

October 04, 2021
European Society for Organ Transplantation
ESOT Transplant Fellowship Program

Re: ESOT Transplant Fellowship 2020 Report by Ilker Iskender, MD, MSc

The honour of receiving ESOT Transplant fellowship grant was delivered on a December evening in 2019, while I was spending my holidays in Turkey with parents. I had research and clinical fellowships in Toronto-CA, Birmingham-UK, and Zurich-CH before applying for a clinical fellowship position in Leuven-BE related to the ESOT Fellowship Program.

The journey has started almost a decade ago. At that time, lung transplantation was an establish therapy in the Western World, however the first successful lung transplantation in an adult patient could only be performed in 2009 under the leadership of Prof. Cemal Asim Kutlu at Sureyyapasa Chest Center in Istanbul-TR, where I completed my residency in general thoracic surgery. Thereafter, I became dedicated to expanding my scientific and clinical skills in the field of lung transplantation.

It took almost 2 years to start a research fellowship in Toronto-CA in 2011. The Toronto Program has the reputation of performing the first successful adult lung transplantation in mankind back in 1983. Throughout the years, the program has become one of the largest lung transplant centers in the world and advanced the lung transplant procedures by implementing the current lung preservation solution in clinical practice and promoting ex vivo lung perfusion (EVLP) in donor lung management. As a tradition, the program receives significant number of fellows and visitors every year. During my fellowship, I have studied experimental models of lung transplantation in rats and pigs related to ischemia-reperfusion injury. I had also opportunities to participate clinical EVLP assessments at the Toronto General Hospital. Furthermore, I have completed a Master of Science Degree program at the University of Toronto under supervision of Drs. Shaf Keshavjee and Mingyao Liu. I coauthored almost a dozen of other projects during my fellowship, which was finished at the end of 2014. The Toronto experience was very educative and productive. Thereafter, I have decided to continue my training in lung transplantation in Europe.

With the support of a fellowship grant from the Scientific and Technological Research Council of Turkey, I started a clinical research fellowship in Zurich-CH in 2015. At that time the Zurich Program was led by Prof. Walter Weder, one of the pioneers of thoracic surgery in the world. I had opportunities to participate in the peri-operative management of lung transplant patients and continued research activities in pig models of EVLP and lung transplantation. During my fellowship in Zurich, I completed the necessary exams and became a registered medical practitioner in the United Kingdom. The structure of the program and excellent patient care in Zurich had a significant impact in my career and future goals.

After spending almost 5 years in research setting, I was delighted to be back to the clinical practice in the UK. While I was establishing connections with the transplant centers, I initially served as a resident medical officer in a private health care setting. Approximately 6 months after, I started a cardio-pulmonary retrieval fellowship at the Queen Elizabeth

Hospital, Birmingham-UK. Other than gaining experience in thoracic organ retrieval, I had opportunities to participate in the perioperative management of heart and lung transplant patients. Furthermore, I worked as an honorary clinical fellow at Heartlands Hospital to participate perioperative management of general thoracic surgical patients. I had good relationships and memories during my fellowship in Birmingham, UK.

Zurich again! I decided to move back to the department of thoracic surgery at the University Hospital Zurich, Switzerland as a clinical fellow after spending a year and a half in the UK. During my first year I mainly worked in the research laboratories and continued to improve my German language skills. Thereafter, I started to participate in clinical duties actively as a resident doctor. Perioperative management of thoracic surgical patients, outpatient clinics, emergency consultations and night calls were some of the duties of resident doctors, including myself. I developed sincere relationships with my colleagues and patients. During my second year, Dr. Laurens Ceulemans from Leuven, Belgium has started a fellowship training in Zurich. Due to the nature of surgical training program in Zurich, trainees do not have many opportunities for hands on training during residency years. For this reason, I was investigating the options for the next step in my career development. With the guidance of Dr. Ceulemans, I have applied for a surgical fellowship in Leuven to improve my operative skills. By the end of 2019, I completed a fellowship in Zurich and became an independent procurement surgeon and EVLP specialist. Furthermore, gained valuable experience in the perioperative management of thoracic surgical patients.

At the beginning of 2020, I started a surgical fellowship in Leuven, Belgium, supported by the ESOT Transplant Fellowship Program. Thoracic surgery department in Leuven is a world-known center in the field of general thoracic surgery. The program has a long-standing experience with lung transplantation. The program has performed close to 1300 lung transplants since 1991. Moreover, Leuven Program is one of the few centers that performs esophageal surgery as part of thoracic surgery services in Europe. Around 20 scheduled operations are being performed in 10 elective operating theatres weekly. An additional emergency room is usually occupied for lung transplants and other emergencies throughout the week. The overall program activity is divided into three main subspecialties: lung transplants, upper gastrointestinal (GI) surgery, and lung and mediastinal surgery. Lung transplant candidates and, lung and esophageal cancer patients are discussed routinely during weekly multidisciplinary board meetings. Furthermore, the program performs more than 1000 procedures yearly. There are 8 consultant thoracic surgeons supported with 2 senior surgical fellows and 4 surgical residents. The program is further supported by interns, research and visiting fellows to accommodate the busy operation schedule. I worked as a senior surgical fellow during my fellowship in Leuven.

The aims of this fellowship were to participate actively in thoracic surgical procedures, including lung transplantation and continue performing clinical and basic scientific research. Initially I had difficulties to obtain a medical license, which is a prerequisite for active involvement in surgeries in Belgium. Shortly after my arrival the COVID-19 pandemic has arrived, which had a negative impact in the assessment of my application by the Belgian authorities. All provincial and federal governmental activities were significantly reduced during the first wave. As a result, I could receive a full licensure in July 2020. I used this time to support surgical activities, prepare research proposals and learn Dutch language. It was

important to have a some understanding about the local language to be able to participate discussions actively related to the patient management.

Surgical training:

Lung transplantation: Lung transplant activity was also significantly decreased in Leuven like any other transplant centers across the world during the COVID-19 pandemic. Nevertheless, the Leuven Lung Transplant Program remained active and continued to perform more than 50 transplants yearly. I was fortunate to participate more than 60 lung transplants during my stay in Leuven. With the support of my supervisors, Profs. Van Raemdonck, De Leyn, and Ceulemans, I performed my very first lung implantations for about 20 patients in Leuven. This was an important achievement in my career.

During my stay I observed the following unique aspects of Leuven Lung Transplant Technique: Surgeons avoid performing Clam-shell incisions. As a result, most of lung transplants are performed via bilateral anterior thoracotomies without dividing sternum. During pneumonectomy it is important to keep the lung ventilating until the occlusion of pulmonary vessels in hilum to avoid desaturations. The Technique also avoids ECMO support during implantations whenever possible. Rather than a threshold value for the pulmonary artery pressures, they use pulmonary to systemic arterial pressure ratio to proceed with or without ECMO during implantation. There are traction stitches placed on the pericard and surrounding tissues to improve the exposure. These sutures also help to avoid unnecessary compressions on the heart and great vessels to prevent hemodynamic instability. During implantations, bronchial anastomosis always covered with a fat patch to strengthen the anastomosis. There is a reperfusion break after implantation of the first lung to allow time for acclimatisation of the new lung into the recipient. The short- and long-term outcomes are excellent with the help of dedicated surgical, intensive, and pulmonary care after lung transplantation in Leuven.

Moreover, I continued to perform lung procurements independently during my stay for more than 30 donors. The lung utilization rate (around 40%) is exceptionally high in Leuven. I have witnessed that marginal donor lungs, such as older donors or lungs with consolidations or suspicion of infections could be safely transplanted in Leuven. Moreover, Belgium is one of the leading countries in donation after cardiac death (DCD) organ donation. DCD donors accounts for about 40% of all lung transplant activity in Leuven. I could further improve my understanding and surgical skills about DCD category III and V donation in Belgium. Importantly, I could transfer my knowledge in lung procurement to young surgical trainees during my stay. Undoubtedly, this experience would allow me to establish a high-quality practice in the management of lung transplant patients.

General thoracic surgical training: Other than the surgical treatment of end stage lung diseases, I am primarily interested in lung, mediastinal and chest wall surgeries. Since the completion of my residency in Istanbul, minimally invasive surgeries have become the treatment of choice in thoracic surgery. Herein The Leuven Program offers a long-standing experience in minimally invasive thoracic surgery to its trainees. Majority of lung resections are performed via video or robot assisted approaches, led by Prof. Decaluwe. The clinical director, Prof. De Leyn oversees extended lung and tracheal resections. Prof. Van

Raemdonck performs majority of metastasectomies and mediastinal surgeries using both minimally invasive and open approaches. Lastly, Prof. Ceulemans is in charge of thoracoscopic lung volume reduction surgery and mesothelioma program. Furthermore, there is a very active chest wall deformity program, led by Drs. Van Veer and Coosemans in Leuven. They performed more than 800 minimally invasive procedures for the correction of pectus deformities with excellent outcomes since the initiation of the program. During my stay in Leuven, I have participated close to 200 lung and mediastinal resections and performed a handful of these operations under supervision. Regardless of the COVID-19 pandemic, I had also opportunities to participate large number of chest wall deformity operations and perform significant number of minor VATS and other thoracic surgical procedures during my fellowship in Leuven. These experiences have certainly helped me to improve my surgical skills.

Thoracic surgeons in Belgium have a unique aspect related to their surgical training. As a rule, trainees need to complete a general surgery residency first, and then specialise in thoracic surgery. Generally, the leaders of thoracic surgery clinics have derived from cardiac surgery during the separation of thoracic surgery from cardiothoracic surgery departments across the world. As a result, there are not many thoracic surgery centers that perform esophageal and upper GI surgeries in the world, even though esophagus is an intrathoracic organ. For this reason, I have not had enough opportunities to expose upper GI surgery before coming to Leuven. The Upper GI Surgery Program is another strong aspect of the thoracic surgery department in Leuven. The Program initially popularized by emeritus prof. Lerut and currently led by Profs. Coosemans, Nafteux, and Depypere. The program performs more than 200 esophageal resections yearly. Dr. Ovaere, who was the other senior surgical fellow, took the primary role of joining upper GI surgeries during my stay in Leuven. Nevertheless, I was fortunate to engage in the operative management of esophageal and upper GI surgeries in about 100 patients. Thus, I have significantly improved my understanding about the upper GI anatomy and am now more confident to operate around the esophagus in thorax.

Overall, I participated more than 700 surgeries during my stay in Leuven during the COVID-19 pandemic, which had a negative impact on the number of procedures performed worldwide. This was a significant achievement on the way to become a consultant thoracic surgeon focusing on the treatment of irreversible lung failure and other lung and mediastinal pathologies.

Research activities:

Similarly, there has been a negative impact on the research proposal as part of my fellowship program due to the COVID-19 pandemic. We have proposed to test the beneficial effects of cytokine clearance from perfusate during EVLP of discarded human lungs. Initially, we had difficulties to secure funding from industry to support our proposal. Discussions continued throughout 2020 and the company has agreed to provide us some research funds to do a few pilot experiments. Thereafter, we worked on the setting up the research laboratories for performing simultaneous sing lung EVLP. In the meantime, the COVID-19 pandemic continued to have a negative impact on finding discarded human lungs to

perform this project during my stay in Leuven. Correspondingly, this project could not be performed yet.

In the meantime, we have proposed another multi-center clinical research project related to lung transplant candidates with a history of previous anatomical native lung resection. Patients with a previous anatomical lung resection require special attention regarding selection, preoperative work-up and advanced perioperative planning in the setting of lung transplantation. The knowledge in literature about this unique group of patients is scarce. Members of the ESTS Lung Transplantation Study Group were invited to submit data on patients undergoing single or double lung transplantation after a previous anatomical native lung resection, from segmentectomy till pneumonectomy between 01/2005 and 07/2020. From 7 participating center we identified twenty-six lung transplant recipients (14 men; mean age 36 ± 15 years) with a previous anatomical lung resection accounting for approximately 1% of the transplant activity of participating centers. In this study we concluded that history of anatomical lung resection is a rare clinical entity in lung transplant candidates. Most candidates are young and diagnosed with cystic fibrosis (CF) or non-CF related bronchiectasis. Although the numbers were limited, survival after lung transplantation in patients with previous anatomical lung resection, including pneumonectomy was comparable to reported conventional lung transplants. The results were presented during the 29th European Conference on General Thoracic Surgery in June 2021. The manuscript of this study is currently under preparation.

During my stay in Leuven, we proposed another clinical retrospective single-center review study related to a manual bronchial closure technique after pneumonectomy. Pneumonectomy remains indicated for the treatment of malign and benign lung pathologies. Currently, mechanical stapling devices are preferred for bronchial closure due to its proven safety and efficacy during pneumonectomies. Nevertheless, primary bronchial closure may still be required to address problems with surgical margins or the choice of a surgeon. The Leuven Program utilizes a unique manual bronchial closure technique described by the Dutch surgeon Klinkenbergh. In this study, we aim to review the results of a specific bronchial closure technique, Klinkenbergh in patients undergoing pneumonectomy due to malign or benign pathologies since 2000 at University Hospitals Leuven and highlight the factors affecting the development of bronchopleural fistula. The study is approved by the Ethics Committee and a total of 650 patients were identified from the database. A research fellow will conduct the analysis in the future.

Continuing Medical Education:

Our lives have significantly changed during the COVID-19 pandemic, also for participating scientific meetings and presentations. Virtual meetings have become the norm to overcome the barriers of in-person interaction. During my fellowship in Leuven, I was recognized by 2 invited presentations. The first one was organised by the XVIVO Perfusion group in March 2021. I delivered a talk titled “Attenuation of Ischemia-Reperfusion Injury through Inflammatory Mediators’ Removal during EVLP” in a webinar, which attached more than 150 participants worldwide. Secondly, I was honored to present at the “Future Leaders on Stage” session of the ESOT Meeting 2021 online. I summarised my international experience related to studying Ischemia-Reperfusion Injury in Lung Transplantation.

Furthermore, I participated several webinars and virtual congresses, such as 100th and 101st AATS Annual Meetings, 41st ISHLT Annual Meeting, 29th ESTS Meeting and ESOT Congress 2021. The ESOT 2021 Meeting was a great success for both in-person and online meeting. We will probably see more scientific meetings with a virtual component in the future, a novelty the COVID-19 pandemic has taught us.

Allocation of funds:

Postgraduate education abroad in a foreign country is costly especially when coming from a country where the currency is weak. Moreover, fellowship salaries are usually just enough to cover the cost of living. Throughout my career, I invested funds in personal development by graduating from a post-secondary degree program at the University of Toronto, mastering foreign language skills for English and German, becoming a registered practitioner in the UK, Switzerland, and Belgium. Until the receipt of ESOT Transplant Fellowship grant, I was under the pressure of ongoing financial stress related to these investments. I hereby declare that I have used the half of the funds to pay off the previous loans. The remaining half of the funds were allocated to support my expenses in Belgium. I will always be grateful for the honour of fellowship and the financial support from ESOT.

Conclusion:

After spending 19 months, I am pleased to conclude a productive fellowship in Leuven. First and foremost, I would like to express my sincere gratitude to my supervisors, Profs. De Leyn, Van Raemdonck, and Ceulemans. They were very helpful and supportive from the moment I have been selected as a fellow till the end of my fellowship. The fellowship has reached its aims by participating significant number of operations actively for both lung transplant and general thoracic procedures. Although the COVID crisis had a negative impact on the proposed research study, we could conclude a European multi-center clinical research study during my fellowship. Surely, I will carry the Leuven experience into my future practical life. I will also be committed to support ESOT activities during my career and encourage young professionals to be a part of this exciting society. With this opportunity, I would like to express my sincere gratitude to the selection committee for this honour again.

Sincerely yours,



Ilker Iskender, Leuven, Belgium