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Bronchoscopic Curative Therapy

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The bronchoscopic therapy with curative intent was aimed mainly in the following bronchial diseases: carcinoma *in situ* and early-stage cancer, benign lesions and typical selected carcinoid tumours. The indications are made when the lesions are in the main airways, the margins perfectly and completely visible and the implantation area very small.

Early cancer

Early stage central lung cancer is a malignant tumour defined as: radiographically occult squamous cell carcinoma that is <2 cm in surface area, appears superficial endoscopically, has clearly visible margins and has no invasion beyond the bronchial cartilage assessed either by pathologic assessment or by available imaging including high-resolution computed tomography (HRCT) or endobronchial ultrasound (EBUS) bronchoscopy. Mediastinal lymphoadenopathy or distant metastasis are absent.

Early stage central type lung cancer can be detected by using 'White Light" bronchoschopy and Autofluorescence bronchoscopy. EBUS bronchoscopy is useful in confirming the thickness of the lesions, non invading the wall beyond the cartilage. Even though these cancers are small, in 70% of cases a lobectomy is required and in the remaining 30% either a bilobectomy or pneumonectomy [1] is required.

In addition 1-4% of these patients will have a synchronous lung cancer and the risk of acquiring a second lung cancer after surgery is 14% per year [2]. Disease-free survival after surgical resection is 70% after 5 years in the Stage IA of non-small cell lung cancer (NSCLC) and over 90% in case of Carcinoma in situ. "If bronchoscopic treatments of early-stage lung cancer can provide similar disease-free survival with less perioperative mortality, morbidity and cost, then they may be alternative front-line therapies. Other than resection, Photodynamic Therapy (PDT) may represent the best approach at this time" [3].

Other bronchoscopic options of therapy are Nd:YAG-Laser, Electrocauthery and Argon coagulator, Cryotherapy and Brachitherapy.

Photodynamic Therapy

PDT is based upon the specific photosensitisation of malignant tissue containing hematoporphyrin (Hp) or Hp derivative after exposure to a visible activating light in the red region of the spectrum (630 nm).

Photosensitisation produces a photochemical reaction, releasing singlet oxygen which causes tissue death and damage of the tumour microvascular system. PDT is an effective therapeutic modality for the bronchoscopic treatment of early stage lung cancer, through which complete remission may be achieved [4].

The majority of clinical experience using PDT in early lung cancer has been for treatment of patients who were deemed non surgical candidates and has been performed by Japanese Centers in the last two decades [5, 6]. There are few articles of European centers [7-9].

Mathur *and Coll* [10] reviewed 10 relevant articles obtained by MEDLINE: 191 early NSCLC lesions in 145 patients were treated by PDT. Complete Response (CR i.e. bronchoscopic and histological recovery of the lesion) was achieved in 86% of the lesions, recurrence was observed in 13% of the cases and a long term CR was achieved in 75%. Considering the sizes of the lesions, the early cancer <1.0 cm had CR in 95% of the treatment, but lesions ≥2 cm had a CR only in 46%. The success of the treatment was also dependent on the clear visibility of the distal margins of the cancerous lesions. In the cases in which the lesions were <1.0 cm and the margins were well visible CR was achieved in 98% of the cases *(Level of evidence: III).*

Moghissi K *and Coll* [11] reviewed 13 articles reporting the results of PDT in 523 patients affected by early stage endobronchial cancer or carcinoma in situ. The authors reported a long term CR in 70% of the treated cases and CR in 94% of the lesions <1.0 cm *(Level of evidence: III).* They confirmed the data in a recent review [12]. The reported complications are sunburn (2-28%), respiratory complications (0-18%) and non-fatal haemoptysis (0-7%).

Cortese *and Coll* [13] reported PDT in non surgical patients affected by early stage central

type lung cancer with CR rate of 84% after 1 treatment; a second treatment after recurrence in 39% of the patients and a long time CR rate of 66%. The same authors [14] purposed PDT in the management of early superficial squamous cell carcinoma as an alternative to surgical resection.

Recently Endo C *and Coll* [15] reported their retrospective experience of PDT in 48 patients affected by roentgenographically bronchogenic occult squamous carcinoma with length <1 cm and reported CR rate of 94% and the 5-years and 10 years overall survival rates of 81% and 71% *(Level of evidence: III).*

Electrocauthery

Electrocauthery and Argon Plasma Coagulation are less expensive forms of treatment for early central lung cancer. A small study of 15 cancers with size <1 cm in 13 patients showed CR in 80% of the treatment without any recurrence at 22 months of follow-up [16] *(Level of evidence: III).*

Brachitherapy

Two studies report the efficacy of Brachitherapy performed with I^{192} in a small group of patients.

In the first study the AA treated 19 pts and obtained CR in 83% of the cases at 3 months and in the 75% at 1 year [17]. In the other study 34 pts showed 85% of CR after 2 years [18] *(Level of evidence: III).*

Cryotherapy

One study reports the efficacy of the Crioterapy in a few number of pts: 35 pts with 41 cancers showed the 91% of CR at 3 months and CR of 63% in the follow-up [19] *(Level of evidence: III).*

Nd-YAG-Laser

In two studies Cavaliere *and coll* reported the efficacy of the bronchoscopic Therapy by using Nd YAG-Laser in case of Carcinoma in situ: 22 cases of carcinoma in situ with CR at the follow-up [20]. 38 cases of carcinoma in situ in 28 patients with follow-up of 22 months in 24/38 cases [21].

A review of Lam about the Nd-YAG Laser therapy of early superficial lesions reports a high risk due to the possibility of perforated lesions when the cancer is localised in the small bronchi [22] *(Level of evidence: IV).*

Recommendations

- **For the patients affected by Early Stage Central Type Lung Cancer not surgical candidates there is indication to PDT (Grade B).**
- **The patients affected by Early Stage Central Type Lung Cancer with superficial lesion less than 1 cm in the diameter could be treated with PDT even if surgical candidates (Grade B).**
- **For the patients affected by Early Stage Central Type Lung Cancer with superficial lesion less than 1 cm in the diameter not surgical candidates the endoscopic Electrocauthery, Brachitherapy and Cryotherapy are alternative Therapy to PDT (Grade B).**
- **For the patients affected by Early Stage Central Type Lung Cancer with superficial lesion less than 1 cm in the diameter the endoscopic Therapy with Nd YAG-Laser could be useful but involves perforation risks (Grade B).**
- **In the cases of carcinoma *in situ* of central bronchial airways there is Indication to Endoscopic Therapy (Grade B).**

Typical carcinoid tumours

Typical Carcinoid is a tumour characterised by a number of mytosis of less than 2/2 mm^2, the absence of coagulative necrosis and very rare presence of lymphnodal methastases. In the case of central, typically exclusively endoluminal carcinoid tumour with peduncolated basis, less than 1.5 cm^2 is possible to suppose an endoscopic treatment with curative intent. Only two authors reported their results with bronchoscopic treatments of central typical carcinoids of the bronchi.

Cavaliere *and Coll* [23] reported 47 of 188 carcinoid tumours with the endoscopic characteristics in which was indicated endoscopic Laser therapy: they treated 44 typical carcinoid tumour with curative intent and observed only 1 recurrence after thee years follow-up *(Level of evidence: IV).*

Van Boxem *and Coll* [24] reported the results of endoscopic Laser therapy in 19 central typical carcinoid tumours: the results were CR in 14/19 cases (73%) after a follow-up period of 29 months *(Level of evidence: III).*

Recommendation

- **The central, exclusively endoluminal, typical carcinoid tumours, with base in the bronchial wall less than 1.5 cm^2 or peduncolated could be treated by Nd YAG-Laser endoscopically with curative intent (Grade C).**

Benign tumours

We found only one review regarding 185 cases of benign tumours (4,7% of 3937 treated lesions) of the main airways treated with Bronchoscopy Laser

resection in the Laser Center of Marseille and in Respiratory Endoscopy in Brescia [25]. In this series 53 localized or extensive papillomas are included.

The best indications for laser resection are considered:

1) endoluminal tumours; 2) extent in main airways (trachea, mainstream bronchi, bronchus intermedius); 3) low probability of recurrence; 4) symptomatic patients or patients who may be expected to be so because the location and the extent of the lesion 5) recent collapse of lobe/lung.

The results of the laser resection were "very good" (i.e tumour was completely removed in 1 session of therapy) in 115/185 (62%) and "good" (the tumour was partially removed and required repeated sessions) in 70/185 (38%) *(Level of evidence: III).*

Recommendations

- **For benign intraluminal tumours with visible implantations in trachea, mainstream bronchi and bronchus intermedius could be indicated the Laser assisted bronchoscopy treatment. The Laser therapy could be extended to papillomatous endotracheobronchial lesions (Grade B).**

Summary of Recommendations

- **For patients affected by Early Stage Central Type Lung Cancer who are not surgical candidates there is indication to PDT (Grade B).**
- **The patients affected by Early Stage Central Type Lung Cancer with superficial lesion less than 1 cm in the diameter could be treated with PDT even if they are surgical candidates (Grade B).**
- **For the patients affected by Early Stage Central Type Lung Cancer with superficial lesion less than 1 cm in the diameter who are not surgical candidates the endoscopic Electrocauthery, Brachitherapy and Cryotherapy are alternative Therapy to PDT (Grade B).**
- **For the patients affected by Early Stage Central Type Lung Cancer with superficial lesion less than 1 cm in the diameter the endoscopic Therapy with Nd YAG-Laser could be useful but involves perforation risks (Grade B).**
- **In the cases of carcinoma *in situ* of central bronchial airways there is an indication towards Endoscopic Therapy (Grade B).**
- **The central, exclusively endoluminal, typical carcinoid tumours, with base in the bronchial wall less than 1.5 cm^2 or peduncolated could be treated by Nd YAG-Laser endoscopically with curative intent (Grade C).**
- **For benign intraluminal tumours with visible implantations in trachea, mainsteam bronchi and bronchus intermedius could be indicated the Laser assisted bronchoscopy treatment. The Laser therapy could be extended to papillomatous endotracheobronchial lesions (Grade B).**

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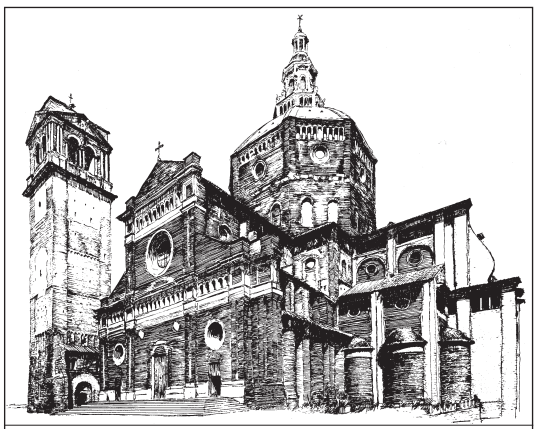

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