confidently the presence of the testis or to establish the absence of an IAT: US detects only 30% of extra-abdominal testicular nubbins and 38% of viable IATs with an overall a sensitivity of 45% and specificity of 78% [3, 8]. In addition, it is time-consuming: imaging ordered by primary care providers may increases the time to referral and delays definitive surgical treatment [23].

Cross-sectional imaging by CT (computed tomography) or MRI (magnetic resonance imaging) is not capable to localize NPTs and may lead to unnecessary exposures to radiation and/or anaesthesia [23]. For testicular localization, MRI has an overall accuracy of 62-67%, which increases to 92-97% supplemented with diffusion weighted imaging [23]. However, if the testis is not detected by MRI, laparoscopy is still required to confirm the absence of the testis, thus avoiding the need for MRI [23].

Use of US or MRI is limited and only recommended in specific and selected clinical scenarios, such as for identification of Müllerian structures in cases of suspicious DSD or when other associated urogenital anomalies are suspected (e.g., renal anomalies, urethral duplications, posterior urethral valves, prune belly syndrome, and spina bifida) [3, 23]. Additionally, imaging studies can be considered for determination of the exact testicular size if needed [3].

4.3.4. Diagnostic laparoscopy

Diagnostic exploratory laparoscopy is the current gold standard with high sensitivity and specificity for identification of NPTs and possibility to be used for treatment subsequently [19]. CPGs from AHRQ, AUA, BAPS/BAUS, CUA, EAU/ESPU both recommended it in cases of NPTs [3, 17, 19-22]. The operative procedure is chosen according to pathoanatomical findings related to the testis and vessels, and to the surgeon's own preference [23, 24]

4.4. Management

4.4.1. Management of retractile testis

Recent guidelines do not offer medical or surgical treatment to boys with RTs [25]. However, monitoring of this condition is important because RTs can become ascending testes, that share the same histopathology with congenital UDTs [19, 26, 27]. AUA and CUA guidelines both offer annual exams for all RTs, while EAU/ESPU recommends the follow-up of RTs until puberty [3, 17, 19, 22].

4.4.2. Management of undescended testis

4.4.2.1. Hormonal therapy

Hormonal therapy in the management of UDTs may occur as a neoadjuvant to induce testicular descent or as an adjuvant to surgery to improve fertility rate after orchiopexy [23]. Preoperative hormonal treatment using human chorionic gonadotropin (hCG), or gonadotrophin-releasing hormone (GnRH) is not recommended: it has a maximum success rate of only 7-68%, and in addition 20% of these descended testes have risk of re-ascending [23, 28-31]. In general, success of the neoadjuvant treatment depends on the testicular position: the higher the testis is located prior, the lower the success rate of the therapy [3, 32]. Short-term side effects include increased scrotal erythema and pigmentation as well as induction of pubic hair and penile growth. In addition, during hCG treatment echocardiographic evidence of increased left ventricular mass was found [23, 29].

As an adjunct to surgical management, its overall benefit is still unclear: existing studies are inconclusive for definitive recommendations [23]. Studies concluded that post-operative hormonal therapy appears to increase testicular size and sperm production after orchiopexy and thereby may be beneficial in select populations (e.g., in patients with hypothalamus-pituitary-gonadal hypofunction) [23, 29].

AUA, CUA, and EAU/ESPU do not advise routine hormonal therapy for NPTs [3, 17, 19, 22]. While AUA and CUA guidelines mention that hormonal treatment has little to no role in the management of UDT, EAU/ESPU states that patients should be individually assessed [3, 17, 19, 22]. However, it should be considered, that investigations on hormonal therapy are small, and results are variable, therefore larger trials are needed in order to make convincing recommendations [23].

4.4.2.2. Surgical therapy

Timing of surgical therapy

Undescended testis is known to be associated with decreased fertility potential and increased malignancy rates [27]. Timely referral to a surgical specialist and timely surgical correction may improve fertility rates and decrease the risk of malignant changes [27]. International guidelines – AUA, CUA, EAU/ESPU, BAPS/BAUS – both recommend surgical referral by primary care providers, especially if there is no descent of UDT by 6 months [3, 17, 19, 21, 22]. In addition, the essence of these guidelines is that boys with a congenital UDT which does not descend spontaneously by 6 months of age should undergo orchiopexy by 18 months [1].

The abnormally high temperature of the cryptorchid testis may be an important reason of germ cell loss: the longer the testes are not placed in their physiologic place in the scrotum the longer the risk period for thermal injury, as well as the older the boy at the time of the orchiopexy, the higher is the risk of no germ cells in the testis **(Figure 1.)** [4, 5, 33, 34]. Performing orchiopexy before puberty reduces the subsequent risk of testicular cancer [35]. Accordingly, cryptorchid boys who undergo orchiopexy after the age of 12 are 2-6 times more likely to have testicular cancer compared to those who receive the surgery before the age of 12 [5, 35].

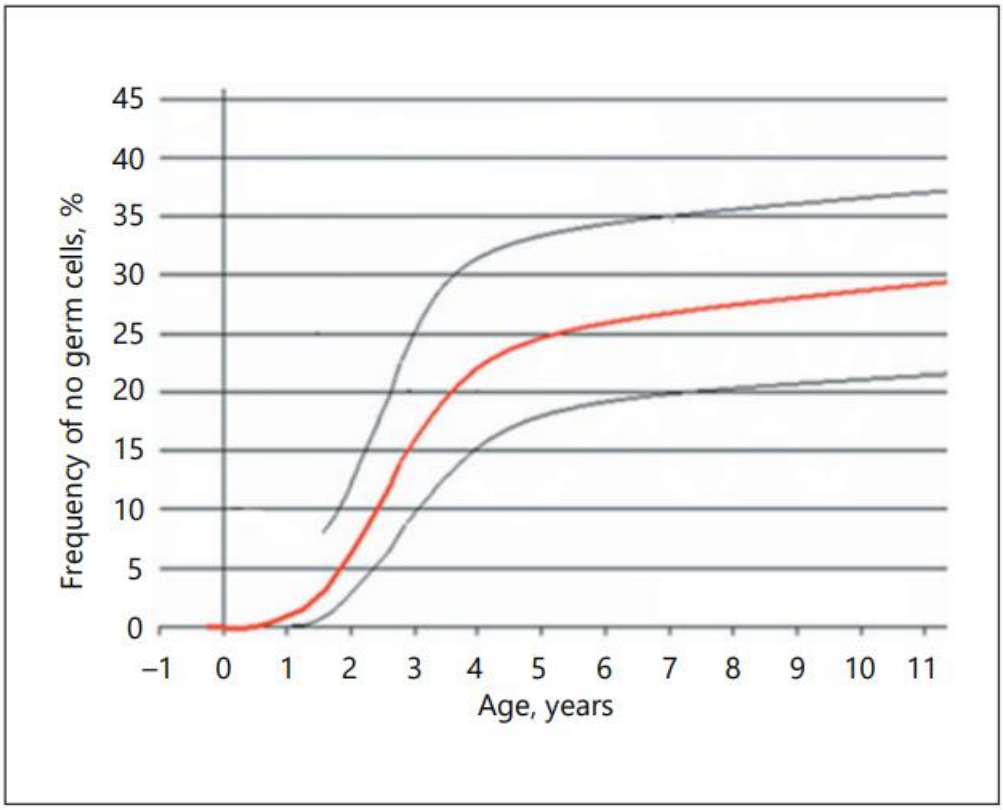

Figure 1 The frequency of no germ cells (%) in testicular biopsies at surgery in 862 consecutive cryptorchid boys <12 years at surgery after Thorup et Cortes 2019 [34].

Palpable testes

Surgery for palpable testes includes orchiolysis and orchiopexy, either via an inguinal or scrotal approach [3]. The latter technique is mainly reserved for low-positioned UDTs [3]. Inguinal orchiopexy is a widely used method with a high success rate of up to 92% [3]. The basic steps of it include high ligation of the processus vaginalis and division of the longitudinal cremasteric, external spermatic, and internal spermatic fibres [1]. Any additional pathology must be dealt

with, such as removal of an appendix testis [3]. Size of the testis can be measured and the connection of the epididymis to the testis can be judged and documented [3]. Finally, the mobilized testis must be placed in a sub-dartos pouch without any tension [3].

A common alternative to the inguinal orchiopexy is the trans-scrotal orchiopexy described by Bianchi and Squire [1, 36]. The ideal patient for a trans-scrotal orchiopexy has an ectopic, ascending, or low palpable testis over the pubic tubercle that can be manipulated into the upper scrotal sac [1]. The incision allows mobilization of the spermatic cord proximally to the external inguinal ring and if a hernia sac is encountered, it can be ligated at the external inguinal ring [1]. Advantages of the trans-scrotal approach include reduced operative time, discomfort, and surgical scarring [1].

Non-palpable testes

Nowadays, diagnostic laparoscopy has been universally agreed to be the gold standard for identifying IAT and to determine the next steps [3, 17, 23, 25, 37]. During laparoscopy, possible anatomical findings include spermatic vessels entering the inguinal canal (40%), an intra-abdominal (40%) or peeping (10%) testis, or blind-ending spermatic vessels confirming vanishing testis (10%) **(Figure 2.)** [3]. If the spermatic vessels enter the inguinal canal, inguinal exploration is suggested because a healthy testis may be present that requires standard orchiopexy [3, 38]. In case of blind-ending spermatic vessels, inguinal exploration is not recommended, the necessity of surgical fixation of the contralateral testis is open to debate [3, 38]. It is crucial to remove any intra-abdominal testicular remnant due to the high incidence of residual germ cells and therefore the potential for malignant transformation that may be unrecognized in an intra-peritoneal location [8]. Peeping testis can be placed down in the scrotum laparoscopically or via an inguinal incision [3].

Despite the high prevalence, surgical treatment of IATs is still challenging. The main limiting factor is the shortness/brevity of testicular vessels, hindering adequate and tension-free placement of the testis into the scrotum. Moreover, too much stretching on the testicular vessels may cause circulatory disorder, sometimes atrophy of the testis. To overcome this factor numerous treatment options have been described. If the testis can reach the scrotum without any tension after careful dissection and mobilization, typically one-stage laparoscopic orchiopexy is performed with a great (85-100%) success rate [8, 39].

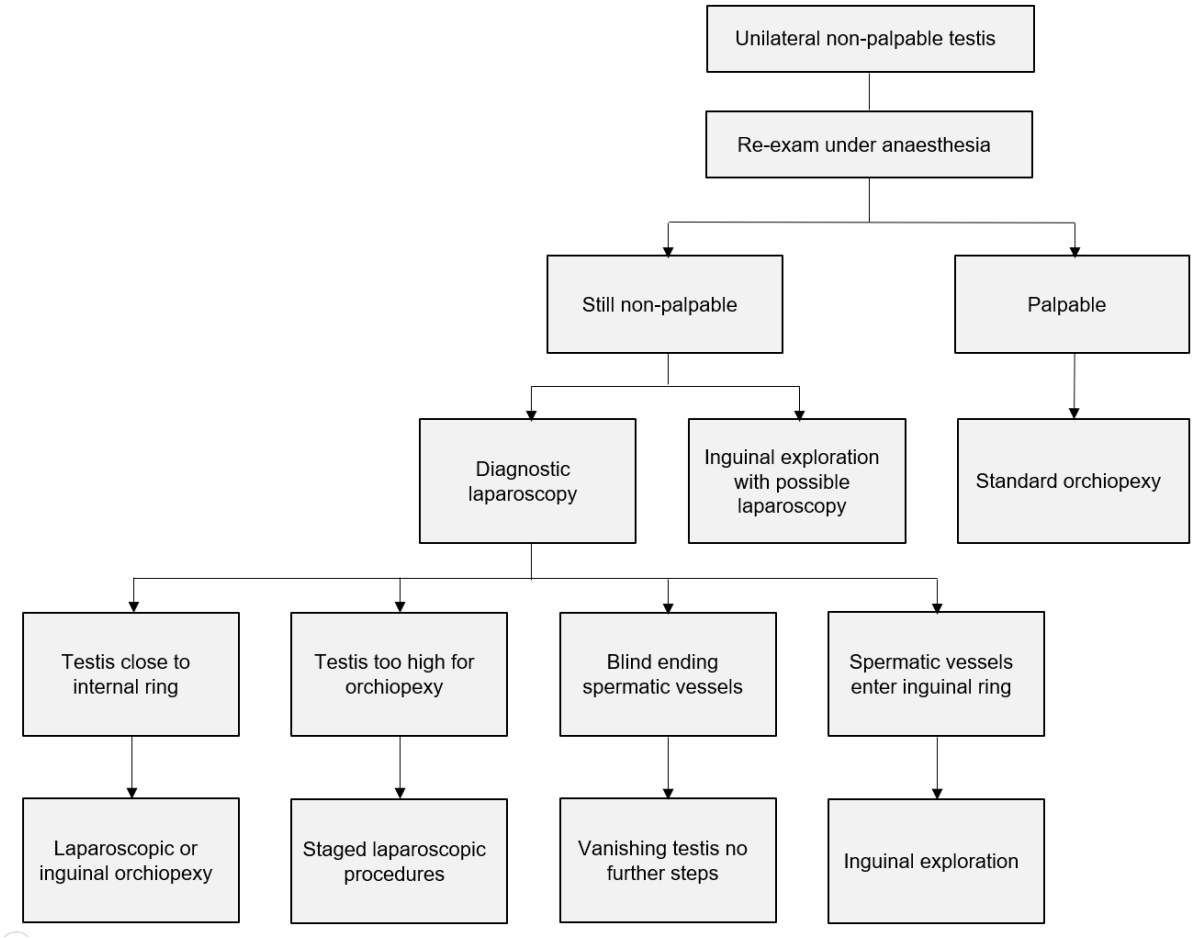

Figure 2 Algorithm for unilateral non-palpable undescended testis based on the guidelines of The European Association of Urology/European Society for Paediatric Urology; modified after Radmayr et al. 2016 [3].

If the vessels are too short, staged orchiopexy should be chosen. One of the most popular techniques is the two-stage Fowler-Stephens orchiopexy (FSO), performed laparoscopically, where the spermatic vessels are transected to gain length to bring the testes to an orthotopic location. An alternative and technically demanding approach is the microvascular testicular auto-transplantation, where the vessels are transected, the testis is brought down to the scrotum, where vessels are re-anastomosed to the inferior epigastric vessels [1, 8, 40, 41]. Pooled estimated success rate of FSO is 80%-85% and 88 % of microvascular orchiopexy, although the functional effect and fertility outcomes are still questionable [8, 42, 43].

To reduce the rate of testicular atrophy Shehata et al. revisited the laparoscopic traction technique with preservation of the main blood supply of the testis in 2008 [Shehata technique or staged laparoscopic traction orchiopexy (SLTO)]. At the first stage, after dissecting the gubernaculum and the lateral peritoneal attachments, the IAT is fixed up to the abdominal wall

near the contralateral anterior superior iliac spine. After three months, the testis is detached and brought down to the scrotum via the anatomical way or by Prentiss manoeuvre **(Figure 3)**. In between the two stages the elongation of the cross-stretched testicular vessels is carried out by gradual traction due the weight of intestine as well because of the respiratory movements of the abdominal wall [44]. So far, surgical results of Shehata technique are mostly single centric, including mainly low number of cases with relatively short-term follow-up, however the preliminary data are satisfactory: success rate is estimated between 65 and 100%, while the failure of the surgery comes almost exclusively from testicular ascent [45-50].

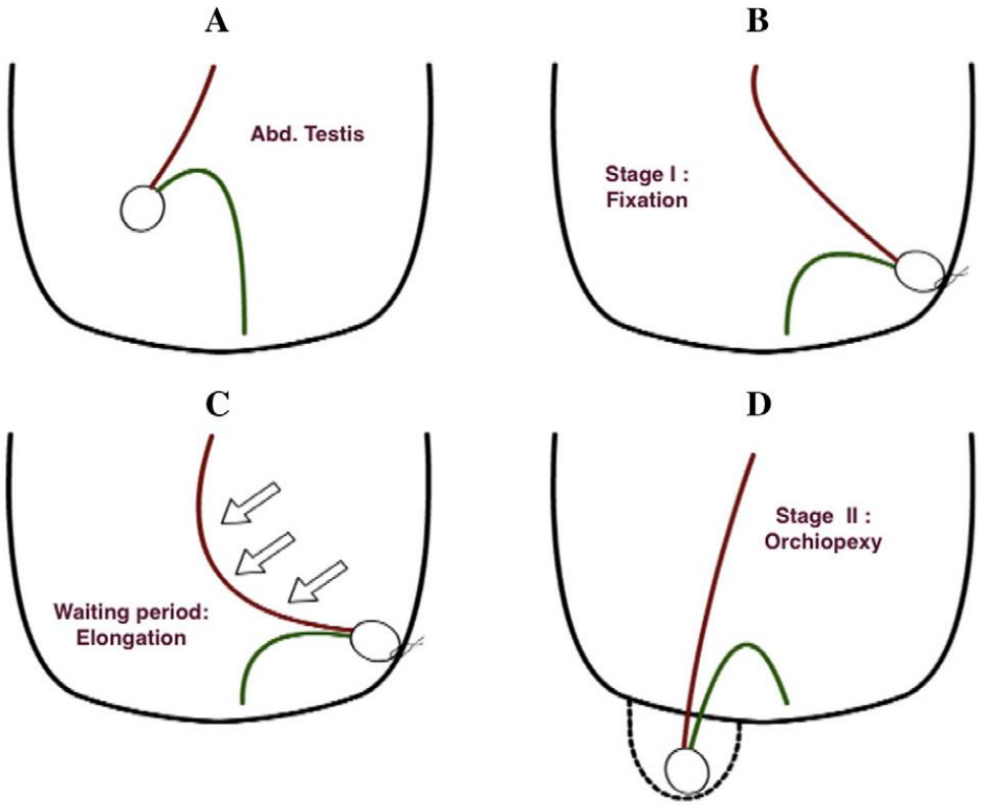

Figure 3 Schematic diagram showing the steps of staged laparoscopic traction orchiopexy. **A** right intra-abdominal testis, **B** stage I: laparoscopic fixation above contralateral anterior superior iliac spine, **C** possible mechanism of elongation by weight of intestine, **D** stage II: laparoscopic-assisted placement in scrotum after Shehata et al. 2016 [45]. Abd. Testis = intra-abdominal testis.

Complications of surgical therapy

The most common complications after orchiopexy include retraction of the testis out of the scrotum and testicular atrophy observed in 1.2-6% of all UDTs [1, 14]. Causes of testicular retraction include underdeveloped scrotal sac, incomplete retroperitoneal mobilization of the

spermatic cord, failure to close the hernia sac, and overzealous dissection – outside the scrotal border – during creation of a dartos pouch, allowing the testis to migrate out of the scrotum [1].

Testicular atrophy is typically a result of injury to the spermatic vessels during surgery, tension on the spermatic cord, with subsequent ischaemia, iatrogenic torsion, and intentional ligations of the testicular vessels as an integral part of FSO [3]. Other rare complications include vas deferens injury, local wound infection, dehiscence, and haematoma [3]. **Table 1** contains the recommendations of the EAU/ESPU for the management of UDTs [3].

Recommendations of the European Association of Urology/European Society for Paediatric Urology for the management of undescended testis		
	LE	**GR**
Do not offer medical or surgical treatment to boys with retractile testes but closely follow-up until puberty.	2a	A
Offer surgical orchiolysis and orchiopexy before the age of 12 months, and by 18 months at the latest.	2b	B
Evaluate male neonates with bilateral non-palpable testes for possible DSD.	1b	A
In cases of non-palpable testes and no evidence of DSD, offer laparoscopic intervention because of its excellent sensitivity and specificity in identifying an intra-abdominal testis, as well as the possibility for subsequent treatment in the same session.	1a	A
Do not routinely offer hormonal therapy, either in an adjuvant or neo-adjuvant setting for testicular descent. Patients have to be evaluated on an individual basis.	2a	C
In cases of bilateral undescended testes, offer endocrine treatment to possibly improve further fertility potential.	4	C
For an undescended testis in a post-pubertal boy or older, with a normal contralateral testis, discuss removal with the patient/parents because of the theoretical risk of a later malignancy.	3	B

Table 1 Treatment recommendations for undescended testis according to the European Association of Urology/European Society for Paediatric Urology guidelines after Radmayr et al. 2016 [3]. DSD = Disorders of sexual development; GR = Grade of recommendation; LE = Level of evidence.

Follow-up after surgical therapy

After orchiopexy apart from the routine follow-up of patients regarding postoperative complications and monitoring the viability and proper position of the testis, there are two important additional parameters which correlate with the management of UDTs: impairment of fertility and potential risk of malignancy [3]. Counselling and educating parents and patients regarding these possible long-term effects and proper self-exam of the testes is crucial, as well as long-term follow-up, even up to puberty is recommendable [3, 14].

4.5. Long-term outcomes

4.5.1. Undescended testis and fertility

Men with a history of UDT have an increased risk of infertility and about 10% of infertile men have a history of cryptorchidism and orchiopexy [34, 51, 52]. The association seems to be a result of multiple factors, including germ cell loss, impaired germ cell maturation, Leydig cell diminution, and testicular fibrosis [3]. Although boys with unilateral UDTs have a lower fertility rate, they have a similar paternity rate to general population [3]. In contrast, boys with bilateral UDTs suffer from lower fertility and paternity rates too: they have a 6-fold higher risk of being infertile when compared with unilaterally cryptorchid men and general population [3, 52, 53]. Though, it is important to consider, that fertility rate is the number of offspring born per mating pair, individual of population, whereas paternity reflects the actual potential of fatherhood [3].

Adult men with persisting cryptorchidism have azoospermia in 85% of bilateral and 15-20% of unilateral cases, because unilateral UDT may involve the same pathological mechanism in both testes [54]. The reduction in germ cell count begins as early as 6 months of age [52]. To improve fertility, it is suggested that orchiopexy should be performed between 6 and 12 months of age and completed by 18 months at the latest [3]. Besides the timing of treatment, the later fertility is also related to the original location and size of the testis [34]. In general, the higher the testicular position at the time of therapy, the fewer the number of germ cells [52]. Testicular biopsy at the time of orchiopexy can provide significant information on the future fertility [52]. Regarding severely retractile/ascending testis, they should be operated after the diagnosis is settled [34].

4.5.2. Undescended testis and malignancy

Cryptorchidism is the most widely accepted risk factor for testicular cancer [34]. Boys who are treated for an UDT have an approximately 1.6-7.5-fold increased risk of developing testicular malignancy, and it is estimated that 5-9% of all men with testicular cancer have a history of persistent cryptorchidism [5, 55-57]. This risk is raised further in the setting of bilateral UDTs, while in unilateral cases the unaffected testis has also a slightly higher predisposition [58]. Based on epidemiological studies, pre-pubertal orchiopexy may reduce the risk of testicular cancer, however not to the level of normal controls, in addition, the younger the child at surgical therapy, the lower the odds ratio for later testicular germ cell cancer [34, 56, 59]. Since early orchiopexy seems to have a protective effect, timely referral to a surgical specialist and early surgical correction is mandatory to reduce malignancy rates related to UDTs [34, 60, 61]. In addition, screening, and self-examination during and after puberty is recommended to facilitate early cancer detection [3, 27].

In postnatal testis gonocytes or stem cells transform into spermatogenic stem cells or undergo apoptosis at 3-9 months of age [4, 27]. This step is confused in cases cryptorchidism, and arrested gonocytes can cause germ cell malignancies after puberty [4, 27]. Intratubular germ cell neoplasia (ITGCN) is the precursor lesion for invasive testicular germ cell tumours of adolescents and young adults [58]. Approximately 50% of patients with ITGCN will develop an invasive of testicular germ cell tumour within 5 years [62]. ITGCN is present in 5% to 8% of men with a history of cryptorchidism, and this rate is further elevated in patients with syndromic cryptorchidism, especially in cases with genital ambiguity and/or chromosomal disorders [34, 58, 63]. Based on these findings, in this patient group some authors suggest taking testicular biopsy at the time of orchiopexy [34, 63]. Testicular microlithiasis is more prevalent in boys with history of cryptorchidism, however, it alone has not been shown to conclusively be a predictor of future testicular cancer [23].

Optimal management of UDT in a post-pubertal male remains unknown [8]. Due to the related histologic changes and increased risk of malignancy, EAU/ESPU recommends surgeons offer orchiectomy for patient of this age with an UDT and a normal contralateral descended testis, while AUA suggests considering orchiectomy in case of an IAT and a normal contralateral testis [3, 8, 17].

5. OBJECTIVES

To improve patient care, we evaluated the current treatment of UDTs in Hungary. The aims of our comprehensive study were as follows.

I. Evaluation of the adherence of primary care paediatricians (PCPs) to current recommendations, regarding screening newborns for cryptorchidism, referral of suspicious cases to paediatric surgical specialists, management of retractile testes, and long-term follow-up after surgical therapy.

II. To assess the adherence of paediatric surgical specialists to the current EAU/ESPU and Hungarian Ministry of Human Resources (MHR) guidelines regarding the management of UDTs, with particular emphasis on diagnostic imaging, surgical and hormonal therapy.

III. To investigate, whether surgical procedures currently used by paediatric surgeons, comply with the latest literature recommendations.

IV. Retrospective analysis of medium-term results of SLTO on a larger cohort in a national multicentre study.

V. Determination of the effects of traction on the circulation/viability of the testes using Doppler ultrasound (US) examination.

VI. To investigation the effects of the type of fixation stitch (monofilament or braided) to the success of the surgery.

6. METHODS

6.1. Current management of undescended testes in Hungary at the level of primary and speciality care

6.1.1. Study design

The study was approved by the National Scientific and Ethical Committee (approval number: BM/15215-1/2023). To assess the management of UDTs in Hungary a web-based questionnaire (Survio®) was completed in 2023 among the members of The Association of the Hungarian Primary Care Paediatricians (AHPCP) and The Hungarian Association of Paediatric Surgeons (HAPS). Survey data were collected on a voluntary and anonymous basis, respondents provided informed consent to participate in this examination. The questions for assessing the patient management of PCPs were edited by the employees of the University of Szeged. The analysis of the patient management of paediatric surgical specialist care was carried out applying a Hungarian translation of a questionnaire edited by Aubert et al. and approved by The European Paediatric Surgeons' Association (EUPSA) [64].

The first part of the survey covered sociodemographic data. During the translation of the EUPSA approved questionnaire, these questions were adapted to the Hungarian conditions. The second part of the survey focused on the patient management including diagnostics, referral of suspicious cases to paediatric surgical specialists, surgical and hormonal therapy, application of new surgical procedures, management of RTs, long term follow-up after orchiopexy and adherence to national and international CPGs, with particular regard to the EAU/ESPU 2016 guidelines and to the Hungarian MHR 2021 guidelines about the management of UDTs [3, 38].

6.1.2. Statistical analysis

Based on the first part of the questionnaire sociodemographic data including qualification, location, and level of institution as well as number of practicing years comprising residency were described. According to the second part of the survey patient management (average number of diagnosed UDTs and performed orchiopexies per year, age for screening children for UDT, the optimal timing and type of specialist care for the referral of suspicious cases, applications of medical imaging, optimal time and type of surgical treatment, indications of hormonal therapy, application of new surgical procedures, management of RT, long term follow-up after orchiopexy, adherence to national and international CPGs) was analysed.

Descriptive statistics were used to summarize the outcomes; variables were displayed using frequencies and/or percentages.

6.2. Assessment of the medium-term results of Shehata technique

6.2.1. Study design

The study was approved by the ethical committees of the institutions (IRB number and date of approval: 87/2017-SZTE, 22/05/2017). Patients with NPT treated with SLTO were enrolled in the study from three Hungarian centres (University of Debrecen, University of Pécs and University of Szeged) between January 2013 and October 2020. Medical records were retrospectively reviewed for demographic data, operative findings, as well as postoperative events. The follow-up of the patients was carried out by the surgeon's own preference.

All patients were called back for an additional check-up in 2021 to collect the actual status of their testicles. The position of the testes was determined by physical examination. The viability was determined by Doppler US examination: testicular atrophy was diagnosed if no testicular tissue or no blood flow was detectable. Relocation or ascent was identified if the testicle was placed outside the scrotum. Success was defined as proper scrotal position and blood flow on Doppler US. Furthermore, testicular size was assessed by US and compared to the contralateral descended testicle.

6.2.2. Inclusion criteria

All boys diagnosed with NPTs were subjected to diagnostic laparoscopy. Atrophic IATs or remnants were removed. If a viable IAT was found, stretching test was performed to determine the feasibility of SLTO: in case the testis reached the contralateral internal inguinal ring tension free – it could be mobilized to the scrotum without tension – standard single-stage laparoscopy was done. When single-stage laparoscopy was not feasible the testis was mobilized to the fixation point: if it occurred with moderate tension the patient underwent the first step of SLTO.

6.2.3. Operative technique

Operative technique was performed according to the initial description of Shehata et al [45, 65]. The patient was positioned in supine position. Re-examination was done under general anaesthesia and if the testis was non-palpable, diagnostic laparoscopy was carried out. Testicular morphology was evaluated by inspection.

After dividing the gubernaculum, stretching test was performed. The testis was mobilized with the division of the lateral peritoneal attachments and was fixed to the abdominal wall one inch above and medial to the contralateral anterior superior iliac spine using a single stitch, which was a 3-0 braided, non-absorbable suture with 17 mm ½ circle round needle or 3-0 monofilament, non-absorbable suture with 17 mm ½ circle round needle. The suture was inserted through a small skin incision at the determined point into the abdominal cavity. After taking an appropriate amount from the testis, the suture was pulled out through the skin incision, tied extracorporeal and buried subcutaneously.

The second stage was performed average 3 months after the first operation. The abdominal cavity was inspected for any adhesive bands, internal herniation, slippage of the suture or adhesion of the spermatic cords in bilateral surgeries. The atrophic testes were removed. Degree of elongation of testicular vessels was measured indirectly by passing a forceps behind them at the midline and by elevating them toward the anterior abdominal wall. Then, the fixation stitch was divided, and the testis was delivered to the contralateral internal inguinal ring (stretching test). If the testis can't be brought to the contralateral internal ring, redo traction (refixation of the testis) was performed. If the length of testicular vessels was appropriate an ipsilateral scrotal incision was made, and the testis was delivered through a new hiatus medial to the inferior epigastric vessels (Prentiss manoeuvre) or through the inguinal canal into a sub-dartos pouch and sutured to the scrotal wall using an absorbable suture.

6.2.4. Follow-up details

Testicular blood flow, position and size were prospectively analysed in 2021. Physical examination occurred to determine the position of the testes. The viability was assessed by Doppler US examination: testicular atrophy was diagnosed if no testicular tissue or no blood flow was detectable. Relocation or ascent was identified if the testicle was placed outside the scrotum. In these cases, our treatment strategy was redo open orchiopexy. Success was defined by appropriate scrotal position by physical examination, with appropriate flow on Doppler US. Testicular volume was determined by scrotal US; testicular dimensions were measured, and volume was calculated using the ellipsoid formula (volume = $r1 \times r2 \times r3 \times 0.52$). In unilateral surgeries testicular volume of the operated testis was compared to descended contralateral one.

6.2.5. Statistical analysis

Demographics including age, laterality, comorbidities, and operative data such as intraoperative testicular location, testicular morphology, type of suture used for testicular fixation to the abdominal wall, fixation of the testis in the scrotum, time interval between first and second stages, number and outcomes of redo tractions, conversions and perioperative complications were analysed retrospectively. Prospectively testicular viability, location, size, and success rate were assessed, and follow-up period was described. Descriptive statistics were used to analyses the data. Categorical variables were expressed as frequencies and/or percentages in each category. Continuous variables were presented as mean (range).

7. RESULTS

7.1. Management of undescended testes in Hungary at the level of primary health care

Sixty-nine registered members of the AHPCP (approximately 7%) participated in the survey. **Table 2** contains the percentage distribution of their answers to the questions. The majority of them (92.8%) have been practising (including residency) for more than twenty years. Forty-two percent work in Budapest or in Pest County; the other counties are separately represented by 0-8.7% of them.

Most of the contributing PCPs (82.6%) declare following the Hungarian MHR 2021 guidelines when managing UDTs. Unawareness of the guidelines (13.0%) was the most common reason of non-adherence. In addition, roughly the half of them (55.1%) follow the EAU/ESPU 2016 guidelines in their clinical practice. On the management of UDTs the participants are influenced mostly by their experience during their specialty training (65.2%): awareness of national (50.7%) and international (18.8%) guidelines are less authoritative.

Almost all responders (98.6%) screen newborns for UDT and 88.4% refer any suspicious cases at first detection or before 6 months of age for paediatric surgical or paediatric urological examination. In general, they (91.3%) consider necessary to evaluate male neonates with bilateral NPTs for possible DSD. Although more than 85% of the participants are aware of the possible complications of cryptorchidism, only two-thirds of them know the appropriate time for surgical therapy. Long-term follow-up after orchiopexy is recommended by 39.1% of them until puberty while in the majority of cases (46.5%), the controls end when school-age is reached. Additionally, 59.4% of them consider the management of RTs to be primarily conservative, and 60.8% of them offer close follow-up until puberty.

When do you check the position of the testes at the first time?	
I do not examine the testes (0%)	3-12 months (1.4%)
<3 months (98.6%)	>12 months (0%)
When do you refer suspicious cases of UDT to specialist in order to assess the need for surgery?	
On first detection (15.9%)	> 1,5 years of age (1.4%)
If there is no change by the age of 6 months (72.5%)	> 2 years of age (2.9%)
	> 3 years age (0%)
> 1 year of age (7.3%)	Other (0%)
To which surgical specialist do you refer the suspicious cases of UDT?	
To paediatric surgical or paediatric urological specialist (100%)	Under the age of three to paediatric surgical or paediatric urological specialist, over the age of three to adult urological specialist (0%)
To adult urological specialist care (0%)	Other (0%)
Do you evaluate male neonates with bilateral non-palpable testes for possible DSD?	
Yes (91.3%)	No (5.8%)
For selected cases (2.9%)	
According to your knowledge, what is the ideal time for surgical treatment of UDTs?	
<12 months (33.3%)	<3 years (8.7%)
<18 months (33.3%)	Other (2.9%)
<2 years (21.8%)	
According to your knowledge, what can be the long-term consequences of UDT treated beyond the optimal time? (multiple answers may apply)	
Testicular atrophy (85.5%)	Malignant testicular tumours (87.0%)
Reduced fertility (97.1%)	
How long do you follow children after orchiopexy?	
The follow-up occurs at the surgery/urology (2,9%)	Until puberty (39.1%)
For one year (7.2%)	Other (4.3%)
Until school-age (46.5%)	
According to your knowledge, what is the primarily recommended management of retractile testicles?	
Conservative (observation) (59.4%)	Hormonal therapy (hCG or GnRH) (13.1%)
Surgical intervention (23.2%)	Other (4.3%)
Do you follow up boys with retractile testes until puberty?	
Yes (60.8%)	No (17.4%)
For selected cases (21.8%)	
Do you follow the EAU/ESPU 2016 guidelines when managing UDT?	
Yes (55.1%)	No (44.9%)
Do you follow the Hungarian Ministry of Human Resources 2021 guidelines when managing UDT?	
Yes (82.6%)	No (17.4%)
In your clinical practice which factor has the greatest influence on the management of UDT? (multiple answers may apply)	
Personal experience over the years (42.0%)	National guidelines (50.7%)
Established practice in our institute (11.6%)	What I was trained (65.2%)
Consultant's preference (1.4%)	Other (0%)
International guidelines (18.8%)	

Table 2 Results of the questionnaire regarding management of undescended testis at the level of primary health care. The table contains the percentage distribution of the answers of 69 primary care paediatricians to the questions. DSD = disorder of sexual development; EAU = European Association of Urology; ESPU = European Society for Paediatric Urology; GnRH = Gonadotropin-releasing hormone; hCG = Human chorionic gonadotropin; UDT = undescended testis.

7.2. Management of undescended testes in Hungary at the level of paediatric surgical specialist care

Fifty-six active members of the HAPS (approximately 49%) participated in the survey: 44 paediatric surgical specialist (78.6%) and 12 trainees (21.4%). The results of their answers are summarized in **Table 3**. The distribution of the number of years spent practising (including residency) were as follows: < 5 years: 10.7%; 5 to 10 years, 23.2%; 10 to 20 years, 35.7%; and >20 years: 30.4%. Level of care was reported as tertiary in 91.1%, secondary in 7.1%, and primary in 1.8%. Thirty-eight of participants reported that they work in Budapest or in Pest County. Baranya, Csongrád-Csanád and Hajdú-Bihar Counties are each represented by 16.1% of the respondents in accordance with the location of the university centres. The participation rate from the other counties can be put between 0-5.4%.

When managing UDTs, almost all participants (98.2%) declare following EAU/ESPU 2016 guidelines, and the majority of them (92.9%) follow the Hungarian MHR 2021 guidelines, too. Based on their answers, international (66.1%) and national (39.3%) guidelines influence mostly their patient management regarding cryptorchidism.

Most of the responders (98.2%) offer orchiopexy before 1.5 years of age. In case of NPTs, 71.4% prefer diagnostic laparoscopy and 28.6% primarily recommend ultrasonography. If a peeping testicle is found during laparoscopy, 67.9% perform inguinal or laparoscopic assisted orchiopexy. Treatment of HITs – located >2 cm proximal to the ipsilateral internal inguinal ring – occur primarily (82.1%) with minimally invasive Shehata technique. If blind ending spermatic vessel are identified, further management is heterogenous: 39.2% finish the operation, 25.0% fix the contralateral testis, 19.7% explore the inguinal canal to remove testicular nubbin and 9.0% explore the inguinal canal and additionally fix the contralateral testis. A significant part of them (69.6%) considers necessary to evaluate male neonates with bilateral NPTs for possible DSD. RTs are treated primarily conservative (87.5%), and their follow-up is mainly (80.4%) is offered until puberty. Additionally, hormonal therapy – GnRH or hCG – is not recommended in general either to facilitate testicular descent (91.0%) or to improve fertility potential (94.6%).

At what age do you offer an orchiopexy to your patients with undescended testis?	
<12 months (37.5%)	<3 years (0%)
<18 months (53.6%)	Other (7.1%)
<2 years (1.8%)	
How do you manage retractile testes?	
Conservative (observation) (87.5%)	Hormonal therapy (hCG or GnRH) (0%)
Surgical intervention (5.4%)	Other (7.1%)
Do you offer close follow up until puberty to boys with retractile testes?	
Yes (80.4%)	No (16.0%)
In selected cases (3.6%)	
Do you evaluate male neonates with bilateral non-palpable testes for possible DSD?	
Yes (69.6%)	No (12.5%)
For selected cases (17.9%)	
In cases of non-palpable testes what would you recommend?	
Diagnostic laparoscopy (71.4%)	Exploration of the inguinal canal (0%)
Magnetic resonance imaging (0%)	Other (0%)
Ultrasound examination (28.6%)	
Do you offer hormonal therapy (hCG or GnRH) to facilitate testicular descent? (multiple answers possible)	
Never (91.0%)	In unilateral impalpable undescended testis (0%)
In unilateral palpable undescended testis (0%)	In bilateral impalpable undescended testis (1.8%)
In bilateral palpable undescended testes (5.4%)	Other (1.8%)
Do you offer hormonal therapy to improve fertility potential? (multiple answers possible)	
Never (94.6%)	In unilateral impalpable undescended testis (0%)
In unilateral palpable undescended testis (0%)	In bilateral impalpable undescended testis (3.6%)
In bilateral palpable undescended testes (0%)	Other (1.8%)
If at laparoscopy a peeping testicle (testis close to internal ring) is identified, how would you proceed?	
Inguinal or laparoscopic assisted orchiopexy (67.9%)	Shehata technique (17.9%)
Single-stage Fowler-Stephens (1.8%)	Other (10.6%)
Staged Fowler-Stephens (1.8%)	
If at laparoscopy a high testicle (>2cm from the internal ring) is identified, how would you proceed?	
Inguinal or laparoscopic assisted orchiopexy (0%)	Shehata technique (82.1%)
Single-stage Fowler-Stephens (12.5%)	Other (5.4%)
Staged Fowler-Stephens (0%)	
If at laparoscopy blind ending spermatic vessels are identified, how would you proceed?	
No further steps (39.2%)	Exploration of the inguinal canal with removal of testicular nubbin + fixation of the contralateral testis (9.0%)
Exploration of the inguinal canal with removal of testicular nubbin (19.7%)	Other (7.1%)
Fixation of the contralateral single testis (25.0%)	
Do you follow the EAU/ESPU 2016 guidelines when managing UDT?	
Yes (98.2%)	No (1.8%)
Do you follow the Hungarian Ministry of Human Resources 2021 guidelines when managing UDT?	
Yes (92.9%)	No (7.1%)
In your clinical practice which factor has the greatest influence on the management of UDT? (multiple answers may apply)	
Personal experience over the years (23.2%)	National guidelines (42.9%)
Established practice in our institute (28.6%)	What I was trained (33.9%)
Consultant's preference (14.3%)	Other (0%)
International guidelines (69.6%)	

Table 3 Results of the questionnaire regarding management of undescended testis at the level of paediatric surgical specialist care. The table contains the percentage distribution of the answers of 56 members of The Hungarian Association of Paediatric Surgeons. DSD = disorder of sexual development; EAU = European Association of Urology; ESPU = European Society for Paediatric Urology; GnRH = Gonadotropin-releasing hormone; hCG = Human chorionic gonadotropin; UDT = undescended testis

7.3. Medium-term results of Shehata technique

Patient demographics, operative data, and details of follow up are listed in **Table 4.** The course of the clinical study is summarized in **Figure 4.** In the study period, 48 patients (55 testes) were treated with SLTO in the participating centres. From these, 23 IAT were right-sided, 18 were left-sided and 7 bilateral surgeries occurred. The latter were operated in the same session. Associated conditions – partial androgen insensitivity and prune belly syndrome – were seen in two patients. Mean age at first stage was 2.9 (0.8-12.6) years. At the operation, the majority (52.1%) of the children was older than 1.5 years, in addition 16.7% of the patients were beyond 6 years. HIT were found in 16.4% of the cases. Morphological abnormalities (testicular hypoplasia or vas deferens and epididymis anomaly) were observed in 60%. The type of suture used for testicular fixation to the abdominal wall was monofilament in 67.3% and braided in 29.1%. In 3.6% the suture material was not recorded.

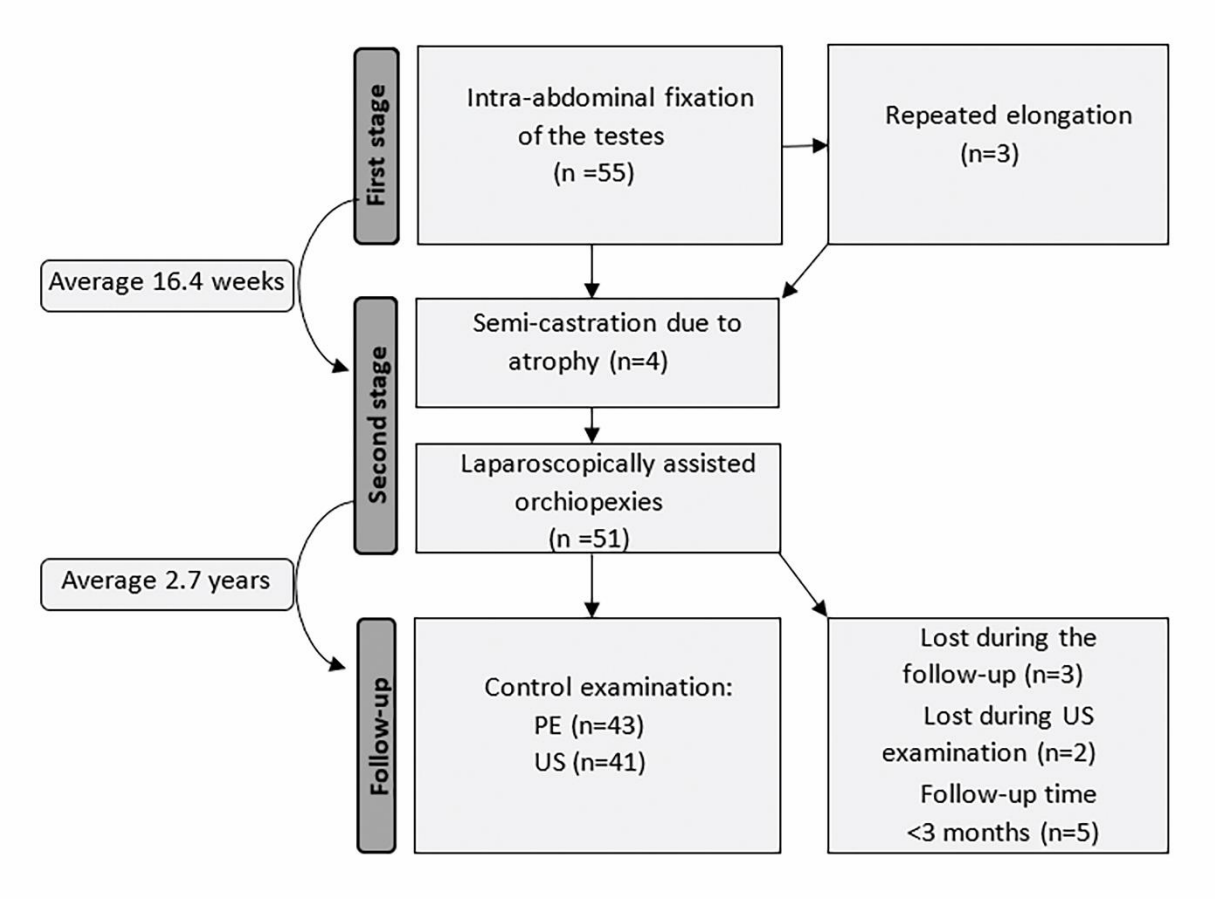

Figure 4 Flow diagram describing the course of study analysing the medium-term results of staged laparoscopic traction orchiopexy (SLTO) or Shehata technique. (PE = physical examination, US = ultrasound)

The mean elapsed time between the two stages were 16.4 (5.1-48.1) weeks. The traction interval passed uneventfully without any serious complications. Failure to achieve adequate elongation occurred in three cases (5.5%); redo traction was done in all of them. Testicular atrophy developed in four cases between the two stages, two of them after redo traction. All the removed testes already showed morphological abnormalities at the first visual evaluation during the first stage and histology examination showed hypoplasia in all four cases. In three out of the four atrophic testes, slippage of the traction stitch leading to insufficient elongation was observed as well. The fourth case was a bilateral IAT, where cross adhesions between the testicular vessels was reported due to the simultaneous cross traction. After separation of the spermatic cords, one testicle was successfully brought down to the scrotum and the other atrophic testicle was removed. Slippage of the fixation stitch (which means that the suture cut through and the testis was found floating in the abdomen) occurred in 11 cases (20%), where 10 from 11 (90.9%) were monofilament suture material.

Testicles were brought down scrotum using Prentiss manoeuvre in 70.6 %, and via the inguinal canal in 29.4 % of the cases. One conversion was necessary due to technical problem. Postoperatively, four wound healing disorders (7.3%) and one temporary hydrocele (1.8%) were reported. The wound healing disorders included two cases of mild port-site wound inflammation, a case of port-site seroma, and a case of suture granuloma. All complications resolved spontaneously. Scrotal testicular position was achieved in 51 (92.7 %) cases.

Thirty-eight patients (43 testes) showed up on control physical examinations and thirty-six patients (41 testes) had US examinations available as well. The mean follow-up period was 2.7 (0.34-7.9) years. Forty testes (93.0%) were found in adequate scrotal position. Testicular ascent occurred in three patients (7.0%). Colour Doppler US identified testicular atrophy in one case (2.4%). In the remaining 97.6 % of the patients, the circulation in the testes to the was appropriate. The overall success rate of the surgery was 82.2 %. In unilateral SLTOs, size of the operated testes measured by US was compared to the contralateral one and the average volume difference was 34.3%. In two out of the three relocated cases redo open orchiopexy was performed via inguinal approach and the scrotal location has been satisfactory ever since. In the third case open orchiopexy is planned.

Demographics	mean (range)	n (%)
Laterality		
Unilateral		41 (85.4)
Bilateral		7 (14.6)
Age distribution at the first stage		
Age at first stage (years)	2.9 (0.8-12.6)	
<=1.5 years		23 (47.9)
1.5-6 years		17 (35.4)
<=6 years		8 (16.7)
Operative data		
Time interval between first and second stages (weeks)	16.4 (5.1-48.1)	
Intraoperative testicular location		
High intra-abdominal testis		9 (16.4)
Low intra-abdominal testis		46 (83.6)
Testicular morphological characteristics		
Hypoplasia and/or dissociation		33 (60.0)
Normal or not mentioned		22 (40.0)
Fixing suture		
Monofilament, non-absorbable		37 (67.3)
Braided, non-absorbable		16 (29.1)
Not recorded		2 (3.6)
Fixation of the testis in the scrotum		
Prentiss manoeuvre		36 (70.6)
Through the inguinal canal		15(29.4)
Redo traction		3 (5.5)
Perioperative complications		
Fixation suture slippage		11 (20.0)
Attached spermatic cords		1 (1.8)
Surgical site infection		4(7.3)
Hydrocele		1(1.8)
Intraoperative testicular atrophy		4(7.3)
Follow up (assessment in 2021)		
Available for physical examination (testes)		43 (84.3)
Available for ultrasound examination (testes)		41 (80.4)
Follow-up duration (years)	2.7 (0.34-7.9)	
Outcomes		
Testicular atrophy		1 (2.4)
Testicular retraction		3 (7.0)
Success rate		82.2%

Table 4 Medium-term results of staged laparoscopic traction orchiopexy (SLTO) or Shehata technique: demographics, operative data and follow up details. Data of SLTO performed in three paediatric surgical centres between 2013 and 2020 were analysed retrospectively. In 2021, physical and Doppler ultrasound examinations were performed to determine the position and viability of testes. Success was defined as an intra-scrotal testicle without atrophy.

8. DISCUSSION

8.1. Current management of undescended testis in Hungary

8.1.1. Timing of the surgical therapy

In cases of UDT early diagnosis, timely referral and optimal surgical therapy are essential to maximize fertility and reduce the risk of malignant changes [1]. The diagnosis is based on physical examination [38]. According to the Decree No. 51/1997 (XII. 18.) of the Ministry of Welfare, the evaluation of the testicular position is an essential part of neonatal screening performed by general practitioners [66]. According to national and main international guidelines, boys with a congenital UDT which does not descend spontaneously by 6 months of age should undergo orchiopexy by 18 months [1, 3, 17, 23, 25, 37, 38]. Treatment of the disease out of the optimal time may cause some consequences [38]. The elevated temperature results in arrest of maturation processes [1, 38]. Consequently, the lack of development of germ cells to into A type dark spermatogonia is associated with infertility [1, 38]. After the age of 1.5-2 years secondary testicular atrophy begins, which becomes irreversible within a few years [38]. Histological examinations demonstrated that the mean tubular fertility index, the number of germ cells, and spermatogonia will lower in UDTs, with a progressive increase in peritubular fibrosis [1, 38, 67]. In untreated cases, there is a 2 and 1% risk per month, respectively, of germ cell loss and Leydig cell depletion each month beyond 1 year of age which can lead to complete lack of germ cells by puberty [1, 68, 69]. Furthermore, gonadotropic regulation of both Leydig and Sertoli cells becomes abnormal [38].

Based on our questionnaire survey, the screening, referral, and surgical management of UDT in Hungary is mainly carried out in accordance with the recent recommendations. Almost all participating PCPs evaluate of testicular position in newborns at the first time before three months of age. Most of them, if a testicle is not palpable in the scrotum, refer the child proper time – on first detection, or if there is no change, by the age of 6 months – for paediatric surgical or paediatric urological examination. Specialists know the proper time for orchiopexy: they offer surgical therapy to their patients before the age of 1.5 years.

Despite, Fadgyas et al. demonstrated, that a significant proportion of orchiopexies are performed in Hungary out the optimal time: the average age of children (n=205) treated with UDT in Pál Heim National Institute of Paediatrics between 2010 and 2019 was 4.5 years [70]. In addition, during the multicentre study of the medium-term results of the Shehata technique,

we also found that the average age of children is higher than recommended. In accordance with our result, English language studies have been reported, that the majority of orchiopexies are done well outside of the suggested age ranges [23]. Reasons cited for non-adherence to established guidelines include a lack of knowledge in primary care physicians, children in lower socio-economic settings with poor access to health care, children in rural areas where referral to subspecialty care is less available, public insurance with poor health care access, children in whom testicular descent was documented early in life but noted at a later age to have an ascending testis, attempts at hormonal treatment prior to surgical referral, and neurologically impaired children with less attention to testicular physical exam [23].

In this study, nearly one third of PCPs consider that the appropriate time for surgical therapy of UDT is over 1.5 years of age. The reason for this can be assumed that their patient management are mainly influenced mostly by the experience during their specialty training instead of national and international guidelines. This fact can be especially alarming, because most of the participating primary care providers have been working in patient care for more than twenty years. In order to modernize patient management, we consider important to provide nationwide educational programs by paediatric surgeons to primary care providers. In addition, dissemination of new recommendations on scientific meetings and conferences as well as publishment of current guidelines in paediatric journals would be necessary.

8.1.2. Management of non-palpable testes

While NPTs represents only a small portion of all UDTs, they remain a clinical challenge for paediatric surgeons [8]. Diagnosis primarily based on physical examination: imaging studies – US examination, MRI – are not recommended due to their low sensitivity and specificity [3, 8, 17, 23, 25, 37, 38]. Despite, ultrasonography is performed still often unnecessarily in our country. Although it is a non-invasive tool as well as widely available, we must note, that it cannot confirm the presence or absence of the testis and therefore, it does not influence the indication of the surgery [3, 38]. Moreover, it can delay the definitive treatment of UDTs [3, 38]. Consequently, the use of different imaging modalities for NPTs is only recommended in specific and selected clinical scenarios (e.g., identification of Müllerian structures in cases with suspicion of DSD) and determination of exact testicular size if needed [3].

Currently, diagnostic laparoscopy has been universally accepted as gold standard for identifying IATs and to determine the further treatment [3, 17, 23, 25, 37, 38]. If during the laparoscopy the testicular vessels enter the inguinal canal, inguinal exploration is recommended

because a healthy testicle may be present that needs to undergo standard orchiopexy [3, 38]. In case of blind-ending spermatic vessels, inguinal exploration is not suggested, the necessity of surgical fixation of the contralateral testis is controversial [3, 38]. Consequently, when vanishing testis is detected, the decisions of the participating specialists in this survey is heterogeneous: 39.2% finish the operation, 25% fix the contralateral testis, 19.7% explore the inguinal canal to remove testicular nubbin and 9.0% explore the inguinal canal and additionally fix the contralateral testis. According to current guidelines of EAU/ESPU a peeping testis can be placed down in the scrotum laparoscopically or via an inguinal incision [3]. In our country, treatment is mainly provided according to this or with minimally invasive Shehata technique.

The main limiting factor in the treatment of IATs is the shortness/brevity of testicular vessels, hindering adequate and tension-free placement of the testis into the scrotum. If the vessels are too short, staged orchiopexy should be chosen [3, 38]. One of the most popular techniques is the two-stage FSO, performed laparoscopically, where the spermatic vessels are transected to gain length to bring the testes to an orthotopic location. [8, 42, 43]. SLTO or Shehata technique is a novel treatment method for IATs based on elongation of the testicular vessels without dividing them [44]. Of the two surgical interventions, the testicular atrophy rate of the latter is clearly more favourable [48-50, 71]. Treatment of IATs in Hungary can be considered up to date: SLTO was introduced nationwide and the second largest multicentre study on the efficiency of the technique – after Shehata's own investigation – occurred in our country.

8.1.3. Hormonal therapy

Hormonal treatment in the management of UDTs arises as both a neoadjuvant to induce testicular descent and as an adjuvant to surgery to improve fertility after orchiopexy [23]. Formulating a clear recommendation is aggravated by the fact, that most of the studies on hormonal treatment have been of poor quality, with heterogeneous and mixed patient populations, testis location, schedules, and dosages of hormonal administration and in addition, long-term data are almost completely lacking [3, 25]. Results of hormonal therapy as primary management are against its use: successful testicular descent occurs in only 7-63% of the patients, and its use may delay definitive surgical treatment [23, 28-31]. However, its applying as an adjuvant in select patients – e.g., congenital hypogonadotropic hypogonadism or partial androgen insensitivity – may improve fertility [23, 27]. The current national and main international guidelines do not routinely offer hormonal therapy, either in an adjuvant or neoadjuvant setting for testicular descent: patients have to be evaluated on an individual basis [3, 17, 23, 26, 38]. Accordingly, patient management in Hungary regarding hormonal therapy

can be considered modern: its routine use has practically disappeared from patient management. However, it is important to note that in special circumstances, it should take into consideration as an additional treatment.

8.1.4. Management of retractile testes

Retractile testis has completed its descent into the scrotum but can be located either in the upper scrotum or inguinal canal because of an overactive cremasteric reflex [12]. One notable feature of an RT, that it can be pulled gently to the bottom of the scrotum and remain there for a finite period of time [12]. These testes usually become fully descended (non-retractile) at puberty and are thought to retain normal fertility [72]. However, their classification as a normal variant is controversial: according to some studies, up to 50% of them may develop to an ascending testis, which may explain the bimodal distribution for age at orchiopexies with two peaks occurring at 2 and 10 years [1, 12, 27, 72]. Ascending testes seems to share similar histological features as seen in congenital cryptorchidism: during their examination, a reduced number of germ cells was described, and therefore it can be assumed that fertility is affected [26].

Both MHR 2021 and ESPU/EAU 2016 guidelines offer RTs close follow-up for boys with until puberty instead of medical or surgical treatment [3, 38]. The Hungarian recommendation emphasizes that the control examination can also be performed by PCPs or health visitors [38]. According to our results, RTs are not managed completely in accordance with the current recommendations: less than two-thirds of the members of the AHPCP consider the management of RTs to be primarily conservative, and less than two-thirds of them offer close follow-up until puberty. Regular education about the treatment of RTs is necessary to implement nationwide up-to-date care and thereby to screen ascending testis early. Currently, the level of follow-up care is not clearly defined: clarifying of this would help the precise monitoring until puberty. Due to the centralized nature of paediatric surgery in Hungary, it would be advantageous if the follow-up was performed by PCPs, as well as and it would also be beneficial if the two professions officially agreed on this issue.

8.1.5. Long-term follow-up after orchiopexy

Long-term follow up after orchiopexy is obligatory to check the viability, position, and structure of the testes. When atrophy is detected, the patient can be offered a testicular prosthesis to improve body image, and reduce stress caused by monorchidism, while in case of secondary cryptorchidism, repeated orchiopexy is recommended to prevent late complications [3, 8, 38]. Cryptorchidism is a well-characterized risk factor for malignancy: men with a history of

cryptorchidism are 1.6-7.5 times more likely to develop testicular cancer, compared with the general population [56, 57]. Because of this, counselling and educating parents and patients regarding these possible long-term effects is essential. [3].

The current recommendation of MHR suggests annual exam until puberty for children after orchiopexy; monitoring can be performed by paediatric surgeons, PCPs, or health visitors [38]. Furthermore, the EAU/ESPU emphasize the importance of proper monthly self-examination of the testes [3]. Based on our results, in Hungary the tendency of control examinations does not follow the current trends: the follow-up is not sufficiently coordinated neither at the level of primary health care nor at the level of paediatric surgical specialist care and in most cases, annual control exams finish upon reaching school-age. The reason for this may be that the level of follow-up is not clearly declared in the recommendations. Besides, the causal role of incomplete communication between the surveyed groups also arises.

8.1.6. Strengths and limitations

According to our best knowledge, no study has been previous conducted in Hungary to analyse the nationwide management of UDTs. Our results can provide a good basis for the targeted development of patient care, as well as for the wider dissemination of current CPGs. The main limiting factor of this research is the relatively low response rate among the members of the AHPCP. In addition, we would like to emphasize, that questionnaire surveys only show the main trends of patient management, while each patient requires individualized therapy.

8.2. Medium-term results of Shehata technique

8.2.1. General considerations

In our clinical practice, the management of UDTs is based on the current EAU Guidelines on Paediatric Urology [25]. Accordingly, in the diagnostic of NPTs, imaging modalities are not routinely used: following a thorough physical examination, laparoscopy is our first choice. In cases of NPTs or bilateral UDTs and any sign of DSD, like concomitant hypospadias, genital ambiguity, or scrotal hyperpigmentation, urgent endocrinological and genetic evaluation is performed.

Treatment of IATs is planned between 6 and 18 months of age. The cause of the relatively high mean age (2.9 years) at the first stage of the surgery is due to the delayed referral to the

participating paediatric surgical centres. This treatment performed late may have an adverse effect on the outcomes, such as relatively greater mean size difference between the operated testis and the contralateral one, as well as a higher atrophy rate, compared to previous studies. Despite this, our results can still be considered successful. With our publication, we would like to draw attention to the importance of timely referral of UDTs to paediatric surgical or urological units.

Following the encouraging results of the Shehata technique, our primary treatment for IATs – which are not suitable for one-stage laparoscopic orchiopexy – became SLTO. We reserve the Fowler-Stephens technique for cases where the testis cannot reach the fixation point without undue tension. The operative technique of SLTOs followed the initial description of Shehata et al [45, 65]. In this study, we did not routinely perform testicular biopsy during orchiopexy in HIATs. In the future, we are planning further examinations to evaluate more accurately the success of the surgery, involving its long-term impact on future fertility, in which a testicular biopsy can be considered in order to predict future testicular function.

Postoperative follow-up is carried out by the surgeon's own preference: in general, the patients are being followed up in the outpatient clinic after at 7 days and at 3, 6 and 12 months. Testicular US is not routinely performed, therefore the use of it was part of the study itself.

8.2.2. Complications

In our series, perioperative complications occurred altogether in 38.2% of the operations including fixation suture insufficiency of the fixation suture, adhesion of the spermatic cords, testicular atrophy, wound healing disorders and a hydrocele. We have found that the recommended traction period (12 weeks) is sufficient to achieve adequate elongation of the testicular vessels without any signs of inflammation or other drawbacks. We believe that this timeframe is suitable to achieve adequate elongation and good results.

8.2.2.1. Internal herniation, intestinal obstruction

Traction interval passed uneventfully without any serious complications. Although, there is a theoretical chance for internal herniation and/or strangulation of the intestines through testicular vessels passing across the abdominal cavity, this complication did not occur neither in the previous reports nor in our series [45-50]. However, it is important to consider its possibility and inform parents accordingly.

8.2.2.2. Fixation suture insufficiency

Slippage of the stitch which fixes the testis to the abdominal wall during the traction period was the significant complication following the traction technique causing insufficient elongation of testicular vessels as well as inappropriate scrotal positioning. Therefore, redo traction is sometimes necessary before the second stage. In our investigation fixation suture insufficiency occurred in 11 cases (20%) due to cutting through the suture, while in the previous studies, this complication was reported between 0 and 27.3% of the cases [45-50].

In two publications about Shehata technique this complication was reported limited to older children, in which Abouheba observed it in children older than 6 years and Dawood in children older than 7 years of age considering consequence of limited stretchability and elasticity of short testicular vessels [47, 50]. Interestingly, in our study only 27.3% of the children with fixation suture insufficiency were out of the recommended age. We observed that insufficient fixation 10 out of 11 testes happened when monofilament sutures were used, in contrast to the braided sutures: braided suture seems to be a better choice to fix the testes up to the abdominal wall. Earlier reports support our observation: the frequency of this complication was higher with monofilament suture material (27.3% vs. 9.1-14.7%) [45, 47, 49, 50]. Although further research is required to clarify this reason for this observation.

8.2.2.3. Adhesion of the spermatic cords while a bilateral fixation at the same time

According to the original description of Shehata technique, the technique can be applied for bilateral cases simultaneously at the same time [45], however our experience shows, that it can lead to complications: cross adhesion of spermatic cords and subsequent division of them affords the possibility of testicular vessel and/or spermatic duct injury with consequent testicular atrophy and impaired fertility.

Adhesion between the crossed structures was reported to be 10.5% [45-47]. In our investigation, the frequency of this complication was 14.3%. Additionally, this adhesion caused consequent unilateral testicular atrophy in one case, which cannot be neglected. To avoid this complication, separate traction intervals are recommended in bilateral cases.

8.2.2.4. Testicular atrophy

Testicular atrophy is the most serious complication of orchiopexy affecting testicular function and fertility. In the earlier studies of Shehata technique the diagnosis of atrophy was mostly

based on the percentage of testicular volume-loss compared to preoperative data or to contralateral testis. Because IATs are frequently underdeveloped compared to the contralateral testes we also used US to check the viability of testes. Atrophy defined as undetectable testicular tissue or lack of blood flow on Doppler US examination. In previous studies on SLTO, the reported atrophy rate was zero [45-50]. In contrast, in our analysis the sum atrophy rate was 11.1%. Four atrophies occurred between the two stages of the surgery requiring unilateral orchiectomies, two of them following redo traction. In all four cases, a macroscopically shrunk testis was found intraoperatively, and after removal, histology confirmed the hypoplasia with structural abnormalities. Probably, the reason for this is insufficient circulation in the already underdeveloped testes. During the follow up, testicular atrophy evolving after the second stage was detected only in one patient. In all of these, morphological abnormalities (testicular hypoplasia or vas deferens and epididymis anomaly) were already documented at the first operation. Furthermore, three of them were originally localized in high abdominal position, which may have a negative effect on our results.

There is no consensus on what constitutes an adequate determination of testicular viability postoperatively [73]. In our study Colour Doppler US provided a reliable tool for evaluation of testicular atrophy: in our all cases the presence or absence of testicular circulation was obviously determinable and due to the lack of testicular vascularity testicular atrophy was clearly identified. Comparing the results of physical examination with US findings no remarkable difference was observed.

8.2.2.5. Other (minor) complications

In this series, the noted minor postoperative complications, such as wound healing disorders and hydrocele recovered spontaneously. In previous publications adhesions to the abdominal wall was reported in one case managed uneventfully.

8.2.3. Redo traction

According to the original description of Shehata, in case of fixation insufficiency, refixation of the testis is recommended for another 12 weeks to achieve an adequate elongation [45]. This technique was employed in four of the six earlier studies on SLTO and occurred in 9.1-14.7 % of testes in corresponding articles, in total of 24 cases. In three publications the refixation-period lasted for 12 weeks, and in one report this time interval was not available. All testes that have undergone redo traction were successfully brought down to the scrotum [45-47, 49].

In our study, if the testis did not reach the scrotum after the traction interval, redo traction was performed. Three testes required refixation; two of them because of slippage of the traction stitch. Time frame was defined by the surgeon's own preference, the mean retraction interval was 10.5 (7.7-14.4) weeks. One of them was brought down successfully to the scrotum and two testes have atrophied requiring unilateral orchiectomy. In the atrophied cases, macroscopic morphological abnormalities were already documented at the first stage.

Due to poor outcomes of redo traction in our series, other options can be considered. Elsherbeny et al. reported two cases with failure to achieve adequate elongation. In one of them the vessels were cut (converted to FSO), and the testis was brought to the scrotum, while in the other one, the vessels were spared, and the testis was brought to the upper part of the scrotum [46]. Dawood et al. presented two cases with suture slippage and consecutive inadequate elongation; they underwent staged FSO following the first stage [50]. Testis fixed in the upper part of the scrotum or inguinal area can also be attempted to be brought down to the scrotum later during another operation. In addition, microvascular testicular auto-transplantation can be also a possible treatment.

8.2.4. Testicular ascent

Appropriate scrotal location is desirable to maximize fertility and for early detection of possible malignancy [42]. However, there is no consistent definition of adequate testicular position following orchiopexy: in some of the previous studies low or mid scrotal testis was considered successful, while in others the proper position of the testes in the scrotum has not been defined. In our study adequate scrotal position was defined as intra-scrotal testis determined by physical examination. In the previous reports about Shehata technique proper position was achieved in 72.2-100% [45-50]. Our study showed similar results to the earlier outcomes: 92% of testes were in adequate scrotal position and three cases showed evidence of testicular ascents requiring redo open orchiopexy.

While 70.6% of the testes were brought down to the scrotum with Prentiss manoeuvre, in some cases the elongation was so successful, that the testicle could be brought down directly through the inguinal canal itself. However, the most preferred way was the Prentiss manoeuvre. During the follow up relocation was detected in similar proportion: in 6.7% of the cases of Prentiss manoeuvre and in 8.2% of the cases when the testis was brought down through the inguinal canal.

8.2.5. Testicular volume difference

Evaluating the results, Shehata determined normal testicular size – defined within 75-100% of the other side by US examination or to normal controls – as one of criteria of the success of the operation [45]. Except for Dawood et al., the other authors did not apply the exact volume difference of the testes as a criterion of the success of SLTO [46-50].

In our case series the mean volume difference between the operated and descended testes was 34.3%. Despite this, we do not consider our operations unsuccessful. It is well known, that IATs are usually smaller than the contralateral physiologically descended testes, and because of this volume difference this should not be considered a surgical complication [49].

Abdelhalim et al. in 2019 studied the testicular volume changes in laparoscopic staged FSO. They found that small testicular volume following staged FSO is mostly the result of abnormal development – at follow up, 83.3% of the testes, which were smaller than the mean (50th percentile) for age measured by US, were small for age at baseline – and less commonly due to damage of blood supply during the operation [74]. This is supported by our results too: morphological abnormalities such as testicular hypoplasia or anomaly of the vas deferens and epididymis were observed in 60% of the cases. For this reason, we consider the marked volume difference in our results a consequence of abnormal testicular development.

8.2.6. Success-rate

Overall success rate is defined as proper scrotal position with no testicular ascent without any signs of atrophy. According to this definition in our study the success rate was 82.2%, which is comparable to the previously reported series (65-100%) **(Table 5.)** [45-50]. Traditionally, if an IAT can't be mobilized intra-abdominally toward to contralateral internal inguinal ring without tension after careful dissection, one- or two-stage FSO is performed [8]. Two-stage method may be significantly superior [39]. In a few large series of two-stage FSO success rate was reported between 67 and 98% [75]. According to the same studies, in two-stage FSO the number of atrophies and relocations contributes to the failure of surgery similarly: atrophy occurs in 3.5 to 10.3% and ascent in 1.7 to 8.8% [74, 75].

According to the original hypothesis of SLTO the gradual lengthening of the intact testicular vessels may lead to better lower atrophy rate in contrast to dividing them [65]. The previous studies supported this theory: according to the results, the main difference between SLTO and FSO was, that in SLTO, the failure of the surgery arise completely from testicular ascent

(11.4%) while no testicular atrophy was reported [45-50]. However, our results with 11.1% testicular atrophy do not support this previously expected excellent atrophy rate, though, the overall success rate turned out to be beneficial. However, further long-term studies are required to provide more information about the success of this technique.

	Shehata 2016	*Elsherbeny 2018*	*Abouheba 2019*	*Liu 2021*	*Bawazir 2021*	*Dawood 2021*	*Present study*	*All results*
Number of SLTOs	140	22	34	22	11	20	55	304
Mean follow-up (years)	1.3	1	0.5	2	1	0.7	2.7	1.4
Success rate (%)	**84**	**90.5**	**NR**	**100**	**81.8**	**65**	**82.2**	**84.1**
Completed with orchiopexy	140	21	34	22	9	18	51	295
Followed operations	125	20	34	21	11	18	41	270
Atrophies	0	0	0	0	0	0	1+4	1+4
Relocations	20	1	NR	0	0	5	3	29

Table 5 Outcomes of published staged laparoscopic traction orchiopexies. NR = not reported; SLTO = staged laparoscopic traction orchiopexy.

8.2.7. Limitations

The present study has some limitations. Firstly, its retrospective nature with a relatively low number of patients and different follow-up periods. Although, the number of patients of our multicentre study is the 2nd highest published so far, still, to draw the proper conclusions even bigger cohort is needed. Our plan is to continue our study in order to obtain more data and longer-term results. Secondly, mean age of the children at the surgery was relatively old compared to the current recommendations. Although this may have an adverse effect on the outcomes, our results were favourable.

9. CONCLUSIONS AND SUMMARY OF NEW FINDINGS

I. Current treatment of UDTs in Hungary is mainly up to date, although, the knowledge of PCPs on some important issues – optimal timing of surgery, follow-up of RTs and children after orchiopexy – is incomplete. In order to modernize patient management, we consider important to provide nationwide educational programs by paediatric surgeons to primary care providers. In addition, dissemination of new recommendations on scientific meetings and conferences as well as publishment of current guidelines in paediatric journals would be necessary.

II. Hungarian paediatric surgical care provides a modern, often minimally invasive approach: most recommendations of EAU/ESPU and MHR are being followed by participant HAPS members. However, ultrasonography is performed often unnecessarily in NPTs, delaying definitive treatment. Accordingly, awareness of the role of imaging studies in the diagnosis of UDTs could be improved.

III. Based on our results, in Hungary, neither the management of RTs nor the follow-up after orchiopexy occur according to the current trends: monitoring is not sufficiently coordinated neither at the level of primary health care nor at the level of paediatric surgical specialist care. Currently, the level of follow-up care is not clearly defined: clarifying of this would help the precise monitoring until puberty.

IV. SLTO or Shehata technique is a safe and feasible method for the treatment of IATs with excellent medium-term results: success rate was comparable with previously described techniques. In addition, this treatment option was associated with no serious intra- or postoperative complications.

V. Doppler US examination is a suitable minimally invasive tool for determining testicular viability during the follow-up of children treated with Shehata technique. Confirmed by Doppler US, preservation of the testicular vessels provides appropriate circulation of the testes with low atrophy rate.

VI. Braided suture is better to fix the testis to the abdominal wall; frequency of fixation suture slippage was lower, when braided suture material was used instead of monofilament.

10. SUMMARY

Introduction: Modern treatment of undescended testis (UDT) in children is essential to avoid long-term morbidities including infertility and malignant changes. Although both national and international guidelines support the appropriate decisions, our clinical experience indicates, that in Hungary a considerable proportion of children with UDT are treated beyond the optimal time frame. Staged laparoscopic traction orchiopexy (SLTO) is a novel technique for the intra-abdominal testis (IAT) based on elongation of the testicular vessels without separating them. This technique was also introduced in our country. So far, surgical results of SLTO are mostly single centric, including mainly low number of cases with relatively short-term follow-up.

Objectives: Firstly, this study evaluated the current management of UDT in Hungary: we assessed the adherence of primary care paediatricians (PCPs) and paediatric surgical specialists to current national and international recommendations with particular regard to the European Association of Urology (EAU)/ European Society for Paediatric Urology (ESPU) 2016 guidelines and to Hungarian Ministry of Human Resources (MHR) 2021 guidelines. Secondly, we aimed to evaluate in a national multicentre investigation to retrospectively analyse the medium-term results of SLTO on a larger cohort.

Methods: In the first part of this study a web-based questionnaire on the treatment of UDTs was completed among the members of The Association of the Hungarian Primary Care Paediatricians and The Hungarian Association of Paediatric Surgeons. The second part of our investigation analysed retrospectively data of SLTOs performed in three paediatric surgical centres between 2013 and 2020. Furthermore, in 2021, physical and Doppler ultrasound (US) examinations were performed to determine the position and viability of testes. Success was defined as an intra-scrotal testicle without atrophy. Data were analysed descriptively.

Results: When managing UDTs, PCPs (n=69) are influenced mostly by their experience during specialty training (65.2%). However, paediatric surgical specialists (n=56) are influenced mainly by international guidelines (66.1%). Most PCPs (98.6%) screen newborns for UDT and refer any suspicious cases (88.4%) in proper time for surgical examination, but only two-third of them know the appropriate time for orchiopexy. Additionally, 59.4% of them consider the management of retractile testes (RTs) to be primarily conservative, and 60.8% of them offer close follow-up until puberty. After orchiopexy long-term follow-up until puberty is recommended by 39.1% of them. Specialists (98.2%) know the proper time for orchiopexy;

however, they recommend ultrasonography relatively often (28.6%) in cases of non-palpable testes. Treatment of high intra-abdominal testes (HITs) occur primarily (82.1%) with minimally invasive Shehata technique.

Between 2013 and 2020, SLTO was performed on 48 cases (55 testes, 7 bilateral) in the centres participating in the study. Mean age at first stage was 2.9 (0.8-12.6) years. HITs were found in 16.4% and in 60% morphological abnormalities were observed. To fix the testes to the abdominal wall monofilament suture was used in 67.3%, braided in 29.1%. Mean time between the two stages was 16.4 weeks; three testes required redo traction. Perioperative complications occurred in 21 patients (38.2%) including insufficient fixation (11), testicular atrophy (4), wound complications (4), adhesion of the spermatic cords (1) and hydrocele (1). In case of insufficient fixation monofilament sutures were used in 90.9%.

In 2021 38 patients (43 testes) had physical and 36 patients (41 testes) had US examinations. Mean follow-up was 2.7 (0.34-7.9) years. Altogether five atrophies were identified, and three testicular ascents (7.0%) occurred. The overall success rate was 82.2%.

Conclusions: Current treatment of UDTs in Hungary is mainly up to date, although, the knowledge of PCPs on some important issues – optimal timing of surgery, follow-up of RTs and children after orchiopexy – is incomplete. Paediatric surgical care provides a modern, often minimally invasive approach; however, ultrasonography is performed often unnecessarily. Regular education about the management of UDTs is necessary to implement nationwide up-to-date care.

In addition, minimally invasive SLTO – introduced nationwide in Hungary – is a safe and feasible method for the treatment of IATs with good medium-term results. Doppler US findings confirmed that preservation of the testicular vessels provides appropriate circulation of the testes with low atrophy rate. According to our results, braided suture seems to be better to fix the testicle to the abdominal wall. Additionally, in bilateral cases separate traction intervals instead of simultaneous operation should be considered. However, further studies are still needed to evaluate the success of the surgery, involving very importantly its long-term impact on future fertility.

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13. ANNEX

PAPER I.

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Medium-Term Results of Staged Laparoscopic Traction Orchiopexy for Intra-abdominal Testes: A Multicenter Analysis

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ABSTRACT

Background: Staged laparoscopic traction orchiopexy (SLTO) is a novel technique for the intra-abdominal testis (IAT) based on elongation of the testicular vessels without separating them. This multicenter study evaluated the medium-term results of this technique.
Methods: Data of SLTO performed in three pediatric surgical centers between 2013 and 2020 were analyzed retrospectively. In 2021, physical and Doppler ultrasound examinations were performed to determine the position and viability of testes. Success was defined as an intra-scrotal testicle without atrophy.
Results: SLTO was performed on 48 cases (55 testes, 7 bilateral). Mean age at first stage was 2.9 (0.8 −12.6) years. High intra-abdominal testes were found in 16.4% and in 60% morphological abnormalities were observed. To fix the testes to the abdominal wall monofilament suture was used in 67.3%, braided in 29.1%. Mean time between the two stages was 16.4 weeks; three testes required redo traction.
Perioperative complications occurred in 21 patients (38.2%) including insufficient fixation (11), testicular atrophy (4), wound complications (4), adhesion of the spermatic cords (1) and hydrocele (1). In case of insufficient fixation monofilament sutures were used in 90.9%.
In 2021 38 patients (43 testes) had physical and 36 patients (41 testes) had ultrasound examinations. Mean follow-up was 2.7 (0.34–7.9) years. Altogether five atrophies were identified, and three testicular ascents (7.0%) occurred. The overall success rate was 82.2%.
Conclusions: SLTO may be a feasible alternative to conventional treatments of IATs. Additionally, braided suture seems to be a better option to fix the testicle to the abdominal wall.
Level of Evidence: LEVEL IV.

1. Introduction

Undescended testis (UDT) is the one of the most common disorders in boys concerning approximately 3.5% of male newborn's [1]. The etiology and pathogenesis seem to be multifactorial with potential contribution of several mechanisms, including genetic, hormonal, and mechanical factor [2]. There is a left-sided predominance, and association is possible with comorbidities such as cardiac or genitourinary anomalies, as well congenital syndromes [3].

The retained testes can be located anywhere between the abdominal cavity and the entrance of the scrotum, typically along the normal path of descent [4]. Generally, 20% of UDTs are non-palpable (NPT) and 15–34.1% of NPTs falling into intra-abdominal category [3,5]. Testes situated ≥2 cm proximal to the ipsilateral internal inguinal ring are defined as high intra-abdominal testes (HIT) (Ain Shams classification Type 4) [6]. Currently, diagnostic laparoscopy has been universally accepted and recommended, as gold standard, for identifying IAT and to determine the further treatment [7,8].

Recent guidelines such as recommendations of the American Urological Association (AUA) and The European Association of

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Abbreviations

AUA	American Urological Association
DSD	disorders of sex development
EAU	The European Association of Urology
FSO	Fowler Stephens orchiopexy
HIT	high intra-abdominal testes testis
IAT	intra-abdominal testis
NPT	nonpalpable testis
SLTO	staged laparoscopic traction orchiopexy
UDT	undescended testis
US	ultrasound

Urology (EAU) advocate orchiopexy between 6 and 18 months of age to maximize fertility potential and to decrease the risk of malignant changes [8–10]. Despite the high prevalence, surgical treatment of intra-abdominal testis (IAT) is still challenging. The main limiting factor is the shortness/brevity of testicular vessels, hindering adequate and tension-free placement of the testis into the scrotum. Moreover, too much stretching on the testicular vessels may cause circulatory disorder, sometimes atrophy of the testis. To overcome this factor numerous treatment options have been described. If the testis can reach the scrotum without any tension after careful dissection and mobilization, typically one-stage laparoscopic orchiopexy is performed with a great (85–100%) success rate [3,11].

If the vessels are too short, staged orchiopexy should be chosen. One of the most popular techniques is the two stage Fowler Stephens orchiopexy (FSO), performed laparoscopically, where the spermatic vessels are transected to gain length to bring the testes to an orthotopic location. An alternative and technically demanding approach is the microvascular testicular auto-transplantation, where the vessels are transected, the testis is brought down to the scrotum, where vessels are re-anastomosed to the inferior epigastric vessels [1,3,12,13]. Pooled estimated success rate of FSO is 80%–85% and 88% of microvascular orchiopexy, although the functional effect and fertility outcomes are still questionable [3,14,15].

To reduce the rate of testicular atrophy Shehata et al. revisited the laparoscopic traction technique with preservation of the main blood supply of the testis in 2008 (Shehata technique or two-stage laparoscopic traction orchiopexy [SLTO]). At the first stage, after dissecting the gubernaculum and the lateral peritoneal attachments, the intra-abdominal testis is fixed up to the abdominal wall near the contralateral anterior superior iliac spine. After three months, the testis is detached and brought down to the scrotum via the anatomical way or by Prentiss maneuver. In between the two stages the elongation of the cross-stretched testicular vessels is carried out by gradual traction due the weight of intestine as well because of the respiratory movements of the abdominal wall [16].

So far, surgical results of Shehata technique are mostly single centric, including mainly low number of cases with relatively short-term follow-up. The aim of the present national multicenter study was to retrospectively analyze the medium-term results on a larger cohort.

2. Methods

2.1. Study design

Patients with NPT treated with SLTO were enrolled in the study from three Hungarian centers between January 2013 and October 2020. Medical records were retrospectively reviewed for demographic data, operative findings, and details as well as post-operative events.

The follow-up of the patients was carried out by the surgeon's own preference.

All patients were called back for an additional check-up in 2021 to collect the actual status of their testicles. The position of the testes was determined by physical examination. The viability was controlled by Doppler ultrasound (US) examination: testicular atrophy was diagnosed if no testicular tissue or no blood flow was detectable. Relocation or ascent was identified if the testicle was placed outside the scrotum. Success was defined as proper scrotal position and blood flow on Doppler US. Furthermore, testicular size was assessed by US and compared to the contralateral descended testicle.

The study was approved by the ethical committees of the institutions (IRB numbers and date of approval: 87/2017-SZTE, 22/05/2017).

2.2. Inclusion criteria

All boys diagnosed with non-palpable testes were subjected to diagnostic laparoscopy. Atrophic IATs or remnants were removed. If a viable IAT was found, stretching test was performed to determine the feasibility of SLTO: in case the testis reached the contralateral internal inguinal ring tension free – it could be mobilized to the scrotum without tension – standard single stage laparoscopy was done. When single stage laparoscopy was not feasible the testis was mobilized to the fixation point: if it occurred with moderate tension the patient underwent the first step of SLTO.

2.3. Operative technique

Operative technique was performed according to the initial description of Shehata et al. [7,17]. The patient was positioned in supine position. Re-examination was done under general anesthesia and if the testis was nonpalpable, diagnostic laparoscopy was carried out. Testicular morphology was evaluated by inspection.

After dividing the gubernaculum, stretching test was performed. The testis was mobilized with the division of the lateral peritoneal attachments and was fixed to the abdominal wall one inch above and medial to the contralateral anterior superior iliac spine using a single stitch, which was a 3-0 braided, non-absorbable suture with 17 mm ½ circle round needle or 3-0 monofilament, non-absorbable suture with 17 mm ½ circle round needle. The suture was inserted through a small skin incision at the determined point into the abdominal cavity. After taking an appropriate amount from the testis, the suture was pulled out through the skin incision, tied extracorporeal and buried subcutaneously.

The second stage was performed average 3 months after the first operation. The abdominal cavity was inspected for any adhesive bands, internal herniation, slippage of the suture, or adhesion of the spermatic cords in bilateral surgeries. The atrophic testes were removed. Degree of elongation of testicular vessels was measured indirectly by passing a forceps behind them at the midline and by elevating them toward the anterior abdominal wall. Then, the fixation stitch was divided, and the testis was delivered to the contralateral internal inguinal ring (stretching test). If the testis can't be brought to the contralateral internal ring, redo traction (refixation of the testis) was performed.

If the length of testicular vessels was appropriate, an ipsilateral scrotal incision was made, and the testis was delivered through a new hiatus medial to the inferior epigastric vessels (Prentiss maneuver) or through the inguinal canal into a sub-dartos pouch and sutured to the scrotal wall using an absorbable suture.

2.4. Follow-up details

Testicular blood flow, position, and size were prospectively analyzed in 2021. Physical examination occurred to determine the position of the testes. The viability was controlled assessed by Doppler US examination: testicular atrophy was diagnosed if no testicular tissue or no blood flow was detectable. Relocation or ascent was identified if the testicle was placed outside the scrotum. In these cases, our treatment strategy was redo open orchiopexy. Success was defined by appropriate scrotal position by physical examination, with appropriate flow on Doppler US. Testicular volume was determined by scrotal US, testicular dimensions were measured and volume was calculated using the ellipsoid formula (volume = r1 × r2 × r3 × 0.52). In unilateral surgeries testicular volume of the operated testis was compared to descended contralateral one.

2.5. Statistical analysis

Demographics including age, laterality, comorbidities, and operative data such as intraoperative testicular location, testicular morphology, type of suture used for testicular fixation to the abdominal wall, fixation of the testis in the scrotum, time interval between first and second stages, number and outcomes of redo tractions, conversions and perioperative complications were analyzed retrospectively. Prospectively testicular viability, location, size, and success rate were assessed, and follow-up period was described.

Descriptive statistics were used to analyze the data. Categorical variables were expressed as frequencies and/or percentages in each category. Continuous variables were presented as mean (range).

3. Results

Patient demographics, operative data, and details of follow up are listed in Table 1. The course of the clinical study is summarized in Fig. 1. In the study period, 48 patients (55 testes) were treated with SLTO in the participating centers. From these, 23 IAT were right-sided, 18 were left-sided and 7 bilateral surgeries occurred. The latter were operated in the same session. Associated conditions – partial androgen insensitivity and Prune Belly syndrome – were seen in two patients. Mean age at first stage was 2.9 (0.8–12.6) years. At the operation, the majority (52.1%) of the children was older than 1.5 years, in addition 16.7% of the patients were beyond 6 years. High IAT were found in 16.4% of the cases. Morphological abnormalities (testicular hypoplasia or vas deferens and epididymis anomaly) were observed in 60%. The type of suture used for testicular fixation to the abdominal wall was monofilament in 67.3% and braided in 29.1%. In 3.6% the suture material was not recorded.

The mean elapsed time between the two stages were 16.4 (5.1–48.1) weeks. The traction interval passed uneventfully without any serious complications. Failure to achieve adequate elongation occurred in three cases (5.5%); redo traction was done in all of them. Testicular atrophy developed in four cases between the two stages, two of them after re-do redo traction. All the removed testes already showed morphological abnormalities at the first visual evaluation during the first stage and histology examination showed hypoplasia in all four cases. In three out of the four atrophic testes, slippage of the traction stitch leading to insufficient elongation was observed as well. The fourth case was a bilateral IAT, where cross adhesions between the testicular vessels was reported due to the simultaneous cross traction. After separation of the spermatic cords, one testicle was successfully brought down to the scrotum and the other atrophic testicle was removed. Slippage of the fixation stitch (which means that the suture cut through and the testis was found floating in the abdomen) occurred in 11 cases (20%), where 10 from 11 (90.9%) were monofilament suture material.

Table 1
Demographics, operative data and follow up details.

Demographics	mean (range)	n (%)
Laterality		
Unilateral		41 (85.4)
Bilateral		7 (14.6)
Age distribution at the first stage		
Age at first stage (years)	2.9 (0.8–12.6)	
≤1.5 years		23 (47.9)
1.5–6 years		17 (35.4)
≤6 years		8 (16.7)
Operative data		
Time interval between first and second stages (weeks)	16.4 (5.1–48.1)	
Intraoperative testicular location		
High intra-abdominal testis		9 (16.4)
Low intra-abdominal testis		46 (83.6)
Testicular morphological characteristics		
Hypoplasia and/or dissociation		33 (60.0)
Normal or not mentioned		22 (40.0)
Fixing suture		
Monofilament, non-absorbable		37 (67.3)
Braided, non-absorbable		16 (29.1)
Not recorded		2 (3.6)
Fixation of the testis in the scrotum		
Prentiss maneuver		36 (70.6)
Through the inguinal canal		15(29.4)
Redo traction		3 (5.5)
Perioperative complications		
Fixation suture slippage		11 (20.0)
Attached spermatic cords		1 (1.8)
Surgical site infection		4(7.3)
Hydrocele		1(1.8)
Intraoperative testicular atrophy		4(7.3)
Follow up (assessment in 2021)		
Available for physical examination (testes)		43 (84.3)
Available for ultrasound examination (testes)		41 (80.4)
Follow-up duration (years)	2.7 (0.34–7.9)	
Outcomes		
Testicular atrophy		1 (2.4)
Testicular retraction		3 (7.0)
Success rate		82.2%

Testicles were brought down scrotum using Prentiss maneuver in 70.6%, and via the inguinal canal in 29.4% of the cases. One conversion was necessary due to technical problem. Postoperatively, four wound healing disorders (7.3%) and one temporary hydrocele (1.8%) were reported. The wound healing disorders included two cases of mild port-site wound inflammation, a case of port-site seroma, and a case of suture granuloma. All complications resolved spontaneously. Scrotal testicular position was achieved in 51 (92.7%) cases.

Thirty-eight patients (43 testes) showed up on control physical examinations and thirty-six patients (41 testes) had US examinations available as well. The mean follow-up period was 2.7 (0.34–7.9) years. Forty testes (93.0%) were found in adequate scrotal position. Testicular ascent occurred in three patients (7.0%). Color Doppler US identified testicular atrophy in one case (2.4%). In the remaining 97.6% of the patients, the circulation in the testes to the was appropriate. The overall success rate of the surgery was 82.2%. In unilateral SLTOs, size of the operated testes measured by US was compared to the contralateral one and the average volume difference was 34.3%. In two out of the three relocated cases redo open orchiopexy was performed via inguinal approach and the scrotal location has been satisfactory ever since. In the third case open orchiopexy is planned.

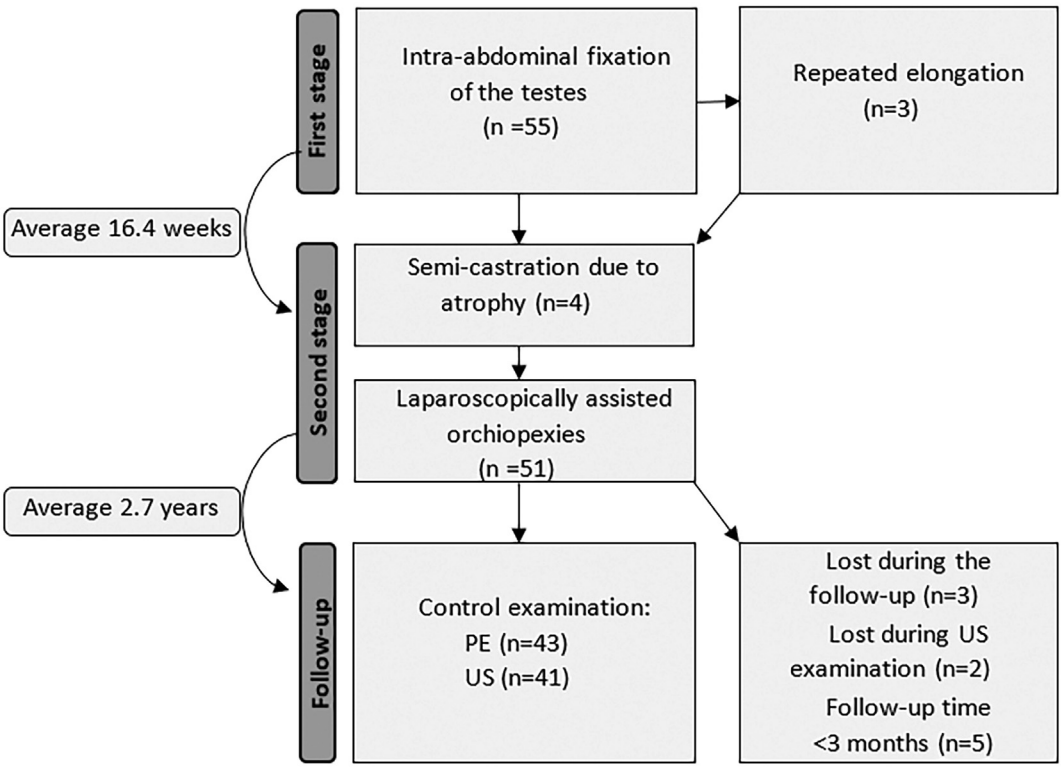

Fig. 1. Flow diagram describing the course of study (PE – physical examination, US – ultrasound).

4. Discussion

Until now, surgical results of Shehata technique were mainly resulted from a single center, including relatively low number of cases with short- or medium-term follow-up. Since 2008, six articles were published providing results of 249 SLTOs (Table 2) [17–22]. Our recent study is the second largest and represent the longest follow-up series of IATs treated with SLTO after Shehata's procedure up to now. In our study, additional color Doppler US was performed to confirm the viability of the operated testes.

All study, listed in Table 2., support that SLTO is a safe and feasible treatment of IATs, with comparable success rates with FSO and microvascular autotransplantation.

4.1. General considerations

In our clinical practice, the management of UDTs is based on the current EAU Guidelines on Paediatric Urology [8]. Accordingly, in the diagnostic of NPTs, imaging modalities are not routinely used: following a thorough physical examination, laparoscopy is our first choice. In cases of NPTs or bilateral UDTs and any sign of disorders of sex development (DSDs), like concomitant hypospadias, genital ambiguity, or scrotal hyperpigmentation, urgent endocrinological and genetic evaluation is performed.

Treatment of IATs is planned between 6 and 18 months of age. The cause of the relatively high mean age (2.9 years) at the first stage of the surgery is due to the delayed referral to the participating pediatric surgical centers. This treatment performed late may have an adverse effect on the outcomes, such as relatively greater mean size difference between the operated testis and the contralateral one, as well as a higher atrophy rate, compared to previous studies. Despite this, our results can still be considered successful. With our publication, we would like to draw attention to the importance of timely referral of UDTs to pediatric surgical or urological units.

Following the encouraging results of the Shehata technique, our primary treatment for IAT – which are not suitable for one-stage laparoscopic orchiopexy – became SLTO. We reserve the Fowler-Stephens technique for cases where the testis cannot reach the fixation point without undue tension. The operative technique of SLTOs followed the initial description of Shehata et al. [7,17]. In this study, we did not routinely perform testicular biopsy during orchiopexy in high IATS. In the future, we are planning further examinations to evaluate more accurately the success of the surgery, involving its long-term impact on future fertility, in which a testicular biopsy can be considered in order to predict future testicular function.

Postoperative follow-up is carried out by the surgeon's own preference: in general, the patients are being followed up in the outpatient clinic after at 7 days and at 3, 6 and 12 months. Testicular US is not routinely performed, therefore the use of it was part of the study itself.

4.2. Complications

In our series, perioperative complications occurred altogether in 38.2% of the operations including insufficiency of the fixation suture, adhesion of the spermatic cords, testicular atrophy, wound healing disorders and a hydrocele. We have found that the recommended traction period (12 weeks) is sufficient to achieve adequate elongation of the testicular vessels without any signs of inflammation or other drawbacks. We believe that this timeframe is suitable to achieve adequate elongation and good results.

4.2.1. Internal herniation, intestinal obstruction

Traction interval passed uneventfully without any serious complications. Although, there is a theoretical chance for internal herniation and/or strangulation of the intestines through testicular vessels passing across the abdominal cavity, this complication did not occur neither in the previous reports nor in our series [17–22].

Table 2
Outcomes of published staged laparoscopic traction orchiopexies (NR – not reported).

	Shehata 2016	Elsherbeny 2018	Abouheba 2019	Liu 2021	Bawazir 2021	Dawood 2021	Present study	All results
Number of SLTOs	140	22	34	22	11	20	55	304
Mean follow-up (years)	1.3	1	0.5	2	1	0.7	2.7	1.4
Success rate (%)	**84**	**90.5**	**NR**	**100**	**81.8**	**65**	**82.2**	**84.1**
Completed with orchiopexy	140	21	34	22	9	18	51	295
Followed operations	125	20	34	21	11	18	41	270
Atrophies	0	0	0	0	0	0	1 + 4	1 + 4
Relocations	20	1	NR	0	0	5	3	29

Bold values signifies the success rate is the most frequently used indicator of the success of the operation.

However, it is important to consider its possibility and inform parents accordingly.

4.2.2. Fixation suture insufficiency

Slippage of the stitch which fixes the testis to the abdominal wall during the traction period was the significant complication following the traction technique causing insufficient elongation of testicular vessels as well as inappropriate scrotal positioning. Therefore, redo traction is sometimes necessary before the second stage. In our investigation fixation suture insufficiency occurred in 11 cases (20%) due to cutting through the suture, while In in the previous studies, this complication was reported between 0 and 27.3% of the cases [17–22]. In two publications about Shehata technique, this complication was reported limited to older children, in which Abouheba observed it in children older than 6 years and Dawood in children older than 7 years of age considering consequence of limited stretchability and elasticity of short testicular vessels [19,22]. Interestingly, in our study only 27.3% of the children with fixation suture insufficiency were out of the recommended age. We observed that insufficient fixation 10 out of 11 testes happened when monofilament sutures were used, in contrast to the braided sutures: braided suture seems to be a better choice to fix the testes up to the abdominal wall. Earlier reports support our observation: the frequency of this complication was higher with monofilament suture material (27.3% vs. 9.1–14.7%) [17–19,21,22]. Although further research is required to clarify this reason for this observation.

4.2.3. Adhesion of the spermatic cords while a bilateral fixation at the same time

According to the original description of Shehata technique, the technique can be applied for bilateral cases simultaneously at the same time [17], however our experience shows, that it can lead to complications: cross adhesion of spermatic cords and subsequent division of them affords the possibility of testicular vessel and/or spermatic duct injury with consequent testicular atrophy and impaired fertility.

Adhesion between the crossed structures was reported to be 10.5% [17–19]. In our investigation, the frequency of this complication was 14.3%. Additionally, this adhesion caused consequent unilateral testicular atrophy in one case, which cannot be neglected. To avoid this complication, separate traction intervals are recommended in bilateral cases.

4.2.4. Testicular atrophy

Testicular atrophy is the most serious complication of orchiopexy affecting testicular function and fertility. In the earlier studies of Shehata technique the diagnosis of atrophy was mostly based on the percentage of testicular volume-loss compared to preoperative data or to contralateral testis. Because IATs are frequently underdeveloped compared to the contralateral testes we also used US to check the viability of testes. Atrophy defined as undetectable testicular tissue or lack of blood flow on Doppler US examination. In previous studies on SLTO, the reported atrophy rate was zero [17–22]. In contrast, in our analysis the sum atrophy rate was 11.1%. Four atrophies occurred between the two stages of the surgery requiring hemicastration of affected testes unilateral orchiectomies, two of them following redo traction. In all four cases, a macroscopically shrunk testis was found intraoperatively, and after removal, histology confirmed the hypoplasia with structural abnormalities. Probably, the reason for this is insufficient circulation in the already underdeveloped testes. During the follow up, testicular atrophy evolving after the second stage was detected only in one patient. In all of these, morphological abnormalities (testicular hypoplasia or vas deferens and epididymis anomaly) were already documented at the first operation. Furthermore, three of them were originally localized in high abdominal position, which may have a negative effect on our results.

There is no consensus on what constitutes an adequate determination of testicular viability postoperatively [23]. In our study Color Doppler US provided a reliable tool for evaluation of testicular atrophy: in our all cases the presence or absence of testicular circulation was obviously determinable and due to the lack of testicular vascularity testicular atrophy was clearly identified. Comparing the results of physical examination with US findings no remarkable difference was observed.

4.2.5. Other (minor) complications

In this series, the noted minor postoperative complications, such as wound healing disorders and hydrocele recovered spontaneously. In previous publications adhesions to the abdominal wall was reported in one case managed uneventfully.

4.3. Redo traction

According to the original description of Shehata, in case of fixation insufficiency, refixation of the testis is recommended for another 12 weeks to achieve an adequate elongation [17]. This technique was employed in four of the six earlier studies on SLTO and occurred in 9.1–14.7% of testes in corresponding articles, in total of 24 cases. In three publications the refixation-period lasted for 12 weeks, and in one report this time interval was not available. All testes that have undergone redo traction were successfully brought down to the scrotum [17–19,21].

In our study, if the testis did not reach the scrotum after the traction interval, redo traction was performed. Three testes required refixation; two of them because of slippage of the traction stitch. Time frame was defined by the surgeon's own preference, the mean retraction interval was 10.5 (7.7–14.4) weeks. One of them was brought down successfully to the scrotum and two testes have atrophied requiring unilateral orchiectomy. In the atrophied cases, macroscopic morphological abnormalities were already documented at the first stage.

Due to poor outcomes of redo traction in our series, other options can be considered. Elsherbeny et al. reported two cases with failure to achieve adequate elongation. In one of them the vessels

were cut (converted to FSO), and the testis was brought to the scrotum, while in the other one, the vessels were spared, and the testis was brought to the upper part of the scrotum [18]. Dawood et al. presented two cases with suture slippage and consecutive inadequate elongation; they underwent staged FSO following the first stage [22]. Testis fixed in the upper part of the scrotum or inguinal area can also be attempted to be brought down to the scrotum later during another operation. In addition, microvascular testicular auto-transplantation can be also a possible treatment.

4.4. Testicular ascent

Appropriate scrotal location is desirable to maximize fertility and for early detection of possible malignancy [14]. However, there is no consistent definition of adequate testicular position following orchiopexy: in some of the previous studies low or mid scrotal testis was considered successful, while in others the proper position of the testes in the scrotum has not been defined. In our study adequate scrotal position was defined as intra-scrotal testis determined by physical examination. In the previous reports about Shehata technique proper position was achieved in 72.2–100% [17–22]. Our study showed similar results to the earlier outcomes: 92% of testes were in adequate scrotal position and three cases showed evidence of testicular ascents requiring redo open orchiopexy.

While 70.6% of the testes were brought down to the scrotum with Prentiss maneuver, in some cases the elongation was so successful, that the testicle could be brought down directly through the inguinal canal itself. However, the most preferred way was the Prentiss maneuver. During the follow up relocation was detected in similar proportion: in 6.7% of the cases of Prentiss maneuver and in 8.2% of the cases when the testis was brought down through the inguinal canal.

4.5. Testicular volume difference

Evaluating the results, Shehata determined normal testicular size – defined within 75–100% of the other side by US examination or to normal controls – as one of criteria of the success of the operation [17]. Except for Dawood et al., the other authors did not apply the exact volume difference of the testes as a criteria of the success of SLTO [18–22].

In our case series the mean volume difference between the operated and descended testes was 34.3%. Despite this, we do not consider our operations unsuccessful. It is well known, that IATs are usually smaller than the contralateral physiologically descended testes, and because of this volume difference this should not be considered a surgical complication [21].

Abdelhalim et al., in 2019 studied the testicular volume changes in laparoscopic staged FSO. They found that small testicular volume following staged FSO is mostly the result of abnormal development – at follow up, 83.3% of the testes, which were smaller than the mean (50th percentile) for age measured by US, were small for age at baseline – and less commonly due to damage of blood supply during the operation [24]. This is supported by our results too: morphological abnormalities such as testicular hypoplasia or anomaly of the vas deferens and epididymis were observed in 60% of the cases. For this reason, we consider the marked volume difference in our results a consequence of abnormal testicular development.

4.6. Success-rate

Overall success rate is defined as proper scrotal position with no testicular ascent without any signs of atrophy. According to this definition in our study the success rate was 82.2%, which is comparable to the previously reported series (65–100%) [17–22].

Traditionally, if an IAT can't be mobilized intraabdominally toward to contralateral internal inguinal ring without tension after careful dissection, one- or two- FSO is performed [3]. Two-stage method may be significantly superior [11]. In a few large series of two-stage FSO success rate was reported between 67 and 98% [25]. According to the same studies, in two-stage FSO the number of atrophies and relocations contributes to the failure of surgery similarly: atrophy occurs in 3.5–10.3% and ascent in 1.7–8.8% [24,25].

According to the original hypothesis of SLTO the gradual on lengthening of the intact testicular vessels may lead to lower atrophy rate in contrast to dividing them [7]. The previous studies supported this theory: according to the results, the main difference between SLTO and FSO was, that in SLTO, the failure of the surgery arise completely from testicular ascent (11.4%) while no testicular atrophy was reported [17–22]. However, our results with 11.1% testicular atrophy do not support this previously expected excellent atrophy rate, though, the overall success rate turned out to be beneficial. However, further long-term studies are required to provide more information about the success of this technique.

4.7. Limitations

The present study has some limitations.

Firstly, its retrospective nature with a relatively low number of patients and different follow-up periods. Although, the number of patients of our multicenter study is the 2nd highest published so far, still, to draw the proper conclusions even bigger cohort is needed. Our plan is to continue our study in order to obtain more data and longer-term results.

Secondly, mean age of the children at the surgery was relatively old compared to the current recommendations. Although this may have an adverse effect on the outcomes, our results were favorable.

5. Conclusion

Staged laparoscopic traction orchiopexy is a safe and feasible method for the treatment of intra-abdominal testes with good medium-term results. Doppler US findings confirmed that preservation of the testicular vessels provides appropriate circulation of the testes with low atrophy rate. According to our results, braided suture seems to be better to fix the testicle to the abdominal wall. Additionally, in bilateral cases separate traction intervals instead of simultaneous operation should be considered.

Further studies are still needed to evaluate the success of the surgery, involving very importantly its long-term impact on future fertility.

Previous communication

None.

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PAPER II.

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Tisztelt Dr. Varga Alexandra!

Az Orvosi Hetilap Szerkesztősége örömmel értesíti, hogy a

„Varga Alexandra dr., Tardi Réka dr., Kovács Tamás dr., A hereleszállási zavarok kezelése Magyarországon – hol tartunk most?”

című közleményük elfogadásra került, és a kézirattal kapcsolatos nyomdai munkálatok megkezdődtek.
Terveink szerint a cikk január második felében jelenik meg az Orvosi Hetilapban.
A közlemény nyilvántartási száma: DOI: 10.1556/650.2024.32957

Budapest, 2022. december 12.

Papp Zoltán dr.
professor emeritus
főszerkesztő

Hungarian Medical Journal

A hereleszállási zavarok kezelése Magyarországon – hol tartunk most?

Az Orvosi Hetilap Szerkesztősége felkérésére készített tanulmány, melyet a Szerzők Dr. Altorjay István, az első magyar gyermeksebész professzor emlékének ajánlanak halálának 25. évfordulóján.

--Manuscript Draft--

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Full Title:	A hereleszállási zavarok kezelése Magyarországon – hol tartunk most? Az Orvosi Hetilap Szerkesztősége felkérésére készített tanulmány, melyet a Szerzők Dr. Altorjay István, az első magyar gyermeksebész professzor emlékének ajánlanak halálának 25. évfordulóján.
Secondary Full Title:	Current management of undescended testes in Hungary – where are we now?
Article Type:	Eredeti közlemény
Keywords:	Hereleszállási zavar; diagnosztika; kezelés; utánkövetés; szakmai irányelv
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Abstract:	Bevezetés: A hereleszállási zavarok korszerű gyermekkori kezelése nélkülözhetetlen a hosszútávú morbiditás – infertilitás, malignus heretumorok – kialakulásának elkerüléséhez. Célkitűzés: Az ellátási gyakorlat fejlesztése érdekében vizsgálatunkban fel kívántuk tárni, hogy a kórkép magyarországi ellátása megfelel-e az aktuális hazai és főbb nemzetközi, elsősorban európai irányelveknek. Módszer: Az alap- és szakellátás felméréséhez 2023-ban online kérdőíves vizsgálatot végeztünk a Házi Gyermekorvosok Egyesületének, valamint a Magyar Gyermeksebész Társaság tagjai körében. A válaszokat leíró statisztikai módszerekkel elemeztük. Eredmények: A hereleszállási zavarok kezelését a felmérésben résztvevő alapellátók (n=69) esetében elsősorban szakképzésük során tanultakat (65,2%), míg a szakellátás képviselőinek körében (n=56) döntően a nemzetközi irányelvek (66,1%) befolyásolják. A kérdőívet kitöltő házi gyermekorvosok 98,6%-a ellenőrzi a herék újszülöttkori helyzetét, és eltérés észlelésekor 88,4%-uk megfelelő időben utalja szakrendelésre a gyermeket. Az orchidopexia optimális idejét 66,6%-uk ismeri. A retraktilis herék kezelése 59,4%-uk ismeretei szerint elsősorban konzervatív és 60,8%-uk végzi pubertáskorig utánkövetésüket. Orchidopexiát követően 39,1%-uk végzi kamaszkorig a gondozást. A szakellátás képviselői (98,2%) az orchidopexiát megfelelő életkorra időzítik, azonban nem tapintható herék észlelésekor 28,6%-uk kér preoperatív

	ultrahang vizsgálatot. A magas hasüregi herék kezelése elsősorban (82,1%) a minimál invazív Shehata műtéttel történik. Megbeszélés: A hereleszállási zavarok hazai kezelése döntően az aktuális irányelvek szerint zajlik, mindemellett az alapellátás képviselőinek ismeretei néhány fontos kérdésben – műtéti ellátás optimális időzítése, retraktilis herék és orchidopexián átesett gyermekek gondozása – hiányosak. A gyermeksebészeti szakellátás modern szemléletű, korszerű minimál invazív technikák alkalmazásával, azonban ultrahang vizsgálat sok esetben feleslegesen történik. Következtetés: A hereleszállási zavarok kezelésére vonatkozó ismeretek szélesebb körű terjesztése szükséges az országos szintű, minden tekintetben korszerű ellátás megvalósulásához és a hosszútávú morbiditás csökkentéséhez.
Secondary Abstract:	Introduction: Modern treatment of undescended testis (UDT) in children is essential to avoid long-term morbidities including infertility and malignant changes. Objective: This study evaluated the current treatment of UDT in Hungary. Method: A web-based questionnaire was completed among the members of The Association of the Hungarian Primary Care Paediatricians and The Hungarian Association of Paediatric Surgeons. Data were analysed descriptively. Results: Primary care paediatricians (PCPs) (n=69) were influenced mostly by their experience during specialty training (65.2%). However, paediatric surgical specialists (n=56) were influenced mainly by international guidelines (66.1%). Most PCP (98.6%) screen newborns for UDT and refer any suspicious cases (88.4%) in proper time for surgical examination, but only two-third of them know the appropriate time for orchidopexy. Additionally, 59.4% of them consider the management of retractile testes to be primarily conservative, and 60.8% of them offer close follow-up until puberty. After orchiopexy long-term follow-up until puberty is recommended by 39.1% of them. Specialists (98.2%) know the proper time for orchiopexy; however, they recommend ultrasonography relatively often (28.6%) in cases of nonpalpable testes. Treatment of high intra-abdominal testes occur primarily (82.1%) with minimally invasive Shehata technique. Discussion: Treatment of UDT in Hungary is mainly up-to-date, although, the knowledge of PCPs on some important issues – optimal timing of surgery, follow-up of retractile testes and children after orchidopexy – is incomplete. Paediatric surgical care provides a modern, often minimally invasive approach; however, ultrasonography is performed often unnecessarily. Conclusion: Regular education about the management of UDTs is necessary to implement nationwide up-to-date care.
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Response to Reviewers:	

Kísérőlevél

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Tisztelt Főszerkesztő Úr!

Örömmel nyújtjuk be a **„A hereleszállási zavarok kezelése Magyarországon – hol tartunk most?"** című kéziratunkat az Orvosi Hetilapban történő eredeti közleményként való publikálásra.

A hereleszállási zavarok korszerű gyermekkori kezelése nélkülözhetetlen a hosszútávú morbiditás – infertilitás, malignus heretumorok – elkerülése érdekében. Vizsgálatunkban fel kívántuk tárni, hogy a kórkép magyarországi ellátása megfelel-e az aktuális hazai és főbb nemzetközi, elsősorban európai irányelveknek. Az alap- és szakellátás felméréséhez 2023-ban online kérdőíves vizsgálatot végeztünk a Házi Gyermekorvosok Egyesületének, valamint a Magyar Gyermeksebész Társaság tagjai körében. Eredményeinket az ellátási gyakorlat fejlesztésére kívánjuk használni.

Kijelentjük, hogy a közlemény más folyóiratban korábban nem jelent meg és máshová beküldésre nem került. A kézirat végleges változatát valamennyi szerző jóváhagyta, és kijelenti, hogy tartalmáért felelősséggel tartozik. A levelező szerző a szerzői útmutatót elolvasta. A cikk elkészítéséért a szerzők nem részesültek anyagi támogatásban, érdekeltségeik nincsenek.

Köszönjük, hogy időt szán kéziratunkra.

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Szeged, 2023. október 17.

„A tanulás a legerősebb fegyver, amivel megváltoztathatod a világot." Nelson Mandela

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A hereleszállási zavarok kezelése Magyarországon – hol tartunk most?

Current management of undescended testes in Hungary – where are we now?

Az Orvosi Hetilap Szerkesztősége felkérésére készített tanulmány, melyet a Szerzők Dr. Altorjay István, az első magyar gyermeksebész professzor emlékének ajánlanak halálának 25. évfordulóján.

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A közlemény más folyóiratban korábban nem jelent meg, és máshová beküldésre nem került.

A levelező szerző a szerzői útmutatót elolvasta.

Anyagi támogatás: A cikk elkészítéséért a szerzők nem részesültek anyagi támogatásban.

Szerzői munkamegosztás: K. T., V. A.: Szerzői koncepció. V. A.: Irodalomkutatás, a vizsgálat kivitelezése és a kézirat elkészítése. T. R.: Adatok elemzése. K. T.: Nyelvi és szakmai lektorálás. A cikk végleges változatát valamennyi szerző elolvasta és jóváhagyta.

Érdekeltségek: A szerzőknek nincsenek érdekeltségeik.

Köszönetnyilvánítás: A szerzők köszönetüket fejezik ki a Házi Gyermekorvosok Egyesületének és a Magyar Gyermeksebész Társaságnak szakmai támogatásukért, valamint a vizsgálat kivitelezésében nyújtott segítségükért, továbbá a kérdőíveket kitöltő kollégáknak a kutatásban való részvételért.

Összefoglalás

Bevezetés: A hereleszállási zavarok korszerű gyermekkori kezelése nélkülözhetetlen a hosszútávú morbiditás – infertilitás, malignus heretumorok – kialakulásának elkerüléséhez.

Célkitűzés: Az ellátási gyakorlat fejlesztése érdekében vizsgálatunkban fel kívántuk tárni, hogy a kórkép magyarországi ellátása megfelel-e az aktuális hazai és főbb nemzetközi, elsősorban európai irányelveknek.

Módszer: Az alap- és szakellátás felméréséhez 2023-ban online kérdőíves vizsgálatot végeztünk a Házi Gyermekorvosok Egyesületének, valamint a Magyar Gyermeksebész Társaság tagjai körében. A válaszokat leíró statisztikai módszerekkel elemeztük.

Eredmények: A hereleszállási zavarok kezelését a felmérésben résztvevő alapellátók (n=69) esetében elsősorban szakképzésük során tanultakat (65,2%), míg a szakellátás képviselőinek körében (n=56) döntően a nemzetközi irányelvek (66,1%) befolyásolják. A kérdőívet kitöltő házi gyermekorvosok 98,6%-a ellenőrzi a herék újszülöttkori helyzetét, és eltérés észlelésekor 88,4%-uk megfelelő időben utalja szakrendelésre a gyermeket. Az orchidopexia optimális idejét 66,6%-uk ismeri. A retraktilis herék kezelése 59,4%-uk ismeretei szerint elsősorban konzervatív és 60,8%-uk végzi pubertáskorig utánkövetésüket. Orchidopexiát követően 39,1%-uk végzi kamaszkorig a gondozást. A szakellátás képviselői (98,2%) az orchidopexiát megfelelő életkorra időzítik, azonban nem tapintható herék észlelésekor 28,6%-uk kér preoperatív ultrahang vizsgálatot. A magas hasüregi herék kezelése elsősorban (82,1%) a minimál invazív Shehata műtéttel történik.

Megbeszélés: A hereleszállási zavarok hazai kezelése döntően az aktuális irányelvek szerint zajlik, mindemellett az alapellátás képviselőinek ismeretei néhány fontos kérdésben – műtéti ellátás optimális időzítése, retraktilis herék és orchidopexián átesett gyermekek gondozása – hiányosak. A gyermeksebészeti szakellátás modern szemléletű, korszerű minimál invazív technikák alkalmazásával, azonban ultrahang vizsgálat sok esetben feleslegesen történik.

Következtetés: A hereleszállási zavarok kezelésére vonatkozó ismeretek szélesebb körű terjesztése szükséges az országos szintű, minden tekintetben korszerű ellátás megvalósulásához és a hosszútávú morbiditás csökkentéséhez.

Kulcsszavak: Hereleszállási zavar, diagnosztika, kezelés, utánkövetés, szakmai irányelv

Summary

Introduction: Modern treatment of undescended testis (UDT) in children is essential to avoid long-term morbidities including infertility and malignant changes.

Objective: This study evaluated the current treatment of UDT in Hungary.

Method: A web-based questionnaire was completed among the members of The Association of the Hungarian Primary Care Paediatricians and The Hungarian Association of Paediatric Surgeons. Data were analysed descriptively.

Results: Primary care paediatricians (PCPs) (n=69) were influenced mostly by their experience during specialty training (65.2%). However, paediatric surgical specialists (n=56) were influenced mainly by international guidelines (66.1%). Most PCP (98.6%) screen newborns for UDT and refer any suspicious cases (88.4%) in proper time for surgical examination, but only two-third of them know the appropriate time for orchidopexy. Additionally, 59.4% of them consider the management of retractile testes to be primarily conservative, and 60.8% of them offer close follow-up until puberty. After orchiopexy long-term follow-up until puberty is recommended by 39.1% of them. Specialists (98.2%) know the proper time for orchiopexy; however, they recommend ultrasonography relatively often (28.6%) in cases of nonpalpable testes. Treatment of high intra-abdominal testes occur primarily (82.1%) with minimally invasive Shehata technique.

Discussion: Treatment of UDT in Hungary is mainly up-to-date, although, the knowledge of PCPs on some important issues – optimal timing of surgery, follow-up of retractile testes and children after orchidopexy – is incomplete. Paediatric surgical care provides a modern, often minimally invasive approach; however, ultrasonography is performed often unnecessarily.

Conclusion: Regular education about the management of UDTs is necessary to implement nationwide up-to-date care.

Keywords: Undescended testis, diagnostics, therapy, follow-up, guideline

Rövidítések

DSD = (disorder of sexual development) a szexuális fejlődés rendellenessége; EAU = (The European Association of Urology) Európai Urológus Társaság; EMMI = Emberi Erőforrások Minisztériuma; ESPU = (The European Society for Paediatric Urology) Európai Gyermekurológus Társaság; EUPSA = (The European Paediatric Surgeons' Association) Európai Gyermeksebész Társaság; GnRH = (gonadotropin-releasing hormone) gonadotropint felszabadító hormon; hCG = humán choriogonadotrophin; HGYE = Házi Gyermekorvosok Egyesülete; MGYST = Magyar Gyermeksebész Társaság, NM = Népjóléti Minisztérium

A hereleszállási zavar a nemi szervek egyik leggyakoribb fejlődési rendellenessége; a fiú újszülöttek kb. 3,5%-át érinti [1]. Koraszülöttekben incidenciája magasabb, terminustól függően 20-100% közé tehető [2]. A herék csecsemőkori spontán leszállásának következtében előfordulása egy éves korra kb. 1%-ra csökken [2]. Kialakulását multifaktoriális eredetűnek feltételezik genetikai, hormonális és mechanikai faktorok közreműködésével [3]. Társulhat többek közt a szív és a húgyivarszervek fejlődési rendellenességeivel, valamint bizonyos szindrómákkal (pl. Down-, Noonan- vagy Prune belly szindróma) [4]. A kórkép lehet egy- vagy kétoldali; az egyoldali esetek jobboldali túlsúllyal (70–80%) fordulnak elő [5]. Az érintett here elhelyezkedhet a normális leszállás vonalában vagy azon kívül, ektópiásan [5]. A herezacskón kívül elhelyezkedő herék kb. 80%-a tapintható [6]. A nem tapintható herék kb. 40%-át a hasüregi herék teszik ki [7].

A hereleszállási zavar korai felismerése és korszerű kezelése elengedhetetlen a fertilitás megőrzése és a malignus heretumorok kialakulásának megelőzése érdekében. Bár hazai és nemzetközi irányelvek is segítik az ellátást, korábbi vizsgálati eredményeink, valamint klinikai tapasztalataink egyaránt azt mutatják, hogy a rejtett herével született gyermekek nem elhanyagolható része az optimális időkereten túl kerül ellátásra hazánkban [8]. Jelen vizsgálatunk során ennek okait kerestük, valamint azt kívántuk felmérni, hogy a hereleszállási zavarok magyarországi kezelése (alap-és szakellátás) megfelel-e az aktuális irányelveknek, különös tekintettel az Emberi Erőforrások Minisztériumának (EMMI) 2021-es, valamint Európai Urológus Társaság (The European Association of Urology [EAU]) és az Európai Gyermekurológus Társaság (The European Society for Paediatric Urology [ESPU]) 2016-os közös irányelvére [6,7]. Eredményeinket az ellátási gyakorlat fejlesztésére kívánjuk használni.

Módszer

A hereleszállási zavarok hazai kezelését online kérdőív (Survio®) alkalmazásával vizsgáltuk. Szakmai-etikai engedélyünk száma: BM/15215-1/2023. A kérdőív a Házi Gyermekorvosok Egyesületének (HGYE) és Magyar Gyermeksebész Társaság (MGYST) aktív tagjai számára e-mailben került kiküldésre. A válaszadás önkéntes és anonim módon zajlott, a résztvevők az eredmények tudományos céllal történő feldolgozásához és az összesített adatok publikálásához hozzájárultak. Az alapellátás vizsgálatára a kérdőívet a Szegedi Tudományegyetem munkatársai állították össze. A szakellátás elemzése egy, az Aubert és mtsai. által szerkesztett, az Európiai Gyermeksebész Társaság (The European Paediatric Surgeons' Association, EUPSA) által jóváhagyott kérdőív magyar nyelvű fordításának segítségével történt [9]. A

kérdőívek első része a válaszadók szociodemográfiai adatait – szakképzettség, orvosként a betegellátásban eltöltött évek száma, munkahely vármegyénkénti elhelyezkedése, valamint progresszivitási szintje – mérte fel. Az angol nyelvű kérdőív fordítása során a fenti kérdéseket a magyarországi viszonyokra adaptáltuk. A kérdőívek második része az ellátási gyakorlatra fókuszált: diagnosztika, szakellátóhelyre történő beutalás, kezelés, utánkövetés, hazai és nemzetközi egészségügyi szakmai irányelvek ismerete. A válaszokat leíró statisztikai módszerekkel elemeztük százalékos megoszlások megadásával.

Eredmények

Alapellátás

Az alapellátásban résztvevő orvosok – HGYE 69 tagja, kb. 7%-os kitöltési arány – kérdőívre adott válaszainak százalékos megoszlását az *1. táblázat* tartalmazza. A felmérésben résztvevők döntően (92,8%) több, mint húsz éve dolgoznak orvosként a betegellátásban. Negyvenkét százalékuk Budapesten vagy Pest vármegyében praktizál, a többi vármegyét külön-külön a válaszadók 0-8,7%-a reprezentálja.

A hereleszállási zavarok ellátása során többségük (82,6%) követi az EMMI hatályban lévő irányelvét, míg 13,0%-uk önkitöltős válasz formájában jelezte, hogy a módszertani levél nem jutott el hozzá. Az EAU/ESPU jelenlegi ajánlásának ismerete a válaszadók 55,1%-ára jellemző. A kérdőívet kitöltők többsége – 65,2% – a rejtett heréjű gyermekek ellátását leginkább befolyásoló tényezőként a szakképzés során tanultakat jelölte meg: a hazai és nemzetközi irányelvek ismerete 50,7% ill. 18,8%-uk döntéshozatalában mérvadó.

A válaszadók csaknem mindegyike (98,6%) három hónapos kort megelőzően dokumentálja első alkalommal a herék helyzetét. Többségük (88,4%), amennyiben a herezacskóban nem tapint herét, már vagy az első észlelést követően, vagy legkésőbb a csecsemő hat hónapos korában gyermeksebészeti vagy gyermekurológiai szakrendelésre irányítja a beteget. Kétoldali, nem tapintható here esetén a kérdőívet kitöltők 91,3%-a tartja szükségesnek a gyermek DSD irányában történő kivizsgálását. A válaszadók 59,4%-ának ismeretei szerint a retraktilis herék kezelése elsősorban konzervatív, emellett 60,8%-uk végzi pubertáskorig utánkövetésüket. Bár a nem megfelelő időben történő kezelés lehetséges szövődményeit a több, mint 85%-ban ismerik, a műtéti kezelés ideális időpontját közel egyharmaduk (30,4%) teszi 1,5 éves kor felettire. A kérdőívet kitöltők mindössze 39,1%-a ellenőrzi orchidopexiát követően a

herék helyzetét pubertáskorig; az utánkövetés az esetek többségében (46,5%) az iskoláskor elérésekor befejeződik.

Szakellátás

A hereleszállási zavarok szakellátására vonatkozó kérdőív eredményeit a *2. táblázat* foglalja össze. A felmérésben a MGYST 56 aktív tagja (kb. 49%-os kitöltési arány) vett részt: 44 gyermeksebész szakorvos (78,6%) és 12 gyermeksebész szakorvosjelölt (21,4%). A kérdőívet kitöltők 30,4%-a több, mint húsz éve dolgozik orvosként a betegellátásban. A tíz és húsz ill. az öt és tíz év közötti munkaviszonnyal rendelkezőket a válaszadók 35,7 és 23,2%-a képviseli. Az 5 évnél kevesebb tapasztalattal rendelkezők aránya 10,7%. Túlnyomórészt III. (91,1%), míg kisebb arányban II. (7,1%) illetve I. (1,8%) progresszivitási szintű ellátásban vesznek részt. A válaszadók munkahelyének vármegyénkénti aszimmetrikus eloszlása a gyermeksebészet centralizált voltát tükrözi. A kérdőívet kitöltők közel 38%-a Budapesten vagy Pest vármegyében dolgozik, míg Baranya, Csongrád-Csanád és Hajdú-Bihar vármegyéket – a vidéki egyetemi centrumok elhelyezkedésének megfelelően – egyenként a válaszadók 16,1%-a képviseli. A többi vármegyéből kikerülők részvételi aránya 0-5,4% közé tehető.

A hereleszállási zavarok kezelése során a felmérésben résztvevők 98,2%-a követi az EAU/ESPU jelenlegi ajánlását, emellett az EMMI aktuális irányelvét 92,9%-uk alkalmazza. Ellátási gyakorlatukat leginkább befolyásoló tényezőként szintén a nemzetközi (66,1%) ill. hazai (39,3%) egészségügyi szakmai irányelveket jelölték meg.

Az válaszadók 98,2 %-a az orchidopexia ideális időpontjának 1,5 évesnél fiatalabb életkort tartja. Nem tapintható herék esetén 28,6%-uk ultrahang vizsgálat elvégzése mellett dönt, míg 71,4%-uk betegellátása során a laparoszkópos explorációt nem előzi meg képalkotás. Amennyiben a diagnosztikus laparoszkópia során a belső lágyékgyűrű közelében elhelyezkedő herét észlelnek, a felmérésben résztvevők többsége (67,9%) inguinális vagy laparoszkóppal asszisztált orchidopexiát végez, míg magas hasüregi here (>2cm a belső lágyékgyűrűtől) esetén 82,1%-uk elsődlegesen Shehata-műtét mellett dönt. A lágyékgyűrű előtt vakon végződő gonadális erek észlelésekor a válaszadók 39,2%-a további teendőt nem tart szükségesnek, 25%-uk elvégzi az ellenoldali here rögzítését a herezacskóban, 19,7%-uk feltárja a lágyékcsatornát a here maradványának eltávolítása érdekében, míg 9,0%-uk ez ellenoldali orchidopexiát és a lágyékcsatorna feltárását egyaránt elvégzi. Kétoldali, nem tapintható here esetén a kérdőívet kitöltők 69,6%-a tartja szükségesnek a gyermek DSD irányában történő kivizsgálását. A retraktilis heréket 87,5%-uk elsősorban konzervatívan kezeli; szoros utánkövetésüket 80,4%-

uk javasolja pubertáskorig. Hormonális kezelést (gonadotropint felszabadító hormon, gonadotropin-releasing hormone [GnRH] vagy humán choriogonadotrophin [hCG]) a válaszadók legnagyobb része sem a herék leszállásának elősegítése (91,0%) sem a fertilitás fokozásának érdekében (94,6%) nem javasol.

Megbeszélés

A hereleszállási zavarok kezelésében (műtéti időpont, műtéti módozatok, hormonkezelés kérdése stb.) jelentős változások következtek be az elmúlt kb. három évtizedben. Kérdőíves vizsgálatunkban korszerű kezelésük jelenlegi helyzetét kívántuk felmérni Magyarországon. A felmérés az alap- és szakellátás megkérdezésével történt. Ehhez a HGYE, valamint az MGYST aktív tagjai számára e-mailben kérdőíveket küldünk, majd ezek eredményeit dolgoztuk fel. A vizsgálat szakellátásban résztvevő orvosok kb. 49%-át képviseli, ami megfelelő kitöltési aránynak tekinthető. Szeretnénk azonban hangsúlyozni, hogy felmérésünk – a többszöri megkeresés ellenére – az alapellátásban résztvevő házi gyermekorvosok rendkívül kis százalékát (7%) reprezentálja és emiatt ez utóbbi csoportban jelentősebb következtetések levonásával óvatosnak kell lenni. Eredményeinket, az ellátásai gyakorlat célzott fejlesztésére kívánjuk használni.

A műtéti ellátás időpontja

A hereleszállási zavarok kezelésének legfőbb célja a fertilitás megőrzése, valamint a rosszindulatú heretumorok kialakulási esélyének csökkentése [1]. Ehhez nélkülözhetetlen a here kóros helyzetének korai felismerése, a beteg megfelelő időben történő szakirányú beutalása, valamint a kórkép megfelelő életkoran történő műtéti korrekciója. A rejtettheréjűség diagnosztikájában elsődleges a fizikális vizsgálat, mely az 51/1997. (XII. 18.) NM (Népjóléti Minisztérium) rendeletben foglaltak szerint az újszülött hazaadását követő első háziorvosi vizit kötelező része [10]. Amennyiben a here vagy a herék helyzete kóros, és ebben változás nem történik, a hazai és a főbb nemzetközi ajánlások szerint 6 és 18 hónapos életkor között orchidopexia elvégzése javasolt [2, 6, 7, 11-13].

A betegség nem megfelelő időben történő kezelése számos következménnyel járhat [6]. A magasabb hőmérséklet hatására a gonocyták úgynevezett sötét A típusú (type A dark) spermatogóniumokká való érése zavart szenved, ami infertilitáshoz vezethet [1, 6]. Másfél-két éves kort követően megkezdődik a here másodlagos sorvadása, ami néhány éven belül irreverzibilissé válik [6]. Szövettani vizsgálatok során az átlagos tubuláris termékenységi index,

a csírasejtek és spermatogóniumok számának csökkenése, valamint progresszív peritubuláris fibrózis igazolódott [1, 6]. Egy éves kor feletti kezeletlen esetekben a csírasejtszám-csökkenés esélye kb. 2%, a Leydig-sejtek kimerülésének esélye kb. 1% havonta, ami pubertáskorra a csírasejtek elvesztéséhez vezethet [1]. Emellett mind a Leydig-, mind a Sertoli-sejtek gonadotróp szabályozása abnormálissá válik pubertáskort követően [6].

A felmérésben részt vevők válaszai alapján Magyarországon a rejtettheréjűség szűrése és kezelése a döntően az ajánlásoknak megfelelően történi. A kérdőívet kitöltő házi gyermekorvosok csaknem kivétel nélkül a herék helyzetét első alkalommal három hónapos életkort megelőzően dokumentálják. Többségük, amennyiben a herezacskóban nem tapint herét, már vagy az első észlelést követően, vagy legkésőbb a csecsemő hat hónapos korában gyermeksebészeti vagy gyermekurológiai szakrendelésre irányítja a beteget. A szakellátás felmérésben résztvevő képviselői amennyiben szükséges, az orchidopexiát csaknem mindannyian 1,5 éves életkort megelőzően tervezik.

Ugyanakkor két hazai tanulmány is beszámol arról, hogy hazánkban az orchidopexiák jelentős része az optimális életkornál később történik [8, 14]. A Heim Pál Országos Gyermekgyógyászati Intézet beteganyagában a 2010 és 2019 között hereleszállási zavar miatt operált gyermekek (n=205) átlagos életkora 4,5 év volt, míg a debreceni, pécsi és szegedi gyermeksebészeti centrumban a 2013 és 2020 között hasüregi here miatt Shehata-műtéten átesett gyermekek (n=48) átlagos életkora 2,9 év volt [8, 14]. Több külföldi tanulmány is leírta, hogy az orchidopexiák jelenetős része az ajánlott életkornál később történik, aminek hátterében az alapellátásban résztvevő orvosok hiányos ismereteit, a műtéti ellátást igénylő gyermek alacsony szocioökonómiai státuszát, a szakellátás korlátozott mértékű elérhetőségét, a retraktilis herék aszcenzusát, valamint a műtétet késleltető hormonális terápiát feltételezik [13]. Fontos megjegyeznünk, hogy a vizsgálatban résztvevő házi gyermekorvosok közel egyharmada a műtéti ellátás ideális időpontját 1,5 éves kor felettire helyezi. Ez adódhat abból, hogy a kérdőívet kitöltő HGYE-tagok többségének betegellátását a hazai és nemzetközi irányelvek helyett elsődlegesen a saját szakképzésük során tanultak befolyásolják. Ez különösen azért adhat okot aggodalomra, mivel a válaszadók többsége már több, mint húsz éve dolgozik orvosként a betegellátásban. Az ellátás korszerűsítésének érdekében fontosnak tartjuk a gyermeksebészek részéről a hereleszállási zavarok kezelésére vonatkozó információkat országos szintű továbbképző tanfolyamokon, tudományos üléseken átadni, valamint az aktuális irányelveket gyermekgyógyászati témájú folyóiratokban publikálni.

Nem tapintható herék kezelése

Bár a nem tapintható herék a hereleszállási zavarok csupán kis részét képviselik, kezelésük továbbra is kihívást jelent a gyermeksebészeti ellátásban [4]. A diagnózis felállításában elsődleges a fizikális vizsgálat, képalkotó vizsgálatok (ultrahang vizsgálat, mágneses rezonanciás képalkotás) rutinszerű elvégzése alacsony szenzitivitásuk miatt nem ajánlott [2, 6, 7, 11-13]. Helyettük kötelezően elvégzendő vizsgálómódszer a diagnosztikus laparoszkópia a kezelési stratégia meghatározása érdekében [2, 6, 7, 11-13].

Vizsgálati eredményeink alapján a nem tapintható herék észlelését követően hasi ultrahang vizsgálat még mindig sok esetben feleslegesen történik. Bár viszonylag könnyen elérhető és noninvazív, a here hiányának egyértelmű igazolására alkalmatlan, emiatt a műtéti indikációt nem befolyásolja, a definitív ellátást viszont késleltetheti, valamint az amúgy is túlterhelt radiológiai ellátó rendszert feleslegesen terheli [6, 7]. A jelenlegi irodalom elsősorban válogatott esetekre (pl. DSD gyanúja esetén a Müller-vezeték eredetű képletek azonosítása vagy a here méretének meghatározása) szorítja létjogosultságát [7].

A diagnosztikus laparoszkópia során az alábbi anatómiai szituációkat észlelhetjük: a gonadális erek a lágyékcsatornába lépnek (kb. 40%), a gonadális erek a belső lágyékgyűrű előtt vakon végződnek („vanishing testis") (kb. 10%), a herét a belső légyékgyűrű közelében észleljük („peeping testis") (kb.40%), a here a hasüregben helyezkedik el (kb. 10%) [7]. A lágyékcsatornába kilépő gonadális ereket észlelésekor a lágyéktáj feltárása javasolt, mivel a lágyékcsatornában életképes here helyezkedhet el [6, 7]. Vakon végződő gonadális erek észlelésekor a lágyékcsatorna feltárása nem javasolt; az ellenoldali here rögzítéséről a vélemények megoszlanak, ennek megfelelően „vanishing testis" észlelésekor a vizsgálatban részvevők döntései heterogének [6, 7]. Az EAU/ESPU aktuális irányelve (peeping testis") esetén laparoszkópos vagy inguinális orchidopexiát javasol, hazánkban az ellátás döntően ennek megfelelően, vagy a minimál invazív Shehata műtéttel történik [7].

A hasüregi herék sikeres kezelését leginkább a here belső lágyékgyűrűtől való távolsága határozza meg. Amennyiben túl magasan helyezkednek el, többlépcsős eljárások alkalmazása indokolt [6, 7]. A hagyományosan alkalmazott laparoszkóposan asszisztált Fowler-Stephens eljárás során az elégtelen hosszúságú testicularis ereket lekötik, majd a kollaterális keringés megerősödését követően rögzítik a herét scrotumban, míg a közelmúltban leírt, szintén laparoszkóposan asszisztált Shehata műtét során a testicularis ereket megkímélik, azok fokozatos megnyúlása biztosítja a második lépésben történő orchidopexiához a megfelelő

hosszúságot [1, 4, 15, 16]. A két műtéti típus közül a hereatrófiák aránya Shehata műtét esetén kedvezőbb [8, 17-20]. Megnyugtató, hogy a Magyarországon a hasüregi herék kezelése jól történik: a jelenleg legkorszerűbbnek tekintett minimál invazív eljárást, a Shehata műtétet országszerte alkalmazzák, a műtét eredményességéről szóló, Shehata saját beteganyagát követően második legnagyobb esetszámú, multicentrikus vizsgálat hazánkból került publikálásra [8].

Hormonális kezelés alkalmazása

A hormonális kezelés (hCG vagy GnRH) alkalmazása a rejtettheréjűség kezelése során két időpontban merül fel: használható neoadjuváns kezelésként a here leszállásának elősegítésére, valamint orchidopexiát követően adjuvánsként a fertilitás fokozása érdekében [13]. A hormonterápiára vonatkozó egyértelmű ajánlás megfogalmazását nehezíti, hogy a kapcsolódó tanulmányok jellemzően heterogének, emellett hosszú távú eredményeket gyakorlatilag nem tartalmaznak [2]. Neoadjuváns kezelésként való alkalmazása ellen szól, hogy a here leszállása a kezelésben részesült betegek mindössze 7-63%-ban következik be, emellett alkalmazása a műtéti ellátást késleltetheti [13, 21-24]. Adjuvánsként való alkalmazása válogatott betegcsoport esetén – kongenitális hypogonadotrop hypogonadismus, parciális androgén inszenzitivitás, kétoldali rejtettheréjűség – megfontolandó [25]. A jelenleg érvényben lévő hazai, és főbb nemzetközi ajánlások a hormonterápia rutinszerű alkalmazása ellen érvelnek [2, 6, 7, 11, 13]. A hormonális kezelés tekintetében a hazai ellátás korszerűnek mondható, alkalmazása a rutinszerű ellátásból gyakorlatilag kikerült. Fontos azonban megjegyezni, hogy válogatott esetekben kiegészítő kezelésként fel kell, hogy merüljön a gyermek ellátása során.

Retraktilis herék

Retraktilis (visszahúzódó) herék esetében a normál leszállás megtörtént, azonban az élénk reflextevékenység hatására a here a lágyékcsatorna és a herezacskó között „ingázik” [26]. Fizikális vizsgálat során nehézség nélkül a scrotum aljára húzhatóak és ezt követően tartósan ott helyezkednek el [26]. Az esetek többségében pubertáskorra „elvesztik retraktilitásukat” és tapinthatóvá válnak a herezacskóban [27]. Normál variánsként történő besorolásuk azonban ellentmondásos: egyes vizsgálatok alapján akár egyharmadukból aszcendáló (felszálló) here alakulhat ki, ami az orchidopexiák életkor szerinti gyakoriságában megfigyelt bimodális eloszlás – legnagyobb gyakoriság 2 és 10 éves korban – egyik magyarázataként szolgálhat [1, 26-28]. Az aszcendáló herék szövettani jellemzői a primer rejtett herékéhez hasonlóak:

vizsgálatuk során a csírasejtek csökkent számát írták le és azáltal a termékenység érintettségét feltételezik [29-30].

Az EMMI, valamint ESPU/EAU egyaránt a retraktilis herék hormonális vagy műtéti kezelése helyett kamaszkorig történő évenkénti ellenőrzésüket javasolja [6, 7]. A magyar nyelvű ajánlás kiemeli, hogy az ellenőrzést az alapellátásban résztvevő háziorvosok, védőnők is végezhetik [6]. Vizsgálatunk eredményei arra engednek következtetni, hogy Magyarországon a retraktilis herék ellátása csupán korlátozott mértékben történik a jelenlegi ajánlásoknak megfelelően: a felmérésben résztvevő házi gyermekorvosok kevesebb mint kétharmada tartja a konzervatív kezelést elsődlegesnek, emellett szintén kevesebb, mint kétharmaduk végzi kamaszkorig szoros utánkövetésüket. a retraktilis herék a gondozásra vonatkozó ismeretek célzott és szélesebb körű terjesztése lehet szükséges az aszcenzus időben történő felismerése érdekében. Jelenleg az utánkövetést végző szint nincs egyértelműen deklarálva, ennek egyértelművé tétele segíthetné a precíz, serdülőkorig tartó gondozást. A gyermeksebészet centralizált volta miatt kézenfekvő, hogy a gondozás helye a házi gyermekorvosoknál legyen, illetve hasznos lenne, ha erről a kérdésről a két szakma hivatalosan megállapodna.

Az orchidopexián átesett gyermekek gondozása

Az orchidopexián átesett gyermekek gondozásának elsődleges célja a here életképességének, megfelelő helyzetének és szerkezetének ellenőrzése. Atrófia esetén hereimplantátum beültetése ajánlható fel a testkép javítása, valamint a monorchismus okozta stressz csökkentésére érdekében, szekunder retenció kialakulásakor a késői szövődmények megelőzése céljából ismételt orchidopexia javasolt [4, 6, 7]. A rejtettheréjűség a hererák egyértelmű rizikófaktora, kialakulási esélyét 1,6-7,5-szörösére növeli [31, 32]. Időben történő felismerése érdekében fizikális vizsgálattal történő szűrése, valamint a szülők és a gyermek önvizsgálatról történő edukációja a kontroll vizsgálatok részét kell, hogy képezze [7].

Az EMMI hatályban lévő ajánlása az orchidopexián átesett gyermekek ellenőrzése kamaszkorig évente legalább egy alkalommal javasolja; a gondozást az alapellátásban résztvevő háziorvosok, védőnők is végezhetik [6]. Az EAU/ESPU aktuális irányelve a rendszeres ellenőrzés mellett az önvizsgálat fontosságára helyezi a hangsúlyt [7]. Vizsgálati eredményeink arra engednek következtetni, hogy az orchidopexián átesett gyermekek gondozása Magyarországon sem gyermeksebészi, sem házi gyermekorvosi szinten nem megfelelően koordinált. Az utánkövetés az aktuális irányelveket nem követi: a pubertáskorig tartó ellenőrzés az esetek többségében elmarad. Ez részben abból következhet, hogy a

gondozást végző ellátási szint az ajánlásokban nincs egyértelműen kijelölve, emellett a megkérdezett orvoscsoportok közötti hiányos kommunikáció oki szerepe is felmerül.

Erősségek és korlátok

Tudomásunk szerint Magyarországon a hereleszállási zavarok országos szintű ellátásának felmérése korábban még nem történt meg. Kutatásunk eredményei jó alapot szolgáltatnak az ellátási gyakorlat célzott fejlesztéséhez, valamint az egészségügyi szakmai irányelvek szélesebb körű terjesztéséhez. Tanulmányunk egyik korlátja a részt vevő kollégák alacsony hányada HGYE tagjai körében. Emellett szeretnénk hangsúlyozni, hogy a kérdőíves felmérések csupán az ellátás fő tendenciáit mutatják, miközben minden beteg személyre szabott terápiát igényel [33].

Következtetés

Vizsgálati eredményeink alapján elmondható, hogy a hereleszállási zavarok hazai ellátása a kérdőívet kitöltő házi gyermekorvosok körében döntően az aktuális ajánlásoknak megfelelően történik: ismereteik alapvetően megfelelőek, azonban néhány fontos kérdésben – műtéti ellátás optimális időzítése, retraktilis herék kezelése és utánkövetése, orchidopexián átesett gyermekek gondozása – hiányosak. Emiatt fontosnak tartjuk a korszerű ellátásra vonatkozó ismeretek továbbképző tanfolyamokon, tudományos üléseken történő átadását, valamint az aktuális irányelvek gyermekgyógyászati témájú folyóiratokban történő publikálását. Emellett az internet alapú egészségkommunikációs lehetőségek szintén jó alapot szolgáltathatnak az új ismeretek terjesztéséhez [34].

A hereleszállási zavarok gyermeksebészeti ellátása korszerűen történik a vizsgálatban résztvevők körében. Ennek talán legjobb indikátora, hogy a hasüregi herék kezelése a jelenleg legmodernebbnek számító minimál invazív Shehata műtéttel történik. Szeretnénk azonban felhívni a figyelmet, hogy a nem tapintható herék észlelésekor még mindig sok esetben feleslegesen kért ultrahang vizsgálat a műtéti ellátást késlelteti.

A retraktilis herékkel rendelkező, valamint az orchidopexián átesett gyermekek gondozása jelenleg nem megfelelő. Ez adódhat abból, hogy jelenleg az utánkövetést végző szint nincs egyértelműen deklarálva. Ennek egyértelművé tétele segíthetné a precíz, serdülőkorig tartó gondozást. Emellett az alap- és szakellátásban is fontos hangsúlyozni a retraktilis herék hosszútávú gondozásának fontosságát, mivel ezek az évek során műtéti ellátást igénylő valódi rejtettheréjűséggé alakulhatnak át.

Javaslataink célja elsősorban, hogy a nem descendált herék ellátása hazánkban minden szinten a hazai és nemzetközi ajánlásoknak megfelelően történjen a hosszútávú morbiditás, infertilitás és a felnőttkori malignus heretumorok kialakulási esélyének csökkentése érdekében.

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