

EUROTRANSPLANT newsletter

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Eurotransplant Newsletter is a publication of the Eurotransplant International Foundation. The editor welcomes articles pertaining to organ donation, allocation and transplantation. If there are issues not discussed in the Eurotransplant Newsletter, that you would like to see, please contact the editor. Send copy preferably via e-mail:
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Introduction

In this issue of the ET Newsletter you will find information on the latest developments within Eurotransplant. Much of the snow has melted, but the results of the ET winter meeting remain. They are presented in a brief report by the chairmen of the respective workshops.

A summary is given of the meeting of the Eurotransplant Board on 25 January 2012 including a number of recommendations that were approved.

From the reports of our Advisory Committees you will see proof of the constructive work performed in the past months by the ETKAC, ELIAC, EThAC, OPC, TTAC and ETEC.

A key issue to improve old-for-old programs may be the combination of age matching with HLA-DR compatibility. The ET Senior DR-compatible Program (ESDP) is currently relaunched to study the impact of this altered allocation principle in the elderly transplant recipients. The background, study design and logistic support are addressed in this issue.

The ET duty desk presents news on the LAS adaptations as well as on the implementation of RLAC03.10 regarding two additional lab values that are to be reported to ET upon listing and MELD update.

Eurotransplant is looking forward to meeting you (again) in Leiden on 11 & 12 October 2012 on occasion of the annual ET meeting during which ET will celebrate its 45th anniversary.

Arie Oosterlee
General Director

Statistics

PRELIMINARY CUMULATIVE STATISTICS EUROTRANSPLANT : JANUARY 01 - MARCH 31

NUMBER OF ORGANS FROM DECEASED DONORS USED FOR TRANSPLANTATION

	Donor country	Austria	Belgium	Croatia	Germany	Hungary	Luxembourg	Netherlands	Slovenia	Non ET	Total
2012	Kidney	114	100	32	487	-	-	110	22	-	865
2011	Kidney	83	109	63	470	-	2	104	16	-	847
2012	Heart	19	15	6	88	3	-	9	8	2	150
2011	Heart	14	18	8	71	-	-	8	3	1	123
2012	Liver	39	55	22	238	-	-	34	13	3	404
2011	Liver	29	64	33	234	2	2	42	6	5	417
2012	Lung	29	53	8	143	14	-	41	2	20	310
2011	Lung	18	48	6	103	36	-	36	4	8	259
2012	Pancreas	5	12	6	39	-	-	13	2	-	77
2011	Pancreas	4	23	3	33	-	-	13	1	-	77

NUMBER OF TRANSPLANTS PERFORMED

	Transplant Country	Ki	BKi	Li	SLi	Pa	Ki + Pa	He	BLu	SLu	He + BLu	Li + Ki	SLi + Ki	Li + Pa	He + Ki	He + Li	BLu + Li	Total
2012	Austria	112	2	39	-	-	4	17	36	1	-	-	-	-	1	-	-	212
2011	Austria	90	1	28	1	-	4	12	32	-	-	-	-	-	-	-	1	169
2012	Belgium	101	1	44	-	9	2	12	27	2	1	5	-	-	-	-	-	204
2011	Belgium	96	3	56	-	18	5	13	23	7	1	5	-	1	2	1	-	231
2012	Croatia	27	-	20	1	-	2	8	-	-	-	-	1	-	-	-	-	59
2011	Croatia	49	1	32	2	1	1	11	-	-	-	-	-	-	-	-	-	97
2012	Germany	419	10	240	5	6	42	88	64	10	1	2	-	-	1	-	-	888
2011	Germany	415	8	232	14	2	34	68	48	12	-	4	-	1	2	-	-	840
2012	Hungary	-	-	-	-	-	-	2	-	-	-	-	-	-	-	-	-	2
2011	Hungary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	Netherlands	96	2	30	3	3	9	10	17	5	-	-	-	-	-	-	-	175
2011	Netherlands	101	-	33	1	6	4	9	14	2	-	1	-	-	-	-	-	171
2012	Slovenia	11	-	14	-	-	-	8	-	-	-	-	-	-	-	-	-	33
2011	Slovenia	8	-	4	-	-	-	4	-	-	-	-	-	-	-	-	-	16
2012	Non ET	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
2011	Non ET	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	Total	766	15	387	9	18	59	146	144	18	2	7	1	-	2	-	-	1574
2011	Total	759	13	385	18	27	48	117	117	21	1	10	-	2	4	1	1	1524

He-Heart Ki-Kidney Pa-Pancreas Li-Liver SLu-Lung BKi-both Kidneys BLu-Both Lungs SLi-Split Liver

Calendar of Events

32ND ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR HEART & LUNG TRANSPLANTATION (ISHLT)

April 18 – 21, 2012
Prague, Czech Republic
For information visit www.ishlt.org

CONGRESS OF THE INTERNATIONAL LIVER TRANSPLANTATION SOCIETY (ILTS)

May 16 – 19, 2012
San Francisco, USA
For information visit www.iltts.org

49TH CONGRESS OF THE EUROPEAN RENAL ASSOCIATION – EUROPEAN DIALYSIS & TRANSPLANTATION ASSOCIATION (ERA-EDTA)

May 24 – 25, 2012
Paris, France
For information visit www.eraedta2012.org

AMERICAN TRANSPLANT CONGRESS (ATC)

June 2 – 6, 2012
Boston, USA
For information visit www.atcmeeting.org

XXIV CONGRESS OF THE TRANSPLANTATION SOCIETY (TTS)

July 15 – 19, 2012
Berlin, Germany
For information visit www.tts.org

21. JAHRESTAGUNG DER DEUTSCHEN TRANSPLANTATIONSGESELLSCHAFT (DTG)

July 15 – 19, 2012
Berlin, Germany
For information visit www.d-t-g-online.de

45TH ANNUAL MEETING OF EUROPEAN SOCIETY FOR PEDIATRIC NEPHROLOGY (ESPN)

September 6 – 9, 2012
Krakow, Poland
For information visit www.espn2012krakow.org

EUROPEAN LIVER INTESTINE TRANSPLANT ASSOCIATION (ELITA) – LICAGE LIVER MEETING &

4th ELITA split-liver course
September 13 – 15, 2012
Ghent, Belgium
For information visit www.esot.org

EUROTRANSPLANT ANNUAL MEETING 2012

October 11 – 12, 2012
Leiden, the Netherlands
For information: Mrs. Marianne Franzen
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24TH EUROPEAN TRANSPLANT COORDINATORS ORGANISATION (ETCO) – EUROPEAN DONATION COMMITTEE (EDC) MEETING

October 5 – 7, 2012
Dubrovnik, Croatia
For information visit www.esot.org

EUROPEAN SOCIETY FOR ORGAN TRANSPLANTATION (ESOT) AND AMERICAN SOCIETY OF TRANSPLANTATION (AST) JOINT MEETING – TRANSFORMATIONAL THERAPIES AND DIAGNOSTICS IN TRANSPLANTATION

October 12 – 14, 2012
Nice, France
For information visit www.esot.org

26. JAHRESTAGUNG DER ÖSTERREICHISCHE GESELLSCHAFT FÜR TRANSPLANTATION, TRANSFUSION UND GENETIK – AUSTROTRANSPLANT

October 17 – 20, 2012
Rust (Burgenland), Austria
For information visit www.austrotransplant.org

THE LIVER MEETING OF THE AMERICAN ASSOCIATION FOR STUDY OF LIVER DISEASES (AASLD)

November 9 – 13, 2012
Boston, MA, USA
For information visit www.aasld.org

3RD ETHICAL LEGAL AND PSYCHOSOCIAL ASPECTS OF ORGAN TRANSPLANTATION (ELPAT) CONGRESS

April 20 – 24, 2013
Rotterdam, the Netherlands
For information visit www.esot.org

33RD ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR HEART & LUNG TRANSPLANTATION (ISHLT)

April 24 – 27, 2013
Montreal, QC, Canada
For information visit www.ishlt.org

Summary of the meeting of the Eurotransplant International Board on Wednesday, 25 January 2012 in Alpbach, Austria

Laura van Hattum, secretary to the Eurotransplant International Board

The Board was informed on the progress of the implementation of recommendations. First of all, the Board got an update regarding the LAS score. The technical implementation went without problems.

The ESDP study is slowly developing now a new CRO has taken over the duties of the former organization that went bankrupt.

Concerning the disentanglement of the shared services of ET, the Dutch Transplantation Foundation (NTS) and BISLIFE, the Board was informed about the progress of this project. The separation of the ENIS tissue system from the ENIS organ system is in progress and will be finalized mid-March 2012. As soon as the systems are separated, the shared services with BISLIFE could be ended. ET wants to sustain a distance towards tissue related issues. For this reason the shared services with BISLIFE are being terminated. Also discussions are currently taking place on how shared services with NTS should best be continued.

With regard to housing, the Board was informed the re-housing project is half-way. Because of problems at NTS due to a delay in receiving supplies, the re-housing project is expected to experience a two week delay and therefore is expected to be completed mid April 2012.

The technical part of the joining of Hungary went without problems. Until this moment there has been no organ exchange in the context of the preliminary cooperation.

ET's general conditions were discussed. All ET countries besides Germany have accepted the general conditions. A meeting took place with the German Bundesärztekammer in which almost all the outstanding issues were resolved.

The Board formally agreed to the lung twinning agreement between Romania and Vienna.

The attendees were informed about the current status regarding a possible follow-up to the EFRETOS project. ET expects that the EU will decide by the end of January 2012 whether setting up a European registry of registries for transplant follow-up data is supported by the EU and a corresponding budget will be assigned. There are doubts whether the set-up of a European registry of registries will be financed, since there are three other joint action programs currently being funded by the European Commission, all in the area of transplantation. The good news is that EFRETOS was preselected as one of the projects that is considered as an "Outstanding EU project".

Next, the Board was informed regarding the formalization of the relationship between ET and Belgium. A draft contract has been made and has been agreed upon by the Belgian ministry. A few minor changes will be adapted where after it is expected to have a signed contract in the near future.

Reports of the ET Kidney Advisory Committee (ETKAC), ET Liver Intestine Advisory Committee (ELIAC), the ET Pancreas Advisory Committee (EPAC), the ET Thoracic Advisory Committee (EThAC), the Organ Procurement Committee (OPC), the ET Tissue Typing Committee (TTAC) and the ET Ethics Committee (ETEC) were discussed.

Since the reports will be published in this issue of the ET Newsletter, there is no need to further elaborate on them in this summary.

The Board gave its approval for the ET budget for 2012.

Due to recent incidents involving the listing and transplantation of non-resident patients, the Board decided to re-discuss the development of a non-resident policy for all organs. The directors were asked to adapt the proposed ET policy and recommendation which will be discussed during the next Board meeting.

The Board discussed a proposal to make a clear distinction between recommendations and policies. At the moment, recommendations can be subdivided into recommendations that need formal approval by the respective authorities of all countries, which after approval are binding for all centers and can be enforced by ET and recommendations that concern a working procedure or policy of ET which are only sent for information to the national authorities. Their main goal is to increase transparency of the working procedures of ET and its partners. The second type of recommendations will be named "policies" to make this important difference immediately transparent. The Board agrees to the proposal.

Finally the Board discussed a joint action from the European Union regarding facilitating cooperation on organ donations between national authorities within the EU. Since no organization has the level of experience in the field of organ exchange as ET, the EU has asked ET to participate in this project. The Board agreed that ET takes part in this project.

The following recommendations have been discussed and approved by the Board:

KIDNEY ADVISORY COMMITTEE

RKAC01.10 (rephrased)

In addition to the option of performing a combined liver+kidney transplant, the option of a kidney-after-liver transplant should be made possible in selected cases. If a recipient is listed for a liver and kidney transplant, the center can decide to perform a simultaneous liver+kidney transplant or a kidney-after-liver transplant. In the latter case the recipient gets 500 extra points in the kidney allocation system (ETKAS) during the period of 90 to 360 days after the liver-only transplant, under the condition that the creatinine clearance is <15ml/min within this period.

In case a patient was not listed on the kidney waiting list prior to the liver transplantation, the kidney-after-liver bonus will be granted on request of the transplant centre. If the recipient had been on dialysis for at least 6 weeks prior to the liver transplantation. All other requests for the kidney-after-liver bonus are to be audited by the ETKAC.

This recommendation will be forwarded to the national authorities for authorization.

RKAC04.11

Kidneys from deceased donors are classified according to donor age, kidney function and co-morbidities; the following age categories apply:

1. Donor age 0-15 years;
2. Donor age 16-49 years;
3. Donor age 50-64 years;
4. Donor age \geq 65 years.

Donors from the categories 2 and 3 who at least meet one of the following criteria will be categorized into the next higher category:

- creatinine prior to donation is >1,5 mg/dl or
- the cause of death is cerebrovascular or
- the donor suffers from diabetes mellitus or
- a severe hypertension.

These categories will be used in the calculation of the national balances to be used for the balancing factor in ETKAS. The balances should not be limited to one year, but increase over time.

In addition to these donor categories, the balances will also be divided according to the donor ABO blood group.

The effect of RKAC04.11 will be monitored during the first 2 years after implementation and adapted if necessary.

This recommendation will be forwarded to the national authorities for information.

PANCREAS ADVISORY COMMITTEE

RPAC03.11

Patients, who are in need of an urgent pancreas-only re-transplantation, following a pancreas graft failure within the first two weeks after transplantation, are eligible for the urgency code 'Special Urgency'. The SU request must have been received by the ET office within two weeks after transplantation. If re-registration takes place between 14 days and 6 months after transplantation, the recipient is eligible for return of waiting time but not for the SU status. After this period no bonus whatsoever will be granted.

Including the addition of a regulation regarding return of waiting time, RPAC03.11 replaces RPAC01.07.

This recommendation will be forwarded to the national authorities for authorization.

THORACIC ADVISORY COMMITTEE

RThAC04.11

In order to complete the registration for a lung transplant, it will be required that at time of listing for a lung transplant in Eurotransplant all LAS and LASplus waiting list and post-transplant items have to be provided to the ENIS system. A patient will not be considered for a lung offer in case these items are missing. An exception is made for pulmonary artery systolic pressure, pulmonary artery mean pressure (only for sarcoidosis) and pulmonary capillary wedge mean pressure. In case the values are missing for these three factors, a normal value will be used.

This recommendation will be forwarded to the national authorities for authorization.

ORGAN PROCUREMENT COMMITTEE

ROPC01.11

If a recipient is willing to accept an organ of HIV+ donors, this must be indicated in the donor profile of the recipient.

The following points should be respected as a policy of ET on HIV+ donors:

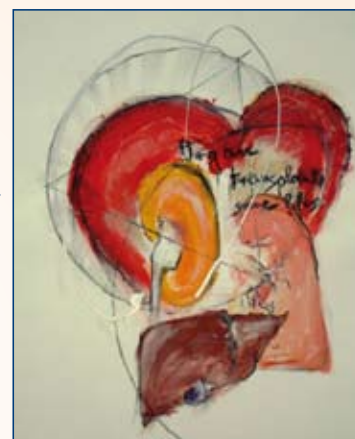
1. Proper and extensive categorization should be performed;
2. Organs of HIV+ donors should be allocated to and accepted for HIV+ recipients;
3. Transplantation of organs from HIV+ donors should take place in the framework of a standardized protocol;
4. Procurement teams themselves should decide whether they are willing to procure the organs of HIV+ donors. If the local team is not willing to perform the procurement, the transplant coordinator must inform ET as soon as possible in order to enable ET to inform the transplant center and to make arrangements for procurement by the transplant center.

This recommendation will be forwarded to the national authorities for information.

Announcement

Eurotransplant Meetings 2012-2013

Mark your calendar!



2012	Annual meeting	October 11 – 12, Leiden, the Netherlands
2013	Winter meeting	January 23 – 25, Alpbach, Austria
	Annual meeting	October 10 – 11, Leiden, the Netherlands

The following reports from the Advisory Committees were discussed by the Eurotransplant International Board on 25 January, 2012 in Alpbach, Austria

Please note that all approved recommendations mentioned in the following reports, are published elsewhere in this Newsletter.

Report of the meeting of the Eurotransplant Kidney Advisory Committee (ETKAC)

Chairman: Prof.Dr. U. Heemann

Secretary: Dr. J. de Boer

The ETKAC met on Tuesday, December 6, 2011

Members present: 13 + 1 external advisor + 1 director + 1 ET co-worker

Members excused: 3

A. Code of Conduct for kidney audits

The Code of Conduct for kidney audits had already been approved by the ETKAC last year but due to the fact that not all national authorities had given their approval so far it was again addressed during this ETKAC meeting.

It was questioned whether such a document should be subject to national formal and binding regulations or just be regarded as a guideline. It was decided to have the ETKAC members once again check the Code of Conduct and to indicate which items should be subject to legal regulations and which should only be regarded as guidelines.

B. Status of the ET Senior DR matching (ESDP) study

The ETKAC was informed that after suspension of the project due to financial problems of the Clinical Research Organization (CRO), a new CRO has to be found. It was reported that recently a suitable company has been identified, that negotiations are under way and that a new three party contract has to be set up. It has been decided to divide the study in a registry part that will include the kidney pairs that are not participating in the extensive data collection of the clinical trial. It was furthermore addressed that an estimate on the sample size for the registry part of the study as well as a vote from an external ethics committee is needed.

C. Special request for bonus points for kidney-after-liver transplantation

The ETKAC discussed a special request for the kidney-after-liver bonus of 500 points in the kidney allocation system (ETKAS). Due to a clerical error a recipient was not listed for a kidney transplant prior to the liver transplant. The recipient involved was however on dialysis prior to the liver transplant.

In general the ETKAC is not against granting the bonus to recipients who are registered too late due to a clerical error. However, it should be clear and beyond any doubt that forgotten timely registration of the recipient is concerned rather than cheating the system.

After ample discussion it was decided that recipients who are on dialysis for at least 6 weeks prior to the liver transplant will be granted the kidney-after-liver bonus upon request of the transplant center. For all other cases a request has to be audited by the ETKAC (RKAC01.10 rephrased).

D. Consideration to grant bonus points for kidney-after-pancreas transplantation

The ETKAC was informed that based on the fact that for several reasons donor pancreas are sometimes lost for allocation, the EPAC is investigating the willingness of pancreas centers to accept pancreas-only for a selected group of pancreas-kidney recipients. Subsequently, the option of a kidney-after-pancreas bonus – in analogy to RKAC01.10 kidney-after-liver bonus – was proposed to the EPAC. The EPAC could however not immediately come to a conclusion and decided to further discuss this issue in depth and asked the ETKAC for its input in the EPAC discussion.

The ETKAC discussed that, in case this concept is accepted the allocation sequence for pancreas-only should be: pancreas-only recipients before pancreas-kidney recipients who are eligible for pancreas-only offers. It was agreed upon to give the EPAC a positive feedback and to propose to have the same rule implemented as for kidney-after-liver transplantation (granting a 500 points bonus during the period of 90-360 days after the pancreas-only transplant, provided that the creatinine clearance is <15ml/min).

E. Joint ETKAC/OPC meeting on machine perfusion trial

Due to the absence of several key persons a previously meeting had to be canceled. During the ETKAC meeting the ETKAC key persons were identified and it was agreed upon to ask the OPC to also appoint their key persons. Thereafter a new meeting between ETKAC and OPC key persons will be scheduled.

The ETKAC members again expressed their wish for an 'intention to treat' analysis of the machine perfusion trial data. In order to avoid any kind of bias the donors where the machine perfusion failed should also be included in this analysis.

F. Data validation for recipients on the waiting list

Based on a recent incident it was discussed how to prevent intended or unintended wrong data entries into ENIS by the transplant centers that can have an influence on the allocation. Already right now ET is performing for several data plausibility checks and/or (random) audits. The most allocation relevant and critical item for kidney transplant is the date of the start of dialysis. The ETKAC discussed what measures should be in place to avoid errors or misuse of entering the starting date of dialysis.

It was decided that a limit of 3 years should be taken into consideration. If the duration of dialysis at time of registration on the waiting list is more than 3 years, the nephrologist should send in a statement confirming the date of dialysis. In addition ET should enforce that, in case of multiple organ listing, for each organ a competent physician should be responsible (e.g. in case of kidney a nephrologist). It was concluded that prior to drawing any conclusions these suggestions should be broadly discussed by the ET Board.

G. Suggestion to set pediatric age limit for pediatric recipients to 18 years

The external ETKAC advisor for pediatric transplantation informed that the majority of the European organ procurement organizations have set the age limit for pediatric recipients to 18 years and that it would be in line with the European harmonization that ET should follow this rule. In addition he stated that the current system (age limit at 16 years with inclusion of the bone age) is a disadvantage to female recipients who in general mature earlier than male recipients.

It was remarked that the aim of entering the bone age was to diminish the adverse influence of chronic renal failure on the maturation for which reason there seems no reasoning for changing the system.

It was decided to perform further analysis with respect to the number of recipients that were put on the waiting list between the age of 16 and 18 years and on the question how many of them have received the child bonus and how many of them have not received this bonus. This issue will be further discussed based on the results of this analysis.

H. Adaptation of the kidney allocation system

The ETKAC chairman introduced a proposal – extensively discussed by an expert group consisting of ETKAC members and tissue typers – to categorize donors according to age and ABO blood group. At the beginning these categories should only be used in the national balance points. In a later stage however these categories should also be used on purpose of matching donor quality with the recipient's medical needs.

The rationale for this categorization arose from the fact that donor age is by far the most important factor influencing graft survival. Data on the kidney exchange over the past year has shown that the number of kidneys exchanged per donor category, especially in the elderly donor category, is very small. Therefore the risk exists that smaller countries cannot be compensated in time due to lack of suitable recipients and consequently the incentive to report these donors might diminish. As a solution it was suggested to start by balancing between countries within the categories and in the long run extend it to the allocation system itself.

After a discussion about the division of the age categories and the criteria to categorize donors in the next higher level the ETKAC formulated RKAC04.11.

Next the ideas that the expert group wants to discuss in the near future were presented:

- A. Adjustment of waiting time;
- B. DR/DR+ matching;
- C. Extension of ESP;
- D. Creating supra national regions.

The ETKAC members were asked which topic should be addressed first.

Finally it was decided to discuss the adjustment of waiting time in a workshop during the ET winter meeting (January 2012) and to discuss the DR/DR+ matching in a joint ETKAC/TTAC meeting.

The ETKAC is not in favor of addressing the topic of creating supra national regions. The reason is that the objective of this option is shortening the CIP, within the current limits however the CIP seems still acceptable. In addition recent analyses of ET showed that CIP is in many cases independent of the distance between donor and recipient center.

As the ESP is mainly a national concern it is decided to leave the decision regarding modifications of the ESP system to the national expert groups and authorities.

Report of the meeting of the Eurotransplant Liver Intestine Advisory Committee (ELIAC)

Chairman: Prof.Dr. X. Rogiers
Secretary: Dr. A. Rahmel

The ELIAC met on Monday, November 14, 2011
Members present: 8 + 1 ET co-workers
Members excused: 3

A. LAS and accepted combined organs

The ELIAC was informed that due to the change in lung allocation, in the future there will be no "Accepted Combined Organ" (ACO) status for lung transplantation in combination with other organs anymore.

Instead, patients in need of a combined organ transplantation including lungs will be assigned by an expert group a so-called Exceptional LAS (Lung Allocation Score). As only the lung transplant expert group has experience with assigning a LAS, the task of the ELIAC members will only be to identify, whether a combined transplantation with priority is indicated in this individual. If the liver expert agrees to this, it is up to the LAS expert group to assign the appropriate LAS.

The ELIAC agreed to this approach. The liver transplant centers within ET will be informed about the new approach.

B. Reports from the national ELIAC representatives

The ELIAC was informed on national developments in liver donation, allocation and transplantation by the Austrian, Belgian, Croatian, Dutch, German and Slovenian representatives in the ELIAC.

With regard to Germany, the ELIAC was informed that the working group of the German Bundesärztekammer regarding liver transplantation, the following standard exceptions have been discussed and will be modified for Germany:

- a) For the SE 'Biliary sepsis and secondary sclerosing cholangitis' the matchMELD will be calculated based on labMELD and a higher increase of the 3-months mortality than in the past (+30% 3-months mortality instead of +20% 3-months mortality). Analyses of the ET data have shown that this higher increase of the MELD score better reflects the urgency of this patient group.
- b) For primary sclerosing cholangitis the diagnostic criteria have been modified and the assignment of the standard exception MELD is now built similar to the one for the HCC (initial SE-MELD equivalent to 15% 3-months mortality and thereafter 10% 3-months mortality increase every 3 months).

The chairman of the ELIAC expressed his concern that the allocation rules, specifically in Germany, get more and more complex. He has the idea that at the moment experts and

transplant centers do not know all details of the allocation rules anymore. Additional refinements that are currently proposed in Germany can lead to even further confusion.

C. Correctness of data reported to ET for the calculation of the MELD score

The ELIAC was informed about the possible manipulation of data being used for the calculation of the MELD score. In a recent case there was substantial doubt whether the patient, of whom it was claimed that he was on dialysis, indeed received dialysis. So far, ET checks the correctness of laboratory values used for calculation of the MELD-score by asking the transplant centers for copies of the original lab data (in case of MELD score of higher than 25 in every case, below this threshold the check is done in a random manner). So far, it has not been checked, whether a patient claimed to be on dialysis or hemofiltration indeed received this treatment. The correctness of this information provided to ET was trusted upon.

Thereupon, the ELIAC discussed to what extent ET in fact can and has to check the provided information. In the interest of transparency of the system and with the idea to document also a statement of an expert that is not directly involved in the liver transplantation, the ELIAC developed RLAC01.12.

Furthermore, ongoing concern was shared with the ELIAC regarding the possibility to manipulate the measurement of the lab values used for the calculation of the MELD score. One possibility, claimed to be used in this context, is the sending of blood samples on Friday evening so they can only be analyzed the following Monday. The measurement of bilirubin and INR could be systematically influenced by this approach.

The ELIAC discussed whether establishing central laboratories in the different ET countries would be an adequate approach to prevent any bias in this measurement of the MELD lab values. After extensive discussion, the ELIAC concluded that such an approach would result in huge organizational challenges without any clear effect on the accurateness of the data. Nevertheless, the ELIAC stated it might be an option to discuss this question on a national level.

D. PRO-DUCT study

The ELIAC discussed the study by the Berlin transplant center. It is stated to be essential that it is monitored by the steering committee of the planned study that none of the centers involved in the study, includes more than 10 patients as foreseen in the study protocol. This is considered important in order to prevent misuse of the study.

The ELIAC agreed to the study protocol.

E. Study proposal on the correlation of extended donor criteria with MELD score

The Vienna transplant center presented the study proposal to the ELIAC. The basic idea of the study is to use donor and recipient data from transplants performed between 2007 and 2010 to see which of the donor and recipient factors have an impact on outcome after transplantation.

The ELIAC pointed out some issues, which should be taken into consideration. Furthermore, it is stated that a similar study is performed by the Leiden University Hospital. Finally, the ELIAC concluded that both study groups will receive data from ET. Also cooperation with ELTR is suggested. Also, a liaison person within the ELIAC is appointed, who will cooperate with both study groups. This way, it would also be possible to facilitate interaction between the study groups.

F. Request for bonus points in relation to kidney-after-liver transplantation

The ELIAC was informed about cases, in which centers claimed that they forgot to register a patient for combined liver and kidney transplantation prior to liver transplantation, although the patient already had end stage renal failure. They only became aware of this mistake after the liver transplantation and now the centers ask for bonus points for kidney-after-liver transplantation as foreseen by the respective recommendation.

The opinions in the ELIAC differed. On the one hand there is the opinion that patients should not be punished for human errors of the transplant centers. On the other hand, the ELIAC expressed concern that allowing a later registration for kidney-after-liver transplantation might lead to abuse of the system. The ELIAC concluded there should be clear evidence that the patient already had end stage kidney failure prior to the liver transplantation for the bonus. In order to come to clear and manageable rules for this, it has been suggested to bring this topic to the attention of the ETKAC and ask them for a proposal how to best handle this situation.

G. Update on developments in liver allocation

A very recent analysis of liver transplant data was presented to the ELIAC. Concerns were expressed with regard to the very low rate of patients that receive their donor liver via labMELD and standard allocation (the percentage dropped below 20% recently). The reason for this is the very high rate of rescue allocations especially in Germany on the one hand and the increasing number of recipients that get their donor liver allocated via a Standard Exception. The German representative in the ELIAC is asked to bring this issue forward in national discussions because the situation might undermine the basic idea of the MELD allocation system.

Report of the meeting of the Eurotransplant Thoracic Advisory Committee (ETHAC)

Chairman: Prof.Dr. G. Laufer

Secretary: Dr. J. Smits

The ETHAC met on Tuesday, December 13, 2011

Members present: 13 + 1 external advisor + 1 director + 3 ET co-workers

Members excused: 2 + 1 external advisor

A. Discussion on the interface between the lung allocation system based on LAS and on urgency tiers

In summary the new lung allocation policy is based on the following rules:

1. Only the **total balance** will be used for leveling out the organ exchange between the countries.
2. All **international** transplant candidates, i.e. patients on the match list of a donor from another country will be **ranked by LAS**. National allocation – this is the scheme applied for ranking patients from the same donor country – will not change in the non-LAS countries, except for the blood group rules and the age matching (see 5. and 6.)
3. International patients from a country with a negative total balance with the donor country will have priority on the list. Of these international patients, those with a high LAS will come on top of the match list, those with a low LAS will be sorted among the national patients.
4. If the donor country is a non-LAS country the international patients with a high LAS and a negative total balance will come on top of the national list of the donor country and will be sorted by LAS. The international patients without a negative total balance will come after the national patients and will be sorted by LAS. The low LAS international patients with a negative total balance will be sorted among the elective national patients, sorted by waiting time.
5. *Blood group rules*
All countries agreed to allocate lungs first according to the modified ABO compatible rule (AB0-0 to AB0-0 and -B; AB0-A to AB0-A and -AB; AB0-B to AB0-B; AB0-AB to AB0- AB) and then according to the ABO compatible rule (AB0-0 to AB0-0, -B, -A and -AB; AB0-A to AB0-A and -AB; AB0-B to AB0-B and -AB; AB0-AB to AB0-AB).
6. *Donor-patient age matching*
All countries agreed to allocate lungs from donors <12 years of age, first to patients <12 years, then to patients aged 12 - 17 years, then to patients aged ≥18 years; from donors aged 12 - 17 years first to patients 12 - 17 years, then to patients <12 years, then to recipients ≥18 years.

In all countries except in Germany, donors aged ≥ 18 years are first allocated to patients ≥ 12 years and then to patients < 12 years.

5. An additional urgency status will be created for transplant candidates < 12 years, patients who are hospitalized will get priority above patients who are not hospitalized.
6. The threshold value for high LAS is defined at 50.
7. A detailed imputation scheme has been agreed upon.

B. Audit process

The general rules of the audit process for judging requests for exceptional LAS were discussed and agreed upon. Both review boards (RB) are advised to strictly adhere to these rules and to exchange their experience.

In order to avoid split decisions among the RB members, it is advised to concur prior to sending one final decision to ET.

C. Mandatory submitting of LAS / LASplus data

After consulting the other transplant centers, the national EThAC representatives confirmed on behalf of their country that they agree with RThAC04.11.

D. Standardization on donor items

The EThAC representative in the OPC informed that during the recent OPC meeting the Dutch representatives asked for adding additional items to a list of standardized donor data. As this list had previously been designed by the EThAC, the OPC now kindly asked for a judgment of this new proposal.

All EThAC members recognized the need for obtaining standardized and detailed data.

It was stated that – in view of the forthcoming trial on heart preservation, for which purpose the DSO (German procurement organization) has already adapted its forms – inconsistency between these two forms is not beneficial. Therefore it was decided to take care that both lists will be matching.

Report of the meeting of the Eurotransplant Organ Procurement Committee (OPC)

Chairman: Prof.Dr. D. Ysebaert

Secretary: Dr. I. Tieken

The OPC met on Wednesday, November 23, 2011

Members present: 8 + 1 director + 1 ET co-worker

+ 1 observer

Members excused: 6 + 3 observers

A. Presentation of the Community Concept

The ET manager Finance/IT presented the various functionalities of the Community Concept platform that ET is currently piloting and assessing with regard to its usefulness for the ET-community. He explained that this platform in comparison with other platforms has more possibilities and it has the appropriate functionality for security of privacy and data which enables of having open but also very restricted groups. These different groups can discuss and work on documents together.

First a pilot phase will start after which ET will determine the usefulness of the concept and its various functionalities.

Some OPC members are rather sceptical about the certain functionalities and the usefulness of such a platform and raised several critical questions and remarks about the concept.

The pilot is expected to provide insight in different groups of ET's community.

B. Risk assessment of communicable diseases of potential ET member states

The OPC members were presented with a document on this issue that was prepared by some members of the ET medical staff together with the ET Directors. The OPC chairman explained to the members that with the increasing number of countries showing interest to become an ET member the prevalence of communicable diseases might increase. For this reason the ET Board and Directors expressed the wish to create a risk assessment tool of communicable diseases. In order to be able to create such a risk assessment it is necessary to have an overview of communicable diseases in the current ET member states. In this respect it was decided to research at first those infectious diseases that fall under the group VII 'Diseases under routine national surveillances'. Next the question was discussed who should be asked or where the information could be found. The conclusion of this discussion was that the information should be collected by the WHO. During the next OPC meeting the profiles of communicable diseases in the ET member states in comparison to that of the new preliminary ET member country Hungary will be discussed.

The OPC members then discussed another document 'Assessment tool for logistic risks'. The general Director of ET explained that not only communicable diseases could lead to problems but also logistics (e.g. transport of organs, procurement teams etc.).

After a discussion on this issue the OPC concluded that the additional issues are to be added to the document on assessment of logistic risks.

C. Establishment of an information platform for infectious diseases

During a previous OPC meeting it was already concluded that ET should only give basic information regarding infectious diseases through its website. Giving information through our website might lead to problems such as stirring up expectations, incorrect publication etc. for which ET cannot take the responsibility. Besides it is questioned whether transplant surgeons will read information at time of an organ offer and if so that this might lead to unnecessary declines as transplant surgeons do not want to take any risks. All national representatives in the OPC were asked whether they favor information on the ET website on infectious diseases. All except for one ET country indicated that they do not. The OPC members then came to the conclusion that no information on infectious diseases should be published on the ET website at all. Instead it was suggested to ask transplant coordinators – i.e. in the future via the community concept – whether they feel the need for a platform. If they are enthusiastic about having the information provided on the ET website, ET will have to consider this again.

D. Protocol for reporting and allocation of HIV+ donor organs

The presented protocol for reporting and allocation of HIV+ donor organs led to a discussion after which ROPC01.11 was formulated.

In the framework of this discussion the OPC chairman stated that the Advisory Committees should indicate whether a change or a new feature must be regarded as a recommendation or as a policy.

The Board should make definitions of a policy and of a recommendation. The consequences of the choice should be clear e.g. a recommendation would probably take more time in comparison with a policy because national authorities must give their consent to recommendations as they are binding which does not hold true for policies which are without engagement.

E. Example of allocation / procurement problems

The OPC was informed about a center that discarded an organ without informing ET and did not reply to several requests for an explanation of violating the ET regulations. All members of the OPC agree that this is not acceptable. A center that violated the rules of ET and is asked for an explanation must respond.

The OPC discussed what should be done in the future with such cases. The medical director explained that he recently decided that after two reminders the responsible Advisory Committee should be asked what to do. The OPC is of the opinion that national authorities could be involved at an earlier stage and that the ET Board should make a policy on what steps ET can take if such incidents occur.

F. Procedure towards electronic quality forms / application

The discussion focused on 'Logistics: filling out and returning the quality form by the transplant surgeon'. As paper quality forms and the quality form application both have advantages as well as disadvantages it was concluded that both will be made available.

G. Establishment of organizational framework on donor pretreatment

The OPC chairman presented the members with a document in which is explained that nowadays every study needs to have informed consent of the recipients besides the approval of an ethics committee. A study in the domain of donor pretreatment becomes problematic because every possible recipient has to give his consent for every study.

The OPC discussed the suggestion to ask every new recipient on the waiting list for approval for receiving organs being allocated in the framework of a study. This could then be added to the donor profile such as "ECD donor".

Later, if the recipient receives an organ within a study and additional data is needed, the recipient should be asked if he will give his consent for gathering of specific data and / or for the carrying out of tests that are needed for the study. The OPC members questioned this approach as an enormous pressure would be laid on the shoulders of a recipient to accept study related donor organs otherwise having a considerable longer waiting time.

The discussion was concluded by the agreement that a proposal should be formulated and that every ET country should be asked for their comments. Besides during the upcoming ET winter meeting (January 2012) a workshop on this issue will be organized.

Report of the meeting of the Eurotransplant Tissue Typing Advisory Committee (TTAC)

Chairman: Prof. Dr. F. Claas
Secretary: Prof. Dr. I. Doxiadis

The TTAC met on Wednesday, December 7, 2011
Members present: 10 + 1 ET director
Members excused: 0

A. Reports from Advisory Committees and ET countries

- *ISWG*

The TTAC was informed about a presentation of the so-called Community Concept that might possibly be introduced in ET. The TTAC is of the opinion that such way of communication will not improve the discussion between centers. The TTAC will analyze primary results obtained by the transplant coordinators and will re-discuss this issue at a later occasion.

The TTAC was furthermore informed that the ISWG discussed the need for simulation models which idea was adopted by the TTAC.

The return rate for organs which have been sent to recipient centers with an expected negative crossmatch has been briefly discussed. According to a study of the TTAC secretary, presented at last year's Tissue Typers meeting, the rate is about 3%.

- *National societies*

Germany

Germany will introduce the concept of unacceptable antigens (virtual cross match) in the guidelines. This will decrease cold ischemia times. A concept of reporting HLA typing results of transplant candidates for other than kidney organs will be passed to the laboratories and centers soon.

The Netherlands

An education day, organized by the Dutch Transplantation Society (NTV) and EFI, took place in Nijmegen. The topic was HLA in relation to anything but transplantation.

B. News on new countries

Hungary has signed a preliminary agreement with ET for a period of one year. After evaluation a full membership could be possible. EFI accreditation of the laboratory is a prerequisite.

There is no news with regard to Serbia and with regard to Estonia the TTAC is informed that Estonia has now an accredited laboratory but that logistics are very difficult.

C. Problems with the ET administration regarding labels, allocation and report of data

The protocol for retyping inconsistencies is still in the pipeline.

D. External Proficiency Testing (EPT)

The TTAC secretary informed the TTAC about the new way of reporting EPT results and on the new organization of the EPTs. CDC (complement dependent cytotoxicity) will be mandatory for all participants and in case solid phase assays are used an analysis can only be done if 10 or more participants report results. In addition some screening samples will be used for the definition of acceptable mismatches.

E. Dutch pilot study for organ shipment with our cross match in the donor center

This prospective study will be discussed during a consensus meeting with all transplant and tissue typing centers in the Netherlands. A date is not yet appointed.

F. New allocation parameters

The TTAC chairman reported from the last ETKAC meeting where the new allocation parameters were discussed. There will be four donor categories in the ages of 0-15, 16-49, 50-64 and ≥ 65 years. These will form also the basis for the pay-back system in ET.

The next TTAC meeting will be used for the discussion on the implementation of an HLA-DR identity between patients and donors and the influence of class I which is a risk for re-transplants.

Report of the meeting of the Eurotransplant Ethics Committee (ETEC)

Chairman: Drs. M. Bos
Secretary: Dr. A. Rahmel

The ETEC met on Friday, October 14, 2011
Members present: 4
Members absent: 3

A. Non-heart-beating (NHB) donation guidelines (minimal standards) – current status

The ETEC was informed that the Board is in principal content with the interest by the ETEC for looking into the question of NHBD (DCD) in the different ET countries. However, it was stated that it is not the role of ET to come up with detailed

guidelines regarding the determination of death in NHBD, since the topic of determining death in potential donors does not fall under the responsibility of ET.

It was reported that in the Netherlands as well as in Belgium NHB donation is currently reviewed by respectively a committee of the Dutch Health Council and a working group of the Belgium Transplantation Council. Both groups agreed to exchange ideas in the process of developing national guidelines. It is expected that in Spring 2012 a document can be presented, which will be subdivided in two major parts:

- a) A best practice paper which describes the current practice and the rules surrounding NHB donation
- b) Position paper which addresses the ethical and legal basis of NHB donation.

The ETEC was furthermore informed that the topic of NHB donation will not be discussed in Croatia at the moment since it might endanger the reached consensus in the community regarding organ donation as well as the public trust in organ transplantation.

B. Deviation from allocation rules after blood group incompatible heart transplantation

The ETEC was informed about a blood group incompatible heart transplantation followed by acute retransplantation with deviation from the heart allocation rules. ETEC concluded that the right decision in this matter was taken. Furthermore, the ETEC concluded that cases like this should be reported to the ETEC in any case. If time allows, a member of the ETEC should be involved in future cases. The role of the ETEC member would not be to give formal consent to any deviation from the allocation rules but rather to give advice taking ethical arguments into account.

C. Recent developments regarding transplantation of non-residents

Two recent cases regarding transplantation of non-residents were presented to the ETEC. In one case, after the transplantation took place, an anonymous accusation was made that the case involved organ trade. After discussing the case, the ETEC clearly stated that it is not a case of organ trade because no money was paid to influence the allocation of the organ. The allocation went according to the allocation rules of ET.

Critical remarks/questions formulated by the ETEC in this matter were:

- How did the patient get access to the waiting list?
- How and why did the patient get the urgency status (MELD score) that led to the allocation of the organ?
- It is considered of some concern that a company was involved in mediating the contact between the foreign hospital and the ET Transplant Center. The ETEC is of the opinion that contact with the ET hospital should have

been established by the foreign Hospital or insurance company.

- Why was the patient not transplanted in his home country? (Liver transplants are performed in his home country).

With regard to the last question, the ETEC concluded that a transplant center, situated within ET, should only accept a patient from outside ET if there is immediate contact to the treating physician in the home country. Furthermore, it should be explicitly asked whether the recipient had been referred for transplantation in the home country and if no, why not. In case a referral has been tried and rejected, reasons for this rejection have to be asked. Also, it would need to be clarified, prior to accepting any non-resident for transplantation, whether the necessary treatment after transplantation can be provided in the home country.

The ETEC considers the fact that money was paid for the transplantation as a limited problem, as long as the payment took place according to the hospital regulations and as long as the payment had been in line with payment for general transplantations of the same type in the recipient center. However, the ETEC stated that it has to be prevented that depending on the amount of money a patient can pay, access to the waiting list is allowed.

The ETEC discussed how to go ahead with non-resident transplantation in the future within ET. Different scenarios were discussed. One option could be to go for a complete 0% non-resident rule, not allowing any non-resident to be transplanted. There are concerns within the ETEC whether this is ethically and legally possible. Another option would be to allow the transplantation of non-residents only if there is a formal agreement with the home country of the recipient which takes into account:

- a) Equal access to transplantation of all patients within the home country;
- b) Reciprocity (for every patient transplanted from the country of the non-resident, a donor organ of the same type has to be provided to ET);
- c) Medically sound follow-up of the patient.

Another option could be that every non-resident transplantation has to be analyzed by an independent committee that specially focuses on the question whether any ethically or legally not acceptable circumstances were involved in the referral and acceptance of the non-resident patient. However, concerns were expressed how these criteria should be defined and how it could be investigated. It was felt that such control cannot be provided by ET but only by independent national authorities that also have immediate access to the transplant center.

In summary, the ETEC stated to be in favor of having transparency in the area of non-resident transplantation.

Announcement of the 2012 Henk Schippers Young Investigator Award



Henk Schippers became the first Eurotransplant Director in 1970. After 5 years, he was appointed Secretary Treasurer of the Board until his death in 2003. Henk laid the foundations for the administration of Eurotransplant. He successfully completed negotiations with the insurance companies and initiated the interna-

tional network, which is now a hallmark of Eurotransplant. To commemorate his pioneering work for Eurotransplant a young investigator award in his name was established in 2003.

Purpose

The purpose of this award is to encourage young clinical and/or scientific investigators to pursue a career in the field of organ and tissue transplantation. It is our hope that this research will be invigorated by the work of young, talented individuals supported by stable multi-year funding. The Henk Schippers Young Investigator Award is especially meant to enable the investigator to present his/her results of clinical and/or scientific organ transplantation related investigations at well recognized and respected international transplantation congresses or symposia, e.g. European Society for Organ Transplantation (ESOT).

Eligibility

Candidates (<40 years) must have attained a masters or PhD degree. Individuals at the Associate Professor level are not eligible. Clinicians and investigators must have completed their residency or post-doctoral training no more than five years prior to applying. Applications coming from the entire European area will be accepted.

Terms

The recipient will receive € 2.500. This award will be made available to the individual applicant and must be used for direct expenses. A progress report will be required. Applicants can provide a paper, also after presentation at a specific meeting and the candidate chosen can use the money in the next year. The Eurotransplant International Foundation will retain the right to unilaterally cancel any awards for non-compliance or non-performance.

Application procedure

Candidates must submit:

- A completed curriculum vitae;
- An application letter with
 - the publication on which the application is based
 - for which purpose he/she will use the award with a short description of the research project (limited to three pages);

- A list of publications abstracts and previous research in the field of transplantation (limited to two pages);
- Applications must also contain a letter of nomination from a faculty sponsor who will accept responsibility for monitoring the awardee;
- Applications must be entirely in the English language.

One original and one copy of all parts of the application must be received on or before the due date at the office of Eurotransplant International Foundation in Leiden, the Netherlands.

At least one copy of the application must contain original signatures.

Non-complying applications will be returned without review.

Deadline

The application deadline is August 12, 2012

Selection

The Award Committee consisting of Board members of the Eurotransplant International Foundation, will consider all proposals. Decisions of the Award Committee will be announced by **the second week of September**.

The award will be presented at the annual Assembly / Presidential Symposium of Eurotransplant. The winner of the award will be invited to present his/her data (15 minutes talk including discussion) either at the annual Presidential Symposium or at the annual ET Winter Meeting. Travel costs will be reimbursed.

Award management

Award payments will be made following written acceptance by awardee.

Change in status of awarded

Awards are to remain solely with the designated awardee and may not be transferred to any other person. If a recipient decides not to attend the anticipated congress, the award will be terminated as described above.

Inquiries

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The Eurotransplant Senior DR-compatible Program

Age and HLA-DR matching for the Elderly

On behalf of the ESDP Study Group
Prof. dr. Johan W. de Fijter, Leiden University Medical Center

The ageing kidney transplant recipient

Over the past decades, there have been significant changes in demographic characteristics of patients with end-stage renal disease, mainly due to an increase in elderly patients over the age of 65 years and, in more recent years, over 75 years. There is substantial evidence to support transplantation in elderly, since it is relatively safe and provides a life expectancy exceeding that on dialysis¹. Clearly the magnitude of improved patient survival is not uniform across patient subgroups such as the elderly and/or those with diabetes mellitus². Nevertheless, several studies have reported acceptable outcomes for selected patients over the age of 70 years, or even 80 years^{1,3}. In addition, also recipients over 65 years of age who received expanded criteria or marginal kidneys lived on average 3.8 years longer than their waiting listed counterparts, despite lower graft outcomes⁴. Preclusion of elderly for renal transplantation based on age alone is considered not fair. Some reluctance is however also justified given the excess initial mortality. In addition, there is the lifelong need for immunosuppressive therapy, while in the elderly infectious causes are among the leading primary causes of death⁵. The difficulty of selection, taking biological age and co-morbid conditions along with an increased operative risk into account, continues to pose a significant challenge to the nephrology and transplant community.

The challenge to kidney allocation

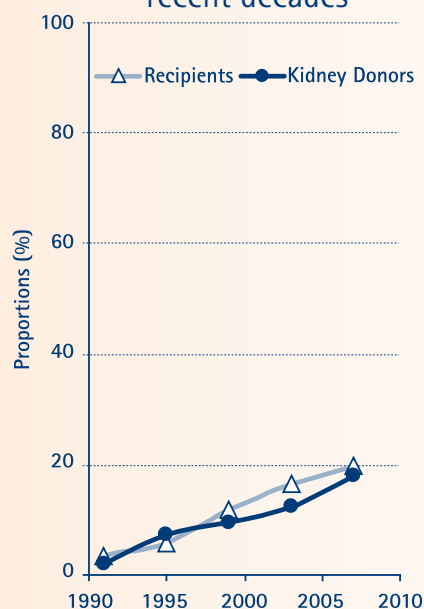
Allocation of the limited number of available kidneys also poses a constant challenge to maintain an acceptable balance between equity of access, medical utility, efficiency in terms of logistics and finances as well as balance between participating countries. In the Eurotransplant (ET) Kidney Allocation System all kidneys are virtually offered to the pool. Each patient receives a transparent point score on the basis of human leukocyte antigen (HLA) matching based on the “broad” class I antigens and splits for class II, waiting time, mismatch probability, distance to the transplant center, and balance for donation rates between the participating countries⁶. This system has been very effective in terms of histocompatibility. Between 1996 and 2005, more than 20% of recipients received a zero mismatched kidney and almost all patients (97%) received at least a zero or one HLA-DR mismatched kidney⁷.

The inevitable consequence of prioritization of HLA matching for all loci is that some patients have to wait longer for a suitable organ and accumulate on the waiting list. This may

occur specifically if they express HLA antigens or a haplotype not prevalent in the organ donor population. Nowadays, however, median waiting times within ET are approaching five years, but differ between countries. An allocation policy dominated by waiting time inherently carries the unintended consequence of a disadvantage directly related to life expectancy, i.e. the elderly ESRD patient. The key issue remains that annual mortality rates on dialysis still by far exceed the improved transplantation rates. As a consequence, especially the elderly carry a significant risk for not surviving before they reach the end of the queue⁸.

Since 1999, the ET Senior Program (ESP) preferentially allocates kidneys from older (≥ 65 years) deceased donors, without prospective matching for HLA antigens, to older (≥ 65 years), local or regional, transplant candidates. Allocation without the effort to achieve matching for HLA antigens at that time constituted a significant deviation from European allocation standards. The rationale behind this policy was to expedite the change of the elderly to receive a transplant and to reduce the incidence of delayed graft function⁹. Currently, the program also includes repeat transplants or sensitized patients, provided that unacceptable antigens are identified and excluded. The result has been that in the past decade, there has been an annual increase in the proportions kidney transplant recipients ≥ 65 years from less than 4% to well over 20%¹⁰. The ESP allocation principle encouraged the use of older donor organs that otherwise might have been discarded and also expedited the chance of the elderly to receive a transplant (Figure 1).

Kidney Transplantation in the Elderly in recent decades



Improve outcome in the elderly

Several studies have shown that outcome after deceased donor transplantation is influenced by several independent parameters as cold ischemia, donor and recipient age, degree of sensitization, and HLA compatibility^{11;12}. Studies have also documented that kidneys from older donors are more vulnerable to ischemia/reperfusion injury, to the vasoconstrictive toxicity of calcineurin inhibitor therapy, more likely to experience acute rejection as well as less likely to mount an inadequate repair response following injury. The key objective is to minimize toxicity, but at the same time achieve the current low acute rejection rates seen with kidneys from the regular donor pool. HLA-DR matching was shown to be most important in the first period of transplantation, followed by HLA-B, and finally HLA-A¹³. More recently, a significant beneficial effect of HLA-A and -B matching was only found in patients receiving a full HLA-DR compatible kidney¹⁴. Also in the current era of very effective immunosuppressive therapy, the principle advantage of HLA compatibility is still evident from the superior graft survival of HLA six-antigen matched kidney grafts. The excellent results achieved with living unrelated kidney donation have indicated that HLA-matching and donor age may be of less relative importance in case there is the benefit of receiving a (selected) kidney with normal renal function without the summation of insults associated with brain death and cold storage¹⁵. As the lowest graft survival rates have been observed in six HLA-mismatched kidney transplants, the decision to preferentially allocate kidneys from older deceased donors to senior citizens without prospective matching is, on hindsight, less straightforward.

Both acute rejection and subclinical rejection are associated with the degree of incompatibility for HLA-DR antigens^{16;17}. Asymptomatic infiltrates in early biopsies after living donor transplantation most likely represent a donor-specific immune response as it correlated with HLA-DR mismatching, underscoring the fact that current clinical immunosuppressive regimen remain imperfect^{16;18}. At present, the outcome parameters in the elderly are, however, dominated by increased death from infectious disease causes¹⁹. The impact of increasing age on death-censored graft outcome appears to be amplified if also the age of the kidney donor is taken into account. The therapeutic index for clinical immunosuppressive therapy appears to be even narrower in the elderly than in younger renal transplant recipients. A direct causative relation between the need to treat rejection and increased mortality may be difficult to establish, but there is no doubt that extra boluses of steroids or treatment with antibodies add significantly to post-transplant morbidity.

A more sophisticated way to improve the balance in the elderly is to combine age-matching with the old virtue of prospective matching for HLA-DR antigens. Foreign tissue antigens tend to be ignored unless the tissue is injured in which case it is more likely that they provoke and activate an immune response²⁰. Grafts from older deceased donors already have more age related injury and inflammation at

the time of procurement and transplantation²¹, which in turn may increase immune recognition. After deceased donor transplantation, older donor age and the presence of chronic lesions, defined by interstitial fibrosis and tubular atrophy, at the time of implantation were found to be associated with subclinical inflammation in protocol biopsies obtained 3 months after transplantation¹⁷. The effect of matching for HLA-class II antigens on the incidence of acute rejection in the elderly remains to be determined¹⁴. Of note, in the past decade only 7% of all kidneys have been allocated with two HLA-DR mismatches and therefore experience with HLA-DR mismatched transplants within the ET community is still very limited.

Synopsis of the ESDP study

Objective: The primary aim is to assess the efficacy and safety of allocating kidneys from older deceased donors to elderly recipients based either A) on waiting time, without prospective matching for HLA antigens [current practice in ESP] or B) on HLA-DR compatibility (defined by zero HLA-DR mismatches) followed by waiting time.

Study population: The ESDP study will include patients aged 65 years or older, who have been listed for kidney transplantation and the ET Senior Program (ESP) in particular.

Study design: In this non-interventional observational allocation study paired kidneys from donors ≥ 65 year of age will be randomized at the center or (cooperating) regional level: the first kidney according to current ESP allocation (waiting time, no prospective matching for HLA antigens) and the contra-lateral kidney aimed at zero mismatches for HLA-DR followed by waiting time. Cold ischemia times should preferentially remain under 20 hours.

Main study parameters/endpoints: The primary read out will be the incidence and severity (need for antibody therapy) of biopsy-proven acute rejection at 6 months post-transplantation. Optimal scientific evaluation of the modified allocation primarily based on DR-compatibility requires a widely accepted standard of clinical immunosuppressive therapy. The ESDP Study also aims to assess secondary outcomes such as the impact on graft function and patient and (death-censored) graft survival up to five years.

Nature and extent of the burden and risks associated with participation: The proposed HLA matching will, according to all medical knowledge, not negatively but rather positively influence the outcome of the selected patients. Treatment regimens and outpatient department visits are according to (evidence-based) standard medical care for renal transplant recipients and their follow-up.

Logistic support for the ESDP study

It is also a great personal pleasure to be able to inform you, that (after the declaration of insolvency of ClinTrio and the retreat of Roche Germany as subsidiary partner) with the continued full support of Astellas we have been able to relaunch the ESDP study.

Leiden University Medical Center (as sponsor) in close cooperation with ET and Astellas we have selected and contracted a new contract research organization, being MEDIDATA based in Konstanz, Germany.

MEDIDATA GmbH is an independent, privately owned contract research organization (CRO) that has been providing end-to-end services for clinical trials and for observational studies for more than 25 years. The headquarters are located in Konstanz, Germany and its field based monitoring group has sites all over Germany. Currently employing over 60 professionals, MEDIDATA GmbH combines experience with the quality, dedication, and flexibility of a mid-sized organization. Since the company's early days MEDIDATA has managed a large number of international observational studies in different indication areas. MEDIDATA has now taken over the project management of the observational ESPD study and will kindly support you regarding study advancement.

Clinical Project Manager for the ESDP study is Tamara Rupp. Contact details: Tamara Rupp, Clinical Project Manager,

MEDIDATA GmbH

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As of day one ET International Foundation has been a collaborating partner in the ESDP trial. To facilitate an optimal allocation process for the ESDP study, a new tailor-made allocation algorithm has been incorporated in the ENIS system. In addition, a user friendly (internet based) electronic Case Record Form (e-CRF) has been created within ENIS to collect the predefined follow-up data. ET provides all participating centers with the option of a training-by-telephone session to facilitate the use of the eCRF and offers direct user support for the duration of the study. Centers will be periodically informed about any missing data. Marieke van Meel was appointed to coordinate the activities within ET regarding the ESDP trial. Marieke currently is the registry coordinator with ET and will coordinate the process of data collection and reimbursement for the ESDP study.

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Currently we are in the process of contacting all transplant centers in Austria, Belgium, Germany and the Netherlands in order to relaunch the ESDP study and renew the study contracts with the sites. With the help of the principal investigators for the different countries: Austria (Prof. Mühlbacher, Vienna), Belgium (Dr. Peeters, Ghent), Germany (Prof. Krämer, Mannheim and Prof. Heemann, Munich), Netherlands (Prof. De Fijter, Leiden) and the ETKAC we are working hard to achieve participation of as many (but preferentially all) transplant centers as possible and start inclusion as of May 2012.

Conclusion

Last but not least it is important to emphasize that this observational study has a paired design allocating one kidney according to the current ESP program and the contra-lateral kidney according to the ESDP principle. We therefore do need the continued and, if possible, the full support of you all, the ET family, to regain momentum in ESDP study and also to bring this collaborative initiative to its ultimate goal, being better allocation principles based on solid scientific data. The important perspective for our patients remains that a successful transplant, even with a marginal donor kidney, will be associated with a substantial further improvement in longevity and in quality of life.

Thank you in advance for your continued support!



Reference list

1. Rao PS, Merion RM, Ashby VB, Port FK, Wolfe RA, Kayler LK. Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007; 83: 1069-1074
2. Wolfe RA, Ashby VB, Milford EL *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant [see comments]. *N Engl J Med* 1999; 341: 1725-1730
3. Huang E, Poommipanit N, Sampaio MS *et al.* Intermediate-term outcomes associated with kidney transplantation in recipients 80 years and older: an analysis of the OPTN/UNOS database. *Transplantation* 2010; 90: 974-979
4. Ojo AO, Hanson JA, Meier-Kriesche H *et al.* Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; 12: 589-597
5. Meier-Kriesche HU, Ojo AO, Hanson JA, Kaplan B. Exponentially increased risk of infectious death in older renal transplant recipients. *Kidney Int* 2001; 59: 1539-1543
6. De MJ, Persijn GG, Wujciak T, Opelz G, Vanrenterghem Y. The new Eurotransplant Kidney Allocation System: report one year after implementation. Eurotransplant International Foundation. *Transplantation* 1998; 66: 1154-1159
7. Doxiadis II, Smits JM, Persijn GG, Frei U, Claas FH. It takes six to boogie: allocating cadaver kidneys in Eurotransplant. *Transplantation* 2004; 77: 615-617
8. Schold J, Srinivas TR, Sehgal AR, Meier-Kriesche HU. Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. *Clin J Am Soc Nephrol* 2009; 4: 1239-1245
9. Frei U, Noeldeke J, Machold-Fabrizii V *et al.* Prospective Age-Matching in Elderly Kidney Transplant Recipients-A 5-Year Analysis of the Eurotransplant Senior Program. *Am J Transplant* 2007;
10. de Fijter JW. An old virtue to improve senior programs. *Transpl Int* 2009; 22: 259-268
11. Morris PJ, Johnson RJ, Fuggle SV, Belger MA, Briggs JD. Analysis of factors that affect outcome of primary cadaveric renal transplantation in the UK. HLA Task Force of the Kidney Advisory Group of the United Kingdom Transplant Support Service Authority (UKTSSA). *Lancet* 1999; 354: 1147-1152
12. Nyberg SL, Matas AJ, Kremers WK *et al.* Improved scoring system to assess adult donors for cadaver renal transplantation. *Am J Transplant* 2003; 3: 715-721
13. Thorogood J, Persijn GG, Schreuder GM *et al.* The effect of HLA matching on kidney graft survival in separate posttransplantation intervals. *Transplantation* 1990; 50: 146-150
14. Doxiadis II, de Fijter JW, Mallat MJ *et al.* Simpler and equitable allocation of kidneys from postmortem donors primarily based on full HLA-DR compatibility. *Transplantation* 2007; 83: 1207-1213
15. Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. *N Engl J Med* 1995; 333: 333-336
16. Choi BS, Shin MJ, Shin SJ *et al.* Clinical significance of an early protocol biopsy in living-donor renal transplantation: ten-year experience at a single center. *Am J Transplant* 2005; 5: 1354-1360
17. Naesens M, Lerut E, Damme BV, Vanrenterghem Y, Kuypers DR. Tacrolimus exposure and evolution of renal allograft histology in the first year after transplantation. *Am J Transplant* 2007; 7: 2114-2123
18. Shapiro R, Randhawa P, Jordan ML *et al.* An analysis of early renal transplant protocol biopsies--the high incidence of subclinical tubulitis. *Am J Transplant* 2001; 1: 47-50
19. Meier-Kriesche HU, Ojo AO, Hanson JA, Kaplan B. Exponentially increased risk of infectious death in older renal transplant recipients. *Kidney Int* 2001; 59: 1539-1543
20. Zinkernagel RM, Hengartner H. Antiviral immunity. *Immunol Today* 1997; 18: 258-260
21. Nyengaard JR, Bendtsen TF. Glomerular number and size in relation to age, kidney weight, and body surface in normal man. *Anat Rec* 1992; 232: 194-201

News from the Eurotransplant duty desk

Overview of adaptations to the LAS request form since implementation

- The field Current pCO₂ is no longer linked to the fields Highest and Lowest pCO₂. The value for the Current pCO₂ can be filled in and for the other fields the option N/A can be chosen. The Highest and Lowest pCO₂ values remain linked, both can be left open or both can be filled in.
- In the exceptional request forms the diagnosis 'Other' is added to the list of diagnosis codes. If this option is chosen, specifications need to be filled in as well.
- The text to the field Pulmonary artery catheter is changed from 'Previous three months' to 'Max. 1 year old' reflecting current practice.
- The field 'Pap mean' is still automatically calculated, but can be adapted.

Arterial PCO₂

Current pCO₂ N/A

Current pCO₂ unit

Highest/Lowest pCO₂ N/A

Lowest pCO₂ (previous six months) unit

Highest pCO₂ (previous six months) unit

Implementation of RLAC03.10

The following recommendation submitted by the ET Liver Intestine Advisory Committee (ELIAC) and approved by the ET International Board is operational as of 21 March 2012.

RLAC03.10

At time of listing and with every MELD update the following two additional lab values have to be reported to Eurotransplant:

1. Serum Ferritin
2. Serum Cholinesterase

The rationale behind this recommendation is that recent data indicate that these lab values might increase the predictive value of MELD especially with regard to outcome after liver transplantation. These lab values might therefore be helpful in further improving liver allocation via a modified MELD-score.

In the event that the lab values involved have not been tested or if a country did not approve this recommendation then centers can enter N/A (= not available).

If you have any questions about the above regulation, please do not hesitate to contact Laura Boogert, assistant secretary of the ELIAC at l.boogert@eurotransplant.org

Na+ Unit N/A CHE Unit N/A Ferritin Unit N/A

Comment

Eurotransplant Winter Meeting provides useful opportunities for exchanging ideas

Lively discussions in Alpbach

Again the Eurotransplant (ET) Winter Meeting proved to be an excellent opportunity for professionals to meet, exchange ideas and create energy. The attendance of 153 active participants was, together with last year, an all time high. With a choice of carefully chosen topics, the mixture of interactive workshops and plenary sessions was well balanced. The transplant community and the competent authorities of eight European countries work together in a constructive and interactive fashion within ET. Knowing each other helps create a common understanding. This forms the basis for exchanging ideas, organs and data. Occasions like the Winter Meeting are therefore indispensable for this productive cooperation.

This Winter Meeting was the last time Ellen Houwaart was involved in the organization. Since then she has become a mother. Ellen successfully helped develop and organize the Winter Meeting, since it was held in Alpbach for the first time. She transferred her responsibilities as secretary to the Board, as well as that of organizer of the Winter Meeting to Laura van Hattum.

This article describes in a nutshell the topics and discussions of the workshops during the Winter Meeting in Alpbach, Austria from 25 to 27 January.

Organ tourism

The Ethics Committee held the workshop '*The responsibility of transplant professionals to deal with potential organ tourists*'. Chairman Michael Bos started with an update on organ tourism, both globally and within Europe/ET. The number of organ tourists from ET-countries is relatively low, but still the issue deserves attention. India, Pakistan, Philippines have recently put a legal ban on selling organs to foreign patients, but organ tourism shifted to Colombia, Peru, Vietnam, Kenya.

How can the transplant doctor deter or discourage kidney patients who have plans to obtain a kidney abroad? In recent (draft) guidelines of the Canadian Council on Transplantation a proactive approach is advocated. The advice is to inform all new patients on the waiting list of the risks of overseas transplants. Recent research shows a lower graft survival and a higher complication rate. If a patient has plan to go abroad (or is suspected of plans), the doctor should seek contact and actively discourage him or her, by pointing out the unethical/illegal aspects of organ tourism and the potential damage to the donor. However, a returning organ tourist must be cared for and should receive normal medical follow-up.

In general the participants of the workshop felt that all patients on the waiting list should receive information on the risks of (paid) donation, but there was reluctance to confront individual patients who might be inclined to obtain a kidney abroad. If, on the other hand, a patient would openly express this intention, the doctor/center should in no way facilitate such plan and actively discourage the patient. Facilitating an illegal donation/transplant is a violation of the national law in all ET-countries. However all participants agreed that on return an organ tourist must receive medical follow-up care. There was discussion over the question on what to do if the kidney is rejected shortly after the transplant: back on the waiting list with return of waiting time, or at the end of the queue?

Kidney allocation

Prof. Uwe Heemann (Munich, Germany) handled the different aspects of kidney allocation during the workshop '*Further development of kidney allocation*'. At the moment, different waiting times in ET countries affect allocation. In Germany, kidneys are mainly allocated on basis of waiting time; matching is a factor of lesser importance. A solution for this could be to correct the amount of points given for waiting time, based on the difference between the mean national waiting time and the mean waiting time.

Furthermore, the country balance does not reflect the actual situation as it is based on the number of transplants performed in the previous year. This could be resolved by the introduction of a continuous country balance. Finally, ET countries have different point systems for local/regional and national donors i.e. Slovenia 100 points for local, 100 points for regional and 100 points for national versus the Netherlands (= one region) where everybody gets 300 points for national. This affects the import/export rate between countries. By having the same national points for allocation between countries this issue could be resolved.

Analysis of audit cases

The ET medical staff received several requests for an upgrade for HU liver transplantation. As these cases were considered to be outside the standard HU criteria, members of the ELIAC audited these cases. During the workshop both chairmen Xavier Rogiers (Ghent, Belgium) and Herold Metselaar (Rotterdam, the Netherlands) presented six of these cases. The audience could vote by showing a green or red card to grant or deny the request. In some cases the audience had a different opinion than the original auditors. The lively discussions resulted in several statements, which will be discussed with the ET staff. The audience was very

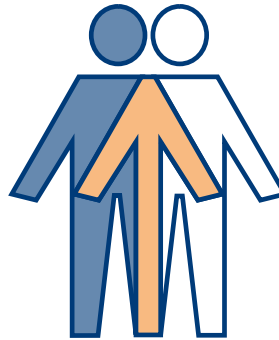
enthusiastic about the workshop and suggested to repeat this next year.

Organ loss in pancreas procurement

Prof. Wolfgang Schareck (Rostock, Germany) and Dr. Stefan Farkas (Regensburg, Germany) held a presentation on how to prevent organ loss in pancreas procurement and transplantation. The average waiting time for a pancreas transplantation has increased significantly in recent years. Possibilities for improvement can be found in management of the donor pool, the process of allocation and logistics, the decision process after an organ offer and in qualifying retrieving surgeons to improve trust between centers.

Scientific studies in organ donation

In this workshop with Prof. Dirk Ysebaert (Antwerp, Belgium) as a chair the different aspects regarding scientific research in organ donation were discussed. Information was exchanged regarding the difficulties of this issue taking into account the different laws and ethical issues in each ET member state. This information will be used for a position paper on the legal, ethical and organizational framework for scientific research in organ donors. This position paper can be used and challenged in all European countries.



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