Kidney Transplantation in Emerging Countries - Macedonian Experience for Improvement of the Program

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BSN, August 30, 2013, Budapest, Hungary
Kidney transplantation – best treatment option in ESRD

Gap between supply & demand

Deceased donors:

Living donation
  – related / unrelated / paid

The Declaration of Istanbul

The facts about KTx in Balkans

SEEHN initiative

Improvement in the MK kidney transplant program

Future perspectives!
Transplantation is best option for the ESRD patients

Schnuelle P, JASN 1998
Death-censored graft survival estimated by Cox proportional hazard analysis

Herwig-Ulf Meier-Kriesche, Kidney Int 2003; 58, 1311–1317
Kaplan–Meier Estimates of Allograft Survival According to the Use or Nonuse of Long-Term Dialysis before Kidney Transplantation from a Living Donor

Graft survival - HLA matching (LURD, LRD & CAD grafts)
Organ Exchange Organizations

- Scandiatransplant
- UK Transplant
- ABM, France
- SwissTransplant
- Lusotransplante
- ONT, Spain
- Eurotransplant (ET) - 125 M – 7 states
- Poltransplant
- Czechtransplant
- Hungarotransplant
- CNT, Italy
- HNTO, Greece
Eurotransplant: gap between supply & demand

- Deceased donors
- Transplants
- Active waiting list

Year 2000: 1,748
Year 2001: 1,732
Year 2002: 1,747
Year 2003: 1,896
Year 2004: 1,795
Year 2005: 2,245
Year 2006: 2,299
Year 2007: 2,411
Year 2008: 2,232
Year 2009: 2,305

- +21.2%
- +31.9%
- +11.8%
Each day, 12 European citizens die whilst waiting for a suitable organ transplant, that’s over 4,000 people on a yearly basis*

*4,019 deaths on the waiting list, Council of Europe data 2006
Waiting for an organ transplant in Europe

Facts & Figures
Total waiting list - Europe*

*Council of Europe data 2009, 32 countries: 517.3 million population
Challenge:

*how to increase organ donation?*
Organ donor categories

- **Deceased donors:**
  - heart-beating donors (brain dead)
    - Standard Criteria Donors (SCD)
    - Extended Criteria Donors (ECD)
  - non-heart-beating donors (donation after cardiac death, DCD)

- **Living donors:**
  - related
  - unrelated
Factors impacting on donation rates - CAD

- Potential for donation
- Legislative environment
- Organizational measures
- Professional education
- Health-economic variables
- Cultural & religious barriers
Median recipient age – Eurotransplant (WL)
Median donor age - Eurotransplant
Fig. 1. Graft survival (immunological failures only) for donors more and less than 50 years old. $P < 0.01$ by log-rank and Breslow tests.
- Priority allocation for kidneys from donors over age 65 to recipients over age 65 years (‘old-for-old’)
- Regional allocation
- Only for unsensitized candidates, first transplant
- No HLA-matching
- (Restricted) ABO-compatibility
  - O-donors to O and B recipients only
‘Expanded criteria’ donor organs …

… are like vintage cars: when knowing and respecting their limits, and on condition they’re well preserved, they still can do the job!
Living organ donation !?
Living (un)related kidney transplantation in Eurotransplant
How to improve living donation?

In a kidney exchange, donor will donate their kidney to another recipient that also has an incompatible or poorly compatible donor. The transplant operations would generally take place at the same time!
Living organ donation

- Altruism
- Organ trafficking
- Transplant tourism
- Exploitation of the poor

Istanbul Declaration (WHO, TTS)
Transplantation medicine in the SEE Health Network countries is presently **underdeveloped**; fewer **transplants** are being performed when compared to other European countries.

**Transplants PMP in 2010**

are 204 transplanted patients (24%) [152 M (74.5%)] with ESRD that have received a kidney transplant either in Albania or abroad. Majority of the renal transplantations have been performed in Turkey (45.2%), followed by Greece (22.0%), Albania (18.2%), Italy (8.4%), Pakistan (3.2%), Austria (2.1%) and Hungary (0.5%). The greatest proportion of the kidney recipients received the transplanted kidney from a living donor [131 (95.6%)], and only 6 patients (4.3%) received it from a cadaveric one.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>574</td>
<td>69.2</td>
</tr>
<tr>
<td>Peritoneal Dialysis</td>
<td>51</td>
<td>6.2</td>
</tr>
<tr>
<td>Kidney Transplant</td>
<td>204</td>
<td>24.6</td>
</tr>
</tbody>
</table>
Federation of Bosnia and Herzegovina
Kidney transplantation

Live donor transplantation
Cadaver transplantation
Montenegro – KTXs in different centers:

- **Total number:** 83
- Clinical Center of Serbia 33 (41.25%)
- Moscow 12 (14.63%)
- Pakistan 12 (14.63%)
- Military Medical Academy-Belgrade 11 (13.42%)
- Clinical Center Rijeka-Croatia 7 (8.54%)
- India 3 (3.65%)
- Paris 2 (2.44%)
- Lion 1 (1.22%)
- Viena 1 (1.22%)
Macedonia - Transplant program 1977 - 1995

A successful and sad story!

- Deceased donor transplantation possible
- Results achieved mainly enthusiastically

![Graph showing transplant numbers from 1976 to 1995]
1977-1995

- Total 35 Kidney transplants
- 22 CAD kidneys explanted
  - A dedicated procurement person - neurosurgeon
  - Complementary funeral expenses coverage by the University hospital
  - Results achieved mainly enthusiastically
  - Missing organizational infrastructure - 4D program
  - Governmental support
    - Legislation from the former YU federation
    - 1995 improvement in the Legislation of R. Macedonia
Macedonia - KIDNEY Tx - facts

1996 – 2011 (average 13.5 / year)

- 216 LD Tx and only 2 CAD
- 18 LD Tx for citizens of Kosovo
- 23 Explantations or lethal complications ≈ 10%
- Team: 1 urologist = 192; 1 = 14 Txs; 3 = 10 Txs; 3 nephrologists
The outcome of commercial kidney transplant tourism in Pakistan


Abstract: The lack of cadaver organs for transplantation motivates some Balkan patients to go to developing countries to buy a kidney. We have followed 36 patients who received kidney transplants in Lahore and Rawalpindi, Pakistan. The patients had not been cleared for transplantation with a standard pre-transplant work-up: 80% were hepatitis-C virus (HCV) or HBsAg positive. During follow-up, seven patients died. Sixteen patients experienced wound infections with post-operative hernias, and three patients developed peri-renal hematomas. Six abscesses and four lymphoceles occurred, and four urinary fistulas were surgically treated. Nephrectomy was performed in three patients because of renal artery thrombosis. Nine patients developed active hepatitis C, and four patients manifested cytomegalovirus disease. Three patients developed steroid diabetes, and three patients experienced acute myocardial infarction. Nine patients had one or more rejection episodes. Urinary tract infection with Pseudomonas or Escherichia occurred frequently. The one-yr patient and graft survival rates were 80% and 68%, respectively. Paid unregulated renal transplantation is not recommended for both ethical reasons and because of an association with excessive morbidity and mortality.
The outcome of commercial kidney transplant tourism in Pakistan

<table>
<thead>
<tr>
<th>Medical and surgical complications in patients returning from Pakistan between January 2006 and March 2008 (%)</th>
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</thead>
<tbody>
<tr>
<td>Wound infection</td>
</tr>
<tr>
<td>Perirenal hematomas</td>
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<tr>
<td>Perirenal abscesses</td>
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<tr>
<td>Lymphoceles</td>
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<tr>
<td>Urinary leakage</td>
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<tr>
<td>Renal artery thrombosis</td>
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<tr>
<td>Renal artery mycotic aneurysm</td>
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<tr>
<td>Nephrectomies</td>
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<tr>
<td>Postoperative hernias</td>
</tr>
<tr>
<td>Deaths</td>
</tr>
<tr>
<td>Sepsis (bacterial and fungal)</td>
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<tr>
<td>CMV disease</td>
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<tr>
<td>Hepatitis C</td>
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<tr>
<td>DM (steroid)</td>
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<tr>
<td>Myocardial infarction</td>
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<tr>
<td>Cerebrovascular stroke</td>
</tr>
<tr>
<td>Rejection episode</td>
</tr>
<tr>
<td>CAN</td>
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<tr>
<td>UTI</td>
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</tbody>
</table>

CMV, cytomegalovirus; CAN, chronic allograft nephropathy; UTI, urinary tract infection (*Pseudomonas, Escherichia*).
Dear Sir,

Ivanovski et al. (1) nicely reported about the problem with patient’s organ trafficking in the presence of an insufficiently developed deceased donor program in the Balkan region. Because it is necessary to discourage this act, it should be essential to understand the circumstances staying behind this desperate organ purchasing. The fact that Balkan’s recipients are at the edge of poverty and sometimes selling even their houses to buy a kidney, should be especially considered. In addition, as professionals, we should completely recognize the problem and try to prevent it by maximizing our efforts to comply with the increasing demand of kidney transplantations. Unfortunately, it seems that the healthcare systems and professionals in developing countries fail to enable organ transplantation as basic human right for best treatment option in patients with CKD which should be equally distributed all over the world. In
Can we decrease organ trafficking in the Balkans?

Finally, a repeatedly raised question is what has to be done by the transplant professionals aiming to increase the number of transplantations which is considered as best option to discourage the organ trafficking (10). Certainly, the number of living-related transplants should be increased as an immediate and prompt action. Furthermore, an official waiting list of candidates for deceased donor transplantation, composition of a few committed surgical teams, and a greater number of educated transplant nephrologists should be considered as a prerequisite for development of deceased donor transplant program. Here, the governmental support with necessary organizational and infrastructural investments to update the legislation, establish the national coordinative body, and transplant coordinators raising the awareness on the number of potential deceased donors is ultimately recognized as essential.
CROATIAN DONATION PROGRAM
A successful story!

- In the year 2000 donor rate was only 2.7 donors pmp
- Donor rate in Croatia was lagging far behind the European average
- Transplantations were limited and below expectations
HOW TO INCREASE DONOR RATE
Actions taken to increase donor rate in Croatia

- **2000-2010**
  - National Transplant Coordinator appointed in the ministry
  - 24 hour Coordination “duty desk “established at the Ministry
  - In-house transplant coordinators nominated in each hospital
  - New legislation adopted
  - Training programs for coordinators have been launched
  - Incentives paid to donor hospital implemented
  - Public awareness campaign EDD and National Donor Day
  - International cooperation established - Eurotransplant membership
  - Donor quality assurance program/inspections
World Health Organization

The Transplantation Society
The Declaration of Istanbul on Organ Trafficking and Transplant Tourism

To address the growing problems of organ sales, transplant tourism and trafficking in organ donors in the context of the global shortage of organs, a Summit Meeting was held in Istanbul of more than 150 representatives of scientific and medical bodies from 78 countries around the world, and including government officials, social scientists, and ethicists.

Istanbul Summit
April 30th – May 2, 2008
Objectives of the SEE(HN) project

- Strengthen regional cooperation among SEE countries in the field of organ donation and transplantation through exchange of good practice/knowledge, policy development, research, advocacy, collaboration and networking among SEE countries

**Individual Tx development**

- Promote the relevant WHO guiding principles, CoE Guidelines/recommendations, EU safety and quality standards in organ donation and transplantation medicine, in the Region
Accomplishments:

- **The RHDC’s role, objectives, and collaborative partners** were presented
- Network of SEE country partners (**via National Focal Points**) was established and presented (personal relationships)
- **Operational tool for assessment** of the specific country needs was presented and finalised (in concert with Skopje meeting)
National Focal Point by Country

- **ALBANIA:** Pellumb Pipero, Ministry of Health
- **BOSNIA AND HERZEGOVINA:**
  - Lada Sarajlić, Federation BIH MoH
  - Andreja Subotić Popović, Republic of Srpska (MoH)
- **BULGARIA:** currently (not known)- Executive Agency for Transplantation
- **MACEDONIA:** Goce Spasovski, Medical Faculty, University of Skopje
- **MOLDOVA:** Igor Codreanu, Transplant Agency
- **MONTENEGRO:** Marina Mugosa Ratković, Clinical center of Montenegro
- **ROMANIA:** Irinel Popescu and Executive Agency for Transplantation
- **SERBIA:** Mirjana Laušević, Clinical Center of Serbia
2nd Meeting, Skopje, Macedonia, May 27-28, 2011

- Comparative analysis and review of current country donation and transplantation practices, polices, legislation and public awareness situation (based on completed country questionnaires);
- Assessment of the specific country needs – Action Plan Booklet
- Organised by Professional Societies (TTS, ESOT, ISODP, ETCO)
## RHDC – Creation of Action Plan Booklet

### 2nd Meeting, Skopje, Macedonia, May 27-28, 2011

- Action Plans created based on comparative analysis (Action Plan Booklet)
- Summarizes major priorities by country

<table>
<thead>
<tr>
<th>Country</th>
<th>First Priority</th>
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<tbody>
<tr>
<td>Albania</td>
<td>Creation of a National Waiting List</td>
</tr>
<tr>
<td>Bosnia and Herzegovina (2)</td>
<td>Competent Authority (1), National Coordination Center (2)</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>Education of coordinators and transplant teams</td>
</tr>
<tr>
<td>Croatia</td>
<td>Full functionality of the RHDC</td>
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<tr>
<td>Montenegro</td>
<td>Train professionals/ ICU staff</td>
</tr>
<tr>
<td>Moldova</td>
<td>National Program in Transplant including budget</td>
</tr>
<tr>
<td>Romania</td>
<td>Improve accredited donor hospitals</td>
</tr>
<tr>
<td>Serbia</td>
<td>Competent Authority</td>
</tr>
<tr>
<td>Macedonia</td>
<td>Competent Authority, Registries, ICU/TC education</td>
</tr>
<tr>
<td>Slovenia</td>
<td>Education, auditing, and motivating ICU staff</td>
</tr>
</tbody>
</table>

**Table:** First priority by country, as stated in Country Action Plan presented at 2nd RHDC Meeting, Skopje May 2011
The RHDC Croatia on Organ Donation and Transplant Medicine would like to recognize and thank the following partners:

- WHO Regional Office for Europe
- SEEHN
- Council of Europe
- European Commission
- Professional Societies and Organisations;
  - The Transplantation Society (TTS)
  - The European Society for Organ Transplantation (ESOT)
  - International Society of Organ Donation and Procurement (ISODP)
  - European Transplant Coordinators Organisation
- Eurotransplant International Foundation
- Sloveniatransplant
- Other partners countries /institutions/organisations
RHDC – Annual Meetings 2012

3rd Meeting, Ljubljana, Slovenia, March 2012

- Training in brain diagnostics - ICU doctors

4th Meeting, Ohrid, Macedonia, June 2012

- ERA-EDTA CME Course on Transplantation
- TAIEX Workshop on Transplantation
Miodrag Radunović, MD, MSc, PhD
Minister of Health,
Montenegro

Dear Minister Radunović:

It is very encouraging that a well developed action plan is underway with the alliance of the Ministry of Montenegro and the experienced leadership of Professor Marina Ratkovic.

However, key components needed for success were identified at our May 5th meeting that we wish to bring to your attention. These include:

- the capacity to determine death by neurologic criteria in the Intensive Care Units of the University Hospital of Montenegro;
- the engagement and commitment of the Director of the Hospital to assemble a multidisciplinary team to conduct the donation and transplantation program.
RHDC – SEEHN success – First LD KTx in Montenegro - September 2012

Historical First Living Related Kidney Organ Transplantation in Montenegro

Croatian Minister of Health Ostojic with Montenegrin Minister of Health Radunovic
Vasile Cepoi, M.D.
Minister of Health
Republic of Romania

Dear Minister Cepoi:

The action plan of Romania to increase deceased donation entails three priority initiatives:

- the identification of a Key Donation Person in the employ of County Hospitals with intensive care unit services;
- the appointment of an in-house transplantation coordinator at centers that you would deem appropriate for such designation;
- higher level of care classification of county hospitals participating in the national transplant program.
2012 – Start of the new KTx era in MK:
Between 22 March, 2012 – 10 July, 2013 = 51 KTx
LURD – 7

Team: 4 urologist =51; 4 nephrologists; 1 vasc. Surg.

Complications: 4 kinking, 2 trombosis – reoperated, 4 lymphc.
1 perirenal haematoma, 2 wounds opened - healed per sec.
Macedonia - KIDNEY Tx - facts

- 51 Tx since March 22, 2012
- 2 graft lost – HUS? Tromb.
- 1 ex. - sepsis/DIC (mycosis)
- 6Txs with double arteries – successfully performed Tx!

- 7 - Emotionally related donors (spouse, partner, brother in law)
- ATG – rescue treatment in 4 AR
Action Plan Priorities Status

- HCF reimbursement per Tx increased to 10-15.000 Eur
- DRG code for organ donation – 5000 Eur
- Established WL for LD Tx under the composed priorities
- WL for cadaveric transplantation – under construction
- Bylaws under the new law completed – legal adoption
- NTC & HTC - expected nomination in the near future
- WKD topic on organ donation
- DDD – donor donation day – first time in MK
- First meeting of all professionals involved in DD Tx-18 May
- Sec. meeting of all professionals involved in DD Tx-25 Sep
- MSNDTAO- International Congress - TAIEX workshop on Tx
- 6 ICU doctors & 2 neurologists past TC/BD course (2011/12)
- First DD expected in the forthcoming months
Living donor kidney transplantation in MK
Results - New treatment policy

- Lower CIT and sec. WIT, Standardized MAP>85mmHG
- Average hospital days reduced to 10 (7-21) days
- Urocathether removal on average 6 (4-15) days
- Decreased rate of urinary tract infections
- Decreased use of an expensive antibiotic treatment

Benefits:
- Patients – shorter stay with no complications
- Department – decreased expenses and higher turnover through the Tx center
- Society – improved cost efficacy of KTx vs dialysis
- Up to >40 KTx – best results ever achieved
- Start of Deceased donor transplantation program once bylaws from the Ministry of health are issued
- Maintaining of the increased number of KTx in the following years
- Positioning as new regional KTx center
- Meeting of the Tx societies from MK, Al, Kos (29.09.2012 – Pristina), endorsed event by the ISN and KDIGO – awaiting first patients
ORGANISATION - PARAMOUNT IMPORTANCE
HOPE WE CAN ALL MAKE IT!

Thank You!