

RESEARCH ARTICLE

Editorial Process: Submission:09/11/2017 Acceptance:06/26/2018

Elective Neck Dissection for Management of Early- Stage Oral Tongue Cancer

Zeiad S Gad^{1*}, Osama A El-Malt¹, Mostafa A T El-Sakkary¹, Mohamed M AbdalAziz²

Abstract

Background: The occult neck metastasis rate is very high with tongue cancers. The aim of this study was to assess the current role of elective neck dissection (END) in management of early-stage oral tongue cancer with a focus on lymph node metastasis. In addition, effects of END on regional or systemic disease recurrence and survival were investigated. **Methods:** This retrospective study included patients with stage I and II tongue cancer recruited from our National Cancer Institute (NCI) over a time period of six years (2007-2013). The collected data were analyzed for disease free survival (DFS) and recurrence rate. **Results:** A total of 144 patients presented to our NCI with oral tongue cancer but only 88 were staged clinically and radiologically as early stage (stage I, stage II). Some 53% were smokers. Most lesions were dealt with by surgery, either by wide local excision (22%) or hemiglossectomy (78%). Treatment of neck lesions was either by neck dissection (85.2%) or “wait and see” (14.8%). The rates for local and nodal recurrence were 7.9% and 20.4%, respectively. Analysis of associations between DFS and different factors revealed significance for adoption of adjuvant therapy and the dissected lymph node status. **Conclusion:** Controversy still exists regarding neck management.

Keywords: Elective neck dissection- occult metastasis- squamous cell carcinoma

Asian Pac J Cancer Prev, 19 (7), 1797-1803

Introduction

Cancer of the anterior 2/3 of the tongue accounts for about 37% of newly diagnosed cases of malignancy involving oral cavity (Parkin et al., 2005). Cervical metastasis is the most significant factor in the prognosis of oral squamous cell carcinoma (SCC) as early detection and treatment may prevent distant metastases (Brown et al., 2000).

The assessment of cervical lymph nodes is difficult clinically and radiodiagnosis lacks considerable power to detect occult neck metastasis making the non-invasive neck staging methods limited to a maximum accuracy of 76% (Kovacs et al., 2000). Rate of occult neck metastasis is high in oral tongue cancer taking the risk of regional recurrence by application of “wait and see” policy. Franceschi et al., (1993) reported a 31% incidence of occult nodal metastasis in the clinically N0 neck for early oral tongue cancer and a 35% cervical node metastases on follow-up in patients with T1 or T2 lesions who did not undergo elective neck dissection (END). For T1 or T2 N0 oral SCC, sentinel lymph node biopsy could predict a pathologically negative neck in 96% of patients (Agrawal et al., 2010). Skip metastasis is rare in early-stage tongue cancer (T1,T2 SCC), so inclusion of

level IV is not mandatory in END for clinically negative neck (Battoo et al., 2012).

There are currently three policies advocated for management of an N0 neck; elective neck irradiation (ENI), END or close observation (wait and see). The choice takes into consideration T stage, site of primary, grade, compliance for follow-up, or the probability for occult metastasis (Shah and Gil, 2009).

Some prefer to adopt a “wait and see” policy, although this requires both great compliance from the patient and great expertise of the physician to identify metastasis early (Capote et al., 2007). Another argument in favor of END is the significant deterioration of the survival rate when neck dissection is due after clinical disease is detected (Godden et al., 2002). Elective Supraomohyoid neck dissection (SOHND) detects occult metastases in early node-negative oral tongue SCC and is sufficient to remove the majority of lymph node metastases. Patients with early oral SCC exhibiting occult metastases should be considered as high risk patients (Cheng et al., 2008).

Our aim was to verify the current role of END in management of early-stage oral tongue cancer through studying the prevalence of occult and skip lymph node metastasis, and evaluating the role of END in minimizing disease failure whether regionally or systemically and its

¹Department of Surgical Oncology, National Cancer Institute, Cairo University, ²Department of Surgical Oncology, Faculty of Medicine, Alexandria University, Egypt. *For Correspondence: z_gad@yahoo.com

role in improving survival.

Materials and Methods

This retrospective study included patients with early-stage oral tongue cancer presented at our National cancer institute (NCI) during six years (2007-2013).

Inclusion criteria:

Stage I and II tongue cancer

- Tumors <4 cm without invasion to surroundings clinically or following pathological examination.
- Negative neck either by clinical examination, by FNAC or by radiological investigation

Exclusion criteria

- Tumors >4cm or invading surrounding tissues either by examination or by pathological examination.
- Positive neck.

Data were collected by revising hospital records of patients diagnosed as early stage oral tongue cancer. Data included; age, sex, initial clinical presentation, laboratory investigations, U/S and CT results, biopsy results, treatment for the tongue lesion [wide local excision (WLE) or hemiglossectomy], treatment for the neck (type of neck dissection if performed, radiotherapy, or Observation), pathological features (tumor size, grade, margins, and lymph node status), post-operative course and follow up (postoperative complications, local recurrence and regional or distant failure). Data was statistically analyzed for:

- Disease free survival (to the date of recurrence whether local or distant)
- Local failure (recurrence)
- Distant failure (recurrence)

Statistical methods

Data were analyzed using IBM SPSS advanced statistics version 20 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation (SD) or median and range as appropriate. Qualitative data were expressed as frequency and percentage (%). For quantitative data, comparison between two groups

was done using Mann-Whitney test (non-parametric t-test). Comparison between 3 groups was done using Kruskal-Wallis test (non-parametric ANOVA) then post-Hoc “Scheffe test” was used for pair-wise comparison based on Kruskal-wallis distribution. Survival analysis was done using Kaplan-Meier method and comparison between two survival curves was done using log-rank test. All tests were two-tailed. P<0.05 was considered significant.

Results

This study included 144 patients presented with oral tongue cancer but only 88 patients were staged clinically and radiologically as early stage (stage I/II), the remaining 56 patients were stage III/IV.

These 88 patients with early stage had complete data with almost regular follow-up visits. Their mean age was 59.2 yrs with 52% (n=46/88) of them <60 years old, while 48% (n=42/88) of them were ≥60 years old. Half of cases (n=44/88) were males. We considered that smoking was the most important habit special to search for, and we found that 53% (n=46) of patients were smokers. There were different types of presenting symptoms with tongue ulcer being the most common presentation in 35% (n=31/88) of cases, followed by tongue mass in 23% (n=20/88), then ulcerating mass in 16% (n=14/88), followed by tongue nodule in 15% (n=13/88), then rubbery areas in 8% (n=7/88), followed by other presentations in 3% (n=3/88). Most lesions were at lateral margins (right or left) with about 53.4% and 40.9% for each one respectively and only 4.5% for midline lesions. The maximum diameter of the lesions varied from 0.5-5

Table 1. Frequency of Nodal Recurrence among Cases Who Had Neck Dissection in Relation to the Type of Dissection Used to Treat Them

Type of neck dissection	Total number	Number of recurrence (%)
MRND	40	12 (30)
SOHND	23	2 (8.7)
RND	12	2 (16.7)
Wait and see	13	2 (15.3)
Total	88	18 (20.4)

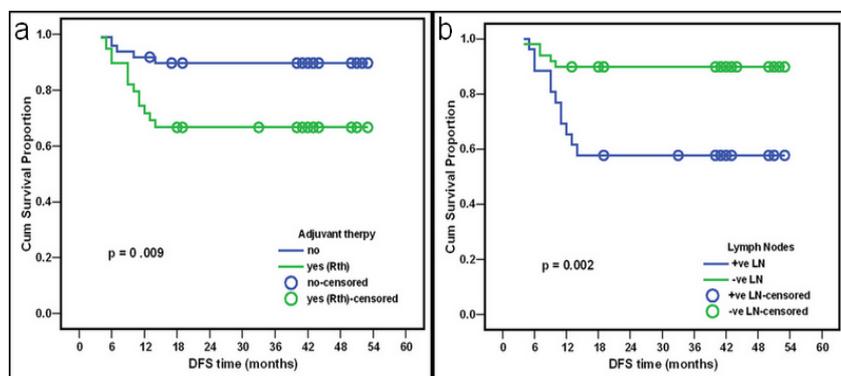


Figure 1. A. Comparison between Cases that Had Postoperative Adjuvant Therapy Versus Those Who Hadn't as Regards Cumulative Survival. Test Statistics for Equality of Survival Distributions for adjuvant therapy (P=0.009). B. Comparison between pathological results of neck dissection (positive versus negative) as regards cumulative survival. Test Statistics for Equality of Survival Distributions for Positive LNs (P=0.002).

Table 2. Association between Disease free Survival and Different Factors Implicated in the Study (Age, Sex... etc.) at 54 Months of Follow up

	Number	Disease free survival	P-value
Early stage tongue cancer	88	79.88%	
Age			
<60 yrs	46	73.91%	0.180
≥60 yrs	42	85.71%	
Gender			
Male	44	72.73%	0.124
Female	44	86.36%	
Special habits			
Smoker	46	73.91%	0.169
Non smoker	42	85.71%	
Site of primary			
Rt lateral margin	47	78.72%	
Lt lateral margin	36	80.56%	
Post 1/3, midline	5	80%	0.981
Presentation			
Ulcer	31	83.87%	
Mass	20	75.00%	
Nodule	13	92.31%	0.558
Rubbery areas	10	70.00%	
Ulcerating mass	14	72.43%	
Surgery for primary			
Hemiglossectomy	69	81.16%	0.404
WLE	19	79.55%	
Type of neck dissection			
Supraomohyoid ND	23	91.30%	
RND	12	83.33%	0.123
MRND	40	70.00%	
Grade			
G1	11	63.64%	0.242
G 2,3	72	80.50%	
LN status			
Positive LN	49	89.80%	
Negative LN	26	57.69%	0.0017
Adjuvant therapy			
Had adjuvant therapy	49	89.80%	
Hadn't adjuvant therapy	39	66.67%	0.0086
Neck treatment			
Wait and see	13	84.62%	
Neck dissection	75	78.67%	0.616

cm with a median of 2.5 cm.

Biopsy was done for confirmation in 70.5% of patients (n=62/88) and assessment of the neck status by either U/S neck in 64% (n=56/88) of patients) or CT head and neck was done in 36% (n=32/88) of patients.

Most lesions had been dealt with by surgery and not radiotherapy, either by WLE in 22% (n=19/88) or hemiglossectomy in 78% (n=69/88); hemiglossectomy was the main treatment modality. The treatment of the neck was either by neck dissection in 85.2% (n=73) or "wait and see" policy in 14.8% (n=15). The most common type of neck dissection used in this study was MRND in 53.3% (n=40), followed by SOHND in 30.7% (n=23),

then RND in 16% (n=12).

As regards pathology of the primary tongue lesion, we found that SCC formed about 95% of cases while other types like adenocarcinoma, cylindroma, adenoidcystic carcinoma and malignant melanoma formed 5%.

In this study, most cases were SCC with grade 2 as the most common grade (75%) followed by grade 1 (12.5%) then grade 3 (6.8%), verrucous subtype was only found in one case.

Lymph node (LN) dissection was carried out in 75 cases out of the 88 ones (85.2%), the number of the harvested LN ranged from one to 38 with a median of 17.

The cases that had positively harvested LN were 26 cases (34.7%), and cases that had negatively harvested ones were 49 (65.3%).

Number of positively harvested LN ranged between 1 to 16 with a median of 5, while negatively harvested ones ranged between 2 to 38 with a median of 15.

As regards adjuvant therapy that was mainly in the form of radiotherapy, 39 cases (44.3%) had postoperative radiotherapy.

As regards postoperative recurrence, in our study we found that local recurrence occurred in 7 cases out of the 88 cases (7.9%). Out of the 69 cases treated by hemiglossectomy there were 4 cases of local recurrence (5.8%) while the other group treated by WLE (19 cases) there were 3 cases of recurrence (15.8%).

As regards nodal recurrence, out of the 88 cases there was recurrence in 18 cases (20.4%). Among who adopted wait and see policy (13 cases) 2 cases had nodal recurrence (15.4%), those who had ND (75 cases) recurrence occurred in 16 cases (21.3%); nodal recurrence was lowest in SOHND that seemed to be superior to other modalities (Table 1).

The time of recurrence considered from the date of surgery to the date of appearance of recurrence at either neck or tongue was in the range of 4 to 14 months with a median of 9 months.

As regards postoperative recurrence treatment in this

Table 3. Overall Survival in All Cases (n=144)

	Number	Overall survival rate	P-value
Whole group	144	49.89%	
Age			
<60 yrs	70	53.78%	0.148
≥60 yrs	74	49.19%	
Gender			
Male	75	49.93%	0.054
Female	69	59.03%	
Grade			
G1	11	66.86%	0.098
G 2	66	49.08%	
G 3&4	62	39.67%	
Stage			
Local	39	66.88%	
Regional	49	37.69%	0.003
Distant	56	8.98%	

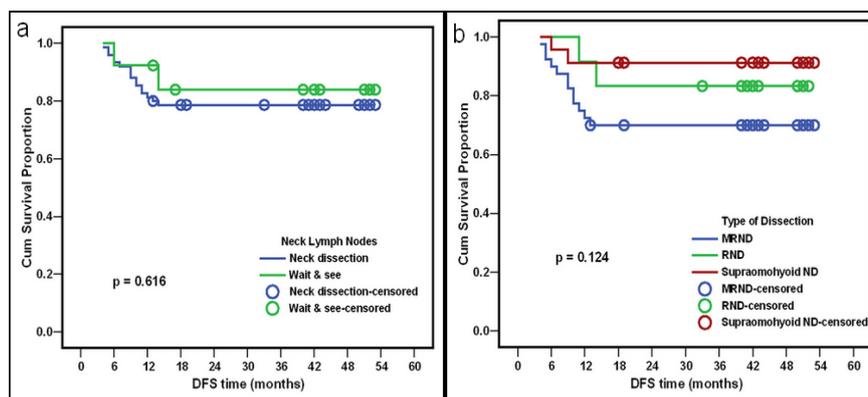


Figure 2. A. Comparison between the Two Different Modalities for Neck Treatment as Regards Cumulative Survival. Test Statistics for Equality of Survival Distributions for Neck LN ($P=0.616$). B. Represents the type of neck dissection in relation to cumulative survival. Test Statistics for Equality of Survival Distributions for Dissection type ($P=0.124$).

study, there were 2 modalities of treatment for managing postoperative recurrence (surgery and radiotherapy). Surgery was adopted in 66.7% ($n=12$) of patients, while radiotherapy was given to 33.3% ($n=6$) of patients.

In our study disease free survival (DFS) was estimated from the end of surgery to the date of appearance of 1st Recurrence (in cases who suffered of recurrence) or last follow up and during which the patient was completely free (in non-recurrent cases). The disease free survival period ranged between 4 and 53 months with a median of 42 months (The patient had a follow up range between 13 to 54 months with a median of about 43 months).

Analysis of the association between DFS and different factors implicated in this study at 54 months of follow up revealed that there was statistical significance association between DFS and 2 factors (adoption of adjuvant therapy and the status of dissected LN). It was clear that DFS was longer in patients who received adjuvant therapy (Table 2, Figure 1a) and in patients who had negative LN (Table 2, Figure 1b). It also raised the question of adoption of wait and see policy for treatment of N0 (negative neck) in early-stage tongue cancer as there was neither statistical significance in DFS between patients who had neck dissection and who had watchful waiting (Table 2, Figure 2a) nor between different types of neck dissection done in this study (Table 2, Figure 2b).

The overall survival rate has been estimated for all cases (early and late onset cases) ($n=144$) to be 49.89%. Studying the association between the overall survival rate and the studied variables revealed a significance association between the overall survival and the tumor stage ($P=0.003$); survival decreased from 66.88% in patients with local stage to 37.69% in regional stage then to 8.98% in distant stage (Table 3). Comparing the overall survival in between patients with clinically early stage tongue cancer ($n=88$) and those not clinically staged as early cases ($n=56$) revealed no significant difference (48.54% vs 49.89% respectively) ($P=0.258$).

Discussion

The study tried to highlight the importance of which strategy we have to follow in management of the neck in node negative patients (N0), in patients with early-stage

tongue cancer.

As regards early-stage cases at our NCI there were about 144 cases of tongue cancer during last 6 years but only 88 (61%) were staged as stage I, II. The neck was staged clinically and radiologically as N0 but about 34% of them harbor metastasis from primary tongue lesion by pathological examination of dissected LN. U/S is ideal for examining superficial structures in the neck, but examination of large necks and deep structures is more difficult making it an inappropriate technique for local staging of many primary head and neck cancers. Ultrasound is extremely useful in differentiating solid from cystic mass lesions, and can detect calcification. Evaluation of the internal structure and the margins of neck nodes will facilitate differentiation between benign and malignant nodes (Ferlito et al., 2001).

The pattern of local spread of oral cavity tumors is mainly along muscle fibers, which may be associated with displacement, infiltration or obliteration of fatty facial planes and interfaces, with later involvement of neurovascular bundles and periosteal surfaces as the tumor enlarges. Subsequently a soft tissue mass may be detectable as it enlarges by CT (Creager et al., 2001). In our study we found that about 64% of cases had US neck done and the other had CT head and neck for staging the disease that might reflect that early-stage tongue cancer cases could be staged clinically and we might depend on US neck beside clinical examination to accurately stage the neck. Biopsies of tongue lesions should endeavor the deep margin of the tumor in addition to mucosa at the periphery of the tumor. Deep biopsies may give an indication of tumor depth, but also multifactorial histological malignancy grading of the most dysplastic areas of the invasive form may help in assessing the risk of cervical metastasis (Woolgar, 1999). In our study 62% of patients had a biopsy of the tongue primary lesion before surgery and the other group of patients used the excision biopsy as both diagnostic and treatment tool for the primary lesion.

In our study the strategy for attacking the primary was mainly based on surgery and not radiotherapy nor the trend of photodynamic therapy. Both WLE and hemiglossectomy were used. In general, tongue cancer is usually treated surgically and additional adjuvant

therapy is carried out if patients have advanced cancers (Yokoyama et al., 2000).

Lesions of the oral tongue are more likely to be symptomatic than lesions of the base of the tongue. The majority of patients with cancer of the oral tongue present with stage I/II disease which contrasts significantly with cancers of the base of the tongue that are usually stage III/IV at presentation (Anderson et al., 1996). In our study we found that the most common presentation was ulcer at the tongue mainly on lateral sides followed by mass and nodule.

Oral SCC continues to affect more males than females with a ratio of 1.5-1 in the fifth or sixth decade of their lives. However, there is an increasing trend of oral cancer affecting young people under the age of 45 years (Jay et al., 2010). This was similar to what has been found in our study as the highest incidence was between the ages of 50-70 years (about 56%) and there was considerable incidence in the age between 30-50 years (about 22%). Males and females were equally affected in contrast to male predominance in most other studies.

The dominant risk factors are tobacco and alcohol abuse, which are strongly synergistic. Alcohol and tobacco account for 75% of the disease burden of oral malignancies in Europe, the Americas and Japan (Oakley et al., 2004). This study revealed association between smoking and development of tongue cancer as 53% were smokers but it didn't seem to affect DFS when comparing smokers and non-smokers.

Pathological examination of the primary tongue lesion revealed that about 95.5% of our cases were SCC confirming that SCC is the most prevalent type of malignancy in the tongue (Roodenburg et al., 2006).

About 35% of cases that had neck dissection showed positive nodes (occult metastasis), this was similar to others (Hindle et al., 2000). The lymph nodes at highest risk of occult metastases from oral cavity cancers are those at levels I, II, and III. The metastatic rates to these sites are 58% (level I), 51% (level II), 26% (level III), 9% (level IV), and 2% (level V) (Poddar et al., 1990).

There is no debate as regards the suggestion that node-positive patients with SCC of the oral tongue should undergo therapeutic neck dissection. However, what remains controversial is whether END should be performed for the clinically node-negative patients. Because of the high incidence of occult nodal metastasis in these patients, many authors have proposed prophylactic neck dissection of N0 cases. However, the cosmetic and functional defects associated with radical neck dissection are sometimes very severe, markedly hampering the activities of daily living of these patients. There have also been some negative reports about prophylactic neck dissection (Eckardt et al., 2002).

Currently the treatment dilemma that most head and neck oncology surgeons face is the treatment of the N0 neck in oral SCC. Three treatment options are available; observation with therapeutic neck dissection once regional metastases becomes apparent, END or ENI (Jalisi, 2005).

There is great controversy regarding the optimal therapy for clinically negative necks. The proponents of observation cite the morbidity of END as a reason to

observe. Another argument for close observation is that with close follow-up, any cervical metastasis can be detected early and then treated with adequate therapy. Moreover the occult metastatic rate to the neck from oral cavity cancer is 34%. Hence, it is argued that nearly 2/3 of patients would be exposed to the morbidity of a neck dissection unnecessarily (Poddar et al., 1990).

Study comparing glossectomy and neck observation versus glossectomy and neck dissection for T1 and T2 SCC of the oral tongue concluded that survival in the observation group was 33%, compared with 55% in the neck dissection group, and that locoregional control increased from 50% to 91% when neck dissection was performed (Shah and Lydiatt, 1995). Cassisi (1980) showed that ENI reduced the neck failure rate in patients with controlled primary tumors and N0 necks from 18% to 1.9%. Another study reported that END provided a 95% control rate for neck recurrences compared with 38% without ENI in T1 N0 SCC of the oral tongue (Spaulding et al., 1991).

In the current study there were about 75 cases out of 88 ones who had neck dissection and the remaining cases had a watchful waiting policy as treatment for N0 neck; the comparison between the 2 strategies in treatment as regards DFS showed that there was no statistical significance with DFS of 78.67% in patients who had neck dissection and 84.62% in patients who had watchful waiting. The recurrence in patients who had neck dissection was 21.2% and in patients who had a watchful waiting was 15.4% with total of 18 cases who had recurrence out of 88 (20.5%). This might be explained by either that follow up period wasn't long enough or that watchful waiting was a trustable strategy.

There has been a debate about the relative efficacy of SOHND and that of a classic RND. Several studies have shown that there is no statistically significant difference in locoregional recurrence between a selective neck dissection and a RND (Myers et al., 1997). McGill (1997) noted a skip metastasis rate of 15% to level IV in SCC of the oral tongue and advocated that dissection of level IV should be included in a selective neck dissection. It has been demonstrated that level IV need to be dissected only if there are suspicious nodes in level II or III.

There is voluminous literature supporting the use of selective neck dissection for surgical treatment of N0 necks in oral cavity carcinoma. This procedure has relatively low morbidity when compared with the classic RND. In our study, there was use of RND in 16% of patients, MRND in 53% of patients and SOHND in about 30% of cases. It was clear that node +ve ND results bad impact on survival that was statistically significant. Unfortunately during revision of pathological reports there was no specification about which level was involved except in few cases so identification of the level with high frequency of involvement couldn't be accomplished. But there was no significant association between the type of neck dissection and DFS.

The use of postoperative radiation therapy (PORT) following neck dissection is advised in the presence of multiple metastatic lymph nodes and any node with

extracapsular spread (ECS). The use of PORT for limited nodal disease is more controversial. The variability in the proposed indications for PORT raises the following question: should PORT be performed for patients with any histologically positive node or only for patients with more than three nodes (Martin et al., 2008). There is study that showed that among the patients with ECS, the survival rate was significantly lower in the PORT group than in the non-PORT group in patients with a fewer number of metastatic lymph nodes, whereas there was no significant difference in the survival between the PORT group and non-PORT group in patients with more than three metastatic lymph nodes, suggesting that PORT might be effective for patients with a larger number of metastatic lymph nodes (Wang et al., 2010).

In comparison with our study, there was about 44.3% who had PORT. The DFS was statistically significant between the two groups ($P < 0.001$). DFS for patients who had PORT was 89.8% while those who hadn't was 66.67%. It was clear that PORT was an important factor to minimize recurrence at both primary site and neck.

As regards recurrence whether local at primary site or at the neck, out of the 88 cases there was 7 cases of recurrence at the tongue primary site (92%) and 18 cases had nodal recurrence (20.4%) on follow up. In comparison with other study with a median follow-up of 66 months, the 5-year rates of local recurrence-free survival, regional recurrence-free survival, and disease-specific survival were 89%, 79.9%, and 85.6%, respectively. Regional recurrence was ipsilateral in 61% of patients and contralateral in 39% of patients. Patients who developed recurrence in the neck had a significantly poorer disease-specific survival compared with those who did not (33% vs 97%) (O'Sullivan et al., 2013). These results were comparable to our study. Another study also concluded that END significantly reduced mortality by lymph nodal metastasis and increased the 5-year free survival especially in patients with stage T2 oral SCC and suggested END as a preferred treatment strategy for tongue carcinoma in stage T2 (Guo et al., 2014).

Finally, the current study showed that MRND was the ideal as regards node yield for examination (not SOHND like other studies). NO necks have to be dealt with although both watchful waiting and ND results as regards DFS were equal but follow up in Egypt isn't regular to make it reliable option.

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