REVIEW

Illuminating the use of photodynamic therapy in urologic oncology

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Introduction: *We report the first scoping review of the clinical urologic literature for photodynamic therapy (PDT) among multiple urologic malignancies.*
Materials and methods: *A scoping review using Medline and Embase was performed for treatment of urologic malignancies with PDT.*
Results: *There were 84 papers included with the majority involving bladder and prostate cancer. Upper tract urothelial cancer (UTUC) only comprised three publications and there was no clinical data for renal or testicular cancer. Utilizing PDT in prostate cancer led to a negative biopsy rate of 30%-100%. Bladder cancer treatment with PDT had a 3-month complete response rate of 31.5%-100%. UTUC management with PDT reported at least 50% complete response rate.*
Conclusions: *Ultimately, PDT has been established as a safe and effective treatment for urologic malignancies and we provide the first comprehensive review of the literature regarding the utility of this treatment modality.*

Key Words: quality of life, photochemotherapy, prostatic neoplasm, urinary bladder neoplasms, hematoporphyrin derivative, erectile dysfunction, hematuria, urinary incontinence, photodynamic therapy

Introduction

Photodynamic Therapy (PDT) is a method of treating cancer involving administering a drug that is taken up by cancer cells and activated by a light source. This activated compound within the cancer cells goes through a series of reactions, killing the cancer cell.[1] The first clinical use of PDT was by Dougherty et al in 1978, who successfully treated 111 out of 113 patients with malignant squamous cell carcinoma with hematoporphyrin derivative (HpD) followed by red light exposure.[2] Since then, many medical specialties have used PDT in clinical practice. PDT has been used to treat dermatologic lesions, including actinic keratosis, basal cell carcinoma, and squamous cell carcinoma.[3] Additionally, it has demonstrated benefits in intra-thoracic tumors such as non-small cell lung cancer and esophageal carcinoma.[4,5] PDT may be less invasive than many surgical approaches to treating cancer and has fewer general side effects than many systemic antineoplastic treatments.[6] Its major drawback is that it can only be used in areas where light can be directly applied, making it difficult to treat cancers where direct contact with the tumor is more challenging to achieve.[7,8]

Urologic cancers have a wide range of treatment options available. Various medical and surgical options are available depending on cell type, depth

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of invasion, or spread. Extensive research has proven these treatment methods effective in targeting and eradicating urologic neoplasms. Unfortunately, these treatments have many side effects can cause many adverse events. Transurethral resection of the bladder tumor (TURBT) is typically the first step in the surgical management of non-muscle invasive bladder cancer (NMIBC). While effective, patients undergo the risk of subsequent urinary tract infections, hematuria, or bladder wall rupture.[9] Furthermore, for prostate cancer, radical and whole gland external beam radiotherapy or brachytherapy can cause urinary incontinence and erectile dysfunction.[10] With these side effects in mind, urologists need to continue to explore treatment options that both maximize the efficacy of eradicating the cancer as well as maximize the quality of life of the patient.

A descriptive review in 2012 reported on some of the current applications, as well as the pros and cons of using PDT in urologic oncology.[11] We expand on these findings with a more robust search strategy and update any findings by performing a systematic scoping review of the current clinical data reporting the clinical use of PDT for urologic malignancies. We will identify trends in data reporting over time and aim to identify gaps in knowledge within the scientific literature.

Materials and methods

A scoping review was performed in January 2024 using PubMed (MEDLINE) and Embase (Elsevier) databases. The protocol for this scoping review was developed through the guidance of the Joana Briggs Institute (JBI) methodology for scoping reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist.[12,13] The methods for this scoping review were developed within this a priori protocol and were strictly adhered to throughout this study. Our protocol, search strategy, and data extraction files can be found on Open Science Framework. We provide these materials to increase the transparency and reproducibility of our findings.

Inclusion and exclusion criteria

The inclusion and exclusion criteria were developed following the JBI "PCC" model: Population, Concept, and Context. The population of this review included literature of the following study designs: clinical trials, retrospective database reviews, systematic reviews, meta-analyses, cross-sectional analyses, cohort studies, and case-control studies. Additionally, only literature published in English was included in this study. To address the concept of the review, only studies on the use of phototherapy within urologic oncology were included. Finally, to address the context of the review, we limited our study population to those examining urologic cancers supported by AUA guidelines, which include the following: renal cancer, upper tract urothelial carcinoma, bladder cancer, prostate cancer, and testicular cancer.[14,15]

Exclusion criteria included any study: (1) that was written in a language other than English, (2) that was conducted on a topic unrelated to phototherapy for cancer, (3) that failed to analyze one of the listed cancers, (4) that was written as a commentary, correspondence, or letter to the editor, or (5) was in the preclinical stage (in vitro, in vivo in animals). Each stage of the review process, including title and abstract screening, full-text screening, and data extraction, was performed in a duplicate, double-blind fashion between two investigators. Any discrepancies were dealt with through conversation, and if a consensus could not be met, a third investigator was brought in to reconcile. The results of each step of the literature search, as well as the reasoning for the exclusion of studies, can be found in the included PRISMA diagram.

Synthesis

SPSS version 18 (IBM) software was used to summarize our data in the following ways: (1) frequencies of publications by cancer type, phototherapy type, and study design over time (2) longitudinal analysis of publications for the most publicized cancers over time.

Results

PRISMA flowchart

Our initial literature search resulted in 6512 records. After removing 1514 duplicates, 4998 abstracts were eligible for initial screening. After screening titles and abstracts, 169 full-text articles were retrieved for full-text review. Of those 169 articles, 86 met the final inclusion criteria for data extraction, Figure 1.

Publications per cancer

The cancer type with the most published clinical data was bladder cancer (50%), followed by prostate cancer (46.42%). Upper tract urothelial cancer (UTUC) only comprised three publications (3.57%). The gap discovered through this scoping review is that no clinical data was found for either renal or testicular cancer. When looking at trends in publications for specific cancers over time, we found that the earliest

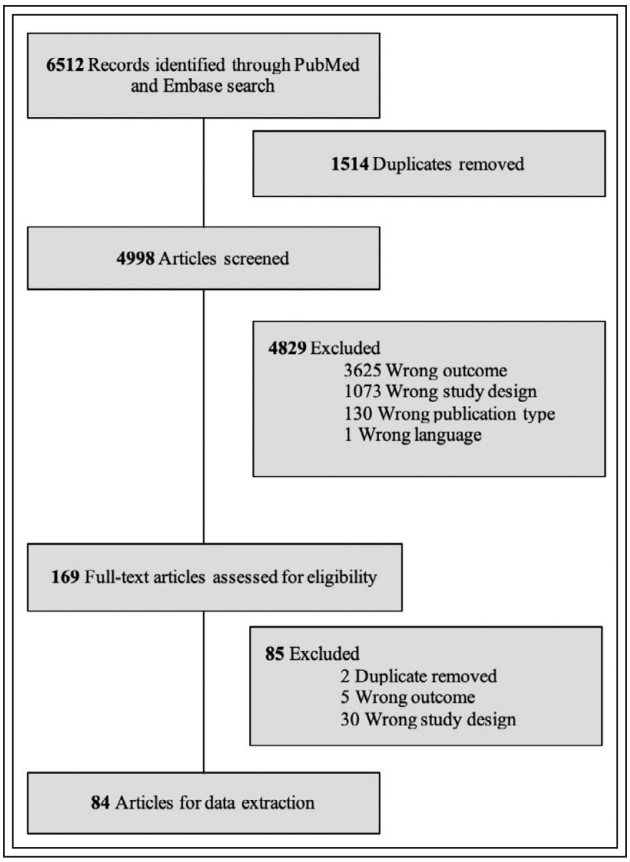

Figure 1. PRIAMA flowchart.

reports of the clinical use of PDT in urologic oncology were for bladder cancer. From 1980 until 2000, bladder cancer dominated the published literature (28 publications), with UTUC just beginning to emerge with one publication in that time frame. With the turn of the century, prostate cancer became the main focus in published clinical data with 37 reports, bladder cancer with 15, and UTUC with 2, Figure 2.

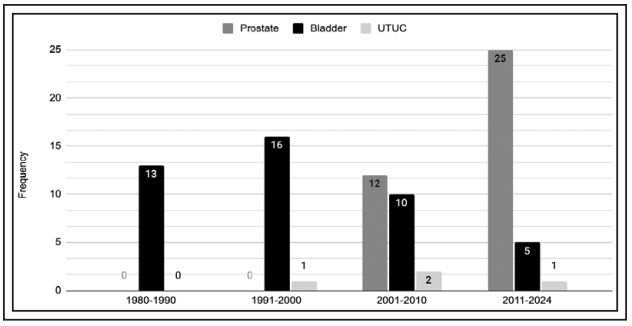

Figure 2. Total publications of individual cancer by year. Note: Renal and Testicular cancer are not included in the figure due to the absence of publications on these cancer types.

Publications per study design

Most (74%) of the included reports were clinical trials. Systematic reviews and meta-analyses comprised 13.6% of our included study cohort, with case series, retrospective database reviews, retrospective chart reviews, and surveys making up the remainder (12.4%) of our report cohort, Table 1.

Number of patients enrolled in RCTs per cancer yype

A great deal of variation was found among the number of patients enrolled in clinical trials between the different types of urologic malignancies, Table 2. UTUC had the least amount of enrolled clinical trial patients with 23. Even though there was a similar number of clinical trials identified between bladder cancer and prostate cancer, there was a significant disparity between the number of enrolled clinical trial patients between the two. Bladder cancer had a total of 685 patients within retrieved clinical trials, while prostate cancer had nearly double that amount with 1409 patients.

TABLE 1. **Number of publications per study design**

Study design	Clinical trial	Systematic review/MA	Case series	Database review	Chart review	Survey
Total #	64 (76.19%)	11 (13.1%)	4 (4.76%)	2 (2.38%)	2 (2.38%)	1 (1.19%)

TABLE 2. **Number of patients enrolled in RCTs per cancer type**

Cancer type	Bladder	Prostate	UTUC	Renal	Testicular
Total pts	685	1409	26	0	0

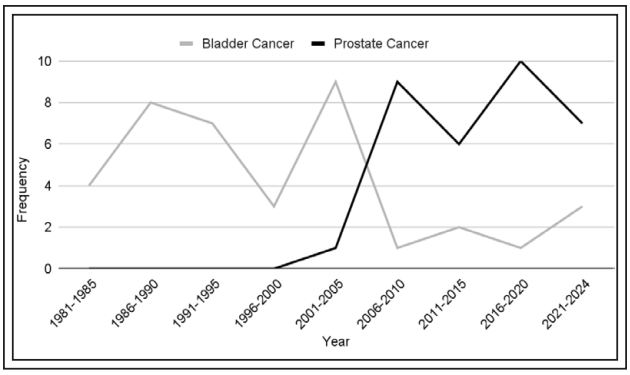

Figure 3. Number of RCT/SR for bladder and prostate cancer by year.

Longitudinal analysis of RCT/SR over time

We analyzed the general publication trends of randomized control trials and systematic reviews/meta-analyses for the most publicized urologic cancers over time, such as bladder and prostate cancer, Figure 3. These two study designs comprise the highest level of evidence, so we wanted to examine trends in their prevalence and frequencies.[16] Bladder cancer held the most publications of RCT/SRs from 1980-2006, with 2001-2005 being the most prolific timeframe for publications of these study designs for this cancer. Beginning in 2006, prostate cancer publications of RCT/SR began to be more prevalent than bladder cancer, with an average of 6-10 reports in each 5-year span.

Discussion

Prostate

The 39 papers utilized the following phototherapy types: temoporfin (mTHPC), padeliporfin (TOOKAD/WST1/palladium-bacteriopheophorbide), motexafin lutetium, and 5-aminolevulinic acid (5-ALA).[17-55] The majority of research utilized padeliporfin, with a total of 26 papers utilizing this type.

Prostate cancer classification

The vast majority of papers included low-risk prostate cancer patients, with some being only Gleason Grade 3+3 = 6 and others including low-volume 3+4 = 7. There were 3 papers that included low and intermediate-risk patients,[17,34,40] and 1 paper that included low risk through high-risk (Gleason 6-9).[42] There were 9 papers regarding the utilization of PDT for recurrent disease after radiotherapy.[22,25,29,30,32,35,36,44,50] There were 2 papers discussing the feasibility of radical prostatectomy after PDT.[20,53]

Effect on PSA

Surprisingly, of the 39 papers, there were 19 that did not discuss the effect on PSA. At 6-12 months there is a pooled reduction in PSA of 0.11-4.9,[21,26,27,31,38,45,51,54,55] or by 35%-67% at 6-12 months.[18,24,26,42] Interestingly, Patel et al measured PSA 24 hours after PDT and found that 24 hours after PDT, patients had a PSA increase of 98% ± 36%, but 1 month after treatment the levels decreased to baseline.[22] Betrouni et al found that when comparing PDT to AS, the PSA was lower in the treatment group and had a 0% PSA failure compared to 2% in the AS cohort at 6 months.[43]

MRI response (post-treatment MRI)

Twenty-one papers did not include post-treatment imaging with MRI. Several papers obtained an MRI at 1 week showing intra- and extra-prostatic necrosis.[19,24,29,30,32,35,38,45,46,51,52] Moreover, the majority of these papers showed a positive correlation between the percentage of intra-prostatic necrosis with either improved PSA reduction or likelihood of negative biopsy at 6 months.[29,30,35,51,52] Specifically, Trachtenberg et al found that > 60% necrosis on the 1-week MRI was a predictor for a patient having a complete response.[35] Additionally, Azzouzi et al found that the mean percentage of necrosis on MRI at 1 week was significantly higher in patients treated with a therapeutic light density index (LDI) of ≥ 1 compared to < 1, where LDI was defined as the ratio of the length of fibers (cm) to the planned treatment volume (mL). Azzouzi found that patients had a higher percentage of having a negative biopsy (78.6%) for LDI ≥ 1 versus 63.0% for LDI < 1.[45] These findings of optimal LDI > 1 allowing for improved ablation volume were also supported in Taneja et al's study, which found that for men undergoing optimal WST11 dosing (4 mg/kg) with LDI ≥ 1, 73.3% had a negative biopsy.[38] Similar findings were found by Azzouzi and Moore, with a negative biopsy rate of 68.4% and 83%, respectively.[51,52]

Prostatic necrosis was noted to resolve between 2-6 months on MRI.[30,33,35,46] There was an initial increase in prostate size due to edema, but an ultimate decrease in prostate size between 55-62%, usually due to fibrous scar within the prostate.[24,25,33,46] Additionally, several papers discussed extraprostatic necrosis. Chelly et al reported a negative correlation between extraprostatic necrosis and the success of erectile dysfunction (ED) treatment and further found that extraprostatic necrosis was an independent risk factor for being prescribed a medication for ED treatment.[19] Extraprostatic necrosis involved the levator ani muscles, obturator internus, periprostatic veins, pubic bone marrow, and anterior rectal wall; however, they noted there was no clinical

significance of this.[19,29,35,38,46,51] Moreover, Trachtenberg and Kulik reported that by 6 months, the blood flow to the extraprostatic areas was restored or with only small areas of residual necrosis.[35,46]

Lastly, MRIs suspicious for malignancy after treatment were more frequently associated with a positive biopsy. For example, Noweski et al reported that of the 20 patients who had scans suspicious for malignancy, 6 were in the untreated lobe, 14 were in the treated lobe, and ultimately 12 had malignancy on biopsy.[31] Barrett et al reported that if the 1-week MRI demonstrated residual tumor, this was supported on the 6-month biopsy with a 100% sensitivity, 60% specificity, 83.3% positive predictive value, 100% negative predictive value, and accuracy of 86.7%.[44] Lastly, Flegar et al reported that if an MRI was not suspicious if prostate cancer was detected on a biopsy, it was clinically insignificant.[55]

Biopsy results

Thirty-two of the papers included biopsy results. Biopsies were performed most commonly at 6 months or 1 year. There was a negative biopsy rate of 305-100%[17,18,27-29,32,35,40,42,45,47,51,52,54,55] or no significant cancer in 49%-89% for biopsies between 6-24 months.[17,18,26] Positive biopsy rates varied from 19.4%-68%, with malignancy more commonly being in the non-treated lobe.[23,31,34,38,53]

Erectile dysfunction

Potency rates were of 0%-86%, with most being > 50%.[17,18,31,42,51,55] Most studies reported no difference or only 1-point drop in Sexual Health Inventory for Men (SHIM) or International of Erectile Function (IIEF-5) scores at 6-24 months follow up.[18,19,27,30,39,41,52] Conversely, at 6 months, three studies noted IIEF-5 scores that were reduced by 4 points from baseline,[45,51,54] and Barret et al reported a 10-point drop in median IIEF-5 score at 1 year.[21] Notably, Flegar et al compared patients with unilateral low-risk prostate cancer who underwent PDT with padeliporfin versus prostatectomy and reported preserved erectile function in 71% versus 30%, respectively.[55]

Voiding dysfunction

Men were given an International Prostate Symptom Score (IPSS) at baseline, and by 6-12 months, the score either improved back to baseline,[21,30,38,40] or had a decrease in IPSS score by 1.3-3.1 points, indicating stable or improved urinary symptoms.[45,51,52,54] Wang et al reported a reduction in IPSS score of 29.1% for 6 studies, though it is important to note that one of the studies showed significantly decreased IPSS scores, the others only were reduced by 1-2 points.[42] There was only 1 paper that reported adverse voiding outcomes, with 6 patients returning to baseline and 7 with worsened voiding dysfunction, but these findings were reported at 3 months rather than the 6-12 months other papers reported.[25] There were 2 papers that discussed pad-free rates, which were reported to be 93%-100%.[49,55] Flegar et al compared the PDT versus prostatectomy cohorts and found that 100% of the PDT group versus 30% of the prostatectomy group were pad-free.[55]

Adverse events

The most common adverse reactions were transient voiding symptoms and perineal pain that resolved without sequelae.[24,27,31,37,40,45,47,50-52,54,55] Perineal pain was reported in 7.2%-15.4%,[27,31,47,51,54] dysuria in 7%-34%,[45,50-52,54] UTI in 2.5%-14%,[37,45,47,50,54] temporary retention 4.8%-28.6%,[45,50,52,54] and hematuria 2%-19%.[37,51,52,54] There was 1 paper that reported 2 patients developed a stricture requiring dilation[27] and two papers that reported 2% prostatitis risk.[40,54]

Feasibility of performing RP after PDT

Two papers discussed the feasibility of performing a salvage prostatectomy after PDT. Pierrard et al reported that a salvage prostatectomy was feasible with non-blinded surgeons rating the prostatectomy as "easy" for 69% of patients.[20] Additionally, they found an average estimated blood loss (EBL) of 200 mL and that PSA was undetectable at 6-12 months for 88% of patients. Lebdai et al supported this study and found that the surgery was feasible with average EBL of 400 cc with 84% of patients maintaining an undetectable PSA with median follow up of 10 months.[53] Lebdai et al reported a positive surgical margin rate of 31% positive surgical margins,[53] Flegar et al reported no biochemical recurrence.[55]

Bladder

Forty-three papers utilized the following phototherapy types: hexaminolevulinate (HAL), 5-aminolevulinic acid (5-ALA), hematoporphyrin derivatives (HpD) such as dihematoporphyrin ether (DHE) or Photofrin (Porfimer sodium), argon ion pumped dye laser, Radachlorin, ruthenium-based photosensitizer (TLD1433), and Fotolon (chlorin e6-polyvinylpirrolidone).[56-98] The most commonly studied was Photofrin (Porfimer sodium) which was utilized in 17 papers.

Bladder cancer classification

There was extreme diversity among the bladder cancer grading that was included. The majority of papers included intermediate or high-risk NMIBC (HgTa, T1, CIS), early recurrence after intravesical therapy,

or recurrent Ta/CIS/T1 and not eligible for or refused cystectomy.[56-71,73-89,93-96,98] Fewer papers also included T2 or T3 disease.[57,61,62,65,66,89,91] Only one paper utilized PDT for T4 disease.[90] For patients with recurrent disease, there were 4.5-7.4 mean recurrences prior to PDT treatment.[60,67,72,97]

Efficacy on cystoscopy

For the papers utilizing HpD and whole bladder treatment, there was a pooled 3-month complete response rate of 31.5%-100%.[57,58,61-63,65,67,69-71,74,76,79,81,82,84,85,87,90,94] There was an overall durability of complete response rate in 31%-91% of patients with a mean follow up of 9-60 mo nths.[65-67,71,73,74,79,82,84,90] Some papers, such as Naito et al studied the light dose on disease response, finding a CR rate of 71.4% at 10 J/cm^2, with 50% of these patients remaining disease-free at 29.6 ± 18.4 months.[70] There was a CR rate of 73.3% at 20 J/cm^2, with 26% remaining tumor-free interval for 13.8 ± 8/2 months. At 30 J/cm^2, the CR rate was 60%, with only 1 patient (33%) remaining disease-free on interval cystoscopy. In total, in those with a complete response at 3 months for the different light doses, 58.3% remained disease-free on follow up.[70] Similar findings were reported by Hisazumi et al with CR rates of 71.4, 70%, 60% for light doses of 10, 20, and 30 J/cm^2, respectively.[83] The tumor-free periods for 10 J/cm^2 was 51.3 months and for 20 J/cm^2 was 13.2 months, with all patients recurring in the 30 J/cm^2 by 1 year.[83] Therefore, both studies concluded 10-20 J/cm^2 would be adequate for treatment. Lastly, Schaffer et al and Nseyo et al both discussed performing cystectomy after photofrin therapy with both papers reporting feasibility.[90,91]

For the papers utilizing 5-ALA, there was a pooled 3-month complete response rate of 57.1%-100%.[57,59,60,72,80,97,98] There was an overall durability of complete response rate in 215-78% of patients with a mean follow up of 12-24 months.[59,60,72,78,80,97]

Bader et al was the only study to utilize HAL and they reported 52.9% were tumor-free at 6 months and 11.8% tumor-free after 21 months.[56]

For the papers utilizing chlorin, there was a pooled 3-month complete response rate of 80%-100%. There was an overall durability of complete response rate in 40%-91.6% at 24-29 months.[77,88,96]

Kulkarni et al was the only paper that utilized ruthenium (tld1433) and found a complete response rate in 66% with durability to 18 months.[93]

Repeat cytology

The majority of papers reported cytologies were obtained with cystoscopies, but typically these were not addressed. The papers that addressed cytologies were those with positive cytology without visual disease on cystoscopy, leading to a partial response.[57,66] Specifically, four papers reported that a cytology could be positive for up to 3 months after PDT even in those with a complete visual response. Therefore the authors recommended caution in a positive cytology with caution in the setting of negative cystoscopy.[66,70,84,85]

Adverse events

The most commonly reported side effects included dysuria, frequency, urgency, and hematuria which occurred in the majority of patients.[56-58,61,63,64,66-68,70-83,89,93,95,96,98] Most voiding symptoms were transient lasting 2-12 weeks, with those exposed to increased dose having more severe symptoms or length of symptoms. For those with irritative voiding symptoms, Filonenko et al and Waidelich et al recommended 10 mg of rectal scopolamine,[59,72,97] while Walther et al reported significant relief with NSAIDs.[68] Shackley at al reported a lidocaine dwell was effective for 3% ALA treatment, but those undergoing treatment with 6% ALA had higher reported pain.[75]

Some papers reported no events of cutaneous photosensitization,[56,59,60,72,78,80,81,88,97] though several of these papers reported strict sun avoidance precautions. Other papers reported transient sunburn in 8.6%-50% of patients that resolved without sequelae.[57,61-63,66,67,70,74,79,82,8387,89,95] Four papers reported 80%-100% of patients had slight skin erythema after sunlight exposure, but no severe reactions.[65,70,76,85]

Two papers reported development of crystalline bladder deposits composed of varying amounts of calcium oxalate monohydrate, calcium oxalate dihydrate, brushite, and hydroxyapatite.[63,68]

There were two reported instances of fistula, with Windahl et al reporting one instance of rectourethral fistula,[66] and Lee et al reporting one enterovesical fistula.[88] Lee et al did note that the patient underwent partial cystectomy and ileal conduit with no malignancy present in the specimen.

Two papers, both by Waidelich et al reported hypotension (defined as a decrease in mean arterial pressure of 20% or more) or tachycardia (defined as a heart rate increase by 20% or more).[72,97] It was reported that all patients who experienced these effects had prior known severe cardiovascular disease. They treated hypotension with etilefrine and, if needed gave dopamine or norepinephrine given. Tachycardia was managed with esmolol. All cardiovascular side effects were resolved after 12 hours.

Long-term voiding dysfunction/strictures/contracture

For the majority of patients, there was no change in bladder capacity or episodes of bladder contracture

(reduction in capacity by 50% or more) at the conclusion of the studies.[56,60,72,76,78,80,88,97] Others reported permanent bladder contracture in 5%-22.2% of patients.[57,82,95] Several of papers discussed that since the majority of patients had prior bladder resections or intravesical treatments, that the baseline capacity was lower than the average population, with pre-treatment capacity reported as 120-400 cc.[62,64,70,71,74] Many papers reported decreased bladder capacity by 75-200 cc at 1-4 months with some patients regaining capacity at 1-2 years post-treatment.[58,62,64,70,71,83] Moreover, some papers reported the dose-dependent response associated with reduction in capacity. Specifically, Nseyo et al reported 39% of patients who received a photofrin dose of 2 mg/kg and light dose of 15 J/cm^2 or higher had bladder contracture with grade II-III vesicoureteral reflux, which was not seen in any patients receiving 2 mg/kg dosage with 10 J/cm^2 light or 1.5 mg/kg dosage and 10-15J/cm^2 light.[79] They also reported 24% had both bladder contracture and vesicoureteral reflux, which resulted in 8 getting cystectomy.[79] Lastly, there was only 1 reported urethral stricture, found in the study by Walther et al.[63]

Upper tract urothelial carcinoma (UTUC)

Three UTUC papers utilized the following phototherapy types: 5-aminolevulinic acid (5-ALA), Photofrin (Porfimer sodium), and padeliporfin (TOOKAD/WST1).[99,100,101]

UTUC classification

In all cases, the patient's pathology would have been recommended by guidelines for nephroureterectomy, but patients were either poor surgical candidates, unwilling to undergo surgery, or would have had to go on hemodialysis, and therefore were planned for PDT. The pathology included residual or recurrent malignancy after endoscopic treatment, high-grade malignancy, extensive spread of low-grade malignancy, and multifocal disease.[99,100,101]

Response on ureteroscopy (URS)

Coombs et al published their work in 2004, highlighting 2 of 3 patients without recurrence between 6-24 months of follow up.[101] Waidelich et al described their work in the *Journal of Urology* in 1998 with complete response in 2 of 4 patients, but with the remaining 2 patients having significant reduction of papillary tumors to allow for laser ablation treatment following at 4 and 13 weeks.[100]

The most recent paper published in 2023 in the *Journal of Urology* by Yip et al discusses the results from their phase I trial with padeliporfin (TOOKAD/WST1), which had a 30-day treatment response of 94% (50% complete response, 44% partial response) [34]. Based on the trial's results, they were able to initiate a phase III clinical trial (ENLIGHTED) for low-grade upper tract disease.[99]

Renal function

Yip and Waidelich reported unchanged renal function, with Coombs not discussing it.[99,100]

Adverse events

The adverse reactions were all reported to be transient with most reporting hematuria and discomfort. Yip et al reported overall low adverse reactions including transient flank pain (79%) and transient hematuria (84%).[99] All papers found no incidence of ureteral stricture.[99,100,101] The only major reactions reported were by Waidelich et al who reported patients with prior cardiovascular history had hypotension and tachycardia that required transient catecholamines.[100]

Renal

There were no clinical studies on renal PDT that were found for inclusion in this paper. This study did not include pre-clinical research of which there is a significant amount of UTUC and renal and will potentially have clinical data within the future.

Testicular

There were no clinical studies on testicular PDT that were found for inclusion in this paper.

Strengths and limitations

Strengths of this current study include the methods and reproducibility. The methods were derived from a strong framework established by the JBI methods manual and PRISMA-ScR, which have set the foundation for many publications. Additionally, we released our a priori protocol and search strategy on Open Science Framework, which allows other investigators to replicate our results. Screening and data extraction were completed in duplicate, which adds to the validity of our study. Limitations of this review include the restrictions that we placed on study designs, primarily excluding any pre-clinical data and non-English papers. Additionally, human error within the screening and data extraction steps of our review could have led to missing studies or pieces of data to report in this manuscript. Finally, it is possible that our search strategy did not capture the entire scope of our intended study population, leaving possible manuscripts missed for inclusion.

Conclusion

This is the first scoping review of the urologic literature for PDT among multiple urologic malignancies. Utilizing PDT in prostate cancer led to a negative biopsy rate of 30%-100% with potency rates > 50% and stable urinary symptoms. Bladder cancer treatment with PDT had a 3-month complete response rate of 31.5%-100% with transient symptoms of dysuria, frequency, urgency, and hematuria. UTUC management with PDT reported at least 50% complete response between the three papers. Gaps in the literature include renal and testicular data, of which there is no clinical data published at this time. Upper tract urothelial carcinoma has only 3 existing clinical papers, but this will be supplemented in the future by the ongoing ENLIGHTED Trial, which is a phase III multicenter study evaluating padeliporfin PDT for low-grade UTUC. Ultimately, PDT has been established as a safe and effective treatment for urologic malignancies and we provide a comprehensive review of the literature regarding the utility of this.

Disclosures

Dr. Robert Grubb is a site principal investigator for the ENLIGHTENED Trial with Steba Biotech. None of the other authors have conflicts of interest to disclose. No financial disclosures. □

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