

# THORACIC SURGERY AND TRANSPLANTATION

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## ABSTRACT

Major changes are bringing a new dimension to thoracic surgery and lung transplantation. This article reports the foremost recent advancements within the field. The most important advancement in thoracic surgery is certainly the widespread use of uniportal video-assisted thoracic surgery in the common practice of most thoracic operations, including major resections for lung cancer. In oncological thoracic surgery, to avoid unnecessary operations in the future, prospective randomised trials are ongoing to demonstrate why some patients with a 'resectable' malignancy within the chest will not survive as long as expected. Lung transplantation has progressed on multiple fronts but a significant advancement is the possibility to perform minimally invasive techniques to insert the lung into the chest of the recipient.

In conclusion, the search for minimal invasiveness has a prominent role in thoracic surgery but further research is essential to demonstrate the real advantages of technological surgical innovations. Worldwide co-operation will permit the collection of data faster and allow the completion of randomised controlled studies to this end.

Keywords: Thoracic surgery, lung cancer, lung transplantation, video-assisted thoracic surgery (VATS), uniportal, minimally invasive surgery.

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## INTRODUCTION

Major changes are bringing a new dimension to the future of thoracic surgery and there is no doubt that as technology is evolving so rapidly, it is sometimes difficult to follow all of the true advancements. In this brief article, the author analyses modern, major advancements within the field of thoracic surgery and lung transplantation, and the possible impact that some of these advancements will have in the future.

## THORACIC SURGERY

The most important recent advancement in thoracic surgery is certainly the widespread use of uniportal video-assisted thoracic surgery (VATS) in common practice. The concept of uniportal VATS was introduced in Europe (Catania, Italy) in 1998 and the first results were published between 2000 and 2003,<sup>1-6</sup> but only recently is the technique becoming known worldwide.<sup>7-11</sup> Briefly, uniportal VATS permits the execution of many thoracic

operations, from pleural biopsy to major lung resection, through a single, small skin incision. It is performed by a team of one or, at a maximum, two surgeons. Some authors have also been able to perform more sophisticated operations using this technique, such as bronchial sleeve resection.<sup>12</sup>

Robotic-assisted thoracic surgery is performed in only a few European centres with high-quality results,<sup>13</sup> but controversy remains regarding the application of robotic surgery because of the lack of well-established evidence.<sup>14-16</sup> Robotic-assisted thoracic surgery is still too expensive for the majority of hospitals, mainly because of the cost of the 'robot' and the long length of operating room usage reported.<sup>13</sup>

Awake thoracic surgery has successfully been used to perform wedge resections of the lung for diagnostic purposes, pneumothorax, and tracheal resections,<sup>17</sup> but recently its use for major lung resection has brought about ethical concerns;<sup>18,19</sup> on the contrary, the concept of enhanced recovery

(‘fast-track’) after thoracic surgery and anaesthesia has allowed an increased number of video-assisted parenchymal lung resections to be performed in managing primary lung cancer.<sup>20</sup>

Surgery for oesophageal cancer, one of the most complex operations, is nowadays more frequently performed using minimally invasive techniques, becoming the preferred method of approach to reduce postoperative complications and help patients to recover from surgery quickly. Scientists are trying to establish which extended surgery techniques patients are more likely to benefit from. The Society of Thoracic Surgeons (STS) recently published practice guidelines on ‘the role of multimodality treatment for cancer of the esophagus and gastroesophageal junction’.<sup>21</sup> It is important that surgeons and physicians fully understand that evidence-based guidelines are recommendations, not absolutes, and are intended to assist healthcare providers in clinical decision-making by reviewing a range of acceptable approaches for the management of specific conditions. The most important messages included in the guidelines are that patients without metastatic disease, in whom surgical resection can be safely performed, should receive oesophageal resection.<sup>21</sup>

Recent publications in thoracic surgery, including important scientific messages, are not yet widespread. This is becoming problematic as personal surgical experience operating on patients with extended malignant disease is starting to count less than before, and this is because patients are asking for evidence of survival, and not just an opinion based on difficult past experiences. On this subject, Treasure et al<sup>22</sup> recently wrote that the ‘E’ in EBM (evidence-based medicine) stands for evidence, not for eminence, experience, expertise, eloquence, or any words that have been used to give authority to one or a group of surgeons.

In the last few years it has become evident, for example, that indications for the surgery of mesothelioma and pulmonary metastasectomy are very weak, and based on case series instead of prospective randomised trials.<sup>23-25</sup> Moreover, few meta-analyses have been published.<sup>26</sup> Rigorous scientists agree that to answer heavily disputed topics such as surgery for mesothelioma or lung metastases, only prospective randomised trials will help.<sup>27</sup> Regarding mesothelioma, only two prospective randomised papers have been

published.<sup>28,29</sup> The first demonstrated that extended surgery for mesothelioma does not prolong survival and is possibly harmful to patients,<sup>28</sup> while the second showed that pleurectomy/decortication and talc pleurodesis have similar long-term results. In a few words, it seems that for mesothelioma in particular, the less the patient is put through, the better.<sup>29</sup> Although morally, surgeons give ‘hope’ but not ‘false hope’ to patients with mesothelioma,<sup>30</sup> some studies have been initiated with the intention to report results of pleurectomy/decortication with hyperthermic intraoperative intrathoracic chemotherapy (HITHOC) versus talc pleurodesis alone.<sup>31,32</sup> The rationale to use HITHOC is justified by the fact that under *ex vivo* hyperthermic conditions, cisplatin diffuses into human lung tissue with a median penetration depth of approximately 3-4 mm.<sup>33</sup>

Around lung metastases, only one prospective randomised trial exists: the PulMiCC trial.<sup>34</sup> Launched in 2010, this trial investigated lung metastases of colorectal cancer, with the main goal of giving a definitive answer to whether or not surgical resection of pulmonary metastases from colorectal cancer lengthens survival. Although the trial was initiated in the UK, it is now open internationally and is recruiting patients in both Europe and China.<sup>35,36</sup> Recently, a staging system for lung metastases has been proposed to the scientific community.<sup>36</sup> It is difficult to obtain data on the long-term survival rates of ‘rare’ and complex surgeries, and therefore the need to include these patients in a worldwide collaborative, prospective multicentre trial has become mandatory, otherwise their best treatment options remain uncertain. An ethical approach in thoracic oncologic extended operations (but not only) when long-term survival is uncertain should probably stay between patient and surgeon needs, always keeping in mind the oath to do no harm.<sup>37</sup> In the future, efforts must be made to demonstrate evidence that the surgical practice used for every oncological disease remains effective at prolonging survival and improving quality of life. For example, the progression of metastasis is still not well known, but it seems that it is mainly caused by a small fraction of tumour cells with the capability to navigate away from primary tumour cells to result in end-organ metastasis.<sup>38</sup> For this reason it is possible that in the future, the so called liquid biopsy could be used to detect the presence of circulating tumour DNA in the blood of patients with lung metastasis burden.<sup>38</sup>

## MOBILE TECHNOLOGY AND THORACIC SURGERY

The use of mobile technology, such as smart phones or tablets, is also influencing daily practice of thoracic surgery; the surgeon is able to see images from home or wherever he/she is, and consequently, medical opinions can be delivered to the junior doctor without the need to reach the hospital, as was required 20 years ago.<sup>39-42</sup> There are several advantages of this method, such as the possibility to simultaneously inform all members of the team regarding the clinical situation and decisions taken about every single patient in the unit; and the ability to connect with remote colleagues who work where there is not, for example, a thoracic unit. The most important possible limitation of this form of communication is the possibility to change the relationship between the doctor and patients, and between doctors themselves, and that it may challenge patient privacy; consequently, medico-legal issues could arise.<sup>42</sup> Nevertheless, the use of this technology needs a well-documented study to demonstrate its effectiveness.

## LUNG TRANSPLANTATION

Following the first transplant performed in 1963,<sup>43</sup> the lung probably remains a difficult organ to transplant because of its fragility, which easily facilitates injuries and infections. Several questions remain unresolved, and between them, the shortage of lung donors is a chronic problem worldwide. In 2015, the International Society for Heart and Lung Transplantation (ISHLT) published guidelines to help physicians and surgeons in their decision making, writing that: "in the absence of high-grade evidence to support decision making, these consensus guidelines remain part of a continuum of expert opinion based on available studies and personal experience. Some positions are immutable. Although transplant is rightly a treatment of last resort for end-stage lung disease, early referral allows proper evaluation and thorough patient education. Subsequent waiting list activation implies a tacit agreement that transplant offers a significant individual survival advantage. It is both the challenge and the responsibility of the transplant community globally to ensure organ allocation maximises the potential benefits of a scarce resource, thereby achieving that advantage."<sup>44</sup> Recently, sophisticated devices have been introduced to recondition sub-lobar donor

lungs to make the organs suitable for transplant. Machines have been designed to enhance lung function by ventilating and perfusing the organ for up to 6 hours after the lungs' retrieval from a donor.<sup>45</sup> This permits an extended assessment and provides time for the lungs to recover from the inflammatory shock following brain death. Another emerging innovation in lung transplantation includes the possibility to perform minimally invasive techniques to insert the lung into the chest of the recipient. A recent study from Harefield Hospital, UK, evaluated 194 bilateral sequential lung transplant patients between April 2010 and November 2013, compared with 124 patients who underwent clamshell incision and 70 patients who underwent bilateral anterior thoracotomies.<sup>46</sup> Results showed that minimally invasive techniques have early postoperative and mid-term clinical benefits compared with the traditional approach of clamshell operations.<sup>46</sup> These observations warrant larger definitive studies to further evaluate the impact of minimally invasive lung transplantation on physiological, clinical, and patient-reported outcomes.<sup>46</sup> Only a few months ago, some authors reported experience on the impact of cell death signals at 24 hours and 48 hours following lung transplantation on short and long-term clinical outcomes of 60 bilateral lung transplant recipients. They demonstrated that recipient plasma concentration of epithelial cell death markers after lung transplantation negatively correlated with early graft performance and long-term survival.<sup>47</sup>

## THE FUTURE

From what it is possible to determine from recently published papers, it appears bizarre that although the use of uniportal VATS was born in Europe, nowadays it is less used in Europe and the USA compared with China, where two major hospitals including the Shanghai Pulmonary Hospital perform over 8,000 anatomic and sub-anatomic lung resections per year. Although there is not a clear explanation for this behaviour, the common feeling is that uniportal VATS will be more frequently used worldwide in the near future.<sup>48</sup> The use of smaller incisions to treat cancer should never place patients at risk, and therefore the use of uniportal VATS will require approval by scientific societies following evidence of improvement, or at least maintenance, of similar outcomes for both benign and malignant diseases. Moreover, the next generation of thoracic surgeons should receive formal training for all the available VATS techniques (single incision, multiple

port, and robotic-assisted), and after training, the surgeon should be able to decide to operate according to the approach that suits him/her best.<sup>49</sup> To note, if in the next decade the indications and the number of operations for lung cancer remain the same, fewer surgeons will be needed because uniportal VATS and robotic surgery are performed by a single surgeon.<sup>50</sup>

No less important is the future of lung transplantation, which appears bright with progress on multiple fronts.<sup>51</sup> Indications for surgery in malignant diseases with uncertain postoperative

long-term survival will have an answer after prospective randomised trials are completed. To avoid the possibility of unnecessary operations,<sup>52</sup> more efforts need to be executed to demonstrate why some patients with a 'resectable' malignant disease in the chest will not survive as long as expected, and therefore the completion of further research is essential to demonstrate that surgical innovations given by technology are true advantages for both patients and surgeons.<sup>53</sup> Worldwide co-operation will permit the collection of data promptly and finishing randomised controlled studies will ultimately benefit humanity.

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