Review Article

Tuberculosis: mother of thoracic surgery then and now, past and prospectives: a review

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Abstract: Knowledge on ontogenesis of thoracic surgery is essential not only for understanding present concepts and debates on surgery for tuberculosis, but it also contributes to the further developments in operative treatment of lung cancer. Both diseases have been the leading cause of death in their respective ages. History of tuberculosis follows the classic algorhythm: diagnostic, causistic and therapeutical stages. Villemin followed by Virchow, and, finally, Koch revealed the pathoanatomy and the cause of tuberculosis. The therapeutic phase of lung cancer has been reached without identified cause of the disease. Chest surgery, eradication of the macrosocopic focus by physical interference with the involved tissue mass, in both diseases preceeded medical treatment. Identification of phenotypes of lung cancer—if it is a single disease at all—does not contravene the concept: the tumor mass should be eliminated. However, causation is not an absolute sine qua non of an effective treatment, as the tuberculosis-lung cancer analogy also proves. Surgical approach of both diseases suffered from the same paradoxon: eradication without direct interference with the causative factor. While lung cancer seems to be controlled by an emerging array of new drugs, tuberculosis poses a new challenge, as multidrug resistant and extensively drug resistant Koch bacteria are emerging and fragile societies' immunity is weakening. Thoracic surgery has a significant share in the fight against tuberculosis, when drugs and/or society fail. Palliative and radical adjuvant surgery multiplies the chance of cure in those cases, where not much hope is left. The jury is still out in a series of questions, but it is obvious, that surgery is only an option and not a panacea where medicines and their providers fail. Deeper understanding of our past and present failures with tuberculosis and its surgery might contribute to new concepts in coping with lung cancer as well.

Keywords: Tuberculosis; history of medicine; thoracic surgery; Koch bacillus; lung surgery; carcinoma of lung

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Introduction

This paper is an attempt to build a solid bridge between the past and the present of chest surgery in order to increase understanding of rationale of tuberculosis surgery and revive many techniques undeservedly neglected, some forgotten. Mycobacterium tuberculosis infects around one-third of the world's population and kills between two and three million people annually, an enormous burden, indeed (1). Present surgical concepts and techniques to treat lung cancer are rooted in surgery for tuberculosis, or phthisiosurgery. Renewed spread of tuberculosis calls for review of the still active surgical methods and for a search for new ones. Thoracic surgery is one and indivisible, and the different surgical techniques and considerations are relevant on all walks of it, should we serve our patients' suffering either from lung cancer or tuberculosis.

The article is structured into three sections. A sketch of historical development of the surgical techniques for tuberculosis is followed by a comparative analysis of the conceptual parallelisms between tuberculosis and lung

cancer. The critical overview of the contemporary chest surgeon's armamentarium in the present fight against tuberculosis is completing the overview.

Tuberculosis has been with us from the very beginning of the human history. It is debated if we are facing a renewed attack of the disease or we just became aware of the problems due to the migration crisis. It is very true that lung cancer shadowed all infective lung diseases in the biased euroatlantic pulmonological discurses in the past four decades or so. The Old Testament of the Holy Bible already refers to phtyisis or dry disease (2) and Hyppocrates, the Greek father of medicine, makes interesting observations (3). The names of the disease are numerous, starting with the dry disease, frequently referred to as consumption, and most recently phtysis (4,5). Till the advent of the microbiological identification by Robert Koch (1882) and the birth of radiology (Conrad W. Röntgen, 1896), the clinical picture itself served as an umbrella diagnosis, covering many only seemingly similar pathologies. Oncologists and lung specialists in the future might look back at our present attempts at curing lung cancer with a somehow similar surprise and disdain, as so many essentially different diseases were treated under the same code: lung cancer.

Surgery for tuberculosis

Space management I: artificial pneumothorax

Our forefathers very early recognised the importance of the space problem in order to arrest the tuberculous inflammatory process. In a broader sense of the word, public health observations proved that a small narrow living space (combined with bad air and poor hygiene) is responsible to a certain degree for the disease. In a more focused manner, the pleural spaces were scrutinised in the late 18th and early 19th centuries. The general concept of rest as a natural healing power was connected to the diseased lung by Bourru in 1774 and Carson in 1822 (5,6). Breathing movements of the lung prevented the approximation of the cavity walls. Permanently moving tissue was supposed to be the main obstacle of the elimination of tuberculotic foci and of the restoration of normal anatomy. Arrest of the lung disease was aimed by immobilisation in form of induced collapse of the lung, similar to how the Achilles tendon heals only when in rest. Two patients of Carson failed to prove the concept at his attempts to induce pneumothorax (7). Other surgeons and their patients were not luckier, either (5). In 1885 Cayley induced artificial pneumothorax in a patient who had had a pulmonary hemorrhage. The pleural space was always entered using a scissor or scalpel, resulting in entering of an uncontrollable amount of air (8). Only the introduction of the sharp-ended small bore injection needle, simultaneously invented by Pravaz and Wood (9) in the second half of the 19th century, permitted a controlled air fill of the pleural sac. The Italian Forlanini, (6,10,11) used a needle for the delivery of nitrogen via a water level pressure controller in the same year when Koch identified the causative organism, 1882 (12). The method gained acceptance only after the extremely innovative John B. Murphy (13) presented it in the USA in 1898. Murphy's assistant, Lemke (14) treated 350 cases by I902, but he had no followers till 1912 in the USA. Artificial pneumothorax became a standard form of therapy of tuberculosis in Europe by the turn of the century. The paradigmatic tuberculosis novel, Thomas Mann's *Magic Mountain*, frequently makes references to pneumothorax therapy. Brauer, in Germany, Saugman, in Denmark, Dumarest and Rist, in France, and Lillington, in England, (15) were the pioneers of the method in Europe. The USA was "reinfected" by the concept just prior the Great War, 1914-18. (5). The simplification of the method, by substituting air for nitrogen, and the use of highly sensitive manometers helped a lot (16). In the first half of the 20th century, in the pre-Streptomycin era, artificial pneumothorax became a standard method or as a pre-surgery modality. Thirty-three to fifty percent of patients who were institutionalised in sanatoria received pneumothorax therapy (5). The procedure was widely used until the 1940s in spite of the complication rate of around 10%. The mortality of the disease treated by artificial pneumothorax varied between 20–44% at 5 years (17). Pleural adhesions preventing the much desired lung collapse were electrocauterised by Jacobeus' thoracoscopy method published from 1910 onwards (18,19). As usual, the method had been discovered well before Jacobeus, but remained dormant for 50 years (20).

Obsession with senseless prophylactic measures is not new. On the zenith of enthusiasm for pneumothorax, some physicians were suggesting collapse of healthy lungs to prevent tuberculosis (5). The advent of the antituberculous drugs, crowned by rifamycin, and the avaibility of safe resective lung surgery put the treatment of the pleural space and the beautifully designed beachwood and copper pneumothorax machines to an end by the mid 1960s (21,22).

Space management II: treatment of dead space

Creating artificial pneumothorax was an answer to the need for favourable biological conditions by means of intrapleural pressures permitting elastic lung tissue to relax. Interplay of pressures (intrapleural and pulmonary) were seeen as the key to recovery of diseased lung parenchyma. Pleural cavity space management was commanded by the concept of "horror vacui"—the tendency to fill all empty spaces. However, the 300 to 500 mL of injected air or nitrogen was absorbed quite quickly and a definitive solution was needed if treatment failed. Reducing the space or expanding the lung were the two solutions for the lung/chest cavity mismatch. The dead space had to disappear.

Thoracoplasty

The removal of series of ribs in order to collapse the chest wall providing rest for the tuberculous cavities in the underlying parenchyma was perfected in the late 19th and early 20th centuries (23). The first convincing series of cases was presented by Schede (24) following de Cerenville's "first" in 1885 to perform thoracoplasty. In 1908 Friedrich (25) widely extended the degree of collapse of the lung by removing large segments of the second to ninth ribs. The first rib debate took its origin from here. Leaving the periosteum intact provided a potential for at least partial rib regeneration. Mortality was reduced significantly when Brauer (26) switched to the two-stage technique and others followed. The procedures were performed under local anesthesia (early nonintubated, awake surgery). In 1911 Wilms (27) perfected a technique resecting the posterior part of the chest wall. Wilms and his contemporary, Sauerbruch, (15) established the extrapleural paravertebral thoracoplasty. The originally extensive resections were reduced heralding the "less invasive thoracic surgery" led by Semb (28). It was OV Björk, in 1954, (29) who closed the long list of authors, where no eminent thoracic surgeon missed the chance to develop his own modification (30). Thoracoplasty was not an "a priory" procedure. It was usually preceded by failed bedrest therapy followed by series of artificial pneumothorax and in some cases phrenicolysis (see below). The long preoperative period made a "natural selection of patients" leading to a serious bias when the method is evaluated retrospectively. Postoperative deformity of the thorax, shrinkage of the operated side, and retraction of the heart and mediastinum were the price of the procedure and of becoming free of tuberculosis. In properly selected cases the mortality rate was low, and collected sanatorium statistics showed that about 70% of the patients eventually achieved an "arrested" status (5).

In fact, thoracoplasty remained the most popular treatment of choice until the arrival of Streptomycin (21,23). By the end of the 1950s, the boom of thoracoplasty was definitely over, and it became a (nearly) completely forgotten operation.

Soft thoracoplasty: diaphragm

The floor of the chest cavity, the diaphragm, a potent structure in narrowing the thoracic cavity where the diseased lung is struggling for survival, was targeted early in the 20th century. The phrenic nerve was paralysed first in 1911, by Stuertz (31). The method and its indications were refined later by Sauerbruch and Schepelman in 1913, and by Felix and Goetze in 1922 (5). The elevated diaphragm compressed the diseased lung. A passive elevation of the diaphragm from below was the next logical step. Pneumoperitoneum, pushing the diaphragm upwards, was popular in Europe. To secure a safe way to inflate the abdomen, the Veress needle (32) was introduced: a method which is the quintessence of laparoscopy and in many cases of video-assisted thoracoscopic surgery (VATS). Banyai (33) published promising results of pneumoperitoneum with phrenicectomy in case of previously failed artificial pneumothorax in 1946 (15,16). However the results were not convincing enough and pneumoperitoneum was reduced mainly to an adjunct role as preliminary measure prior to resection in poor risk patients (34).

Space occupying by fluids and solid material

Other space occupying methods included oleothorax (35), when intrapleurally instilled oil collapsed the lung. Wax and synthetic materials (lucith balls) were used later, as pioneers of plastic breast surgery later to come (36,37). Extrapleural pneumothorax, suggested by Mayer (38) in 1913, gained popularity only two decades later. Plombs of the extrapleural space ranged from fatty tissue to paraffin (21,39). Thoracic empyema was not an uncommon complication (40). Extrathoracic muscle transfer into the chest cavity came later in the 1970s (41).

Space management by evacuation

Drainage of tuberculous thoracic empyema laid the foundation of chest surgery (15,16,21,41). Monaldi choose a conceptually different way: approaching the tuberculous cavity deeply within the parenchyma through the relatively intact parenchyma in 1938 (42,43). A tube was inserted

into the tuberculous cavity and approximated the caverna walls by applying suction for long periods of time. Monaldi took the first step on a long road, which led to the vaccum assisted space management of thoracic empyema and other intrathoracic, focal inflammatory processes (44,45).

Space management III: the trapped lung

Freeing the trapped lung under the thick cover of inflammatory pleural cortex offered a solution for the danger of "horror vacui" in an inside-out way. Decortication, originally described independently by Fowler and Delorme (15,46,47) in 1883, meant the radical removal of the fibrous cortex and required safe general anaesthesia, which was not available until the 1950s. The more gentle form of treating the trapped lung, chemical decortication via local application of trypsin, streptokinase and similar agents, still survives nowadays for the treatment of postpneumonic stage I–II thoracic empyema (45).

Space management IV: lung resection

Looking back from our present stance, it is not easy to understand why the resection of the circumscript lesion took so long to be an option (48). There were, so to speak, two and a half heavy obstacles on the road to lung resection: fear of sudden increased intrapleural pressure and lack of anaesthesia were the main problems, while blood loss was a relatively minor one. As a generation of surgeons returned from the trenches of the First World War (WW1), with reassuring experience on the management of lung injuries (41), they turned their attention to the White Death (49). However, it was very soon realised what the tuberculous lung tissue meant compared with the lung injuries of otherwise young and fit men with healthy lungs. Resection for tuberculosis was not a real option (50) in spite of the promising animal experiments of Gluck (51), back in 1881, and of Bionda, in 1883. The first lung resection in a human had terrible consequences in 1883: the patient died and at autopsy there was no evidence of tuberculosis (15,21,52). The surgeon, Block, shot himself. In 1884, Krönlein (53) resected apical tuberculous lesions in two patients, but they died just like Ruggi's patients 1 year later. Tuffier (54) was the first to successfully remove the apical portion of a tuberculous lung in 1891. Babcock was the pioneer in the USA in 1908, but his patient did not survive the right lower lobectomy (48). Lung resection before WW1 was mainly a theoretical question (55). A safe procedure depended on three pillars: securing hilar vessels, closure of lung parenchyma and managemenet of pleural space. Hilar tourniquet and ligation gave answers to the first question. Positive pressure ventillation won over the negative pressure operational chamber and solved the management of the pleural space intraoperatively (15,21). Postoperative drainage made recovery safer (56). The first lobectomy with hilar disection in 1912 (57) was followed by the technically less demanding pneumonectomy 21 years later: Graham's historical first pneumonectomy for lung cancer (58). Two years later, Freedlander performed a successful lobectomy for tuberculosis (59). The years between 1933 and 1940 saw the refinement of the individual ligation techniques and of the methods of bronchial stump closure (60-63). In spite of the technical improvements, around the 1940s, pneumonectomy and lobectomy for tuberculosis were associated to mortality rates of 40.2% and 20.5%, respectively (21,64). The chest trauma experience of the WW2 (41)—intubation, positive pressure ventilation, bronchoscopy, physiotherapy—contributed to the establishment of lung resection as one of the standard therapies of tuberculosis. In 1943, Churchill and Klopstock redefined the indications, recommending lobectomy as a primary procedure in selected cases (65). Generally speaking, lung resection in the pre-Streptomycin era was restricted to patients in whom other collapse measures had failed. Advent of Streptomycin reshifted the overall picture when it became generally available in the early 1950s (64). Chamberlain (66) further reduced surgical agressivity advocating segmentectomy in circumscript cases. Physiological approach (external parenchyma compression) and mechanical eradication (parenchyma removal) were competing modalities. In spite of slowly expanding resective policies in lung tuberculosis, collapse therapy kept its place till Streptomycin arrived. Overholt, in 1950, was among the first to recommend simultaneous thoracoplasty and pulmonary resections (64). Ten years later, the deforming procedures of thoracoplasty practically disappeared from the thoracic surgical armamentarium. The pre and postoperative administration of streptomycin reduced the hazard of complications caused by spread of the disease. The 60-day postoperative mortality of around 9% paid off with a 80% success rate (64). Pulmonary resection gained now a supplementary role, instead of being a competitor of drug treatment. With the advent of further antituberculous drugs and safer anaesthesia, resectional therapy virtually replaced collapse therapy by the late 1950s. One decade later, the newly arrived surgical staplers promised a safer

and quicker lung surgery. Ravitch (67) was a pioneer in the use of the Russian staplers (68), which applied the Petz machine concept born in 1922 (69). Antituberculous drugs and highly reliable stapled suture lines together made a final breakthrough in the surgery for tuberculosis in the 1970s (70). The happy days did not last long: the new wonder drug rifamycin was a near-panacea relegating tuberculosis into the no-go zone of most thoracic surgeons in the high income, low tuberculosis incidence part of the world. Paradoxically enough, the safety of the lung operations significantly improved due to the antituberculous agents at the same time when the demand for the resective solutions fell sharply exactly for the same reason. Improving systemic treatment definitely reduced the need for surgery except in some geographic regions, for complex reasons. Since the 1980s, surgery for tuberculosis has been a rare indication in Western and Central Europe, and in the USA and Japan as well. Surgical morbidity and mortality did not fall as expected because surgeons had to cope with more complex and high risk cases. As the turn of milleneum approached, celebrations were prepared for the final victory over the White Death. The Third World and Eastern Europe knew it better, and from the mid 1980s the self-indulged optimism vanished with the spread of multi-drug resistant (MDR) and extensively drug resistant (XDR) tuberculosis. Even "simple, drug sensitive cases" can be made very complicated by socioeconomic and political factors. This is a challenge that no modern thoracic surgeon can deny, and where this article takes off.

Tuberculosis surgery laid the way of lung cancer surgery.

Development of modern surgical techniques

Modern thoracic surgical techniques were developed originally from procedures to treat tuberculosis (5,16,21). Present VATS techniques take their origin in Jacobeus' thoracoscopy (18,19) invented to free the lung from adhesions before artificial pneumothorax. Veress needle (32,71) is the cornerstone of induced pneumoperitoneum and pneumothorax. Thoracic surgical staplers, sine qua non of VATS and robotic surgery, are derivates of the "Russian staplers" (68,70) originated in the Petz machine (69). Thoracoplasty, performed in local anesthesia for many decades, is nothing but generic awake/non-intubated thoracic surgery of today (72). Covered bronchial stump following neoadjuvant therapy in order to reduce bronchopleural fistula is a reborn surgical procedure from the tuberculosis heritage (21). Concurrent drug administration, implementation of the double and triple combination antituberculous regime protocol patterns resurfaced in the cancer treatment schemes and resulted in improvement of antitumour therapy efficacy in the 1970s (73,74). Anti-cancer chemotherapy protocols followed the strategy of antituberculous therapy with combinations of drugs, each with a different mechanism of action. Reducing the parenchymal loss in lung cancer surgery humbly followed the similar paradigm shift in tuberculosis many decades before (65,66). The recent debate over neoadjuvant *vs.* adjuvant therapy for > Stage Ib non-small cell lung cancer (NSCLC) reflects to the bygone dispute on resection before or after antituberculous medical treatment. The different modalities are no mutually exclusive options, but complementary ones. Pre-surgical treatment is for patients to make them operable; post resectional adjuvant therapy is to make recovery safer, disease-free interval longer for many and cure for a few.

Tuberculosis of the lung is a systemic disease caused by the Koch bacillus, best treated by drugs with additional surgical removal of the focus of the disease if necessary. The disease has a fairly good chance of around 90% of to be cured (75). The treatement response rate is predictably high as the causative organism is targeted directly. The role of surgical removal of the pathologic focus is limited and more or less properly established. The prognostic factors (cure-rate, relapse) include the drug resistance of the bacterium, the extent of the process and the functional and immunological reserves of the patient. However, it must be accepted that, just because the Koch bacillus is the same all around the world, the disease has many different faces, as the patients (and the society around them) on the receiving end are frequently and highly different. This explains the significant differences in cure and response rates, and the divergent policies of care givers.

Stage I to III lung cancer is a local manifestation of a systemic disease without sufficiently identified aetiology, except the cloudy category of epidemiologic causality (76). Therapy response is understood at cohort level, but it is unpredictable where the individual patient's fate is concerned. Epidemiological causality offers some sort of clue to the pathogenesis as far as inhaled noxas and genomics are concerned. For reasons unknown, mechanical eradication offers the best chance for cure in early stages of the tumour. Apart from the biological features of the malignant tissue growth (cell-type/differentiation), three

tumour related factors are serving as outcome predictors. Size, extension and location of the primary growth, (T), lymph node involvement (N) and distant metastasis (M) are counted as components of tumour extent and prognostic elements. It is unclear if recent modest improvements in survival are due to refined imaging techniques that facilitated earlier diagnosis or the results of less collateral damages of new therapies. Sceptics argue that improved operability rather than increased resectability results in a positive shift in the surgical outcomes.

Parallelisms in role of surgery in treating tuberculosis and lung cancer

There were three distinctive steps in the understanding and treatment of tuberculosis. The diagnostic, causative and therapeutic periods can be distinguished, but overlap each other at certain times. Surgery (space management procedures and resection) preceded medical treatment by half a century.

While the timing of the pathologic diagnostic phase of lung cancer nearly matched with that of tuberculosis, in case of lung cancer it was followed by therapeutic stage without any identified cause. In 1878, malignant lung tumours represented only around 1% of the cases in large centers, with a disturbingly 4:1 man/women ratio well before the launch of tobacco industry. Following a slow increase before WW1, it reached 15% by the 1930s (15,73). The theory of mechanical eradication of the malignant tumour was born very early (77) as chemotherapy was nowhere prior 1950. Even radiotherapy preceded drug treatment (78). Attempts at surgical resection faced the same technical problems that tuberculosis presented. However pneumonectomy for lung cancer was performed earlier than for tuberculosis.

There are at least four remarkable paralellism between tuberculosis and lung cancer.

Search for prognostic factors

When progress takes a standstill categorization, fever takes over. Hilar and mediastinal lymph nodes are the central elements of the Ghon complex and its calcified result, the Ranke complex (79) of the tuberculous lung. The same lymph nodes are the cornerstones of the TNM system (80,81). The desire to find a strong prognostic element resulted in a perpetual search. Gaffky, disciple of Koch, seemed to find the key in tuberculosis (82). The Gaffky index—number of Koch bacillus in the smear of sputum—was intended to work as a prognostic tool (83). Real life did not confirm the supposed close correlation, and the Gaffky index became completely forgotten soon. Is there a chance that all the discussions of stations and size of lymphnodes in lung cancer (84) will share the fate of the Gaffky index? What we are looking for is a predictive factor, rather than a prognostic one (85).

Long silence

Similarities in the phenomenon of a late relapse/recurrence in both diseases offers analogues in spite of their obvious differences. The dormant Koch bacillus vs exogenous reinfection debate (86,87) is paralleled by the dormant cancer cell hypothesis (88). DNA analysis can differentiate in both cases, but the shared phenomenon of long period hiding remains to be a disturbing question.

Bloodborne factors

Infectivity of the circulating Koch bacillus, hotly debated in the 1920s, and its supposed prognostic value (89) are comparable to the present circulating tumor cell question. Connection between tumour in the bloodstream and in the bone marrow and the metastasis seems to be plausible. While the question of the *Mycobacterium tuberculosis* in the bloodstream settled down by 1950 (90), the circulating lung cancer cells are subject of intense research (91,92) The "seed and and soil" theory might offer a clue for the distant metastasis formation (93,94): a shared feature of both pathologies. The impressive similaritities in the predominance of the involvement of segment 2 and 6 in both tuberculosis and lung metastasis formation is a considerable observation.

Peeling of the onion

The truth is approached by the serial removal, layer by layer, of misdiagnoses, oxymorons and misconceptions. Till the 1960s all tuberculosis seemed to be the same, until atypical tuberculosis was identified and the victims of the *Mycobacterium xenopi* and other similar organisms were able to leave their stigmatic diagnostic box (95). Certain phenotypes of the adenocarcinoma *in situ* (previously known as bronchioloalveolar adenocarcinoma: BAC) behaves definitely in a more benign way than any other cell type NSCLC (96). Further genetic mapping might reveal the underlying difference from the rest of the malignant lung parenchymal processes, adding one more parallelisms to the tuberculosis question.

The big question is, what happens after the complete removal of the tumour mass? Surgery of infectious disease

is more liberal: following the removal of the main volume of the pus and the dead tissue, the inherent reparatory processes are called in. The last existing tumour cell is not the last clinically detected one. Overkill or simply destroy what was identified during the procedure? What is an absolute prerequisite of making the patient tumour-free? When seemingly all tumour cells are removed, we are wrong in our victorious assumptions. Were we right, there would be no local recurrence, bone marrow micrometastasis, detected tumour cell in the blood stream and so on. Every long-term survivor is an evidence for a contender in the agnostic corner. The present state of lung cancer surgery is the same as that of lung surgery for tuberculosis before the Streptomycin era. We attempt to eradicate the local manifestation of a systemic disease, unknown in origin, just because we do not have better option. The cause of cancer is as unknown now as was the cause of tuberculosis before the Laennec-Villemin-Koch chain of revelations (12,50,97,98). It took more than 60 years following Koch's identification of the cause to find the first effective agent, Streptomycin. In 2018, we still do not know what is the single causative agent (if it exists at all) of the lung cancer (if it exists at all as a single entity), but we have a quite effective armamentarium against the disease, and scalpel is definitely one of them. White Death, as tuberculosis was known more than a century ago, is replaced by now by the not less deadly lung cancer. In respect to the causation of lung cancer, we are still in square one, waiting for the Copernican revolution in tumour biology. The main message of tuberculosis surgery to present day oncosurgeons is that no one can forget the interaction between tumour and patient and his/her socioeconomic status around the pathologically identified focus.

Surgery for tuberculosis in 2018

The protean behaviour of the tuberculosis and the differences of the geopolitical and economic influences on the disease make the answer to the question regarding the place of surgery in its management very difficult. The answer depends on where you are, what you have and who your patients are (99,100). The surgical attitude is defined by the drug sensitivity of the Koch bacillus, by the particular socioeconomic and cultural features of the patient cohort and by the capabilities of the relevant health care system. Significantly different theoretical and surgical heritage issues are obstructing discussions, based on usually incomparable results. For example, the 76% medical treatment efficacy of the MDR cases in Switzerland, opposed by the Russian 23.6%, offers an explanation of differences in their attitudes toward surgery. A significant amount of the so called tuberculosis surgery cases in Western and Central Europe and USA are solitary pulmonary nodules (SPN) that turned to be tuberculomas under the microscope (101). Tuberculoma is a lucky finding in oncologic thoracic surgery, while all other tuberculous pathologies challenge the full armamentarium of septic chest surgery. Sharp distinction and application of clear categories help to avoid false generalisations with regard to operability and resectability. The modern thoracic surgeon is a member of the multidisciplinary team, but the only one whose action is irreversible (102). With a rule of thumb a newly recognised SPN has a chance of >80% of being a malignant tumor in Western and Central Europe, USA and Japan. The chance of malignancy for the same lesion is less than 50% in, say, Ukraine, Moldova or Rumania, and is below 20% in many parts of the low income, high tuberculosis incidence countries of the world. The different approaches are dictated by and are justified in their own environment. It is generally agreed that tuberculosis of the lung is primarily a medical disease. The cure/treatment success rate of proper medical treatment is around 85–90%, according to the 2015 World Bank data (103). The definition of cure is an asymptomatic patient who has three negative cultures. However, the absolute number of individuals behind the abstract and meaningless double digit of 10–15% is shockingly high. To make bad things worse, a significant number of the "active cases" are MDR or XDR tuberculosis patients. The smear/sputum positive cases are walking Koch-bacterium sources, and their social impact is enormous, indeed. Surgery should have an adjunct role when the Koch bacillus is resistant to the drugs or the patients and/or their treatment adherence are too weak. Massoud Dara led an internet-based panel of eminent experts to put the questions into shape in 2015 (104). Many questions were resolved by consensus, others were better defined than before, and not a few remained open for the future.

Indications

At handbook level, the surgical indications for tuberculosis are clear-cut and well established (105). The majority of the surgical interventions are diagnostic, opposed to the more challenging therapeutical interventions. There is a general consensus concerning the diagnostic roles. The place of

resective surgery is open for discussion as there are many divergent opinions. Language barriers accepted, it is obvious that there is a distinct way, led by the robust Russian (and ex-Soviet Union states) experience (106,107), of favouring resection, while the majority of publications from the Far East show a more restrained attitude (100,108-110). There is an undestandably highly conservative attitude in the high income low incidence countries, a stance recently challenged by mass migration and global tourism.

Diagnosis

Diagnostic procedures include exploration and evacuation of the pleural space, identifying SPN if all previous methods failed (image guided biopsies) and procedures involving the exploration of mediastinal lesions (usually lymph nodes). Recurrent massive pleural effusion accompanying, pleural dissemination might require a surgical approach, usually VATS under general anesthesia and double lumen intubation. The recent rebirth of awake patient surgery/non-intubated anaesthesia are worth considering (72,111). Short hospital stay/day case surgery options are benefits of the approach, regardless of the closed chest tube drainage or the VATS evacuation (112). The danger of re-expansion oedema is disputed, but in an absence of hard data (113) a relatively slow release of the fluid (5–8 minutes pause between 1,000 mLs) makes the procedure safe. Mediastinal lymphadenopathy is approachable by endoscopic (transbronchial, transesophageal) and guided biopsy. Less rich and generous health systems, unable to afford these tools rely on surgical sampling. Cervical mediastinoscopy is limited to the upper-anterior mediastinum and parasternal mediastinoscopy (the Stemmer/Chamberlain procedure) allows an extension down to the hilum. All other parts of the hemithorax are amenable by VATS or by limited thoracotomy with or without the assistance of an endoscope.

Non-verified, suspicious, ususally solitary lesions within the lung parenchyma pose the double challenge of diagnosis and therapy. Multifocal intrapleural lesions need biopsy only. The approach is usually by VATS, with the exception of those patients who do not tolerate one-lung ventilation. The increasing number of unidentified, small-volume lesions picked up by low-dose CT screenening poses a real challenge. Disease-free resection line is a common requirement for lung cancer and tuberculosis surgery as well, even in diagnostic procedures. VATS technology, well established in lung cancer surgery, has an increasing popularity in tuberculosis (114). This is an obvious choice when the tuberculous lesion is small enough (115). The advantage of VATS (116) is less clear when the lesion is larger than 4–5 cm, as harvesting of the specimen needs an incsion of around 6–7 cm: the same length of a definitely cheaper limited thoracotomy incision. Robotic surgery is not excluded from surgery of tuberculosis (117), an unrealistic technology for low and many middle income countries.

Therapy

Failure of medical therapy might be a calling for surgery, if the patient is fit for the required intervention. The degree of fitness of the patient and the patho-anatomical attributs of the disease are the two major factors to decide which type of surgery and for which patient should be performed. There is a relative consensus in the first group of indications for surgery (99,104). Failure of adequate medical therapy beyond 4–6 months of sputum-positive multidrug-MDR and XDR tuberculosis patients who have limited lesion(s) (usually a cavity) is a generally accepted indication for resection (100). Sputum/smear negative, but culture positive, patients with similar focal lesions are also candidates for surgery (118) if the radical removal of the involved lung is deemed possible and the patient's pulmonary reserve allows the operation. The culture reversion (relapse) in a patient with a recurrent limited lesion during or after treatment is also amenable for surgery. The onset of quinolone resistance is a srong pro-surgery argument, as a signal of the impeding MDR to XDR transition. Persisiting bronchopleural fistula of M/XDR patients with focal disease is also an indication for surgery (120,121). Drug intolerance, allergy, liver/kidney diseases contraindicating standard antituberculous medication and special social indications (addictions, patient compliance etc.) are among the rare situations where sugical therapy as an adjunct to medical treatment can be considered.

Absolute indications for surgery include tension pneumothorax, toxic thoracic empyema leading to sepsis, and massive haemoptysis, if all other methods fail, regardless of drug sensitivity.

Residual focus

Surgery of destroyed lung parenchyma without evidence of culture positivity is a debated topic. No reasonable surgeon wants to perform an operation until less risky, but equally

efficient methods, are still available. However, waiting for too long is what Hippocrates warned: "opportunity fleeting" (occasio praeceps). Generally speaking, resection of residual lesions at the end of a successful medical treatment in a sputum-negative and asymptomatic patient is not justified. However, cavitary lung lesions with negative sputum/culture where the lesion is larger than 8–10 cm might be subjected for resection (122,123). These lesions have the potential of reactivation, causing relapse. The frequency of transformation of the cold cavity to a hot one is 20–30% according to Russian experience, justifying an active surgical attitude even in culture-negative cases. Indeed, if a large pulmonary cyst/bulla is an accepted surgical indication, then why to exclude a definitely less innocent cavity with thick, frequently calcified, fibrotic wall? Other experts' attitude in asysmptomatic patients is less agressive, but resection is not absolutely excluded. The thoracic surgeons of high income low incidence countries are even more conservative in this particular case. The 10% relapse rate of medically treated patients is a cause of concern (124,125).

Therapy-resistant caseous pneumonia, infiltrative pulmonary tuberculosis, positive sputum after 6–8 month of treatment are indications for resection for some Russian authors, if no other option was left. This sort of desperate situation is unknown to the thoracic surgical communities of other parts of the world. The question is not so troubling, if one make the comparation with lung gangrene, where the resection is accepted and justified as the last resort (126,127).

Persisting tuberculoma, larger than 2 cm in a sputum/culture negative patient, is usually treated with extended antituberculous medication. Others argue that the inflammatoriy barrier is the hindrance of the sufficient drug concentration. The saying: "*the greatest danger of a tuberculoma*, *that it is not a tuberculoma at all*" is relevant in the high and medium income, low incidence regions.

Sequels and complications

Secondary (tuberculous) pneumothorax is complicated by the fact that the underlying, frequently destroyed lung parenchyma is unable to fully expand (128). The general concept of secondary pneumothoraces is to be applied, with the drug treatment for tuberculosis. With a hint to the artificial pneumothorax treatment of the tuberculosis in the pre-streptomycin era, one might suppose that a controlled pneumothorax could be more beneficial than chasing the mirage of a full expansion and a fine chest X-ray. The lack of modern studies on artificial pneumothorax prevents the author from further discussions. Thoracic empyema with or without bronchopleural fistula is treated with established methods (45), regardless of the causative organism. Haemoptysis needs consideration of less aggressive therapeutic methods, like selective bronchial artery embolisation first, before going for resection. Fibrothorax might benefit from decortication, stripping the encapsulating cortex and freeing the trapped lung. Chemical decortication, as a less invasive alternative (45), might also be considered. Expansion oedema, cytokine storm of a suddenly expanding lung, needs a close cooperation between surgeon and anesthesist (112). VATS decortication is a relative newcomer in the list of procedures (130). No surgery is advised in the central airways during an active process. Post-tuberculous tracheobronchial strictures and stenonis need a prove of the viability of the distal parenchyma. Preoperative angiography and even positron emission tomography–computed tomography (PET-CT) might help in the decision. Permanent chest wall sinuses (with or without rib osteomyelitis) (131) call for active intervention following proven local sterilisation.

Surgical details

Preoperative bronchoscopy to exclude extensive bronchitis and to obtain samples for bacteriology cultures and biopsies in case of doubt are integral parts of the preoperative work-up. The contralateral side needs extra attention. The tracheobronchial tree should be made as dry as possible. Keeping a minimum of 1-cm free bronchus stump and a safe margin zone in the parenchyma resection line are mandatory. In spite of the challenge that the hilum of the tuberculous lung means, anatomical resections are to be preferred. Sublobar and especially non-anatomical (atypical wedge) resections are alternatives to doing nothing, rather than alternatives to lobectomy. Removal of a tuberculous mass is a sort of give-and-take type compromise procedure, where the body has a chance. Small, encapsulated tuberculomas are obvious exceptions.

The distribution of the procedures are broadly different from center to center. The choice of extent of resection varies from center to center, according to local policy and patient type. The frequency of pneumonectomy varies between 11–50%; for lobectomy, 30–54%; and for sublobar resections, around 20–35% (106,108,118,119,132). Where segmentectomy is considered, preference for lesions in segments 2 and 6 or lingula is obvious. Frequently, more than one procedure is required (lobectomy/

pneumonectomy with thoracoplasty, parenchyma resection with decortication, same-stage cavernostomy and myoplasty, etc.). Fragile patients might benefit from staged procedures (106,107). Operations for bilateral lesions need significant functional reserve and good judgement (107). Multi-stage operations give a chance for recovering, while bilateral resections give hope to those who otherwise have no choice. While the published data on bilateral resections are encouraging (107), the devil, as usual, is in the details. One's lifelong experience and the old fox's seventh sense in patient selection are hard to explain in numbers like odd ratios and P values. Those who start with the more affected/complicated side argue that the main burden must be eliminated first. Others prefer starting with the less involved side, saying that the more parenchyma is spared for next stage operation, the better. The debate is familiar to surgeons with an ardent interest in resection of bilateral lung metastases.

Palliative surgery—apart from procedures in the pleural space and adjacent underlying lung—consists mainly of extrapleural thoracoplasty (133), in some series with combination of intrabronchial valves. Thoracoplasty and open thoracic window/cavernostomy are for the high risk patients, usually with bilateral cavities. Extensive fibrosis, destroyed lung causing shunt circulation, and/or recurrent non-specific inflammations might make patients candidates for surgery, even following successfully completed medical therapy.

Transsternal occlusion of the main bronchi is a rare last-resort procedure. Originally developed for re-resection of stump in case of main bronchus insufficency (134), there are some surgeons who apply it to close definitely the central airway supplying the infective focus (135). The problem of space management is solved by leaving the destroyed lung in place. Lung transplantation for destroyed lung remains a curiosity (136).

Postoperative treatment

The postoperative antituberculous treatment depends on the Koch bacillus status of the patient at the time of surgery. Sensitive/susceptible patients require a 4–6 month postoperative medication. In MDR cases, a maximum of 18 months is recommended in case of smear/culture positivity. In XDR cases, 18–24 months are recommended, if the patient was positive at the time of the operation. Successfully converted negative cases, confirmed by sputum culture, need definitely shorter medical treatment, if they were operated on. Previously susceptible bacteria need 4 months and M/XDR patients require 6–8 months. An 18-month window seems to be needed following the conversion. Reports on robust series, critical retrospective analyses and collective expert opinions based on thousands of cases should be respected. Double-blind randomised multicentre trials are not the exclusive sources of reasonable knowledge in the vast field of tuberculsosis, especially as the outcomes also are deeply influenced by non-medical factors. The 10% relapse rate of the medically treated cases explains cautious policy (124).

Results

The reported results are strongly connected to the patient selection policy of the different study teams, reflecting the influence of their respective environments. This fact makes comparation very hard, sometimes impossible, indeed. All conclusions are subjected to the „fog of preselection bias" behind the frequently returning oily, ambiguous pseudo-definition: "properly selected cases". The main task of the surgical intervention is bacteriological conversion in sputum and culture alike. Life threatening conditions like haemoptysis, sepsis due to thoracic empyema or tension pneumothorax require only the stabilisation of the patient. In the cases where the culture-negative patient is operated on, the indication is prophylactic. This is the territory where the decisions are harder to make and the experts' opinions are mostly divergent.

The cure rate among those who underwent a radical operation is between 83–93% (106,108,118,119). Success rate among drug sensitive cases is 98% (106). The success rate of palliative procedures (thoracoplasty +/- valve, thoracostomy) is not more than 40–50%. In spite of the paucity of data, the overall cure rate is around 75% at a price of mortality between 1–4%.

MDR recurrence rate is between 1.3% and 5%. Complication rates are varying between 1% and 16%. The mainly inflammatory postoperative complications are 6–7 times more frequent, than the intraoperative bleeding, a most sly and malevolent incident indeed. The nutritive status (BMI) and the cardio-respiratory reserves are the main prognostic factors. The list of the negative outcome predictors is long and they are frequently interplaying: HIV positivity, diabetes, liver and kidney disease, chronic obstructive pulmonary disease (COPD) and alcoholism. Patient compliance is hard to formulate, but its role is more than obvious.

Conclusions

Surgery for tuberculosis opened up the way to lung cancer surgery (and also opened the chest for cardiac surgery). Now, it is time to think again and repay a part of the bill. Extrapolating present knowledge into the future is one of the riskiest businesses. One of the teachings of tuberculosis is that the disease is more than a interesting but basically simple interaction between the acid fast Koch bacillus and the pneumocyte. It became obvious that it is more than a pathologic entity, involving a segment, or even more than a rather complex disease of the lung. Not only the cells of the body are affected, but the soul as well. The message is wider—tuberculosis made obvious, the immunology of a society is reflected sharply by the statistics of tuberculosis. Results of lung cancer surgery also seem to reflect the immune status of the individual patient as well as on the protective capabilities of the science and the society. Wangensteen's words should be cited: "*what greater amalgamating influence is there than a common great need? There has been, and always will be, an interdepence of each medical discipline upon the others, including too an increasing expectant dependence upon the fragmenting segments of the natural sciences, particularly chemistry and physics*." (137). Here and now, we, thoracic surgeons, have influenced the outcome of lung cancer and tuberculosis patients alike by the thoughtful use of our full knowledge and thoracic surgical weaponry collected by our ancestors against both of theses enemies of the humankind.

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Footnote

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