



Diagnostic performance of narrow-band imaging and photodynamic diagnosis compared to white light cystoscopy for non-muscle invasive bladder cancer: A network meta-analysis of randomized trials

Se Young Choi^{1,*}, Yun-Jung Yang^{2,*}, Kyung Chan Min¹, Yong Seong Lee³, Joongwon Choi³,
Jung Hoon Kim³, Chung Un Lee³, Eun-Jung Yang⁴, Jong Hyun Tae¹

¹Department of Urology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, ²Department of Convergence Science, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, ³Department of Urology, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Gwangmyeong, ⁴Department of Plastic and Reconstructive Surgery, Institute for Human Tissue Restoration, Yonsei University College of Medicine, Seoul, Korea

Purpose: To compare the diagnostic performance of white light cystoscopy (WLC), photodynamic diagnosis (PDD), and narrow-band imaging (NBI) in the detection of non-muscle invasive bladder cancer (NMIBC) through a network meta-analysis of randomized controlled trials (RCTs).

Materials and Methods: A systematic literature search of PubMed, Embase, CENTRAL (Cochrane Central Register of Controlled Trials), and Web of Science was conducted in February 2024. RCTs comparing WLC, NBI, and PDD in patients with NMIBC were included. Six RCTs comprising 2,439 patients were analyzed. Diagnostic outcomes evaluated included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false-positive rate, and carcinoma *in situ* (CIS) sensitivity. A random-effects network meta-analysis was performed using Stata software. Risk of bias was assessed using the RoB 2 tool.

Results: Both NBI and PDD demonstrated significantly improved sensitivity compared to WLC (odds ratio [OR] for NBI 7.66, 95% confidence interval [CI] 2.91–20.19; OR for PDD 7.85, 95% CI 3.76–16.38). PDD showed the highest CIS sensitivity (OR 13.37, 95% CI 4.38–40.89). WLC had the highest specificity (OR for PDD 0.29, 95% CI 0.08–1.00). NBI achieved the highest NPV (OR 8.28, 95% CI 1.34–51.28), while PDD showed the lowest PPV (OR 0.16, 95% CI 0.09–0.29). SUCRA (surface under the cumulative ranking curve) rankings supported these findings.

Conclusions: NBI and PDD improve NMIBC detection sensitivity over WLC, notably PDD for CIS, despite lower specificity. WLC remains the most specific, and NBI offers a favorable balance between sensitivity and diagnostic precision.

Keywords: Bladder cancer; Cystoscopy; Fluorescence; Narrow band imaging; Sensitivity and specificity

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Corresponding Author: Jong Hyun Tae <https://orcid.org/0000-0001-5826-3469>

Department of Urology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, 102 Heukseok-ro, Dongjak-gu, Seoul 06973, Korea
TEL: +82-2-6299-3794, E-mail: jjongee13@gmail.com

*These authors contributed equally to this study and should be considered co-first authors.

INTRODUCTION

Bladder cancer is one of the most common malignancies worldwide, with nonmuscle invasive bladder cancer (NMIBC; stages Ta, T1, and carcinoma *in situ* [CIS]) accounting for approximately 75% of initial diagnoses [1]. Accurate endoscopic detection and complete resection of tumors are vital for minimizing recurrence and preventing progression to muscle-invasive disease [2]. However, white light cystoscopy (WLC)—the standard for diagnosis and surveillance—has limited sensitivity, missing up to half of CIS lesions, with detection rates ranging between 62% and 84% [3,4]. These diagnostic shortcomings significantly contribute to high NMIBC recurrence rates, affecting up to 50%–70% of patients within five years despite standard treatment [1,5].

To address these limitations, enhanced imaging techniques—including photodynamic diagnosis (PDD) using photosensitizers such as 5-aminolevulinic acid (5-ALA) or hexaminolevulinate (HAL), and narrow-band imaging (NBI)—have been introduced. PDD causes tumor-specific red fluorescence under blue light by preferential accumulation of porphyrins in neoplastic urothelium, while NBI enhances mucosal microvasculature contrast by filtering the light spectrum to wavelengths absorbed by hemoglobin [6,7]. Randomized and prospective studies indicate that PDD and NBI can elevate overall tumor detection rates to over 90%, with CIS sensitivity reaching as high as 95%—compared to approximately 77% overall and 58% CIS detection using WLC alone [4,6–8]. Recent studies have emphasized the prognostic significance of regular cystoscopies in the diagnosis and surveillance of bladder cancer, while research is also actively underway to improve the diagnostic performance of non-invasive diagnostic markers [9,10].

Nonetheless, head-to-head comparisons between NBI and PDD remain scarce, with significant heterogeneity in photosensitizer type, trial methodology, and outcome definitions. Existing meta-analyses have mostly focused on recurrence or progression outcomes, while few have systematically compared diagnostic performance metrics—such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false-positive rate, and CIS-specific sensitivity—using unified network meta-analytic approaches [11,12]. To fill this gap, we conducted a network meta-analysis restricted to randomized controlled trials (RCTs), evaluating the diagnostic accuracy of WLC, NBI, and PDD in NMIBC detection across six key outcomes. By synthesizing both direct and indirect evidence, this study aims to clarify the relative strengths and limitations of each modality and inform evidence-based decisions in bladder cancer diagnostic

pathways.

METHODS

This review focused on adult patients with non-muscle-invasive bladder cancer (Population), evaluating the diagnostic performance of NBI or PDD (Interventions) compared with conventional WLC (Comparator), with outcomes including sensitivity, specificity, predictive values, false-positive rate, and CIS detection (Outcomes).

This network meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA 2020) and its extension for network meta-analyses. This review has been registered in PROSPERO (CRD420251149512).

1. Search strategy and study selection

A systematic literature search was performed in four electronic databases: PubMed, Embase, the CENTRAL (Cochrane Central Register of Controlled Trials), and Web of Science. The search was conducted in February 2024. Search terms are provided in the supplementary materials (Supplementary Table 1), and the detailed results of the search are summarized in Supplementary Table 2. No restrictions were placed on publication year or language. After removal of duplicates, two reviewers (J.H.T. and S.Y.C.) independently screened titles and abstracts, followed by full-text assessment to determine eligibility according to predefined inclusion and exclusion criteria. Discrepancies were resolved through discussion and consensus.

2. Inclusion and exclusion criteria

Studies were included if they met the following criteria: (1) RCT design; (2) involved adult patients with suspected or confirmed NMIBC; (3) compared WLC, NBI, PDD; and (4) reported at least one diagnostic outcome measure, including sensitivity, specificity, PPV, or NPV. Studies were excluded if they were non-RCTs, review articles, editorials, commentaries, case reports, technical descriptions, or previously published meta-analyses.

3. Data extraction

Two reviewers independently extracted data using a standardized data collection form. Extracted variables included first author, publication year, study design, intervention modality, total sample size, diagnostic performance (sensitivity, specificity, PPV, NPV), and data specific to CIS when available. Disagreements were resolved by consensus after discussion.

4. Risk of bias assessment

Risk of bias in the included studies was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials. This tool evaluates five domains: (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result. Each domain was rated as 'low risk,' 'some concerns,' or 'high risk' of bias. The overall risk of bias for each study was determined based on domain-level judgments.

5. Statistical analysis

A network meta-analysis was conducted using a random-effects model to compare diagnostic performance among WLC, NBI, and PDD. Odds ratios (ORs) and 95% confidence interval (CI) were calculated for each outcome. The ranking probabilities for each modality were assessed using the surface under the cumulative ranking curve (SUCRA), probability of being best (PrBest), and mean rank. Higher SUCRA values indicate a greater likelihood of being the most effective modality among those compared. Network meta-analysis was conducted using Stata software version 19 (StataCorp). Inconsistency within the network was evaluated using a design-by-treatment interaction model. Due to the limited number of studies, publication bias was not formally assessed, as funnel plot-based methods are unreliable when fewer than 10 studies are available.

6. Characteristics of interventions

Among the three included studies evaluating PDD, two studies used intravesical HAL, and one study used oral 5-ALA. Although both agents are clinically validated for

PDD, they differ in administration route and pharmacodynamics. These variations were noted during data extraction but not used as stratification variables in the network meta-analysis.

RESULTS

A total of 1,269 records were identified across the four databases: PubMed (n=200), Embase (n=362), CENTRAL (n=630), and Web of Science (n=77). After removal of 774 duplicates, 495 records remained for title and abstract screening. Of these, 249 records were excluded because they were replies, commentaries, editorials, case reports, or reviews and meta-analyses. A total of 246 full-text articles were assessed for eligibility, with 240 excluded due to irrelevant intervention, unavailable full-text, lack of diagnostic accuracy data, or non-randomized design. Finally, a total of six RCTs [13-18], involving 2,439 patients, were included in this network meta-analysis. Three studies compared NBI with WLC, and three compared PDD with WLC. All six studies reported overall sensitivity and specificity, and five studies provided CIS-specific diagnostic data. Sample sizes ranged from 113 to 1,242 patients. A summary of the study characteristics and diagnostic performance is presented in Table 1. The PRISMA flow diagram is shown in Fig. 1. Risk of bias was assessed using the RoB 2 tool; detailed results are presented in Fig. 2 (traffic light plot) and Fig. 3 (domain-level summary plot).

1. Sensitivity

All six RCTs reported overall sensitivity for tumor detection. Compared to WLC, both NBI and PDD demonstrated significantly improved sensitivity. In the network

Table 1. Summary characteristics of the six included RCTs, including study design, sample size, diagnostic modality, and CIS-specific outcomes

Study	Design	Intervention	Total no. of samples	Overall diagnostic outcomes	No. of CIS lesions	CIS specific outcomes
Shen et al. [18] (2012)	RCT	NBI/WLC	309	Sensitivity: WLC 77.7%, NBI 92.9% Specificity: WLC 82.7%, NBI 73.5%	41	Sensitivity: WLC 68.3%, NBI 87.8% Specificity: WLC 82.9%, NBI 77.1%
Ye et al. [17] (2015)	RCT	NBI/WLC	300	Sensitivity: WLC 75.5%, NBI 98.8% Specificity: WLC 58.65%, NBI 60.9%	11	N/A
Dalgaard et al. [15] (2019)	RCT	NBI/WLC	147	Sensitivity: WLC 80.0%, NBI 97.5% Specificity: WLC 44.8%, NBI 19.4%	9	Sensitivity: WLC 66.7%, NBI 88.9%
Fradet et al. [14] (2007)	RCT	PDD/WLC	113	Sensitivity: WLC 68.0%, PDD 92.0% Specificity: WLC 69.0%, PDD 61.0%	113	Sensitivity: WLC 68.0%, PDD 87.8% Specificity: WLC 69.0%, PDD 61.0%
Taoka et al. [13] (2025)	RCT	PDD/WLC	1,242	Sensitivity: WLC 61.1%, PDD 95.3% Specificity: WLC 95.2%, PDD 61.0%	148	Sensitivity: WLC 26.4%, PDD 93.9%
Jocham et al. [16] (2005)	RCT	PDD/WLC	328	Sensitivity: WLC 77.0%, PDD 96.0% Specificity: WLC 74.0%, PDD 63.0%	62	Sensitivity: WLC 68.0%, PDD 95.0%

RCTs, randomized controlled trials; CIS, carcinoma *in situ*; NBI, narrow-band imaging; WLC, white light cystoscopy; PDD, photodynamic diagnosis; N/A, not available.

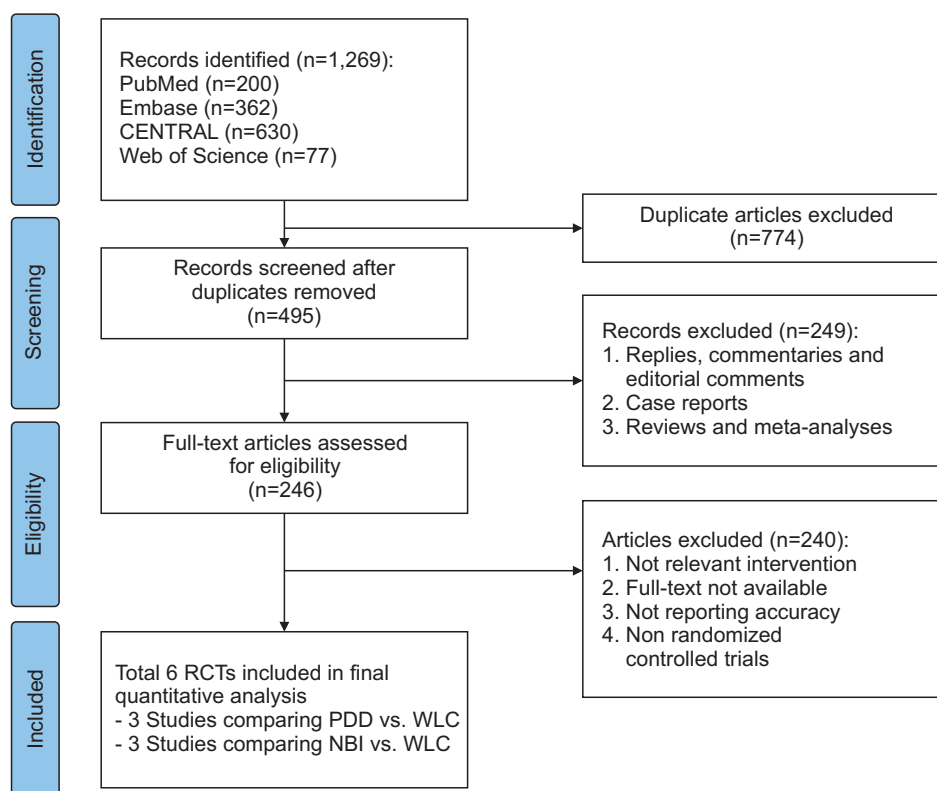


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram outlining the study selection process for the network meta-analysis. A total of 1,269 records were identified from PubMed (n=200), Embase (n=362), CENTRAL (n=630), and Web of Science (n=77). After removal of 774 duplicates, 495 records were screened by title and abstract. Of these, 246 full-text articles were assessed for eligibility, and 240 were excluded for reasons including irrelevant intervention, unavailable full-text, lack of diagnostic accuracy data, or non-randomized design. Finally, six randomized controlled trials (three comparing photodynamic diagnosis with white light cystoscopy, and three comparing narrow band imaging with white light cystoscopy) were included in the quantitative analysis. CENTRAL, Cochrane Central Register of Controlled Trials; RCTs, randomized controlled trials; PDD, photodynamic diagnosis; WLC, white light cystoscopy; NBI, narrow-band imaging.

meta-analysis, NBI showed an OR of 7.66 (95% CI 2.91–20.19) versus WLC, while PDD showed an OR of 7.85 (95% CI 3.76–16.38) versus WLC. Both enhanced modalities were strongly favored over standard WLC.

In terms of relative ranking, the SUCRA values were 75.0% for PDD and 74.9% for NBI, whereas WLC ranked lowest with 0.0%. The PrBest was 50.1% for PDD and 49.9% for NBI, with both sharing a mean rank of 1.5 (Table 2). These results indicate that both NBI and PDD offer substantial improvements in sensitivity over WLC, with nearly identical performance between the two enhanced techniques. Fig. 4A displays the network forest plot for sensitivity. The SUCRA ranking across all diagnostic metrics is shown in Fig. 5.

2. Specificity

All six RCTs also reported specificity. In contrast to the findings for sensitivity, WLC demonstrated the highest specificity. Compared to WLC, PDD was associated with a lower specificity (OR 0.29, 95% CI 0.08–1.00), as was NBI

(OR 0.59, 95% CI 0.17–2.07). Although these results suggest a trend toward reduced specificity for PDD and NBI, the CIs crossed unity, indicating that the findings were not statistically definitive.

The SUCRA value for WLC was highest at 88.0%, followed by NBI at 49.0%, and PDD at 13.0%. WLC also had the highest PrBest (76.8%) and the lowest mean rank (1.2) (Table 2). These findings suggest that while NBI and PDD increase sensitivity, this may come at the expense of specificity, with WLC remaining the most conservative modality for minimizing false-positives. The forest plot for specificity is presented in Fig. 4B, and overall rankings are shown in Fig. 5.

3. False-positive rate

The false-positive rate was reported across all studies. NBI showed an OR of 1.69 (95% CI 0.48–5.92) compared to WLC, while PDD showed an OR of 3.47 (95% CI 1.00–12.06). The SUCRA value was highest for WLC at 88.7%, followed by NBI at 49.9%, and lowest for PDD at 11.4% (Table 2). These results suggest that PDD may be associated with



Fig. 2. Risk of bias summary (traffic light plot) for the six included randomized controlled trials based on RoB 2 domains.



Fig. 3. Domain-level risk of bias summary bar plot for the included studies.

a higher rate of false-positive findings compared to WLC. However, the estimates for NBI were not statistically significant. Forest plots are provided in Fig. 4C.

4. NPV

NBI showed the highest NPV among the three modalities, with an OR of 8.28 (95% CI 1.34–51.28) compared to WLC. PDD also showed a higher NPV compared to WLC (OR 4.81, 95% CI 0.39–59.04), though the CI was wide. The SUCRA score for NBI was 80.5%, compared to 63.5% for PDD and 5.9% for WLC. NBI had the highest PrBest (62.5%), supporting its

reliability in ruling out disease (Table 2). These findings are visualized in Fig. 4D.

5. PPV

PDD demonstrated the lowest PPV among the three techniques, with an OR of 0.16 (95% CI 0.09–0.29) compared to WLC. NBI was similar to WLC, with an OR of 1.11 (95% CI 0.65–1.90). SUCRA scores for NBI and WLC were 82.3% and 67.7%, respectively, while PDD had a SUCRA of 0.0% (Table 2). These results indicate that although PDD increases sensitivity, it may lead to more false-positive results. For-

Table 2. SUCRA scores, PrBest, and mean ranks for each modality by diagnostic outcome

	Intervention	Sensitivity	Specificity	FP	NPV	PPV	CIS sensitivity
SUCRA scores	WLC	0.0	88.0	88.7	5.9	67.7	1.4
	NBI	74.9	49.0	49.9	80.5	82.3	54.6
	PDD	75.0	13.0	11.4	63.5	0.0	93.9
PrBest	WLC	0.0	76.8	77.6	0.0	35.4	0.0
	NBI	49.9	20.5	20.3	62.5	64.6	12.1
	PDD	50.1	2.7	2.1	37.5	0.0	87.9
Mean rank	WLC	3.0	1.2	1.2	2.9	1.6	3.0
	NBI	1.5	2.0	2.0	1.4	1.4	1.9
	PDD	1.5	2.7	2.8	1.7	3.0	1.1

Values are presented as % or rank.

SUCRA, surface under the cumulative ranking curve; PrBest, probability of being best; WLC, white light cystoscopy; NBI, narrow-band imaging; PDD, photodynamic diagnosis; FP, false-positive rate; NPV, negative predictive value; PPV, positive predictive value; CIS, carcinoma *in situ*.

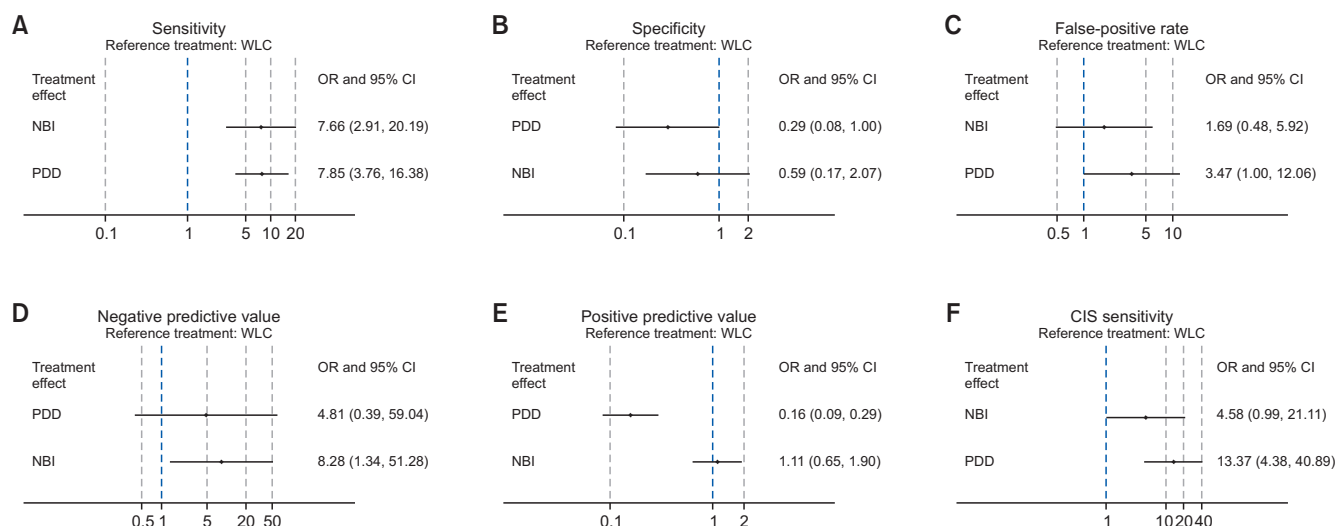


Fig. 4. Network forest plot for sensitivity (A), specificity (B), false-positive rate (C), negative predictive value (D), positive predictive value (E), sensitivity for CIS (F). WLC, white light cystoscopy; NBI, narrow-band imaging; PDD, photodynamic diagnosis; OR, odds ratio; CI, confidence interval; CIS, carcinoma *in situ*.

est plots for PPV are shown in Fig. 4E.

6. Sensitivity for CIS

Five RCTs reported sensitivity for detecting CIS lesions, which are known to be flat and often missed by conventional cystoscopy. PDD showed the highest sensitivity for CIS, with an OR of 13.37 (95% CI 4.38–40.89) compared to WLC. NBI also demonstrated improved CIS detection over WLC (OR 4.58, 95% CI 0.99–21.11), though the result did not reach statistical significance. The SUCRA values were 93.9% for PDD, 54.6% for NBI, and 1.4% for WLC. PDD had the highest PrBest (87.9%) and the lowest mean rank, reinforcing its superiority in CIS detection (Table 2). These results are visualized in Fig. 4F.

DISCUSSION

This network meta-analysis compared the diagnostic performance of WLC, NBI, and PDD in the evaluation of NMIBC, synthesizing data from six RCTs involving 2,439 patients. Both NBI and PDD demonstrated significantly higher sensitivity compared to WLC, with ORs of 7.66 (95% CI 2.91–20.19) and 7.85 (95% CI 3.76–16.38), respectively. In contrast, WLC showed the highest specificity, outperforming NBI (OR 0.59, 95% CI 0.17–2.07) and PDD (OR 0.29, 95% CI 0.08–1.00). Notably, PDD provided the greatest sensitivity for detecting CIS, with an OR of 13.37 (95% CI 4.38–40.89) versus WLC, compared to an OR of 4.58 (95% CI 0.99–21.11) for NBI. These findings were supported by SUCRA rankings, with PDD and NBI scoring 75.0% and 74.9%, respectively, for overall sensitivity, and PDD leading in CIS sensitivity (SUCRA 93.9%).

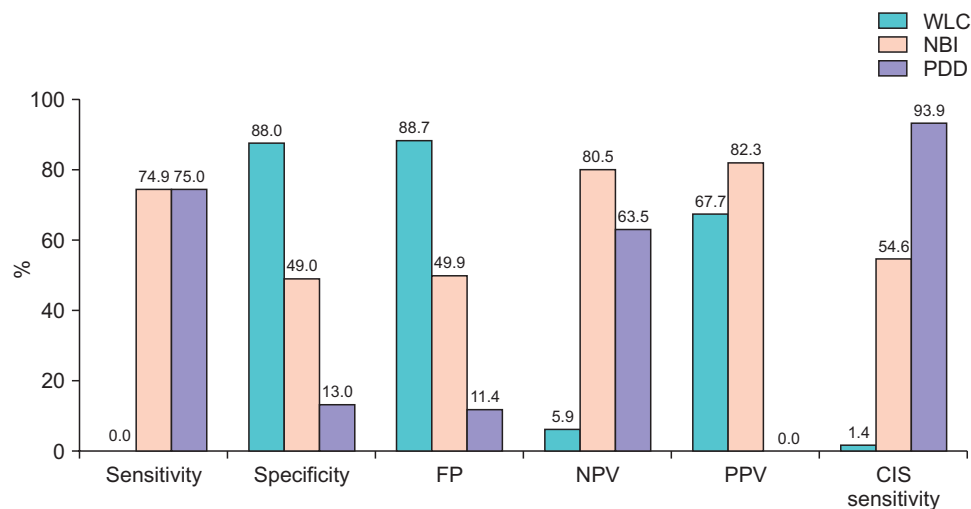


Fig. 5. SUCRA-based ranking plot for sensitivity, specificity, PPV, NPV, and CIS detection. SUCRA rankings designates better performing modalities as higher ranks. SUCRA, surface under the cumulative ranking curve; WLC, white light cystoscopy; NBI, narrow-band imaging; PDD, photodynamic diagnosis; FP, false-positive rate; NPV, negative predictive value; PPV, positive predictive value; CIS, carcinoma *in situ*.

These results highlight a clear trade-off between enhanced detection and diagnostic precision. While NBI and PDD offer meaningful improvements in sensitivity, they may also increase the rate of false-positive findings. PDD, in particular, was associated with a higher false-positive rate (OR 3.47, 95% CI 1.00–12.06) and the lowest PPV (OR 0.16, 95% CI 0.09–0.29). Conversely, WLC yielded the best specificity (SUCRA 88.0%) and the lowest false-positive rate (SUCRA 88.7%), making it the most conservative modality when diagnostic accuracy is prioritized over lesion detection. NBI had the highest NPV among the three modalities (OR 8.28, 95% CI 1.34–51.28, SUCRA 80.5%), supporting its utility for safely ruling out residual tumor following transurethral resection. These differences may inform patient-specific decision-making in clinical settings, balancing the risks of overtreatment against the potential for underdiagnosis.

Our results are consistent with previous meta-analyses. Fan et al. [19] similarly found that both PDD and NBI outperform WLC in sensitivity and CIS detection, while Russo et al. [11] confirmed superior lesion-level sensitivity for enhanced imaging modalities. However, our analysis expands upon prior work by incorporating only RCTs, performing updated risk of bias evaluation using the RoB 2 tool, and quantifying diagnostic rankings using SUCRA scores, PrBest, and mean rank.

Several methodological strengths support the validity of our findings. We restricted inclusion to RCTs, ensuring high-quality data. The network meta-analytic framework allowed integration of both direct and indirect comparisons. Diagnostic metrics were evaluated across multiple clinically relevant outcomes, including CIS detection and NPV. In addition, bias

was systematically assessed and visualized, improving transparency and interpretability.

Nonetheless, this study has limitations. Heterogeneity in the photodynamic agent used—HAL in two studies and 5-ALA in one—may affect generalizability. Some diagnostic outcomes, especially those related to CIS and NPV, had wide CIs due to limited event counts and sample size. The small number of studies prevented formal subgroup or meta-regression analyses. Moreover, although a comprehensive search was conducted, due to the limited number of studies, publication bias was not formally assessed. Furthermore, the heterogeneity detected in our network estimates likely reflects methodological and clinical diversity among trials. Important contributors may include differences in photosensitizer agents (5-ALA vs. HAL), variability in operator expertise, multicenter versus single-center design, and inconsistent definitions of positive findings or CIS across studies. These factors may have influenced the observed effect sizes, and therefore the pooled estimates should be interpreted with caution.

Future research should address these gaps. Head-to-head comparisons of 5-ALA and HAL are needed to determine the relative diagnostic value of each agent. Further large-scale, multicenter RCTs with standardized reporting of outcomes are essential. Emerging technologies such as artificial intelligence-driven image enhancement or multimodal integration with clinical variables may further advance the accuracy of endoscopic diagnosis. Finally, health economic evaluations and integration studies are needed to assess the feasibility of adopting these enhanced cystoscopic modalities into routine practice.

CONCLUSIONS

Among patients undergoing diagnostic evaluation for NMIBC, both NBI and PDD offer substantial improvements in tumor detection compared to standard WLC. PDD showed the highest sensitivity, particularly for CIS, while WLC demonstrated superior specificity and the lowest rate of false-positives. NBI provided the most favorable balance, combining high sensitivity with the strongest NPV. These findings suggest that enhanced imaging techniques can be selectively applied based on clinical priorities—whether maximizing tumor detection, minimizing overtreatment, or confidently ruling out residual disease.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Se Young Choi and Jong Hyun Tae. Data acquisition: Jong Hyun Tae and Yun-Jung Yang. Statistical analysis: Yun-Jung Yang. Data analysis and interpretation: Yun-Jung Yang and Jong Hyun Tae. Drafting of the manuscript: Jong Hyun Tae. Critical revision of the manuscript: Jong Hyun Tae. Obtaining funding: Se Young Choi. Administrative, technical, or material support: Kyung Chan Min, Yong Seong Lee, Joongwon Choi, Jung Hoon Kim, Chung Un Lee, and Eun-Jung Yang. Supervision: Se Young Choi. Approval of the final manuscript: all authors.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via <https://doi.org/10.4111/icu.20250547>.

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