Diagnostic Performance Between White Light Endoscopy and Narrow Band Imaging in Detection of Nasopharyngeal Carcinoma
A Systematic Review and Meta-Analysis

Pamuji M.A.[1,3,*], Utomo B.S.R.[2], Marlina L.[2], Trixie J.A.[1], Tasya L.[1], Hutagalung V.N.[1], and Esterini D.N.[1]

[1] *Faculty of Medicine, Universitas Kristen Indonesia, Jakarta, Indonesia*
[2]*Department of Otorhinolaryngology, Head and Neck Surgery Faculty of Medicine Universitas Kristen Indonesia, General Hospital of Universitas Kristen Indonesia, Jakarta, Indonesia*
[3]*Pamuji MA; Faculty of Medicine, Universitas Kristen Indonesia*
[*]*Corresponding author. Email: maurin.asyita@gmail.com*

ABSTRACT
Nasopharyngeal Carcinoma (NPC) is an epithelial carcinoma originating from the nasopharynx mucosa lining. It is the most common head and necks malignant globally, especially in Asia. NPC is mostly located in Fossa of Rosenmüller, an area that is hard to observe. To diagnose NPC, radiologic imaging and endoscopic examination are necessary. White Light Endoscopy (WLE) is a basic standard endoscopy examination that can be used to diagnose NPC. On the other hand, many studies were expecting for another examination, Narrow Band Imaging (NBI), to be more sensitive in diagnosing NPC than WLE. This meta-analysis aimed to compare the diagnostic performance between WLE and NBI in NPC detection. A literature search was performed using medical literature databases such as PubMed, BMC, Research Gate, and Medical Journal. The studies that we used were published in 2011-2021. Review Manager 5.4.1 was utilized to analyze data extraction and the risk of bias. Seventeen studies were expecting used in this meta-analysis. All of those studies had fulfilled inclusion criteria. The WLE's sensitivity was 2-90 % and its specificity was 0-100% (95% CI). Meanwhile, NBI's sensitivity was 60-100% and its specificity was 0-100% (95% CI). NBI was more sensitive in diagnosing NPC than WLE, but both had the same specificity value. Further studies might be useful to validate this examination.

Keywords: *Nasopharyngeal Carcinoma, Narrow Band Imaging, White Light Endoscopy.*

1. INTRODUCTION

Nasopharyngeal carcinoma is one of four most commonly found malignancies in Indonesia after cervical cancer, breast cancer, and skin cancer. A study by Adham et al. in 2012 mentioned that in Indonesia, NPC estimated overall incidence is 6.2/100 000 or about 12 000 new cases per year [1]. It is more frequently discovered in adult than children. Moreover, the number increases from age 30 to the peak age between 40 and 60 years old [2,3]. Nasopharyngeal carcinoma is also more likely occurred in men than women with a ratio 2–3:1 [3]. Diagnosing nasopharyngeal carcinoma from clinical symptoms is challenging because of non-specific symptoms. The location of the nasopharynx is also difficult to inspect. NPC can be found in the Fossa of Rosenmüller, which is a hard area to be observe [4]. The definitive method that may be utilized for nasopharyngeal carcinoma diagnosis is a combination between biopsy and endoscopy [5]

Current detection modalities of NPC include endoscopic examination and radiologic imaging [6,7]. 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 [8].

White light endoscopy (WLE) can detect morphologic changes in the superficial mucosa, and it is widely used in the diagnosis of NPC [9,10]. However, for some early-stage NPC, the superficial tumor zone is complicated to identify or differentiate from other pathologies, such as lymphoid follicular hyperplasia [6].

Narrowband imaging (NBI) is a novel optical technology that uses reflected light to improve the visualization of superficial mucosal lesions.[9,10] It provides more in-depth insights into the behaviour of a target lesion to obtain a so-called optical biopsy. It also allows visualization of lesions that are not otherwise visible, which helps reduce the number of unnecessary biopsies and minimises the number of false negatives [2,6]. Thus, this study aims to evaluate the diagnostic performance between WLE and NBI in NPC detection.

2. MATERIALS AND METHODS

Medical electronic databases such as PubMed, BMC Medicine, and ResearchGate were searched with no limitation of publishing year and only with a language that writers understood (English language). The search terms used were the following: “nasopharyngeal carcinoma,” “NPC,” “narrow-band imaging,” and “diagnostic.” The first author searched electronic searches. The eligibility of the studies assessed independently by authors and disagreements were discussed together between all authors.

The data analysis was completed using Review Manager 5.4 (Cochrane Training). Data from each eligible study were extracted by true positive, false positive, true negative, and false negative. The meta-analysis was performed to analyze the sensitivity and specificity with the aim to assess the comparison of NBI and WLE capability in diagnosing NPC. The value of the confidence interval used was 95%. Moreover, the meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement.

3. RISK OF BIAS

Study quality was assessed by QUADAS-2. It is a quality assessment of diagnostic accuracy studies. Four domains related to the risk of bias were assessed in each study: (1) flow and timing (2) reference standard (3) index test (4) patient selection. Review authors’ judgments were categorized as ‘‘low risk,’’ ‘‘high risk,’’ or ‘‘unclear risk of bias.’’ Five authors independently assessed the risk of bias. Discrepancies and disagreements were resolved by discussion

4. RESULTS AND DISCUSSION

4.1 Results

4.1.1 Study Selection and Study Characteristics

From Figure 1, we could understand the data retrieval process. A total of 342 studies were assessed for its eligibility. There were 260, 32, and 50 studies obtained from PubMed, BMC, and ResearchGate, respectively. Afterwards, 22 studies were excluded due to duplication, 39 were excluded due to the incongruous title with the aim of the study, and 24 were excluded within the abstract selection, leaving 11 studies to extract. Then, we included 6 studies from references of a meta-analysis journal so that the number of studies used was 17. All these studies were suitable to be included in this study. In addition, all studies were from Southeast Asia. Each investigator independently abstracted data from each study separately. Data from each eligible study were extracted without modification of the original data onto custom-made data collection forms (Table 1).

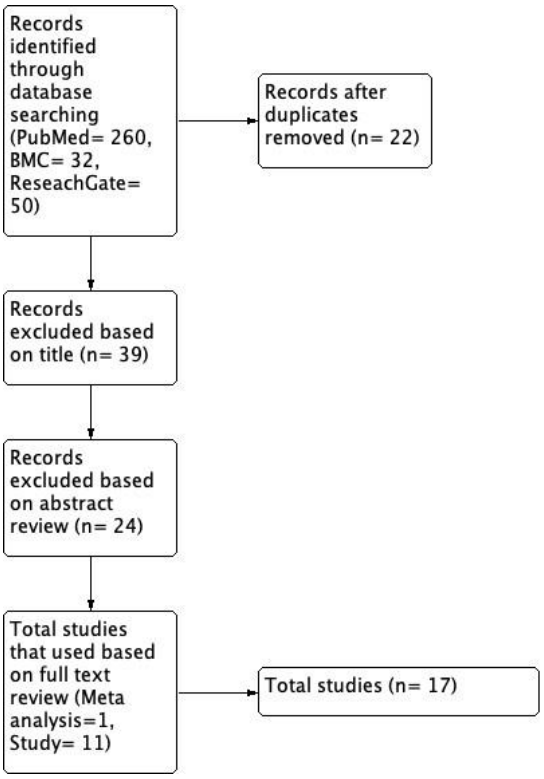

Figure 1. Flowchart of the study.

A total of 17 studies were analyzed (Fig. 2 and 3), for a total of 3,628 subjects where the data were divided into NBI and WLE. Most studies are diagnostic tests that compare NBI and biopsy, or WLE and biopsy.

Table 1 Characteristics of Studies Included in The Meta-Analysis

Author (Year)[a]	Patients:Lesions	Mean Age	M:F	Endoscopist	Diagnostic Standard of nasopharyngeal carcinoma
Si (2018)	119:119	NR	2850:3068	NR	Increased of superficial vessels of the mucosa, increased (expanded) vessel diameter, disordered texture, local circuitry, intensively distributed punctiform vessels, and lumbriciform, or rope-strip-shaped vascular disruptions
Qin (2015)	44:44	47	NR	NR	New vessels with branch- or earthworm-like shape and intraepithelial papillary capillary loop
Ho (2011)	63:63	NR	46:17	NR	An irregular engorged vascular pattern and/or a microvascular proliferative pattern
Wang NBI type II (2011)	79:79	52,2	58:21	2	Type II[b]
Vlantis (2016)	156:156	49,5	90:66	2	Dilated and/or enlarged vessels; vascular tufts
Song (2016)	52:52	51	43:9	NR	A well-demarcated brownish area with scattered brown spots
Vlantis (2018)	156:156	NR	33:20	NR	A well-demarcated brownish area with thick dark spots and/or winding vessels
Wei (2016)	182:182	51	112:20	NR	A well-demarcated brownish area with high density; irregularly dilated new vessels with branch-like or earthworm-like shape
Ge (2016)	80:80	45	62:18	2	New vessels with branch-like or tortuous shapes
Yuniserani (2017)	24:24	NR	16:8	NR	Brownish Spot or irregular Vascular Pattern with Brown Spot
Wang (2012)	106:106	55,9	80:26	NR	A well-demarcated brownish area with scattered brown spots
Wen (2012)	211:211	38	133:78	2	A well-demarcated brownish area with or without irregular type III or IV microvascular patterns
Ho (2013)	211:211	48	93:118	NR	NR
Adham (2014)	56:56	NR	38:18	NR	Clear brown spots are concentrated in one area of the nasopharyngeal mucosa or loss of polygonal follicular pattern with regular arrangement or large mucous capillary blood vessels with irregular arrangement
Yang (2012)	1845:1845	53,1	1153:701	NR	Smooth and had a slightly red- dish area or A clearly demarcated brownish area and scattered brown spots. or well-demarcated brownish areas with hypertrophic vascular loops branching out to several winding vessels or demarcated brownish area with tortuous and expanded micro vessels.
Madana (2015)	15:15	NR	58:21		Loss of normal polygonal follicular architecture of n nasopharyngeal mucosa

Author (Year)[a]	Patients:Lesions	Mean Age	M:F	Endoscopist	Diagnostic Standard of nasopharyngeal carcinoma
Wang (NBI type IV) (2011)	79:79	52,2	58:21	2	Type IV[c]
Wang (NBI type V) (2011)	79:79	52,2	58:21	2	Type V[d]
Ni (2016)	290:290	NR	NR	2	Type V[e]

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

[a]Design of each study: prospective (except Ho, for which the design was not reported).

[b] Irregular microvascular pattern (IMVP) indicates tortuous micro vessels with abnormal dilatation, abrupt alteration in caliber and heterogeneity in shape.

[c] Side-difference indicates presence of light crests (LC) signs or regular capillary network on one side, while absent on the contralateral side.

[d] Presence of either irregular microvascular pattern or side difference. Irregular microvascular pattern indicates tortuous micro vessels 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.

The biopsy method acts as a standard gold examination to compare examination results between NBI and WLE.

Our calculation results in Figure 2 concluded that the sensitivity and specificity values of the NBI were 60-100% and 0-100%, respectively (with 95% CI). Meanwhile, for WLE, shown in Figure 3, the sensitivity value was 2-90% and the specificity was 0-100% (95% CI). These figures showed that the NBI is better in sensitivity, which means that the ability of the NBI to determine a positive result on NPC was better. In addition, WLE has the same specificity value as NBI, which means that both could determine negative results on NPC.

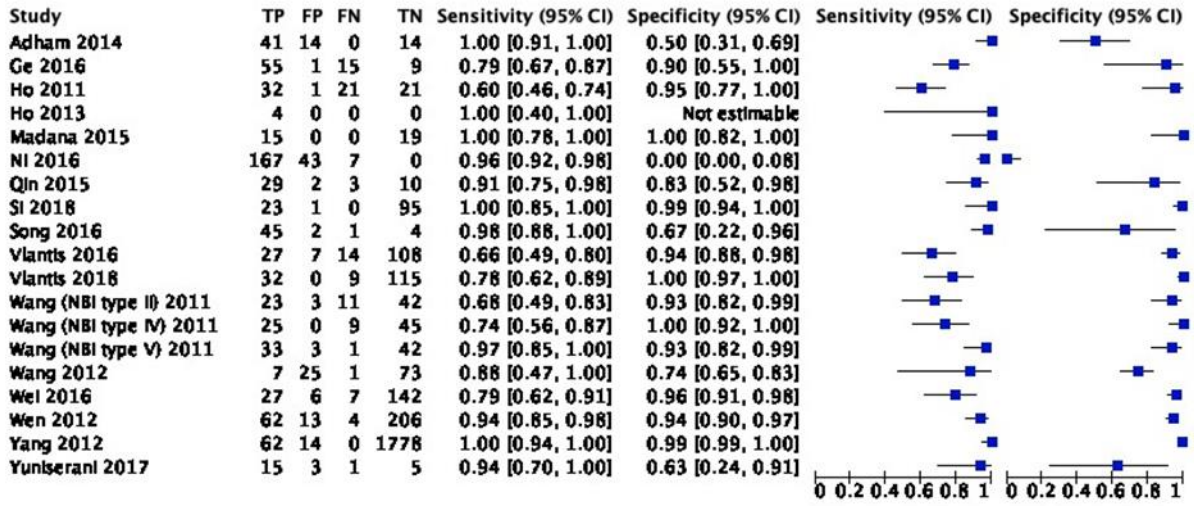

Figure 2. Forest plot for sensitivity and specificity between NBI and biopsy. TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval

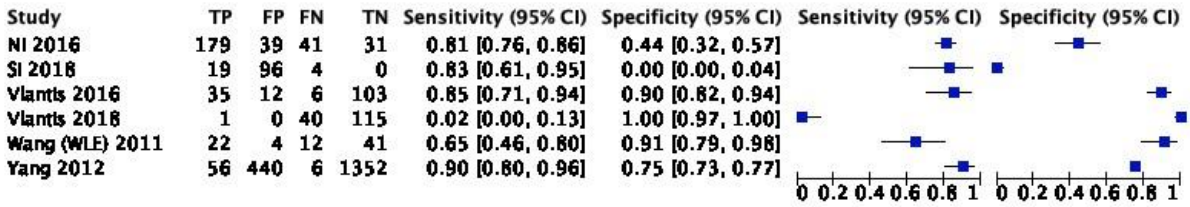

Figure 3. Forest plot for sensitivity and specificity between WLE and biopsy. TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

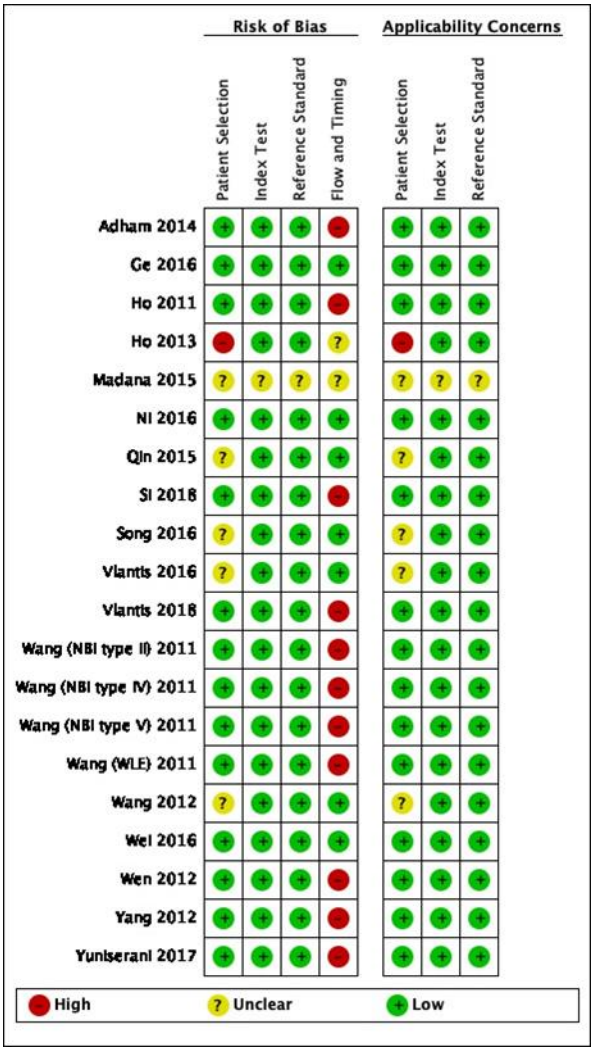

Figure 4 Risk of bias summary of the study

Almost all eligible studies claimed to have a low risk of bias (Fig. 4 and 5), and we found this consistent with our calculations. We rated some parameters as unclear because it did not clearly explain the risk of bias. Within the parameters analyzed, both patient selection, index test, and reference standard showed low risk results. For flow timing, they showed high-risk results.

4.2 Discussion

Nasopharyngeal cancer is the most common in Southeast Asia. The five countries with the highest incidence are China, Indonesia, Vietnam, India and Malaysia [24-26]. Nasopharyngeal cancer has a variety of clinical manifestations, so there is often an error in diagnosis [27]. Whereas early detection is very necessary for the success of therapy [28].

In diagnosing nasopharyngeal carcinoma, beside history taking and physical examination, supporting examinations are also important. One of the supporting examinations in diagnosing nasopharyngeal carcinoma is imaging. The two most commonly used imaging are White Light Endoscopy (WLE) and Narrow Band Imaging (NBI). The results of the analysis of this study indicate that WLE has a sensitivity value of 2% - 90% and a specificity value of 0% - 100%. Meanwhile, the NBI has a sensitivity value of 60% - 100% and a specificity of 0% - 100%. The standard examination used in this meta-analysis is histopathological examination.

NBI is more sensitive in diagnosing nasopharyngeal carcinoma than WLE. However, for specificity both have the same value. The results of this meta-analysis are different from the meta-analysis conducted by Sun., et al. [29]. Those meta-analyses stated that NBI had the same sensitivity and specificity in diagnosing nasopharyngeal carcinoma compared to WLE. Their analysis used 10 studies, in contrast to this meta-analysis which used 23 studies

Figure 5. Risk of bias graph of the study

Similar results were also found in the diagnostic test conducted by Yuniserani, et al (2017) in Bandung, West Java. The study involved 24 patients with histopathological proven nasopharyngeal carcinoma. NBI examination has a sensitivity of 93.75% [16].

The mechanism NBI works with an optical technique that is used to improve the visualization of microvascular patterns and mucosal surfaces. NBI works by filtering white light into more specific light, where this light will be absorbed by hemoglobin, thereby penetrating the tissue surface. This causes the capillaries on the mucosal surface to turn brown and the veins in the submucosa appear cyan on the monitor [30-32].

Therefore, NBI is good at detecting vascular changes associated with malignancy, thereby increasing the detection rate of NPC at an early stage [29,31]. This is in accordance with the results of this meta-analysis. However, it should be noted that NBI is not a substitute for histopathological examination [30].

The shortcoming in this meta-analysis is that most of studies taken were conducted in China. This causes less representation of the purpose of this scientific paper. Furthermore, there are fewer diagnostic tests assessing WLE than studies assessing NBI.

5. CONCLUSION

Although NBI can improve the detection and diagnosing NPC due to the higher sensitivity rather than WLE, both had the same specification value. Further studies might be useful to validate this examination. NBI also offers a timely, convenient, and highly reliable assessment of recurrent NPC. Moreover, it may indicate excellent probability to exclude nasopharyngeal carcinoma possibilities based on the evaluation of changes in nasopharyngeal mucosal features.

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