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Original Research Article

Optimizing Outcomes in Redo Hypospadias Repair: The Impact of Perioperative Hyperbaric Oxygen Therapy on Tissue Healing

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Abstract

Introduction: Redo hypospadias repairs present significant challenges due to tissue scarring and hypovascularity, substantially increasing the risk of complications. Previous literature document complication rates above 40% after three or more previous urethroplasties, highlighting the need for strategies that enhance tissue quality. Postoperative hyperbaric oxygen therapy (HBOT) can improve healing outcomes. However, the role of perioperative HBOT in enhancing tissue quality through neovascularization remains unclear. This study aims to evaluate whether perioperative HBOT (both pre- and postoperative) instead of the senior author's standard of care (SOC) topical nitroglycerin reduces complication rates and improves surgical outcomes in redo hypospadias repair.

Methods: We retrospectively reviewed 47 patients (aged 3 – 18 years) who underwent redo hypospadias repairs between January 2019 and January 2022, following 2-4 prior failed procedures. Inclusion criteria included patients with failed primary repairs, while exclusion criteria included patients with contraindications to HBOT or incomplete follow-up data. Patients were allocated to treatment groups (i.e. perioperative HBOT v. SOC) based on insurance coverage for HBOT rather than randomization. Group 1 (n=31) received perioperative HBOT while Group 2 (n=16) received SOC, consisting of topical nitroglycerin ointment. Additionally, BMG patients in both groups received topical vitamin E for 2-3 weeks post-operatively. HBOT protocol consisted of 20 preoperative sessions and 5-10 postoperative sessions at 2.0 ATA.

Results: The two groups did not differ significantly in hypospadias locations (Group 1: 22 distal, 9 proximal; Group 2: 10 distal, 6 proximal; P=0.795) or operative technique (Group 1: 21 one-stage dorsal inlay grafts [DIG], 10 staged buccal mucosa grafts [BMG]; Group 2: 10 one-stage DIG, 6 staged BMG; P=0.972). The HBOT group demonstrated a reduction in postoperative

complications compared to SOC group (6.4% vs. 25%; P=0.179 95% CI 0.05-1.26), though this difference did not reach the level of statistical significance. Specifically, the HBOT group experienced only two cases of fistula formation, while the SOC group had four total complications: one case of graft contracture and three fistulas. All complications were successfully corrected surgically one year postoperatively using the perioperative HBOT protocol. Subjective clinical assessment also suggested improved tissue quality and pliability in HBOT-treated patients.

Conclusions: This study suggests that perioperative HBOT was associated with a lower, but not statistically significant, complication rate in redo hypospadias repairs. The findings support the potential use of perioperative HBOT in promoting tissue healing and justify further investigation through prospective randomized controlled trials to establish definitive efficacy and optimize treatment protocols for this challenging patient population.

Keywords: Repeat Hypospadias repair, hyperbaric oxygen therapy, tissue preconditioning, reconstructive urology

Introduction

Redo hypospadias surgeries represent one of the most challenging scenarios in pediatric reconstructive urology. These cases are characterized by the compromised structural and functional integrity of penile tissues following previous failed repairs. Each subsequent operation often results in increased scar tissue formation, diminished tissue elasticity, and a progressively hypovascular wound bed. The cumulative effects of these changes create conditions that are fundamentally unfavorable for successful surgical repair and optimal wound healing.

The pathophysiologic changes in previously operated hypospadias cases contribute substantially to elevated complication rates. Re-operative urethroplasty after failed hypospadias repair demonstrates a dramatic escalation in complication rates with each successive operation. While primary distal and proximal repairs show 12% complication rate, re-operative procedures demonstrate significantly higher failure rates: 32% for repeat tubularized incised plate (TIP) repairs, 35% for inlay repairs, and 40% for two-stage repairs. Most critically, logistic regression analysis reveals that each prior surgery increases the odds of subsequent complications 1.5-fold, with complications rates reaching 40% in patients who have undergone three or more prior operations.[1] The most common complications—urethrocutaneous fistulas, graft shrinkage, strictures, and wound dehiscence—are directly related to the impaired healing capacity of scarred, ischemic tissues.[2,3,4,5] These high failure rates underscore that compromised tissue quality and inadequate wound healing are critical determinants of poor outcomes in repeat repairs.

Hyperbaric oxygen therapy (HBOT) represents a potential adjunctive intervention to address the underlying pathophysiologic mechanisms in these cases. HBOT involves the administration of 100% oxygen at pressures greater than atmospheric pressure, typically 2.0-2.4

atmospheres absolute (ATA).[6] This approach markedly increases the dissolved oxygen content in blood plasma, enhancing oxygen delivery to tissues independent of hemoglobin-bound oxygen. The biological effects of HBOT include stimulation of angiogenesis, reduction of tissue edema, enhancement of fibroblast proliferation, and augmentation of collagen synthesis—all critical elements for improved wound strength and healing.[7,8]

In related fields such as plastic surgery, perioperative HBOT has demonstrated efficacy in reducing postoperative complications, enhancing graft take, and improving overall wound healing outcomes.[7] This report by Friedman et al. demonstrated that preconditioning HBOT reduced post-abdominoplasty complications in a large series of patients.[7] Furthermore, the senior author's prior experience in severely scarred and re-operative epispadias and bladder exstrophy contributed to his conviction that preconditioning HBOT rejuvenated the hypovascular tissues.[5] Application of this rationale to hypospadias repair suggests that perioperative HBOT could potentially reduce complication rates by optimizing tissue vascularity and regenerative capacity prior to surgical intervention. Additionally, post-operative HBOT may also support healing processes through enhanced tissue oxygenation and cellular repair mechanisms. Given that compromised vascularity appears to be a fundamental mechanism underlying the exponentially increasing failure rates in redo cases, interventions specifically targeting tissue perfusion and oxygenation represent a logical therapeutic approach.

We hypothesized that a perioperative HBTO regimen (encompassing both pre-operative and post-operative HBOT) would reduce complication rates in redo hypospadias repairs by promoting neovascularization in scarred tissues and enhancing overall wound healing capacity. This study aims to evaluate whether perioperative HBOT instead of SOC reduces complication rates and improves surgical outcomes in redo hypospadias repairs.

Methods

This investigation represents a retrospective cohort study of patients treated in the senior author's private practice. These patients were referred to him as a private practicing surgeon and the hospital location, where he had surgical privileges, was chosen by him and determined by the patient's address and his surgical schedule. The study received Institutional Review Board approval (IRB #17-53), and the IRB approved a waiver of informed consent for analysis of de-identified data. The study compares outcomes in patients who underwent redo hypospadias repairs with perioperative HBOT versus standard of care.

We conducted a systematic retrospective review of all patients who underwent redo hypospadias repairs by a single senior pediatric urologist between January 2019 and January 2022. Inclusion criteria encompassed: (1) age 3-18 years, (2) history of 2+ prior failed hypospadias repairs, (3) at least four months follow-up post-operatively. Exclusion criteria included patients with either contraindications to HBOT, incomplete follow-up data, or minor revisions such as skin chordee, small fistulas, or minor revisions.

The cohort was divided into two groups based on insurance coverage for HBOT, as HBOT was not covered by certain insurance plans during the study period. Of note, all patients were offered HBOT and informed about the implications of HBOT, nonetheless insurance plan coverage was the final determinant. No clinical factors beyond insurance coverage such as degree of scarring, number of prior surgeries, or tissue quality were used for group allocation.

Patients in the HBOT group received a standardized hyperbaric oxygen treatment protocol consisting of 20 preoperative sessions and 5 to 10 postoperative sessions, administered at 2.0 ATA of 100% oxygen for 90 minutes, with 5-minute air breaks every 20 minutes to reduce the risk of oxygen toxicity. The variation in postoperative sessions (5-10) was due to two patients

who were not able to complete 10 postoperative sessions because they moved away from the center and were unable to continue. Sessions were conducted in a hyperbaric chamber under direct medical supervision. The protocol of 20 preoperative HBOT sessions was established based on the senior author's prior clinical experience with similarly complex re-operative cases in bladder exstrophy patients, which demonstrated favorable outcomes with this regimen as no major postoperative complications were seen in the cohort.[5]

All procedures were performed using standardized techniques appropriate for the specific anatomical presentation. Dorsal inlay graft (DIG) repair was utilized for patients with adequate urethral plate tissue and moderate ventral curvature, while staged buccal mucosa graft (BMG) reconstruction was reserved for cases with severe scarring, inadequate urethral plate, or significant ventral curvature requiring two-stage reconstruction.[9] The choice between techniques was based on preoperative and intraoperative assessment of tissue quality, degree of curvature (>30 degrees favoring staged approach), and extent of previous.

The SOC group received 2% nitroglycerine ointment application to the penis at the conclusion of surgery (integrated into the tie-over dressing for staged BMG cases or under gauze/Tegaderm for one-stage DIG cases). The rationale and choice of using nitroglycerin as a vasodilator is based on prior studies demonstrating its efficacy in improving tissue perfusion and reducing flap necrosis.[10, 11] For one-stage DIG SOC patients, parents applied nitroglycerin every 8 hours for 2-3 days after dressing removal. The HBOT group did not receive nitroglycerin ointment in the operating room or at home, as the HBOT was considered the primary vasodilatory intervention.

For patients who underwent repair with BMG in both groups (HBOT and SOC), topical vitamin E was applied to the graft three times daily for 2-3 weeks post-operatively to promote

optimal wound healing and graft pliability. For staged repairs in both groups, graft stretching was performed during the interval period between stages to optimize graft pliability and dimensions. All surgical procedures were performed by the senior author with extensive experience managing complex urologic cases, including redo hypospadias repair. Standard perioperative antibiotic prophylaxis consisting of cefazolin was administered to all patients.

Data were collected on patient demographics, location of hypospadias (distal or proximal), operative technique, number of prior surgeries, and complications. Of note, classification of distal v. proximal location was determined by original meatal location, with distal cases defined as coronal, sub-coronal, or distal penile, and proximal cases defined as mid-shaft, proximal penile, penoscrotal, or scrotal locations. The primary outcome measures included overall complication rates and specific complications, particularly fistula formation and graft contracture. Secondary outcomes included subjective assessment of tissue quality by the treating surgeon. Statistical analysis was performed using IBM SPSS Statistics and categorical variables were analyzed using chi-square or Fisher's exact test. Continuous variables were compared using t-test or Mann-Whitney U test depending on distribution normality. Results were considered statistically significant at $p<0.05$.

Representative photographic documentation was obtained as part of routine clinical care and de-identified for analysis; use of these images was approved under the IRB waiver.

Results

Our search methodology yielded a final study population of 47 patients who met all inclusion criteria during the study period with 31 patients receiving HBOT based on insurance coverage, while 16 patients received SOC with nitroglycerin. The two groups did not differ significantly in terms of hypospadias locations (HBOT: 22 distal, 9 proximal; SOC: 10 distal, 6 proximal; P=0.795) or operative technique (Group 1: 21 one-stage dorsal inlay grafts [DIG], 10 staged buccal mucosa grafts [BMG]; Group 2: 10 one-stage DIG, 6 staged BMG; P=0.972). Table 1 summarizes the baseline characteristics and outcomes for both study groups. Patient demographics and clinical characteristics were comparable between the two groups. Also, patient follow-up ranged from 4 months to 3 years; the median follow-up was 12 months. All patients had ≥ 4 months of follow-up per inclusion criteria.

The HBOT group experienced a total of two cases of fistula formation (6.4%), while the SOC group had four total complications: three cases of fistula formation and one case of graft contracture (25% total complication rate), as illustrated in Figure 1 (p = 0.179, 95% CI 0.05-1.26). All complications were successfully corrected surgically one year postoperative using the same perioperative HBOT protocol (20 preoperative and 5-10 postoperative sessions) as employed in the initial intervention. The two patients from the HBOT group, as well as the four patients from the SOC group, who experienced these complications had the perioperative HBOT protocol incorporated into the treatment plan for addressing the complications. Notably, patients who experienced initial complications and underwent revision surgery with HBOT demonstrated successful healing without any further complications during the follow-up period.

A representative case illustrating the clinical benefits of perioperative HBOT is presented in Figure 2. This case involved a patient with severe penile scarring following three major prior

surgical procedures: dermal graft, urethroplasty, and meatotomy. Pre-operative imaging demonstrated extensive scarring and tissue compromise (Figure 2A). Following 20 preoperative HBOT sessions, marked improvement in tissue quality and pliability was observed (Figure 2B), facilitating subsequent surgical intervention. The surgical procedure involved excision of scar tissue and replacement of corporal wall with dermal graft (Figure 2C), with early healing noted at 10 days post-operatively (Figure 2D). At 3 months post-operatively from the first stage, tissue quality remained optimal (Figure 2E), allowing for successful second-stage surgery involving proximal Duplay urethroplasty and distal inlay graft (Figure 2F-G).[12] Final post-operative results demonstrated good functional and cosmetic outcomes (Figure 2H).

Subjective evaluation of tissue quality and healing was performed by both the senior pediatric urologist and patients' parents throughout the treatment course. This assessment, while clinically valuable, represents observational data without standardized measurement tools or blinded evaluation, which must be acknowledged as a limitation. Parents of patients in the HBOT group consistently reported notable improvement in tissue pliability following the 20 preoperative HBOT sessions. Additionally, the treating pediatric urologist documented that tissues in HBOT-treated patients appeared markedly softer with enhanced overall wound healing quality compared to those in the SOC group. No significant adverse events related to HBOT were observed during the study. No cases of oxygen toxicity, pneumothorax, or claustrophobia requiring treatment discontinuation were documented.

When outcomes are analyzed by hypospadias location, distal cases in HBOT group (n=22) had a 4.5% complication rate (1 fistula) compared to 20% in SOC group distal cases (n=10, 2 fistulas). For proximal cases, HBOT group (n=9) had an 11.1 complication rate (1 fistula) compared to 33.3% in SOC group (n=6, 1 graft contracture and 1 fistula). While these

trends favor the HBOT group in both subgroups, the small numbers preclude meaningful statistical analysis.

Discussion

The management of redo hypospadias repairs remains one of the most challenging scenarios in pediatric reconstructive urology. The cumulative effects of multiple failed operations—including tissue scarring, reduced elasticity, and compromised vascularity—create conditions that significantly increase the risk of complications and surgical failure. Our study suggests that combined pre- and post-operative HBOT may improve outcomes in these challenging cases by addressing the fundamental pathophysiologic deficits of scarred, hypovascular tissues.

The observed reduction in complication rates in Group 1 (6.4% vs. 25%) represents a lower rate, though it did not reach statistical significance (P=0.179, 95% CI 0.05-1.26) due to the small sample size and low absolute number of complications, as seen in Figure 1. However, this finding aligns with prior studies suggesting that HBOT can reduce failure rates in complex reconstructive procedures.[8,13] Notably, our data revealed a trend toward decreased urethrocutaneous fistula formation, which represents one of the most common complications in hypospadias repair.[3] Regarding the patients who experienced complications and required further surgical revision, regardless of initial group allocation, all patients from both the HBOT and SOC groups who experience complications were successfully treated using the same perioperative HBOT protocol as the HBOT group. These patients demonstrated similar subjective tissue quality improvements during their revision surgeries and no complications related to HBOT therapy were observed in our cohort.

The lack of statistical significance demonstrated herein should not overshadow the potential clinical importance of these findings. A post-hoc power analysis demonstrated that 120 total patients would be required to demonstrate statistical significance given the observed effect

size, which only further highlights the need for larger, multicenter studies to definitively establish the efficacy of this HBOT protocol in this patient population.

Several limitations must be acknowledged that could influence the interpretation of our results. The retrospective nature of this study introduces potential selection bias, as patient allocation was determined by insurance coverage rather than clinical factors, which could result in the two treatment groups representing different socioeconomic demographics with potentially different baseline health characteristics, adherence patterns, or access to care. This non-randomized allocation potentially limits both the ability to draw causal inferences from the observed associations and the study's external validity. Additionally, the two treatment groups differed in their adjunctive interventions: SOC patients received nitroglycerin ointment, while HBOT patients received HBOT without this specific adjunct therapy; meanwhile, patients in both groups who underwent graft placement received topical vitamin E treatment. Although there was heterogeneity in treatment protocols across patients: HBOT alone or HBOT and vitamin E for graft patients in the HBOT group versus nitroglycerin alone or nitroglycerin and vitamin E for graft patients in the SOC group; one can still compare both groups to evaluate the role of HBOT as a vasodilatory treatment versus nitroglycerin.

The inclusion of both distal and proximal cases represents another potential confounding factor. Proximal hypospadias repairs are inherently more complex with higher baseline complication rates regardless of intervention. HBOT group had a higher number of proximal cases (9/31 vs. 6/16), which typically have higher complications rates, yet still demonstrated better outcomes. Furthermore, there was no statistically significant difference between the HBOT and SOC group regarding hypospadias location ($p = 0.795$), thus the potential impact of

this “limitation” would be limited. Nonetheless, future studies should stratify outcomes by complexity and anatomical location of hypospadias to better understand the benefits of HBOT.

The subjective assessment of tissue quality outlined herein by both the treating surgeon and parents, while potentially clinically valuable, lacks objective validation and standardization. In fact, multiple studies have shown that clinical assessment of tissue characteristics, even by experienced surgeons, can be limited when compared to objective standards.[14] Future studies should incorporate standardized, blinded assessment of tissue quality protocols and potentially even histological analysis to provide more robust, definitive evidence of tissue quality improvements.

Previous studies have shown that postoperative HBOT can improve healing outcomes in various surgical settings. However, the role of preoperative HBOT in enhancing tissue quality through neovascularization remains in question, particularly in the context of redo hypospadias repairs. The concept of tissue preconditioning through preoperative HBOT is compelling, as it may stimulate neovascularization in scarred tissue before surgical intervention.[13] By enriching the wound bed with new capillaries and increased oxygen tension, HBOT potentially improves oxygen supply during the critical early phases of healing, which may create a more favorable environment for successful repair. This hypothesis is supported by recent findings in similar clinical contexts, such as complex repeat surgeries for bladder exstrophy and epispadias, where preconditioning HBOT significantly reduced postoperative complications and improved wound healing outcomes.[5]

The biological mechanisms underlying these potential improved outcomes are multifaceted. HBOT is known to enhance tissue oxygenation, stimulate angiogenesis, promote fibroblast proliferation, and enhance collagen synthesis.[4] Furthermore, hyperbaric conditions

stimulate growth factors and cytokines critical for tissue repair while simultaneously attenuating inflammatory responses. Additionally, the preoperative application of HBOT may promote neovascularization in scarred tissue, creating a more favorable environment for surgical reconstruction and graft take.

The case presented in Figure 2 provides compelling visual evidence supporting the clinical utility of perioperative HBOT in complex redo hypospadias cases. The dramatic improvement in tissue quality observed between pre-treatment (Figure 2A) and post-HBOT conditioning (Figure 2B) demonstrates the potential for HBOT to reverse some of the pathophysiologic changes associated with repeated surgical trauma. The successful completion of multi-stage reconstruction in this severely compromised case, with good intermediate and final outcomes, supports the hypothesis that HBOT-mediated neovascularization can create conditions more favorable for complex reconstructive procedures. This case also illustrates the practical application of our HBOT protocol in the most challenging clinical scenarios, where conventional approaches might be expected to have higher failure rates.

The integration of HBOT into the surgical workflow presents logistical challenges, including the need for specialized equipment, trained personnel, and significant time commitment from patients and families. The economic impact of HBOT must also be considered, as the upfront costs are substantial. However, if HBOT reduces reoperation rates and overall healthcare utilization, the long-term cost-effectiveness profile may be favorable. A formal cost-utility analysis would be valuable to quantify the economic implications comprehensively.

Future research directions should include prospective, multicenter randomized controlled trials comparing standard care with and without HBOT while stratifying patients by the severity

of tissue compromise, anatomical location, and number of prior surgeries. Such studies should standardize all adjunctive treatments between groups to isolate the specific effects of HBOT. Additionally, regression analysis including variables such as age, number of prior operations, anatomical location, surgical procedure would help identify the most significant predictors of increased risk of complications. These approaches would provide higher-quality evidence regarding the efficacy of HBOT in this context. Furthermore, additional studies are needed to optimize HBOT regimens, determining the optimal number and timing of sessions to maximize benefits while minimizing costs and inconvenience.

Our findings have important implications for clinical practice and future research. For surgeons managing complex redo hypospadias cases, combined pre- and post-operative HBOT represents a potentially valuable adjunct that may improve outcomes in this challenging patient population. The physiological rationale and preliminary clinical evidence suggest that perioperative HBOT may promote neovascularization in scarred tissue, supporting its integration into SOC protocols for complex re-operative cases.

Conclusion

This retrospective study observed a lower - but not statistically significant - overall complication rates with perioperative HBOT in redo hypospadias repairs (6.4% vs. 25%, P=0.179, 95% CI 0.05-1.26). This preliminary evidence suggests perioperative HBOT may be a valuable adjunct in complex redo hypospadias repairs, but definitive conclusions cannot be drawn from the current study design.

Conflict of Interest Statement

All authors that contributed to this manuscript have no known competing financial interests or personal relationships that could have influenced their work on this paper.

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Ethical Approval

This retrospective study involved analysis of de-identified patient data collected as part of routine clinical care. This study was approved by the Institutional Review Board (IRB #17-53). The IRB granted a waiver of informed consent for the use of de-identified clinical data and images. Patient confidentiality was maintained throughout the data collection and analysis process, and no identifiable patient information is included in this manuscript.

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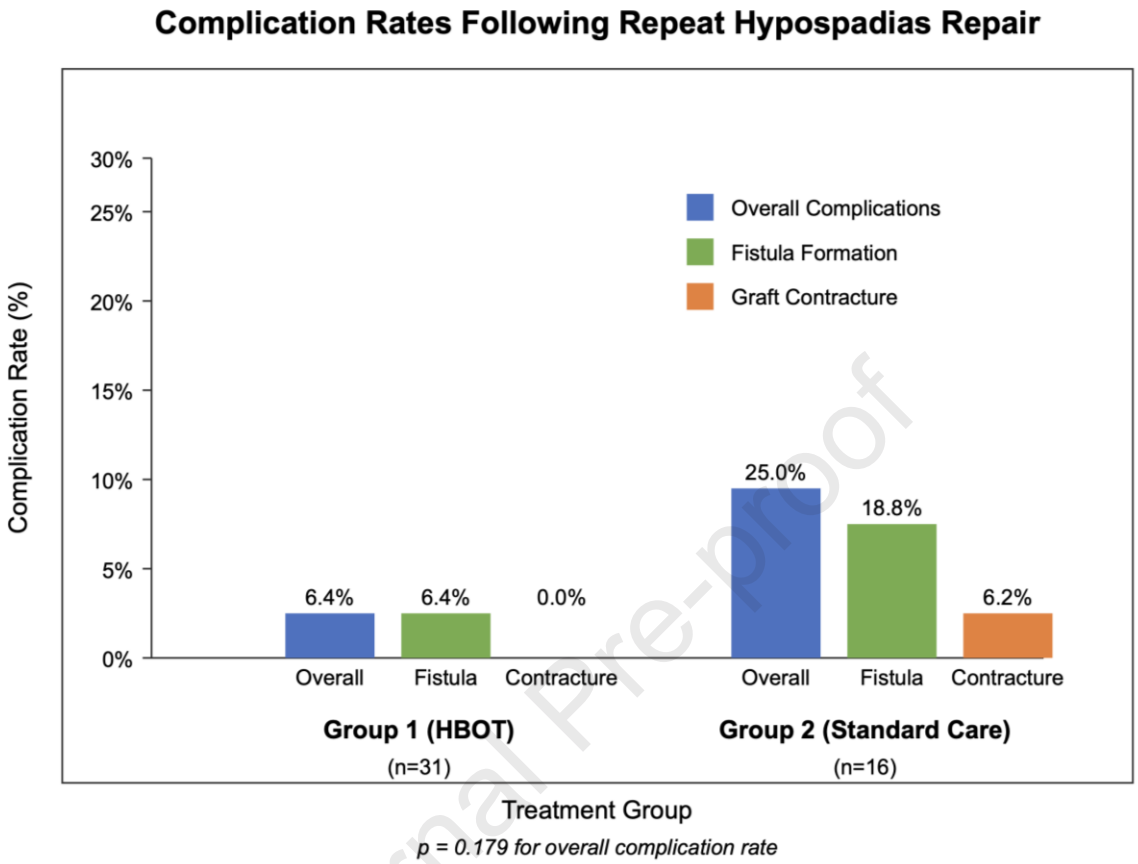
386 **Tables/Figures**



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388 *Figure 1: Comparison of Postoperative Complication Rates in Repeat Hypospadias Repair with*

389 *and without HBOT*

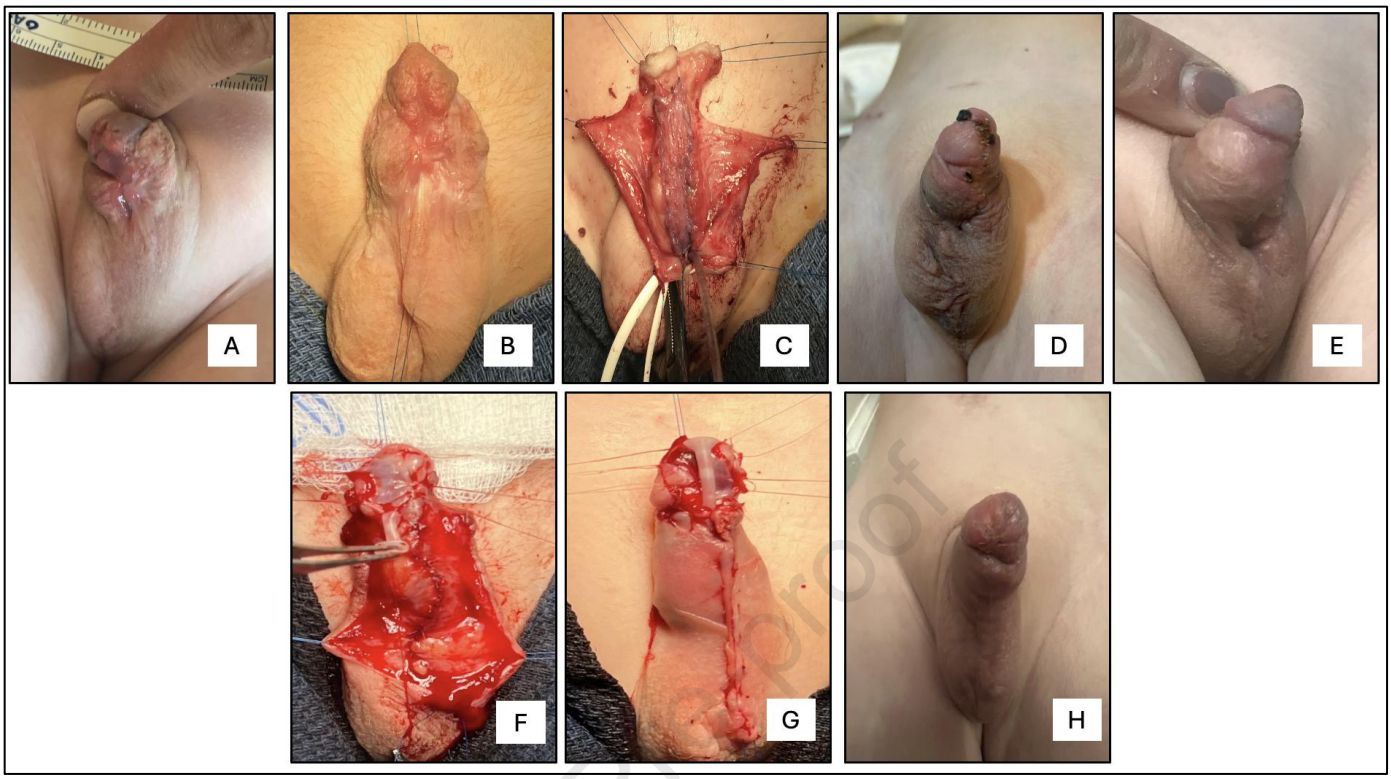

Figure 2: Representative Case Demonstrating Clinical Benefits of Perioperative HBOT in Complex Redo Hypospadias Repair

(A) Pre-operative appearance showing severe penile scarring following three prior major surgical procedures. (B) Tissue appearance after 20 preoperative HBOT sessions, demonstrating improved tissue quality and pliability. (C) Intraoperative view during excision of scar tissue and replacement of corporal wall with dermal graft. (D) Early post-operative healing at 10 days. (E) Tissue quality at 3 months post-operatively from first stage, showing healing. (F-G) Second-stage surgery involving proximal Duplay urethroplasty and distal inlay graft. (H) Final post-operative result demonstrating functional and cosmetic outcome.

Characteristic	Group 1 (HBOT) n=31	Group 2 (SOC) n=16	P-value
Hypospadias Location			.795
Distal	22 (71.0%)	10 (62.5%)	
Proximal	9 (29.0%)	6 (37.5%)	
Surgical Technique			.972
One-stage DIG	22 (71.0%)	10 (62.5%)	
Staged BMG	10 (32.3%)	6 (37.5%)	
Outcomes			
Total Complications	2 (6.4%)	4 (25.0%)	.179 (95% CI 0.05-1.26)
Fistula Formation	2 (6.4%)	3 (18.8%)	.314 (95% CI 0.06-1.85)
Graft Contracture	0 (0%)	1 (6.3%)	.340 (95% CI 0.01-4.12)

Table 1: Baseline Characteristics and Outcomes