Diagnostic Performance of Narrow Band Imaging for Nasopharyngeal Cancer: A Systematic Review and Meta-analysis

Changling Sun, PhD1*, Yayun Zhang, MS2*, Xue Han, MS2, and Xiaodong Du, MD1

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objective. The purposes of this study were to verify the effectiveness of the narrow band imaging (NBI) system in diagnosing nasopharyngeal cancer (NPC) as compared with white light endoscopy.

Data Sources. PubMed, Cochrane Library, EMBASE, CNKI, and Wan Fang databases.

Review Methods. Data analyses were performed with MetaDisc. The updated Quality Assessment of Diagnostic Accuracy Studies–2 tool was used to assess study quality and potential bias. Publication bias was assessed with a Deeks asymmetry test. The registry number of the protocol published on PROSPERO is CRD42015026244.

Results. This meta-analysis included 10 studies of 1337 lesions. For NBI diagnosis of NPC, the pooled values were as follows: sensitivity, 0.83 (95% CI, 0.80-0.86); specificity, 0.91 (95% CI, 0.89-0.93); positive likelihood ratio, 8.82 (95% CI, 5.12-15.21); negative likelihood ratio, 0.18 (95% CI, 0.12-0.27); and diagnostic odds ratio, 65.73 (95% CI, 36.74-117.60). The area under the curve was 0.9549. For white light endoscopy in diagnosing NPC, the pooled values were as follows: sensitivity, 0.79 (95% CI, 0.75-0.83); specificity, 0.87 (95% CI, 0.84-0.90); positive likelihood ratio, 5.02 (95% CI, 1.99-12.65); negative likelihood ratio, 0.34 (95% CI, 0.24-0.49); and diagnostic odds ratio, 16.89 (95% CI, 5.98-47.66). The area under the curve was 0.8627. The evaluation of heterogeneity, calculated per the diagnostic odds ratio, gave an $I^2$ of 0.326. No marked publication bias ($P = .68$) existed in this meta-analysis.

Conclusion. The sensitivity and specificity of NBI for the diagnosis of NPC are similar to those of white light endoscopy, and the potential value of NBI for the diagnosis of NPC needs to be validated further.

Keywords
narrow band imaging, nasopharyngeal cancer, meta-analysis

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nasopharyngeal carcinoma (NPC) is one of the most common malignant tumors of head and neck in Southeast Asia. Current detection modalities of NPC include endoscopic examination and radiologic imaging. Radiologic imaging plays an important role in identifying the extent of tumor invasion, and it provides accurate clinical staging for subsequent treatment; however, it fails to identify superficial mucosal abnormalities. Traditional white light endoscopy (WLE) can detect morphologic changes in the superficial mucosa, and it is widely used in the diagnosis of NPC. However, for some NPCs in the early stage, the superficial tumor zone is difficult to identify or differentiate from other pathologies, such as lymphoid follicular hyperplasia. Therefore, it is of primary importance to establish a more useful screening protocol for NPC diagnosis and to administer treatment in the early stages of disease.

Narrow band imaging (NBI) is a novel optical technology that uses reflected light to improve the visualization of superficial mucosal lesions. It provides more in-depth insights into the behavior of a target lesion to obtain a so-called optical biopsy. It also allows visualization of lesions that are not otherwise visible, which is helpful for reducing the number of unnecessary biopsies and for minimizing the number of false negatives. To date, NBI has been widely studied for the characterization and diagnoses of head and neck cancer. However, to the best of our knowledge, no published meta-analysis has assessed the value of NBI for differentiating lesions of the nasopharynx. The aim of this study is thus to evaluate the diagnostic performance of NBI for NPC with histopathology as the reference standard.

1Department of Otolaryngology–Head and Neck Surgery, Affiliated Hospital of Jiangnan University, Wuxi, China

2Medical College of Jiangnan University, Wuxi, China

*These authors contributed equally to this article.

Corresponding Author:
Xiaodong Du, MD, Department of Otolaryngology–Head and Neck Surgery, Affiliated Hospital of Jiangnan University, Huizhe Road 200, Wuxi, Jiangsu Province, China.
Email: entdxd@sina.com
Methods

Protocol and Registration

The protocol used in this article is published on PROSPERO. The registry number for this study is CRD42015026244.

Search Strategy

Two investigators (X.H. and Y.Z.) searched the PubMed, Embase, Cochrane Library, CNKI, and Wan Fang databases up to January 2017. The search terms were “NBI,” “narrow band imaging,” “nasopharyngeal carcinoma,” “nasopharynx carcinoma,” “nasopharyngeal cancer,” and “nasopharynx cancer.” We also manually searched the reference lists of relevant articles and reviews to identify studies that had been missed.

Study Selection

Inclusion criteria for this meta-analysis were as follows: (1) the articles were based on diagnostic accuracy experiments with NBI among patients with nasopharynx disease suspected on clinical grounds; (2) studies evaluated the lesions in terms of true and false positives and true and false negatives (or values could be calculated from the raw data in the publication); and (3) diagnosis of the lesion came from the gold standard, histopathologic biopsy. Among eligible studies with data published more than once, articles with the largest sample sizes of patients were included. Finally, no language restriction was used in our meta-analysis. The following exclusion criteria were applied: (1) data could not be fully extracted; (2) the articles were reviews, case reports of <10 patients, comments, thesis, or conference abstracts; and (3) lesions had no pathologic confirmation based on the gold standard.

We used a 2-stage process to retrieve studies. First, the titles and abstracts of studies identified by the search strategy were scanned independently by 2 reviewers (X.H. and Y.Z.) to determine whether each study met the inclusion criteria. Second, the full text of the identified studies was reviewed independently by each researcher to assess the eligibility of each article, and disagreements were resolved by consensus.

Data Extraction and Quality Assessment

Two independent reviewers (X.H. and Y.Z.) extracted the following data: first author, publication date, number of endoscopists, diagnostic standard of NPC, and patient characteristics (number of patients and lesions, mean age, sex). The sensitivity, specificity, and lesions of the true and false positive and true and false negative were extracted and cross-checked. Any discrepancies were elucidated by X.D. For data that could not be extracted or for any statement that was not clearly expressed, communication with author was executed via email. If no reply was received, the study was excluded.

Two independent reviewers (X.H. and C.S.) assessed the methodological quality and risk of bias of the included studies using the Quality Assessment of Diagnostic Accuracy Studies–2 (QUADAS-2),12,13 which comprises 4 sections: patient selection, index test, reference standard, and flow and timing. Each section contains a series of questions and is scored as high, low, or unclear.

Statistical Analysis

The diagnostic accuracy effect quantities—including the pooled sensitivity, specificity, likelihood ratio, and diagnostic odds ratio (DOR) with 95% CI—were calculated with Meta-Disc 1.4 (Ramony Cajal Hospital, Madrid, Spain) and were combined with the creation of a symmetric receiver operator characteristic curve. The area under the curve and integrated DOR values were used to analyze the diagnostic precision of NBI for the diagnosis of NPC. The heterogeneity of the studies was assessed with the $Q$ and $I^2$ statistics, and $I^2$ values of 25%, 50%, and 75% represented low, moderate, and high inconsistency, respectively.14,15

Subgroup analysis and sensitivity analysis were performed when heterogeneity was found ($P < .05$). Subgroup analyses were conducted per the number of examined lesions ($n \geq 100$) and recurrent lesions after radiotherapy. We also performed a WLE analysis to assess its diagnostic performance in comparison with NBI.

In this meta-analysis, we used Manager 5.3 software (Cochrane Collaboration, London, UK) for the evaluation of methodological quality, Stata 12.0 (Stata, College Station, Texas) for the assessment of publication bias, and Meta-Disc 1.4 for most statistical analyses.

Results

Eligible Studies

Figure 1 shows a flowchart depicting the article selection process. After the initial computerized search, 46 studies were identified: 16 studies were excluded due to duplication and 7 on the basis of title and abstract review, leaving 23 articles for further selection. After full text review, 13 of the 23 relevant articles were excluded for the following reasons:

Figure 1. Flowchart of the systematic literature search and study.
Table 1. Characteristics of Studies Included in the Meta-analysis.

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Patients:Lesions, n</th>
<th>Mean Age, y M:F, n</th>
<th>Endoscopists, n</th>
<th>Diagnostic Standard of Nasopharyngeal Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ho (2011)16</td>
<td>63:63</td>
<td>NR</td>
<td>46:17 NR</td>
<td>An irregular engorged vascular pattern and/or a microvascular proliferative pattern</td>
</tr>
<tr>
<td>Wang (2011)17</td>
<td>79:79</td>
<td>52.9</td>
<td>58:21 NR</td>
<td>Type V^a</td>
</tr>
<tr>
<td>Wang (2012)18</td>
<td>106:106</td>
<td>55.9</td>
<td>80:26 NR</td>
<td>A well-demarcated brownish area with scattered brown spots</td>
</tr>
<tr>
<td>Wen (2012)19</td>
<td>211:285</td>
<td>38</td>
<td>133:78 NR</td>
<td>A well-demarcated brownish area with or without irregular type III or IV microvascular patterns</td>
</tr>
<tr>
<td>Qin (2015)25</td>
<td>44:44</td>
<td>47</td>
<td>NR NR NR</td>
<td>New vessels with branch- or earthworm-like shape and intraepithelial papillary capillary loop</td>
</tr>
<tr>
<td>Ni (2016)20</td>
<td>290:290</td>
<td>NR</td>
<td>NR</td>
<td>Type V^b</td>
</tr>
<tr>
<td>Vlantis (2016)11</td>
<td>156:156</td>
<td>49.5</td>
<td>90:66 2</td>
<td>Dilated and/or enlarged vessels; vascular tufts</td>
</tr>
<tr>
<td>Song (2016)22</td>
<td>52:52</td>
<td>51</td>
<td>43:9 NR</td>
<td>A well-demarcated brownish area with scattered brown spots</td>
</tr>
<tr>
<td>Wei (2016)23</td>
<td>182:182</td>
<td>51</td>
<td>112:70 NR</td>
<td>A well-demarcated brownish area with high density; irregularly dilated new vessels with branch-like or earthworm-like shape</td>
</tr>
<tr>
<td>Ge (2016)24</td>
<td>80:80</td>
<td>45</td>
<td>62:18 2</td>
<td>New vessels with branch-like or tortuous shapes</td>
</tr>
</tbody>
</table>

Abbreviations: F, female; M, male; NR, not reported.

^aDesign of each study: prospective (except Ho, for which the design was not reported).

^bPresence of either irregular microvascular pattern or side difference. Irregular microvascular pattern indicates tortuous microvessels with abnormal dilatation, abrupt alteration in caliber, and heterogeneity in shape. Side difference indicates presence of light crests (LC) signs or regular capillary network on one side while absent on the contralateral side.

^cIntraepithelial papillary capillary loops are dilated, elongated, and distorted and appear clearly as irregular, twisted, brownish line shapes; they have snake-like, earthworm-like, or branch-like shapes. The microvascular network and submucosal veins are nearly invisible.

(1) the aim of the article was not to reveal the diagnostic accuracy of NBI for NPC; (2) researchers did not use histopathologic results as the reference standard; (3) the articles did not report data that could be used to construct or calculate true-positive, false-positive, true-negative, and false-negative results; and (4) there was data overlap among the articles. Finally, 10 articles^11,16-24 fulfilled the inclusion criteria and were included for meta-analysis. Table 1 summarizes the characteristics of the eligible studies.

Quality Assessment

We assessed the quality of the 10 included articles per QUADAS-2. Figure 2 shows the quality of the eligible studies according to QUADAS-2 criteria. Of the 10 included studies, 2 studies fulfilled 7 items,20,22 and 8 studies met 6 items.11,16-18,21,22,24,25 Among them, the patient selection domain of 8 studies was labeled as unclear, as the authors did not report whether the patients were consecutive or from a random sample.

Diagnostic Accuracy of NBI Basis

Figure 3 presents the forest plot of sensitivity and specificity for NBI in the diagnosis of NPC. The pooled values were as follows: sensitivity, 0.83 (n = 1337; 95% CI, 0.80-0.86); specificity, 0.91 (n = 1337; 95% CI, 0.89-0.93); positive likelihood ratio, 8.82 (n = 1337; 95% CI, 5.12-15.21); negative likelihood ratio, 0.18 (n = 1337; 95% CI, 0.12-0.27); and DOR, 65.73 (n = 1337; 95% CI, 36.74-117.60; Table 2). The area under the curve was 0.9549 (SE = 0.0110), Q^* = 0.8972 (SE = 0.0153; Figure 4), indicating that NBI presents a high level of diagnostic accuracy.

Diagnostic Accuracy of WLE Basis

Seven articles compared the results with a WLE control group; therefore, we analyzed the data to compare the diagnostic performance of WLE with NBI. The pooled values were as follows: sensitivity, 0.79 (n = 1009; 95% CI, 0.75-0.83); specificity, 0.87 (n = 1009; 95% CI, 0.84-0.90); positive likelihood ratio, 5.02 (n = 1009; 95% CI, 1.99-12.65); negative likelihood ratio, 0.34 (n = 1009; 95% CI, 0.24-0.49); and DOR, 16.89 (n = 1009; 95% CI, 5.98-47.66). The area under the curve was 0.8627 (SE = 0.0465), Q^* = 0.7933 (SE = 0.0451).

Heterogeneity Test

The threshold effect is usually one source of heterogeneity. The Spearman correlation coefficient was 0.479 (P = .162), indicating no definite threshold effect-induced heterogeneity for these studies. Heterogeneity was observed with an I^2 value of 0.326 for DOR, which indicates the existence of moderate statistical heterogeneity among the studies. Thus, statistical analyses were performed with a random effect model with Meta-Disc software.

Subgroup analysis identified the source of heterogeneity.26 In this meta-analysis, we performed a subgroup analysis based on the number of examined lesions and recurrent NPC among the studies. The pooled sensitivity and specificity for the studies with examined lesions ≥100 were 0.81 (n = 1019; 95% CI, 0.76-0.85) and 0.91 (n = 1019; 95% CI, 0.89-0.93), respectively. In contrast, the pooled sensitivity and specificity for the articles with examined lesions <100 were 0.87 (n = 318; 95% CI, 0.72-0.99) and 0.91 (n = 318; 95% CI, 0.83-0.96), indicating no significant degree of heterogeneity in the number of lesions. Per subgroup analysis,
the pooled sensitivity and specificity for the studies including recurrent NPC after radiotherapy were 0.81 (n = 286; 95% CI, 0.66-0.91) and 0.87 (n = 286; 95% CI, 0.83-0.91). However, the pooled sensitivity and specificity for the studies not including recurrent NPC after radiotherapy were 0.83 (n = 1051; 95% CI, 0.80-0.86) and 0.93 (n = 1051; 95% CI, 0.90-0.95), indicating no significant heterogeneity among studies regardless of whether recurrent NPC after radiotherapy is included or not.

Table 3 and Figure 6. No study significantly affected the pooled DOR from the results in Figure 6.

Publication Bias Estimate

The Deeks funnel plot (Figure 7) did not display significant asymmetry (P = .68), suggesting that no striking publication bias was present in this study.

Discussion

Principal Findings

NPC occurs at a high frequency in southern China, and it is difficult to obtain an early diagnosis when examined with conventional WLE. NBI is a novel imaging method that has the potential to improve the early diagnostic rate of the nasopharynx lesions. In this study, we performed a systematic review and meta-analysis to evaluate the diagnostic performance of NBI among patients with nasopharyngeal neoplasm. The results showed that NBI had a sensitivity of 0.83 and a specificity of 0.91 for the diagnosis of NPC. In contrast, the pooled sensitivity and specificity for WLE...
Figure 3. Forest plots of (A) sensitivity and (B) specificity for narrow band imaging in the diagnosis of nasopharyngeal cancer. Values are presented as Table 2.

Table 2. Results of the Studies Retrieved from 2 × 2 Tables.

<table>
<thead>
<tr>
<th>Study</th>
<th>Results, n</th>
<th>Value (95% CI)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TP:FN</td>
<td>FP:TN</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>PLR</td>
<td>NLR</td>
<td>DOR</td>
</tr>
<tr>
<td>Ge (2016)²⁴</td>
<td>55:15</td>
<td>1:9</td>
<td>0.79 (0.67-0.87)</td>
<td>0.90 (0.55-1.00)</td>
<td>7.86 (1.22-50.64)</td>
<td>0.24 (0.15-0.39)</td>
<td>33 (3.87-281.44)</td>
</tr>
<tr>
<td>Ho (2011)²⁶</td>
<td>32:9</td>
<td>1:21</td>
<td>0.78 (0.62-0.89)</td>
<td>0.95 (0.77-1.00)</td>
<td>17.17 (2.51-117.33)</td>
<td>0.23 (0.13-0.41)</td>
<td>74.67 (8.80-633.39)</td>
</tr>
<tr>
<td>Ni (2016)²⁰</td>
<td>167:43</td>
<td>7:73</td>
<td>0.80 (0.73-0.85)</td>
<td>0.91 (0.83-0.96)</td>
<td>9.09 (4.46-18.50)</td>
<td>0.22 (0.17-0.30)</td>
<td>40.5 (17.40-94.27)</td>
</tr>
<tr>
<td>Qin (2015)²⁵</td>
<td>29:3</td>
<td>2:10</td>
<td>0.91 (0.75-0.98)</td>
<td>0.83 (0.52-0.98)</td>
<td>5.44 (1.53-19.36)</td>
<td>0.11 (0.04-0.34)</td>
<td>48.33 (7.03-332.38)</td>
</tr>
<tr>
<td>Song (2016)²²</td>
<td>45:1</td>
<td>2:4</td>
<td>0.98 (0.88-1.00)</td>
<td>0.67 (0.22-0.96)</td>
<td>2.93 (0.95-9.11)</td>
<td>0.03 (0.00-0.25)</td>
<td>90 (6.62-1222.94)</td>
</tr>
<tr>
<td>Vlantis (2016)¹¹</td>
<td>27:14</td>
<td>7:108</td>
<td>0.66 (0.49-0.80)</td>
<td>0.94 (0.88-0.98)</td>
<td>10.82 (5.11-22.93)</td>
<td>0.36 (0.24-0.56)</td>
<td>29.76 (10.94-80.92)</td>
</tr>
<tr>
<td>Wang (2011)¹⁷</td>
<td>33:1</td>
<td>3:42</td>
<td>0.97 (0.85-1.00)</td>
<td>0.93 (0.82-0.99)</td>
<td>14.56 (4.87-43.51)</td>
<td>0.03 (0.00-0.22)</td>
<td>462.00 (45.92-468.09)</td>
</tr>
<tr>
<td>Wang (2012)¹⁸</td>
<td>7:1</td>
<td>25:73</td>
<td>0.88 (0.47-1.00)</td>
<td>0.74 (0.65-0.83)</td>
<td>3.43 (2.24-5.26)</td>
<td>0.17 (0.03-1.05)</td>
<td>20.44 (2.40-174.42)</td>
</tr>
<tr>
<td>Wei (2016)²³</td>
<td>27:7</td>
<td>6:142</td>
<td>0.79 (0.62-0.91)</td>
<td>0.96 (0.91-0.98)</td>
<td>19.59 (8.78-43.69)</td>
<td>0.21 (0.11-0.42)</td>
<td>91.29 (28.46-292.80)</td>
</tr>
<tr>
<td>Wen (2012)¹⁹</td>
<td>62:4</td>
<td>13:206</td>
<td>0.94 (0.85-0.98)</td>
<td>0.94 (0.90-0.97)</td>
<td>15.83 (9.31-26.91)</td>
<td>0.06 (0.02-0.17)</td>
<td>245.62 (77.30-780.42)</td>
</tr>
<tr>
<td>Overall</td>
<td>484:98</td>
<td>67:688</td>
<td>0.83 (0.80-0.86)</td>
<td>0.91 (0.89-0.93)</td>
<td>8.82 (5.12-15.21)</td>
<td>0.18 (0.12-0.27)</td>
<td>65.73 (77.30-780.42)</td>
</tr>
</tbody>
</table>

Abbreviations: DOR, diagnostic odds ratio; FN, false negative; FP, false positive; NLR, negative likelihood ration; PLR, positive likelihood ratio; TN, true negative; TP, true positive.
were 0.79 and 0.87, respectively. In addition, when compared with WLE, NBI demonstrated a higher positive likelihood ratio (8.82 vs 5.02) and DOR (65.73 vs 16.89) and a lower negative likelihood ratio (0.18 vs 0.34).

Table 4 shows the statistical analyses of the difference between NBI and WLE in diagnosing NPCs. The difference of sensitivity and specificity between NBI and WLE in the included studies had no statistical significance ($P = .07$ and $P = .31$). The significant difference of DOR is attributed to 2 studies\(^{17,19}\) that included more patients with true-positive and true-negative results than the other studies.

Moderate heterogeneity was found in this meta-analysis. We calculated the Spearman correlation coefficient, and the result indicates that no threshold effect exists ($r = 0.48$, $P > .05$). A subgroup analysis was performed based on the number of lesions and recurrent NPC after radiotherapy among the included studies. The results show that 2 factors did not contribute to heterogeneity. However, we found that the criteria for NBI diagnosis of NPC were not unified. Some studies diagnosed NPC with the evidence of new vessels with branch- or earthworm-like shape.\(^{16,17,24,25}\) In other studies, lesions appearing with well-demarcated brownish areas with scattered brown spots were regarded as NPC.\(^{18,22,23}\) Wen et al\(^{19}\) and Ni et al\(^{21}\) summarized the characteristics of superficial microvessel patterns of different nasopharyngeal mucosal lesions and proposed their own diagnostic criteria. We hypothesize that the observed heterogeneity might arise from the difference of diagnostic criteria.

**Clinical Implication and Future Directions**

The NBI system is an optical technique used for enhanced visualization of microvascular patterns and microsurface structures with narrower bands of blue and green filters. Therefore, NBI is supposedly good at detecting blood vessel changes associated with malignancy, thus promoting the
detection rate of NPC in the early stage. However, our meta-analysis results indicated no statistical significance between NBI and WLE in terms of their sensitivity and specificity. The results indicate that NBI is not more useful than WLE in the detection of NPC. Several reasons may account for this result. First, unlike the hypopharyngeal and esophageal squamous epithelium, lymphoid tissue is rich in the nasopharyngeal region. The microvessels covered with the proliferated lymphoid tissue can not be fully exposed and do not present as typical microvessel changes. In addition, some factors still limit the observation of microvessels, such as secretion coating bleeding and darker image. Second, most NPCs included in the studies are in advanced stages at diagnosis and thus can be easily detected, even by WLE. However, the NBI is supposed to be superior to WLE in detecting ulcerative- and superficial-type NPC in the early stage. Third, there is no unified criteria for microvessels during NBI observation. Different classification criteria can affect the result of diagnostic performance of NBI. For example, Vlantis adopted relatively stricter or narrow criteria that resulted in an extremely low sensitivity, 0.22. Therefore, we proposed that the NBI may serve as a good supplement to WLE in screening high-risk groups of NPC or the follow-up after radiotherapy to detect early-stage NPC.

Magnifying endoscopy enables image magnification compared with traditional endoscopy, and high-magnification endoscopy can enlarge an image 100-fold. Combined with high-magnification endoscopy, NBI might allow a more detailed visualization of microvessels and microstructures within the superficial layer of the nasopharyngeal mucosa and the precise distinguishing of precancerous and cancerous lesions in the nasopharynx. It is foreseeable that the NBI endoscopic system, combined with magnifying endoscopic techniques, can further improve diagnostic sensitivity, helping clinicians to perform more accurate early diagnosis.

Study Limitations
There are several limitations of our study. First, we included only 10 studies, and some of them were not of high quality. For example, only 2 of these 10 studies reported the methods of patient enrollment, and the patient selection of 8 studies was marked as a risk of bias in QUADAS-2. The study design is crucial for reliability of results in the diagnostic accuracy test. Hence, more multicenter studies with strict controls on experimental procedures are needed to provide high-quality data for further analysis. Second, all articles included in our meta-analysis came from China, where the prevalence rate is much higher than in other countries, which may have generated some bias. Consequently, the difference of positive predictive value between NBI and WLE is likely much less in other populations. Third, the pooled sensitivity and specificity in this study were based on per-patient analysis. None of these articles provided specific patient characteristic data. Thus, there may be some differences in the results obtained from the per-patient analysis when compared with the per-lesion analysis. Fourth, heterogeneity existed among studies. Because the subgroup analysis did not find the sources of heterogeneity, we could only speculate on the potential reasons for it.

Conclusion
In conclusion, this meta-analysis indicates that the diagnostic sensitivity and specificity of NBI are similar to those of traditional WLE. Given the limitations mentioned, the potential value of NBI for the diagnosis of NPC needs to be validated further.

Acknowledgments
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Author Contributions
Changling Sun, idea of the study, data analysis, drafting, final approval, accountability for all aspects of the work; Yayun Zhang, design of the study, data analysis, drafting, revising the manuscript, final approval, accountability for all aspects of the work; Xue Han, data interpretation, revising the manuscript, final approval; Xiaodong Du, idea of the study, data analysis, drafting, final approval, accountability for all aspects of the work.


<table>
<thead>
<tr>
<th>Test Statistic</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PLR</th>
<th>NLR</th>
<th>DOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>z*</td>
<td>1.93 (t) b</td>
<td>1.03</td>
<td>0.68</td>
<td>1.85</td>
<td>2.147</td>
</tr>
<tr>
<td>P</td>
<td>.073</td>
<td>.305</td>
<td>.495</td>
<td>.064</td>
<td>.032</td>
</tr>
</tbody>
</table>

Abbreviations: DOR, diagnostic odds ratio; NLR, negative likelihood ration; PLR, positive likelihood ratio.

aThe statistic for the 2-sample t test.
bThe statistic for the 2-sample Wilcoxon rank-sum test.
Disclosures
Competing interests: None.
Sponsorships: None.
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References