Master Thesis

Organ donation:
Organization structure, measures of success, estimation of demand

submitted by

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Declaration

I hereby declare that the following diploma thesis has been written only by the undersigned and without any assistance from third parties. Furthermore, I confirm that no sources have been used in the preparation of this thesis other than those indicated in the thesis itself.

Graz, 5.11.2020 *Vanessa Stadlbauer-Köllner eh*

Preamble

Organ transplantation is a relatively "new" chapter in medicine - the first long-term successful transplants were performed in the late 1960s. The possibility of saving or extending lives by transplanting organs from deceased people often causes debates - ethically, politically, socially, and organizationally. In order to save or extend life through organ transplantation, a functioning organ donation system is required. In Austria, the organ donation process has been optimized in the last decades through political measures and above all through the commitment of outstanding personalities, for example in Prim. PD. Dr. med. Michael Zink, who is also the supervisor of this thesis. Compared to other countries, Austria has achieved a high number of utilized organ donors per million inhabitants. However, despite these high numbers of organ donors, each year 70-80 people die in Austria while on a waiting list for organ transplantations and 20-30 are removed from the waiting list because they are unfit for transplantation (with a high dark-figure because of different policies how waiting list dynamics are managed between centers). Thus, the question arises whether the available number of organ donors is sufficient or whether the demand would actually be greater.

I am working in the field of organ donation and organ transplantation for 22 years and I was and I am covering different roles in this field – from being a perfusionist and a transplantation coordinator as a medical student to leading the research unit transplantation research at the Medical University of Graz, being a local transplantation coordinator and leading a study module for medical students on transplantation medicine. In this thesis I will combine my knowledge in the field of organ donation and transplantation with hospital management aspects by describing and comparing the existing organizational measures to promote organ donation in successful and less successful countries and by aiming to assess the true demand for organ donation in Austria for the example of liver transplantation.

Acknowledgement

I thank my supervisor Prim. Michael Zink for the excellent support during this work, the exciting discussions on organ donation, transplantation and many other topics over the years and for his friendship.

I thank my family - my husband Werner and my daughters Sara and Sophia - for supporting me in my decision to pursue this MBA in Health Care and Hospital Management in addition to my other duties, which limited my already limited time resources even further at the expense of „family time“.

I also wish to thank my boss, Univ. Prof. Dr. Peter Fickert, who supported me to pursue this MBA and the study nurses of the liver clinic Andreas Posch, BSc and Andrea Streit, BSc who assisted me with data collection from the tumor-boards. Finally, I would like to thank Univ. Prof. Dr. Helfried Metzler and his team for the organization the MBA in Health Care and Hospital Management and the great support.

Zusammenfassung

Organspende ist die Voraussetzung für erfolgreiche Organtransplantations-programme. Um eine ausreichende Anzahl an Spenderorganen zur Verfügung zu haben, bedarf es Organisationsstrukturen. Der gesamte Prozess von der Erkennung potentieller hirntoter Organspender*innen über die Kommunikation mit den Angehörigen, die Durchführung der Hirntoddiagnostik, der intensivmedizinischen Betreuung von hirntoten Organspender*innen bis zur Organentnahme und Allokation muss in diesen Organisationsstrukturen abgebildet sein. Da es sich um ein einerseits für manche Beteiligten emotional belastendes und andererseits organisatorische komplexes Feld handelt, sind unterschiedliche Länder unterschiedlich erfolgreich in der Umsetzung des Ziels der „self-sufficiency“ in der Organspende.

Diese Masterarbeit beschäftigt sich mit der Analyse der Prozesse der Organspende aus einer Management-Perspektive und geht der Frage nach, wie hoch der wahre Bedarf an Spenderlebern in Österreich wäre.

Für die Analyse der Prozesse der Organspende wurden die vorhandenen Prozesse und Strukturen in Österreich, Deutschland, der Schweiz und Spanien verglichen und diskutiert. Es zeigt sich, dass trotz ähnlicher Strukturen und Prozesse die Ergebnisse sehr unterschiedlich sein können. Dies hebt hervor, dass neben den Strukturen und definierten Prozessen auch die agierenden Persönlichkeiten eine wichtige Rolle für den Erfolg spielen. Die Analyse der Systeme zeigte außerdem, dass es wichtig ist, relevante Qualitätsindikatoren für Organspendeprogramme zu entwickeln.

Die Analyse des Bedarfs an Spenderlebern in Österreich ergab, dass jährlich 5.7 Leberspender*innen pro Million Einwohner*innen fehlen, um alle Patient*innen auf der Warteliste rechtzeitig zu versorgen. Weitere 8.4 Leberspender*innen pro Million Einwohner wären notwendig um den vorhandenen, aber derzeit nicht abdeckbaren Bedarf im Bereich onkologischer Lebertransplantations-Indikationen decken zu können. Die Umfrage zum Organmangel in Österreich ergab, dass bis zu 10% der Ärzt*innen, die Entscheidungen treffen, ob Patient*innen auf die Leberwarteliste kommen, den Organmangel in ihre Entscheidungen einfließen lassen und mehr Patient*innen für die Warteliste empfehlen würden, wenn es mehr Organe gäbe. Durch den demographischen Wandel und Veränderungen in

der Epidemiologie von Lebererkrankungen ist mit einer weiteren Steigerung des Bedarfs zu rechnen.

Insgesamt besteht in Österreich ein gut funktionierende Organspendesystem. Die von der World Health Organisazion (WHO) geforderte „Selbsterhaltungsfähigkeit“ kann in Österreich bei Lebertransplantationen aber auf Kosten von Todesfällen auf der Warteliste sowie bei strengen Richtlinien für die Auflistung von Patienten mit onkologischen Indikationen noch nicht erfüllt werden. Es ist davon auszugehen, dass 40-45 Organspender*innen pro Million Einwohner notwendig sind, um den aktuellen und zukünftigen Bedarf zu decken. Die weitere Optimierung der Organspendeprozesse, neue Methoden wie Maschinenperfusion und chirurgische sowie organisatorische Fortschritte sowie die Förderung der Organspende nach Herztod sind notwendig um den steigenden Bedarf zu decken. Aufklärungsarbeit und kontinuierliche Evaluierung und Optimierung von Organisationsstrukturen sind relevante Managementmaßnahmen um dieses Ziel zu erreichen.

Abstract

Organ donation is the prerequisite for successful organ transplantation programs. Organizational structures are required in order to have a sufficient number of donor organs available. The entire process from identifying potential brain-dead organ donors to communicating with relatives, carrying out brain death diagnostics, over intensive medical care for brain-dead organ donors to organ removal and allocation must be mapped in these organizational structures. Since this is an emotionally stressful field on the one hand, and an organizationally complex field on the other, different countries have different levels of success in reaching the goal of self-sufficiency in organ donation.

This master thesis aims to analyze the processes of organ donation from a "hospital management" perspective and aims to answer the question of how high the true need for donor livers in Austria would be.

To analyze the processes of organ donation, the existing processes and structures in Austria, Germany, Switzerland and Spain have been compared and discussed. Despite similar structures and processes, the organ donation rates vary between the analyzed countries. This shows that in addition to the structures and defined processes, the personalities involved also play an important role to implement a successful organ donation and procurement program. The analysis of the organ donation systems also showed that it is important to develop relevant quality indicators for organ donation programs.

The analysis of the true need for donor livers in Austria showed that in the last 10 years there was a shortage of 5.7 liver donors per million inhabitants. Another 8.4 liver donors per million inhabitants would be necessary to meet the needs in the area of oncological liver transplant indications. And the survey on donor organ shortage showed that up to 10% of the doctors who make decisions about whether patients should be placed on the liver waiting list would include the organ shortage in their decisions and would recommend more patients for the waiting list if there were more organs available. Demographic changes and changes in the epidemiology of chronic liver diseases will further increase the demand for liver transplantation in the near future.

Overall, there is a well-functioning organ donation system in Austria. Self-sufficiency - as required by the World Health Organisation (WHO) – is not met yet

for liver transplantations at the expense of deaths on the waiting list as well as strict policies for listing patients with oncological indications. 40-45 brain dead organ donors per million population will be necessary to meet the current and near future demand in Austria. Additional measures to optimize the organ donation process, surgical and logistic advances, machine perfusion and the development of donation after cardiac death programs will be necessary to meet the demand. Educational work and continuous evaluation and optimization of organizational structures are relevant management measures to achieve this goal.

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Abbreviations

Liver transplantation LTX

Lokale Transplantationsbeauftragte LTXB

Hepatocellular carcinoma HCC

Transplantation Procurement Management TPM

Transplantation Procurement Management specialist TPMs

Organización Nacional de Trasplantes ONT

World Health Organisation WHO

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1 Introduction

Organ donation is the prerequisite for organ transplantation. For many patients with end-stage disease, organ transplantation is the only therapeutic option to save their lives and/or to improving their quality of life. However, since the demand on organ donation is always higher than the availability. This is also true for Austria, despite a high number of organ donors when compared to many other countries.

A positive attitude of the general public and health care professionals towards organ donation is vital for patients on the waiting list. These patients are dependent on the political attitude towards organ donation, the public opinion influencing the rate of consent or opt-out, and the willingness of hospital staff to report organ donors and perform the organ procurement procedure. In addition to these factors, also professional organization of the process of organ donation is the key to success.

Organ donation is a complex process. During this process many people from different medical disciplines and with different goals need to cooperate to ensure success of the organ donation process: The donor hospitals have to identify potential donors. Before an organ is removed, the unequivocal determination of death by independent physicians is the necessary prerequisite. During that period, intensive care treatment for the potential organ donor needs to continue. The quality of the organs and the opinion of the deceased person regarding organ donation need to be assessed. Different medical tests (blood tests, imaging studies, HLA determination etc.) need to be carried out in advance of any organ removal. During all these procedures the health care professionals have to deal with the bereaved family of the deceased person. Once death is proven, the organ donor is reported to the coordination center in charge. This is typically located at the transplant center. A transplant coordinator from the coordination center supports the donor hospitals in all organizational matters, prepares the tissue typing and organ removal and reports the organ donation to the respective organization – in the case of Austria to Eurotransplant in Leiden (Netherlands).

Austria is a member of Eurotransplant together with the Netherlands, Belgium, Luxembourg, Germany, Croatia, Slovenia and Hungary. Eurotransplant is a non-profit association based in Leiden (the Netherlands). Eurotransplant monitors the quality standards for organ donation and transplantation, keeps the waiting lists of the recipients of all member countries and determines the recipient who should receive the reported organ (organ allocation). As more than 118 million people live in the Eurotransplant region, being a member of this organization increases the chances of finding a suitable organ in good time, especially for patients who urgently need an organ or have rare tissue characteristics.

After the potential recipient has been selected by Eurotransplant, the transplantation center, where the patient is listed, receives an alert with the necessary data of the potential donor organ. When the transplantation center accepts the offer, the patient is informed and gets prepared for the transplantation. At the same time, a surgical team retrieves the organs from the donor in the donor hospital and the organ are transported to the transplantation center in a special transport container. Since the quality of the donor organ and thus its survival depends on the period between organ removal and transplantation (ischemia time), it is important to ensure the fastest possible transport between centers.

It is clearly visible from this short description of the complex process of organ donation that this process involves many people and organizations and also carries an emotional burden for some of the involved people. Therefore, clear and transparent organization and communication is of utmost importance to avoid friction in this process.

1.1 History of organ transplantation and organ donation

1.1.1 From myths to modern medicine

The idea to replace organs or body parts by living human tissue is a fascinating topic since several millennia. Hindu and Greek mythological texts as well as the bible mention procedures that can be interpreted as transplantations, sometimes in great detail. The legend of the Christian saints and physicians Cosmas and Damian, that is shown on several paintings, who “successfully” transplanted an entire leg of a black man to a white man who lost his gangrenous leg, is usually referred as one of the first descriptions of a transplantation, but it is highly questionable if this transplantation really took place. These descriptions however show the fascination of the possibility of successful transplantation over millennials and across cultures. (1)

Figure 1: Cosmas and Damian miraculously transplant the black leg of the Ethiopian onto the white body of the patient, Landesmuseum Württemberg,

Stuttgart, Germany (Wikimedia Commons)

Autogenous skin flaps were most likely the true first successful transplantations that possibly already took place as early as 600 b.c. Several surgeons in the 16th century successfully replaced missing noses or ears with this technique. Also, skin homografts were tested and interestingly, the possibility, that homografts could fail, was ignored over centuries. This ignorance prevented the understanding of immunologic processes in transplantation and impacted negatively on the discovery of mechanisms of transplantation immunology. (1)

Development of successful transplantation of organs and tissues was not only a matter of improved surgical technique but most importantly of the understanding of transplantation immunology. The history of transplantation immunology is turbulent with several scientific dead-ends, ignorance of important findings for several decades due to personal antipathy on the one hand and lucky strikes of other researchers on the other hand. (1)

Although transplantation immunology was already well understood from animal data in the 1950s, the lack of safe immunosuppressants was a major hurdle in successful human transplantation. The first successful human kidney transplantation was performed in 1954 in identical twins. Although this transplantation was not an outstanding scientific achievement – technically kidney transplantation was already well developed and the acceptance of tissues between identical twins has also been demonstrated before – this created a significant impact for the field of transplantation research by widespread enthusiastic reports that were an important stimulus for surgeons to pursue further efforts in transplantation. However, since prevention of allograft rejection was difficult at that time, long-term success of technically functioning kidney transplants was poor outside of the immunologically privileged situation of identical twins. Leading experts in the field of transplantation were heavily discouraged by these results and already discussed discontinuation of transplantation programs. Thomas Starzl was the first transplantation surgeon with satisfying long-term results of kidney transplantation, not so much because of his outstanding surgical skills but because he developed a drug combination to achieve immunosuppression that was tolerated for longer time without the risk of rejection. Between 1963 and 1968 also liver, heart, pancreas and lungs were successfully

transplanted for the first time. In the following years the success of organ transplantation increased steeply, mainly because the protocols for immunosuppression were optimized and new drugs like cyclosporine and tacrolimus were developed. These technical advances transformed organ transplantation from a medical sensation to a standard treatment of many end-stage disease. (1)

1.1.2 History of organ transplantation and donation in Austria

Austria has a longstanding history in organ transplantation. Several “firsts” worldwide have been performed in Austria. Even before human transplantation became a true therapeutic option, research in the field of transplantation was pioneering in Austria. In 1902, the first successful kidney transplant ever was performed by E. Ullmann in Vienna. The first clinical renal transplant in Austria was performed in 1965 by F. Piza in Vienna. Also, the first successful multi-visceral transplant including the entire small bowel worldwide took place in Innsbruck in 1989 with R. Margreiter and A. Königsrainer, two leading personalities in the Austrian (and later also German) transplantation community for centuries, being the surgeons. (2) These and many other pioneering transplants led to three multiorgan- and two kidney-transplant programs in Austria and generated activities that are among the best worldwide in terms of volume, and also quality. As described above, for successful transplantation programs successful organ donation programs are the prerequisite. In 2001 the Federal Health Commission (Bundesgesundheitskommission) initiated a donor action program. The project “Support for organ donation” (Förderung der Organspende) focusses on the implementation of appropriate measures to increase the number of organ donors. The program aims to improve the identification of potential organ donors, the reporting and management of potential and actual organ donors e.g. by supporting the communication with families, supporting the appropriate intensive care management. (3)

1.1.3 Institutionalization of organ donation

In the early years of organ transplantation, there was no necessity to develop a system of organ donation. Most of the earliest kidney transplantation were living donations, the first heart and liver transplantations were performed from donors who died from circulatory death. Because these procedures were highly individualized in the early era, the search for a suitable donor organ started only after a recipient was identified. There is remarkably little information on the dynamics of identifying, consenting, and retrieval of the early cadaveric organs in the early clinical transplantation era in the 1960s. Legal and ethical frameworks as well as organizational structures for organ donation followed the success of organ transplantation. The definition of death, organ sharing networks and organ procurement structures are the framework for successful transplantation programs. (4)

The clear definition of death is the prerequisite for successful, ethically sound and generally accepted transplantation programs. The most important process was the definition of death – while this sounds trivial, it was a huge medical, ethical and legal developmental effort to define death unequivocally and also ensure that organs can be recoverable and functioning in a recipient. The concept of brain death was introduced 1968 by the “Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death” and is still the valid medico-legal basis for todays´ definitions used in all transplantation programs, however, there are differences in some details of how brain death is exactly determined between different countries. The rising demand for cadaveric organs relative to a static cadaveric organ supply in the 1990s led to the development to alternative concepts of organ donation. Donation after circulatory death, e.g. after withdrawal of life support in patients with irreversible conditions and no contraindications for organ donation or after failure of return of spontaneous circulation during resuscitation, was developed to widen the pool of available donor organs. This transformation from a brain-death-only definition to a donation-after-circulatory death definition is critically discussed and remains a major bioethical controversy in the medical community. Interestingly however, before the introduction of the brain death definition in 1968, donation after circulatory death was the common

practice how cadaveric organs were retrieved in the earliest days of clinical transplantation. (4)

1.1.4 Organ donation and procurement process

From a philosophical perspective, organ transplantation is possible due to a new vital cycle, enabling a society which donates and has a transplantation coordination system to benefit from this process. Several processes and factors are important in this new vital cycle: Societies' attitude depending on cultural, religious, economic and educational factors, the organizational structure to ensure organ procurement and sharing to allow that organs are allocated in the most ethical and fairest possible way, transplantation and follow up in authorized centers that allow the best possible success of transplantation. (5)

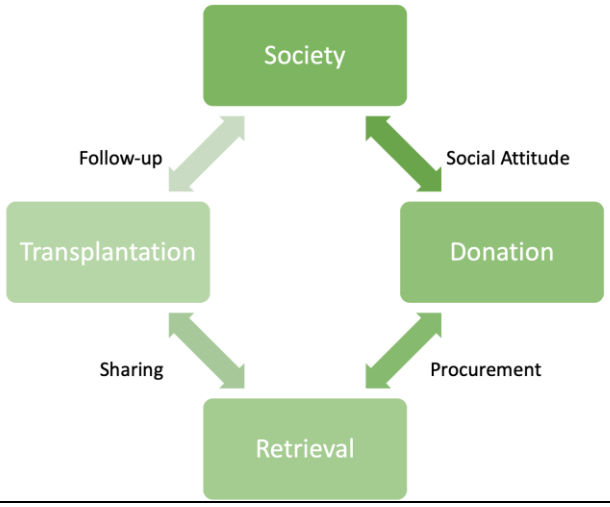

Figure 2: New vital cycle of the donation and transplantation process (adapted from (5))

From a hospital management perspective several key processes during organ donation and organ procurement need to be optimized to increase the number of available donor organs and transplantations. The process that links organ donation to organ sharing and facilitates organ transplantation is called organ procurement process. The most renowned program to optimize the organ procurement process is the Spanish Transplant Procurement Management (TPM®) program. From a hospital management point of view, donor detection and

clinical evaluation, diagnosis of brain death, organ donor management and organ viability assessment, family approach for organ donation and organ retrieval are the key processes that need attention to facilitate a functioning organ procurement process. (5) These processes are highly interrelated and therefore highly skilled personnel is necessary to avoid unnecessary loss of donor organs.

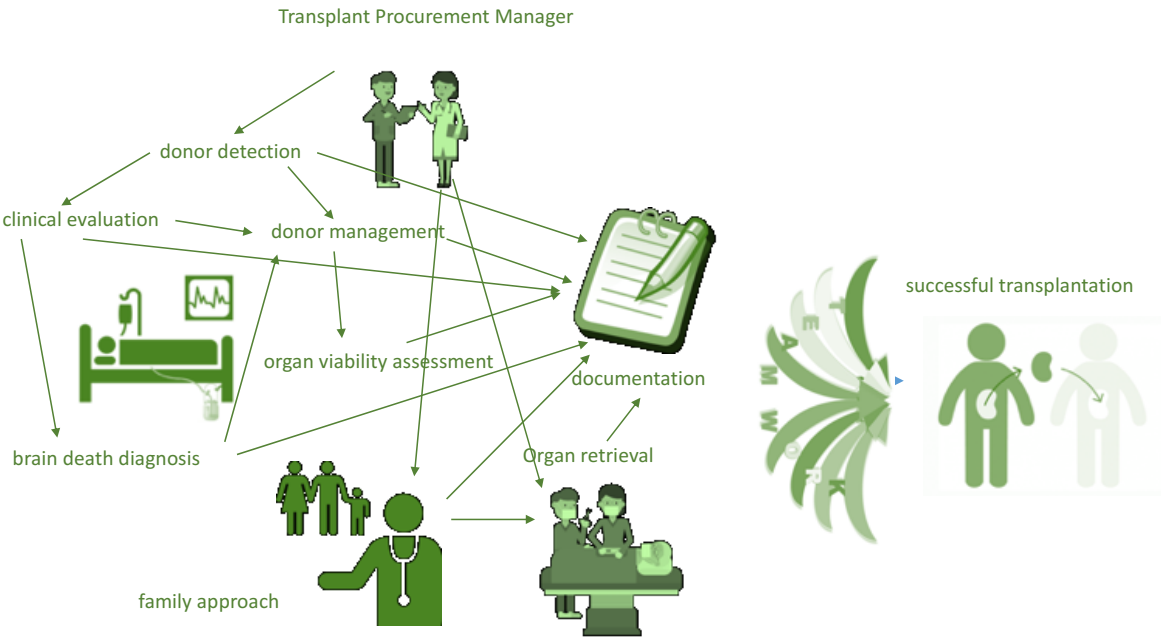

Figure 3 shows the relationship between these processes that ultimately lead to the successful transplantation of organs (all icons were downloaded from Wikimedia Commons under creative commons license)

1.1.5 European organ sharing network - Eurotransplant

Successful organ transplantation programs can – at least for the time being - only exist within an organ sharing network because the obligate ischemia developing in organs after removal from the donor's body do not allow the prolonged banking of organs. To allow the optimal use of all available organs, several centers need to be organized within an organ sharing network. (4) One of the pioneering organ sharing networks in the world was Eurotransplant (Eurotransplant International Foundation), founded in 1967 by Prof Jon J. van Rood from the Leiden University Medical Center in Leiden. The organization started as a scientific experiment of twelve transplant centers who voluntarily shared data on transplant candidates

and donors to optimize matching of donors and kidney transplant recipients. Today the Eurotransplant network consists of Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands and Slovenia, serving a total population of around 137 million people. Furthermore, agreements have been made with 17 other organ exchange organizations in Europe to facilitate international organ exchange on cases when no matching recipient can be found within the Eurotransplant area. (6)

Eurotransplant facilitates the allocation and cross-border exchange of deceased donor organs. Partners in the organ exchange process are hospitals where organ donations take place, national organ procurement organizations, transplant centers, tissue-typing laboratories and national competent authorities. All these parties work together with the aim to ensure that the best possible match between donor organs available and patients on the transplant waiting list is made. (6)

The journey of a donated organ within the organizational structure of Eurotransplant is shown in figure 4. When a deceased organ donor is identified, consent or the absence of an opt-out is assessed in the donor hospital. Medical experts assess in the hospital which organs can be donated (heart, lung, liver, pancreas, kidney, intestine). Thereafter the hospital registers the donor at Eurotransplant. The donor's blood group and tissue characteristics and a predefined medical dataset is sent to Eurotransplant via a secure data connection. Data are transferred in a pseudonymized way. At Eurotransplant, data from the donor organs are matched with patients on the waiting list and allocated to the most suitable recipient. Eurotransplant then offers the donor organs to the respective transplant centers. The transplant centers evaluate the organ offer and accept or decline the offer. Once all organs are allocated, the organs are removed surgically from the deceased donors´ body. The organs may need to be transported from the donor hospital to transplant center by the fastest means possible. The transplantation of the organs is performed immediately after the organ arrives at the transplant center. Recipients receive regular check-ups at the transplant center following transplantation. Data gathered during organ donations and transplantations together with recipient's follow-up data help Eurotransplant to improve the allocation process. (6)

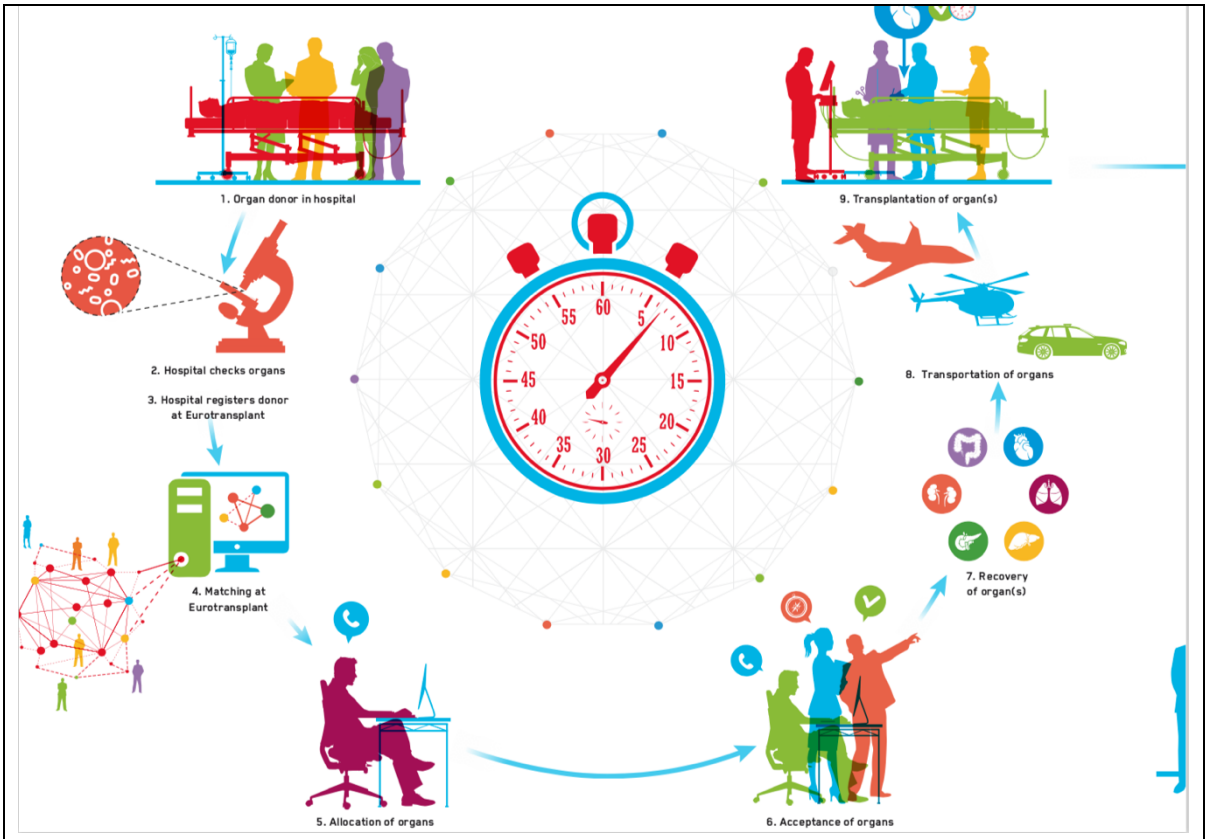

Figure 4 From one human to another: The journey of a donated organ (© Eurotransplant press downloads, downloaded 24.3.2020)

1.1.6 Organ donation potential

Estimating the necessary number of potential organ donors to be able to fulfill the demand is an equally important and difficult task. For the USA, medical records from 36 organ procurement organizations between 1997 and 1999 were analyzed and found out that the rate of potential organ donors (defined as people who died from brain death without an absolute contraindication against organ donation) could be as high as 50/million population whereas the rate of actual organ donors was approximately 21/million population during the study period. (7) The authors identified three factors in the donation process that affected the conversion rate (the number of actual donors divided by the number of potential donors): the rate of hospital referral, the rate of requests made to families, and the rate of consent by families. This publication also showed that larger hospitals (more than 150 beds) and the presence of a neurosurgery service were associated with higher numbers of potential and actual donors. In the USA large variations between different organ-procurement organizations were observed. This paper created

considerable discussion in the community. The optimal measure of success of an organ procurement organization was discussed, since the number of actual donors only weakly correlates with the number of potential donors who become actual donors, which may be the better assessment of performance of different organ-procurement organizations or different geographic regions. Also, the usefulness of labor intensive and time-consuming retrospective audits of medical files was questioned. To allow prospective evaluation and thereby quality management, the claim for the creation of a specific code for brain death in the International Classification of Diseases, that would facilitate studies and comparisons based on mortality data, was made – however without success until today. (7-10)

When looking at the organ donation process from a management point of view, the identification of useful and reliable operating figures is of importance to be able to set realistic goals and to monitor target achievement. A common systematic approach to the process of deceased organ donation is needed to facilitate the practical development and progressive increase of deceased donation activities. Based on the Consultation on Organ Donation and Transplantation of the World Health Organization (WHO) in 2010 a working group developed the critical pathway of organ donation as a systematic approach to the organ donation process. The pathway provides a tool for assessing the potential of deceased donation and for the prospective identification and referral of possible deceased donors. (11, 12) Figure 5 shows the critical pathway of organ donation for donation after brain death.

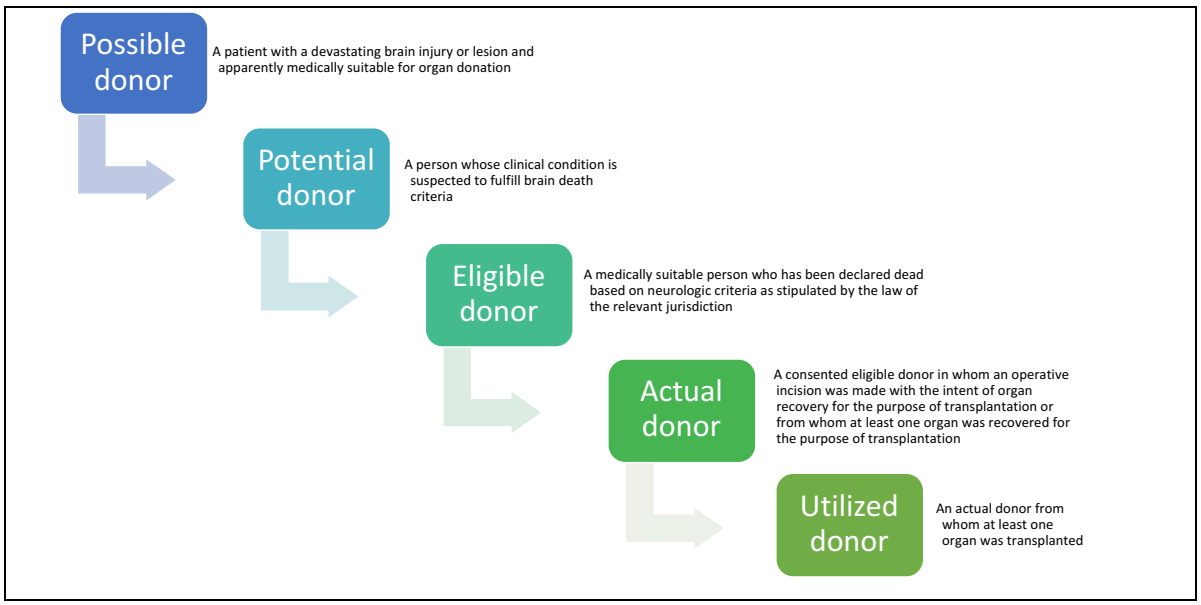

Figure 5 Critical pathway of organ donation, adapted from (1)

2 Aims

This thesis aims to analyze the process of organ donation and organ procurement from a hospital management perspective and aims to quantify the true demand of donor livers in Austria.

The **first aim** is to analyze the organizational structure of the organ donation and organ procurement process in Austria, Germany, Switzerland and Spain and connect this information with the success of organ donation programs in the respective countries.

The **second aim** is to determine, how many donor livers from deceased organ donors in Austria would be needed for self-sufficiency in liver transplantation. To fulfil this aim, the "organ donation gap" for livers in Austria compared to Germany was analyzed over the last decade by assessing how many patients died on the waiting list or were removed from the waiting list due to deterioration of their disease. A questionnaire was distributed to professionals involved in the field of transplantation in Austria to understand the impact of donor organ shortage on decisions to evaluate or list patients for liver transplantation. Further, the potential additional need for liver donations was assessed for the oncological indication of liver transplantation since in this case strict rules are in place which patients can be listed for a transplantation due to the shortage of donor organs while evidence is available that also many patients outside these criteria would benefit from a transplantation.

In conjunction, the information collected in this thesis will serve as a reference on processes to improve rates of deceased organ donation and will define the true demand of liver donation in Austria.

3 Methods

3.1 Review of the organization structure of the organ donation

To fulfill the first aim, which comprises the theoretical part of this thesis, the official websites of the organ donation organizations were used as a starting point. Additional detailed information from either legal texts, scientific publications or books have been gathered. The countries were chosen by the following rationale: Austria, because it is the country of origin of the author of this thesis; Germany and Switzerland as neighboring countries – Germany as a member of Eurotransplant and Switzerland, which is not a member of Eurotransplant but has a comparable legal framework for organ donation to Germany. Spain was chosen as a best practice example because of its success in organ donation.

The primary websites to gather information were:
https://transplant.goeg.at/ for Austria
https://www.dso.de/ for Germany
https://www.swisstransplant.org/de/ for Switzerland

For Spain, the Transplant Coordination Manual (5) was used as primary information, since web based information is mainly available in Spanish.

Additional literature search was performed in Pubmed and Google Scholar using the keywords “organ donation” “organ procurement” and the respective country names.

The assessment of the organ donation and organ procurement process was performed in a structured procedure and contained the assessment of the current status of the following predefined topics during the process of organ donation:

1) Legal framework
2) Process of identification of potential organ donors
3) Process of brain death diagnosis

4) Process of family approach
5) Medical treatment of the donor
6) Process of organ allocation
7) Process of organ retrieval

To assess the success of organ donation and organ procurement in each country the numbers for utilized donors per million population, the number of transplanted organs and the ratio of transplanted organs per donor were assessed for the past 10 years from the Eurotransplant statistical data website and the IRODaT website.

3.2 Assessment of organ donation demand

To assess the true demand of deceased donor livers, three empirical approaches were employed. First, data from the Eurotransplant statistical data service were analyzed to study the dynamics on the waiting list between 2010 and 2018. Patients who were removed from the waiting list because they were unfit for transplantation and those who died on the waiting list were defined as the patient group who would have had a demand for transplantation but did not receive a transplantation in time due to the lack of organ donors. To bring these data into context, the same analysis was attempted for Germany, Switzerland and Spain. Permission to use these data from Austria and Germany was granted on 06.03.2020 by the Eurotransplant statistical data service by Maya de Beer (request number req132.2020). Data for Switzerland and Spain were searched from publicly available sources. Additional data for Switzerland and Spain were requested from Swisstransplant and the IRODaT database, however, despite initial positive feedback (from Swisstransplant in March 2020), no further data could be obtained from Switzerland and Spain.

Literature review in Pubmed and PubPsych revealed that to questionnaire is available to assess organ donation demand. Therefore, a questionnaire was developed by the author of the thesis. Content and face validity was assessed by 10 independent health care professionals. Since no gold standard for this assessment is available, no further tests for validity or reliability could be

performed. Permission to use this questionnaire was obtained from the local research ethics committee (32-324 ex 19/20). The questionnaire was distributed electronically via the Austrian Society of Transplantation (Austrotransplant) and the Austrian Society for Gastroenterology and Hepatology (ÖGGH) as a web-based survey using SurveyGizmo between 22.6.2020 and 14.8.2020. Data were exported as .csv file.

To quantify the potential additional demand of deceased liver donations for oncologic indications, data from all patients who were discussed in the hepatocellular carcinoma (HCC) tumor-board of the Medical University of Graz were assessed regarding their tumor stage at first presentation. Permission to use these data was obtained from the local research ethics committee (32-324 ex 19/20). Raw data were manually collected from paper-based documentations of the tumor-boards in an excel file. Tumor size, number of tumors and alpha-feto-protein levels (AFP) were collected. Analysis of tumor stage was performed manually by categorizing the obtained data into either inside or outside the Milan, up-to-seven, UCSF or Metroticket 2.0 criteria.

All data are presented as ratio of patients per million population. The official population figures from Eurostat were used and rounded to 0.1 million. (13)

For statistical analysis IBM SPSS statistics V26 (IBM, Armonk, NY) was used. Data were analyzed for normality by the Shapiro-Wilk test. Descriptive statistics (frequency, percentage, median and variance) as well as deductive statistics (Chi square tests and Pearson´s correlation) were performed. A $p<0.05$ was considered as statistically significant. Graphs were prepared in Excel for Mac, Powerpoint for Mac and GraphPad Prism 7 for Mac OS.

4 Results

4.1 Organ donation and organ procurement processes

4.1.1 Austria

Austria has an opt-out system for organ donation. People, who do not want to donate their organs after death can enroll in an objection register that is administrated by the "Gesundheit Österreich GmbH". A federal law on the transplantation of human organs (Organ Transplantation Act – OTPG) (14) is in force in Austria since December 14, 2012, which contains regulations on the following sub-areas: Principles of donation, removal of organs from the deceased for the purpose of transplantation, objection register, obligations of the procurement units, living donation, follow-up care for living donors, standard operating procedures, organ and donor characterization, transport of organs, traceability, organ vigilance, records and reports, automation-supported data traffic, international organ exchange and administrative penalty provisions, (3)

The Coordination Office for Transplantation (ÖBIG-Transplant) was established in 1991 on behalf of the federal ministry responsible for health to coordinate activities in transplantation nationwide. ÖBIG-Transplant is responsible for the statistical-administrative part of organ donation in Austria as well as for ensuring important services, such as keeping the objection register, creating guidelines, updating standard operating procedures and supporting donation related projects. (3)

The project "Maßnahmen zur Förderung der Organspende" (support for organ donation) is active since 2001. ÖBIG-Transplant defined guidelines on the specific use of funds. The measures proposed therein aim to ensure continuity in the donor volume at a constantly high level and to further increase the number of reported donors. Several measures were put in place to reach these aims: Payment of reimbursement of costs to hospitals that report donors, since not all services in connection with donor care are covered by the hospital funding; establishment of regional transplantation coordinators (Transplantations-ReferentInnen) who provide educational work in the area of donor recognition and support and support

the intensive care departments in this area; establishment or financing of mobile brain death diagnosis teams in regions with no or insufficient opportunities for brain death diagnosis; payment of reimbursement of costs for the services of the transplant coordination centers, which act as the central point of service for the coordination of organ donation and transplantation; reimbursement to cover organ transport costs; establishment of local transplant coordinators (lokale Transplantationsbeauftragte, LTXB) in selected hospitals who are available as contact persons for all questions regarding organ donation. Further projects to increasing professionalization of the staff in the intensive care units were initiated, such as communication seminars, lectures in nursing schools and training for transplant coordinators.

In Austria donor identification was identified as the most critical step in the organ donation process. Potential organ donors are identified by intensive care staff in hospitals who have many other duties and identifying organ donors may not be their number one priority. Therefore, from 2009, local transplant coordinators, as equivalent to the proposed TPMs (Transplantation Procurement Managers) in the Spanish model (see below), have been established in selected hospitals. These are medical professionals who act as contact persons for all questions regarding organ donation and raise awareness for organ donation. In contrast to Spanish TPMs, these posts are not full-time jobs but are pursued as additional responsibility by full-time hospital employees. The LTXB have specific knowledge in the areas of donor identification and donor management and pass on their knowledge to colleagues. (3) They also retrospectively analyze all deaths with primary or secondary brain damage in intensive care units in order to assess in individual cases why an organ donation did not take place. This survey enables to assess the actual potential of organ donors and to identify potentials for improvement and measures to increase organ donor reports to the transplant centers. (3)

For brain death diagnosis a detailed standard operating procedure has been published by the Supreme Medical Council (Oberster Sanitätsrat). In some regions in Austria, mobile brain death diagnosis teams are available for hospitals where brain death diagnosis cannot be performed due to lack of equipment and/or trained staff. To support intensive care staff with family approach and medical treatment of the donors, recommendations are published and updated regularly.

(3) These recommendations, as well as further region specific details, can also be accessed via a free smartphone or web app. (15) Furthermore, communication training seminars are offered for intensive care unit personnel on how to approach families of potential organ donors. The process of organ allocation and organ retrieval is organized by the transplantation coordinators who are employees of the hospitals and who work according to standard operating procedures in close cooperation with the donor hospital and Eurotransplant. (3)

These efforts led to a high and stable numbers of utilized organ donors over the last decade in Austria. Also, the number of transplanted organs is high in Austria. This resulted in a high and stable rate of organs per donor between 3 and 4 organs. Figures 6-8 show the number of utilized organ donors per million population, the number of transplanted organs per million population and the rate of organs transplanted per donor in Austria between 2010 and 2019. Raw data were provided by Eurotransplant.

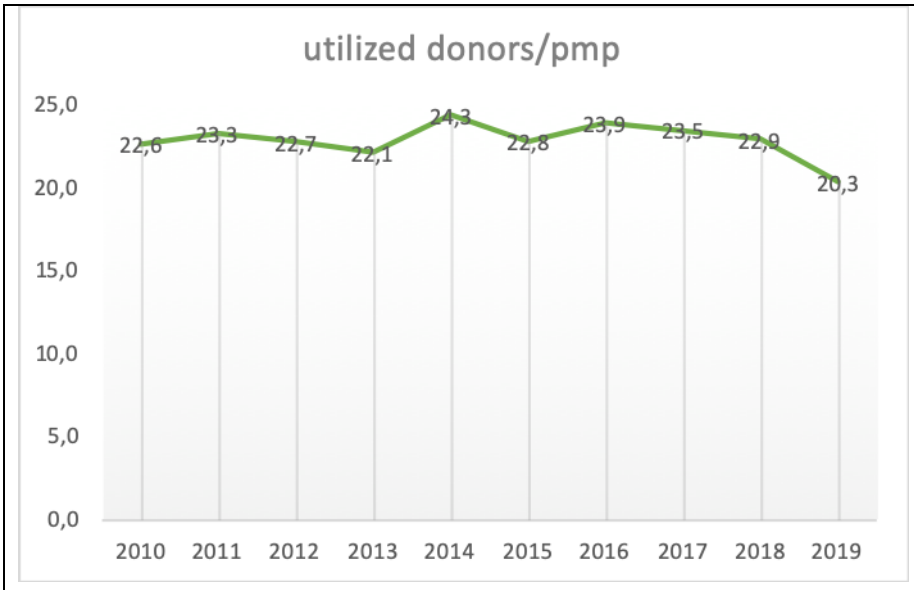

Figure 6 Utilized deceased organ donors per million population (pmp) in Austria between 2010 and 2019 (Data have been provided by Eurotransplant)

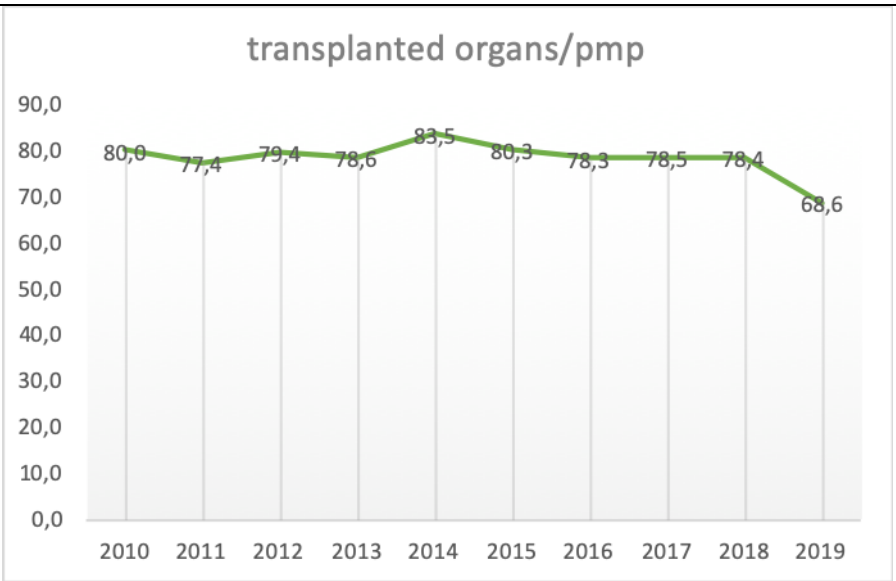

Figure 7 Transplanted organs per million population (pmp) in Austria between 2010 and 2019 (Data have been provided by Eurotransplant)

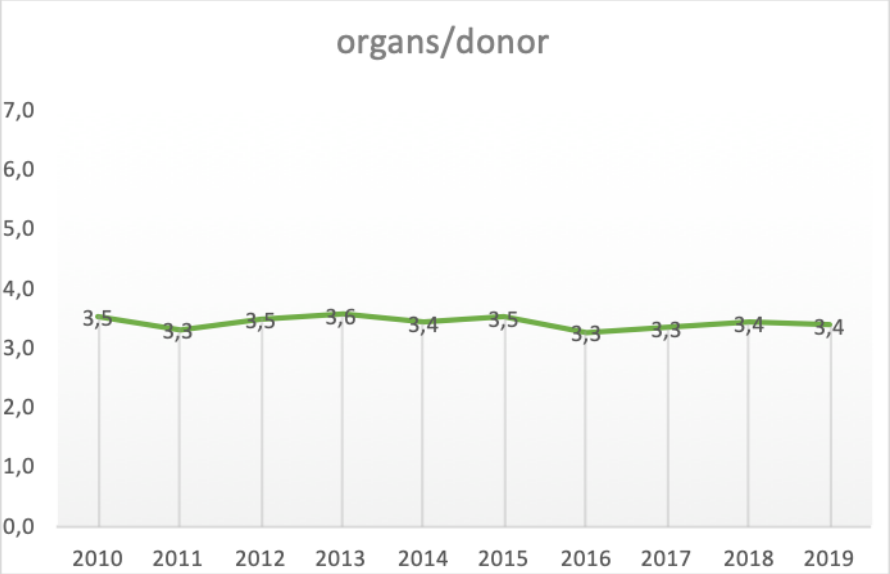

Figure 8 Transplanted organs per donor in Austria between 2010 and 2019 (Data have been provided by Eurotransplant)

4.1.2 Germany

In Germany organ donation and transplantation is regulated in the "Transplantationsgesetz". (16) Germany has an opt-in solution. In 2012 a declaration-based decision model was introduced. Every person in Germany aged 16 and older is now regularly asked by his or her health-insurance carrier to

decide on and document an organ-donation status (“yes,” “no,” “yes with reservations” or transfer of decision-making competence to another person). If no declaration is available, the decision is deferred to the next of kin. This law was under discussion in the last years in Germany, and a poll was demanded on the 26th of January 2020 in the “Bundestag”. The majority of the delegates voted for the existing opt-in law. The German Foundation for Organ Transplantation (Deutsche Stiftung Organtransplantation, DSO) is the nationwide coordination point for deceased organ donation in Germany. The DSO organizes all steps of the organ donation process when they are notified by a donor hospital that there is a potential donor in the hospital until handing over the organs to the transplant centers. All processes from the identification of a potential donor, medical management, organization of brain death diagnosis, organization of all necessary laboratory tests via assistance with family approach to communication with Eurotransplant, and organization of organ retrieval, storage and transport are coordinated by the DSO. The DSO is also responsible for reimbursement of costs for donor hospitals. For all processes detailed standard operating procedures are in place and the responsibilities are clearly laid down in a detailed manual. (17)
Figures 9-11 show the number of utilized organ donors per million population, the number of transplanted organs per million population and the rate of organs transplanted per donor in Germany between 2010 and 2019.

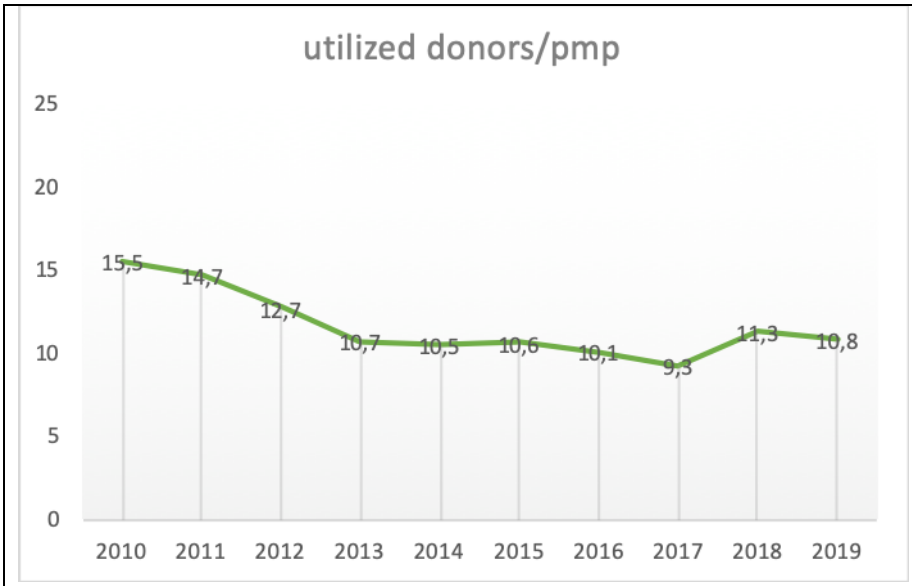

Figure 9 Utilized deceased organ donors per million population (pmp) in Germany

between 2010 and 2019 (Data have been provided by Eurotransplant)

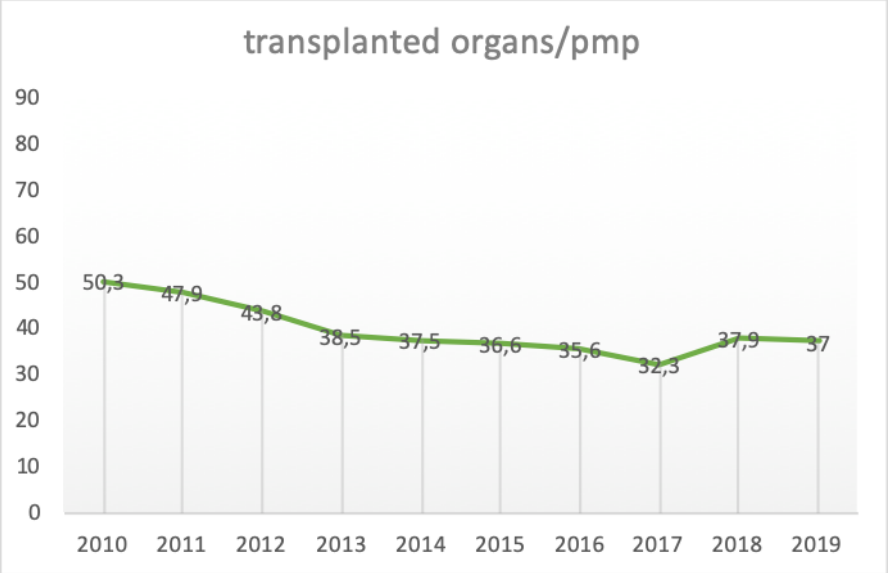

Figure 10 Transplanted organs per million population (pmp) in Germany between 2010 and 2019 (Data have been provided by Eurotransplant)

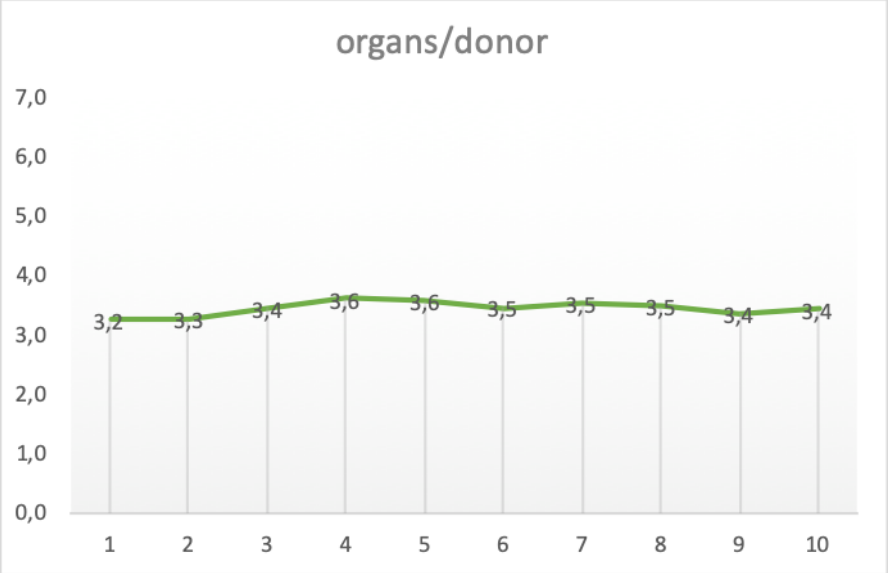

Figure 11 Transplanted organs per donor in Germany between 2010 and 2019 (Data have been provided by Eurotransplant)

4.1.3 Switzerland

In Switzerland, organ donation and transplantation is regulated in the “Bundesgesetz über die Transplantation von Organen, Geweben und Zellen”.(18) In Switzerland a person can be an organ donor after his/her death when the person either declared his/her consent before dying (organ donation card, national register, organ donation app) or, if no documentation of the person’s will is available, the decision is deferred to the next of kin. As in Germany, also in Switzerland, this law is under public discussion at the moment. An action plan for more organs for transplantation was launched 2013 by the Federal Office of Public Health that introduced various measures in Switzerland to increase the number of organ donations. This action plan includes educational efforts, the standardization of processes, quality control and the establishment of clearly defined organizational structures. (19)

All processes are defined in the swiss donation pathway, a document that covers donor detection and reporting, medical treatment of the donor, family approach and communication, coordination of the organ procurement process, transportation of organs. Swisstransplant is the organization that is responsible to develop and implement these standards and to implement processes and structures. Swisstransplant is also responsible for donor management, organ transports and coordination of reimbursements to donor hospitals. (19)

Figure 12-14 show the number of utilized organ donors per million population, the number of transplanted organs per million population and the rate of organs transplanted per donor in Switzerland between 2010 and 2019. Data were extracted from documents available at the website from Swisstransplant. (19)

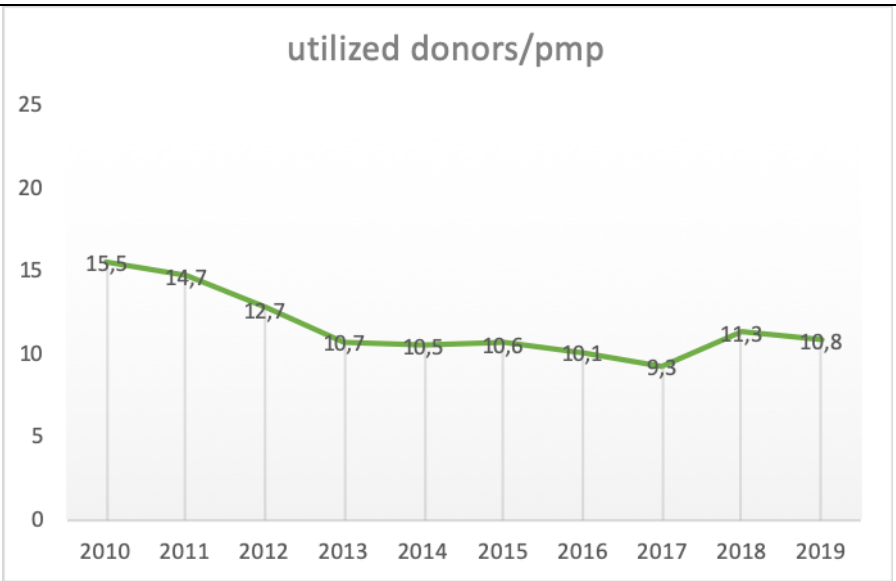

Figure 12 Utilized deceased organ donors (pmp) per million population in Germany between 2010 and 2019 (Data from the public website Swisstransplant)

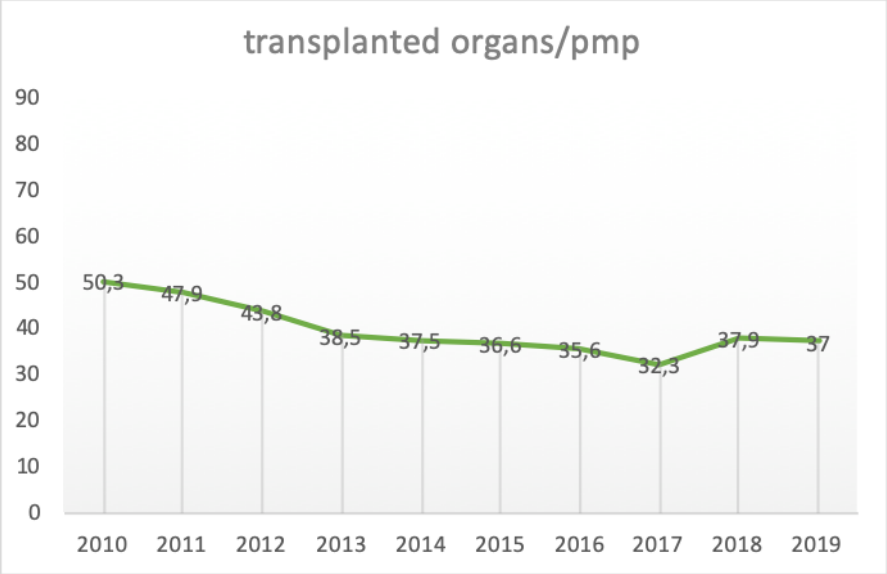

Figure 13 Transplanted organs per million population (pmp) in Germany between 2010 and 2019 (Data from the public website Swisstransplant)

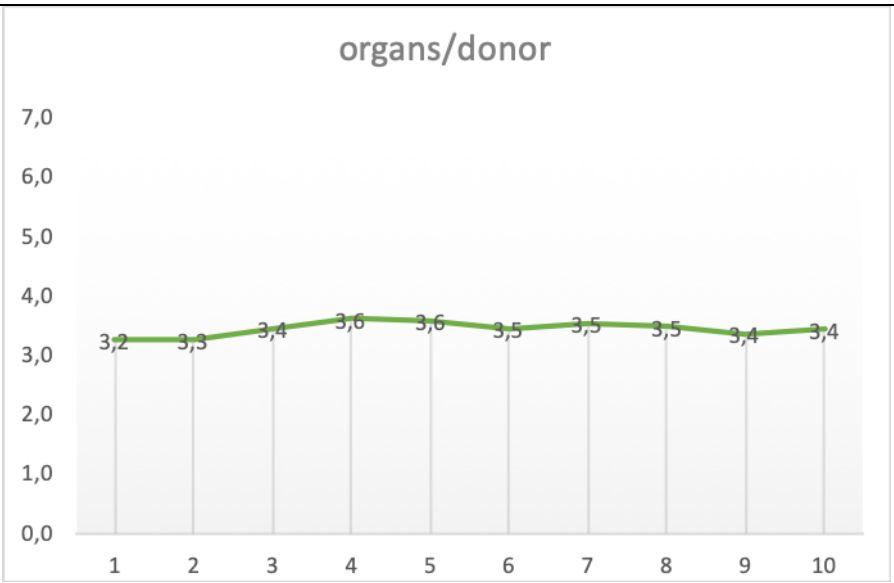

Figure 14 Transplanted organs per donor in Germany between 2010 and 2019 (Data from the public website Swisstransplant)

4.1.4 Spain

Spain has an opt-out system for organ donation. The Spanish Ministry of Health created the Organización Nacional de Trasplantes (ONT) in 1989 as an agency in charge of the coordination and oversight of donation, procurement, and transplantation activities in a politically decentralized country, albeit with an adequate legislative and technical framework from the transplantation perspective. The ONT developed an organized and professionalized model to effectively identify donation opportunities and facilitate their transition to actual donation and to promote public support for donation after death. These measures enabled Spain to double its deceased donation activity in less than a decade and therefore Spain serves as a best practice example for the development of operational organization or organ donation and organ procurement. (20)

From this experience, also an educational program was developed – the Transplant procurement management (TPM). TPM is an international educational program in organ and transplant coordination under academic endorsement of the University of Barcelona. It promotes knowledge transfer and development of professional competences in organ donation as key factors to maximize donor potentiality and conversion rates. The TPM program suggests the role of a TPM

specialist (TPMs), who is professionally trained in all aspects of organ procurement. TPMs are suggested to be physicians who are skilled in personal relations, who are locally accepted and acknowledged, supported by the management and paid for their work, ideally as full-time TPMs. For a TPMs, organ donation must be a goal in itself and not a step on the road to other objectives. TPMs should have specific training in organ procurement. From a management point of view, TPMs are suggested to be best placed independent from the transplant team and other hospital departments and should be experienced intensive care physicians. They should be hospital employees, who report directly to the medical management. TPMs should have resource and process cost management responsibilities. (5) Detailed manuals are available for all processes from detection of potential organ donors until the organs are handed over to the transplantation team. Furthermore, quality control measures are in place.

Figure 15-17 show the number of utilized organ donors per million population, the number of transplanted organs per million population and the rate of organs transplanted per donor in Spain between 2010 and 2019. Data were derived from IRODaT (21). Spain usually only reports actual organ donors, not utilized organ donors. Only for the year 2017 the rate of utilized organ donors per million population was documented in IRODaT: it was 41.1/million population, the rate of actual organ donors was 46.9/million population – showing that the rate of utilized donors in 2017 was approx. 12.5% lower than the rate of actual donors. The graphs below show the numbers of actual donors (solid line) as well as the extrapolated numbers of utilized donors (dashed line).

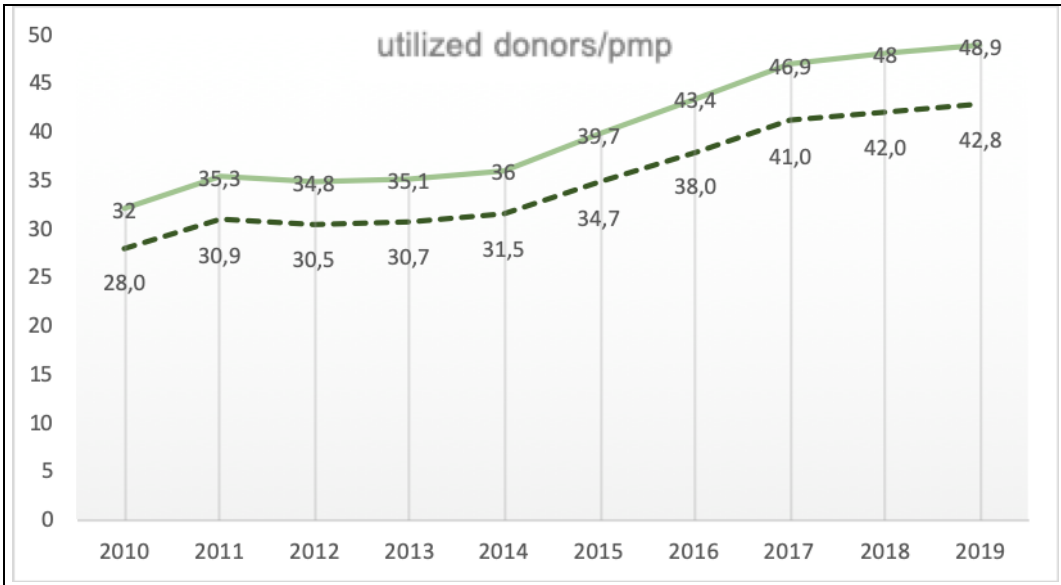

Figure 15 Solid line: Actual deceased organ donors per million (pmp) population in Spain between 2010 and 2019 (Data from the public website IRODat) dashed line: extrapolated utilized deceased organ donors per million (pmp) population in Spain between 2010 and 2019

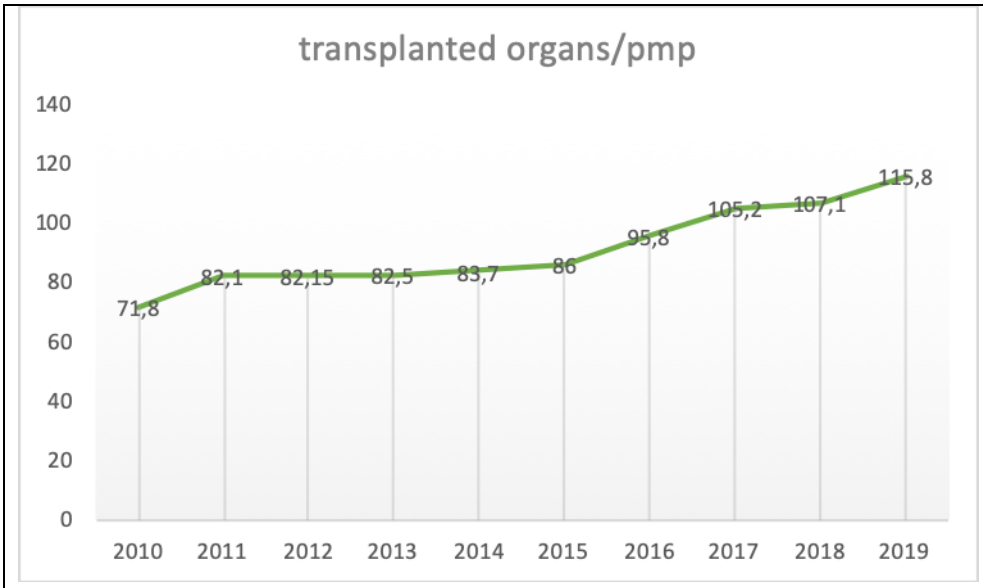

Figure 16 Number of transplanted organs per million population (pmp) in Spain between 2010 and 2019 (Data from the public website IRODat)

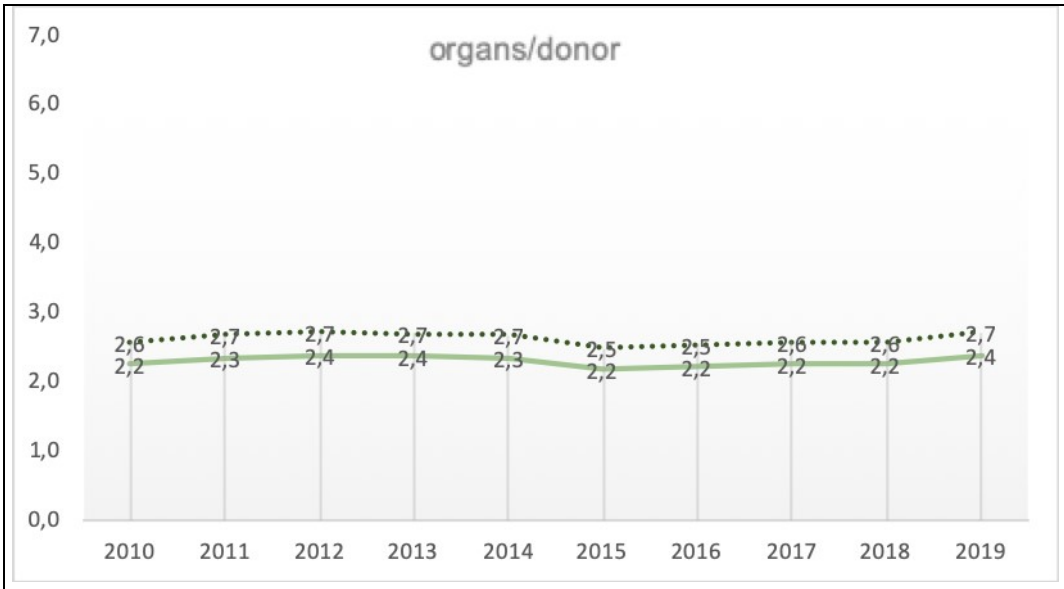

Figure 17 Solid line: Transplanted organs per actual donor in Spain between 2010 and 2019 (Data from the public website IRODat), dashed line: extrapolated transplanted organs per utilized donor in Spain between 2010 and 2019

4.2 Organ donation demand – review of available data

Quantifying the true demand for donor organs is a difficult task. In 2010 the WHO has called upon each country to achieve a national self-sufficiency in the organ donation and transplantation needs of its people. (12) Self-sufficiency is achieved when a country can treat all patients who are at need for organ transplantation. This quite simple definition contains several difficulties. On the one hand, self-sufficiency can be measured by operating figures of a transplantation program: number of organ donors in a country, number of patients on the waiting list and number of transplantations as well as waiting time. From this number it can be conveyed whether all patients from the waiting list get the chance to be transplanted within one year. Additionally, death on the waiting list or removal from the waiting list because of deterioration can be signs for the lack of self-sufficiency. However, this may not be the complete picture: One could speculate, that the need for transplantation would be even higher, but since physicians know that the number of organ donation is limited, they only recommend patients with an expected large benefit for transplantation, whereas those with who are (maybe subjectively or wrongly) not perceived as ideal candidates will not be

recommended for listing. Since success after transplantation cannot be predicted with sufficient accuracy for each individual patient, it can be hypothesized that this practice could disadvantage patients who are perceived to have worse outcome.
In Austria the goal set by the government is to achieve 30 utilized organ donors per million population per year to fulfill self-sufficiency. Spain has set its goal to 40 actual donors per million population and manages to reach and even excel this goal. In a publication from the Spanish ONT it is stated that the global annual number of organ transplants represents less than 10% of the global needs, however without specifying where these numbers come from. There is no solid evidence available to support or refute these number. The next aim of this thesis was therefore to quantify the true need of organ donation for liver transplantation in Austria.

4.3 Liver donation "gap" in Austria

The first approach to quantify the true demand of livers from deceased organ donors in Austria that was used for this thesis was the assessment of the dynamics on the liver waiting list from 2010 to 2018 in Austria in comparison to other countries. The "liver donation gap" was defined as the difference between the number of available donor livers and the number that would be needed to avoid death on the waiting list and removal from the waiting list because of deterioration of the disease.

In Austria within the last 10 years the "liver donation gap" was between 2.4 and 6 liver donors per million inhabitants. Figure 18 shows the number of transplanted livers and the liver donation gap over time. In Austria the liver donation gap decreased during the observed period, while the number of liver transplantations per million population was relatively stable with a tendency to increase.

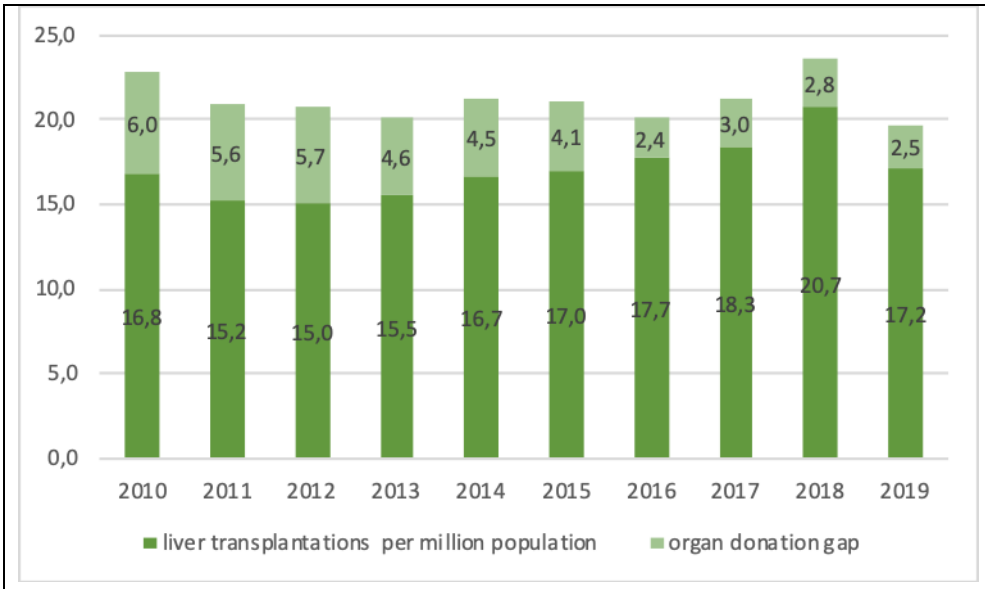

Figure 18 Liver transplantations and liver donation gap between 2010 and 2019 in Austria (Data from Eurotransplant)

When comparing the numbers for liver transplantation with the number of utilized organ donors, on average 1.4 utilized donors are necessary in Austria to be able to procure one liver. When using this factor to calculate the demand of utilized organ donors from the above shown organ donor gap, on average over the 10-year observation period, additional 5.7 donors per million population would be necessary to reach self-sufficiency. When adding these figures to the actual number of utilized organ donors, (see figure 6) on average 28.5 utilized organ donors would have been necessary in Austria to avoid death on the waiting list or delisting due to progression of the disease.

In Germany, within the last 10 years, the gap between the number of available donor livers and the number that would be needed to avoid death on the waiting list and removal from the waiting list because of deterioration of the disease, was between 3.8 and 8 liver donors per million inhabitants. Figure 19 shows the number of transplanted livers and the liver donation gap over time.

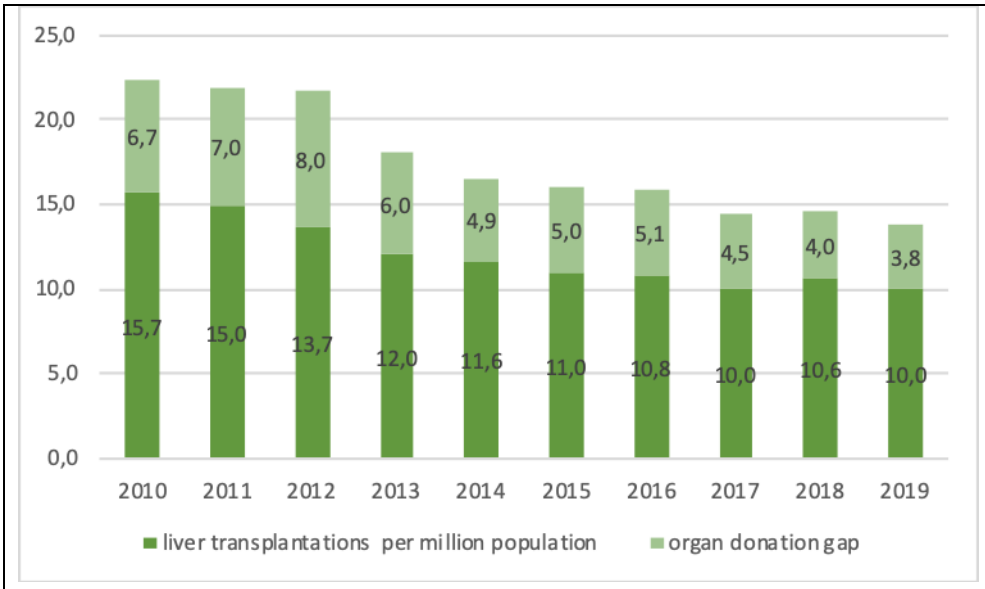

Figure 19 Liver transplantations and organ donation gap between 2010 and 2019 in Germany (Data from Eurotransplant)

Considering the above-mentioned presumptions, over the last 10 years in Germany on average 5.3 additional utilized donors per million population per year would have been needed to avoid deaths on the waiting list and removals due to deterioration of the condition – a figure that is well comparable to Austria.

When correlating the number of liver transplantations per million population with the organ donation gap, an interesting observation can be made: In Austria, a country with high rates of organ donors, an inverse association between the number of liver transplantations per million population with the organ donation gap is observed, indicating that with lower numbers of liver transplantations more patients die on the waiting list or are removed from the waiting list. (Figure 20A) In Germany, the opposite was observed: There is a strong positive association between liver transplantations per million population and the organ donation gap. (Figure 20B)

This discrepancy indicates, that simply increasing the number of donor organs may not be the solution to decrease the organ donation gap. Especially in Germany, other factors than the lack of organ donations alone seem to play a role in evaluation and listing patients for liver transplantation.

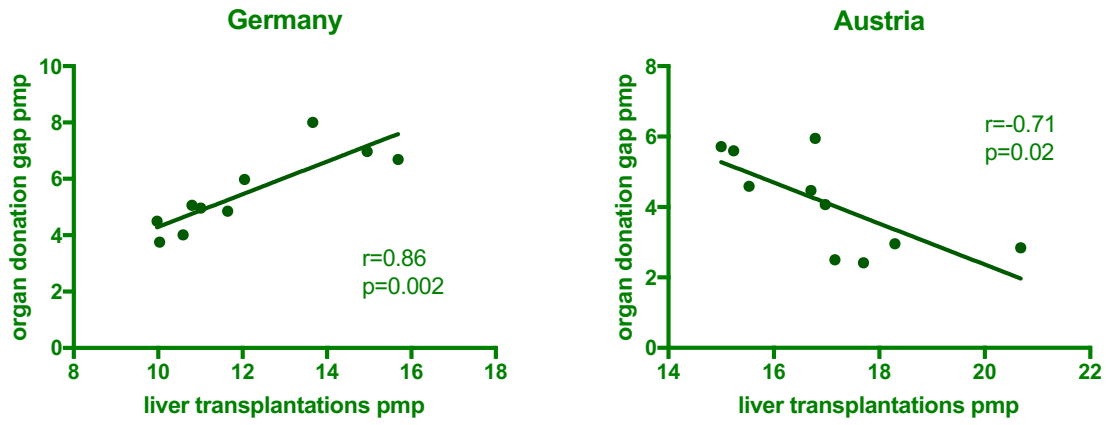

Figure 20 Association between organ donation gap and liver transplantations per million population in Germany (A) and Austria (B), Pearson´ correlation

When data for Austria and Germany are combined, an inverted U shape for the association (using third order polynominal fit) between liver donation rate and organ donation gap can be observed, indicating that the organ donation gap is low when there is an extreme donor organ shortage, then increases with increasing availability of donor organs and decreases again, when reaching “self-sufficiency”.

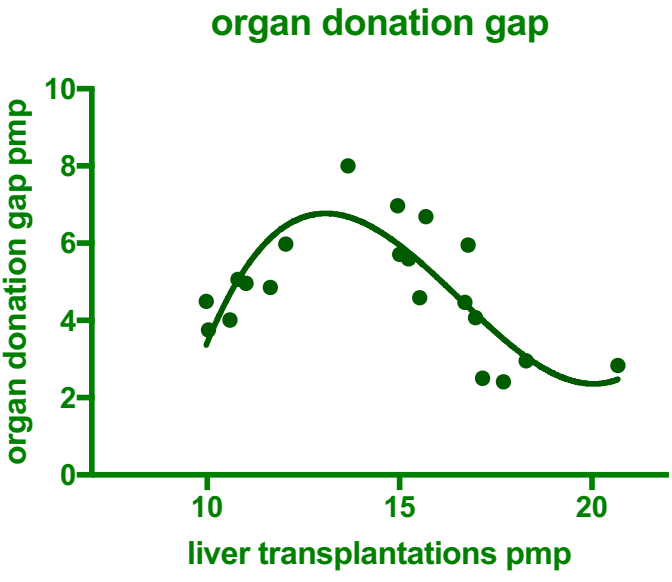

Figure 21 Inverted U-shaped curve for the association (third order polynominal fit) between liver donation rate and organ donation gap per million population (combined data from Austria and Germany 2010-2019)

For data from Spain the transplantation register IRODaT was contacted several times, however no answer was received. For Switzerland Swisstransplant was

contacted several times but despite initial positive feedback, no data could be obtained.

4.4 Subjective organ donation demand in Austria

The above mentioned inverse U-shaped relation between number of liver donations and organ donation gap leads to the hypothesis, that physicians may not recommend patients for liver transplantation in the knowledge of donor organ shortage because they know (or believe) that their patients will not get an organ in time and therefor they do not want to offer this therapeutic option to their patients. Besides “objective” criteria, when a patient is suitable for liver transplantation, there may also be more “subjective” factors that influence the decision-making process of physicians for referring patients for liver transplantation evaluation. This topic has not been studied in detail yet, especially not for Austria. Therefore, an electronic survey was designed and distributed to assess, whether perceived organ shortage influences the decision to refer or select patients for the liver transplantation waiting list.

The survey was sent out to members of the Austrian Society of Organ Transplantation (Austrotransplant) and to the Austrian Society of Gastroenterology and Hepatology (ÖGGH), both societies together have 1721 members. 143 respondents started the survey, 60 did not answer more than 2 questions and data were therefore excluded from the analysis. 83 completed the survey. Since the number of members in both societies who have an interest in liver transplantation and the number of people who are members in both societies is not known, the response rate cannot be calculated accurately. All but 2 respondents were form Austria (2 from Croatia). 53 (63.9%) of the respondents were physicians, 12 (14.5%) surgeons, 3 (3.6%) anesthetists and 15 (18.1%) were other health care professionals (transplantation coordinators, psychologists, nurses). 47 (56.6%) respondents stated that they do not work in a transplantation center, 31 (37.3%) work in a transplantation center and 5 did not answer this question. 35 (42.2%) state that they are not involved in decisions if a patient will be evaluated for liver transplantation; 44 (53.0%) stated that they are involved in these decisions and the remaining 4 respondents did not answer. 59 (71.1%) stated that they are not

involved in decisions if a patient will be accepted on the waiting list, 20 (24.1%) stated that they are directly involved in decisions if a patient will be accepted on the waiting list and 4 did not answer this question.

From the whole cohort, 28 (33.7%) think that there is no donor organ shortage in their hospital,l whereas 51 (61.4%) think that there is a donor organ shortage, the remaining 4 did not answer. When the 44 respondents, who are involved in decisions if a patient will be evaluated for a liver transplantation, were asked if the donor organ shortage influenced their decision, 37 (84.1%) think that this is not the case whereas 7 (15.9%) state that donor organ shortage does impact on their decision. 35 (81.4%) state they would not recommend more patients for evaluation for liver transplantation when there were more donors, but 8 (18.6%) would recommend more patients for liver transplantation in case of higher organ donation rates, 1 person did not answer this question. (Figure 21)

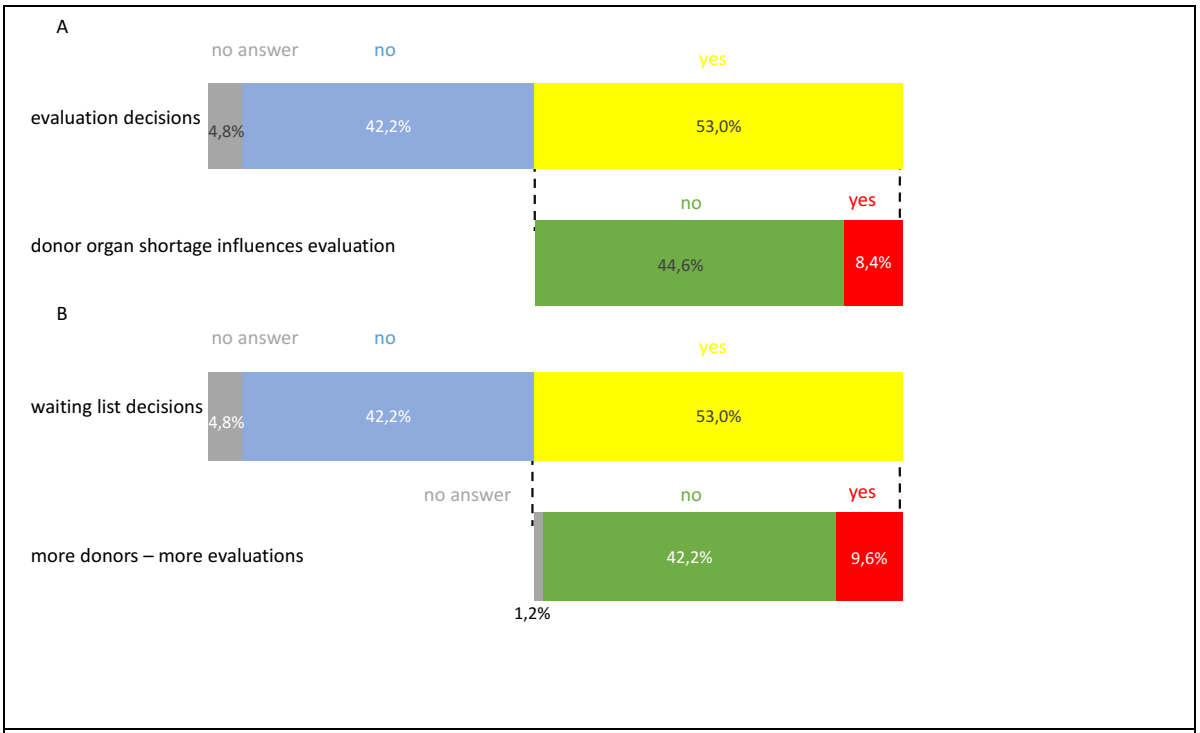

Figure 22 Stacked bar breakdown for the influence of donor organ shortage on decisions to recommend liver transplantation evaluation

Out of the 35 respondents who are not directly involved in decisions if a patient will be evaluated for liver transplantation, 28 (80%) think that donor organ shortage does not influence the decision whether a patient will be evaluated for liver

transplantation, whereas 7 (20%) think that donor organ shortage influences this decision.

Of the 20 respondents who stated that they are involved in the decision if a patient is put on the waiting list for liver transplantation, 17 (85%) state that donor organ shortage does not influence their decision to put a patient on the waiting list, whereas 3 (15%) state that donor organ shortage does impact on their decision. 11 (55%) state they would not put more patients on the waiting list when there were more donors, but 9 (45%) would in that situation put more patients on the waiting list.

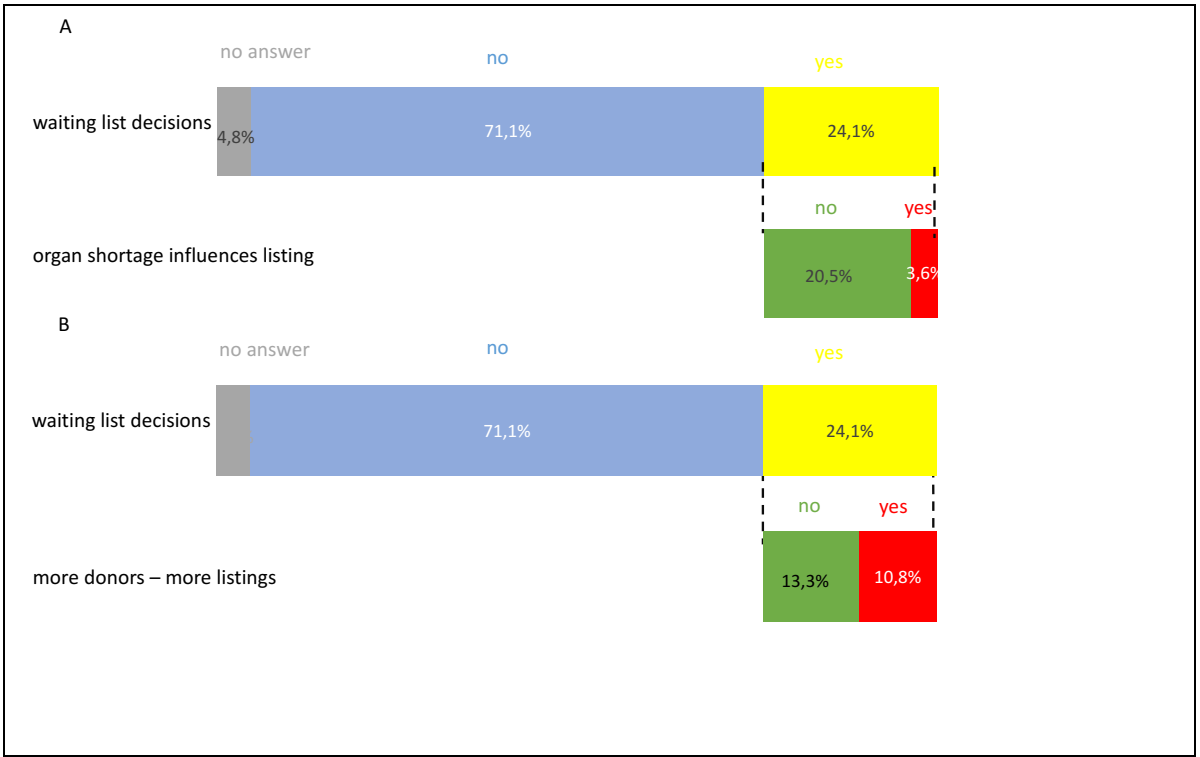

Figure 23 Stacked bar breakdown for the influence of donor organ shortage on decisions to put a patient on the waiting-list

Of the 59 respondents, who are not involved in decisions, if a patient is put on the liver transplantation waiting list, 33 (56.9%) think that donor organ shortage has not influence on the decision if a patient is put on the liver transplant waiting list, whereas 25 (43.1%) think that donor organ shortage has an influence on this decision (1 respondent did not answer this question).

When all respondents were asked, if the organ donation system in Austria is good enough to reach “self-sufficiency” as requested by the WHO, 51 (61.4%) think that this is the case, whereas 26 (31.3%) do not think so (5 did not answer). The majority (70; 84.3%) thinks that organ allocation within Eurotransplant is fair, only 6 respondents (7.9%) disagree with this (7 did not answer this question).

We asked the respondents to estimate the number of utilized organ donors in 2019. The correct number would have been 163 utilized brain-dead organ donors for the year 2019. The number can be found on the public webpage of ÖBIG Transplant and was also part of the press release when the annual report was presented (which took place a few days before the survey was sent out). Respondents stated that they think, that there were 195 brain dead organ donors, however, the range of answers was very high (median 195; CI 150-220, range 0-5000)). When answers were categorized into too low estimates (0-120 donors), appropriate estimates (121-180 donors) and too high estimates (181-5000 donors), respondents working in a transplantation center (25.8% versus 5%, p=0.024) and those who are involved in decisions if a patient is put on the liver transplantation waiting list (36.8% versus 7.5%, p=0.006), were significantly more likely give an appropriate estimate.
When asked for an estimate, how many additional organ donors would be necessary to cover the demand, on average extremely high numbers (median 200, CI 200-500, range 0-5000) were given. Those respondents, who gave an appropriate estimate of utilized organ donors in Austria, stated more often that they would recommend more patients for evaluation to liver transplantation if there was no donor organ shortage (66.7% versus 18.2% of those who gave a too low number and 4.5% of those who gave a too high number, p=0.002).

Figure 23 shows the numbers given by the individual respondents for their estimates of the number of utilized organ donors for 2019 and the number they think would be necessary to meet the demand. On average respondents think that the number of utilized organ donors need to be doubled (median 2, CI 2-2.7, range 1-11) to meet the demand, irrespective of the number of donors they think that are available in Austria.

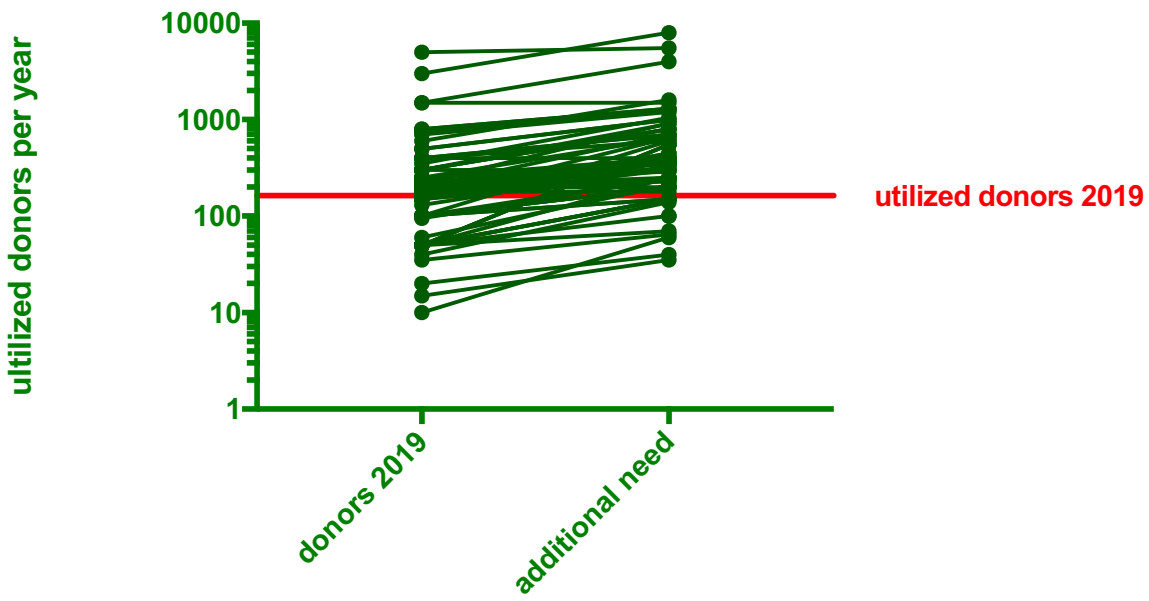

Figure 24 Comparison of the estimated number of utilized organ donors in Austria in 2019 by the respondents of the survey and the number of organ donors the respondents consider appropriate to reach self-sufficiency

Perceived organ donor shortage was independent of the profession, of working in a transplantation center and also independent of involvement in decisions if a patient will be evaluated for liver transplantation or put on the waiting list. These factors also did not influence the opinion on the performance of the Austrian organ donation system or on the fairness of organ allocation within Eurotransplant.

The two open questions regarding the Austrian organ donation and procurement system and the fairness of organ allocation in Eurotransplant were answered by 17 and 3 respondents respectively. Full answers are given in Annex 3 of the thesis. The answers regarding the Austrian organ donation and procurement system discussed problems of communication between different stakeholders (health care professionals but also information of the general public), discussion of responsibilities, the request for clear(er) guidelines, financial compensation as well as the need for more and continuous education. The answers regarding Eurotransplant discuss perceived lack of fairness regarding organ balances between countries and perceived unequal listing policies between centers.

4.5 Demand for additional liver transplantations for hepatocellular carcinoma

As described above, the “liver donation gap” may be underestimating the true demand for deceased donor livers, since the knowledge of organ shortage may influence decision making processes for listing to liver transplantation (either by policies for the selection of transplantation candidates or subconsciously). One situation, where the additional need for liver transplantation can be quantified, are oncologic indications for liver transplantation. Hepatocellular carcinoma (HCC) may be treated in a curative way by liver transplantation, which comprises the cure from the tumor and the cure form chronic liver disease with one procedure. The tumor needs to be confined to the liver to achieve a good outcome after liver transplantation. Several studies have been performed to define, which patients with HCC will benefit from a liver transplantation. The tumor burden plays the most important role in this selection process. Different validated criteria are available, that allow to decide, which HCC patients may benefit from a liver transplantation. (22) However, the definition of “benefit” is also debatable: Currently, because of organ shortage, many countries demand, that the outcome of liver transplantation for HCC has to be comparable to the outcome of non-oncologic indications. (22) However, “correct” comparison would be to compare outcome of liver transplantation to other oncologic therapies. Right now, in Austria (and in many other countries) the consensus between the transplantation centers allows only patients with very small tumor burden, fulfilling for example the “Milan” criteria (22) to be put on the waiting list for a transplantation of a deceased donor organ. (23) So only a small minority (less than 5%) of all patients diagnosed with HCC therefore get the chance of curative treatment by liver transplantation. In an ideal world without donor organ shortage, a much larger proportion of patients with HCC should be entitled to receive a liver transplantation since evidence is available that also patients with more advanced tumor stages would benefit hugely from liver transplantation compared to their currently available therapeutic options with local or systemic anti-tumor therapy. (22)

Table 1 shows the different available criteria to stage early hepatocellular carcinoma and to select patients who would benefit from a liver transplantation. (22)

Table 1 Staging criteria for HCC

Name	Definition
Milan	single tumor ≤5 cm or multiple tumors ≤3 nodules ≤3 cm in size, without vascular invasion
UCSF	single nodule ≤6.5 cm or 2–3 nodules ≤4.5 cm and total tumor diameter ≤8 cm
Up-to-7	sum of the size (cm) of the largest tumor and the number of tumors ≤7
Metroticket 2.0	AFP <200 ng/mL and the sum of number and size of tumors (in cm) ≤7; AFP 200-400 ng/mL and the sum of the number and size of tumors should be ≤5; AFP 400-1000 ng/mL, the sum of the number and size of tumors should be ≤4

For this analysis, all patients who were diagnosed with HCC and discussed in the tumor-board at the Medical University of Graz between 01.01.2017 and 31.12.2019 were assessed. Patients, who fulfilled the criteria for Barcelona Clinic Liver Cancer (BCLC) stage B were identified to be eligible for liver transplantation. Imaging studies from these patients were assessed in detail to assess whether they fulfilled the Milan criteria or the more advanced UCSF, up-to-7 or Metroticket 2.0 criteria. Patients who did not fulfil the Milan criteria but any or all of the other three criteria were considered to be patients who would theoretically benefit from a liver transplantation according to current evidence and who would get the chance to be transplanted if there were more donor organs available.

In the years 2017-2019 160 patients with HCC were discussed in the tumor-board as initial presentations. From these 160 patients 75 (46.95%) were classified as BCLC B at this initial presentation. From these 75 patients, 46 (61.3%) fulfilled the Milan criteria and were therefore in principal eligible for liver transplantation in Austria (not all of them were finally listed or transplanted due to contraindications during the evaluation process as well as patient´s preference for non-surgical therapeutic options). Additionally, 12 patients (16%) were outside the Milan criteria

but inside the UCSF or the up-to-seven or the Metroticket 2.0 criteria and would therefore benefit theoretically from liver transplantation.

When calculating the organ donation gap per million population (1.24 million for the county Styria, which is the main catchment area for the Medical University of Graz), additional 5 liver donations per million population per year would be necessary to cover the demand of these patients, who would medically benefit from a liver transplantation according to current evidence, but do not get one offered right now according to the consensus criteria used in Austria. Considering, that 1.4 deceased organ donations on average are necessary to be able to successfully procure and transplant one liver (in some cases the liver cannot be used due to medical reasons) and that the tumorboard in Graz covers approximately 80% of HCC cases who are presented in the tumorboard (data from KAGES Medical Informatics services, Natalie Zieba MSc), on average 8.4 additional deceased organ donors per million population per year would be necessary to meet the demand for liver transplantations for oncological indications in the county of Styria.

5 Discussion

Organ transplantation is one of the big advances in medicine of the 20th century. 628 people in Austria received a lifesaving solid organ transplantation in 2019. However, even in Austria, a country with a well-developed and successful organ procurement system leading to a high number of organ donations, 90 people died in 2019 while on the waiting list for an organ or were removed from the waiting list because their condition deteriorated and they were unfit for transplantation. This shortage of donor organs chaperons the development of organ transplantation worldwide – without a strong and functional organ donation and procurement program no transplantation program can survive and serve the demand. This phenomenon is referred to as the "Pittsburgh-Necker-Cambridge-Syndrome" which describes the situation of transplant specialists who were trained in these centers and learned transplantation techniques, but when they return to their centers, they are unable to put this into practice because of donor organ shortage resulting from the lack of an organ donation and procurement program. (5) The WHO demands that every country strives for self-sufficiency in organ donation and transplantation. (12) Self-sufficiency would equate to a situation where supply and demand are in an equilibrium.

In this thesis factors during the organ donation process that are associated with successful organ donation programs were analyzed – addressing the "supply" side. Furthermore, in this thesis the magnitude of the organ donation gap in Austria for liver transplantations was defined to understand the current and future "demand" for liver transplantation.

5.1 Comparison of the systems

To analyze the status quo, organization of organ donation and procurement in Austria, Germany, Switzerland and Spain was compared. Differences as well as many similarities were noticed. The legal situation differs – Austria and Spain have an opt-out system whereas Germany and Switzerland have an opt-in system.

While on the first sight the high rates of organ donation in the countries studied here, seem to be associated with the opt-out system, it would be too simplistic to blame the legal system alone. Systematic reviews are contradictory, reporting either that opt-out systems have higher rates of deceased organ donations (24) or that there are no differences between opt-in and opt-out systems (25, 26) depending on the studies and countries included in the analysis. There are indeed examples of highly successful countries with an opt-in system, such as the USA. The switch from opt-out to opt-in does not always result in a sustainable increase of organ donation rate. (27, 28)

From a hospital management perspective, organization of organ donation in Germany, Switzerland and Austria does not differ substantially. However, the Spanish model shows some relevant differences that may explain the success of the Spanish deceased organ donation program. In Spain the position of the TPMs is unique – having a sufficiently experienced intensive care medicine physician with high communication skills in this full-time position is a major advantage in terms of communication and the possibility to optimize processes. The job description includes that the TPMs must have a genuine interest in organ donation and should not only see this position as one step to achieve a different goal. While this system works well in Spain, it cannot easily be transferred to other countries. In comparison to the UK for example, in Spain the number of medical doctors is much higher and salaries are low, therefore such an (adequately paid) position is desirable, whereas in the UK, salaries for doctors, especially consultants, are much higher and the number of doctors is lower, therefore, it is not easy to find somebody for such a demanding position that often requires 24/7 availability and dealing with stressful situations. In Austria a comparable position has been established – the LTXB – who fulfils many, but not all tasks of a Spanish TPMs. LTXB are not working fulltime for organ donation and procurement as opposed to TPMs. In Austria this position has been established in several hospitals since 2009. In a total of 21 hospitals in Austria, 25 LTXB positions were established. The LTXB are available as contact persons for all questions relating to organ donation on site. They implement support, training, motivation, communication and quality assurance measures as required and work closely with the regional transplant consultants and ÖBIG Transplant. Another important task of the LTXB is to retrospectively analyze all deaths with primary or secondary brain damage in

intensive care units in order to assess in individual cases why an organ donation did not take place. This increases awareness of organ donation potential and the analysis of these data enables a realistic assessment of the actual potential of organ donors in Austria and allows to assess if the target value of 30 utilized organ donors per million population is a realistic goal.

When comparing the donation rates between countries, it has to be acknowledged, that Spain reports by far the highest number of organ donations, however one has to consider that Spain (nearly) always reports actual donors and not utilized donors (as it is standard for the Eurotransplant area and Switzerland). The number of utilized donors is always lower than the number of actual donors, especially since Spain has a strong program to facilitate donations from marginal donors. This increases the risk that an actual donor is not converted to a utilized donor because e.g a malignant tumor is found during organ retrieval or that the number of organs that can be used is limited (e.g. kidney only donor). This is also reflected by the relatively lower number of organs per donor (on average 2.5) retrieved in Spain compared to Germany, Switzerland and Austria (on average 3.5). However, due to the fact that utilized donors are not reported, a direct comparison between Austria and Spain regarding this quality indicator is difficult. As an approximation the number of utilized donors in Spain in this thesis was extrapolated from data from 2017, the only year where Spain also reported utilized donors in the IRODaT database. Spain is nonetheless the country with the highest number of organ donors worldwide and therefore also from the countries analyzed in this thesis. For optimal comparison between systems, it would be necessary to use the same quality indicators across different systems.

From the analysis of four different European organ donation and procurement systems it can be concluded, that an organizational framework is crucial to perform organ donation and procurement. However, despite well-organized processes, some countries do not manage to reach sufficient numbers of organ donations. Germany is unfortunately such an example, occupying the penultimate position within Eurotransplant regarding the number of organ donors per million inhabitants. Germany is also at the bottom in comparison with other European countries with comparable political, ethical, religious and social structures. There is

no single factor or general explanation available to account for this unfortunate situation. Possible approaches that have been suggested and discussed by experts in the field are: better education of the population, fostering the general public to indicate their will to donate organs or its rejection, training physicians to recognize potential organ donors, optimizing financial support for transplant officers, and many more. (29) From a hospital management perspective the recognition of potential organ donors and the “frictionless” organization of the procurement procedure are the most important starting points. For an increased recognition of potential organ donors, ongoing education and training of intensive care medicine staff as well as strengthening of the position of a TPMs or equivalent are important. A TPMs or equivalent needs to have enough time resources to perform regular analyses of the situation, to identify weaknesses of the process and has to have the authority to improve these processes.

5.2 Further ways to increase organ donation rates

Further aspects that can increase the number of available donor organs include additional organizational structures such as a mandatory “second opinion” before organ donation is stopped because of “poor organ quality”, support of “donation after circulatory death” programs, machine perfusion for organs with marginal organ quality and technically and logistically advanced organ sharing programs, such as split liver or domino liver transplantation programs.

The mandatory “second opinion” process has been started in Austria in 2019. The standard operating procedure for this process stipulates that in case the transplant center wants to decline an organ donor because of poor organ quality, this can only be done, when the other transplant centers in Austria have reviewed the case and also concluded that poor organ quality does not allow to proceed with organ donation. (30) Future evaluation of this “second opinion process” is necessary to analyze the magnitude of success of this process.

Donation after circulatory death is defined as the retrieval of organs for the purposes of transplantation after death confirmed using circulatory criteria. Donor organ shortage has prompted many countries to re-introduce donation after circulatory death programs (before the definition of brain death in 1968, all donations were donations after circulatory death). The challenges in the practice of

donation after circulatory death include how to identify suitable patients as potential donation after circulatory death donors, how to support and maintain the trust of donor families, and how to manage the consequences of warm ischemia in a fashion that is professionally, ethically, and legally acceptable. Several countries, including Austria, Germany, Switzerland and Spain, have developed concepts with legal and ethical frameworks to allow donation after circulatory death. (31) In these countries, donation after circulatory death accounts for a substantial proportion of deceased organ donors. In Spain, the donation after circulatory death program started in 2012 with 3.4 donations after circulatory death per million population and increased to 15.8 per million population in 2019. In Austria donation after circulatory death donors are reported since 2011, starting with 0.7 per million population but only slowly increasing to 2.4 donations after circulatory death per million population in 2019. In Switzerland donation after circulatory death donors are also reported since 2011, starting with 0.4 per million population and increasing to 6.7 donations after circulatory death per million population in 2019. In Germany, the IRODaT database does not show any donations after circulatory death during these years, although some activities are ongoing in Germany as well.

Donation after circulatory death is increasingly accepted as routine part of end-of-life care in both intensive care and emergency medicine. Results of organ transplantations with organs from donation after circulatory death donors are comparable to donation after brain death. (32) There was some fear that increased rates of donation after circulatory death may lead to a decrease in donation after brain death at the expense of a lower number of transplantable organs and a lower organ quality, however, this does not seem to be the case. The maximum potential of “donation after brain death” to “donation after circulatory death” substitution rate observed was 8% in a retrospective study in the UK. (33)

The increasing use of organs from donors after circulatory death and also the increasing age of organ donors and therefore the increase of marginal donor organs call upon methods to improve organ quality before transplantation to maximize the number of organs that can be transplanted from one donor and to optimize outcome after transplantation. Machine perfusion is an emerging technique to in liver and kidney preservation. For liver transplantation, normothermic machine perfusion may allow to use up to 50% of livers that

otherwise had to be discarded. (34) Technical advances, such as split-liver transplantation to serve two recipients with one donor liver (35) and logistic advances, such as domino liver transplantations, where the explanted liver of one patient (usually with a metabolic disorder that is not expected to harm the recipient) serves as a graft for another patient, can increase the donor pool further. (36)

5.3 Organ donation gap

As described above, self-sufficiency in organ transplantation is the balance between supply and demand. Defining the current and future demand for liver donations in Austria was one of the goals of this thesis. From a hospital management perspective, this analysis is of importance to be able to set a realistic goal for organ donation rates and to generate appropriate quality indicators to be able to calculate and compare the organ donation gap between organs and countries.

Calculating the rate of patients who died on the liver waiting list and the rate of patients who were removed from the waiting list, because they were unfit for transplantation, was chosen as one of the surrogate quality indicators of self-sufficiency of liver donation. For Austria for liver transplantation, this model calculation revealed that over the last decade in addition 5.7 donors per million population would have been necessary to be able to avoid death on the waiting list or removal from the waiting list. On average 28.5 utilized organ donors per million population would have been necessary in Austria to avoid deaths on the liver waiting list or removals from the waiting list due to deterioration of the patients´ conditions. This compares well to the figure of 30 utilized organ donors per million population that is currently set out as goal by ÖBIG-Transplant.

However, this figure may not represent the full picture. When comparing the organ donation gap with Germany, where the number of liver transplantations decreased remarkably during the last 10 years, due to a steep decrease in deceased organ donation, an interesting observation can be made. In Germany, despite a steep decrease in organ donations, the liver donation gap did not increase but rather decreased as well. Since it is unlikely, that in Germany, as opposed to other

countries, the number of patients who would benefit from liver transplantation would have decreased in parallel to the number of available organ donors, this finding can most likely be explained by the fact that in situations of extreme shortage of resources also demand decreases. In other words: in the light of a dramatic donor organ shortage – physicians supposedly decide (consciously or not) to not recommend patients for liver transplantation evaluation because they know that this option is in reality not available for all patients. Therefore, they may offer other therapeutic strategies despite the fact that liver transplantation would offer a longer survival and a better quality of life. When comparing the liver donation rates with the donor organ gap in Germany and Austria together over a period of 10 years, curve fitting shows an inverted U-shaped curve with a low organ donation gap with low and high liver donation rates and a higher organ donation gap in the area of medium organ donation rates. This again underlines the hypothesis that in situations of extreme donor organ shortage, less people are evaluated for liver transplantation, while this number increases as soon as more organs are available – resulting in a higher organ donation gap because not all patients receive their transplantation in time. When organ donation rates start to reach the range of “self-sufficiency”, the organ donation gap decreases again.

To address the potential effects of the known donor organ shortage on decisions to recommend patients to the evaluation for liver transplantation and to put them on the waiting list, a questionnaire was distributed to people working in the field of transplantation in Austria. Since no questionnaire was available from literature, the questionnaire was developed for this thesis. This questionnaire showed that 2/3 of the respondents think that there is a donor organ shortage in their hospital. Those respondents, who are involved in decisions, which patients will be evaluated for liver transplantation and which patients will be listed, indicate in approximately 10% that their decisions are influenced by donor organ shortage and that they would recommend more patients for evaluation and listing when there were more donor organs available. Those respondents who are not directly involved in these decisions, have an even more dramatic view on this; nearly half of them think that decisions may be influenced by donor organ shortage. This finding is alarming, since donor organ shortage may influence decision making processes in a “subconscious” way - outside the current policies – physicians may already

“preselect” candidates for transplantation by not recommending suitable candidates for evaluation for transplantation. From an ethical point of view this preselection increases the risk of unfair decisions, since other factors than the medical urgency and potential benefit of a patient may be considered.
In our questionnaire, the knowledge question regarding the number of utilized organ donors in Austria revealed that only a minority came with their estimation close to the correct number. Knowledge was better in respondents working in a transplantation center and in those who are involved in decisions to put patients on the waiting list. We also asked, how many additional organ donors the respondents think would be necessary in Austria, however, these numbers varied considerably and were unrealistically high or low and it is therefore not possible to conclude on a specific number of necessary additional organ donors. The respondents on average think that the number of organ donors needs to be doubled to meet the demand. Our questionnaire also gave some valuable insights from members of the Austrian transplantation community on areas of improvement, including further educational efforts and improvement of organizational structures.

The data from the survey prove the hypothesis that donor organ shortage not only has direct effects on patients who may not be listed due to strict policies or may die on the waiting-list or deteriorate while listed but also may have indirect effects in the sense that the perceived shortage leads to “rationing” in the minds of the responsible physicians even before patients are listed for a transplantation. In synopsis with the finding of an inverted U-shaped curve between liver donation rate and organ donation gap we can conclude, that with increasing liver donation rates, the demand will also increase. On the other hand, our questionnaire also shows that there is considerable need for continuous education in the field of organ donation and the respondents also state this in the open questions, where they point out the need for continuous education in this field, especially also for medical personnel that is not directly or continuously involved in transplantations.

To further quantify the actual liver donation demand, a specific indication for liver transplantation – HCC – was picked for detailed analysis. For HCC, clearly defined criteria are available to decide who will benefit from a liver transplantation.

However, the definition of “benefit” from liver transplantation for HCC is controversial. An arbitrary threshold of >50% 5-year overall survival is broadly considered a minimum standard for liver transplantation. Right now, in Austria, due to donor organ shortage, only patients with a very low tumor burden (according to “Milan” criteria) are allowed to be evaluated and listed for liver transplantation. However, also patients with more advanced tumor stages would clearly benefit from liver transplantation compared to other treatment possibilities.

Several studies have been performed to define, which patients with HCC will benefit from a liver transplantation. (22) Right now, in Austria (and in many other countries) the consensus between the transplantation centers allows only patients with very small tumor burden, fulfilling the “Milan” criteria (22) to be put on the waiting list for a transplantation of a deceased donor organ. (23) Only a small minority (less than 5%) of all patients diagnosed with HCC therefore gets the chance of curative treatment by liver transplantation. Ideally, a larger proportion of patients with HCC should be entitled to receive a liver transplantation. (22) When comparing the number of donor organs needed for liver transplantation according to Milan criteria and according to more extended criteria (UCLF, up-to-seven, Metroticket 2.0), data from the transplant center Graz suggest that at least an additional number of 8.4 deceased organ donors per million population per year would be necessary to meet the current demand based on the retrospective analysis. The number of patients who would benefit from liver transplantation is likely to increase when surgical techniques and pre- as well as postoperative anti-tumor therapy with new substances advance and would allow more patients to benefit from liver transplantation for a long-term survival advantage compared to current standard oncological therapies.

Also, in other indications, liver transplantation demand may change. The proportion of patients on the liver transplant waiting list for hepatitis C cirrhosis is decreasing. However, the percentages of patients on the waiting list for non-alcoholic steatohepatitis or alcoholic liver disease are increasing. (37) The increase in chronic liver diseases in the general population also leads to an increase in the incidence of HCC, again increasing the need for liver transplantation. (38) In an ageing population, also the upper limit of age for liver transplantation needs to be discussed. While there is currently no absolute upper

age limit, patients over the age of 70, depending on their comorbidities, are only rarely evaluated for liver transplantation, although evidence is available that also patients above 70 years will benefit from a transplantation. (39) In an ideal world with no donor organ shortage, patients who would benefit from liver transplantation should be transplanted without any upper age limit.

5.4 Limitations

The limitation of the theoretical part of the thesis is the lack of standards in reporting organ donations that does not allow full comparison of organ donation systems. The empirical part from this thesis describe the situation regarding liver transplantation partly for Austria (liver donation gap and the survey) and partly for the Transplant Center Graz or the region of Styria (oncological indications) and therefore the figures may be inaccurate in case of large differences between Transplantation Centers. This is however unlikely since all transplantation centers in Austria use the same consensus guidelines for liver transplantation and yearly audits show that there are no major differences in these decisions. It however needs to be assessed in further studies whether these results are transferable to the rest of Austria or other countries. Also, data for calculating the organ donation gap were not available for all studied countries despite several attempts to obtain these data from the respective organizations. The number of completed surveys was not as high as desired, however, the number was acceptable when considering the size of the country and the limited number of potential respondents.

5.5 Lessons learned

Organ donation and procurement is a challenging process involving many people and including a variety of critical steps for the success of the process. The analysis of different organ donation systems showed that the prerequisite for success are structural and procedural concepts. However, despite comparable structures and processes, organ donation rates vary considerably. This shows that also soft factors such as cultural norms and individual personalities involved in the field are factors of success. During the analysis of different organ donation systems and the

available literature on organ donation demand it became evident, that the development of clear, easy to measure and accepted quality indicators is an unmet need in the field of organ donation and transplantation. This already starts with the lack of a code for brain death in the International Classification of Disease coding system and ranges over the lack of comparable organ donation figures across countries to the lack of detailed data on patients who die on the waiting list or are delisted because they did not receive an organ in time. From the quantitative analysis of the liver donation gap in Austria, it can be concluded that approximately 40-45 brain dead organ donors per million population would be necessary to meet the current (and near future) demand for liver transplantation. Figure 25 shows the current and future donor organ supply and demand in Austria based on the data from this thesis to reach self-sufficiency.

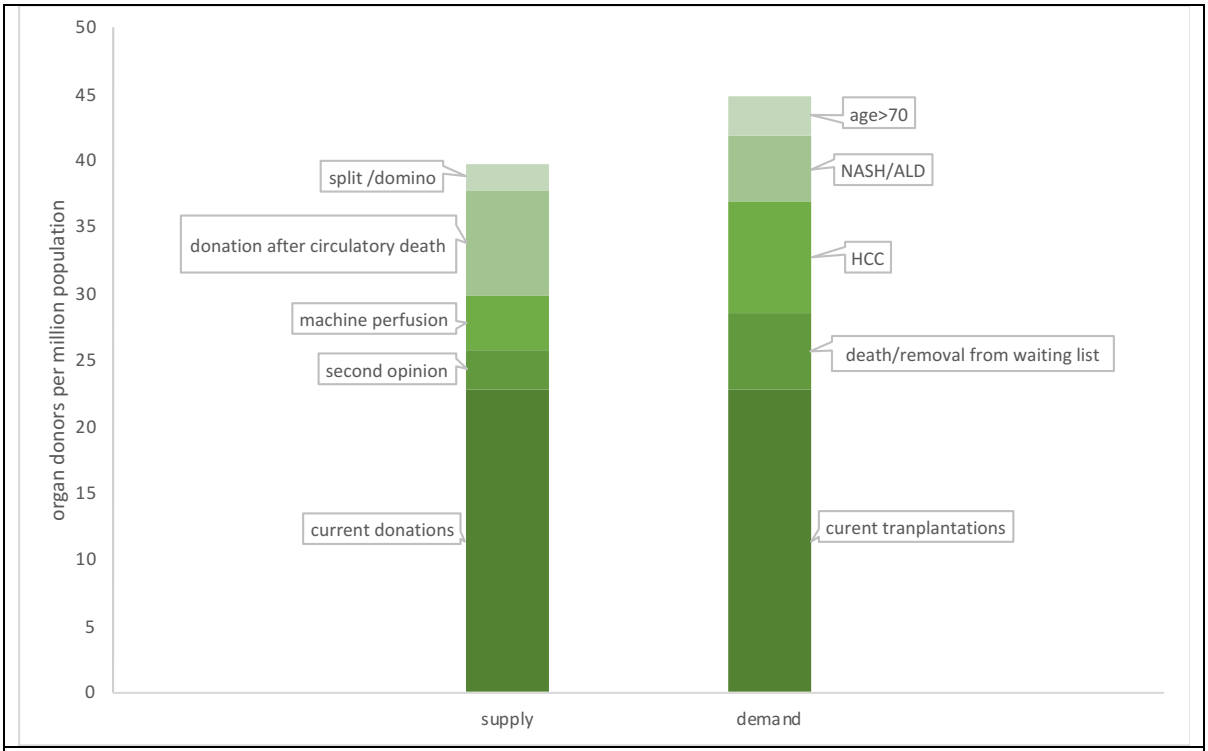

Figure 25 Current and future donor organ supply and demand

From a management point of view, allocation of appropriate resources, implementation of a specific position (equivalent to the Spanish TPM or Austrian LTXB) and continuous educational efforts are essential to maintain high organ donation rates. To be able to analyze potential weaknesses of a system, appropriate and comparable quality indicators need to be developed. Increasing organ donation rates will most likely not immediately reduce the organ donation

gap, since more patients may benefit from organ transplantations who are currently not recommended for transplantation evaluation or listing due to policies that take donor organ shortage into account and also by additional “subconscious rationing” by the involved physicians.

“Don’t take your organs to heaven, heaven knows we need them here”

(M. Scully, 1954-2006)

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7 Annex 1 Study protocol

Study protocol

Version 2

07.04.2020

Author: Vanessa Stadlbauer-Köllner

Assessing the organ donation demand for liver transplantation in Austria

Introduction

Organ transplantation has evolved since the 1960s as a successful therapeutic concept of many end-stage diseases of the heart, the lungs, the liver, the kidney and the pancreas, increasing live expectancy and quality of life for the recipients of organ transplantation. However, this high and increasing demand causes donor organ shortage. Several strategies were developed to reduce donor organ shortage, such as legal frameworks, education, organizational and infrastructure measures and the increasing use of marginal organs.

In the “Third World Health Organization (WHO) Global Consultation on Organ Donation and Transplantation: Striving to Achieve Self-Sufficiency in 2010” the WHO urged its Member States and professionals in the field to regard organ donation and transplantation to meet the health needs of its population as part of every nation’s responsibility in a comprehensive manner and address the conditions leading to transplantation from prevention to treatment. The concept of self-sufficiency was defined as fulfilling the transplantation needs of a given population, by using the resources obtained from within that population, but not excluding opportunities of regulated and ethical regional organ sharing and cooperation. (12)

The benchmarks to compare success in transplantation procurement is the rate of utilized organ donors per million inhabitants as well as the conversion rate of potential donors to utilized donors. (11)

However, the true demand for donor organs cannot be easily quantified. Full self-sufficiency would be reached, when no deaths on the waiting list occur without

having to discard any organs because of the lack of recipients. It is however, unclear, if the number of patients on the waiting list is regulated by the organ donation potential or in other words, if more patients would benefit from organ donation if there were more donor organs available. Furthermore, not all removals from the waiting list may be avoidable by the timely availability of a donor organ.

Aim of the study

This study aims

(a) to quantify the organ donation demand for liver transplantation

(b) to assess whether organ donation rate influences the number of patients put on the waiting list

Methods

To fulfil aim (a), the number of patients with hepatocellular carcinoma that were offered a liver transplantation at the Medical University of Graz between 2017 and 2020 will be assessed. All first presentations of patients to the tumor board will be recorded and classified according to the BCLC criteria. (22) The number of patients who were referred to evaluation for liver transplantation because they fulfilled the Milan criteria and the number of patients who were not recommended for transplantation but would fulfil validated extended criteria (Asan critera, up-to-7 criteria, French alpha-fetoprotein model and Metroticket 2.0 criteria). To assess this, the printout documentations of the hepatocellular carcinoma tumor board from 2017 to 2020 will be manually assessed and a minimal anonymous dataset (age, sex, tumor size, number of tumours, alpha-fetoprotein level, referral to liver transplantation, comorbidities) will be recorded electronically.

For aim (b) a survey (see appendix 1) will be sent to transplant surgeons, transplant physicians and referring physicians in Austria to ask them, if they are restrictive in referring patients to liver transplantation because of donor organ shortage. The survey will be sent out electronically via a web-based platform (SurveyGizmo) to all members of the Austrian Society of Transplantation (Austrotransplant) via the secretary of the society. Each person gets an email with a link to the survey and the anonymously collected data will be exported as a .csv file from SurveyGizmo.

Statistical analysis of the data will be performed with SPSS V26. For aim 1 the difference between the number of referrals to liver transplantation according to the Milan criteria and the potential number of liver transplant recipients when applying extended criteria will be calculated for each year and further data will be described using descriptive statistics. The results of the survey will be assessed by descriptive statistics and chi-square Test.

Ethical considerations

Since all patient data will be collected retrospectively, it is not feasible to obtain informed consent of the patients. Since data are collected anonymously from existing patient documentations and since the results of this analysis will not have any impact on patients´ treatment, this is ethically justifiable.

For the survey, data will also be collected anonymously as described above and participants will be informed before answering the first question that their participation in the survey implies that they consent to statistical evaluation of the results. Since we also will not log IP addresses from participants, in theory one person could therefore fill in the survey more than once. Since we do not give any incentive to participants, we believe that the risk is very low. From our previous experience with online questionnaires we know that logging IP addresses is not useful, since many participants will fill in the questionnaire while logged into their hospital or university network and therefore will show the same outgoing IP address.

Time plan

The collection of patient data will start immediately after the positive vote is received. The survey will be submitted after the positive vote is received, at latest in September 2020.

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VOTUM

gültig bis 28.04.2021

EK-Nummer:	32-324 ex 19/20
Studientitel:	Assessing the organ donation demand for liver transplantation in Austria
Prüfer:	Assoz. Prof. Dr. Vanessa Stadlbauer-Köllner Meduni Graz
Sponsor:	Medizinische Universität Graz, Klinische Abteilung für Gastroenterologie und Hepatologie
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Die o.a. Studie wurde von der Ethikkommission erstmals im 'expedited Review' am 03.04.2020 behandelt. Die Ethikkommission ist zu folgendem Schluss gekommen:

Es besteht kein Einwand gegen die Durchführung der Studie in der vorliegenden Form.

Kommissionsmitglieder, die für diesen Tagesordnungspunkt als befangen anzusehen waren und daher gemäß Geschäftsordnung an der Entscheidungsfindung und Abstimmung nicht teilgenommen haben: keine

Zur Beurteilung vorliegende Dokumente:

Dokumente eingegangen am 24.03.2020, begutachtet im 'expedited Review' am 03.04.2020	
✓ Cover Letter Microsoft Word - Anschreiben.doc Kopie na	24.03.2020
✓ Antragsformular ECS	24.03.2020
Originalprotokoll Study protocol_V1 1	05.03.2020
✓ Conflict of Interest Erklärung Microsoft Word - Interessenskonflikte.doc Kopie na	24.03.2020
✓ CV CV_16032020 na	16.03.2020
Sonstiges: FragebogenV1 1	24.03.2020
Dokumente eingegangen am 03.04.2020 (in der nächsten Begutachtung mitbegutachtet)	
✓ Letter of Authorization	03.04.2020
Dokumente eingegangen am 07.04.2020 (in der nächsten Begutachtung mitbegutachtet)	
✓ Originalprotokoll 2	07.04.2020
✓ Fragebögen 2	07.04.2020
✓ Sonstiges: Stellungnahme zur Bearbeitungsmitteilung	07.04.2020
Dokumente eingegangen am 17.04.2020, begutachtet im 'expedited Review' am 28.04.2020	
✓ Antragsformular ECS Unterschriftenseiten	24.03.2020

Die Ethikkommission geht - rechtlich unverbindlich - davon aus, dass es sich um keine klinische Prüfung nach AMG bzw. MPG handelt.

Es handelt sich um eine Studie im Rahmen einer Diplomarbeit.

Das Votum der Ethikkommission berührt in keiner Weise die alleinige Verantwortung der Prüferin / des

Prüfers / der Prüfer für die ordnungsgemäße Durchführung der Studie unter Einhaltung aller einschlägiger gesetzlicher Bestimmungen und Richtlinien.

Weiters machen wir darauf aufmerksam, dass der Kommission unverzüglich zu melden sind:

- Abweichungen vom Protokoll aus Sicherheitsgründen oder Protokolländerungen

- Änderungen, die das Risiko der Teilnehmer/-innen erhöhen oder die Durchführung der Studie wesentlich beeinflussen

- Mutmaßliche unerwartete schwerwiegende Nebenwirkungen - SUSARs (AMG-Studien ab 1.5.2004) oder schwerwiegende unerwünschte Ereignisse - SAEs (andere Studien)

- Jegliche Information über sonstige Umstände, die die Sicherheit der Teilnehmer/-innen oder die Durchführung der Studie beeinträchtigen können

zusätzliche Auflagen: Die behördlich vorgeschriebenen Maßnahmen hinsichtlich der COVID-19 Pandemie müssen beachtet werden. Der Prüfer und der Sponsor müssen in ihrem jeweiligen Wirkungskreis unter allfälliger Beachtung von Leitlinien gewährleisten, dass keine zur Bekämpfung der Pandemie benötigten Ressourcen gebunden werden bzw. ausreichend Personal vorhanden ist und die TeilnehmerInnen durch ihre Studienteilnahme keiner zusätzlichen Infektionsgefahr ausgesetzt werden.

Dieses Votum gilt für ein Jahr ab dem Datum der Ausstellung. Bei längerer Studiendauer ist rechtzeitig vor Ablauf der Gültigkeit des Votums ein Zwischenbericht vorzulegen (Berichtsformular), um eine etwaige Verlängerung zu erlangen.

Graz, 28. April 2020

Univ.Prof.DI Dr.Josef Haas
Vorsitzender

Univ.Prof.Dr.Hans Dimai
Stv. Vorsitzender

Achtung: Bitte bei allen das Projekt betreffende Schreiben oder telefonischen Anfragen die EK-Nummer angeben!

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Rechtsform: Juristische Person öffentlichen Rechts gem. UG 2002. Information: Mitteilungsblatt der Universität. UID: ATU 575 111 79. Bankverbindung: Raiffeisen Landesbank Steiermark IBAN: AT443800000000049510, BIC: RZSTAT2G

Annex 2– Questionnaire

Organspendebedarf in Österreich

Hintergrund und Ziel des Fragebogens

Fragen

1) Sind Sie?
( ) ChirurgIn
( ) InternistIn
( ) AnästhesistIn
( ) Sonstige : _____

2) Arbeiten Sie in einem Transplantationszentrum
( ) ja
( ) nein

3) Sind Sie direkt an der Entscheidung, ob jemand zur Lebertransplantationsevaluierung vorgestellt wird, beteiligt?
( ) ja
( ) nein

4) Sind Sie direkt an der Entscheidung beteiligt, ob jemand auf die Lebertransplantationswarteliste kommt?
( ) ja
( ) nein

5) Gibt es Ihrer Meinung nach in Ihrem Krankenhaus einen Mangel an OrganspenderInnen nach Hirntod?
( ) ja
( ) nein

6) Hat ein Mangel an OrganspenderInnen nach Hirntod einen Einfluss darauf, ob Sie PatientInnen zur Lebertransplantationsevaluierung vorstellen?

( ) ja
( ) nein

7) Würden Sie bei einer höheren Zahl an OrganspenderInnen nach Hirntod mehr PatientInnen zur Lebertransplantationsevaluierung vorstellen?
( ) ja
( ) nein

8) Hat Ihrer Meinung nach ein Mangel an OrganspenderInnen nach Hirntod einen Einfluss darauf, ob jemand PatientInnen zur Lebertransplantationsevaluierung vorgestellt wird?
( ) ja
( ) nein

9) Hat ein Mangel an OrganspenderInnen nach Hirntod für Sie einen Einfluss darauf, ob Sie jemanden für die Lebertransplantationswarteliste empfehlen?
( ) ja
( ) nein

10) Würden Sie bei einer höheren Zahl an OrganspenderInnen nach Hirntod mehr PatientInnen auf die Leberwarteliste aufnehmen?
( ) ja
( ) nein

11) Hat ein Mangel an OrganspenderInnen nach Hirntod Ihrer Meinung nach einen Einfluss darauf, ob jemand auf die Lebertransplantationswarteliste kommt?
( ) ja
( ) nein

12) Schätzen Sie bitte, wieviele OrganspenderInnen nach Hirntod es letztes Jahr in Österreich gab, von denen zumindest ein Organ auch transplantiert wurden ("utilized" OrganspenderInnen)?

_____

13) Wieviele zusätzliche OrganspenderInnen nach Hirntod müsste es Ihrer Meinung nach in Österreich geben, um den Bedarf zu decken?

_____

14) Sind Sie der Meinung, dass die Organisation des Organspendewesens in Österreich gut genug ist um die von der WHO geforderte „self-sufficiency“ zu erreichen?

( ) ja

( ) nein

15) Was gehört Ihrer Meinung nach geändert?

_____

_____

_____

_____

16) Sind Sie der Meinung, dass die Organverteilung im Eurotransplant-Raum, zu dem Österreich gehört, fair funktioniert?

( ) ja

( ) nein

17) Was gehört Ihrer Meinung nach geändert?

_____

_____

_____

_____

_____

Danke!

Annex 3– Full free text answers

Sind Sie der Meinung, dass die Organisation des Organspendewesens in Österreich gut genug ist um die von der WHO geforderte „self-sufficiency“ zu erreichen?

Stärkere Verbindlichkeiten von potentiellen Spenderhäusern, potentielle Spender auch tatsächlich zu melden und zu führen. Die Spendermeldungsrate ist offenbar von Haus zu Haus sehr unterschiedlich.

Es haben sich auch die Auswahlkriterien für die Organspende in den letzten Jahrzehnten immer wieder geändert. Das haben vielleicht noch nicht alle potentiellen Spendermelder mitbekommen. Lebendspende ist in Österr. noch unterrepräsentiert im Internat. Vergleich

Finanzielle Entschädigung für die Abwicklung von Organspendern.

Jemanden als Organspender in Betracht zu ziehen, ist häufig für denjenigen mit viel Aufwand verbunden, deshalb wird es häufig nicht gemacht. Wir brauchen mehr Aufkärungsarbeit auch in kleineren Häusern und möglicherweise eigene Teams, die dann in die Häuser gehen oder Belohnungen für Krankenhäuser, wenn sie Organspender aquirieren.

Vereinfachte Entnahmeprozesse, Verbesserung der Transplantatvorbereitung, NHBD
besser Aufklärung und Kommunikation mit Tpl Zentrum

Besserer Einbindung peripherer Krankenhäuser.

Procedere nach Meldung eines Spenders an peripherem Krankenhaus

Proaktive, transparente Kommunikation. Mehr personelle und monetäre Ressourcen für das Transplantwesen. Zentren-übergreifende Audits.

Intensive Information der Population, die als Organspender in Frage kommen.

Sensibilisierung aller Österreicherinnen und Österreicher zu dieser Problematik.

1. Mehr Tx-Beauftragte 2. Bessere Umsetzung der gesetzlichen Regelung bzgl. Widerspruchslösung 3. Bessere Aufklärung der Bevölkerung bzgl. Hirntot 4. Optimierte Nutzung der NHBD 5. Flächendeckender Einsatz von Maschinenperfusion zur Verwendung Erweiterung des Spenderpools (extended Donor criteria)

Aufklärung, Post Entnahme Optimierung der Organe durch Perfusion, Reduktion der nicht Meldung durch TX ablehnende Ärzte und Ärztinnen, Werbung, Verpflichtende Meldung und Durchführung der Organspende nach Kreislauf Tod, Reduktion der Zuschüsse an Spitäler mit niedrigen Organspende Zahlen.

Verpflichtende Organspendermeldung

mehr Informationen vor allem in peripheren krankenhäusern um mehr Bewusstsein zu schaffen dafür
Zentrale Organisation

Professioneller Support der Zentren inkl PR für public opinion
Bewusstseinsbildung auch auf kleineren Intensivstationen hinsichtlich Hirntod und Organspendemöglichkeit.

Allokationssystem, Informationspolitik, Kontrolle möglicher Organspender die nicht verwirklicht wurden. Jährliche Schulung von ICU Teams.

Was gehört Ihrer Meinung nach geändert?

Keine Abhängigkeit des Rankings nach Anzahl der Organspendekapazitäten wie es inoffiziell sicher passiert Einheitliche Organspendegesetzgebung im Euroraum

Es kann nicht sein das Österreich Nettoexporteur ist. Ein Verbund mit Ungarn, Tschechien, Kroatien wäre ideal ohne Rest von ET ...

Abstellen des Transplantationszentrums-Hopping, mehr Ehrlichkeit und Fairness!