Role of Chromoendoscopy in Screening High Risk Population for Dysplasia in Esophagus

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ABSTRACT

Background and Objectives: Screening of subjects at high risk for development of esophageal cancer (EC) at an early stage is vital. In the present study, we aimed to determine that Lugol’s chromoendoscopy (LCE) can detect dysplasia and malignancy at an early stage and result in a better outcome as subjects can be offered curative treatment modalities.

Methods: Two hundred and fifty five subjects (240 men), mean age of 51.65 [10.65] years, at high risk for esophageal carcinoma (chronic tobacco chewing >10 gms/day for at least 10 years, smoking cigarettes/beedies >10/day for minimum 10 years and/or alcohol abuse >150 ml/day for minimum 10 years; and patients with head and neck cancers, tylosis or achalasia cardia were prospectively evaluated. At endoscopy, LCE with 4 quadrant biopsy at 5-cm interval cephalad to Z line was done. If an unstained area of >0.5 cm was noted an additional targeted biopsy was obtained. Dysplasia noted on histopathology was followed up with repeat LCE and biopsy at 3 and 6 months.

Results: LCE revealed unstained areas in 85 subjects. Squamous dysplasia was detected in 105/255 (41.1%) cases with mild dysplasia in 62/255(24.31), moderate in 36/255(14.11%), severe in 7/255(2.74%). Most of these lesions were associated with esophagitis. On follow up, among moderate-severe dysplasia patients, 50% had persistent moderate-severe dysplasia. Amongst patients having dysplasia 38 were alcoholics, 20 and 24 were smokers and tobacco chewers respectively.

Conclusion: There is a higher frequency of multiple risk factors for esophageal cancer in Indian men. LCE is an easy and inexpensive method. It improves the detection of dysplasia and should be added to conventional upper GI white light endoscopy in patients at risk for EC. (J Dis Endosc 2012;3(1):1-8)

Key Words: Lugol’s chromoendoscopy (LCE) – Endoscopy – Dysplasia – Biopsy - Esophageal cancer.

Introduction

Esophageal cancer is amongst the first five common malignancies in India. The incidence of EC in India varies from 40/100,000 population in Kashmir to 8-12/100,000 population in the rest of the country [1]. Esophageal cancer carries a poor prognosis since more than 90% of patients are at an advanced stage when they are first diagnosed. Most patients die within a year and the 5-year survival is less than 10%. The prognosis of EC closely correlates with the stage of the disease at the time of diagnosis [2].

Early diagnosis offers a chance of curative treatment. However, in its early stage patients are usually asymptomatic or may have trivial symptoms which do not bring them to the attention of a physician. Screening of subjects at high risk for development of EC by performing Lugol’s chromoendoscopy (LCE) can detect this malignancy at an early stage. LCE is an easy and probably cost-effective screening modality for detecting precancerous and early lesions of EC. Tobacco chewing, chronic alcoholism and smoking have been identified as important risk factors (relative risk of 2.0 – 3.0).
5.0) for EC [1,3,4]. Patients with head and neck malignancies with corrosive or sclerosant induced esophageal damage, achalasia cardia and tylosis have also been found to have a higher risk of EC[5-7]. Surveillance programs done in high incidence countries like China have shown that the prognosis improves with early detection of the disease. Despite a moderately high incidence of EC, no mass screening program has so far been conducted in India. So far no published data on endoscopic surveillance to detect this disease at an early stage has been reported from India. This study was done to evaluate the role of chromoendoscopy in screening for early esophageal malignancy (dysplasia and carcinoma in situ) in Indian patients at increased risk of EC.

Materials and Methods
This prospective study evaluated individuals at high risk for the development of EC at a tertiary referral center in Mumbai. Two hundred and sixty six patients were screened and eleven were excluded because of esophageal varices (n=5) and inadequate biopsy material (n=6). Finally 255 (240 men and 15 women) subjects with mean age of 51.65 (10.65) years were enrolled for the study. Patients having single or combination of following risk factors were evaluated: tobacco chewing (≥ 10 gm/day for more than 10 years), smoking beedies or cigarettes (> 10/day for a minimum of 10 years), alcohol abuse (> 150 ml/day for a minimum of 10 years), patients with head and neck cancers, tylosis and achalasia cardia. Patients with esophageal varices, bleeding diathesis, thyroid disease and severe cardiorespiratory disease were excluded. After initial evaluation which included presence or absence of esophageal symptoms and a complete clinical examination, all subjects underwent an upper gastrointestinal endoscopy with chromoendoscopy. Esophagitis was graded using the Hetzel classification [8]. Biopsies were obtained from the esophagus and histological assessment was performed for the presence of dysplasia or cancer. Patients with dysplasia were given acid suppressive therapy (lansoprazole 30 mg for 3 months) and followed up with a repeat chromoendoscopy and biopsies after three months. Patients with mild dysplasia and esophagitis were not considered for second LCE considering that they are inflammatory lesions. Patients with documented carcinoma-in-situ underwent curative surgical resection.

Chromoendoscopy
Patients underwent upper gastro-intestinal endoscopy after an overnight fast and application of lignocaine pharyngeal spray. Sedation (intravenous diazepam 5mg) was used only if the patient demanded. Endoscopy was done with the video-endoscope (EG-2901, Pentax, Japan). After initial endoscopic visualization of the upper gastro-intestinal tract, the esophagus was washed with 20-40 ml of sodium bicarbonate (7.5% w/v; Hindustan Pharmaceuticals) by using a spray catheter (Wilson cook) to remove the mucus. After 15 minutes, the esophagus was sprayed with 20 ml of 2% Lugol’s iodine solution (Research Lab, Mumbai) starting from the distal esophagus to the proximal using the spray catheter. After a contact time of one minute, the esophageal mucosal staining pattern was observed. The staining pattern was graded as follows: grade I – hyper staining; grade II – greenish brown; grade III - less intense; grade IV – unstained areas [9-11]. The size of this unstained area was measured using an open biopsy forceps. Biopsies were taken from any unstained area of more than 5 mm; if the esophageal mucosal staining pattern was uniform, four-quadrant biopsies were taken from the Z line (squamo-columnar junction) and at 5 and 10 cms above it. Before withdrawing the endoscope, excess iodine solution was aspirated. Biopsy material was processed using hematoxylin-eosin stain and Alcian blue at pH 2.5. The biopsy was read by a qualified pathologist who was unaware of the endoscopic findings. The criteria of dysplasia and carcinoma-in-situ were based on the method of Enterline and Thompson [12-15]. Ethical clearance was obtained from the research society of the hospital prior to the beginning of the study.

Statistics analysis
Data are as mean (SD). \( \chi^2 \) test for proportions was used to calculate the difference in frequency between groups.

Results
Among the 255 patients enrolled, the risk factors for EC included tobacco and alcohol abuse – 240 (94.1%) subjects, head and neck cancer patients – 11 (4.3%), achalasia cardia – 2 (0.8%) and tylosis –2 (0.8%). 186 (72.9%) subjects chewed tobacco, 195 (76.5%) subjects were smokers, 153 (60%) abused alcohol. Only one risk factor was seen in 46 subjects, while two and three risk factors each were seen in 115 and 86 subjects, respectively. Three risk factors were noted in 33/62 of mild, 20/33 moderate and 4/7 of severe where as only in 30 /150 of no dysplasia group. Whereas 2 risk factors were noted in 20/62, 17/33 and 2/7 in mild, moderate and severe dysplasia as against 32/150 of no dysplasia group were noted. The mean tobacco intake was 15.2 (6.1) g/day for a mean duration of 25.4 (11.7) years, with the corresponding values for alcohol

<table>
<thead>
<tr>
<th>Table I: Demographic profile of high risk subjects</th>
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<tbody>
<tr>
<td>Male</td>
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<tr>
<td>Female</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Tobacco</td>
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<tr>
<td>Alcohol</td>
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<tr>
<td>Head &amp; Neck cancer</td>
</tr>
</tbody>
</table>

| Tobacco | 106 (20.6%) | 62 (22.2%) | 33 (27.3%) | 6 (85.7%) |
| Alcohol | 103 (21.8%) | 51 (20%) | 28 (23.1%) | 6 (85.7%) |

intake were 207.5 (94.5) ml/day and 19.9 (9.9) years respectively. The mean quantity of smoking was 26.4 (11.1) cigarettes or beedies/day for a mean duration of 25.7 (10.5) years. Among head and neck cancer patients, nine smoked while seven and five consumed tobacco and alcohol, respectively. The patients with achalasia studied were eight and ten years respectively after diagnosis. The two patients with tylosis were aged 20 and 45 years, and were asymptomatic.

**Symptoms**

One hundred and sixty-six (65.1%) subjects were asymptomatic while heartburn and regurgitation were the commonest symptoms observed in 67 (26.3%) patients; followed by chest pain (n = 51), dysphagia (n = 12), odynophagia (n = 12) and hoarseness of voice in 2 patients.

**Endoscopy**

On upper digestive white light endoscopy following abnormalities were detected:

**Esophagus**

Esophagitis (grade I: 40, grade II: 22, grade III: 8) was seen in 70 (27.5%) subjects. Hiatus hernia, esophageal candidiasis and endoscopic Barrett’s esophagus were seen in 35, 5 and 4 subjects respectively. Esophageal nodule and ulcer were seen in 2 subjects each while inflammatory polyp, Schatzki’s Ring and mucosal tear were seen in 1 subject each.

**Stomach/Duodenum**

Carcinoma stomach was seen in 2 patients and 15 patients had evidence of antral gastritis, 2 had gastric ulcers and 4 had duodenal ulcers.

**1st Chromoendoscopy**

Chromoendoscopy revealed uniform staining in 170 subjects (67%) and unstained (Figure 1) areas in 85 subjects (33%), (upper esophagus - 14, middle esophagus – 46, lower esophagus – 25). The mean size of unstained areas was 1.8 (range 0.5-4 cm) (0.8; CI 1.6-1.9). Unstained areas with sharp, well defined margins were seen in 46/85(54.11%) subjects. Multiple unstained areas were seen in 14/85 (16.47%) subjects (< 0.5 cm – nine, 0.5-1.0 cm – five).

Chromoendoscopy was well tolerated with 9 subjects having chest pain and 3 had persistent hiccups during and following the procedure for less than 2 hours. None of them required any therapy. No allergic reactions were noted.

**Histology**

Changes of esophagitis were seen in 77 subjects (mild esophagitis- 40, moderate - 29 and severe - 8). Most lesions were found in lower third of esophagus. Dysplasia was found in 105 patients [mild dysplasia - 62 (Figure 2), moderate dysplasia - 36 (Figure 3) and severe dysplasia -7 (Figure 4). For analysis purpose the single case of carcinoma in situ is clubbed with severe dysplasia. Eighteen (17.1%), 62 (59.1%) and 25 (23.8%) dysplastic lesions were located in upper, middle and lower third of esophagus, respectively. Unstained areas were present in 35/62 (56.45%) cases with mild dysplasia, 19/36 (52.77%) with moderate and in all the 6 with severe dysplasia. Dysplasia was from uniformly stained area in 45 patients (mild dysplasia - 27, moderate – 17, severe dysplasia - 1). Mean size of unstained area was 1.8 (4) cm in mild dysplasia, 2.2 (2) cm in moderate dysplasia and 2.4 (3) cm in severe dysplasia (p=NS (Table 2).
Specialized columnar epithelium sites (n = 10) had uniform and normal staining. In one patient with an unstained area in the lower third of the esophagus, the histology showed carcinoma in situ which was treated with esophageal resection (Figure 5).

Patients with dysplasia
There was no difference in the age and sex ratio among patients with or without dysplasia. Single factor alcohol abuse was seen in 38 patients with dysplasia, while 20 and 24 patients with dysplasia smoked and chewed tobacco, respectively. Alcohol abuse, tobacco chewing or smoking were not individually, but in combination were associated with dysplasia (p = 0.039).

Follow Up
Patients with dysplasia were treated with oral lansoprazole 30 mg/day for 3 months. Thirty of 43 patients who had moderate to severe grade dysplasia reported for second LCE. Mild heartburn and chest pain were noted in 2 of severe and 5 of moderate dysplasia bearing patients. Second LCE showed that 20 of these 30 patients now had unstained area. On repeat histology 5 subjects had no dysplasia, 10 had mild dysplasia, 9 had moderate and 6 had severe dysplasia; mild esophagitis (8/10) was still present in patients who had moderate and severe grades of dysplasia (Figure 6).

Discussion
Presence of squamous dysplasia was studied using

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### Table 2: Clinical and endoscopic features

<table>
<thead>
<tr>
<th></th>
<th>No dysplasia (n=150)</th>
<th>Mild dysplasia (n=62)</th>
<th>Moderate dysplasia (n=36)</th>
<th>Severe dysplasia (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>37</td>
<td>18</td>
<td>5</td>
<td>7</td>
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<tr>
<td>Regurgitation</td>
<td>13</td>
<td>10</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Odynophagia</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>12</td>
<td>5</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Chest pain</td>
<td>29</td>
<td>12</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Hiatus hernia</td>
<td>19</td>
<td>9</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>28</td>
<td>26</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Barrett’s esophagus</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other lesions</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Gastric lesions</td>
<td>33</td>
<td>20</td>
<td>2</td>
<td>3</td>
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### Table 3: Chromoendoscopic and histological features

<table>
<thead>
<tr>
<th></th>
<th>No dysplasia (n=150)</th>
<th>Mild dysplasia (n=62)</th>
<th>Moderate dysplasia (n=36)</th>
<th>Severe dysplasia (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstained areas (n)</td>
<td>25</td>
<td>35</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>Margins Sharp</td>
<td>10</td>
<td>23</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Irregular</td>
<td>15</td>
<td>12</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Histological esophagitis (n)</td>
<td>2</td>
<td>32</td>
<td>36</td>
<td>7</td>
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<tr>
<td>Grade 1</td>
<td>0</td>
<td>30</td>
<td>11</td>
<td>2</td>
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<tr>
<td>Grade 2</td>
<td>2</td>
<td>2</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Specialized columnar epithelium</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Follow up for third chromoendoscopy was done in 10 patients who had moderate to severe dysplasia at second LCE. On third chromoendoscopy, 8 of 10 patients had unstained areas; all 8 had sharp margins. Histology revealed no dysplasia and, mild dysplasia in 1 each, moderate in 5 and severe dysplasia in 3.
Chromoendoscopy for esophageal dysplasia

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Chromoendoscopy and histology in 255 subjects. The mean age increased with increasing grades of dysplasia, but fell short of significance. The study group consisted predominantly of men, possibly due to the higher frequency of risk factors in Indian males because of socio-cultural reasons. The extent of tobacco and alcohol abuse in the present study is much higher than described in previous reports. Similar to other studies[1,3,4] there was a statistically significant association of the presence of all the three factors (in 84 subjects) with dysplasia. Kaneko et al studied the effect of alcohol and/or smoking in Chiba, Japan. Approximately 70% of high grade dysplasia (HGD) individuals, but only 13% of low grade dysplasia (LGD) individuals, both smoked and consumed alcohol [3].

In the present study, 26% of subjects had esophageal symptoms. There was, however, no difference in the frequency of symptoms between patients with or without dysplasia. Previous studies have shown esophageal symptoms in 8.2%–71.5% of patients with early esophageal cancer (EEC). Sugimachi et al [16] have reported no symptoms related to esophageal lesion in 63.7% of patients with EEC.

Incidence of squamous dysplasia in the present study was 16.8%, considering the facts that mild dysplasia is considered as a benign lesion as reported by Meyer et al [17]. Previous studies[17-21] have reported a frequency of squamous dysplasia ranging from 1% to 20%. Higher incidence of squamous dysplasia in our study may be due to the higher extent of alcohol and tobacco abuse.

We did not find any specific morphological mucosal changes on routine endoscopy to suggest dysplasia, as highlighted by Crespi et al [18]. Alternatively, it may be due to insufficient knowledge of endoscopic appearances of esophageal dysplastic lesions. Macroscopic examination using Lugol failed to identify minute foci of early carcinoma in achalasia patients in a Brazilian study by Yamamura [22].

Chromoendoscopy revealed unstained areas in 85 patients. Fagunde’s et al found unstained areas in 23 of 190 male patients at risk of squamous cell cancer of the esophagus undergoing Lugol’s chromoendoscopy. These areas were not picked up by routine endoscopy and six of these were dysplastic on biopsy [4]. In their series LCE showed a sensitivity of 46%, a specificity of 90%, a positive predictive value of 26% and a negative predictive value of 96% when unstained areas were compared to stained ones. Muto et al showed amongst 389 of their head and neck cancer patients 55% of the patients with many irregular-shaped multifocal Lugol-voiding lesions had synchronous secondary primary esophageal squamous cell carcinomas [6]. A French study consisting of 62 centers revealed, of the 35 carcinomas detected in the 1095 patients, seven (20%) were early lesions, and 20% were only detected after Lugol staining (p=0.02) [23].

Chromoendoscopy using Lugol’s solution is not without hazards. Local irritation of the esophageal mucosa may cause retrosternal pain. General allergic reactions include laryngospasm, bronchospasm, and even cardiac arrest. The concentration of the solution used in studies ranges from 0.5% to 5%, and higher concentrations (3–5%) may be associated with a higher risk of complications. A Japanese study reported that washing the mucosa with sodium thiosulphate may neutralise the iodine solution and reduce retrosternal discomfort. Only two cases of gastric mucosal erosions have been reported after the application of iodine. In this study oropharyngeal and chest burning was noticed when 3% Lugol’s iodine was used. Hiccups were noted in three patients; all side effects subsided spontaneously. In contrast few authors have suggested sodium thiosulfate spray for relief of above symptoms [9].

In our study, unstained areas correlated fairly well with carcinoma in situ, severe dysplasia (6/7, 85.7%) and moderate dysplasia (19/36, 52.8%). However, there was a poor correlation of unstained areas with mild dysplasia, with close to 50% of mild dysplasias having uniform staining. Also, most of the moderate (3/36) & severe dysplastic lesions (7/7) were associated with esophagitis.

The size of the unstained areas corresponding to dysplasia varied from 0.5 to 4 cm in the present study. This is similar to previous studies by Misumi et al [24] and Haruma et al [25]. Ban et al found that most of the unstained lesions turned out to be inflammatory. They considered an unstained lesion as significant when it was >5 mm [19].

Most of the dysplastic foci were present in the middle and lower third of the esophagus. Sugimachi et al [26] have also shown that the majority of the unstained areas were located in middle third, followed by the lower and upper third of the esophagus. This matches the distribution of EEC study of Bonavina et al [27].

Shimizu showed multicentric low grade dysplasia component in 43% of patients who underwent resection of esophagus for early invasive carcinoma [28].

Mori et al [13,15] have shown that the transition from adjacent normal squamous epithelium to the lesion was sharp on iodine staining in invasive carcinoma, carcinoma in situ or severe dysplasia. As against this transition was gradual showing a dull and irregular margin in moderate to mild dysplasia, atrophy and esophagitis. In this study, one carcinoma in situ, 6 high grade dysplasia lesions and 12/36 moderate dysplasia lesions had unstained areas with sharp margins. They reported that most of the grade IV (unstained) lesions were invasive carcinomas, carcinoma-in-situ, and intraepithelial extension of carcinomas which were not obvious on routine endoscopy. On the other hand moderate to mild dysplasia or atrophy showed grade III staining. Grade IV lesions showed well demarcated sharp margins, whereas grade III lesions showed ill demarcated dull margins. Histological evaluation disclosed that the staining intensity reflected the change in the glycogen containing cell layer, in the lesion. The sharpness of the margin reflected the abrupt
or gradual change from the glycogen containing to non-containing areas [18].

Histology of the 85 unstained areas revealed carcinoma in situ in one and various grades of dysplasia in 60 subjects. This contrasts with a similar study by Meyer et al [17]. They reported 125 unstained areas, of which 108 were benign lesions (89 esophageal with dysplasia, 9 patches of mucosa with less glycogen, 5 gastric heterotopia, 4 granular cell tumour and 1 low grade dysplasia). Only 17 unstained areas revealed cancerous lesions including 3 high grade dysplasia, 2 intrapithelial carcinoma and 12 invasive carcinoma. In a similar study, Ban et al have reported 79 unstained areas and majority of them (64.6%) turned out to be inflammatory. Squamous carcinoma and dysplasia were present in only 16.5% and 1.3%, respectively. Dawsey et al comparing esophageal lesions with and without iodine stain, demonstrated that the diagnostic lesions in 17 of 31 patients with moderate dysplasia (55%), 8 of 35 patients with severe dysplasia (23%), and none of the 19 patients with invasive carcinoma (0%) were identified only after staining with iodine [29].

In our series many lesions turned out to be esophagitis. Yoshikawa et al showed that LCE could be used to enhance the diagnosis of endoscopy negative reflux disease. Histologically, Lugol unstained mucosa showed a significant thicker basal cell layer and longer papillae [30].

LCE is operator dependent (ie dependent on the skill and experience of the endoscopist). Studies reporting the accuracy of LCE for dysplasia and Barrett’s are mixed, mostly due to the differences in the technique and material used. Esophageal staining is often uneven and patchy, further it may be altered by spray technique. Longer procedure time is another limitation. High false positive rates are reported in the setting of inflammation and gastric type of Barrett’s epithelium. To overcome these limitations, competing magnification and resolution endoscopic technological modifications with or without tissue stains are taking position.

**Narrow Band Imaging (NBI) vs LCE**

NBI is an optical filter technology that radically improves the visibility of capillaries, veins and other subtle tissue structures, by optimising the absorbance and scattering characteristics of light. NBI uses two discrete bands of light: One blue at 415nm and one green at 540nm. Narrow band light displays superficial capillary networks, while green light displays subepithelial vessels and when combined offer an extremely high contrast image of the tissue surface.

Chiu et al at DDW 2007 showed narrow band imaging had equal sensitivity with LCE at 92.3 but higher specificity (91.7 vs 72.2%) but took more procedure time (7.5 vs 5.7 minutes; p 0.001) [31]. Both Lee et al 32 and Ponchon et al [33] found perfect concordance in the detection rate of 100% for NBI and Lugol chromoendoscopy but noted that 75% of specificity of NBI was low. Yi-Chia Lee et al observed low specificity (40%-95%) and PPV (13%-52%) in case of LCE. They felt that NBI could overcome this and improve the accuracy of targeted biopsy. Inflammation and haemorrhage may obscure observation with NBI. Both detection modalities may offer complimentary information that can minimize the risk of false negative results.

**Magnification endoscopy (ME)**

ME is used by some in detecting dysplasia and early cancer in Barrett’s surveillance. It discriminates lesions 10 to 71 microns apart vs 125 to 165 microns apart by naked eye examination. Sharma et al studied 80 patients with columnar lined distal esophagus using indigocarmine dye and 115 magnification endoscopy. Ridged/villous mucus pattern compared to circular type had higher yield of intestinal metaplasia (97%). Magnification chromoendoscopy technique is hoped to identify high yield areas and eliminate the need for random biopsies [31].

Autofluorescence imaging (AFI) is another optic-based chromoendoscopic device designed to detect early lesions. AFI neoplastic areas, that usually involve a thickening of the mucosal layer and increased hemoglobin, emit weaker autofluorescence compared to non-neoplastic areas. In this technique, non-neoplastic areas appear green in color, whereas neoplastic areas are purple or magenta. Some studies have been conducted in the screening of early squamous esophageal lesions and showed that AFI had a higher sensitivity than white-light endoscopy to detect superficial lesions (79% vs 51%, respectively), however, its accuracy was worse than Lugol’s chromoendoscopy or NBI [34,35].

Optical coherence tomography (OCT) is an optical signal acquisition and processing method. It captures micrometer-resolution, three-dimensional images from within optical scattering media (e.g., biological tissue). Optical coherence tomography is an interferometric technique, typically employing near-infrared light. The use of relatively long wavelength light allows it to penetrate into the scattering medium. OCT uses backscattering of light to obtain cross-sectional images of tissue at different axial depths.

Confocal laser endomicroscopy (CLE) and Endocytoscopy (EC) are emerging endoscopic technologies that permit high-resolution assessment of gastrointestinal mucosal histology at a cellular and sub-cellular level. Endomicroscopy and endocytoscopy dramatically expand the imaging capabilities of flexible endoscopy by their ability to obtain “optical biopsies” of nearly any accessible endoluminal surface.

Confocal laser endomicroscopy (CLE) is based upon the principle of illuminating a tissue with a low-power laser and then detecting fluorescent light reflected from the tissue. The laser is focused at a specific depth and only light reflected back from that plane is refocused and able to pass through the
pinhole confocal aperture. As a result, scattered light from above and below the plane of interest is not detected, increasing spacial resolution. The area being examined is scanned in the horizontal and vertical planes and an image is reconstructed. In this manner, microscopic imaging of biological tissue bearing dysplasia or neoplasia in vivo is possible due to the high lateral resolution of confocal imaging.

Endocytoscopy (EC) is based on the principle of contact light microscopy. EC enables real-time visualization of the cellular structures of the superficial epithelial layer in a plane parallel to the mucosal surface. The technology uses a fixed-focus, high-power objective lens that projects highly magnified images from a minute sampling site (0.5-mm diameter) onto a charge-coupled device. EC instruments include probe-based and endoscope-based systems and are currently available only as prototype devices. EC achieved 81% sensitivity and 100% specificity in identifying neoplasia, based on the blinded evaluation of endocytoscopic images of macroscopically visible lesions in one study [36].

To summarise, Our results suggest that there is a higher frequency of multiple risk factors for esophageal cancer in Indian men. Symptomatology does not differentiate patients with or without dysplasia. No morphological mucosal changes could be identified on routine endoscopy to predict presence of dysplasia. Incidence of moderate to severe squamous dysplasia in the present study was 16.8%. LCE revealed unstained areas in 85 patients and it histologically correlated well with carcinoma in situ, moderate and severe dysplasia but poorly with mild dysplasia. Also, most of the lesions were associated with esophagitis. LCE revealed unstained areas with sharp margins in carcinoma in situ and all high grade dysplasias. LCE is an easy and inexpensive method available worldwide. It improves the detection of dysplasia and should be added to conventional upper GI endoscopy in patients at risk for EC. One of the limitations of our study was non availability of comparative data of magnification and high resolution endoscopy as they were not well established at the time of designing this study.

Acknowledgement

Endoscopy assistance extended by Dr. Satheesh G Kulkarni & Dr. Pankaj S Dhawan: Pathology assistance by Dr. Anjali Amarapurkar.

References


