Psychosocial Characteristics Predictive of Post-operative Mental Health in Living-related Liver or Kidney Donors:
A Systematic Literature Review

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Background: It has been demonstrated that psychosocial outcome following living donation is predominantly favorable. However, little is known about which factors at time of screening of the donor predicts poor mental health in living liver and kidney donors after donation. A systematic literature review was initiated to identify the available empirical research on these predictors for post-donation vulnerability. The long-term objective is producing evidence-based guidance that may support clinicians in donor screening, monitoring and counseling.

Methods: Eligible studies for this review incorporate assessment of mental illness parameters both pre- and post-donation, according to a validated assessment tool, in a population of living liver or kidney donors. No restrictions were used regarding language and date of publication. Scientific reports were searched for through PubMed, PsychInfo, and Embase. Two independent reviewers evaluated major outcomes, socio-demographic donor characteristics, and properties of design and measurement tools.

Results: Out of 227 abstracts screened, 54% merely focused on either recipient physiological safety or ad hoc measurements of well-being of the donor, focused on the recipient, and/or used often post transplantation measurements. Seven studies fully met the inclusion criteria. The mean sample size of donors enrolled was 44, with two of seven studies being non-European. Main concepts of interest were mood (n = 6), quality of life (n = 3) and DSM-IV disorders (n = 2). Overall, results indicated no signs that quality of life, mood or the psychosocial status was impaired after donation. Only two studies sought for factors predictive of worse psychological outcome, and found that higher levels of anger and lower levels of self-esteem in the donor prior to transplantation related to less favorable outcomes.

Conclusions: The published evidence so far does suggest that living donation does not affect mental health. However, the low sample sizes might have influenced the low incidence of psychosocial problems found, and their subsequent lack of predictive capacity.

Key words: kidney, liver, donor, transplantation, psychology, review
Background

It has been demonstrated that psychosocial outcome following living donation is predominantly favorable. However, little is known about factors predicting poor mental health in a subpopulation of living liver and kidney donors after donation. A systematic literature review was initiated in 2008 by the ELPAT Psychological Care working group to identify the available empirical research on these psychosocial vulnerability markers in potential living donors. The occurrence of psychological disorders after living liver or kidney donation has been observed all around the world: from Japan (Fukunishi, Sugawara et al. 2001) to Germany (Walter, Papachristou et al. 2002) and from Australia (Smith, Trauer et al. 2003) to the USA (Johnson, Najarian et al. 1997), but the available data on predictive markers has not been reviewed. The aim of this research is to systematically review all the data needed to produce evidence-based guidelines that may support clinicians in donor screening, monitoring, and counseling. Therefore the research question is “What psychosocial characteristics determine vulnerability of potential liver or kidney donors with regard to (relapse of) mental illness and other outcomes post-donation?”

Over the course of 2008 and 2009 a search string was devised and carried out. Two independent researchers reviewed all the retrieved literature and reported their findings to the ELPAT Psychological Care working group in November 2009.

Methods

Systematic Literature Search

Search strategy
The databases PubMed, Embase (Elsevier) and PsycInfo (Ovid) were searched for the following terms: “kidney transplantation”, “liver transplantation”, “tissue donors”, “living donors”, “mental disorders”, “mental illness”, “depression”, “behavioral symptoms”. All search terms were scanned in titles and abstracts, in full text articles and in their related terms by means of so-called MeSH terms. The search strings were formatted to match the different queries in PubMed, Embase and PsycInfo by an information specialist of the Erasmus MC Medical Library. The formatted search strings can be found under Appendix I.

Inclusion criteria
The following inclusion criteria were applied in title and abstract screening by two independent researchers to filter the desired literature:
1. Population: Living kidney or liver donors
2. Design: Longitudinal, i.e., pre- and post assessment
3. Assessment of psychosocial variables
   a) Mental illness (e.g., depression, anxiety, adjustment, personality disorder)
   b) QOL as outcome measure
4. A-priori defined assessment tools
5. Possible predictive markers (pre-donation):
   a) Demographic and personality characteristics
   b) Social and/or environmental characteristics

Exclusion criteria
The following were excluded:
1. Case reports
2. Review articles
3. Conference abstracts
4. Articles published before 1990

Management of retrieved articles
All retrieved articles were reviewed by two independent researchers to filter the desired literature. The exclusion criteria were applied and any disagreement was discussed with the whole ELPAT working group. Only articles that they agreed on were included in the systematic literature review. The code of inclusion and exclusion criteria was used until consensus was reached.

Study selection
Two independent researchers reviewed all the retrieved articles. The following inclusion criteria were applied in full text articles:
1. Population: Living kidney or liver donors
2. Design: Longitudinal, i.e., pre- and post assessment
3. Assessment of psychosocial vulnerability markers: the inclusion criteria were applied in full text articles and their related terms by means of so-called MeSH terms. The search strings were formatted to match the different queries in PubMed, Embase and PsycInfo by an information specialist of the Erasmus MC Medical Library. The formatted search strings can be found under Appendix I.

4. A-priori defined assessment tools
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Results

Systematic Literature Search
The search string was devised and carried out. Two independent researchers reviewed all the retrieved literature and reported their findings to the ELPAT Psychological Care working group in November 2009.
Exclusion criteria
The following exclusion criteria were applied during title and abstract screening:
1. Case reports
2. Review papers
3. Consensus reports
4. Articles describing current screening practice

Management of references
All retrieved literature was merged into one Endnote X file. Duplicates were automatically removed after which the list was manually checked for remaining duplicates. The literature was shared with all involved researchers. A coding was invented to report whether the article fitted all criteria.

Study selection
Two independent members of the research team reviewed all the titles and abstracts of all retrieved literature following the set inclusion and exclusion criteria. A code was applied for the measure of relevance. Articles rated zero were irrelevant to our review. The main reasons for discarding articles were a focus on recipients, a focus on medical aspects of the process, or that they were descriptions of current screening practices.

Code one meant that the articles were potentially relevant to the study; they were selected for full-text screening if at least one of the researchers rated the article with a 1. The codes were reported in the Endnote X file and compared; differences were discussed until consensus was reached.

All included literature was then reviewed based on full text. A member of the research (JG) team screened these full text articles, while closely following a data extraction form. The verdict on all articles was reported in the Endnote X library, including their respective reasons for exclusion.

Results

Systematic Literature Search
The search string resulted in 227 unique articles from the electronic databases (fig. 1) after removing all duplicates. 206 articles were excluded during the title and abstract screening process, which resulted in 21 articles up for full text screening. Full text screening resulted in the exclusion of 14 articles. In the end 7 papers were included in the review.

Out of 227 abstracts screened, 54% merely focused on either recipient physiological safety or ad hoc measurements of well-being of the donor, focused on the recipient, and/or used often only post transplantation measurements. Seven studies fully met the set inclusion criteria. The mean sample size of donors enrolled was 44, with two of seven studies being non-European. Main concepts of interest were mood (n = 6), quality of life (n = 3) and DSM-IV disorders (n = 2). Overall, results indicated no signs that quality of life, mood or the psychosocial status was impaired after donation. Only one study sought for factors predictive of worse psychological outcome, and found that higher levels of anger and lower levels of self-esteem in the donor prior to transplantation related to less favorable outcomes (Walter et al., 2002).
Evidence table
To report all relevant information retrieved from the 7 included articles an evidence table was created. All articles were compared on the factors “author”, “year”, “location”, “population”, “sample size”, “relation to recipient”, “study outcomes”, “tools”, “moment(s) of post test”, and “main results”. The evidence table can be found as Appendix to this article.

Discussion
This systematic literature review has shown that the psychosocial outcome of living kidney or liver donation is predominantly favourable. Most studies find no significant impairment of psychosocial functioning after living liver or kidney donation. This study has also shown that there is still a lack of publications describing the predictive markers for negative outcome for donors. Furthermore, the low sample sizes might have influenced the low incidence of psychosocial problems found, and their subsequent lack of predictive capacity.

Limitations
Limitations of this study include search terms used to conduct initial appraisals of the included studies, the low number of search terms used for the ELPAT invitational manual, and the low number of search terms used for the ELPAT Psychosocial outcomes Database. Furthermore, this study aimed to critically appraise the included studies to determine the validity of the findings.

Strengths
The systematic literature review was conducted in collaboration with a diverse group of experts in the field of psychosocial outcomes. This resulted in a clear understanding of the factors that influence the psychosocial outcome of living kidney or liver donation. Additionally, this study included a clear list of search terms, which ensured the identification of relevant studies.

Recommendations for future research
Recommendations for future research include:
- The use of more relevant search terms.
- The use of a comprehensive list of criteria to appraise the value of the included studies.
- The use of a more comprehensive list of criteria to appraise the value of the included studies.

Clinical implications
From a clinical point of view, it appears that the psychosocial outcome of living kidney or liver donation is not as favourable as that of other organ donation procedures. Therefore, there is a need for further research to identify the factors that influence the psychosocial outcome of living kidney or liver donation.
Limitations
Limitations of this review might be the low number of articles found, the low number of search terms used in the review process, too few inclusion criteria and the lack of a critical appraisal of the included articles. The first two limitations might be related: because of the low number of search terms a pool of only 227 articles was found and reviewed. At the EL-PAT invitational meeting in Juan les Pins, November 2009 these results were discussed with the EL-PAT Psychological Care working group. The group was not fully satisfied yet with the results found. Furthermore that group suggested that the inclusion criteria used for title and abstract screening and for full text screening might not have been formulated clearly enough, resulting in the exclusion of too many articles. The group also pointed out that we did not critically appraise the quality of the included literature. Therefore there was no possibility to compare the articles on their strengths and weaknesses.

Strengths
The strength of this review is the approach to defining a search strategy by the research team in collaboration with an information expert from the Erasmus MC medical library and the clear results of the analysis. Also the structure of the review process was clearly defined, closely guarded and strictly maintained by all members of the research team. Another strength of this research is the close cooperation with the working group within the EL-PAT organisation. This collaboration gave us the possibility to check any decisions with a large group of experts before carrying out any changes.

Recommendations for further research
Because of the limitations the EL-PAT group suggested a revision of this systematic literature review. Firstly we will extend the number of articles screened by including more search terms. Additional to the original search string we will add: "quality of life" and "life quality". This might have a large impact on the results.

A second recommendation was to adjust the inclusion criteria. The next research should reconsider all criteria and formulate them as clear and sharp as possible in order to include more relevant literature. For instance: articles describing only a post-measure can be included, if they search for predictive value in relatively stable personal characteristics. On the other hand, the use of quality of life as a predictor is debatable: It might be useful as an outcome measure but is not clearly defined enough to use as a predictor of negative psychological outcome of living graft donation. For the next review we benefit from the recommendation to use DSM IV-tr criteria, mood scales, socio-demographics and personality traits as predictors.

Lastly the research team recommends critically appraising all included literature. An appraisal criteria list must be invented to serve this purpose, since most existing lists are designed to appraise the value of clinical research and experiments.

Clinical implications
From a clinical point of view these favourable results are reassuring for the current practice. The vast majority of donors suffer no psychosocial harm by psychiatric standards. This raises the hope that the issue of psychological impairment caused by the living donation of a kidney or liver is not as serious as the ad hoc reports of psychological disorders after living liver or kidney donation suggest.
Closing remarks
Our review confirms that living organ donation is mostly harmless to the psychological well-being of the donor. A new version of this systematic literature review will be initiated on a very short term, based on all suggestions and ideas from the ELPAT working group meeting.

References

Appendices
PubMed:
n=173

PsycINFO:
(kidney transplantation*.mp. OR liver transplantation*.mp. OR renal transplantation*.mp. OR hepatic transplantation*.mp.) AND (tissue donor*.mp. OR living donor*.mp.) AND (exp
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mental disorders/ OR mental disorder*.mp. OR mental illness*.mp. OR depression.mp.

Embase:
(„kidney transplantation”/exp OR „liver transplantation”/exp OR „kidney transplantation”:ti,ab OR „liver transplantation”:ti,ab OR „renal transplantation”:ti,ab OR „hepatic transplantation”:ti,ab OR „kidney transplantations”:ti,ab OR „liver transplantations”:ti,ab OR „renal transplantations”:ti,ab OR „hepatic transplantations”:ti,ab) AND (donor/exp AND (liver.mp. OR kidney.mp. OR donor.mp. OR liver donor.mp. OR kidney donor.mp. OR donor donor.mp. OR liver donors.mp. OR kidney donors.mp. OR donor donors.mp.) OR tissue donor:ti,ab OR „tissue donor”:ti,ab OR „living donor”:ti,ab OR „living donors”:ti,ab OR „tissue donors”:ti,ab OR „living donors”:ti,ab) AND („mental disease”/exp OR „mental disorder”:ti,ab OR „mental illnesses”:ti,ab OR „mental disorder”:ti,ab OR „mental disorders”:ti,ab OR „mental illnesses”:ti,ab OR depression:ti,ab OR „mood disorder”/exp)
n=102

remaining after deduplication: 227
PubMed: 173
PsycInfo: 1
Embase: 53

n=4 (1 over na dedupl)
<table>
<thead>
<tr>
<th>Title</th>
<th>Author et al.</th>
<th>Year</th>
<th>Location</th>
<th>Population</th>
<th>Sample size</th>
<th>Study outcomes</th>
<th>Tools</th>
<th>Moments of post-test</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric and psychological outcomes of Japanese living donors following live transplantation</td>
<td>Shiwaku, Oyama et al.</td>
<td>2009</td>
<td>Tokyo (Japan)</td>
<td>Liver</td>
<td>6</td>
<td>1 the son, 1 the husband, 1 the in-laws, 1 the father; 2 mothers</td>
<td>POMS &amp; STAI</td>
<td>Data collected between 15 days and 1 months</td>
<td>POMS' psychometric score significantly decreased. The STAI score suggested that donors had little anxiety or depression following the donation. (Donors will be measured.</td>
</tr>
<tr>
<td>Impact assessment in living kidney donation: psychological aspects in the donor</td>
<td>Tave, Fonseca et al.</td>
<td>2009</td>
<td>Porto (Portugal)</td>
<td>Kidney</td>
<td>32</td>
<td>28 donors were siblings, 11 parents, 1 daughter</td>
<td>Psychosocial impact and quality of life</td>
<td>Data collected between 12.5 and 14.8 months</td>
<td>Global functioning scale improved. No significant side effects. Depression, anxiety, and daily stress were all markedly increased post-donation. Donors did not report their medication and social mood to others.</td>
</tr>
<tr>
<td>Depression in quality of life in living related renal transplantation</td>
<td>Vircigl et al.</td>
<td>2007</td>
<td>Catania (Italy)</td>
<td>Kidney</td>
<td>40</td>
<td>32 donors were parents, 1 spouse and 4 siblings</td>
<td>Depression and quality of life</td>
<td>4 months</td>
<td>Living donor kidney transplantation did not affect the level of donors. Social anxiety was assessed at 6 months with a normal QOL. It can influence the psychosocial status.</td>
</tr>
<tr>
<td>Psychological and somatic aspects of living kidney donor: preoperative assessment and postoperative course</td>
<td>Walter, Pascher et al.</td>
<td>2009</td>
<td>Berlin (Germany)</td>
<td>Liver</td>
<td>40</td>
<td>38 patients, 12 patients 1 parents, 5 siblings, 2 aunts, 1 cousin, 1 niece, 1 teenager</td>
<td>Global measurement of mood and physical complaints</td>
<td>Berlin Mood Questionnaire &amp; General Complaint Questionnaire</td>
<td>6 months</td>
</tr>
<tr>
<td>Psychiatric situation of living donors: Mood, symptoms, and well-being before and after live transplantation</td>
<td>Walter, Ostermann et al.</td>
<td>2009</td>
<td>Berlin (Germany)</td>
<td>Liver</td>
<td>30</td>
<td>not reported</td>
<td>Measurement of mood and well-being</td>
<td>Scores on Berlin Mood Questionnaire, General Complaint Questionnaire &amp; Nurstein Inventory for QOL</td>
<td>6 months</td>
</tr>
<tr>
<td>Prospective psychosocial monitoring of living kidney donors using the Short Form 36 health survey results at 12 months</td>
<td>Smith, Trauer et al.</td>
<td>2004</td>
<td>Melbourne (Australia)</td>
<td>Kidney</td>
<td>48</td>
<td>not reported</td>
<td>SF-36 &amp; Patient Health Questionnaire: psychological aspect</td>
<td>SF-36 &amp; Patient Health Questionnaire: psychological assessment</td>
<td>4 months &amp; 12 months</td>
</tr>
<tr>
<td>Psychiatric stress of living donors after living donor kidney transplantation</td>
<td>Walter, Papachristou et al.</td>
<td>2002</td>
<td>Berlin (Germany)</td>
<td>Liver</td>
<td>36</td>
<td>31 patients, 12 donors, 2 bows, 1 sister; 3.4 years, 1 aunt</td>
<td>Relation between complications following LDD and stress perception</td>
<td>Scores on Berlin Mood Questionnaire, and Potentially Stress Questionnaire</td>
<td>6 months</td>
</tr>
</tbody>
</table>