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Indications for Diagnostic Bronchoscopy in Adults

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Introduction

Diagnostic bronchoscopy is indicated in several clinical situations and pathological conditions.

Evidence-based guidelines concerning the indications for diagnostic bronchoscopy do not exist in the literature. The list of indications published in books and in the previous editions of Italian Pulmonology Associations Guidelines [1], are based on historical references reported before the advent and diffusion of some imaging techniques, especially thorax CT scan. Therefore, the indications and timing of bronchoscopy in many disorders should be redefined on the basis of CT scan findings.

Furthermore, there are several indications for which the need to perform a bronchoscopy is so obvious that controlled randomised studies to demonstrate its value can not be proposed.

On the contrary, there are conditions in which the role of bronchoscopy is not well defined and the risk and cost of the procedure may be not justified by the expected results.

Finally, there are situations in which the utility of bronchoscopy is unquestionable, but it should be defined the timing of its performance.

Methods

The indications for diagnostic bronchoscopy will be divided in two groups.

Group 1: indications for which there is no controlled randomised study, since the value of diagnostic bronchoscopy appears obvious and there is large consensus on its utility.

Group 2: indications for which the utility of diagnostic bronchoscopy is not clearly evident and/or there is no consensus about the timing of its performance.

For each indication of Group 2, the literature references published in English language from 1990, on the basis of Medline research, have been analysed.

Special indications (lung transplantation, paediatric bronchoscopy and bronchoscopy in intensive care unit) are not reported, since they will be discussed in other reports.

GROUP 1

Group 1 includes the following conditions:

1) Pulmonary lesions observed at CT scan (consolidation, atelectasis, masses, localised hyper-transparency), located in central areas (reachable with the flexible bronchoscope);
2) Staging of lung cancer (evaluation of the endobronchial extension of the tumour and/or transbronchial needle aspirations of enlarged lymph nodes; pre-operative evaluation; restaging after therapy);
3) Mediastinal lesions or masses (evaluation of compression of the airways; transbronchial needle aspiration for diagnosis)
4) Presence of atypical cells in the cytological examination of the sputum;
5) Clinical or CT scan suspicion of tracheal stenosis;
6) Clinical or CT suspicion of endobronchial foreign body;
7) Clinical suspicion of bronchopleural or tracheal/broncho-oesophageal fistula;
8) Thoracic trauma, when there is the suspect of airways obstruction (blood cloths, foreign bodies, secretions) or airways rupture (haemoptysis, mediastinal and/or subcutaneous emphysema);
9) Infiltrative lung diseases (to perform bronchoalveolar lavage and/or transbronchial lung biopsy, according to the indications provided by high resolution CT scan);
10) Suspicion of mucociliary dyskinesia syndrome (to perform mucosal biopsies for electronic microscopy study);
11) Evaluation of patients with tracheal cannula, before decannulation.

Most of these indications are supported by imaging-technique findings, particularly by thorax CT scan. Indications between n. 1 and n. 9 require the performance of CT scan.

Especially with the suspicion of neoplastic conditions or in the field of infiltrative diffuse lung

diseases, CT scan provides essential information for guiding bronchoscopic manoeuvers and therefore it should be performed prior to a bronchoscopy.

In a randomised study [2], 171 patients suspected of suffering from lung cancer underwent bronchoscopy with (group A) and without (group B) prior thorax CT scan. Bronchoscopy was diagnostic in 73% of group A patients and in 54% in group B. The percentage of patients that required further invasive investigation to obtain diagnosis was 8% in group A and 18% in group B.

This study demonstrates that CT scan performed before bronchoscopy increases the diagnostic yield of the endoscopic procedures and reduce the need for further invasive manoeuvres *(Level of evidence: Ib)*.

Even in the field of diffuse infiltrative lung diseases CT scans play a major role in providing a diagnostic definition of the process [3] and indicating the site and type of bioptic approach [4] *(Level of evidence: III).*

Recommendation

- **Bronchoscopy should be performed after thorax CT scan, especially when neoplastic disease is suspected (Grade A) or in the case of diffuse infiltrative lung disease (Grade B).**

GROUP 2

Group 2 includes the following conditions:

1) Chronic cough;
2) "Non-resolving" or "Slow-resolving pneumonia";
3) Dyspnoea of unknown origin;
4) Haemoptysis;
5) Pleural effusion of unknown origin;
6) Vocal cord or diaphragm paralysis;
7) Peripheral lung lesions and pulmonary nodules;
8) Staging of oesophageal cancer;
9) Staging of thyroid cancer.

1) Chronic cough

There are several studies that do not support the indication for routine bronchoscopy in patients with chronic cough (i.e. cough that lasts more then 3 weeks) and negative CT scan.

In a prospective study on 108 patients with chronic cough [5] the cause of the symptom was post-nasal drip in 41%, asthma in 24%, gastro-oesophageal reflux in 21%, chronic bronchitis in 5%, bronchiectasis in 4% and other causes in 5%.

Bronchoscopy allowed diagnosis just in 5 patients (4%) affected by tumour, sarcoidosis and bronchiectasis, but in all these cases a CT scan would have provided a diagnostic suspicion. The Authors conclude that bronchoscopy has a limited role in patients with chronic cough and a negative CT scan *(Level of evidence: III)*. In a retrospective study on 48 patients affected by chronic cough [6], bronchoscopy did not provide useful diagnostic or therapeutical information in any case *(Level of evidence: III).* In another retrospective study on 25 patients [7], bronchoscopy provided useful information in 7 (28%) (broncholitiasis in 2, osteochondroclastic tracheopaty in 2, bronchial tuberculosis, laryngeal dyskinesia and arytenoideus polyp in 1), but in four of these patients CT scan would be positive and in two a laryngoscopy could have provided the diagnosis.

In the ACCP Evidence-based Clinical Practice Guidelines on diagnosis and management of cough [8, 9], bronchoscopy is mentioned in the following situations: a) to confirm the suspicion of eosinophilic bronchitis, with bronchoalveolar lavage examination in alternative to induced sputum; b) to exclude a suppurative non-bronchiectasic disease of the airways; c) to identify non-common causes of cough (tracheobronchomalacia, osteochondroclastic tracheobronchopaty, tracheobronchomegalia, tracheobronchial amiloidosis, foreign bodies, broncholitiasis, tracheo-oesophageal fistula), after exclusion of all the common causes and after having performed a thorax CT scan *(Level of evidence: IV).*

Recommendations

- **Bronchoscopy is not routinely indicated in patients with chronic cough and negative CT scan (Grade B).**
- **Bronchoscopy may be indicated in patients with chronic cough, after exclusion of all the common causes and after a thorax CT scan, in the suspicion of eosinophilic bronchitis, suppurative non-bronchiectasis disease or uncommon pathologies of the airways (Grade C).**

2) Non-resolving or Slow-resolving pneumonia

Non-resolving or slow-resolving pneumonia are usually considered to be an indication for bronchoscopy.

In a retrospective study [10] on 35 patients treated for community acquired pneumonia (CAP) that did not show an improvement after one week, bronchoscopy provided a diagnosis in 12 cases (3 pneumocystis, 2 tuberculosis, 2 bronchoalveolar carcinoma, 2 adenocarcinoma, 1 citomegalovirus, 1 actinomicosis and 1 eosinophilic pneumonia). Diagnostic sensitivity of bronchoscopy was lower in older patients (>55 yrs), COPD smokers and immunocompromised patients with lobar or segmental infiltrates, while it was greater in younger patients, non smokers with multi lobar infiltrates. The Authors conclude that bronchoscopy is useful for diagnosis of non-resolving pneumonia, especially in immunocompetent young patients (<55 yrs) without comorbidities, in which the persistence of pneumonia makes alternative causes more likely *(Level of evidence: III)*. In three prospective

studies [11-13] on patients with CAP that did not show improvement after 72 hours from the beginning of antibiotic therapy, bronchoscopy provided useful information (identification of the infectious agent or alternative diagnosis) in the majority of cases *(Level of evidence: III).* In the study of Aranciba *et al*. [13], different bronchoscopic techniques of sampling were evaluated in 49 patients that did not show improvement after 72 hours of therapy. Protected specimen brush, bronchoalveolar lavage and transbronchial pulmonary biopsy demonstrated a capability to identify the agent responsible of the pneumonia respectively in 40, 42 and 57% of cases. The indication for bronchoscopy in patients affected by CAP that does not respond to therapy or in patients seriously ill is also recommended in review papers [14] and in several guide lines proposed by Scientific Societies [15-18]. The British Thoracic Society guidelines suggest to perform bronchoscopy even in patients with persistence of symptoms and/or imaging abnormalities after 6 weeks from the end of treatment *(Level of evidence: IV).*

Recommendation

- **Bronchoscopy is not indicated routinely in patients affected by CAP. Bronchoscopy is indicated in patients affected by CAP who do not improve after 72 hours from the beginning of therapy (Grade B), in seriously ill patients (Grade B) or if symptoms and/or imaging abnormalities persist after 6 weeks from the end of therapy (Grade C).**

3) Dyspnoea of unknown origin

A Medline revision using as search criteria "*Dyspnoea AND bronchoscopy*" provided several references that have been analysed. No conditions with non-indicative clinical-functional data and with negative CT scan have been identified, for which bronchoscopy may be diagnostic.

Stenosis of trachea and/or of major bronchi may be suspected on the basis of a CT scan that must be performed before bronchoscopy, except in cases where there is the clinical suspicion of tracheal stenosis that require bronchoscopy in an urgent setting.

The only condition that may determine dyspnoea and for which CT scan may be negative (if not performed in dynamic modality) is tracheobronchomalacia [19, 20] *(Level of evidence: IV).*

Recommendation

- **In cases of dyspnoea of unknown origin with CT scan negative, bronchoscopy is not indicated except in cases with clinical suspicious of tracheal stenosis or of tracheobronchomalacia (Grade C).**

4) Haemoptysis

While there is a general consensus on the indication for bronchoscopy in cases of haemoptysis, the timing (before or after CT scan? Early or delayed bronchoscopy?) and the modalities to perform the procedure (flexible or rigid bronchoscopy?) are still debated.

In a blind prospective study [21], 57 patients with non life-threatening haemoptysis were evaluated with CT scan and bronchoscopy. Radiologists did not know the result of bronchoscopy and bronchoscopists were not informed as a result of a CT scan. The CT scan was able to identify a lesion of airways and/or parenchymal causes of haemoptysis in 63% of cases, while bronchoscopy provided a diagnosis in 49% and defined the site of bleeding in 40%. Both the techniques, considered together, were able to obtain a diagnosis in 81% of cases. The Authors conclude that CT scan and bronchoscopy are complementary techniques and that CT scan should be performed before bronchoscopy in non-massive haemoptysis, since it optimises the bronchoscopic procedure *(Level of evidence: III)*. Others Authors agree on the use of a CT scan as the first line of investigation in stable patients with non-massive haemoptysis [22].

There is evidence that early bronchoscopy (performed during haemoptysis or within 48 hours after cessation of bleeding) is more effective than delayed bronchoscopy (more than 48 hours after cessation of bleeding) to identify the site of the bleeding; on the contrary early bronchoscopy does not allow a greater percentage of haemoptysis causes to be found or to modify the outcome [23, 24] *(Level of evidence: III).*

The management of massive haemoptysis (life-threatening condition) may be divided in three steps, and in every step bronchoscopy is indicated [25]. The first goal is to protect the airways and to stabilise the cardio-respiratory conditions. In this step the patient needs to be undergoing endotracheal intubation and bronchoscopy may be indicated to verify the correct position of the tube, to remove bleeding and clots and to assess the side of bleeding.

In the second phase bronchoscopy may be employed to diagnose the cause of bleeding. It is better to use a large calibre tube as it easily allows a flexible bronchoscope to be inserted through the tube itself [26] *(Level of evidence: IV)*. The third steps concerns the possible employment of a bronchoscopic therapeutical procedure.

85% of participants in a survey on the management of life-threatening haemoptysis, conducted among pulmonologists attending a Symposium on Respiratory Emergency during the ACCP Meeting in 1998 [27] agreed on the need for early intubation. 64% of the participants considered useful an early bronchoscopy, within 24 hours *(Level of evidence: IV).*

Some Authors [26] suggest that, in cases of massive haemoptysis, intubation should be performed with a rigid bronchoscope, that allows the patient ventilation, the airways toilette and also the

identification of the bleeding site and cause at the same time *(Level of evidence: IV).* However, it must be considered that rigid bronchoscopy is seldom available in a First Aid Unit or in an emergency setting.

Recommendations

- **Haemoptysis is an indication to the performance of bronchoscopy (Grade B).**
- **In massive haemoptysis (life-threatening) bronchoscopy should be performed as early as possible with rigid bronchoscopy or with a flexible bronchoscope introduced through a tracheal tube (Grade C).**
- **In non-massive haemoptysis, with a stable patient, bronchoscopy should be performed after CT scan (Grade B), possibly within 48 hours to better identify the site of bleeding (Grade C).**

5) Pleural effusion of unknown origin

Several retrospective and prospective studies underline the fact that bronchoscopy has a low diagnostic yield in pleural effusions, when there is no clinical or imaging evidence of bronchial or pulmonary involvement [28-33] *(Level of evidence: III).*

In a retrospective study on 245 patients affected by pleural effusion [28], bronchoscopy was diagnostic in 13, most of which with cough or imaging evidence of lung masses or consolidations. The Authors conclude that bronchoscopy has a limited role in the study of a pleural effusion, except for patients with clinical and radiological evidence of pulmonary involvement. Evaluating 115 patients with pleural effusion, Poe *et al.* [31] reported a diagnostic bronchoscopy in 6 patients out of 12 with haemoptysis, in 8 out of 12 with CT scan evidence of pulmonary mass or infiltrate and in 11 out of 25 patients with atelectasis. Bronchoscopy resulted diagnostic also in 7 patients out of 18 with massive effusion, while it was non-diagnostic in 97.9% of patients with a small or moderate effusion. The Authors conclude that bronchoscopy may be helpful in cases of pleural effusion if there is haemoptysis or imaging evidence of lung masses or infiltrates or in cases of massive effusion or if cytological evaluation of pleural fluid is positive for cancer. On the contrary, bronchoscopy should not be performed routinely in cases with small or moderate amount of fluid, without radiological evidence of pulmonary lesions *(Level of evidence: III).*

In a 2001 ERS/ATS Statement [32] is reported that, in cases of pleural effusion, bronchoscopy should not be performed routinely, but it is indicated when there is the suspicion of endobronchial lesion (haemoptysis, atelectasis, massive effusion without controlateral shift of the mediastinum, failure of lung re-expansion after therapeutical thoracentesis) *(Level of evidence: IV).* According to these literature evidences, the British Thoracic Society Guidelines for the investigation of a unilateral pleural effusion in adults [34], assess that bronchoscopy should not be performed routinely in patients affected by undiagnosed pleural effusion but it should be considered if haemoptysis is present or in cases suggestive for endobronchial lesion.

Recommendations

- **Bronchoscopy should not be performed routinely in cases of undiagnosed pleural effusion (Grade C).**

Bronchoscopy is indicated in cases of pleural effusion if:

- **There are clinical signs suggestive for endobronchial involvement (cough and/or haemoptysis) (Grade B).**
- **There is imaging evidence of parenchimal involvement (atelectasis, masses, infiltrates) (Grade B).**
- **Pleural effusion is massive, without contralateral shift of the mediastinal structures (Grade C).**
- **There is evidence of cancer cells in the cytologial evaluation of pleural fluid (Grade C).**
- **There is failure of lung re-expansion after therapeutical thoracentesis (Grade C).**

6) Vocal cord or diaphragm paralysis

The bibliographic references obtained by MedLine using as key words "vocal cord paralysis AND bronchoscopy" have been analysed. No pathological conditions have been found, in which bronchoscopy could be helpful without CT evidence of pulmonary or mediastinal lesions.

The same results have been obtained using the key words "*diaphragm paralysis AND bronchoscopy*".

Recommendation

- **Vocal cord or diaphragm paralysis, without CT scan evidence of lung or mediastinal lesions, are not indications to bronchoscopy (Grade C).**

7) Peripheral lung lesions and pulmonary nodules

Peripheral lung lesions are defined as the lesions that are located in the peripheral lung parenchima and originate in bronchi that are beyond the visible range of the flexible bronchoscope. Included in this group of lesions are the peripheral solitary nodules (isolated lesions with a diameter of less than 3 cm, not associated with at-

electasis or hilar-mediastinal lymph nodes enlargement).

The indication for bronchoscopy in patients with peripheral pulmonary nodules is still debated in today's literature.

In a retrospective paper on 91 patients affected by solitary pulmonary nodule, bronchoscopy did not eliminate the need for surgery and did not modify the surgical strategy [35] *(Level of evidence: III)*.

Purely on the basis of this paper, ACCP Guidelines on lung cancer [36] have recommended that bronchoscopy is not indicated in patients with a peripheral solitary nodule. This statement caused some criticism in the international scientific community [37]. It was observed that bronchoscopy may be useful before surgery because: 1) it allows eventual anatomical variants of the bronchial tree to be identified, the knowledge of which may be important in order to plan surgery; 2) it allows to identify synchronous tumours of central airways, that are not rare in cases of lung cancer; 3) transbronchial approach, even if not diagnostic, permits to identify the pulmonary segment in which the lesion is located *(Level of evidence: IV).*

Furthermore, in a retrospective study [38] (not mentioned in the ACCP Guidelines) on 64 patients with peripheral nodule or mass and no CT scan evidence of endobronchial lesions, bronchoscopy found central bronchial pathologies in 11 patients (17%), four of which with pulmonary nodule less than 3 cm. The Authors concluded that other studies are necessary before abandoning pre-operative bronchoscopy in patients with peripheral pulmonary nodule *(Level of evidence: III)*. Finally, it should be underlined that several patients with a solitary pulmonary nodule are not good candidate for surgery and in these cases a cyto-histological assessment is essential to define the therapeutic programme.

Transbronchial approach to peripheral pulmonary lesions should be performed utilising guidance systems, since bronchoalveolar lavage, that can be performed without guidance, has a lower sensitivity respect to forceps biopsy and transbronchial needle aspiration [39, 40] *(Level of evidence: III).* BAL provides a sensitivity ranging from 43 to 60%, but it should be utilised in cases suspected for bronchoalveolar carcinoma, lymphangitis carcinomatosis or in patients with coagulation disorders [40] *(Level of evidence: III).* Traditionally, fluoroscopic guidance has been used in most of the studies.

The sensitivity of transbronchial approach to peripheral lung lesions ranges from 45 to 75% [39-43]. The diagnostic yield is related to the size of the lesions and to the sampling instrument utilized. Among the different sampling instruments, transbronchial needle aspiration seems to provide a better sensitivity (60-67%) in comparison to forceps biopsy (46-52%) and to brushing (45-52%) [39-43] *(Level of evidence: III).* Sensitivity of transbronchial approach increases further if more than one sampling instrument is used [41-43] *(Level of evidence: III).*

In recent years, other guidance techniques, such as endobronchial ultrasounds or electromagnetic navigation system, have been proposed for the bronchoscopic approach to peripheral lung lesions. From the preliminary studies [44-47], it seems that these systems may provide a global diagnostic sensitivity comparable to that of fluoroscopic guidance, but that the diagnostic yield is better for small nodules less than 2 cm *(Level of evidence: III).*

Recommendations

- **Bronchoscopy is indicated for bioptic approach to peripheral lung lesions, when a cyto-histological assessment is required (Grade B).**
- **In patients with a peripheral pulmonary lesion, bronchoscopy should be performed with the availability of a system of guidance (fluoroscopy, electromagnetc navigation system, endobronchial ultrasound) (Grade B).**
- **Transbronchial needle aspiration should be used preferentially as sampling instrument (Grade B).**

8) Staging of oesophageal cancer

Two prospective studies [48, 49] were performed, respectively on 116 and on 166 patients, to evaluate the role of bronchoscopy in staging of oesophageal cancer located above the level of tracheal carina. Bronchoscopy was the only procedure able to exclude a surgical approach in 9,7-18,1% of patients. The positive predictive value of bronchoscopy is low when based just on the endoscopic appearance, especially in patients that underwent radiotherapy. Staging accuracy of 95.8 % was obtained with multiple samples of the mucosa, using brushing, bronchial lavage and biopsies. The accuracy of bronchoscopy to evaluate the airways invasion was higher than CT scan. The Authors conclude the bronchoscopy with multiple sampling should be used as last staging procedure, to evaluate for surgery patients with oesophageal cancer located above the level of tracheal carina *(Level of evidence: III).*

Recommendation

- **Bronchoscopy with multiple histological and cytological samples is indicated as staging procedure in patients affected by oesophageal cancer, potentially resectable, located above the level of tracheal carina (Grade B).**

9) Staging of thyroid cancer

In a prospective study on 37 patients affected by thyroid cancer with suspicion of laryngo-tra-

cheal invasion [50], the results of bronchoscopy (localized reddening and/or edema and/or erosion of the mucosa, teleangectasis) were compared with post-operative pathological findings.

12 patients that presented at bronchoscopy a localised reddening of the mucosa required a larger resection, because of a tracheal wall involvement. The Authors conclude that bronchoscopy is useful in the staging of thyroid cancer and surgeon should perform a larger resection in presence of localised reddening of tracheal mucosa at bronchoscopy *(Level of evidence: III).*

Recommendation

- **Bronchoscopy is indicated in the preoperative staging of thyroid cancer, when there is the suspicion of laryngotracheal invasion (Grade B).**

Summary of Recommendations

- **Bronchoscopy should be performed after thorax CT scan, especially in the suspicion of neoplastic disease (Grade A) or in case of diffuse infiltrative lung disease (Grade B).**
- **Bronchoscopy is not routinely indicated in patients with chronic cough and negative CT scan (Grade B).**
- **Bronchoscopy may be indicated in patients with chronic cough, after exclusion of all the common causes and after a thorax CT scan, in the suspicion of eosinophilic bronchitis, suppurative non-bronchiectasis disease or uncommon pathologies of the airways (Grade C).**
- **Bronchoscopy is not indicated routinely in patients affected by CAP.**
- **Bronchoscopy is indicated in patients affected by CAP that do not improve after 72 hours from the beginning of therapy (Grade B), in seriously ill patients (Grade B) or if symptoms and /or imaging abnormalities persist after 6 weeks from the end of therapy (Grade C).**
- **In cases of dyspnoea of unknown origin with CT scan negative, bronchoscopy is not indicated except in cases with clinical suspicious of tracheal stenosis or of tracheobronchomalacia (Grade C).**
- **Haemoptysis is an indication for bronchoscopy (Grade B).**
- **In massive haemoptysis (life-threatening) bronchoscopy should be performed as early as possible with rigid bronchoscopy or with a flexible bronchoscope introduced through a tracheal tube (Grade C).**
- **In non-massive haemoptysis, with a stable patient, bronchoscopy should be performed after CT scan (Grade B), possibly within 48 hours to better identify the site of bleeding (Grade C).**
- **Bronchoscopy should not be performed routinely in cases of undiagnosed pleural effusion (Grade C).**
- **Bronchoscopy is indicated in cases of pleural effusion if:**
  - **There are clinical signs suggestive for endobronchial involvement (cough and/or haemoptysis) (Grade B).**
  - **There is imaging evidence of parenchimal involvement (atelectasis, masses, infiltrates) (Grade B).**
  - **Pleural effusion is massive, without contralateral shift of the mediastinal structures (Grade C).**
  - **There is evidence of cancer cells in the cytologial evaluation of pleural fluid (Grade C).**
  - **There is failure of lung re-expansion after therapeutical thoracentesis (Level of recommendation: C).**
- **Vocal cord or diaphragm paralysis, without CT scan evidence of lung or mediastinal lesions, are not indications for bronchoscopy (Grade C).**
- **Bronchoscopy is indicated for bioptic approach to peripheral lung lesions, when a cyto-histological assessment is required (Grade B).**
- **In patients with a peripheral pulmonary lesion, a bronchoscopy should be performed with the availability of a system of guidance (fluoroscopy, electromagnetc navigation system, endobronchial ultrasound) (Grade B).**
- **Transbronchial needle aspiration should be used preferentially as sampling instrument in the bronchoscopic approach to peripheral pulmonary lesions (Grade B).**
- **Bronchoscopy with multiple histological and cytological samples is indicated as staging procedure in patients affected by oesophageal cancer, potentially resectable, located above the level of tracheal carina (Grade B).**
- **Bronchoscopy is indicated in the preoperative staging of thyroid cancer, when there is the suspicion of laryngotracheal invasion (Grade B).**

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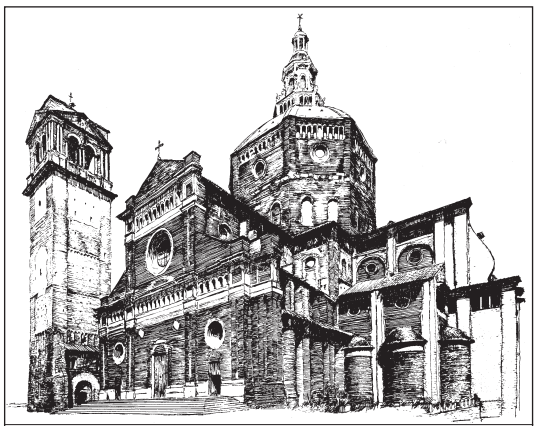

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