Chapter from the book *Emerging Research and Treatments in Renal Cell Carcinoma*

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Health-Related Quality of Life After Radical Nephrectomy and Kidney Donation

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1. Introduction

Radical nephrectomy (RN) is a treatment of choice for the patients with renal cell carcinoma (RCC) achieving excellent results, especially in local stages of the disease. Oncological results of RN are well evaluated on a large number of patients. However, studies on a postoperative health-related quality of life (HRQoL) of these patients are very limited (Novara G et al., 2010; Poulakis V et al., 2003; Clark PE et al., 2001). There are no publications available comparing the HRQoL of patients after RN with that of healthy individuals and other forms of nephrectomy.

Living kidney transplantation provides excellent results with the lowest complication and the highest graft and patient survival rates (Hariharan et al., 2000). However, it should not be forgotten that donors are healthy persons voluntarily donating an organ and their postoperative health and HRQoL should be a matter of utmost importance. It has been shown that kidney donation does not cause serious medical problems like: deterioration of kidney function, arterial hypertension or proteinuria (El-Agroudy et al., 2007). Although advocated in the literature, psychosocial assessment and monitoring of living kidney donors is not yet routinely performed. There are only limited reports in the literature examining HRQoL issues in the donors.

The HRQoL concept is well-known in clinical medicine and is frequently applied for the assessment of surgical or other treatment modalities to determine their therapeutic success. HRQoL has become a leading criteria in many outcome studies alongside with somatic and economic factors and is frequently listed as outcome parameter in medical societies' guidelines. Despite methodological difficulties in making HRQoL measurable, there are numerous surveys and questionnaires used for this purpose. The Short Form-36 (SF-36), Giessen Subjective Complaints List-24 (GBB-24) and Zerssen’s Mood-Scale (Bf-S) are internationally validated and frequently used questionnaires for this purpose (Ware & Sherbourne CD, 1992; Giessing et al., 2004; Zerssen D, 1976).

The importance of this topic is underlined by the fact, that available data on psychological well-being and HRQoL of the patients after RN and kidney donors are limited and somewhat controversial. It would be very interesting to know as to whether there are differences between countries, races, or social groups, with regard to HRQoL of the patients and donors. While some of these studies are providing evidences that the donor HRQoL is at least comparable or even better than that of the general population (Giessing et al., 2004;
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Ibrahim et al, 2009; Feltrin et al, 2008; Johnson et al, 1999; Smith et al, 2003; Isotani et al, 2002; Fehrman-Ekholm et al, 2000; Tanriverdi et al, 2004; Lima et al, 2006), others are showing the negative impact of the donation on donors’ HRQol (Giessing et al., 2004; Johnson et al, 1999; Smith et al, 2003; Jackobs et al., 200; Reimer et al., 2006; Schover et al., 1997; Zargooshi, 2001; Tellioglu et al., 2008). There are no studies comparing the HRQol of kidney donors with the patients who underwent nephrectomy due to the urological diseases.

The aim of the current study was to assess the HRQol of the patients who underwent RN due to the RCC and compare it with age- and sex-matched healthy persons and our kidney donors.

2. Subjects and methods

The study population consisted of:

Group I: 52 patients who underwent nephrectomy due to the RCC

Group II: 120 age- and sex matched healthy individuals

Group III: The kidney donors operated at our institution from January 2005 to December 2008 (n=57).

The patients (Group I) and the kidney donors (Group III) have been followed-up prospectively. The questionnaires have been sent to them after a follow-up of at least 3 months.

The Group I consisted of the 98 consecutive patients operated at our institution for RCC. Three questionnaires (SF-36, GBB-24 and Bf-S) have been mailed to all the patients. 7 (7%) patients have been reported as dead at the time of evaluation, 10 (10%) were lost of follow-up and 29 (30%) didn’t respond. We’ve received the completed questionnaires from 52 patients (53%). The mean follow-up was 28 months (range: 4-35 months). None of the patients had clinical signs of renal insufficiency or other substantial co-morbidities (diabetes etc). Radical or partial nephrectomy without adjuvant immunotherapy was performed in all patients. The pathological stage distribution of the tumors was the following: T1 – 21 (40%); T2 – 13 (25%); T3 – 18 (35%) patients. 14 (27%) cancers were G1, 20 (38%) - G2 and 18 (35%) - G3. Morphological evaluation revealed clear cell RCC in all 52 patients. 2 patients had lymph node and 1 patient had distant metastases at the time of surgery. 18 (34.6%) tumors were discovered incidentally, 29 (55.8%) were locally symptomatic and 5 patients (9.6%) had a systemic disease symptoms. All patients were operated on in one department.

The control group has been generated by using probability-based methods to ensure representativeness of the general population of the Country. The subjects from other psychological surveys have been provided by the national psychological association for this purpose. The control group consisted of 120 healthy volunteers with the mean age of 51±9 years (18-70 years). They were matched with the donors and patients on the basis of: age, sex, race and ethnicity. Exclusion criteria were chronic diseases, with the exception of controlled systemic hypertension and previous non-major surgical interventions.

61 living kidney transplants have been performed at our institution since January 2005 to December 2008. The mean follow-up of the donors was 32 months (range: 4-57 months). All the transplants were performed from genetically related donors. 19 donors (31%) were male and 42 (69%) were female. The mean donor age was 49±9 years. The most frequent form of donation was parent to child (86.5%). In 2.7% of cases organ was offered by sibling and in 5.4% - by cousin and uncle each.
All transplant operations were approved by the ethical committee of the Ministry of Health of Georgia. All the patients and donors were studied according to protocols accepted at our centre. Donor nephrectomy was done by open extraperitoneal approach. All transplants have been performed according to ABO compatibility and negative direct cross-match.

All the donors are alive. They have been followed either by our nephrology department or by associated institutions, with which our center cooperates closely. Three questionnaires (SF-36, GBB-24 and Bf-S) have been mailed, e-mailed, or handed out to all the donors who could be contacted, with a follow-up of at least 3 months. If no answer was returned, we called the donor, motivated him or her for participation, and sent the questionnaires again. If the donor could not be contacted, we talked to the recipient and asked for assistance. Thus, we have received answers from 57 (93%) donors who could be contacted.

The evaluation procedure was completely anonymous and all the respondents were free of any charges related to filling or sending the questionnaires.

2.1 Short form-36 questionnaire

The SF-36 questionnaire was developed in the United States (Ware & Sherbourne CD, 1992). It is a standardized instrument for measuring HRQoL on eight different scales: physical function (PF), physical role (PR), social function (SF), general health perception (GH), vitality (V), bodily pain (BP), mental health (MH), and emotional role (ER). Thirty-six questions have to be answered, and a score is computed for each scale, ranging from 0 (least well-being) to 100 (greatest well-being). This form has been adapted by psychologists for use in Georgia with adequate translation and minor changes to the content of the form.

2.2 Giessen subjective complaints list-24 questionnaire

Giessen Subjective Complaints List-24 questionnaire (GBB-24) assesses physical complaints attributable to psychosomatic reasons (Giessing et al., 2004). The questionnaire has six questions, each referring to four items (cardiac complaints, gastric complaints, limb pain and fatigue tendency) for which participants are asked to rate their complaints (0-no complaints, 4-strong complaints). The sum of these four items reflects the fifth item, “overall subjective complaints” (0–96 points).

2.3 Bf-S questionnaire

Bf-S questionnaire is a self-rating scale developed by Zerssen in 1975 (Zerssen D, 1976). It is a 28 question scale designed to assess the person’s mood. The questionnaire has been used for the analysis of patient’s self-feeling pre- and/or post event (operation, donation etc.).

The study design was approved by the internal review board of the institution as conforming to the provisions of the Declaration of Helsinki. All participants provided written informed consent.

2.4 Statistical analysis

Statistical analysis was performed using computer software (SPSS 12.0 for Windows, Lead Technologies Inc. 2003. Chicago, IL.). Normality of data distribution was examined with
Kolmogorov-Smirnov test. The different scores in the groups were compared with ANOVA, Mann Whitney and Kruskal Wallis tests. Age-dependency of the scores was analysed by the Pearson correlation and linear regression. A p value of less than 0.05 was considered significant.

3. Results

The age, sex distribution and mean follow-up was not different between the groups. At the time of the study, 97.8% of the recipients were alive and 89% of these had a functioning graft. Overall, 12 minor complications occurred in 9 donors (15%) (table 1).

<table>
<thead>
<tr>
<th>Complication</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2</td>
<td>3.5</td>
</tr>
<tr>
<td>UTI</td>
<td>3</td>
<td>5.2</td>
</tr>
<tr>
<td>Postoperative hernia</td>
<td>3</td>
<td>5.2</td>
</tr>
<tr>
<td>Impaired wound healing</td>
<td>3</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Table 1. Postoperative donor complications

Fig. 1. Comparison of the mean (±SE) SF-36 scores between the groups

* p=0.0001 vs. Group II and p=0.0209 vs. Group I
† p=0.0357 vs. Group III and p=0.0375 vs. Group II
‡ p=0.0478 vs. Group II and p=0.0006 vs. Group I
£ p=0.0128 vs. Group I
For the SF-36 items: “Social function”, “Bodily pain” and “Vitality”, donors scored significantly better than controls and patients. “Bodily pain” and “Vitality” indexes of the controls were significantly higher than that of the patients (Fig. 1). The SF-36 scores were not different between males and females.

We analyzed the age dependency of the SF-36 scores in all three groups. The correlation coefficients, corresponding p values and 95% CIs of the eight different SF-36 scores against age are shown in Table 1. The correlation coefficients of “Social function” in Group III; “Social function”, “Mental health” and “Vitality” in Group II were moderately high (-0.541, -0.341, -0.292 and -0.292, respectively); their 95% CIs were narrow (-0.768–0.195, -0.568–0.067, -0.530–0.012 and -0.529–0.011, respectively) and their p values were significant (0.0037, 0.0158, 0.0413 and 0.0416, respectively), showing a negative correlation with age. Low correlation coefficients of other SF-36 scores, especially in Group I, together with a wide range of 95% CIs including 0, indicated that these scores were not age-related (Table 2).

<table>
<thead>
<tr>
<th>SF-36 score</th>
<th>Group I</th>
<th>Correlation Coefficient</th>
<th>P value</th>
<th>95% Lower CI</th>
<th>95% Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PF</td>
<td>-0.235</td>
<td>0.7345</td>
<td>0.7345</td>
<td>-0.925</td>
<td>0.817</td>
</tr>
<tr>
<td>PR</td>
<td>-0.792</td>
<td>0.1282</td>
<td>0.1282</td>
<td>-0.986</td>
<td>0.310</td>
</tr>
<tr>
<td>SF</td>
<td>0.334</td>
<td>0.6238</td>
<td>0.6238</td>
<td>-0.778</td>
<td>0.939</td>
</tr>
<tr>
<td>BP</td>
<td>-0.703</td>
<td>0.2167</td>
<td>0.2167</td>
<td>-0.978</td>
<td>0.472</td>
</tr>
<tr>
<td>MH</td>
<td>-0.326</td>
<td>0.6323</td>
<td>0.6323</td>
<td>-0.938</td>
<td>0.781</td>
</tr>
<tr>
<td>ER</td>
<td>0.212</td>
<td>0.7610</td>
<td>0.7610</td>
<td>-0.825</td>
<td>0.922</td>
</tr>
<tr>
<td>V</td>
<td>-0.670</td>
<td>0.2521</td>
<td>0.2521</td>
<td>-0.976</td>
<td>0.520</td>
</tr>
<tr>
<td>GH</td>
<td>-0.312</td>
<td>0.6479</td>
<td>0.6479</td>
<td>-0.937</td>
<td>0.787</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SF-36 score</th>
<th>Group II</th>
<th>Correlation Coefficient</th>
<th>P value</th>
<th>95% Lower CI</th>
<th>95% Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PF</td>
<td>-0.219</td>
<td>0.1307</td>
<td>0.1307</td>
<td>-0.471</td>
<td>-0.066</td>
</tr>
<tr>
<td>PR</td>
<td>-0.243</td>
<td>0.0924</td>
<td>0.0924</td>
<td>-0.491</td>
<td>0.041</td>
</tr>
<tr>
<td>SF</td>
<td>-0.341</td>
<td>0.0158</td>
<td>0.0158</td>
<td>-0.568</td>
<td>-0.067</td>
</tr>
<tr>
<td>BP</td>
<td>-0.212</td>
<td>0.1439</td>
<td>0.1439</td>
<td>-0.466</td>
<td>0.073</td>
</tr>
<tr>
<td>MH</td>
<td>-0.292</td>
<td>0.0413</td>
<td>0.0413</td>
<td>-0.530</td>
<td>-0.012</td>
</tr>
<tr>
<td>ER</td>
<td>-0.017</td>
<td>0.4236</td>
<td>0.4236</td>
<td>-0.386</td>
<td>0.0169</td>
</tr>
<tr>
<td>V</td>
<td>-0.292</td>
<td>0.0416</td>
<td>0.0416</td>
<td>-0.529</td>
<td>-0.011</td>
</tr>
<tr>
<td>GH</td>
<td>-0.116</td>
<td>0.4313</td>
<td>0.4313</td>
<td>-0.384</td>
<td>0.171</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SF-36 score</th>
<th>Group III</th>
<th>Correlation Coefficient</th>
<th>P value</th>
<th>95% Lower CI</th>
<th>95% Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PF</td>
<td>-0.045</td>
<td>0.8724</td>
<td>0.8724</td>
<td>-0.529</td>
<td>0.461</td>
</tr>
<tr>
<td>PR</td>
<td>-0.140</td>
<td>0.6106</td>
<td>0.6106</td>
<td>-0.595</td>
<td>0.382</td>
</tr>
<tr>
<td>SF</td>
<td>-0.541</td>
<td>0.0037</td>
<td>0.0037</td>
<td>-0.768</td>
<td>-0.195</td>
</tr>
<tr>
<td>BP</td>
<td>-0.058</td>
<td>0.8340</td>
<td>0.8340</td>
<td>-0.538</td>
<td>0.451</td>
</tr>
<tr>
<td>MH</td>
<td>0.008</td>
<td>0.9784</td>
<td>0.9784</td>
<td>-0.490</td>
<td>0.501</td>
</tr>
<tr>
<td>ER</td>
<td>-0.304</td>
<td>0.2573</td>
<td>0.2573</td>
<td>-0.695</td>
<td>0.226</td>
</tr>
<tr>
<td>V</td>
<td>0.284</td>
<td>0.2923</td>
<td>0.2923</td>
<td>-0.246</td>
<td>0.684</td>
</tr>
<tr>
<td>GH</td>
<td>-0.068</td>
<td>0.8069</td>
<td>0.8069</td>
<td>-0.545</td>
<td>0.443</td>
</tr>
</tbody>
</table>

Table 2. Pearson correlation analysis of the age dependency of SF-36 scores in different groups
The four scores which showed significant correlations with age (“Social function” in Group III; “Social function”, “Mental health” and “Vitality” in Group II) were evaluated further with a linear regression model. Figs. 2 and 3 show the regression plots of the three scores (“Social function” in Group III; “Social function” and “Vitality” in Group II) against age. Regression analyses confirmed the results of the Pearson correlation regarding the linearity of their relationship with age. As to “Mental health” in Group II, regression analyses didn’t verify linearity of the relationship.

In all five GBB-24 items the donors scored higher than the controls and patients. For the “gastric complaints” the difference was statistically significant. In this item the patients scored significantly worse than controls and donors (Fig. 4). The GBB-24 scores were not correlated with age. Comparison of the scores between males and females showed that in the Group II, in four out of five items (“Overall complaints”, “Fatigue tendency”, “Limb pain” and “Cardiac complaints”) males scored significantly higher than females (Fig. 5). The differences in other groups were not significant (data not shown).
Fig. 3. Regression plots of the SF-36 scores for “social function” (a) and “vitality” (b) against age in the control group.

For social function:
\[ Y = 118,649 - 0.781 \times X; \quad R^2 = 0.190; \quad p=0.0003 \]

For vitality:
\[ Y = 111,364 - 0.848 \times X; \quad R^2 = 0.073; \quad p=0.0290 \]
Fig. 4. Comparison of the GBB-24 scores between the groups

* p=0.0080 vs. Group I and p=0.0293 vs. Group II

Fig. 5. Comparison of the GBB-24 scores between males and females in the control group

* p=0.0067, † p=0.0433, ‡ p=0.0088, £ p=0.0326.
The mood analyses have shown that Bf-S scores of the donors were significantly higher than that of the controls and patients. The controls scored better than the patients (Fig. 6). The Bf-S scores were not age-related and didn’t differ between males and females (data not shown).

4. Discussion

RN and nephron sparing surgery are the treatments of choice for the patients with RCC. Oncological results and complications of these forms of treatment are extensively evaluated showing excellent outcomes in the patients with local disease stages. However, information on the HRQol of these patients is scarce. There are very few publications assessing and comparing the HRQol of the patients after different forms of surgical treatment of RCC.

The studies on the donors’ psychological well-being and HRQol have been conducted since the early years of kidney transplantation. Yet, this topic remains largely under-evaluated and unknown. Most of the existing studies have limitations such as: retrospective design; lack of matching the groups for age or gender; use of non-standardized and validated questionnaires; comparison of the results with references validated for another cultural background; too few participants or low response rates. Nonetheless, these studies suggest hypotheses that require evaluation in a well-designed prospective manner. It should be considered that disparities among the countries in terms of religion, culture, customs, environment, and other factors can influence the HRQol.

In this study we assessed postoperative HRQol of the patients who underwent RN in comparison with our living kidney donors and age and sex matched healthy individuals.
Three different questionnaires have been used to complexly evaluate their: postoperative HRQol (SF-36), subjective complaints (GBB-24) and mood (Bf-S). This type of design is original in existing literature and gives an opportunity to deeper analyse physical, psychosocial and spiritual well-being of the patients after RN in comparison with healthy, non-operated individuals and persons who underwent the same operation for non-medical indications.

We have shown that in three SF-36 items: “Social function”, “Bodily pain” and “Vitality” donors scored significantly better than the controls and patients. In “Bodily pain” and “Vitality” items the patients scored worse than both, the donors and healthy individuals. In all five GBB-24 items the donors had higher scores than the controls and patients, but only for the “Gastric complaints” the difference reached statistical significance. Incomplete sample number may be the reason of it. In mood analyses the patients scored significantly worse than the controls and donors, with both these differences being substantial.

The reason of worse scores of the patients in comparison with the healthy subjects should be physical complaints related to the main disease and/or operation performed. Also, it should be considered that after passing through the treatment process they do not feel themselves completely healthy. The better scores of the donors in somatic parameters can be explained by the fact that they are selected group of individuals, well-evaluated and with better general health than representatives of the common population. The better scores in psychosocial parameters is caused by the fact that donating an organ is associated with giving a second life to the family member and/or close relative, psycho-social mobilization of the donor and consequently, the better mood.

The new findings of this study are: negative correlation of HRQol scores with age; and gender differences in subjective complaints. We have shown that “Social function”, “Mental health” and “Vitality” indexes of the healthy individuals are decreasing with age. The same was true only for the “Social function” of the donors. Significant postoperative improvement in some of the HRQol parameters could be the reason why these differences have not been detected in the donors. As to the “Social function”, this domain is much more dependent on time and external factors than “Mental health” or “Vitality” and kept negative correlation with age.

Four out of five GBB-24 scores were found to be significantly higher in males as compared with females. Again, this difference was evident in the control group and disappeared in the donors and patients. This result corresponds with the outcomes of early studies showing that: a) females tend to have more health complaints than their male counterparts; b) they do receive more diagnostic workups; and c) they receive prescriptions more often during office visits than men do (Verbrugge & Steiner, 1985). Significant postoperative HRQol worsening in the patients and HRQol improvement in the donors was probably the reason why the difference was not evident in these groups. Both of these concepts need further evaluation with higher sample numbers in order to assess importance of the findings.

This study has some limitations. The most important is a lack of an ideal control group. We’ve used the healthy individuals from general population as controls. As far as the donors are, on the whole, healthier than representatives of the general population, it would be even more informative to compare their results with the persons who were evaluated and accepted as donors, but finally didn’t donate a kidney. However, this kind of analyses
would be impossible to perform with relatively small number of transplants performed in our country. An ongoing multicenter study from the US is addressing this issue and will probably come up with the results in the next few years (http://www.clinicaltrials.gov/ct2/results?term=NCT00608283). Relatively small sample number, especially in Group III, can be considered as another shortcoming of this study. Nevertheless, taking into consideration that they comprise 85% of transplants performed in Georgia, and a very high response rate, this group is representative for the Country.

Prospective design and high response rate are the most important advantages of this study. The response rate of 94% is the highest reported in the literature using these questionnaires. It was caused by the fact that the questionnaires have been handed out personally to almost all the donors by nephrologists. On the contrary, the questionnaires have been mailed to the patients (Group I) and only half of them responded. Another advantage of this study is a comparison of pairs of subjects and controls matched for gender and age. Only few studies have evaluated the matched pairs (Fehrman-Ekholm et al, 2000) whereas others have compared their findings with the scores of general population (Johnson et al, 1999; Karrfelt et al, 1998). The present study is also the first to include post-nephrectomy patients, and apply the Bf-S questionnaire to the study groups.

5. Conclusion

In conclusion, the HRQol of living kidney donors and healthy individuals is similar and better than HRQol of the patients operated due to the medical indications. The future prospective studies with higher number of participants will enhance our knowledge of factors influencing HRQol of the living kidney donors and patients after nephrectomy.

6. References


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The field of renal cell cancer has undergone a significant resurgence. This book summarizes up-to-date research and innovative ideas for the future in this rapidly changing field, which encompasses medicine, surgery, radiation oncology, basic science, pathology, radiology, and supportive care. This book is aimed at the clinician or scientist who has an interest in renal cell cancer, whether they are academic or nonacademic. The book covers tumor biology, molecular biology, surgery techniques, radiation therapy, personal testimonies, and present and future treatments of the disease that are on the horizon. The goal was to produce a textbook that would act as an authoritative source for scientists and clinicians and interpret the field for trainees in surgery, medicine, radiation oncology, and pathology.

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