e-ISSN:3023-7289

SoC
Surgery on Children

Volume: 2 Issue: 1 Year: 2025

MHA
MEDIHEALTH ACADEMY

EDITOR-IN-CHIEF

ASSOCIATE EDITOR-IN-CHIEF

EDITORIAL BOARD

At DAWN,

I believe we had favorable success in the first anniversary of the journal "Surgery on Children," going to a more significant target for better circumstances of children's health. The journal itself is a very fruitful base for authors who have concerns about treating the pediatric age group holistically. Collaborative management is the journal's only task, which is why it is named "Surgery on Children."

To work together, one must be part of a "writer" academic persona. Conversation and good intentions can never be sufficient if writing and "being capable of writing" are absent. So, the mission of the journal demonstrates itself at this point.

Previous year, we had four issues with 24 articles. These articles ranged from case studies and research papers to reviews and editorials. Most importantly, various branches of health-caring tasks contributed to the journal. Nurses, anaesthesiology specialists, pediatric urologists, pediatric surgeons, orthopaedists, nuclear medicine specialists, plastic surgeons, ear-nose-throat surgeons, and pediatric specialists submitted articles to give their hands to this calling. That concludes the success of the journal in the last year.

Contributing to the journal not only provides a platform to share your expertise but also fosters collaboration and learning across different medical specialties. We look forward to welcoming contributions from ophthalmologists, neurosurgeons, emergency and intensive care specialists, pathologists, radiologists, thoracic surgeons, and technicians, as their unique perspectives will enrich our content and further our mission.

Of course, we encountered some functional and academic difficulties during this time. However, we are resolutely committed to overcoming these obstacles with the support of our respected publisher, Medihealth Academy. This commitment should reassure you of our dedication to the journal's continued success.

As a result, I believe the period we passed gives me a humble right to define the ongoing process as a "dawn." We are filled with an increasing eagerness to continue our mission. The journal is at dawn, and we are inspired to keep pushing forward.

Best Regards

Atilla ŞENAYLI

Editor-in-Chief

ORIGINAL ARTICLES

REVIEWS

CASE REPORT

LETTER TO THE EDITOR

MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

doi: 10.51271/SOC-0025

The effect of combined use of oxybutynin and fulguration in children with PUV: experience in a tertiary center in Bangladesh

Ipsita Biswas[1], Sadia Sultana[2], Umama Huq[2], Abhi Kumar Chakraborty[3]

[1]Department of Pediatric Urology, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh
[2]Department of Pediatric Surgery, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh
[3]Department of Pediatric Surgery, Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh

Received: 02/10/2024 ◆ **Accepted**: 25/10/2024 ◆ **Published**: 20/01/2025

Cite this article: Biswas I, Sultana S, Huq U, Chacraborty AK. The effect of combined use of oxybutynin and fulguration in children with PUV: experience in a tertiary center in Bangladesh. *Surg Child.* 2025;2(1):1-4.

Corresponding Author: Ipsita Biswas, ipsitabiswas74@gmail.com

ABSTRACT

Aims: Posterior urethral valve (PUV) is a common congenital urethral obstruction leading to significant morbidity. Despite successful fulguration of PUV, the bladder dysfunction persists in most of the cases. Oxybutynin, an anticholinergic drug is commonly used to manage this bladder dysfunction. This study aimed to assess the impact of oxybutynin on bladder and urinary tract function in children with valve fulguration.

Methods: A retrospective observational study was conducted on 41 children who underwent PUV fulguration at a tertiary care center in Bangladesh between 2020 and 2023. All subjects received oxybutynin for at least 6 months post-fulguration. Bladder wall morphology, hydronephrosis, vesicoureteral reflux (VUR), and post void residues (PVR) were assessed. Side effects of oxybutynin were also documented.

Results: All patients had bilateral hydroureteronephrosis (HUN), except one, who was with unilateral HUN during primary diagnosis. Complete resolution of bilateral HUN was seen in renal USG 14 patients at 6 months post fulguration. Correction of VUR documented in 13 units out of 32 units. Mean serum creatinine decreased to 0.52±0.22from 0.73±0.52 within 6 months of fulguration. Four patients exhibited significant PVR, leading to clean intermittent catheterization (CIC) initiation.

Conclusion: Combined with PUV fulguration and oxybutynin therapy appears to be effective in improving bladder function. Further prospective studies incorporating urodynamic evaluations are warranted to validate these findings.

Keywords: Posterior urethral valve, oxybutynin, fulguration

INTRODUCTION

Posterior urethral valve (PUV) stands as a prevalent form of congenital urethral obstruction, with an incidence of 1 in 2500 to 1 in 5000 male births.[1] This condition is recognized as a primary surgical cause of chronic kidney disease in children necessitating renal replacement therapy.[1] During the development of a normal fetal bladder, bladder cycling generates a stretch force on the bladder that causes a decrease in collagen content in the bladder wall and also a decrease in smooth muscle tension. In patients with PUVs, this normal bladder cycling hampers. It causes structural and functional alteration in the bladder and thus produces bladder dysfunction. Due to the loss of strength and elasticity of the bladder wall, there is a gradual loss of bladder compliance, reduction in capacity, and development of high storage pressures.[2,3] The presence of PUV typically gives rise to bladder hypertrophy and hydroureteronephrosis (HUN), evident on ultrasound scans. While ultrasound serves as an effective diagnostic tool, the gold standard investigation for comprehensive evaluation remains the micturating cystourethrogram (MCU). The MCU offers a detailed portrayal of the condition, showcasing not only the dilated posterior urethra but also providing insights into bladder dimensions, trabeculation, and the presence of vesicoureteral reflux (VUR).[4] Early valve fulguration is proven to be superior to diversion procedures (vesicostomy/ureterostomy) and is considered the optimal management modality following initial stabilization of deranged renal function, metabolic parameters, and coexisting urinary tract infection (UTI).[5,6]

Despite timely interventions such as valve ablation, bladder dysfunction manifested by frequency, dribbling, and daytime and nighttime incontinence, persists in a substantial proportion of patients, often becoming a crucial determinant

of long-term outcomes.[5,7] This dysfunction results from the remaining pathological changes in the bladder that is hypertonic, hyperreflexic, small capacity, and noncompliant bladder. The type of bladder dysfunction after valve fulguration is unpredictable. The clinical challenges are to identify those individuals who are at risk of bladder dysfunction.

Oxybutynin, an anticholinergic drug, emerged as the preferred therapeutic choice for managing post-fulguration bladder dysfunction. Oxybutynin, by inhibiting muscarinic action, exerts an antispasmodic effect on the bladder's smooth muscles.[6] Several studies mentioned that oxybutynin improves this dysfunction.[2,8] It improves the bladder compliance, increases bladder capacity, and decreases the storage pressure.[8] Because of this property, it becomes the drug of choice in treating bladder dysfunction in children with PUVs.[8]

This study sought to evaluate the effectiveness of oxybutynin in the management of children following PUV fulguration.

METHODS

The study was conducted with the permission of the Ethics Committee of Bangladesh Shishu Hospital and Institute (Date: 07.03.2022, Decision No: 2023712(l)). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. This was a retrospective observational study among the children who underwent fulguration for PUV in Bangladesh Shishu Hospital and Institute, a tertiary care center in Bangladesh between 2020-2023. All children who underwent fulguration from the neonatal period to 5 years of age and on oxybutynin were included in the study. Children with PUV were treated with oxybutynin at 0.2 mg/kg/day in two divided doses for 6-month post fulguration. Exceptions are those who have good bladder morphology as noted during cystoscopy and without complaints of frequency, dribbling, and daytime and nighttime incontinence, those with significant persistent post void residues (PVR) on post fulguration follow-up ultrasound, and those who did not tolerate oxybutynin. Basic demographic details, brief antenatal and neonatal medical history, biochemical parameters, renal ultrasonogram, MCU, DMSA scan reports were assessed in follow up. Bladder wall morphology, the status of HUN, and PVR were compared between preoperative and postoperative ultrasound scans. VUR was assessed in MCUs. The status of renal scarring was determined by DMSA scans. Data regarding the side effects of oxybutynin were collected by asking the parent as well as by going through their medical records.

Statistical Analysis

Data analysis was performed with SPSS Statistics for Windows, Version 20.0. Statistical significance was set at $p<0.05$.

RESULTS

There was a total of 44 children who underwent fulguration for PUV between January 2020 and December 2023. Of these, 3 children were excluded as they were lost to follow up. Thus, at the time of final follow-up 41 children were available.

The age at presentation ranged from 9 days to 3 years 8 months (Table 1). The relevant clinical features are summarized in Table 2. The most common clinical presentation was poor urinary stream noted in 30/41 children, UTI in 18/41 children and acute renal failure in 8/41, antenatal diagnosis 10/41.

Table 1. Age of presentation of the patients

Age	n	Frequency
<6 months	21	51%
6months-1year	7	17 %
1year-5year	13	32 %

Table 2. Clinical characteristics f the study population

Clinical presentation	n	Frequency
Poor urinary stream	30	73.17%
Urinary tract infection	18	43.90%
Acute renal failure	8	19.51%
Antenatal diagnosis	10	24.39%

Renal ultrasound revealed bilateral HUN in 40/41 patients and unilateral HUN in 1 patient at presentation (Table 3). In follow up USG at 6 months revealed, 35% (14/40) of those with bilateral HUN had complete resolution. In the remaining 26 patients with bilateral HUN, improvement in HUN was seen in 12 children. There was no change of HUN was observed in 14 patients with bilateral HUN and 1 patient with unilateral HUN (Table 3).

Table 3. Pre and post operative renal ultrasound

		Bilateral HUN	Unilateral HUN
Preoperative USG		40	1
Postoperative USG	Complete resolution	14	0
	Improved	12	0
	Not improved	14	1

HUN: Hydroureteronephrosis

Initial MCU revealed a total of 32 refluxing units (Table 4). In follow up, complete resolution was noted in 8 patients, 13/32 units (41%), and no change in 3 patients. In 7 patients the grade of VUR was improved. However, 2 patients with no VUR had developed new unilateral VUR.

Table 4. Pre and post operative MCU

Preoperative MCU		Bilateral VUR	Unilateral VUR
		13	6
Postoperative MCU	Complete resolution	5	3
	Improved	5	2
	Not improved	3	1

MCU: Micturating cystourethrogram, VUR: Vesicoureteral reflux

Four patients had documented significant PVR in follow-up. This was probably due to the combined effect of oxybutynin with ineffective bladder emptying. All of them were started on clean intermittent catheterization (CIC).

The preoperative mean serum creatinine was 0.73±0.52 and after 6 months of fulguration mean serum creatinine was 0.52±0.22. There was a significant fall in the mean creatinine ($p=.001$) after fulguration (Table 5).

Most of our patients, 35/41 with oxybutynin for more than 6 months after fulguration, were asymptomatic with a good urinary stream in follow-up. 2 children had daytime

incontinence which was improved with time and 3 children had recurrent UTI which was treated with antibiotics.

Table 5. Laboratory findings

	Pre intervention		Post intervention		p
Creatinine	n	Mean (SD)	n	Mean (SD)	
	41	0.73±0.52		0.52±0.22	.001

SD: Standard deviation

DISCUSSION

We conducted a retrospective observational study to find out the course of disease in children diagnosed with PUV and on oxybutynin for at least 6 months with fulguration. The most common presenting complaints in our study population were poor urinary stream and recurrent UTI which was similar to the study done by Norris JJ et al.[9] 55.56% of their patients presented with poor urinary stream and 41.67% with UTI. In our study only 5 (5/41) patients presented at the age of <1 month and 24.39% of our patients had antenatal diagnosis. These findings differed from other studies. Ezel et al.[10] reported a single-center experience of 22 years with 64 children where the median age of diagnosis of PUV was one month (range 1-132 months) and 51.5% were diagnosed antenatally. Another retrospective study over 29 years reported that 42.5% (n=77/181) of the total 181 South African boys with PUV were diagnosed in their first month of life.[11] This is probably due to the lack of proper antenatal screening facilities in our country. We have observed that ultrasound during antenatal period paid very little attention to the detection of congenital anomalies.

In our study, we found improvement in lower urinary tract symptoms and having a good urinary stream in patients with the use of oxybutynin for at least 6 months after ablation. A similar finding was mentioned by Noris JJ et al.[9] There was a decrease in postoperative mean serum creatinine than mean preoperative serum creatinine in our study.

The combined use of oxybutynin and PUV fulguration also caused resolution of the HUN in renal ultrasound scans and the resolution of VUR in MCU in this study. All of these reflect improved bladder function in our PUV patients. These findings were similar to Kim et al.[12] who used anticholinergic medication. Other studies observed that oxybutynin improves bladder compliance, and detrusor overactivity, increases the bladder capacity, and decreases the storage pressure.[8,13] Wani SA et al.[14] mentioned in their study that early use of oxybutynin immediately after the diagnosis of PUV improves the urodynamic parameters in these patients. In our country, urodynamic study cannot be done before 5 years of age. This makes it difficult to identify the specific bladder dysfunction in our setting. We can only assess the improvement of lower urinary tract symptoms, and USG and MCU parameters during follow-up after 6 months of fulguration.

The main concern in using anticholinergic therapy is a reversible iatrogenic myogenic failure causing the overdistended bladder, worsening reflux, and incontinence.[15] We had 4 patients for whom PVR was significant. MCU of these children showed moderate capacity bladder, presence of PVR, and resolution of reflux in 3 patients but increased the grade of reflux in 1 patient. So it was unlikely for the patients to have myogenic failure. However urodynamic evaluation was necessary to confirm. The treatment for myogenic failure is to stop the anticholinergic therapy and start CIC to facilitate bladder emptying.[15,16] So, we treated these 4 patients with CIC and stopped the oxybutynin.

The combined use of oxybutynin and PUV fulguration has resulted in resolution of the HUN in renal ultrasound scans and the resolution of VUR in MCU, thereby reflecting an improvement in bladder function. A comparative study revealed, the observation group where oxybutynin was not given after valve fulguration hydronephrosis was improved in 16/50 (34.8%) renal unit, which was significantly lower than the oxybutynin group.[17] Our study showed improvement of hydronephrosis in 52/81 (64%) renal units.

Oxybutynin has some side effects, these include dry mouth, dry eyes, constipation, and urinary retention.[18] Dryness of the mouth is usually the most common side effect encountered. However, we did not observe these side effects as our patients were mostly below 3 years of age and they could not comprehend the dryness of mouth.

Limitations

Our study has a few limitations. The data were collected retrospectively. It was also not possible to have a control group as management of PUV with oxybutynin and fulguration have become the standard of care. The accuracy of valve fulguration is also predicted by improvement in symptoms and investigations in follow-up. Therefore, it is difficult to mention the outcome of adequate valve fulguration and the use of oxybutynin individually. The other major limitation is the unavailability of urodynamic study in our country So urodynamic correlation could not be possible in our study.

CONCLUSION

Adequate valve fulguration and oxybutynin therapy in children with PUV can improve the function of bladder and helps in preventing structural damage to the upper tracts.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Ethics Committee of Bangladesh Shishu Hospital and Institute (Date: 07.03.2022, Decision No: 2023712(l)).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Bain A, Lavoie C, Rodriguez-Lopez S, Kiddoo D. Renal outcomes of children born with posterior urethral valves at a tertiary center: a 15-year retrospective review. *Can Urol Assoc J*. 2023;17(4):111-116. doi:10.5489/cuaj.8102
2. Hyman M, Groutz A, Blaivas J. Detrusitor instability in men: correlation of lower urinary tract symptoms with urodynamic findings. *J Urol*. 2001; 166(2):550-552.
3. Planta D, Gerwinn T, Salemi S, Horst M. Neurogenic lower urinary tract dysfunction in spinal dysraphism: morphological and molecular evidence in children. *Int J Mol Sci*. 2023;24(4):3692. doi:10.3390/ijms24043692
4. Bingham G, Leslie SW, Rentea RM. Posterior urethral valves. [Updated 2024 May 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560881/ 2024.
5. Peters CA, Bolkier M, Bauer SB, et al. The urodynamic consequences of posterior urethral valves. *J Urol*. 1990;114(1):122-126.
6. McCrery RJ, Appell RA. Oxybutynin: an overview of the available formulations. *Ther Clin Risk Manag*. 2006;2(1):19-24.
7. Sarhan OM, Wadie B, Al-Kawai F, Dawaba M. Bladder function in children with posterior urethral valves: impact of antenatal versus postnatal diagnosis. *Int Braz J Urol*. 2022;48(1):78-86. doi:10.1590/S1677-5538.IBJU.2021.0046
8. Casey JT, Hagerty JA, Maizels M, et al. Early administration of oxybutynin improves bladder function and clinical outcomes in newborns with posterior urethral valves. *J Urol*. 2012;188(4 Suppl):1516-1520.
9. Norris JJ, Raj JP, Thomas TT, Maleperambil TT, Shubha AM. Effects of oxybutynin in children with posterior urethral valves post fulguration: report in a select cohort of children. *J Family Med Prim Care*. 2021;10(10): 3706-3711.
10. Ezel Çelakil M, Ekinci Z, BozkayaYücel B, Mutlu N, Günlemez A, Bek K. Outcome of posterior urethral valve in 64 children. Single center experience of 22 years. *Minerva Urol Nefrol*. 2019;71(6):651-656.
11. Petersen KL, Moore DP, Kala UK. Posterior urethral valves in South African boys: outcomes and challenges. *S Afr Med J*. 2018;108(8):667-670.
12. Kim YH, Horowitz M, Combs AJ, Nitti VW, Borer J, Glassberg KI. Management of posterior urethral valves on the basis of urodynamic findings. *J Urol*. 1997;158(3 Pt 2):1011-1016.
13. Greenland JE, Brading AF. The effects of bladder outflow obstruction on detrusor blood flow changes during the voiding cycle in conscious pigs. *J Urol*. 2001;165(1):245-248.
14. Wani SA, Babu N, Faheem M, Jadhav V, Ramesh S, Deepak J. Early use of bladder relaxant (oxybutynin) in posterior urethral valve patients. Is it justified? *Med Sur Urol*. 2019;8:222. doi: 10.24105/2168-9857.8.222
15. Misseri R, Combs AJ, Horowitz M, Donohoe JM, Glassberg KI. Myogenic failure in posterior urethral valve disease: real or imagined? *J Urol.* 2002; 168(4 Pt 2):1844-1848.
16. Sharma S, Joshi M, Gupta DK, et al. Consensus on the management of posterior urethral valves from antenatal period to puberty. *J Indian Assoc Pediatr Surg*. 2019;24(1):4-14.
17. Abdelhalim A, El-Hefnawy AS, Dawaba ME, Bazeed MA, Hafez AT. Effect of early oxybutynin treatment on posterior urethral valve outcomes in infants: a randomized controlled trial. Journal of Urology [Internet]. 2020 Apr 1 [cited 2024 Oct 17];203(4):826–31. Available from: https://doi.org/10.1097/JU.0000000000000691
18. Lieberman JA. Managing anticholinergic side effects. *Prim Care Companion J Clin Psychiatry*. 2004;6(Suppl 2):20-23.

MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

doi: 10.51271/SOC-0026

Role of intramuscular testosterone therapy for the position of meatus as well as the changes in the degree of chordee on proximal penile hypospadias in children: a non-randomized clinical trial

Refoyez Mahmud, Samiul Hasan, Nazmul Islam, Ashrarur Rahman Mitul

Department of Neonatal Surgery, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh

Received: 11/11/2024 ◆ **Accepted**: 03/12/2024 ◆ **Published**: 20/01/2025

Cite this article: Mahmud R, Hasan S, Islam N, Mitul AR. Role of intramuscular testosterone therapy for the position of meatus as well as the changes in the degree of chordee on proximal penile hypospadias in children: a non-randomized clinical trial. *Surg Child.* 2025;2(1):5-10.

Corresponding Author: Refoyez Mahmud, sipummc@gmail.com

ABSTRACT

Aims: The aim of the current study was to evaluate and compare the changes in meatal position and degree of chordee in children with proximal penile hypospadias before and after intramuscular testosterone therapy.

Methods: This was a single center, parallel arm, non-randomized clinical trial which was conducted in the surgery out-patient department (SOPD) of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh from June 2022 to March 2024 for a period of 22 months. Patients with proximal penile hypospadias attended in SOPD in Bangladesh Shishu Hospital & Institute during the study period. Several variables were recorded like position of meatus as well as the degree of chordee. A preparation of testosterone depot, containing testosterone propionate, phenylpropionate, isocaproate, and decanoate, was administered via intramuscular injection in the buttock to a patient with proximal penile hypospadias. The dosage was 2 mg/kg of body weight, following the specified flowchart. If the desired effect was achieved, either by the growth of the penile length proximal to the meatus resulting in a change in the severity from proximal penile to mid/distal penile hypospadias, or by a reduction in the degree of chordee to less than 30°, or both, the testosterone therapy was discontinued.

Results: A total number of 20 children presented with hypospadias were recruited for this study after fulfilling the inclusion and exclusion criteria. The mean age with the SD of the study population was 42.10±25.37 months. All the position of the meatus of the study population were in the proximal position which was 20((100.0%) cases before intramuscular testosterone therapy. However. After the therapy, the proximal position was found in 10(50.0%) cases and mid position was in 10(50.0%) cases (p=0.002). During testosterone therapy, the mean with the SD of degree of chordee was 55.0±8.73 mm and 43.25±14.26 mm in before and after intramuscular testosterone injection respectively (p=0.0001).

Conclusion: In conclusion the degree of chordee is significantly change before and after intramuscular testosterone injection.

Keywords: Hypospadias, proximal penile hypospadias, chordee, testosterone

INTRODUCTION

Hypospadias is a congenital defect resulting from an abnormal penile development, which leads to the urethral meatus being situated abnormally along the penile shaft, scrotum, or perineum instead of its usual location at the tip of the glans. It is the second most common birth anomaly, occurring in approximately 1 out of every 300 males.[1]

The condition arises due to arrest in normal development of the urethra, foreskin, and the ventral aspect of the penis.[2] Hypospadias classification is based on factors such as the positioning of the urethral opening, the presence of penile curvature (chordee), and the extent of related abnormalities.[3] Proximal hypospadias which account for 20% of all cases of hypospadias among them one-fourth of the hypospadias are associated with chordee.[4,5] The position of the meatus and degree of chordee determine the severity of hypospadias.[6]

Hypospadias was classified according to position of meatus into four categories: first-degree (with the urethral opening at the coronal or distal area of the penis), second-degree (with the urethral opening located between the mid-penile and sub-coronal area), third-degree (with the urethral opening in the perineum or proximal penile area), or categorized as not otherwise specified (NOS).[7] The degree of the chordee can be classified according to the angle of the chordee, with mild chordee defined as <20°, moderate chordee as 20-30°, and

severe chordee as >30°.[8] So, according to classification the more proximal the meatal opening more severe the hypospadias additionally degree of chordee is directly proportional to the severity of hypospadias.

Surgical correction is advised to achieve optimal functionality, cosmetic appearance, and minimal complications, addressing the primary objectives of correcting chordee and ensuring an aesthetically pleasing penis.[9] The likelihood of surgical success remains significantly challenging in children with proximal hypospadias with chordee compared to those with a less severe deformity.[5] To enhance the size of the penis and to achieve satisfactory repair, preoperative testosterone is commonly used as androgen therapy.[10]

In order to increase penile length, temporary stimulation has been attempted through the local application of testosterone or dihydrotestosterone (DHT) cream; however, the outcomes were not only irregular but also exhibited variability in absorption.[11] The benefit of using intramuscular (IM) testosterone application over topical is that it ensures an increase in serum testosterone level.[10]

Therefore, IM testosterone stimulation ensures the development of high-quality tissue by promoting an increase in total penile length, the amount of preputial and penile shaft skin.[12] Testosterone also enhances the vascularity of the corpus spongiosum that facilitates to reconstruct a neourethra within the glans penis, allowing for low-pressure voiding within a distensible tube as well as minimizes potential complications.[13]

However, a few effects as secondary sexual characteristics, like the appearance of pubic hair, changes in genital pigmentation, and aggressive behavior were noted following testosterone stimulation.[14] Nonetheless, these effects were observed to regress once hormonal therapy was discontinued. The most common effect of secondary sexual characteristics of IM testosterone found was the appearance of pubic hair.[15-17] A survey indicated that 76% of respondents believed that the side effects could be minimized by administering IM testosterone at a dosage of 2mg/kg body weight.[17]

Despite an increase in total penile length, it has been observed that the distance from the hypospadiac meatus to the tip of the glans does not increase proportionately with the entire length of the penis.[9] However, this study used topical testosterone and measured total penile length and meatus to glans distance but didn't specifically measure penile length proximal to the meatus.

Testosterone stimulation results in a disproportionate increase in penile length, with more significant growth in tissues proximal to the hypospadiac meatus.[12] Furthermore, their research highlights that the increase in tissues proximal to the meatus is greater than that observed in distal tissues which eventually alters the degree of hypospadias. However, this study was done in a single center on a very small number of patients and didn't mention the effect of IM testosterone on the degree of chordee. Considering these facts about IM testosterone, the present study was conducted to evaluate the effect of intramuscular testosterone on proximal penile hypospadias. The purpose to the present study was to observe and compare the changes in the position of meatus as well as the changes in the degree of chordee before and after IM testosterone therapy.

METHODS

Ethical Consideration

Keeping compliance with the Helsinki Declaration for Medical Research Involving Human Subjects, 1964 a consent form was constructed describing the title, objectives, and procedure of the study, the expected outcome, any potential risk to the subject undergoing intervention, and ways to minimize. These statements were written and described in an easily understandable clear local language. Parents or caregivers decided themselves to be or not to be included in the study. This written informed consent was signed duly by the caregiver and the principal investigator. All information from the patients was kept confidential under the responsibility of the principal investigator. An identification number was given instead of using a name for each member of the study group. No other than the investigator, regulatory authorities, and the ethical review committee would have access to collected data. The patient's identity was not disclosed while analyzing or publishing the results of the study. Ethical clearance was taken from the ethical review committee (Date: 19.10.2022, Decision No: 2022692) of Bangladesh Shishu Hospital and Institute, Dhaka. Every ethical issue was discussed with the patient's parents regarding the study and informed written consent was obtained. The study did not involve any social, psychological, or legal risk to the subject or any invasion of privacy. The study did not involve using hospital or medical records. There was no chance of disclosure of any information that was harmful to the patients or others. The patient's parents were informed about the nature and purpose of the study, procedures followed, risks associated with it, and benefits from the study. They were also informed about the right to participate or to withdraw from the study at any time. No compensation for risk or loss of work time was provided. Confidentiality was strictly maintained regarding all data.

Study Settings and Population

This was a single center, parallel arm, non-randomized clinical trial. The study was conducted in the surgery out-patient department (SOPD) of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh. This study was carried out from June 2022 to March 2024 for a period of 22 months. Patients with proximal penile hypospadias attended SOPD in Bangladesh Shishu Hospital & Institute during the study period. A purposive sampling technique was used. Out of the study population, the individual sample units were selected according to clinical judgment until the desired sample size was attained.

Selection Criteria

Patients who had proximal penile hypospadias with age ranging from 1 year to 10 years were included in this study. Patients who developed secondary sexual characteristics, patients who underwent some surgical repair of penis in the past, patients who had taken prior hormonal therapy for penile growth and patient who had a disorder of sexual development were excluded from this study.

Study Procedure

Several variables were recorded like total length of the penis, penile length proximal to meatus, penile length distal to the meatus, position of meatus and degree of chordee. Proximal

penile hypospadias was defined as the urethral opening located proximal to halfway from the tip of the penis to penoscrotal junctions on the ventral aspect of the shaft of the penis will be 'proximal penile' hypospadias. Severe chordee was recorded when chordee was more than 30°. Position the meatus and degree of chordee was used to define severity of hypospadias. The growth of the penile length proximal to the meatus resulting in a change either in position of the meatus from proximal penile to mid/distal penile hypospadias, or by a reduction in the degree of chordee to less than 30°, or both were considered as reduced severity.

At first, the patient attended the SOPD, Bangladesh Shishu Hospital & Institute, was assessed and the diagnosis was established based on clinical grounds and by history taking and proper physical examination. Then they were approached to participate in the study. Before enrollment in the study, all attendants of patients were described about the titles, study aim and objectives, procedure, benefits, and potential dangers of the study. Face-to-face interviews with patient guardians were conducted by using a semi-structured questionnaire.

Measurements

The degree of chordee measurements was taken by a geometric protractor after stretching the penis. Total penile length, penile length proximal to the meatus and penile length distal to the meatus were measured by placing the jaw of the ruler at the penoscrotal junction after stretching the penis.

Intervention

A preparation of testosterone depot, containing testosterone propionate, phenylpropionate, isocaproate, and decanoate, was administered via intramuscular injection in the buttock to a patient with proximal penile hypospadias. The dosage was 2 mg/kg of body weight, following the specified **Figure 1**.

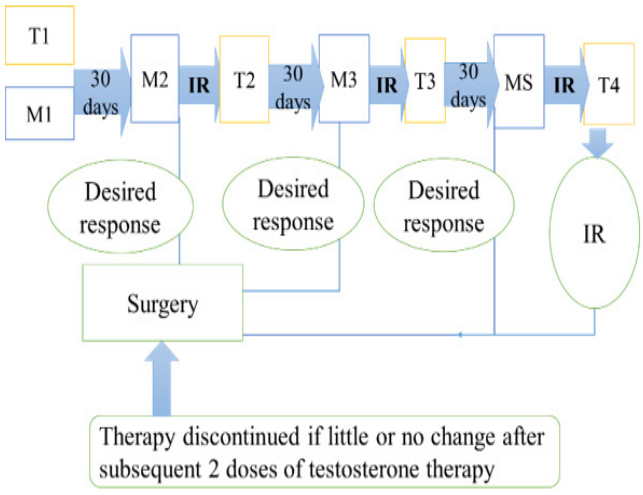


Figure 1. Follow up and outcomes measures
M1: Measurement before 1st injection, T1: 1st dose of testosterone injection, M2: Measurement before 2nd injection, T2: 2nd dose of testosterone injection, M3: Measurement before 3rd injection, T3: 3rd dose of testosterone injection, Ms: Measurement before surgery, T4: 4th dose testosterone injection, IR: Inadequate response.

Follow Up and Outcomes Measures

All patient were followed up and effects of IM testosterone measured according to specified flowchart. If the desired effect was achieved, either by the growth of the penile length proximal to the meatus resulting in a change in the severity from proximal penile to mid/distal penile hypospadias, or by a reduction in the degree of chordee to less than 30°, or both, the testosterone therapy was discontinued and patients were referred to consultant for surgical correction. If there was little to no change in the penile length proximal to the meatus or degree of chordee during subsequent two dosage of testosterone therapy, the therapy was also terminated and patients were referred for surgical consultation as well. Appearance secondary sexual characteristics following IM testosterone therapy like the appearance of pubic hair, genital pigmentation, and aggressive behavior were also observed after therapy. All patients underwent surgical correction within 60 days due to the temporary effects of the intervention. Since this study focused solely on the effects of intramuscular testosterone on penile growth, postoperative outcomes were not assessed.

Quality Assurance Strategy

All the study population was selected very carefully under the close supervision of the guide and inclusion-exclusion criteria was strictly followed. The completeness and quality of the collected data were ensured by regular and routine supervision, checking, and monitoring. The guide randomly scrutinized the data collection procedure. The gathered information from the patient was checked and rechecked with the medical record. Schedule meetings were arranged with the guide at every monthly interval to discuss the progress of data collection. Data cleaning was done before editing in the computer for analysis. After obtaining the results of one-quarter of the study subjects, a review meeting was arranged with the guide, and emerged issues were addressed properly. Before entering data in the computer for analysis random checking of data was done by the guide. Irrelevant and inconsistent data was discarded. After the completion of the data collection, a meeting was arranged with a guide and co-guide to discuss the progress of thesis writing and submission.

Statistical Analysis

The collected data from the participants were analyzed. To maintain consistency, the data were manually checked, edited, and verified before tabulation. The data was then coded, entered, and analyzed using SPSS (Statistical Package for Social Science) version 26 statistical software. The categorical variables were presented as n (% of cases), and the continuous variables were presented as mean±SD. Paired t-tests were carried out to determine the significance of the differences between pre-treatment and post-treatment outcome variables for total penile length, penile length proximal to meatus, penile length distal to the meatus, ratio of distal & proximal penile length and degree of chordee. On the other hand, the McNemar test was used as a test of significance for change in the position of the meatus. A significance level of $p < 0.01$ was considered to be statistically significant. All hypotheses were formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference).

RESULTS

Twenty children with hypospadias were included in this study after meeting the inclusion and exclusion criteria. The age of the participants ranged from 16 to 108 months, with a mean age of 42.10 ± 25.37 months (**Table 1**). Before testosterone therapy, the mean total penile length and proximal penile length were 20.10±4.96 mm and 5.15±2.60 mm, respectively. Following therapy, significant increases (p=0.0001) were observed, with

Table 1. Age Distribution of the study population (n=20)

Age	Values
Mean±SD	42.10±25.37 months
Age range	16.0 to 108.0 months

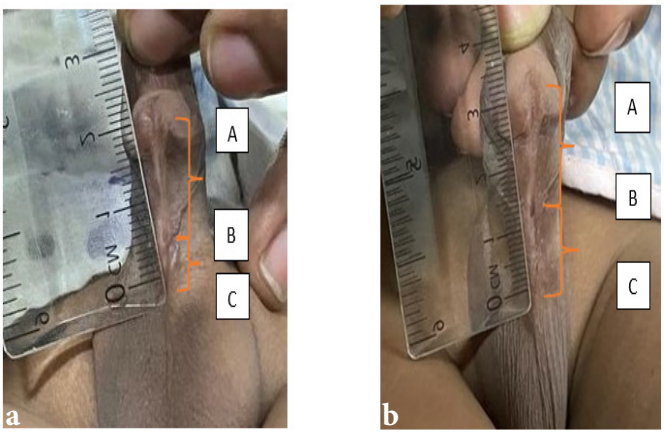
SD: Standard deviation

the total penile length reaching 29.20±5.35 mm (Table 2). The length before and after the testesterone is shown in Figures 2a, 2b and the proximal penile length increasing to 12.15±4.22 mm (Table 3).

Table 2. Comparison of total penile length (AC) before and after testosterone therapy

Testosterone therapy	Total penile length (mean±SD)	99% CI	p value
Before testosterone	20.10±4.96	6.68 to11.61	0.0001
After testosterone	29.20±5.35		

Results were expressed as mean±SD, paired t-test was done as a test of significance, p value <0.01 was considered as significant, CI: Confidence interval, SD: Standard deviation



a.Before testosterone b. After testosterone

Figure 2. Comaprison of penile length; total penile length (AC) and proximal penile length (AB)

Table 3. Comparison of proximal penile length (AB) before and after testosterone therapy

Testosterone therapy	Proximal penile length (mean±SD)	99% CI	p value
Before testosterone	5.15±2.60	4.88-9.11	0.0001
After testosterone	12.15±4.22		

Results were expressed as mean±SD, paired t-test was done as a test of significance, p value <0.01 was considered as significant, CI: Confidence interval, SD: Standard deviation

Before intramuscular testosterone therapy, all 20 participants (100.0%) had the meatus located in the proximal penile position. After therapy, the meatal position was proximal in 10 cases (50.0%) and mid-penile in 10 cases (50.0%), with the change in meatal position being statistically significant (p=0.002) (Table 4). Additionally, the mean degree of chordee decreased significantly, from 55.0±8.73 mm before therapy to 43.25±14.26 mm after therapy. The 99% confidence interval for the mean difference in chordee was 7.44 to 16.06 mm, with the improvement being statistically significant (p=0.0001) (Table 5). The degree of chordee before and after the testesterone therapy are as shown in Figure 3a, 3b.

Table 4. Position of meatus before and after testosterone therapy

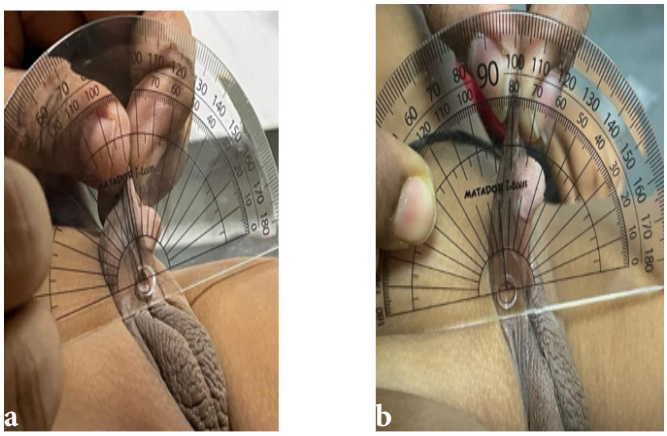
Testosterone therapy	Position	n (%)	p value
Before testosterone	Proximal	20 (100.0%)	0.002
After testosterone	Proximal	10 (50.0%)	
	Mid	10 (50.0%)	

McNemar's test was done as a test of significance, p value <0.01 was considered as significant

Table 5. Comparison of degree of chordee before and after testosterone therapy

Testosterone therapy	Degree of chordee (mean±SD)	99% CI	p value
Before testosterone	55.0±8.73	7.44 to 16.06	0.0001
After testosterone	43.25±14.26		

Results were expressed as mean±SD, paired t-test was done as a test of significance, p value <0.01 was considered as significant, CI: Confidence interval, SD: Standard deviation



a.Before testosterone b. After testosterone

Figure 3. Comparison of degree of chordee

DISCUSSION

The administration of intramuscular testosterone therapy for proximal penile hypospadias has been a subject of considerable interest due to its potential to influence penile growth by promoting cell proliferation and tissue expansion, resulting in a larger and more vascular penis, which may help reduce surgical complications.[18]

In this study total penile length and proximal penile length before testosterone therapy were 20.10±4.96 and 5.15±2.60, respectively. However, total penile length and proximal penile length showed significant increments (p=0.0001) after testosterone therapy, resulting in 29.20±5.35 and 12.15±4.22, respectively. Following this observation, as the penile length increases while the distance from the meatus to the tip of the glans does not grow, similarly to the distance from the meatus to the penoscrotal junction in proximal type, the hypospadias condition effectively shifts to a more distal position compared to its status before treatment.[9,12,19]

All the positions of the meatus of the study population were in the proximal position which was 20 (100.0%) cases before intramuscular testosterone therapy. However, after the therapy, the proximal position was found in 10 (50.0%) cases, and the mid position was found in 10 (50.0%) cases. The difference in the position of the meatus before and after therapy was statistically significant (p=0.002). This finding is also consistent with the findings of another study which showed that the distance from the meatus to the tip did not increase proportionately with the entire penile length, even after testosterone therapy.[12] It has been suggested that the dysplastic nature of the tissue distal to the meatus could be the reason for this discrepancy[13]

Some authors use hormonal stimulation on proximal hypospadias with severe chordee after correcting the chordee due to dysplastic nature of the tissue.[13] Conversely, testosterone stimulation ensures the development of high-quality tissue by enhancing the vascularity of the corpus spongiosum which

alters the severity of hypospadias.[12] In this study, it was found that testosterone therapy significantly reduced the average degree of chordee from 55.0±8.73 degrees to 43.25±14.26 degrees. Similar findings was found by a study who used gonadotropins for hormonal stimulation to reduce the degree of chordee.[20] May be that resulted due to disproportionate growth of penile length proximal and distal to the meatus.[9,19]

The study involved administering IM testosterone to twenty patients, and only one patient (5%) developed pubic hair growth as a result of secondary sexual characteristics. The remaining 95% of the patients showed no signs of pubic hair growth, aggressive behavior, or genital pigmentation. These findings are consistent with few studies which reported similar results with intramuscular testosterone therapy.[15,16,21] These effects could be caused by various factors such as the choice of hormone therapy, timing of administration, appropriate dosage, and method of application (topical or parenteral). A survey reported that administering intramuscular testosterone at a dosage of 2mg/kg body weight could help minimize these effects.[17] Moreover, the single patient who developed pubic hair was the oldest among all the study participants, aged 108 months.

This study did not assess key parameters such as glans width, urethral plate dimensions, and penile shaft diameter, which are essential for a comprehensive understanding of the effects of intramuscular testosterone on proximal penile hypospadias. Additionally, no hormonal tests, such as measuring testosterone levels, were conducted to provide a biological explanation for the observed changes. Hormonal evaluations are needed to establish a link between endogenous testosterone levels and treatment effectiveness. Despite its limitations, this study offers important preliminary evidence that IM testosterone therapy, when used at an appropriate dosage, can reduce the severity of proximal penile hypospadias and minimize side effects. It sets the stage for more extensive research in the future. Well-designed studies are necessary to validate these findings and develop practical clinical guidelines.

CONCLUSION

In conclusion, all patients showed significant increases in proximal penile length, resulting in changes in the position of the meatus more distally. The difference in the position of the meatus before and after therapy is statistically significant. The comparison of the degree of chordee before and after testosterone therapy is also statistically significant.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Ethics Committee of Bangladesh Shishu Hospital and Institute (Date: 19.10.2022, Decision No: 2022692).

Informed Consent

Parents of all patients signed a free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Snodgrass W, Bush N. Recent advances in understanding/management of hypospadias. *F1000Prime Rep*. 2014;6:101. doi:10.12703/P6-101
2. Baskin LS, Ebbers MB. Hypospadias: anatomy, etiology, and technique. *J Pediatr Surg*. 2006;41(3):463-472. doi:10.1016/j.jpedsurg.2005.11.059
3. Mouriquand PDE, Delphine Demède, Daniela Gorduza, Pierre-Yves Mure, eds. HYPOSPADIAS. In: Pediatr Urology. 2nd ed. Saunders/Elsevier; 2010.
4. Montag S, Palmer LS. Abnormalities of penile curvature: chordee and penile torsion. *ScientificWorldJournal.*. 2011;11:1470-1478. doi:10.1100/tsw.2011.136
5. Biswas I, Chakraborty AK, Noor-ul Ferdous KMd, Sultana H. Single stage lateral based flap urethroplasty and two stage urethroplasty in proximal penile hypospadias with chordee : a prospective case control study. *Chatt Maa Shi Hosp Med Coll J*. 2014;13(3):26-29. doi:10.3329/cmoshmcj.v13i3.21018
6. Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, eds. Hypospadias. In: Campbell-Walsh-Wein Urology. 12th ed. Elsevier; 2020.
7. Canon S, Mosley B, Chipollini J, Purifoy JA, Hobbs C. Epidemiological assessment of hypospadias by degree of severity. *J Urol*. 2012;188(6):2362-2366. doi:10.1016/j.juro.2012.08.007
8. Hadidi AT, ed. Hypospadias Surgery: An Illustrated Textbook. Springer International Publishing; 2022. doi:10.1007/978-3-030-94248-9
9. Paiva KCDC, Bastos AN, Miana LP, et al. Biometry of the hypospadic penis after hormone therapy (testosterone and estrogen): a randomized, double-blind controlled trial. *J Pediatr Urol.* 2016;12(4):200.e1-200.e6. doi:10.1016/j.jpurol.2016.04.013
10. Azmy AF. General Princile. In: Hadidi AT, Azmy AF, eds. Hypospadias Surgery. Springer Berlin Heidelberg; 2004:87-92. doi:10.1007/978-3-662-07841-9_7
11. Luo CC, Lin JN, Chiu CH, Lo FS. Use of parenteral testosterone prior to hypospadias surgery. *Pediatr Surg Int*. 2003;19(1-2):82-84. doi:10.1007/s00383-002-0717-3
12. Khokar D, Patel R. Can testosterone alter the degree of hypospadias? a comprehensive study. *J Indian Assoc Pediatr Surg*. 2021;26(1):38. doi:10.4103/jiaps.JIAPS_214_19
13. Hadidi AT, ed. The Meatal-Based Flap Principle. In: Hypospadias Surgery: An Illustrated Textbook. 2nd ed. Springer International Publishing; 2022. doi:10.1007/978-3-030-94248-9
14. Barrett KE, Ganong WF, eds. Function of the Male Reproductive System. In: Ganong's Review of Medical Physiology. 24. ed. A Lange medical book. McGraw-Hill Med; 2012.
15. Ali MA, Palit PK, Hasanuzzaman M. Efficacy of preoperative intramuscular testosterone therapy for micro-phallic hypospadias. *Bangladesh J Child Health*. 2019;43(2):85-89. doi:10.3329/bjch.v43i2.42551
16. Nerli RB, Koura A, Prabha V, Reddy M. Comparison of topical versus parenteral testosterone in children with microphallic hypospadias. *Pediatr Surg Int*. 2009;25(1):57-59. doi:10.1007/s00383-008-2278-6
17. Chua ME, Gnech M, Ming JM, et al. Preoperative hormonal stimulation effect on hypospadias repair complications: meta-analysis of observational versus randomized controlled studies. *J Pediatr Urol*. 2017;13(5):470-480. doi:10.1016/j.jpurol.2017.06.019
18. Bastos AN, Oliveira LRS, Ferrarez CEPF, De Figueiredo AA, Favorito LA, Bastos Netto JM. Structural study of prepuce in hypospadias—does topical treatment with testosterone produce alterations in prepuce vascularization? *J Urol*. 2011;185(6S):2474-2478. doi:10.1016/j.juro.2011.01.035
19. Menon P, Rao KLN, Handu A, Balan L, Kakkar N. Outcome of urethroplasty after parenteral testosterone in children with distal hypospadias. *J Pediatr Urol*. 2017;13(3):292.e1-292.e7. doi:10.1016/j.jpurol.2017.01.001

20. Koff SA, Jayanthi VR. Preoperative treatment with human chorionic gonadotropin in infancy decreases the severity of proximal hypospadias and chordee. *J Urol.* 1999;162(4):1435-1439. doi:10.1016/S0022-5347(05)68333-4

21. Ahmad R, Chana RS, Ali SM, Khan S. Role of parenteral testosterone in hypospadias: a study from a teaching hospital in India. *Urol Ann*. 2011;3(3):138-140. doi:10.4103/0974-7796.84966

MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

doi: 10.51271/SOC-0027

Usage and awareness of nutritional screening tools by nurses caring for pediatric patients in Yozgat province

Kübra Taşdan[1], Yeşim Andıran Şenaylı[2], Zeynep Çiçek[3]

[1]Department of Nutrition, Faculty of Medicine, Yozgat Bozok University, Yozgat, Turkiye
[2]Department of Anesthesiology and Reanimation, Faculty of Medicine, Yozgat Bozok University, Yozgat, Turkiye
[3]Nurse Director, Faculty of Health Sciences, Yozgat Bozok University, Yozgat, Turkiye

Received: 12/11/2024 ◆ **Accepted**: 04/12/2024 ◆ **Published**: 20/01/2025

Cite this article: Taşdan K, Andıran Şenaylı Y, Çiçek Z. Usage and awareness of nutritional screening tools by nurses caring for pediatric patients in Yozgat province. *Surg Child.* 2025;2(1):11-16.

Corresponding Author: Kübra Taşdan, dytkubratasdan@gmail.com

ABSTRACT

Aims: Malnutrition is a significant health issue in children and is closely related to prolonged hospital stays, increased complications, and mortality risk in hospitalized children. Effective use of nutritional screening tools is crucial for early detection of malnutrition. In this context, the active use of nutritional screening tools, the skill to use these tools, and the level of awareness about these tools among nurses who closely care for pediatric patients are vital factors that can potentially improve pediatric patients' health. Our study examines the usage and awareness of nutritional screening tools among nurses caring for pediatric patients in Yozgat province, a region with unique healthcare challenges and opportunities.

Methods: The study was planned as a prospective, descriptive, and cross-sectional design. Ninety-four nurses caring for pediatric patients in Yozgat province and its districts were administered an online questionnaire of 22 questions, which was designed to assess their knowledge, skills, and attitudes towards nutritional screening tools. The questionnaire was distributed through a secure online platform and included both closed-ended and open-ended questions. Data were evaluated using descriptive statistics with SPSS version 27.0.

Results: Of the participants, 78.7% were female and 21.3% were male. 60.6% of the participants were in the age range of 25-34 years, 62.8% had a bachelor's degree, 66% worked at state university hospitals, 30.9% had 6-10 years of professional experience, 74.5% were service nurses, and 39.4% had been involved with pediatric patients for 0-1 years. The most frequently cared age group was 3-6 years (19.9%) and 1-3 years (18.1%). 27.7% of the participants assessed nutrition risk status using visual assessment, 25.5% through anthropometric measurements, and 34% reported referring the physician and dietitian for intervention in risk detection. 47.9% indicated the presence of a screening scale in their institution, 57.1% used the form, 25.5% did not know the name of the screening scale, and 6.4% used the StrongKids scale.

Conclusion: Our study determined that nurses caring for pediatric patients often consider the screening scale as a secondary option for identifying the nutrition risk status, predominantly performing visual and anthropometric evaluations, and did not demonstrate sufficient proficiency or importance regarding screening scales. Although the determination of risk status varies according to the scale used, the significance of screening scales in detecting malnutrition is substantial. Therefore, our study recommends that necessary training be provided to pediatric nurses to use these tools more effectively and that current practices be reviewed. This will not only enable better assessment of the nutritional status of pediatric patients but also instill hope for the implementation of steps to prevent malnutrition.

Keywords: Malnutrition, nutritional screening tools, pediatric patient, pediatric nursing

Presented as an oral presentation at the 41st National Congress of Pediatric Surgery/27th National Pediatric Surgery Nursing Congress (Nevşehir, Turkiye), November 7-10, 2024.

INTRODUCTION

The development of children's nutritional skills can influence their optimal nutritional status, and deficiencies in these skills may lead to chronic diseases and malnutrition in the future.[1] Therefore, efforts are being made to assess individuals' nutritional status.[2,3] Nutritional monitoring is especially crucial for diseases such as cancer.

Malnutrition is a significant health issue and is closely related to prolonged hospital stays, growth retardation in children, increased complications, and mortality risk.[4-7] Adverse outcomes such as muscle tissue loss, delayed wound healing, and prolonged hospitalizations are potential complications in prolonged stays and malnutrition.[3,8]

For these reasons, the effective use of nutritional screening tools is vital for the early detection of malnutrition. Improving individuals' health status can be achieved in this way.[3,4] During the treatment of diseases such as cancer in children, the use

and awareness of screening tools by dieticians and nurses are essential.[2] Various nutritional screening tools such as STRONGkids, pediatric nutrition screening tool (PNST), pediatric Yorkhill malnutrition score (PYMS), and subjective global nutritional assessment (SGNA) are used for this purpose.[3,8-10] Some studies have pointed out that the complexity of existing pediatric screening tools poses a barrier to their widespread clinical application.[9] Therefore, it is suggested that the validity, effectiveness, and ease of use of pediatric nutritional screening tools should be evaluated to improve the nutritional care processes in hospital settings.

Based on this information, nurses caring for pediatric patients' active use of nutritional screening tools, their skills in using these tools, and their awareness about them are vital factors that can potentially improve pediatric patients' health. Studies are being conducted on the content, general characteristics, and validity and reliability of scales used to screen and assess the nutritional status of pediatric patients in Turkey.[5] However, it should also be noted that there is a lack of data in Turkey. The aim of our study is to examine the usage and awareness of nutritional screening tools among nurses caring for pediatric patients in Yozgat province.

METHODS

The study was planned as a prospective, descriptive, and cross-sectional design after obtaining permission from the Ethics Committee of Yozgat Bozok University Social and Human Sciences (Date: 28.06.2024, Decision No: 15/22). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. A 22-question online questionnaire was administered to 94 nurses caring for pediatric patients in Yozgat province and its districts. Data were evaluated using descriptive statistics with SPSS version 27.0. The results were discussed alongside the literature.

RESULTS

Of the participants, 78.7% were female. The group predominantly comprised nurses aged 25-34 (60.6%). 62.8% had a bachelor's degree. 66% worked in state university hospitals. 30.9% of the nurses had been practicing nursing for 6-10 years and constituted the majority. The proportion of service nurses was 78.7%. The percentage distribution of the ages of the patients the employees cared for showed similarities. These distributions are presented in **Table 1**.

Table 1. Demographic information of individuals

Gender	Number (n)	Percent (%)
Female	74	78.7
Male	20	21.3
Age		
18-24	9	9.6
25-34	57	60.6
35-44	22	23.4
45 years and older	6	6.4
Education		
High school	8	8.5
Associate	13	13.8
Bachelor	59	62.8
Master's	11	11.7
Doctorate	3	3.2
Institution worked		
State university hospital	62	66.0
State hospital	8	8.5
City hospital	20	21.3
Private hospital/clinic	1	1.1
Family health center	3	3.2
Years in profession		
0-1 year	7	7.4
2-5 years	20	21.3
6-10 years	29	30.9
11-15 years	23	24.5
16 years and older	15	16.0
Job in the unit		
Service nurse	74	78.7
Clinic nurse	8	8.5
Neonatal nurse	10	10.6
Family health center nurse	2	2.1
Years caring for pediatric patients		
0-1 year	37	39.4
2-5 years	26	27.7
6-10 years	17	18.1
11-15 years	8	8.5
16 years and older	6	6.4
Frequently cared age groups*		
0-1 age range	37	17.1
1-3 age range	39	18.1
3-6 age range	43	19.9
6-9 age range	32	14.8
9-12 age range	27	12.5
12-18 age range	38	17.6

24.8% of the participants reported having heard of the pediatric nutrition risk score (PNRS), 8.5% reported having heard of the SGNA, 17.0% reported having heard of the screening tool for malnutrition assessment in children (STAMP), 4.6% reported having heard of the PYMS, 15.0% reported having heard of the Screening Tool for Nutrition Status and Growth Risk (STRONGkids), 9.8% reported having heard of the PNST, while 20.3% reported having heard of none of these tools. These data are presented in **Table 2**.

51.1% used anthropometric measurements (such as height, weight, and head circumference) for every hospitalized pediatric patient, 11.7% sometimes used them, and 37.2% did not use them at all; 19.9% used a screening scale, 25.5% used anthropometric measurements, 12.8% used biochemical findings, and 27.7% used visual assessment to determine nutrition risk status, while 14.2% did not use any of these methods. These results are presented in **Table 3**.

47.9% of the participants indicated that a screening scale was used to evaluate the nutrition risk status of children in their institution, 28.7% stated it was not used, and 23.4% were unsure. 1.1% indicated they used anthropometric measurements as a form, 1.1% used percentiles, 3.2% used the child health monitoring form, 1.1% used the nutrition status evaluation form, 2.1% used the child nutrition form, 1.1% used the NRS-2002 form, 4.3% used the nutrition form, and 6.4% used the STRONGkids form, while 27.6% did not know which form was used. Results are detailed in **Table 3**.

40.0% of the participants stated they used this form regularly; 1.1% did not use it due to increased workload; 21.1% did not know how to use it, 30.0% indicated that there was no form available; 4.4% said the physician did not request it, and 3.3% stated they did not see the need for it. Results are shown in **Table 3**.

Table 2. Knowledge of nutritional screening tools among individuals

Information on which screening scales nurses have heard of*		
	Number (n)	**Percent (%)**
Pediatric nutrition risk score (PNRS)	38	24.8
Subjective global nutritional assessment (SGNA)	13	8.5
Screening tool for malnutrition assessment in children (STAMP)	26	17.0
Pediatric Yorkhill malnutrition score (PYMS)	7	4.6
Screening tool for nutrition status and growth risk (STRONGkids)	23	15.0
Pediatric nutrition screening tool (PNST)	15	9.8
None	31	20.3
Information on which screening scales nurses have used	**Number (n)**	**Percent (%)**
Pediatric nutrition risk score (PNRS)	31	23.7
Subjective global nutritional assessment (SGNA)	13	9.9
Screening tool for malnutrition assessment in children (STAMP)	13	9.9
Pediatric Yorkhill malnutrition score (PYMS)	6	4.6
Screening tool for nutrition status and growth risk (STRONGkids)	19	14.5
Pediatric nutrition screening tool (PNST)	8	6.1
None	41	31.3

*More than one choices were marked

Table 3. Usage information of nutritional screening tools by individuals

Use of anthropometric measurement for every hospitalized child	**Number (n)**	**Percentage (%)**
Yes	48	51.1
No	35	37.2
Sometimes	11	11.7
Methods for assessing nutrition risk status*		
Screening scale	28	19.9
Anthropometric measurement	36	25.5
Biochemical findings	18	12.8
Visual assessment	39	27.7
None	20	14.2
Intervention methods for nutrition risk identification *		
Referred to physician	82	65.1
Referred to dietitian	37	29.4
Unsure	7	5.6
Use of screening scale for evaluating nutrition risk status of children in the institution		
Yes	45	47.9
No	27	28.7
Unsure	22	23.4
Form used for evaluation**		
Anthropometric measurement	1	1.1
Percentile	1	1.1
Child health monitoring form	3	3.2
Nutrition status evaluation form	1	1.1
Child nutrition form	2	2.1
NRS-2002 form	1	1.1
Nutrition form	4	4.3
STRONGkids	6	6.4
Unsure	26	27.6
Information on the use of form for evaluating nutrition risk status of children by nurses*		
I use it	36	40.0
I don't use it;		
Increases my workload	1	1.1
I don't know how	19	21.1
No form	27	30.0
Physician does not request	4	4.4
I don't feel the need	3	3.3

*More than one choices were marked.
**Evaluated among replies "Yes"

When identifying nutrition risks, 65.1% of the participants referred to a physician, 29.4% referred to a dietitian for intervention, and 5.6% were unsure how to intervene.

DISCUSSION

In our study, participants, composed of nurses, were asked about nutrition evaluation, various screening tests, their knowledge about usage, and what assessments were made in nutrition evaluation. The responses given were evaluated. Among the participants, 20 nurses (14.2%) stated that no nutritional assessment was conducted with any application, and 52.1% of the nurses reported that there was no institutional information provided on this issue, or if there was, they were not informed about it; 27.6% were unaware of any screening tools. The most cited reason for not using screening tools was the absence of a form. Nevertheless, 95% of the nurses said there must be an intervention for patients with a nutritional problem.

Various screening tools used to identify functional nutritional disorders in children are effective, and the significance of screening scales in detecting malnutrition is considerable.[1,4] Some of these tools have demonstrated the ability to quickly and accurately identify nutritional disorders in children. However, it is also recognized that some tools contain numerous questions, making their use complex. Overall, research findings emphasize the importance of selecting an appropriate screening tool for detecting nutritional disorders in children for healthcare professionals.[1] However, it reveals that these tools are generally underutilized and that more studies are needed.[4] Our study also determined that nurses caring for pediatric patients considered the screening scale as a secondary option for identifying the nutrition risk status, predominantly performing visual and anthropometric evaluations, and did not demonstrate sufficient proficiency or importance regarding screening scales. Among the participants, 31 nurses (20.3%) reported they were unaware of the screening tools, and 41 nurses (31.3%) stated they did not use screening tools, which is considered a significant figure. Although it was determined that visual and anthropometric evaluations were being conducted, it was found that 35 nurses (37.2%) did not perform anthropometric measurements. Similar findings were noted in a study conducted in Canada, where more than 50% of nurses underestimated the prevalence of malnutrition in hospitalized patients, yet 92.5% were willing to include a nutritional screening process in inpatient admission procedures.[4] In the same study in Canada, 17% of nurses indicated that helplessness in eating was a significant cause of malnutrition, 39% reported limited access to nutrition education, and 92% expressed interest in such training.

In a study conducted in Korea, 78.7% of nurses believed that nutritional management was necessary, a value lower than what we found in our study. In the same study, 34.9% of nurses claimed to have knowledge of at least one criterion for nutritional assessment, but the percentage of those aware of the normal range for body-mass index (BMI) was only 0.9%, indicating a significantly low level of awareness. Our study similarly found a meager percentage of knowledge regarding screening tools and low usage rates of assessment criteria outside of the screening tools.

Similar results were found in a study conducted in New Zealand. It was observed that the use of nutritional screening tools for pediatric oncology patients was limited, and dieticians had insufficient awareness and resources.[2] Standard screening and assessment methods for detecting malnutrition were recommended. It was understood that the usage issues faced in various world regions share common causes.

Another study found that pediatric malnutrition screening tools are beneficial in clinical use, but some challenges were faced in practice.[11] Newly developed tools effectively monitor malnutrition risk, especially in children who stay in the hospital for a long time. However, it was noted that the most significant barriers faced by healthcare workers in using these tools were time, cost, and resource shortages. The importance of simplifying and integrating these tools into healthcare processes was emphasized.[11]

Another issue regarding usage is that the reliability and validity of nutritional screening tools used to identify pediatric malnutrition may vary.[3] However, it has also been emphasized that these tools are essential for the early detection of malnutrition.[3] A study evaluating the PYMS screening tool and STRONGkids found that PYMS had higher sensitivity and specificity in detecting malnutrition risk than STRONGkids. The sensitivity of PYMS was 95.7%, and its specificity was 66.7%. In contrast, the sensitivity of STRONGkids was 52.2%, and its specificity was 41.7%. The results indicate that PYMS is a more reliable and effective tool for screening malnutrition in children. It is noted that PYMS is a practical screening tool and can be preferred in clinical settings, mainly due to its ability to be applied in a short time.[10] In another study, STAMP, STRONGkids, and the PYMS were found to have moderate validity and reliability in hospital settings.[7] However, it was determined that tools used in community settings did not meet these criteria. The research highlights that the validity and reliability of nutritional screening tools show differences based on the users and that the tools should be standardized. As a result, it is stated that the tools used for detecting pediatric malnutrition need more validation studies.[3,7] Most existing screening tools have not been tested in specific age groups or integrated into electronic health records.[4] Tools like STRONGkids and PNST are essential for the early detection of malnutrition, but there is a need for more valid studies in younger age groups and broader populations. It is emphasized that increasing training and widespread use of the tools in clinical practice is necessary.[4] In this context, it can be concluded that an ideal nutritional screening tool should correctly identify high-risk patients while excluding those with low risk.[3]

In another study, it was determined that both STRONGkids and PNST screening tools could identify the risk of malnutrition in children, but the initially proposed cutoff points were not suitable for the study population.[12] In the same study, adjustments based on ROC curve analysis showed that both tools had better concordance with nutritional status assessment when adjusted cutoff points were applied.[12] In particular, PNST was found to have a higher sensitivity with adjusted cutoff points and was more suitable for clinical use. Both tools could assist in detecting malnutrition, but PNST was noted as the most appropriate tool with the revised cutoff points.[12] In another study, PNST was found to be a simple screening tool that quickly and accurately detects the risk of malnutrition in pediatric patients.[9] The study demonstrated that PNST showed 77.8% sensitivity and 82.1% specificity compared to the

Pediatric SGNA. These results indicate that PNST is a reliable and applicable option for effectively detecting malnutrition risk in pediatric hospital admissions as an alternative to the more complex existing tools. However, it was also noted that PNST has limitations in detecting particularly chronic malnutrition or overweight children.[9]

Some studies have reported positive results and a continuous increase in the use of nutritional screening tools. In a study conducted in Belgium, the STRONGkids screening tool effectively identified malnutrition risk in hospitalized children.[13] The study determined that STRONGkids could detect acute malnutrition with 71.9% sensitivity and a 94.8% negative predictive value (NPV). The tool was also associated with the length of hospital stay, indicating that children who stayed there for 4 days or longer were at risk of malnutrition. The tool also showed a high predictive value (98.9%) for initiating nutritional interventions. As a result, STRONGkids was indicated to be both a practical and a reliable tool for determining the risk of malnutrition in children.[13] In a study conducted in Brazil, the STRONGkids tool demonstrated strong performance in predicting prolonged hospital stays in pediatric patients.[13] It was found that children with 3 points behaved similarly to those at high risk with 4 or 5 points. Therefore, it was concluded that patients scoring 3 points with STRONGkids in hospitals in Brazil should be considered at high risk, similar to those scoring 4 or 5 points. This is an essential step in preventing extended hospital stays and adverse clinical outcomes.[14]

A study conducted in Turkey noted that scales used for screening pediatric nutritional status may not be suitable for every patient and that ethnic, developmental, and disease-specific differences could affect the effectiveness of screening tools.[5] In this study, it was particularly stated that scales such as STRONGkids and the PYMS were widely used to determine the risk of malnutrition in children, but there were limited validity and reliability studies on these scales in Turkey.[5] It was concluded that the simplicity and practicality of existing scales supported their widespread use in practice. The importance of education for healthcare professionals to increase the use of screening and assessment tools was emphasized.[5] Another study conducted in Turkey used the STRONGkids screening tool, which was found to be reliable for assessing nutrition risk in neurology patients. In this study, patients at risk of malnutrition were identified through screening, and opportunities for early intervention were provided. Furthermore, it was concluded that STRONGkids, a simple and practical screening tool, could be widely used in clinical settings. However, it was emphasized that more detailed assessments are needed, especially for identifying advanced malnutrition cases.[6]

In another study, 302 nurses participated in an evaluation in Turkey. The level of knowledge regarding nutrition was around 50%, and it was recommended that nursing education institutions review their curricula in terms of clinical nutrition education and develop a regular nutritional education program. This recommendation is consistent with our conclusions.[15]

In cases with a high rate of underutilization or unawareness of screening tools, awareness-raising efforts should be made to mitigate this situation. For example, a study conducted in Norway aimed to evaluate the changes in clinical nutritional care after ten years of implementing national nutritional guidelines. A study conducted in 2004 revealed that there was a lack of information about nutritional care among doctors and nurses, and inconsistencies were found in practices.[16] A follow-up study with a similar questionnaire in 2014 showed significant improvements in nutritional practices. In a similar study in Norway, while 67% of participants identified the lack of information as a fundamental barrier in 2004, this rate decreased to 57% in 2014 ($p<0.001$).[17] In this study, findings from 2004 indicated that similar to our study, only 46% of nurses had difficulties identifying undernourished patients, assessing their energy needs, and developing a nutritional plan. However, in 2014, it was observed that 57% of the participants were knowledgeable about the topic, indicating an increase in their level of knowledge.[17]

In a study conducted in England evaluating the use of nutritional screening tools, various recommendations were made to increase the use of these tools.[18] It was emphasized that regular routines are essential to maintain nutritional screening effectively. Most participants indicated that they developed various routines, such as conducting weekend screenings, to ensure that the screening process was not interrupted. The importance of nutritional assessment and communication with patients was highlighted regarding good practices in nutritional care. Participants noted that understanding patients' nutritional habits and developing personalized nutrition plans were critical for providing adequate care. It was concluded that nurses should have more autonomy in nutritional care. Nutritional screening is seen as a process that requires clinical judgment, and it is suggested that increasing nurses' decision-making authority will enhance the quality of nutritional care.[18]

CONCLUSION

It is recommended that necessary training be provided to pediatric nurses to use these tools more effectively and that current practices be reviewed. This will enable better assessment of the nutritional status of pediatric patients and the implementation of steps to prevent malnutrition. It is stated that there is a need to increase awareness of nutritional assessment and human resources to ensure the use of the mentioned tools, and steps should be taken to promote the more widespread use of screening tools as indicated in the literature.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of Yozgat Bozok University Social and Human Sciences Ethics Committee (Date: 28.06.2024, Decision No: 15/22).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Litchford A, Wengreen H, Savoie-Roskos MR. Tools available to screen for child feeding dysfunction: a systematic review. *Appetite*. 2021;167:105611. doi:10.1016/j.appet.2021.105611
2. Lovell AL, Laughton S, Wood A, Pugh G. Nutrition screening, assessment, and intervention practices for children with cancer in Aotearoa, New Zealand. *Nutrition*. 2023;116:112218. doi:10.1016/j.nut.2023.112218
3. Oksuz Esen C, Arusoglu G. Nutritional screening tools used in pediatric malnutrition. *TJFMPC*. 2023;17(1):195-206 doi:10.21763/tjfmpc.1067603
4. Becker PJ, Brunet-Wood MK. Pediatric malnutrition screening and assessment tools: analyzing the gaps. *Nutr Clin Prac*. 2022;37(5):1088-1104. doi:10.1002/ncp.10793
5. Zeybek C, Özkaya V. Pediatrik hastalarda beslenme durumunun taranması ve değerlendirilmesinde kullanılan ölçekler. *Sağlık ve Yaşam Bilimleri Dergisi*. 2023;5(3):170-179.
6. Örnek SH. (Tez) Strong kids (bozulmuş beslenme durumu ve büyüme riski için (tarama aracı) nöroloji servisinde yatan 5 ay-18 yaş grubu hastalara uygulanması. Aycan Ünalp (Danışman) 2018, S.B.Ü İzmir Dr. Behçet Uz Çocuk Hastaliklari Ve Cerrahisi Eğitim Ve Araştirma Hastanesi.
7. Becker PJ, Bellini SG, Vega MW, et al. Validity and reliability of pediatric nutrition screening tools for hospital, outpatient, and community settings: a 2018 evidence analysis center systematic review. Academy of nutrition and dietetics. *J Acad Nutr Diet*. 2020;120(2):288-318. doi:10.1016/J.Jand.2019.06.257
8. Oruçoğlu B. Hastanede yatan çocuklarda STRONGkids tarama aracı ile malnutrisyon riskinin belirlenmesi. Tez, Danışman Noğay NH, 2016, Kayseri. Erciyes Üni Sağlık Bilimleri Enst., Beslenme ve Diyetetik AD.
9. White M, Lawson K, Ramsey R, et al. Simple nutrition screening tool for pediatric inpatients. *JPEN J Parenter Enteral Nutr*. 2016;40(3):392-398. doi: 10.1177/0148607114544321
10. Lestari NE, Nurhaeni N, Wanda D. The pediatric Yorkhill malnutrition score ıs a reliable malnutrition screening tool. *Compr Child Adolesc Nurs*. 2017;40(sup1):62-68. doi:10.1080/24694193.2017.1386972
11. Hulst JM, Huysentruyt K, Joosten KF. Pediatric screening tools for malnutrition: an update. *Curr Opin Clin Nutr Metab Care*. 2020;23(3):203-209. doi:10.1097/MCO.0000000000000644
12. Carter LE, Shoyele G, Southon S, et al. Screening for pediatric malnutrition at hospital admission: which screening tool ıs best?. *Nutr Clin Pract*. 2020;35(5):951-958. doi:10.1002/ncp.10367
13. Huysentruyt K, Alliet P, Muyshont L, et al. The STRONG(kids) nutritional screening tool in hospitalized children: a validation study. *Nutrition*. 2013;29(11-12):1356-1361. doi:10.1016/j.nut.2013.05.008
14. Castro JDS, Santos CAD, Rosa COB, Firmino HH, Ribeiro AQ. STRONGkids nutrition screening tool in pediatrics: An analysis of cutoff points in Brazil. *Nutr Clin Pract*. 2022;37(5):1225-1232. doi:10.1002/ncp.10807
15. Yalcin N, Cihan A, Gundogdu H, Ocakci A. Nutrition knowledge level of nurses. *Health Sci J*. 2013;7(1):99-108
16. Lane C, Wedlake LJ, Dougherty L, Shaw C. Attitudes towards and knowledge of nutrition support amongst health care professionals on London intensive care units. *J Hum Nutr Diet*. 2014;27(Suppl 2):339-351. doi:10.1111/jhn.12152
17. Fjeldstad SH, Thoresen L, Mowé M, Irtun Ø. Changes in nutritional care after implementing national guidelines-a 10-year follow-up study. *Eur J Clin Nutr*. 2018;72(7):1000-1006. doi:10.1038/s41430-017-0050-5
18. Chapman C, Barker M, Lawrence W. Improving nutritional care: innovation and good practice. *J Adv Nurs*. 2015;71(4):881-894. doi:10.1111/jan.12571

MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

doi: 10.51271/SOC-0028

Does hypertension develop in children patients who underwent pyeloplasty due to unilateral ureteropelvic junction stenosis?

Derya Yayla[1], Hüseyin Tuğrul Tiryaki[2]

[1]Department of Pediatric Urology, Gaziantep City Hospital, Gaziantep, Turkiye
[2]Department of Pediatric Urology, Ankara Bilkent City Hospital, Ankara, Turkiye

Received: 24/11/2024 ◆ **Accepted**: 12/12/2024 ◆ **Published**: 20/01/2025

Cite this article: Yayla D, Tiryaki HT. Does hypertension develop in children patients who underwent pyeloplasty due to unilateral ureteropelvic junction stenosis?. *Surg Child*. 2025;2(1):17-20.

Corresponding Author: Derya Yayla, dryayla@yahoo.com

ABSTRACT

Aims: Hypertension may develop in children with renal and cardiovascular pathologies. In our study, we aimed to investigate the prevalence of hypertension in children who underwent pyeloplasty.

Methods: We retrospectively evaluated the blood pressure values measured in the postoperative period in children who were diagnosed with ureteropelvic junction stenosis and underwent pyeloplasty in the pediatric urology clinic of Ankara City Hospital between 2007 and 2020.

Results: In our study, 167 patients (48 women, 123 men; mean age 3.6; 58 right, 109 left) who underwent pyeloplasty due to UPJO were evaluated. In the postoperative follow-up, hypertension was detect-ed in 5 patients (2.9%). Bilateral patients were excluded from the study. Of the 5 patients who developed hypertension, one had a pelvic ectopic kidney and one had a contralateral multicystic dysplastic kidney. All of the patients who developed hypertension had intrinsic UPJO; 3 of them were catheterized with a percutaneous nephrostomy catheter preoperatively. The mean MAG3 function was 43.3%. While the mean follow-up period of the patients was 5.6 years, it was ob-served that hypertension developed in an average of 3.5 years. In the postoperative period, there was an average increase of 1.2% in the functions of these five patients in the control scintigraphy. No patient who developed hypertension underwent a second surgical intervention.

Conclusion: In cases where pyeloplasty was performed due to UPJO, blood pressure should be monitored in the postoperative period. Blood pressure should be checked, especially in advanced hydronephrotic patients with a history of percutaneous nephrostomy in the preoperative period.

Keywords: Ureteropelvic junction obstruction, hypertension, pyeloplasty, percutaneous nephrostomy

INTRODUCTION

The prevalence of hypertension in children is considered to be 0.5-1.2%, increasing to 3-5% during adolescence. The causes of hypertension in children are categorized as essential (primary) (2-20%) and secondary (79-98%). Causes of secondary hypertension include kidney diseases, vascular disorders, endocrine factors, neurological disorders, and medication use. Renal parenchymal diseases account for 75-80% of pediatric hypertension cases.[1]

While most glomerulonephritis cases and congenital anomalies are easily detected during initial screening, recurrent urinary infections are often overlooked, which frequently leads to missed diagnoses of reflux nephropathy. Although severe hypertension may develop in some of these patients, clinical findings can remain unclear. Even in congenital obstructions of the urinary system, such as ureteropelvic junction obstructions (UPJO), hypertension may develop. Additionally, hereditary cystic kidney diseases, renal trauma, ischemia, infarction, and compression may lead to renal parenchymal damage, thereby causing hypertension.[2]

In our study, we aimed to investigate the prevalence of hypertension in children who underwent pyeloplasty due to UPJO.

METHODS

The study was conducted with the permission of the Clinical Researches Ethics Committee of Ankara City Hospital No. 1 (Date: 14.05.2020, Decision No: E1-20-592). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Between January 2007 and March 2020, a retrospective review was conducted on 167 patients who underwent pyeloplasty due to ureteropelvic junction obstruction at the Pediatric Urology Clinic of Ankara City Hospital. In the operations,

dismembered pyeloplasty was performed using the Anderson-Hynes technique with a retroperitoneal approach and a mini flank incision. All patients received a perioperative ureteral stent (either external or internal). Postoperatively, an external stent (Pippi Salle catheter) was applied for 10 days, or an internal stent (double-J catheter) was used for one month. Antibiotic prophylaxis was administered only during the first postoperative month while the catheter was in place; it was not continued thereafter. Patients were retrospectively analyzed for gender, age at the time of operation, side of operation, initial presenting symptoms, intrinsic or extrinsic (vascular compression) causes of UPJO, history of antenatal hydronephrosis, urinary ultrasound findings, percentage of renal function, preoperative and postoperative kidney function percentages in MAG-3 scintigraphy, follow-up duration, and blood pressure values. In this study, conducted on patients followed for an average of 6.7 years (±4.2 years), long-term clinical outcomes were evaluated.

Our study included 167 cases (121 boys, 46 girls) (58 right-sided, 109 left-sided). The mean age of the patients was determined to be 44.5±53 months. Demographic characteristics are presented in **Table 1**. Approximately 50% of the patients with preoperative hydronephrosis had a history of antenatal hydronephrosis. None of the patients had a history of hypertension prior to pyeloplasty. Percutaneous nephrostomy was performed preoperatively in 11 patients (6%) with severe hydronephrosis, and postoperative hypertension developed in two of these patients. No cases of hypertension were observed in patients with severely reduced renal function (below 20%) as shown on renal scintigraphy. During an average follow-up period of 3.5 (±1.5) years, hypertension developed in only 2.8% of all patients (5 cases).

RESULTS

In 9 patients (5.2%) who underwent pyeloplasty due to UPJO, vesicoureteral reflux (VUR) was detected on the same side. During follow-up, spontaneous resolution was observed in 7 (4%) cases, while 2 cases with grade 4-5 VUR underwent subureteral injection. None of the patients with both UPJO and VUR on the same side developed hypertension. However, after several years, transient hypertension developed in two patients with stage 2 VUR detected on the contralateral side, with an average follow-up period of 4 years. In these two patients, subureteral injections were performed in case of urinary tract infections (UTI) while they were on antibiotic prophylaxis. These temporary hypertensive patients discontinued their antihypertensive medication once their blood pressure returned to normal, as they did not use the medication regularly.

Renal stones were detected in 21 patients (12.2%). Among these, 10 patients with preoperative stones did not undergo surgery, while 5 patients had perioperative (same session) treatment, 2 patients had treatment before surgery, and 2 patients had laser lithotripsy after surgery. Follow-up showed 3-4 mm stones in 2 cases. No statistically significant correlation was found between nephrolithiasis and VUR (p=0.084). None of the patients with nephrolithiasis developed hypertension.

Postoperatively, drainage with a double-J catheter was performed in 7 patients due to temporary obstruction. The average age of these 6 patients was 13 months, and one patient was 13 years old. Additionally, 5 patients underwent reoperation due to persistent obstruction in postoperative follow-up (4 patients had an average age of 5 months, and one patient was 17 years old). In the 12 patients who underwent reoperation due to temporary or persistent obstruction after pyeloplasty, none developed hypertension during their follow-up.

The characteristics of the patients who developed hypertension after pyeloplasty are shown in **Table 2**. All 5 patients who developed hypertension had intrinsic obstruction as the etiology and underwent pyeloplasty. None of these patients required reoperation after their initial surgeries for UPJO. During follow-up, kidney function values (creatinine, urea) remained normal, and no proteinuria was detected in urine samples. After 24-hour blood pressure holter monitoring, 2 patients with high blood pressure values required antihypertensive medication. Only one of these patients was obese and had a high renal Doppler resistance index. However, hypertension improved with weight control in the obese patient.

Table 1. Summary of patient demographic characteristics

Characteristic	All patients	HT patients
Gender	Female: 4, male: 121	Female: 3, male: 2
Average age (months)	44.5 (±43.3)	46.4
Age groups	<1 year: 74, ≥1 year: 101	<1 year: 2, ≥1 year: 3
Side	Right: 58, left: 109, bilateral: 4	Right: 4, left: 1
Reason for application	AHN: 90, Pain: 64, UTI history: 21	AHN: 4
Preoperative nephrostomy	11	2
Cause	Intrinsic: 154, vascular compression: 21	Intrinsic: 5
Renal function percentage (%)	<20: 13, 21-40: 88, 41-55: 68, >55: 6	<20: 0, 21-40: 2, 41-55: 3
VUR	11 (9 same side, 2 opposite side)	2 (opposite side)
Stone association (pre/postoperative)	19/2	-
Other renal atrophy	2	1
Postoperative renal function increase	2.31%	1.2%
Additional diseases	Cardiac: 4, thyroid: 4, neurological: 6, hematological: 3	Cardiac: 1, neurological: 1
Continuation of postoperative UPJO		
Temporary stenosis	7	-
Permanent stenosis- reoperated	5	-
None	163	5
Follow-up duration (years)	6.7	5.6

Abbreviations: AHN: Antenatal hydronephrosis, VUR: Vesicoureteral reflux, UTI: Urinary tract infection, HT: Hypertension, UPJO: Ureteropelvic junction obstructions

Table 2. Summary of characteristics of hypertensive patients

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender Age (months)	Male 20 days	Male 13 months	Male 10 years	Female 10 months	Female 28 months
Antenatal hydronephrosis	Yes	Yes	No	Yes	Yes
Reason for preoperative referral	AHN	AHN	UTI	AHN	AHN
Co-morbidity	Left MCDR PUV	-	-	Right ectopic renal Right UVJO	Castello syndrome Cardiomyopathy Cerebral dysfunction
Preoperative nephrostomy	Yes	No	Yes	No	No
VUR	No	Left Grade 2 (STING)	No	Left Grade 2 (STING)	No
Postoperative HT development time (years)	1 month	Temporary, 3 years	Temporary, 4 years	Temporary, 5 years	2 years
Blood pressure	High	Normal	Normal	Normal	High
MAG-3 DRF (preop- postop)	50-50%	50-53%	36-37%	34-35%	47-48%
Renin (N: 0.5-5.8) value	1.4 (N)	3.5 (N)	15.73 (High)	1.42 (N)	6.8 (High)
Aldesteron value	25 (N)	21 (N)	31.6 (N)	34 (N)	23 (N)
Blood lipid values	N	N	N	T-Col 158, TG 42, HDL-Col 52	N
Obesity	-	-	-	obesity (+)	-
Renal Doppler RI value	Normal	Normal	Normal	Left 0.84 (high)	Normal
Antihypertensive drug used and duration	Capril (1 year)	-	-	-	Amlodipine, dideral (5 years)
Follow-up duration (years)	6	4	5	6	7

Abbreviations: MCDR: Multicystic dysplastic renal, PCN: Percutaneous nephrostomy, VUR: Vesicoureteral reflux, STING: Subureteric injection, UVJO: Ureterovesical junction obstruction, PUV: Posterior urethral valv, MPS: Muco-polysaccharidosis, AHN: Antenatal hydronephrosis, DRF: Differential renal function on scintigraphy, HT: Hypertension, UTI: Urinary tract infection, Preop: Preoperative, Postop: Postoperative

DISCUSSION

Hypertension is a major risk factor for heart, brain, and vascular diseases in older ages, with roots extending back to childhood. However, the prevalence of hypertension in childhood is lower than in adults (1-2%).[1] The causes of hypertension vary with age. Congenital kidney diseases or cardiovascular factors are leading causes of hypertension in infants and young children. In older children, renal parenchymal diseases, such as reflux nephropathy and chronic glomerulonephritis, are more common.[2] In adolescents, the most frequent cause is primary hypertension. Reflux nephropathy, commonly seen in children, is an important factor in the development of hypertension, with hypertension observed in about 5% of cases.[3] In our study, 5 patients (2.9%) who underwent pyeloplasty due to UPJO developed hypertension after an average of 3.5 years. This rate is higher than the general prevalence of hypertension in children, but lower than the rate seen in reflux nephropathy induced hypertension.

The exact cause of hypertension after pyeloplasty due to UPJO is not yet fully understood. In human and animal models, mechanisms such as the renin-angiotensin system (RAAS), oxidative stress, nitric oxide synthesis disorders, and renal sympathetic activity have been shown.[4] Animal studies have demonstrated that hypertension resolves with the removal of obstruction, and this is salt-dependent.[5] In human studies, it has been shown that hypertension resolves when obstruction is treated or when the damaged kidney is removed.[6] Since there may be several factors contributing to the development of hypertension in UPJO, close monitoring for hypertension after pyeloplasty is important.

There is no established guideline for the ideal follow-up duration for pediatric pyeloplasty. The follow-up period varies due to the absence of standard guidelines and is dependent on physician preference.[7] In our study, 167 patients were followed for an average of 6.7 years. Psooy et al.[7] reported that the likelihood of secondary narrowing was low in children with a non-obstructive renogram after 1-year postoperative follow-up. In our study, 5 patients (2.9%) had reoperation prevented in the first postoperative year, and 7 patients had their obstruction prevented for 3 months with ureteral catheter placement. No hypertension developed in these patients during follow-up.

UPJO can block the flow of urine from the kidney, leading to hydronephrosis and potentially hypertension.[8] Secondary hypertension, including sodium renal hypertension, is associated with increased activity of renin-angiotensin-aldosterone system (RAAS), which leads to increased vascular resistance, abnormal renal autoregulation and water retention.[9] Case reports have shown increased renin levels in the plasma of hypertensive hydronephrotic patients. The degree of RAAS activation appears to be influenced by the duration of obstruction, the presence of a contralateral normal kidney, and other intrarenal factors. Plasma renin activity is high in renal parenchymal and vascular diseases, but it can be low in some disease groups (low-renin hypertension). In cases of hypertension associated with UPJO, plasma renin activity may not always be elevated.[10] The value of this test is limited by factors such as salt intake, antihypertensive medications, and the laboratory's technical capacity. In our study, only two patients had elevated renin levels. One of these patients was a 10-year-old who underwent preoperative percutaneous nephrostomy for intrinsic UPJO, and the other had an additional cardiac disorder. Patients with heart anomalies should be closely monitored for hypertension. Two of the 11 patients who underwent preoperative percutaneous nephrostomy due to advanced hydronephrosis and later pyeloplasty developed hypertension. Preoperative percutaneous nephrostomy may contribute to changes in renal pelvis diameter, oxidative stress, and alterations in the renin-angiotensin system. Similarly, in patients with multicystic dysplastic kidney (MCDK), renin-

mediated hypertension is believed to develop due to RAAS activation caused by the dysplastic kidney.[6]

In patients undergoing pyeloplasty due to UPJO, the high renal Doppler resistance index (RI) in the preoperative period normalized after the obstruction was corrected.[11] In our study, a high renal Doppler RI index was observed in an obese patient. However, no antihypertensive treatment was needed, and hypertension improved with weight control.

Proteinuria can be an important indicator of the severity and prognosis of underlying kidney disease.[9] In our study, no proteinuria was observed in patients who underwent pyeloplasty for UPJO, even with temporary or persistent hypertension after the obstruction was removed. The absence of proteinuria suggests that early pyeloplasty may help prevent glomerular damage.

The severity of UPJO may lead to renal dysfunction, urinary tract infections, nephrolithiasis, and rarely hypertension. To prevent these long-term complications and preserve kidney function, surgical correction of UPJO is necessary.[12] In cases with unilateral UPJO, the development of hypertension may be associated with chronic renal disease. In children, UPJO complications can be prevented with early surgical intervention.[13]

CONCLUSION

In patients where preoperative renal decompression was achieved with percutaneous nephrostomy, the hypertension rate was higher than in other UPJO patients (2/11). In conclusion, blood pressure should be carefully monitored during the postoperative period in patients who undergo pyeloplasty due to UPJO. Hypertension may develop years later, and it should be taken into consideration. Pyeloplasty should be performed early, before obstruction progresses and glomerular damage occurs. In patients with a history of preoperative percutaneous nephrostomy and advanced hydronephrosis, blood pressure should be closely monitored after surgery.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Clinical Researches Ethics Committee of Ankara City Hospital No. 1 (Date: 14.05.2020, Decision No: E1-20-592).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Brewer ED. Evaluation of hypertension in childhood diseases. *Pediatr Nephrol*. 2009:1521-1540
2. Norwood VF. Hypertension. *Pediatr Rev*. 2002;23(6):197-208. doi:10.1542/pir.23-6-197
3. Fidan K, Kandur Y, Buyukkaragoz B, Akdemir UO, Soylemezoglu O. Hypertension in pediatric patients with renal scarring in association with vesicoureteral reflux. *Urology*. 2013;81(1):173-177. doi:10.1016/j.urology.2012.09.003
4. Carlström M. Causal link between neonatal hydronephrosis and later development of hypertension. *Clin Exp Pharmacol Physiol*. 2010;37(2):e14-e23. doi:10.1111/j.1440-1681.2009.05267.x
5. Carlström M, Wåhlin N, Skøtt O, Persson AE. Relief of chronic partial ureteral obstruction attenuates salt-sensitive hypertension in rats. *Acta Physiol (Oxf)*. 2007;189(1):67-75. doi:10.1111/j.1748-1716.2006.01625.x
6. Schlomer BJ, Smith PJ, Barber TD, Baker LA. Nephrectomy for hypertension in pediatric patients with a unilateral poorly functioning kidney: a contemporary cohort. *J Pediatr Urol*. 2011;7(3):373-377. doi:10.1016/j.jpurol.2011.02.020
7. Psooy K, Pike JG, Leonard MP. Long-term followup of pediatric dismembered pyeloplasty: how long is long enough?. *J Urol*. 2003;169(5):1809-1812. doi:10.1097/01.ju.0000055040.19568.ea
8. Carlström M. Causal link between neonatal hydronephrosis and later development of hyperten-sion. *Clin Exp Pharmacol Physiol*. 2010;37(2):e14-e23. doi:10.1111/j.1440-1681.2009.05267.x
9. Chevalier RL. Molecular and cellular pathophysiology of obstructive nephropathy. *Pediatr Nephrol*. 1999;13(7):612-619. doi:10.1007/s004670050756
10. Tian Q, Zhang C, Zhao X, et al. Potential impact of severe hydronephrosis secondary to ureteropelvic junction obstruction on pediatric blood pressure. *J Pediatr Urol*. 2024;S1477-5131(24)00536-9. doi:10.1016/j.jpurol.2024.10.014
11. Sun J, Deng G, Wang F, Mo J. Renal hemodynamic changes and postsurgical recovery in children treated for ureteropelvic junction obstruction. *Ultrasound Q*. 2020;36(1):20-23. doi:10.1097/RUQ.0000000000000477
12. de Waard D, Dik P, Lilien MR, Kok ET, de Jong TP. Hypertension is an indication for surgery in children with ureteropelvic junction obstruction. *J Urol*. 2008;179(5):1976-1979. doi:10.1016/j.juro.2008.01.058
13. Yayla D, Demirtas G, Karabulut B, Tiryaki HT. What is the critical age for the improvement of parenchymal thickness after pyeloplasty? *Urol J*. 2023;20(5):344-349. doi:10.22037/uj.v20i.7301

MHA MEDIHEALTH ACADEMY

Surgery on Children

Review

doi: 10.51271/SOC-0029

Nuclear medicine approaches in the field of oncologic pediatric surgery and review the risk factors for pediatric thyroid nodules

Nilüfer Bıçakcı[1], Güler Silov[2], Ünal Bıçakcı[3], Fatih Batı[2], Banu Kırtıloğlu[1]

[1]Department of Nuclear Medicine, Samsun Training and Research Hospital, Samsun, Turkiye
[2]Department of Nuclear Medicine, Faculty of Medicine, Samsun University, Samsun, Turkiye
[3]Division of Pediatric Urology, Department of Pediatric Surgery, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkiye

Received: 02/06/2024 ◆ **Accepted**: 15/07/2024 ◆ **Published**: 20/01/2025

Cite this article: Bıçakcı N, Silov G, Bıçakcı Ü, Batı F, Kırtıloğlu B. Nuclear medicine approaches in the field of oncologic pediatric surgery and review the risk factors for pediatric thyroid nodules. *Surg Child*. 2025;2(1):21-27.

Corresponding Author: Nilüfer Bıçakcı, niluferbicakci@gmail.com

ABSTRACT

Imaging methods used in nuclear medicine are non-invasive and can be applied to all pediatric age groups, including the neonatal period. F-18 FDG-PET/CT is used for staging, evaluation of treatment response, detection of metastases, and follow-up of various pediatric malignancies. In addition, the incidence of thyroid cancer in childhood has recently increased. In this review, we examined the F-18 FDG PET/CT imaging method that guide the management of the most common malignancies in children. We also discuss in detail the risk factors used in the diagnosis of thyroid cancer frequently encountered by pediatric surgeons.

Keywords: Pediatric surgery, nuclear medicine, PET/CT, thyroid cancer, risk factors

USE OF F-18 FDG PET/CT IN CHILDHOOD MALIGNANCIES

As the incidence of cancer in the childhood age group is lower than that in the adult age group, the incidence of childhood cancers is defined as per million. According to European data, it was reported to be 140 per million in the 0-15 age group and 157 per million in the 0-19 age group.[1] According to between 2014-2018 data from the Department of Cancer of the Public Health Institution of Turkey, the incidence of cancer in boys and girls aged 0-14 years is 10-50 per million, although it varies according to the type of cancer.[2]

Although the incidence of childhood cancers is low, it has serious clinical importance since it is the 2nd most common cause of death in this age group. The most common childhood malignancies are leukemias (30%), central nervous system and brain tumors (20%), lymphomas (14%), neuroblastoma (7%), soft tissue sarcomas (7%), Wilms' tumors (6%), bone tumors (5%), germ cell tumors (3%), retinoblastoma (3%), melanoma (3%), and hepatic tumors (1%).[3]

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) plays an important role in the diagnosis, staging, restaging, response to treatment, and evaluation of prognosis of childhood malignancies.[4] F-18 FDG PET/CT is a noninvasive molecular imaging method that reflects the metabolic properties of the tumor along with its structural status. F-18 FDG PET/CT is being used with increasing frequency in the diagnosis and follow-up of childhood tumors, but the imaging procedure, patient preparation, and calculation of radiation doses require greater care than in the adult age group. It is important to ensure sedation during imaging in pediatric patients. The practice guidelines of the American Academy of Pediatrics can be considered as a guiding example in this regard. In addition, to prevent harmful effects due to radiation, it is necessary to be more careful when calculating radiation doses compared to the adult group. In 2010, the North American Consensus Guideline was published, and the radiopharmaceutical doses to be applied were determined.[5]

CHILDHOOD LYMPHOMAS AND F-18 FDG PET/CT

F-18 FDG PET/CT is a functional and metabolic imaging method that plays a major role in the staging, treatment response evaluation, and residual/recurrence detection of HL and NHL.[6] The sensitivity, specificity, and accuracy (95.9%, 99.7%, and 99.6%, respectively) of 18F-FDG PET/CT were found to be higher (**Figure 1**) than those of other conventional imaging methods (70.1%, 99.0%, and 98.3%, respectively) for initial staging of lymphoma in children.[7]

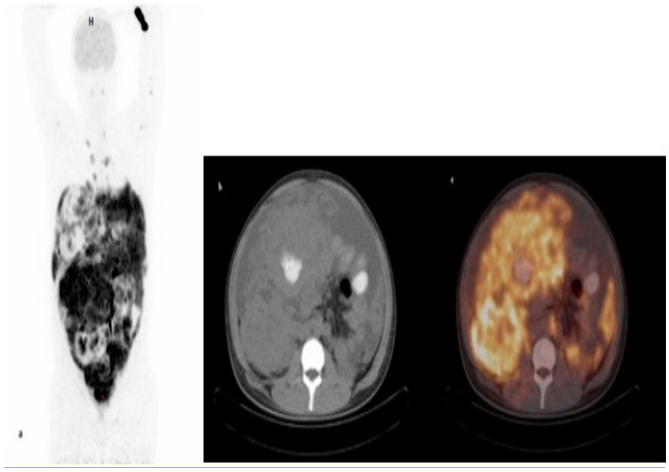


Figure 1. MIP (a), transaxial CT (b) and fusion (c) F-18 FDG PET/CT images of a 15 years-old male patient. Abdominal lymph node biopsy revealed high grade malign B cell lymphoma (Burkitt). On F-18 FDG PET/CT imaging, there were multipl hyper-metabolic mediastinal, abdominal, pelvic lymph nodes, massive abdominal fluid and bone marrow involvement
Figure 1 was obtained from Bıçakçı N, et al.[4]

SYMPATHETIC NERVOUS SYSTEM TUMOURS AND F-18 FDG PET/CT

Neuroblastoma (NB) is the most common tumor in this group, with 90% of cases diagnosed by the age of 5 years. The use of F-18 FDG PET/CT in the diagnosis, staging, and evaluation of response to treatment is limited. In a study, it was reported that F-18 FDG showed moderate uptake in the metaiodobenzylguanidine (MIBG) (-) and (+) groups and was not as successful as MIBG in showing bone and bone marrow metastases.[8]

Treatment modalities for NB usually include 4-6 cycles of induction therapy followed by surgical resection and radiotherapy to the primary site and other active residual disease sites. A recent study evaluated the benefit of surgical resection in a subgroup of patients with poor response to induction therapy (tumor volume >50% of the initial volume after six cycles of induction therapy). The results showed a statistically significant improvement in the 3-year overall survival of patients who responded poorly to induction therapy and underwent tumor resection compared with those who did not undergo surgery.[9] The promising MIBG-labelled PET radiopharmaceuticals, F-18 DOPA (18-F-L 3,4-dihydroxyphenylalanine), Ga-68 DOTA peptids in NB are important for guiding high-dose therapy with I-131 MIBG and Lu-177 DOTA peptids.[10]

WILMS' TUMOR AND F-18 FDG PET/CT

Wilms' tumor (nephroblastoma) is the 4th most common tumor in childhood. Although its etiology is unknown, genetic diseases are associated with 5% of the cases. The overall 5-year survival rate exceeds 90%.[11] Tumor staging, such as tumor location, size, local extension, vascular compression or invasion, and local lymph node metastases, are best assessed by CT, MR imaging, and ultrasonography.[12] The most common site for metastases is the lungs, which are typically assessed by chest CT.[12]

Therefore, the use of F-18 FDG PET/CT for diagnosis and staging has been limited. Wilms tumors show strong 18F-FDG uptake.[13,14] The mean SUV has been reported to be 6.8.[14] Anaplastic Wilms tumors showed particularly high 18F-FDG uptake, and the SUVmax value greater than 5 was due to the highly expressed glucose transporter 1.[13] Apart from this, no significant correlation was found between 18F-FDG uptake and tumour histopathology.[12] F-18 FDG PET/CT appears useful for assessing the response to treatment.[15]

RHABDOMYOSARCOMA AND F-18 FDG PET/CT

Rhabdomyosarcoma (RMS), arising from embryonic mesenchymal cells differentiating into skeletal muscle, accounts for 20% of all solid tumors in children.[16] Although the cases are sporadic, some congenital and genetic diseases increase the risk of RMS (Li Fraumeni syndrome, Beckwith Wiedemann syndrome, Neurofibromatosis type 1, Costilla syndrome, Nooan syndrome). There are embryonal and alveolar histological types of RMS, and the incidence in boys is slightly higher than that in girls (male/female ratio of 1.51).[17]

In the past, aggressive surgical methods such as amputation and pelvic and orbital exenteration had an important role in the treatment of RMS, but in the current treatment of RMS, organ-preserving surgery with chemotherapy and radiotherapy is at the forefront. The survival rate, which was 25% with radical surgical treatment, increased to 70% with the addition of radiotherapy and chemotherapy to the surgical treatment.

F-18 FDG PET/CT is used in RMS to determine the malignancy potential of the lesion, biopsy site selection, staging, and evaluation of response to treatment. This group of tumors showed high FDG accumulation, which increased as the tumor grade increased.

Although F-18 FDG PET/CT is not routinely used for initial staging in pediatric RMS, it is specifically used for the detection of nodal involvement and distant metastatic spread. For nodal involvement, F-18 FDG PET/CT showed a sensitivity of 80%[18] or 100%[19-21] and specificity of 89-100%. F-18 FDG PET/CT has a higher chance of detecting lung metastases larger than 1 cm (**Figure 2**) and bone, and bone marrow metastases than conventional methods. For the detection of distant metastatic sites, PET-CT has a sensitivity of 95%[19] or 100%[18-21] and specificity of 80-100%.

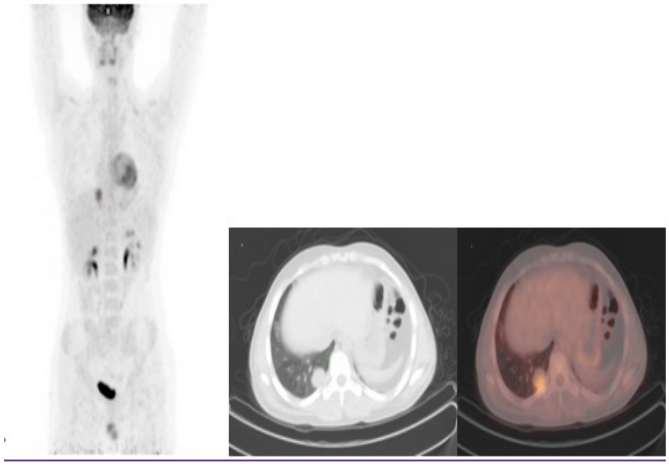


Figure 2. MIP (a), transaxial CT (b) and fusion (c) F-18 FDG PET/CT images of a 16 years-old male patient. Histopathologically diagnosis was rhabdomyosarcoma. On F-18 FDG PET/CT imaging, there were hyper-metabolic metastatic nodule in right lung posterobasal segment
Figure 2 was obtained from Bıçakçı N, et al.[4]

REVIEW OF RISK FACTORS FOR AT THE MANAGEMENT OF PEDIATRIC THYROID NODULES

Clinical Risk Factors for Pediatric Thyroid Nodules

The incidence of childhood thyroid cancer is increasing recently.[22] Despite the rapid increasing incidence, pediatric thyroid cancers constitute less than 2 % of all thyroid cancers.[23] Owing to the high prevalence of thyroid cancer in adults, the main diagnostic and prognostic criteria for thyroid cancer have been developed for adults and were adapted to secondarily applied to children. The American Thyroid Association (ATA) and American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) for reporting sonographic findings and The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) were both developed the management of adult thyroid nodules but are widely used the classification of thyroid nodules in children.[24-26]

Differences in the underlying biology of thyroid tumors between adults and children may affect the risk of malignancy (ROM) predicted by various sonographic and cytopathological findings.

Although thyroid nodules are detected at a much higher rate in adults than in children, they are five times more likely to be malignant in children (26.4%) than in adults (5%).[27] Radiation exposure, autoimmune thyroid disease, and chronic iodine deficiency are well-established risk factors for the development of thyroid malignancies in both adults and children.[28-30]

Childhood thyroid cancer is often diagnosed at a more advanced stage compared to adults, and is more likely to develop regional lymph node and lung involvement and higher recurrence rate. Distant metastases almost always occur in the lungs. These are diffuse and are usually identified by I-131 whole-body imaging (**Figure 3**).[31]

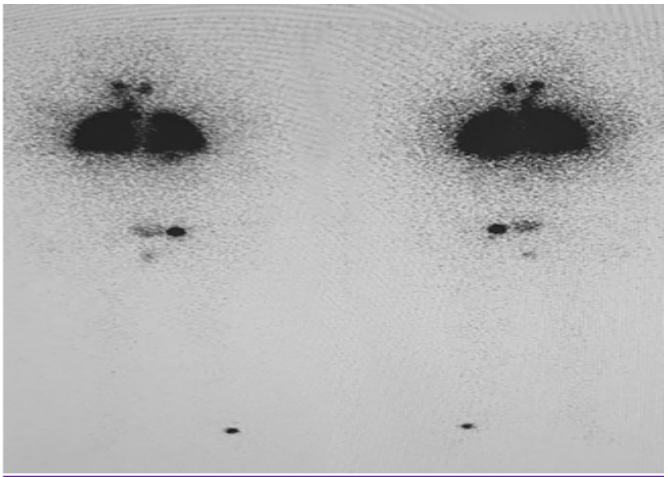


Figure 3. A 12-year-old girl who underwent total thyroidectomy for papillary thyroid cancer. Tg:22.62 µg/L, whole-body scan with 5 mCi I-131 shows diffuse metastatic foci in the lungs, left sacrum and heel of the left
Figure 3 was obtained from Aslı Ayan, MD.

Despite more advanced disease at presentation, children with thyroid cancer have a much lower death rate, with overall cumulative survival rates as high as 97-99%.[32]

The majority of thyroid cancers in children are papillary thyroid carcinoma (PTC) (80-90%), followed by follicular thyroid carcinoma (FTC) (10%), medullary thyroid carcinoma (MTC) (3-5%). Anaplastic thyroid carcinoma (ATC), and poorly differentiated thyroid carcinoma (PDTC) are rarely encountered.[33,34]

ATC is a dedifferentiated thyroid cancer via transformation of differentiated thyroid cancer.[35] It is extremely rare in children. Poor outcomes in children are largely due to regional and distant metastases, rather than the local spread of dedifferentiated tumors as seen in adults.[33]

Genetic Risk Factors for Pediatric Thyroid Cancer

Recent molecular profiling studies have suggested that thyroid cancer in adults and children has different developmental origins, which may explain their different clinical characteristics. PTC is the most common histological type of thyroid cancer in both adult and pediatric populations, although the histological subtype frequencies are different between children and adults.[34,36]

Notably, BRAF V600E, RAS (mostly HRAS and NRAS) point mutations, and gene fusions are mutually exclusive causes of DTC.[37]

Unlike the adult thyroid cancer profile, there is a high prevalence of gene fusion in pediatric PTC. RET, NTRK1, NTRK3, ALK, BRAF, AKAP9, and MET gene fusions are among the most common in pediatric PTC.[38] However, there is a lower frequency of point mutations in the RAS, BRAF and, GNAS genes in children with PTC than in adults.[39] Specific fusions tend to be associated with different histological subtypes of pediatric thyroid cancer. For example, AKAP9-BRAF is a less frequent BRAF alteration associated with classic papillary histology, whereas PAX8-PPARG has a follicular histology.[33]

Pediatric PTCs associated with fusion mutations have a higher frequency of aggressive subtypes, including diffuse sclerosing, tall cell, and solid variant.[36] RET-PTC rearrangements are associated with solid PTC variants. Rearrangements are typical in pediatric patients with radiation-induced PTC.[40]

Between 15-19 years of age, fusion mutations decrease and point mutations potentially lead to dedifferentiation, and radioactive iodine resistance begins to increase as in adults.[41]

Genetic syndromes are also known risk factors for pediatric thyroid cancer, accounting for approximately 5% of all pediatric DTC cases. Some of the more common syndromes affecting the thyroid include PTEN hamartoma tumor syndrome, APC-associated polyposis (e.g., familial adenomatous polyposis), Carney complex, DICER1 syndrome, and Werner syndrome.[33] Medullary thyroid cancer (MTC) is frequently associated with mutations in the RET proto-oncogene and accounts for 5% of all pediatric thyroid cancer cases.[37] Most MTC cases in the pediatric population are hereditary, with germline RET mutations resulting in multiple endocrine neoplasia (MEN) type 2A syndrome (90-95% of childhood MTC), MEN type 2B, or familial medullary thyroid carcinoma (FMTC).[42]

Adult tumors caused by gene fusion do not usually progress to more aggressive diseases. Rather, progression of adult thyroid cancer involves the accumulation of additional point mutations associated with local disease spread, metastasis, and transformation to aggressive dedifferentiated anaplastic and poorly differentiated subtypes. PTC progression is associated with the inclusion of other secondary gene mutations such

as TP53, PIK3CA, and AKT1. These secondary mutations are extremely rare in children and have not been detected in several recent large-scale sequencing studies on pediatric thyroid cancer.[42,43]

Ultrasonographic Risk Classification

Ultrasonography (US) is the most commonly used imaging modality for detecting thyroid nodules, measuring nodule size, and determining nodule shape, borders, location and number, echogenicity, content, and assessment of associated changes in the thyroid gland.[44]

Multiple risk classification systems based on US features of thyroid nodules have been developed to provide general terminology for the identification and classification of nodules at the greatest risk of morbidity and avoiding biopsies of benign nodules.[45]

The ability of the ACR TI-RADS[46] to accurately predict the risk of malignancy in pediatric thyroid nodules is currently unclear, as it was predominantly validated using adult data. However, recommendations for the evaluation and management of pediatric thyroid nodules have historically been based on the adult guidelines.[33]

One of the two most widely used systems in clinical practice is the ACR TI-RADS, which is used by many radiologists, and the other is the ATA guidelines, which is used by many endocrinologists. ACR TI-RADS summarizes this by scoring each of the five ultrasound findings (composition, echogenicity, shape, border features, and echogenic foci of the nodule) and defines the risk levels from TR1 to TR5. Fine-needle aspiration biopsy (FNAB) is recommended for TR3 nodules ≥2.5 cm, TR4 nodules ≥1.5 cm and TR5 nodules ≥1 cm. The biopsy and follow-up criteria according to ACR TI-RADS are summarized in **Table 1**.[45]

The 2009 ATA adult guidelines indicate that the evaluation and treatment of thyroid nodules in children should be the same as those adults.[47] The 2009 ATA adult guideline states that FNAB is not necessary for nodules smaller than 1 cm, unless they are high-risk, has a history of ionizing radiation, or have a pathological regional lymph node. However, the size criterion in children is more problematic because thyroid volume changes with age and nodule size alone does not predict malignant histology. Therefore, US features of malignant lesions, such as hypoechogenicity, irregular borders, microcalcifications, increased intranodular blood flow, and clinical signs, should be given more importance in defining nodules requiring FNAB. US evaluation of cervical lymph nodes should be performed in all children with suspicious nodules.[48,49]

It should also be noted that in the, the diffuse sclerosing subtype which is invasive form of PTC, the tumor shows diffuse microcalcifications without nodules or macroscopic metastases in the cervical lymph nodes.

Evaluation of Pediatric Thyroid FNAB Cytopathology with the Bethesda Classification System

US is often the first step in imaging thyroid nodules. ACR TI-RADS is a well-established tool for evaluating the risk of malignancy in adult thyroid nodules, but its application to pediatric thyroid nodules is still in progress.[50]

Thyroid nodules that are suspicious on US underwent FNAB for differential diagnosis to guide further management decisions. As cytomorphology does not always provide a clear difference between benign and malignant lesions, it is important to have specific diagnostic criteria to stratify the ROM of thyroid nodules based on FNAB results. TBSRTC had been developed and published in 2010.[26] Among the TBSRTC categories, atypia of undetermined significance (AUS), follicular neoplasm (FN), and suspected malignancy (SM) were considered indeterminate. TBSRTC was first updated in 2017 to include non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) as a new histological entity, which may alter the ROM of adult thyroid nodules.[51]

Table 1. ACR-TIRADS classifications and recommendations

Composition (choose one) Spongioform 0 point Cystic 0 point Mixed 1 point Solid 2 point Cannot be determined	**Echogenity (choose one)** Anechoic 0 point Iso/hyperechoic 1 point Hypoechoic 2 point Very hypoechoic 3 point	**Shape diameter (choose one)** Wider than tall 0 point Taller than wide 3 point	**Margin (choose one)** Smooth 0 point Ill-defined 0 point Lobulated 2 point irregular 2 point ETE 3 point	**Echogenic foci choose all that apply** None 0 point Comet like artifact 0 point Macrocalcification 1 point Rim calcification 2 point Small echogenic foci 3 point (microcalcification)
Add points from all categories to determine TI-RADS level				
0 points	1 points	2 points	4-6 points	7 points or more
TR1 benign no FNAB	TR2 not suspicious no FNAB	TR3 mildly suspicious FNAB if ≥2.5 cm follow if ≥1.5cm	TR4 Moderately suspicious FNAB if ≥1.5 cm follow if ≥1 cm	TR5 Highly suspicious FNAB if ≥1 cm follow if ≥0.5 cm
Composition	**Echogenicity**	**Shape**	**Margin**	**Echogenic foci**
Spongiform: Composed predominantly (>50%) of small cystic spaces. Do not add further points for other categories. Mixed cystic and solid: Assign points for predominant Solid component. Assign 2 points if composition cannot be determined because of calcification.	Anechoic: Applies to cystic or almost completely cystic nodules. Hyperechoic/isoechoic/ hypoechoic: Compared to adjacent parenchyma. Very hypoechoic: More hypoechoic than strap muscles. Assign 1 point if echogenicity cannot be determined.	Taller-than-wide: Should be assessed on a transverse image with measurements parallel to sound beam for height and perpendicular to sound beam for width. This can usually be assessed by visual inspection.	Lobulated: Protrusions into adjacent tissue. Irregular: Jagged, spiculated, or sharp angles. Extrathyroidal extension: Obvious invasion=malignancy. Assign 0 points if margin cannot be determined.	Large comet-tail artifacts: V-shaped, >1 mm, in cystic components. Macrocalcifications: Cause acoustic shadowing. Peripheral: Complete or incomplete along margin. Punctate echogenic foci: May have small comet-tail artifacts.

ETE: Extra thyroidal extention, ACR TI-RADS: American College of radiology thyroid imaging reporting and data system, FNAB: Fine-needle aspiration biopsy
Table 1 was established using the ACR TI-RADS guidelines.[24]

Table 2. The 2023 Bethesda system for reporting thyroid cytopathology. This table was established using the 2023 Bethesda system for reporting thyroid cytopathology guideline.[32]

	Adult		Pediatric	
Diagnostic category	ROM mean % (min-max)	Usual management	ROM mean % (min-max)	Usual management
Nondiagnostic (Bethesda I)	13% (5-20)	Repeat FNAB with ultrasound guidance	14% (0-33)	Repeat FNAB with ultrasound guidance
Benign (Bethesda II)	4% (2-7)	Clinical and ultrasound follow-up	6% (0-27)	Clinical and ultrasound follow-up
Atypia of undetermined significance Bethesda III	22% (13-30)	Repeat FNAB Molecular testing Lobectomy Surveillance	28% (11-54)	Repeat FNAB lobectomy
Follicular neoplasm (Bethesda IV)	30% (23-34)	Molecular testing Diagnostic lobectomy	50% (58-100)	Surgical resection
Suspicious for malignancy (Bethesda V)	74% (67-83)	Molecular testing Lobectomy or near-total thyroidectomy	81% (40-100)	Surgical resection
Malignant (Bethesda VI)	97% (97-100)	Lobectomy or near-total thyroidectomy	98% (86-100)	Surgical resection

ROM: Risk of malignancy, FNAB: Fine-needle aspiration biopsy, min-max: Minimum-maximum

A pediatric cohort study reported that the performance of TBSRTC in pediatric populations is unlikely to be affected by the addition of NIFTP.[52] The third edition of the TBSRTC was released in 2023 with updated ROMs (**Table 2**).[53] The new TBSRTC includes two subclassifications of AUS: AUS nuclear atypia and AUS other. In addition, for the first time, the new TBSRTC includes information on its application to pediatric thyroid nodules.

Differences between guidelines have highlighted the need for new methodologies to classify the risk of indeterminate thyroid nodules in pediatric populations. In the third TBSRTC, AUS is divided into two main groups: AUS with nuclear atypia and AUS with any other form of atypia (AUS other).[56] In a retrospective cohort study of 68 pediatric AUS thyroid nodules, there was an increased ROM when there was nuclear atypia (59% for nuclear atypia vs. 6.5% for architectural atypia). The highest ROM was observed in the nodules with both nuclear and architectural atypia (75%). The results of this study demonstrate that risk stratification of AUS pediatric thyroid nodules by atypia type may identify a subset of nodules that require surgical management and reduce overtreatment of nodules that do not have nuclear atypia.[54]

Molecular Techniques for Risk Stratification of Indeterminate Thyroid Nodules

Recently, there have been rapid developments in cytomolecular testing to reduce the need for Bethesda III and IV diagnostic surgery. The Afirma Genomic Sequencing Classifier (Afirma GSC) and Thyroseqv3 (TSv3) performed well, similar to undiagnosed FNAB results (Bethesda III and IV). TSv3 was found to have a relatively high sensitivity and negative predictive value of 90% and 96%, respectively. However, their diagnostic confirmatory performance for malignancy remains limited.[57] Although the use of molecular techniques is increasing, the cost of molecular testing remains the most important problem.

The rate of structural malignancy in BRAFV600E positivity alone in intrathyroidal micropapillary cancer was approximately 1-2%. Bilateral thyroidectomy, lymph node dissection, and RAI treatment are recommended for BRAF-positive intrathyroidal tumors. Active follow-up may be considered for BRAF-negative micropapillary cancers, and lobectomy may be considered for BRAF-negative or BRAF-positive micropapillary cancers. In patients with BRAF V600E+TERT or RAS+TERT promoter mutations, aggressive treatment approaches are selected, even if micropapillary cancer is present.[58]

CONCLUSION

There are many risk stratification systems according to the US characteristics of thyroid nodules, and the most widely used in clinics are the ATA guidelines and ACR TI-RADS. FNAB is the gold standard for evaluating nodules according to US risk stratification. TBSRTC is the most widely used cytomorphological classification for FNAB. The last TBSRTC reporting system covering the adult and pediatric populations was updated in 2023. Recently, there has been a trend towards the use of molecular testing of FNAB specimens, especially those diagnosed as Bethesda III and IV, to reduce the need for diagnostic surgery and to guide treatment.

In conclusion, an excellent prognosis for pediatric DTC may be possible with a review of diagnostic processes and management guidelines for pediatric thyroid cancer.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Steliarova-Foucher E, Stiller C, Kaatsch P, et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCISproject): an epidemiological study. *Lancet*. 2004;364(9451):2097-2105.

2. Türkiye Halk Sağlığı Kanser Daire Başkanlığı http://hsgm.saglik.gov.tr Avalible at. Accessed Ankara 2022.
3. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International classification of childhood cancer, third edition. *Cancer*. 2005;103(7):1457-1467.
4. Bıçakçı N, Elli M. ^{18}Fluorine-fluorodeoxyglucose PET/CT ımaging in childhood malignancies. *Mol Imaging Radionucl Ther*. 2021;30(1):18-27.
5. Society of nuclear medicine guidelines. Avaliable at: http://snmmi.files.cms-plus.com/docs/Pediatric_dose_guidelines_JNM_2011_52_318_1382732155632_11.pdf. Accessed 23.03.2015
6. Jhanwar YS, Straus DJ. The role of PET in lymphoma. *J Nucl Med.* 2006; 47(8):1326-1334.
7. Cheng G, Servaes S, Zhuang H. Value of (18)F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography scan versus diagnostic contrast computed tomography in initial staging of pediatric patients with lymphoma. *Leuk Lymphoma*. 2013;54(4):737-742.
8. Chawla M, Kumar R, Agarwala S, Bakhshi S, Gupta DK, Malhotra A. Role of positron emission tomography in staging and early chemotheraphy in staging and early chemotheraphy responce evaluation in children with neuroblastoma. *Indian J Nucl Med*. 2010;25(4):147-155.
9. Du L, Liu L, Zhang C, et al. Role of surgery in the treatment of patients with high risk neuroblastoma who have poor response to induction chemotherapy. *J Pediatr Surg*. 2014;49(4):528-533.
10. Alexander N, Vali R, Ahmadzadehfar H, Shammas A, Baruchel S. Review: the role of radiolabeled DOTA-conjugated peptides for ımaging and treatment of childhood neuroblastoma. *Curr Radiopharm*. 2018;11(1):14-21.
11. Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adoles- cents with cancer: challenges for the twenty-first century. *J Clin Oncol*. 2010;28(15):2625-2634.
12. Moinul Hossain AK, Shulkin BL, Gelfand MJ, et al. FDG positron emission tomography/computed tomography studies of Wilms' tumor. *Eur J Nucl Med Mol Imaging*. 2010;37(7):1300-1308.
13. Begent J, Sebire NJ, Levitt G, et al. Pilot study of F (18)-fluorodeoxyglucose positron emission tomography/computerised tomography in Wilms' tumour: correlation with conventional imaging, pathology and immunohistochemistry. *Eur J Cancer*. 2011;47(3):389-396.
14. Misch D, Steffen IG, Schönberger S, et al. Use of positron emission tomography for staging, preoperative response assessment and posttherapeutic evaluation in children with Wilms tumour. *Eur J Nucl Med Mol Imaging*. 2008;35(9):1642-1650.
15. Misch D, Steffen IG, Schönberger S, et al. Use of positron emission tomography for staging, preoperative response assessment and posttherapeutic evaluation in children with Wilms tumour. *Eur J Nucl Med Mol Imaging*. 2008;35(9):1642-1650.
16. Weiner E. Soft tissue sarcoma, in Carachi R, Azmy A, Grosfeld JL (eds): The Surgery of Childhood Tumors, Oxford University Press, 2009.
17. Mollen KP, Rodeberg DA. Diagnosis and treatment of rhabdomyosarcoma. In Coran AG, Adzick NS, Krummel TM, et al. (eds): Pediatric Surgery, Philadelphia, Mosby, 2012.
18. Federico SM, Spunt SL, Krasin MJ, et al. Comparison of PET-CT and conventional imaging in staging pediatric rhabdomyosarcoma. *Pediatr Blood Cancer*. 2013;60(7):1128-1134. doi:10.1002/pbc.24430
19. Tateishi U, Hosono A, Makimoto A, et al. Comparative study of FDG PET/CT and conventional imaging in the staging of rhabdomyosarcoma. *Ann Nucl Med*. 2009;23(2):155-161.
20. Volker T, Denecke T, Steffen I, et al. Positron emission tomography for staging of pediatric sarcoma patients: results of a prospective multicenter trial. *J Clin Oncol.* 2007;25(34):5435-5441.
21. Ricard F, Cimarelli S, Deshayes E, Mognetti T, Thiesse P, Giammarile F. Additional Benefit of F-18 FDG PET/CT in the staging and follow-up of pediatric rhabdomyosarcoma. *Clin Nucl Med*. 2011;36(8):672-677.
22. Vergamini LB, Frazier AL, Abrantes FL, Ribeiro KB, Rodriguez-Galindo C. Increase in the incidence of differentiated thyroid carcinoma in children, adolescents, and young adults: a population based study. *J Pediatr*. 2014;164(6):1481-1485.
23. Guille JT, Opoku-Boateng A, Thibeault SL, Chen H. Evaluation and management of the pediatric thyroid nodule. *Oncologist*. 2015;20(1):19-27.
24. Buryk MA, Simons JP, Picarsic J, et al. Can malignant thyroid nodules be distinguished from benign thyroid nodules by clinical characteristics? A review of 89 pediatric patients with thyroid nodules. *Thyroid*. 2015;25(4):392-400.
25. Grant EG, Tessler FN, Hoang JK, et al. Thyroid ultrasound reporting lexicon: white paper of the ACR thyroid imaging, reporting and data system (TIRADS) committee. *J Am Coll Radiol*. 2015;12(12 Pt A):1272-1279.
26. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. *Am J Clin Pathol*. 2009;132(5):658-665.
27. Gupta A, Ly S, Castroneves LA, et al. A standardized assessment of thyroid nodules in children confirms higher cancer prevalence than in adults. *J Clin Endocrinol Metab*. 2013;98(8):3238-3245.
28. Penta L, Cofini M, Lanciotti L, Leonardi A, Principi N, Esposito S. Hashimoto's disease and thyroid cancer in children: are they associated? *Front. Endocrinol.* 2018;9:565.
29. Zimmermann MB, Galetti V. Iodine intake as a risk factor for thyroid cancer: a comprehensive review of animal and human studies. *Thyroid Res*. 2015;8(1):8.
30. Bogović CT, Ilić TM, Girotto N, Grbac IS. Risk factors for thyroid cancer: what do we know so far? *Acta Clin Croat*. 2020;59(Suppl 1):66-72.
31. Karapanou O, Tzanela M, Vlassopoulou B, Kanaka GC. Differentiated thyroid cancer in childhood: a literature update. *Hormones (Athens).* 2017; 16(4):381-387.
32. Zhang B, Wu W, Shang X, Huang D, Liu M, Zong L. Incidence and prognosis of thyroid cancer in children: based on the SEER database. *Pediatr Surg Int*. 2022;38(3):445-456.
33. Paulson VA, Rudzinski ER, Hawkins DS. Thyroid cancer in the pediatric population. *Genes (Basel).* 2019;10(9):723.
34. Hogan AR, Zhuge Y, Perez EA, Koniaris LG, Lew JI, Sola JE. Pediatric thyroid carcinoma: incidence and outcomes in 1753 patients. *J Surg Res*. 2009;156(1):167-172.
35. Jannin A, Escande A, Al Ghuzlan A, et al. Anaplastic thyroid carcinoma: an update. *Cancers (Basel).* 2022;14(4):1061.
36. Balachandar S, La Quaglia M, Tuttle RM, Heller G, Ghossein RA, Sklar CA. Pediatric differentiated thyroid carcinoma of follicular cell origin: prognostic significance of histologic subtypes. *Thyroid.* 2016;26(2):219-226.
37. Agrawal N, Akbani R, Aksoy BA, et al. Integrated genomic characterization of papillary thyroid carcinoma. *Cell*. 2014;159(3):676-690.
38. Pekova B, Sykorova V, Dvorakova S, et al. RET, NTRK, ALK, BRAF, and MET fusions in a large cohort of pediatric papillary thyroid carcinomas. *Thyroid*. 2020;30(12):1771-1780.
39. Monaco SE, Pantanowitz L, Khalbuss WE, et al. Cytomorphological and molecular genetic findings in pediatric thyroid fine-needle aspiration. *Cancer Cytopathol.* 2012;120(5):342-350.
40. Ricarte-Filho JC, Li S, Garcia-Rendueles MER, et al. Identification of kinase fusion oncogenes in post-Chernobyl radiation-induced thyroid cancers. *J Clin Invest*. 2013;123(11):4935-4944.
41. Yamashita S, Saenko V. Mechanisms of disease: molecular genetics of childhood thyroid cancers. *Nat Rev Endocrinol*. 2007;3(5):422-429.
42. Franco AT, Ricarte-Filho JC, Isaza A, et al. Fusion oncogenes are associated with increased metastatic capacity and persistent disease in pediatric thyroid cancers. *J Clin Oncol.* 2022;40(10):1081-1090.
43. Landa I, Ibrahimpasic T, Boucai L, et al. Genomic and transcriptomic hallmarks of poorly differentiated and anaplastic thyroid cancers. *J Clin Invest*. 2016;126(3):1052-1066.
44. Isgor A, Uludag M, Aygun N. Handbook of thyroid parathyroid adrenal. 1st ed. Istanbul: BAU Publications; 2023.
45. Tessler FN, Middleton WD, Grant EG, et al. ACR thyroid ımaging, reporting and data system (TI-RADS): white paper of the ACR TI-RADS committee. *J Am Coll Radiol*. 2017;14(5):587-595.
46. Horvath E, Majlis S, Rossi R, et al. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. *J Clin Endocrinol Metab*. 2009;94(5):1748-1751.
47. Francis GL, Waguespack SG, Bauer AJ, et al. American thyroid association guidelines task force. Management guidelines for children with thyroid nodules and differentiated thyroid cancer. *Thyroid.* 2015;25(7):716-759.
48. McHenry CR, Huh ES, Machekano RN. Is nodule size an independent predictor of thyroid malignancy? *Surgery*. 2008;144(6):1062-1069.
49. Leboulleux S, Girard E, Rose M, et al. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. *J Clin Endocrinol Metab*. 2007;92(9):3590-3594.
50. Ahmad H, al-Hadidi A, Bobbey A, et al. Pediatric adaptions are needed to improve the diagnostic accuracy of thyroid ultrasound using TI-RADS. *J Pediatr Surg*. 2021;56(6):1120-1125.
51. Strickland KC, Howitt BE, Barletta JA, et al. Suggesting the cytologic diagnosis of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): a retrospective analysis of atypical and suspicious nodules. *Cancer Cytopathol.* 2018;126(2):86-93.
52. Rossi ED, Mehrotra S, Kilic AI, et al. Noninvasive follicular thyroid neoplasm with papillary-like nuclear features in the pediatric age group. *Cancer Cytopathol.* 2018;126(1):27-35.

53. Ali SZ, Baloch ZW, Cochand-Priollet B, Schmitt FC, Vielh P, VanderLaan PA. The 2023 Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2023;33(9):1039-1044.

54. Cherella CE, Angell TE, Richman DM, et al. Differences in thyroid nodule cytology and malignancy risk between children and adults. *Thyroid*. 2019; 29(8):1097-1104.

55. Lebbink CA, Links TP, Czarniecka A, et al. European thyroid association guidelines for the management of pediatric thyroiesponse and radioiodine uptaka. *Eur Thyroid J*. 2022;11(6):e220146.

56. Han M, Fan F. Bethesda system for reporting thyroid cytopathology an updated review. *J Clin Transl Pathol*. 2023;3(2):84-98.

57. Patel J, Klopper J, Cottrill EE. Molecular diagnostics in the evaluation of thyroid nodules: current use and prospective opportunities. *Front Endocrinol (Lausanne)*. 2023;14:1101410.

58. Xing M. Genetic-guided risk assessment and management of thyroid cancer. *Endocrinol Metab Clin North Am*. 2019;48(1):109-124.

MHA MEDIHEALTH ACADEMY

Surgery on Children

Review

doi: 10.51271/SOC-0030

Osteogenesis imperfecta-a current overview

Nedim Mujanović

Department of Orthopedic and Trauma Surgery, University Medical Centre, Sarajevo, Bosnia and Herzegovina

Received: 26/09/2024 ◆ **Accepted**: 18/11/2024 ◆ **Published**: 20/01/2025

Cite this article: Mujanović N. Osteogenesis imperfecta-a current overview. *Surg Child*. 2025;2(1):28-32.

Corresponding Author: Nedim Mujanović, nedim_mujanovic@yahoo.com

ABSTRACT

A genetically diverse condition called osteogenesis imperfecta (OI) is characterized by low bone mass and fragility. Over the past few decades, OI has evolved from an illness lacking a known etiology to one with a well-defined and well-mapped genetic background. Pathogenic mutations in COL1A1/COL1A2 with autosomal-dominant inheritance are linked to most cases of OI. The pathophysiology of OI is now well understood thanks to recent gene discoveries, which has opened up new opportunities for treatment development. The main characteristics of OI patient include short stature, bone abnormalities, and repeated fractures. Joint hypermobility, dentinogenesis imperfecta, blue sclera, hearing loss, and, less frequently, muscle weakness, pulmonary, and cardiovascular problems are examples of extraskeletal symptoms. In addition to pharmaceutical therapy, OI requires interdisciplinary care from orthopedic management, rehabilitation, nutrition, dentistry, and other subspecialties. Although the current pharmacologic therapy for OI does not address the matrix defect that is the main cause of bone fragility, it may enhance bone mass and morphology. To develop treatments that will target the genetic flaw and mechanism causing OI, research is still being done.

Keywords: Bone diseases, collagen type 1, genetic background, osteogenesis imperfecta

INTRODUCTION

Osteogenesis imperfecta (OI), also called brittle bone disease, is a genetic disorder affecting the extracellular matrix.[1] It is a systemic connective tissue condition characterized by reduced bone density and fragility, leading to significant morbidity from pain, limited mobility, skeletal deformities, and growth impairment. The weakened bones result in low-trauma fractures or fractures in unusual locations, such as the olecranon and vertebral compression fractures. OI also presents with various extraskeletal symptoms including dental irregularities, blue-gray sclera, hearing impairment, joint hypermobility, and, more rarely, muscle weakness, cardiovascular issues, and pulmonary complications.[2-4] Recent technological advancements have made it possible to diagnose OI as early as the first to early second trimester. In the past, it was only possible to suspect OI in the second trimester using ultrasound, and confirming the diagnosis necessitated invasive genetic testing. Detecting OI early, particularly in severe or lethal cases, could offer ample time to empower the parents in making decisions regarding termination of pregnancy, mode of delivery, resuscitation at birth, treatment options, and seeking genetic counseling for future pregnancies.

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

The incidence of OI is approximately 1 in 10,000.[4] OI is a skeletal dysplasia with genetic diversity and a higher mortality rate compared to the general population. Folkestad et al.[5] discovered that individuals with OI have an increased risk of death due to respiratory and gastrointestinal diseases as well as trauma. In most instances, OI is inherited in an autosomal-dominant manner, although autosomal-recessive and X-chromosome-linked variations of the disease have also been documented. The majority of OI cases (about 85-90%) are linked to dominantly inherited mutations in COL1A1 or COL1A2, which are responsible for encoding type I collagen. To date, over 1500 dominant mutations in the COL1A1 and COL1A2 genes have been identified.[6,7] Pathogenic variants in noncollagenous genes are responsible for the remaining cases, which encode proteins involved in collagen biosynthesis. These variants can also be related to transcription factors and signaling molecules that are involved in bone cell differentiation and mineralization. The inheritance associated with these cases is most commonly autosomal-recessive, but can also be dominant or X-linked.[2-4]

CLASSIFICATION

The severity of OI can vary from a subtle increase in fracture frequency to perinatal death. According to the revised nosology and classification of genetic skeletal disorders, there are 5 clinical forms of OI: OI type I, known as 'nondeforming

with blue sclera'; OI type II, referred to as 'perinatally lethal OI'; OI type III, categorized as 'progressively deforming OI'; OI type IV, labeled as 'moderate severe OI' (**Figure**); and OI type V, which is distinguished by moderate-to-severe bone fragility and a calcified interosseous membrane. OI type V follows an autosomal-dominant pattern, and a hyperplastic callus may form after fractures or surgical interventions.[8-10] There are also other phenotypes, such as Bruck syndrome, a severe OI phenotype that is linked to joint contractures.[11]

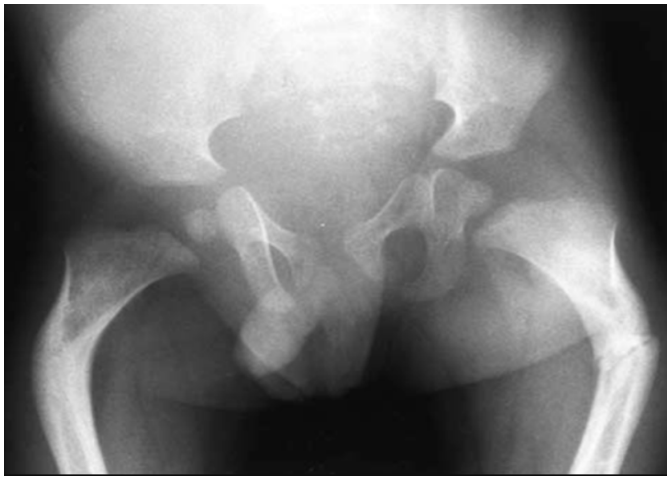


Figure. Osteogenesis imperfecta type IV. Radiograph showing subtrochanteric deformities and a pathological fracture of the femur

DIAGNOSIS

The diagnosis of OI is based on radiographic abnormalities, bone biochemistry, lumbar spine bone mineral density (BMD), history, and clinical examination.[12] It's critical to rule out metabolic causes of osteoporosis. The most significant clinical characteristic, shared by all OI types, is bone fragility, while additional extra-skeletal characteristics may also exist. It is possible to make a diagnosis during pregnancy, at birth, in childhood, or in adulthood.

For the prenatal diagnosis of OI, diagnostic modalities such as ultrasound and molecular testing are crucial. The diagnostic approach is separated into two categories based on whether a family history is present or not.[13] In cases where a known family history of OI exists, the affected family is offered genetic counseling and diagnosis, and future parents may benefit from information on inheritance patterns (e.g., autosomal dominant or recessive). When there is no family history and ultrasound scanning reveals a decrease in femoral length in the second trimester, doctors typically assume fetal OI.[14]

Clinicians and radiologists diagnose patients with mild to moderate OI after birth. Even within the same family, the clinical signs of the mild form of OI can differ within the same mutation.[15] Differentiating mild onset osteoporosis or child abuse from osteoporosis might be challenging at times. Apart from the skeletal symptoms, there are impairments in several tissues that express type I collagen. These include blue-grey sclera, dentinogenesis imperfecta (which manifests as tooth discoloration from a dentin defect, missing permanent teeth, and malocclusion), young-adult onset hearing loss, muscle weakness, reduced respiratory function and cardiac valvular regurgitation.[16] Reduced muscle strength is linked to exercise intolerance, easy fatigability, and gross motor delay. In addition to fractures, bone abnormalities and ligamentous laxity may also contribute to reduced mobility, particularly in cases of severe OI.[17-19] The diagnosis of mild OI is also aided by these symptoms. Progressive bone malformations, like scoliosis, rib cage abnormalities, and long bone bowing, are seen in moderate-to-severe forms of OI.[4,20,21]

While growth deficiency and reduced growth velocity are also noted in the milder OI type I, short stature is a key characteristic in the moderate and increasingly deforming OI, types III–IV (even in the absence of substantial bone abnormalities).[22,23] Aortic root dilatation, valve dysfunction, and infrequently aortic aneurysm and dissection are among the cardiovascular symptoms associated with OI that have been documented.[2,24] In patients with OI, pulmonary problems are a significant source of morbidity and death. These issues can result from both increasingly known intrinsic lung abnormalities and extrinsic causes such as scoliosis, rib fractures, and muscular weakness.[25]

TREATMENT

There is currently no cure for OI. Depending on the patient's age, the disease's severity, and patient's functional status, different therapeutic strategies could be used. Reducing the frequency of fractures, reducing pain, and promoting growth, mobility, and functional independence are all objectives of treatment for OI. Multidisciplinary care should be given, integrating medical genetics, orthopedic surgery, physical therapy, dental expertise, and other subspecialties based on the symptoms and problems, since there can be various skeletal and extraskeletal manifestations.[26] Orthopedic care encompasses the therapy of long bone and spinal abnormalities through surgery as well as fracture repair.[2,21] Intramedullary rodding surgery may be necessary to straighten bowed femurs and tibias in severe cases of OI.[27,28]

In order to support motor growth, boost endurance, reduce pain, gain independence, and aid in the healing process following surgical operations, physical therapy and rehabilitation are crucial.[26,29] Nutritionally speaking, sustaining sufficient levels of calcium and vitamin D is critical to promoting bone health, as well as enhancing the effectiveness and reducing the side effects of using bisphosphonates.[2]

Antiresorptive Treatment

Bisphosphonates, which include zoledronic acid, risedronate, alendronate, and pamidronate, constitute the cornerstone of pharmaceutical management for pediatric OI patients. It has been demonstrated that bisphosphonates enhance bone mass and architecture while also somewhat lowering the risk of fracture. By causing osteoclast apoptosis and inhibiting osteoclast activity, they achieve their desired effect.[30,31] In growing children with OI, bisphosphonates have a significant effect on the vertebra throughout growth and can cause remodeling in cases of vertebral compression fractures.[1] They can be infused intravenously or given orally. According to recent research, intravenous bisphosphonates have a greater impact on BMD and fracture rate than oral bisphosphonates.[32,33]

Intravenous bisphosphonates also have improved absorption, adjusted dosage, reduced gastrointestinal side effects, and resulted in higher patient compliance. The most frequent adverse effects of bisphosphonates, which are normally well

tolerated, include gastrointestinal irritation when taken orally and an acute phase infusion reaction, which usually happens during the first infusion and manifests as hyperpyrexia, myalgia and weakness. Pretreatment with calcium and vitamin D can stop transient hypocalcemia.

Denosumab is a human monoclonal antibody to the receptor activator of nuclear factor kappa-B ligand (RANKL), which is an osteoclast differentiating factor. It inhibits osteoclast formation, decreases bone resorption, increases BMD, and reduces the risk of fracture.[34] Children with SERPINF1, COL1A1, and COL1A2 mutations have been documented to benefit from denosumab treatment, which decreased bone turnover markers and increased areal BMD.[35,36] It is administered by subcutaneous injection. Atypical hip fractures, osteonecrosis of the jaw and hypercalcemia are among the side effects that have been reported.[34]

Growth hormone (GH) therapy-because of its possible anabolic effect on bone, GH has been suggested as a treatment for OI in order to address the growth shortage. According to a preliminary study, certain patients—mostly those with OI type IV—might respond to GH treatment by experiencing a little increase in cancellous bone density along with a rise in linear growth rate.[37] An additional study that contrasted bisphosphonates alone with GH and bisphosphonate therapy found a synergistic effect on growth velocity but no effect on fracture risk.[38]

Anabolic Treatment

The goal of osteo-anabolic therapy is to promote bone growth and osteoblast activity.[39] The first anabolic treatment authorized for use in osteoporosis was teriparatide, also known as recombinant human parathyroid hormone (PTH) 1-34. Osteosarcoma risk was enhanced by preclinical investigations conducted in rats treated with high doses of teriparatide.[40] As a result, it has not been used on pediatric patients and its clinical use is restricted to a 24-month period.

Targeting sclerostin, a glycoprotein that prevents bone formation by blocking the canonical Wnt signaling pathway in osteoblasts, is the goal of sclerostin-inhibitory antibodies (Scl-Ab/Romosozumab). The use of romosozumab in treating osteoporosis was recently approved. Sclerostin inhibition treatment has been shown in preclinical research using animal models of OI to have positive effects on bone formation and BMD.[31]

Transforming growth factor beta (TGFβ) inhibition aims to stop the over-activation of TGFβ signaling, which is connected to controlling bone fragility and mass in OI patients.[31,42,43] Preclinical research on mice with OI treated with TGFβ inhibitory antibody revealed enhanced bone mass and bone strength.[44]

Progenitor cell therapy – it has been suggested that OI's innate bone fragility can be specifically addressed by using progenitor cell therapy, which involves transplanting healthy progenitor stem cells. The rationale is that normal collagen is produced by osteoblasts, which are formed from engrafted healthy donor cells.[31] Although promising thus far, cell therapy is still in its experimental stages because of variable outcomes, safety issues, and ethical constraints.

Methods based on genetic engineering and somatic cells reprogramming into iPSCs (induced pluripotent stem cells)– aim to correct defects in genes. Currently there are multiple methods for modifying transcripts of collagen mutants. The latest method involves silencing or inactivating the mutant gene, resulting in allele suppression and haploinsufficiency, to transform the severe type of OI based on structural deficiencies in collagen I protein into a less severe quantitative form.[45] These techniques are still in the experimental stage, despite the intriguing outcomes.

Fractures and Deformities Treatment

Fractures in OI pediatric patients are treated similarly to those of typical children, while keeping the time of immobilization to minimum. Babies who are severely impacted typically have several fractures at birth, each in a different state of healing. Unstable fractures require a straightforward splint to help with nursing and to lessen pain. Painkillers could also be required and pain normally subsides as the fractures heals over a few weeks. Regular clinic evaluations during the first few months of life are crucial. Support can also be given with intramedullary rods. Although it significantly lowers the number of fractures in the affected bone, it has the drawback that when the bone grows, it bows past the rod and breaks again. Telescopic rod was invented to avoid these problems.[46] When severe cases of OI go untreated, scoliosis and kyphoscoliosis are frequently observed. Arthrodesis combined with spinal instrumentation is suitable in certain cases. However, the vertebral bodies flatten within the first few years of life and scoliosis develops quickly in many children with severe OI. Most of the time, orthotics or plasters are unpractical since the deformation of the chest wall occurs without altering the curve of the spine. The majority of internal fixation techniques are likewise inappropriate for the little and severely osteoporotic vertebrae.[47]

DISCUSSION

This literature review highlights the current challenges faced by clinicians when treating the pediatric population diagnosed with OI. In recent years, numerous additional genetic causes of OI have been discovered, despite the fact that COL1A1/A2 mutations account for the majority of cases. A few of these genes are involved in type I collagen processing. Nowadays we know more about the biomechanics of OI bone, including its material characteristics, the impact of muscle and gait stress, and how to handle fractured bones. With the use of suitable controls, biomechanical models may be able to assist in identifying activities that provide a higher risk of fracture and allow individuals with OI to engage in a wider range of activities in a safer and more comprehensive manner.

The presence of deformities and functional limitations is the keyaspect of OI. There is ongoing discussion in the literature regarding the proportion of patients who have limitations and/or deformities. Although Mrosk's study only included 50 patients, it revealed malformations in terms of bone bowing throughout the entire cohort.[48] In contrast, another study by Li at al.[49] revealed a lower rate of deformities and a higher prevalence of limitations.

Numerous non-bony symptoms of OI are common, affecting various organs and systems and having an effect on the lives of

the patients. Assessing if those characteristics are present in a sizable OI population could provide clinicians with insightful input on how to carry out a diagnostic procedure and treatment. In addition, because of the great variation in type, length, administration method, age at treatment, etc., statistics on drug treatment are sometimes imprecise and challenging to assess and compare.

An essential component of these patients' care is physical therapy. Children with moderate to severe OI are frequently treated with intravenous bisphosphonates. Some of the benefits seen in observational studies have been hard to prove in controlled studies. Other viable OI therapies are being researched. Overall, further research is necessary to understand the precise mechanism and clinical consequences of abnormalities in individuals with OI.

Taking all of the above into consideration, the strength of this study is reflected in highlighting current gaps in knowledge related to the treatment of this condition, and possible future trends in dealing pediatric patients with OI. Limitation of this overview is a lack of systematic searching methods and evaluation. Partial influence of the author's own perspectives and opinions expressed in this review article could be considered as a limitation of this study, in the context of bias.

CONCLUSION

OI is an uncommon multisystem disease with variable clinical characteristics and severity that is typified by primary bone fragility. Children who have OI may require orthopedic and other surgeries on many occasions. The most common causal mutations are on COL1A1 and COL1A2, while more genes have recently been found to contain alterations. The current OI therapy approaches focus on increasing bone mass, managing symptoms, and preventing fractures. Bisphosphonates, denosumab and GH are the three types of drugs most frequently utilized in the treatment of OI in pediatric patients. The main disadvantage of these therapies is their relatively weak efficiency, the lack of effects in some patients or cytotoxic side effects. Genetic engineering and stem cell transplantation are promising approaches for treating OI and other genetic bone diseases in the future.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Palomo T, Fassier F, Ouellet J, et al. Intravenous bisphosphonate therapy of young children with OI: skeletal findings during follow up throughout the growing years. *J Bone Miner Res*. 2015;30(12):2150-2157.
2. Marini JC, Forlino A, Bachinger HP, et al. OI. *Nat Rev Dis Primers*. 2017;3: 17052.
3. Marom R, Lee YC, Grafe I, Lee B. Pharmacological and biological therapeutic strategies for OI. *Am J Med Genet C Semin Med Genet*. 2016; 172(4):367-383.
4. Robinson ME, Rauch F. Mendelian bone fragility disorders. *Bone*. 2019;126: 11–17.
5. Folkestad L, Hald JD, Canudas-Romo V, et al. Mortality and causes of death in patients with OI: a register-based nationwide cohort study. *J Bone Miner Res*. 2016;31(12):2159-2166.
6. Forlino A, Cabral WA, Barnes AM, Marini JC. New perspectives on osteogenesis imperfecta. *Nat Rev Endocrinol*. 2011;7(9):540-557.
7. Marini JC, Forlino A, Cabral WA, et al. Consortium for osteogenesis imperfecta mutations in the helical domain of type I collagen: regions rich in lethal mutations align with collagen binding sites for integrins and proteoglycans. *Hum Mutat*. 2007;28(3):209-221.
8. Van Dijk FS, Byers PH, Dalgleish R, et al. Emqn best practice guidelines for the laboratory diagnosis of OI. *Eur J Hum Genet*. 2012;20(1):11-19.
9. Rauch F, Glorieux FH. OI. *Lancet*. 2004;363(9418):1377-1385.
10. Glorieux FH, Rauch F, Plotkin H, et al. Type V OI: a new form of brittle bone disease. *J Bone Miner Res*. 2000;15(9):1650-1658.
11. Viljoen D, Versfeld G, Beighton P. Osteogenesis imperfecta with congenital joint contractures (Bruck syndrome). *Clin Genet*. 1989;36(2):122-126. doi: 10.1111/j.1399-0004.1989.tb03174.x
12. Trejo P, Rauch F. Osteogenesis imperfecta in children and adolescents-new developments in diagnosis and treatment. *Osteoporos Int*. 2016;27(12):3427-3437.
13. Byers PH, Krakow D, Nunes ME, Pepin M; American college of medical genetics. Genetic evaluation of suspected osteogenesis imperfecta (OI). *Genet Med*. 2006;8(6):383-388.
14. Milks KS, Hill LM, Hosseinzadeh K. Evaluating skeletal dysplasias on prenatal ultrasound: an emphasis on predicting lethality. *Pediatr Radiol*. 2017;47(2):134-145.
15. Bregou Bourgeois A, Aubry-Rozier B, Bonafé L, Laurent-Applegate L, Pioletti DP, Zambelli PY. Osteogenesis imperfecta: from diagnosis and multidisciplinary treatment to future perspectives. *Swiss Med Wkly*. 2016; 146:w14322.
16. Forlino A, Marini JC. OI. Lancet. 2016;387(10028):1657-1671.
17. Veilleux LN, Trejo P, Rauch F. Muscle abnormalities in OI. *J Musculoskelet Neuronal Interact*. 2017;17(2):1-7.
18. Phillips CL, Jeong Y. OI: muscle-bone interactions when bi-directionally compromised. *Curr Osteoporos Rep*. 2018;16(4):478-489.
19. Kruger KM, Caudill A, Rodriguez Celin M, et al. Mobility in osteogenesis imperfecta: a multicenter North American study. *Genet Med*. 2019;21(10): 2311-2318. doi:10.1038/s41436-019-0491-4
20. Castelein RM, Hasler C, Helenius I, et al. Complex spine deformities in young patients with severe OI: current concepts review. *J Child Orthop*. 2019;13(1):22-32.
21. Franzone JM, Shah SA, Wallace MJ, Kruse RW. OI: a pediatric orthopedic perspective. *Orthop Clin North Am*. 2019;50(2):193-209.
22. Jain M, Tam A, Shapiro JR, et al. Growth characteristics in individuals with OI in North America: results from a multicenter study. *Genet Med*. 2019; 21(2):275-283.
23. Barber LA, Abbott C, Nakhate V, et al. Longitudinal growth curves for children with classical OI (types III and IV) caused by structural pathogenic variants in type I collagen. *Genet Med*. 2019;21(5):1233-1239.
24. Balasubramanian M, Verschueren A, Kleevens S, et al. Aortic aneurysm/ dissection and OI: four new families and review of the literature. *Bone*. 2019;121:191-195.
25. Tam A, Chen S, Schauer E, et al. A multicenter study to evaluate pulmonary function in OI. *Clin Genet*. 2018;94(6):502-511.
26. Marr C, Seasman A, Bishop N. Managing the patient with osteogenesis imperfecta: a multidisciplinary approach. *J Multidiscip Healthc*. 2017;10: 145-155.

27. Trejo P, Fassier F, Glorieux FH, et al. Diaphyseal femur fractures in osteogenesis imperfecta: characteristics and relationship with bisphosphonate treatment. *J Bone Miner Res*. 2017;32(5):1034-1039.
28. Azzam KA, Rush ET, Burke BR, et al. Mid-term results of femoral and tibial osteotomies and fassier-duval nailing in children with OI. *J Pediatr Orthop*. 2018;38(6):331-336.
29. Mueller B, Engelbert R, Baratta-Ziska F, et al. Consensus statement on physical rehabilitation in children and adolescents with OI. *Orphanet J Rare Dis*. 2018;13(1):158.
30. Glorieux FH, Bishop NJ, Plotkin H, et al. Cyclic administration of pamidronate in children with severe OI. *N Engl J Med*. 1998;339(14):947-952.
31. Morello R. OI and therapeutics. *Matrix Biol*. 2018;71-72:294-312
32. Bains JS, Carter EM, Citron KP, et al. A multicenter observational cohort study to evaluate the effects of bisphosphonate exposure on bone mineral density and other health outcomes in OI. *JBMR Plus*. 2019;3(5):e10118.
33. Lv F, Liu Y, Xu X, et al. Zoledronic acid versus alendronate in the treatment of children with OI: a 2-year clinical study. *Endocr Pract*. 2018;24(2):179-188.
34. Boyce AM. Denosumab: an emerging therapy in pediatric bone disorders. *Curr Osteoporos Rep*. 2017;15(4):283-292.
35. Hoyer-Kuhn H, Netzer C, Koerber F, et al. Two years inverted question mark experience with denosumab for children with OI type vi. *Orphanet J Rare Dis*. 2014;9(1):145.
36. Hoyer-Kuhn H, Franklin J, Allo G, et al. Safety and efficacy of denosumab in children with OI - a first prospective trial. *J Musculoskelet Neuronal Interact*. 2016;16(1):24-32.
37. Marini JC, Hopkins E, Glorieux FH, et al. Positive linear growth and bone responses to growth hormone treatment in children with types III and IV OI: high predictive value of the carboxyterminal propeptide of type I procollagen. *J Bone Miner Res*. 2003;18(2):237-243.
38. Antoniazzi F, Monti E, Venturi G, et al. GH in combination with bisphosphonate treatment in OI. *Eur J Endocrinol*. 2010;163(3):479-487.
39. Haas AV, LeBoff MS. Osteoanabolic agents for osteoporosis. *J Endocr Soc*. 2018;2(8):922-932.
40. Vahle JL, Sato M, Long GG, et al. Skeletal changes in rats given daily subcutaneous injections of recombinant human parathyroid hormone (1-34) for 2 years and relevance to human safety. *Toxicol Pathol*. 2002; 30(3):312-321.
41. Tauer JT, Robinson ME, Rauch F. OI: new perspectives from clinical and translational research. *JBMR Plus*. 2019;3(8):e10174.
42. Tournis S, Dede AD. O -a clinical update. *Metabolism*. 2018;80:27-37.
43. Rossi V, Lee B, Marom R. OI: advancements in genetics and treatment. *Curr Opin Pediatr*. 2019 12;31(6):708-715.
44. Grafe I, Yang T, Alexander S, et al. Excessive transforming growth factor-beta signaling is a common mechanism in OI. *Nat Med*. 2014;20(6):670-675.
45. Deyle DR, Khan IF, Ren G, et al. Normal collagen and bone production by gene-targeted human osteogenesis imperfecta iPSCs. *Mol Ther*. 2012;20(1): 204-213.
46. Nijhuis W, Verhoef M, van Bergen C, Weinans H, Sakkers R. Fractures in osteogenesis imperfecta: pathogenesis, treatment, rehabilitation and prevention. *Children (Basel)*. 2022;9(2):268. doi:10.3390/children9020268
47. Piantoni L, Noel MA, Francheri Wilson IA, et al. Surgical treatment with pedicle screws of scoliosis associated with osteogenesis imperfecta in children. *Spine Deform*. 2017;5(5):360-365. doi:10.1016/j.jspd.2017.03.002
48. Mrosk J, Bhavani GS, Shah H, et al. Diagnostic strategies and genotype-phenotype correlation in a large Indian cohort of osteogenesis imperfecta. *Bone*. 2018;110:368-377. doi:10.1016/j.bone.2018.02.029
49. Li LJ, Lyu F, Song YW, et al. Genotype-phenotype relationship in a large cohort of osteogenesis imperfecta patients with COL1A1 mutations revealed by a new scoring system. *Chin Med J (Engl)*. 2019;132(2):145-153. doi:10.1097/CM9.0000000000000013

MHA MEDIHEALTH ACADEMY

Surgery on Children

Case Report

doi: 10.51271/SOC-0031

A rare case of primary pulmonary embryonal rhabdomyosarcoma in children

Mehmet Hamdi Şahan[1], Şeyma Eseoğlu[2], Melih Akşamoğlu[1]

[1]Department of Radiology, Faculty of Medicine, Gaziantep University, Gaziantep, Turkiye

[2]Department of Radiology, Gaziantep City Hospital, Gaziantep, Turkiye

Received: 17/10/2024 ◆ **Accepted**: 23/10/2024 ◆ **Published**: 20/01/2025

Cite this article: Şahan MH, Eseoğlu Ş, Akşamoğlu M. A rare case of primary pulmonary embryonal rhabdomyosarcoma in children. *Surg Child.* 2025;2(1):33-35.

Corresponding Author: Mehmet Hamdi Şahan, drmehmetsahan@hotmail.com

ABSTRACT

Rhabdomyosarcoma is one of the most common soft tissue sarcomas in adolescence and young adults. Histologically, rhabdomyosarcoma has many subgroups, including embryonal, alveolar, pleomorphic, and spindle cell/sclerosing rhabdomyosarcomas. More than 50% of embryonal rhabdomyosarcomas occur in the head and neck region. The retroperitoneum and pelvis are less common sites of involvement. Primary pulmonary embryonal rhabdomyosarcoma is extremely rare. A 3-year-old girl presented with symptoms of cough and shortness of breath. A mass lesion with regular contours, approximately 3x3 cm in size, containing millimetric air densities within, and having soft tissue density was detected in the upper lobe of the right lung. According to the results of bronchoscopy and biopsy, a right thoracotomy and right upper lobectomy were performed with the diagnosis of embryonal rhabdomyosarcoma. We present a case whose pathology confirmed the diagnosis of embryonal rhabdomyosarcoma.

Keywords: Embryonal, rhabdomyosarcoma, pulmonary, computed tomography

*This case was presented as a poster presentation at the 42th National Radiology Congress (TÜRKRAD 2021).

INTRODUCTION

Rhabdomyosarcoma is one of the most common soft tissue sarcomas in adolescents and young adults.[1,2] It accounts for an estimated 4.5% of all childhood cancers, with an incidence of six cases per one million annually.[1,3] Histologically, rhabdomyosarcoma has several subgroups, primarily embryonal, alveolar, pleomorphic, and spindle cell/sclerosing rhabdomyosarcomas.[2-5] It is usually seen in children under 15 years of age.[6] More than 50% of embryonal rhabdomyosarcomas occur in the head and neck region.[7] The retroperitoneum and pelvis are less common sites of involvement.[6,8] Primary pulmonary embryonal rhabdomyosarcoma is extremely rare.[3,5,6,8]

CASE

A 3-year-old girl presented with complaints of progressive cough and shortness of breath for 1.5 months. The patient's physical examination revealed weight loss, and laboratory findings were unremarkable. A round opacity with regular contours and approximately 3x3 cm in size was observed in the upper lobe of the right lung on the chest X-ray (Figure 1). A mass lesion with regular contours and millimetric air densities and soft tissue density was observed in the upper lobe of the right lung on chest computed tomography (CT) (Figure 2 a, b). In the patient whose differential diagnosis was considered to be hydatid cyst, *Echinococcus* IHA was negative. The lesion described in the right lung on PET CT examination had an SUVmax value of 2.8 (Figure 3). An endobronchial lesion protruded from the entrance of the upper lobe of the right lung to the trachea was observed in bronchoscopy. The pathology report diagnosed small blue round cell tumor (primarily embryonal rhabdomyosarcoma). Surgery was planned based on the findings. Right thoracotomy and right lung upper

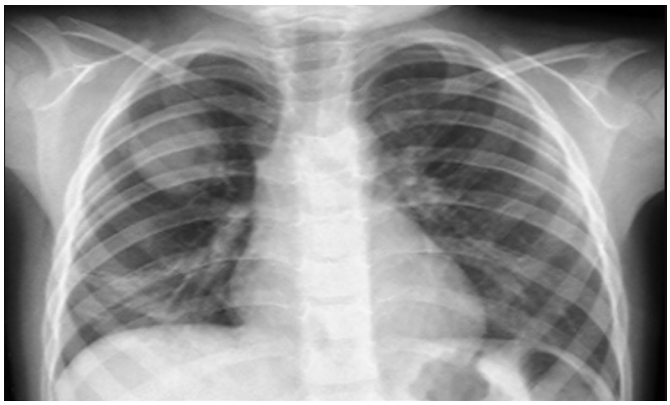


Figure 1. Chest X-ray, round opacity with regular contours in the upper lobe of the right lung

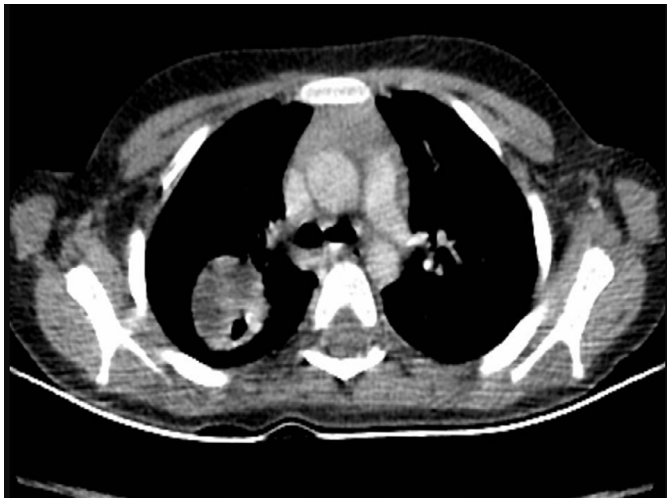


Figure 2a. Thorax computed tomography (mediastinal), a mass lesion with regular borders in the upper lobe of the right lung, containing millimetric air densities and having soft tissue density

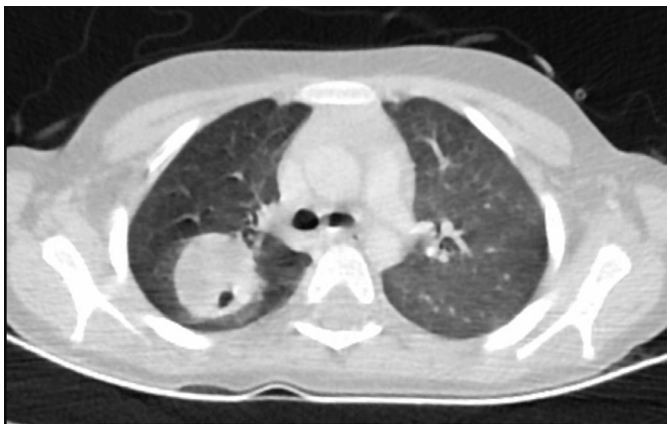


Figure 2b. Thorax computed tomography (parenchymal), a mass lesion with regular borders in the upper lobe of the right lung, containing millimetric air densities and having soft tissue density

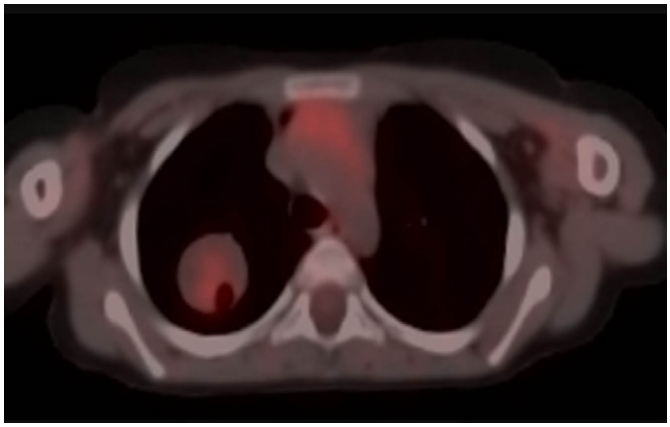


Figure 3. PET CT, a lesion with SUV max value of 2.8 in the right lung

lobectomy were performed. Pathology confirmed the diagnosis of embryonal rhabdomyosarcoma.

DISCUSSION

Rhabdomyosarcoma may develop unusually even in regions without skeletal muscle differentiation.[1,6] Primary pulmonary rhabdomyosarcoma is a very rare site for rhabdomyosarcoma to develop. Pulmonary rhabdomyosarcoma is histopathologically formed in two ways. The first is that the tumor arises from heterotrophic islands of striated muscle. The second is that the tumor arises from metaplasia of undifferentiated mesenchymal cells.[9] These tumors develop either in the context of congenital cystic lesions or from normal lung tissue. The prognosis is different in both groups. Tumors associated with congenital cystic malformations usually have a better prognosis.[9] This is because these cystic lesions are diagnosed early and are usually completely resectable lesions. On the other hand, rhabdomyosarcoma without cystic lesions presents clinically late, reaches a larger size, and cannot be completely resected.[1,6,9] There was no obvious cystic component in our case. Children with tumors smaller than 5 cm generally have a better prognosis than children presenting with larger tumors.[1,6,8-10] In our case, the tumor size was 3 cm and the tumor was completely removed surgically. Most cases present with cough, shortness of breath and chest pain.[9,10] Our case also had similar symptoms.

CONCLUSION

In the differential diagnosis of a child presenting with abnormal opacity on chest X-ray, rare conditions such as lung tumors should be kept in mind. Thus, early surgical intervention can be performed and long-term morbidity and mortality resulting from advanced stages of the disease and treatment complications can be prevented.

ETHICAL DECLARATIONS

Informed Consent

The patient's parents signed the informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Dasgupta R, Fuchs J, Rodeberg D. Rhabdomyosarcoma. *Semin Pediatr Surg.* 2016;25(5):276-283
2. Hafiz B, Bamefleh H. Primary pulmonary alveolar rhabdomyosarcoma in a pediatric patient: a case report with literature review. *Cureus*. 2022;14(1): e21270.
3. Taseer R, Ahmed TT. Embryonal rhabdomyosarcoma presenting as lung metastasis in an adult: an uncommon presentation. *Cureus*. 2021;13(2): e13545.
4. Leiner J, Le Loarer F. The current landscape of rhabdomyosarcomas: an update. *Virchows Archiv.* 2020;476(1):97-108.
5. Skapek SX, Ferrari A, Gupta AA, et al. Rhabdomyosarcoma. *Nat Rev Dis Primers.* 2019;5(1):1-19.
6. Vanhoenacker FM, De Schepper AM, Parizel PM, Gielen JL. Imaging of soft tissue tumors. Springer Science & Business Media. 2006.
7. Beverly Raney R, Walterhouse DO, Meza JL, et al. Results of the Intergroup Rhabdomyosarcoma Study Group D9602 protocol, using vincristine and dactinomycin with or without cyclophosphamide and radiation therapy, for newly diagnosed patients with low-risk embryonal rhabdomyosarcoma: a report from the Soft Tissue Sarcoma Committee of the Children's Oncology Group. *J Clin Oncol.* 2011;29(10):1312-1318.

8. Iqbal Y, Abdullah MF, Al-Jadaan S, Trabichi H, Al Omari A, Al-Sudairy R. Embryonal rhabdomyosarcoma of the lung in a child: case report and literature review. *Ann Saudi Med.* 2002;22(1-2):91-93.
9. Chang HL, Rosenberg AE, Friedmann AM, Ryan DP, Masiakos PT. Primary pulmonary rhabdomyosarcoma in a 5-month-old boy: a case report. *J Pediatr Hematol Oncol.* 2008;30(6):461-463.
10. Özcan C, Çelik A, Ural Z, Veral A, Kandiloğlu G, Balik E. Primary pulmonary rhabdomyosarcoma arising within cystic adenomatoid malformation: a case report and review of the literature. *J Pediatr Surg.* 2001;36(7):1062-1065.

MHA MEDIHEALTH ACADEMY

Surgery on Children

Letter to the Editor

doi: 10.51271/SOC-0032

Evaluation of surgical and non-surgical interventions in pectus excavatum management: nuss procedure vs vacuum bell therapy

Mesut Buz

Department of Thoracic Surgery, Kartal Dr. Lütfi Kırdar City Hospital, İstanbul, Turkiye

Received: 12/07/2024 ◆ **Accepted**: 06/08/2024 ◆ **Published**: 20/01/2025

Cite this article: Buz M. Evaluation of surgical and non-surgical interventions in pectus excavatum management: nuss procedure vs vacuum bell therapy. *Surg Child.* 2025;2(1):36-37.

Corresponding Author: Mesut Buz, mesutbuzmd@gmail.com

Keywords: Pectus excavatum, nuss procedure, vacuum bell therapy

Dear Editor,

Pectus excavatum (PE) is a congenital deformity characterized by a sunken sternum and costal cartilages, resulting in a concave chest wall appearance. It has a prevalence of 1 in 400 to 1 in 1.000 live births, predominantly affecting males. The deformity can lead to physiological complications, such as reduced cardiopulmonary function, and psychosocial distress, particularly during adolescence.[1]

Traditionally, the Nuss procedure, a minimally invasive surgical technique, has been the standard treatment for moderate to severe cases of PE. This method involves the insertion of a concave metal bar beneath the sternum, which is then flipped to correct the depression. Studies have demonstrated its efficacy in achieving significant chest wall correction with minimal complications compared to open surgical techniques.[2]

However, non-surgical approaches, particularly vacuum bell therapy (VBT), have gained attention as alternative treatments for PE, especially for patients who either do not meet surgical criteria or prefer non-invasive options. VBT involves the use of a suction cup device that creates negative pressure to lift the sternum over time.[3]

The Nuss procedure is highly effective in correcting severe PE with documented improvements in Haller index (HI) and patient-reported outcomes. The correction achieved through this procedure is largely stable and results in high patient satisfaction due to the significant cosmetic and functional improvements observed. Nevertheless, the procedure carries risks such as bar displacement, infection, and potential damage to the heart and lungs, which although rare, necessitate careful patient selection and surgical expertise.[4]

VBT has emerged as a viable non-surgical option, particularly for younger patients and those with milder forms of PE. Studies indicate that the efficacy of VBT correlates with the duration and daily hours of usage, with optimal results seen in patients who adhere to a regimen of at least 6 hours daily for a period extending beyond 12 months. A significant reduction in HI and improvements in the thoracic index have been reported, although the degree of correction is generally less pronounced compared to surgical intervention. Moreover, VBT is associated with fewer complications, primarily mild and transient skin changes, making it a safer option for patients unsuitable for surgery.[5,6]

In conclusion, both the Nuss procedure and vacuum bell therapy offer effective solutions for the correction of pectus excavatum, each with distinct advantages and limitations. The choice between these treatments should be guided by the severity of the deformity, patient age, comorbidities, and personal preferences. The integration of these therapeutic options allows for a more personalized approach to managing PE, enhancing patient outcomes and satisfaction.

There is a need for more comprehensive, randomized controlled trials to compare these modalities and better delineate their long-term efficacy and safety profiles. Such data will be invaluable in refining treatment guidelines and enhancing patient care in pediatric surgery.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Prada Arias M, Gómez Veiras J, Rodríguez Iglesias P, Aneiros Castro B, Fernández Eire P, Montero Sánchez M. Treatment of pectus excavatum with vacuum bell during puberty. *Cir Pediatr*. 2023;36(3):116-121.
2. Nuss D, Kelly RE Jr, Croitoru DP, Katz ME. A 10-year review of a minimally invasive technique for the correction of pectus excavatum. *J Pediatr Surg*. 1998;33(4):545-552.
3. Lei W, Shao M, Hu Y, et al. Vacuum bell therapy for pectus excavatum: a retrospective study. *BMC Pediatr*. 2024;24(1):173.
4. Jung Y, Yi E, Lee K, Chung JH, Cho S, Lee S. Surgical versus vacuum bell therapy for the correction of pectus excavatum: a comparison of 1-year treatment outcomes. *J Chest Surg*. 2021;54(6):473-479.
5. Loufopoulos I, Karagiannidis IG, Lampridis S, Mitsos S, Panagiotopoulos N. Vacuum bell: is it a useful innovative device for pectus excavatum correction? *Turk Thorac J*. 2021;22(3):251-256.
6. Luo D, Cheng K, Yuan M, Xu C, He T. Efficacy and determinants of vacuum bell treatment in preschool children with pectus excavatum. *Front Pediatr*. 2022;10:1008437.