**RESEARCH ARTICLE**

**Intensive nutritional counselling obviates a weight gain in kidney transplant recipients with long-term graft survival in Estonia [version 1; referees: 2 approved with reservations]**

Liidia Kiisk, Mai Ots-Rosenberg

Department of Internal Medicine, Faculty of Medicine, Tartu University, Tartu, 51014, Estonia

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**Abstract**

**Background.** After kidney transplantation body weight gain (WG) in patients generally increases and this can be influenced by improved appetite and reversal of the uremic state. Because of a lack of evidence for effective interventions that prevent body WG after kidney transplantation, Ryan *et al.* recently published a randomized controlled trial design in *BMC Nephrology* to assess the effects of intensive nutrition interventions on WG and metabolic parameters. Here we are demonstrating a part of a study performed at our transplantation centre where we also performed an intensive nutritional counselling intervention on kidney recipients. We hypothesised that kidney transplant (KTx) patients who received intensive counselling may have better long-term weight control compared with patients who did not receive such counselling.

**Methods.** During intensive counselling the dietician took into consideration the results of anthropometry, densitometry, biochemistry, food frequency questionnaire and an analysis of 3-day dietary records. Anthropometrical measurements were assessed at 18 months, 36 months, and, finally, 10 years after the kidney transplantation.

**Results.** We noticed WG in all KTx patients (n=56) both in males and females, as follows: in the standard care group the mean WG in males (N=21) was 6.4 kg, females (N=15) 7.0 kg and among intensively counselled males (N=9) 4.6 kg, females (N=11) 1.1 kg. Statistically non-significant weight change was found among counselled living KTx patients with long-term graft survival both in males (p=0.0680) and females (p=0.3166) which was registered 10 years after the KTx compared with the first measurement mean weight. Among standard care control KTx patients, weight change was statistically significant in both males and females (males: p=0.0016; females: p=0.0040) 10 years after the KTx.

**Conclusions.** The long-term WG data clearly showed that in our population of KTx patients, the patients who received intensive individual dietary counselling had much more educated behaviour in the long-term, thereby preventing WG which is a well-known risk factor for long-term graft failure as well as for cardiovascular complications and mortality.

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**Open Peer Review**

**Referee Status:**

<table>
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<tr>
<th>Invited Referees</th>
<th>Report</th>
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1. Edita Ziginskiene, Lithuanian University of Health Sciences Lithuania
2. Ieva Ziedina, Rīga Stradiņš University Latvia

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**Comments (0)**
Corresponding author: Mai Ots-Rosenberg (Mai.Ots@klinikum.ee)

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Grant information: The study was partly supported by the governmental scientific grants SF0182558s03 (PI Prof. A. Peetsalu, subproject leader Prof. M. Ots-Rosenberg), SF0180081s07 (PI Prof M. Lember), IUT2-8 (PI Prof. M. Lember).

Competing interests: No competing interests were disclosed.

Introduction
The management of nutritional status is an important component of the complex care of chronic kidney disease (CKD) patients. Nutritional status, especially a state of malnutrition or obesity in end stage CKD patients, is linked to increased morbidity and mortality. On the other hand, after successful kidney transplantation (KTx), renal function recovers and appetite in kidney recipients tends to increase rapidly, often leading to weight gain (WG), which, together with increased body mass index (BMI), has a negative impact on health, cardiovascular and surgical outcomes. Body WG is an important risk factor for the development of chronic transplant nephropathy. Historically, studies by many researchers have found overall trends in WG over the first couple of years after KTx, with most WG occurring in the first year after surgery. Therefore, appropriate early nutritional management plays an important role in the prevention or reversal of this trend.

Despite the abundance of cross-sectional data on the relationship between body composition and nutrient intake, there are few long-term studies of body composition changes in KTx patients or studies that combine dietary intake and body composition. However, because of a lack of evidence for effective interventions that prevent weight gain after kidney transplantation, Australian researchers have recently designed a randomized controlled study called the INTENT trial (INTEnsive Nutrition interventions on weight gain after kidney Transplantation). The INTENT trial is a single-blind, randomized controlled trial for assessing the effects of intensive nutrition interventions, including exercise advice, on WG and metabolic parameters in the first year after transplantation. Thus, the results may soon provide important data on the effects of intensive nutrition interventions on WG after transplantation and the associated metabolic consequences.

In addition to nutritional counselling after KTx at our transplant centre, which also routinely provides usual dietary guidance for patients, we also initiated more than 10 years ago a program that incorporates nutritional counselling and guidance for the whole CKD patient population. Besides implementing international and local guidelines into clinical practice, we also conducted a longitudinal prospective study in KTx recipients with long-term graft survival at Tartu University Hospital and looked at the impact of longitudinally intensive nutritional counselling on body composition. We hypothesised that patients who received intensive counselling may have better weight control compared with patients who did not receive such counselling. The purpose of the study was to assess the impact of intensive nutritional counselling on KTx patients in the prevention of post-transplant WG compared with standard dietary guidance in KTx patients. The secondary aim was to determine changes in macronutrient intake and body composition in patients after KTx. We further aimed to assess the long-term impact of intensive nutritional counselling 10 years after KTx on WG by comparing groups of intensively counselled and standard care patients.

Methods
Adult consecutive non-diabetic patients with stable kidney function who agreed to participate and gave written informed consent, were recruited for the first measurement (FM) at 18 months and for a follow-up (FU) 36 months after kidney transplantation, performed in our centre between 2003 and 2006.

In total, 75 patients were studied; of these 28 KTx patients (12 males, mean age 42.8 ± 16.1 years and 16 females, mean age 47.0 ± 14.9 years) received intensive nutritional counselling. The remaining 47 KTx patients, who stayed in standard dietary guidance maintenance, formed the control group and this group consisted of 27 males (with a mean age of 45.6 ± 9.4 years and 20 females (with a mean age of 48.7 ± 12.8 years). Anthropometric measurements (body weight, kg; body height, cm; body mass index, kg/m²) were assessed at FM, FU and then, finally, 10 years after the KTx in both groups of patients. WG was estimated taking into account a patients weight measurements at FM and comparing them with measurements after 10 years. Also, laboratory measurements and macronutrient intake were performed on counselled KTx patients twice: at FM and at FU.

All patients at our institution are provided with appropriate usual nutritional guidance before discharge after kidney transplantation. In our study, additional intensive nutritional counselling and dietary guidance at FM (18 months after the KTx) were carried out by a dietician who took into account individual patient’s anthropometrical, laboratory as well as nutritional investigations including the food frequency questionnaire (see Supplementary material 1) and the analysis of 3-day dietary records. Individual nutritional counselling and dietary guidance were performed repeatedly. Nutritional counselling was performed by a dietician who took into consideration the patient’s age, gender, the stage of chronic kidney damage, proteinuria, build of the body, the 24-hour need for food energy and nutrients, and the patient’s eating habits. The consumption of energy and main nutrients content in the 3-day menus of kidney transplant patients was calculated and analysed with the Finnish food composition database program MicroNutrica Nutritional Analysis (https://fineli.fi/). All the data were compared with the Estonian Nutrition Recommendations.

Ethics approval: The study was approved by the Ethics Committee on Human Research of the University of Tartu, Estonia (protocol no 141/30; 2005).

Results

Dataset 1. Raw data supporting the patients’ long-term body weight gain findings in different study groups

http://dx.doi.org/10.5256/f1000research.10035.d141569

In the dataset columns that are not important or would potentially identify the patients (e.g. diagnosis, date of birth, doctors names etc) have been deleted and only columns with necessary data for analysis for the current study remain.

Our previous results of detailed anthropological measurements at 18 and 36 months after KTx showed that females were more accurate to follow dietitians’ advice compared to male patients. We also showed previously that the mean body weight increased significantly among studied male KTx patients and in control KTx patients, both male and females, after the follow-up, but in female KTx patients the BW increase was non-significant.

Now, in our current study 10 years after the KTx we further aimed to clarify the longitudinal effect of intensive nutritional counselling and guidance on WG. We noticed WG in all KTx patients, both...
in males and females, as follows: in the standard care group, the males’ mean WG was 6.4 kg, the females’ 7.0 kg and among intensively counselled males 4.6 kg and females 1.1 kg. But in Table 1, we demonstrate statistically non-significant weight change among counselled living KTx patients with long-term graft survival both in males (N=9, p = 0.0680) and females (N=11, p = 0.3166) which was registered 10 years after the KTx compared with the FM mean weight. Among standard care control KTx patients, weight change was statistically significant in both males and females (males: N=21, p = 0.0016; females: N=15, p = 0.0040) 10 years after the KTx.

We also observed and assessed macronutrient intake, which was determined at FM and at FU (Table 2). The food frequency

### Table 1. Body weight data in kidney transplant patients and control kidney transplant patients compared with body weight data 10 years after kidney transplantation.

<table>
<thead>
<tr>
<th>Study groups</th>
<th>Body weight (kg) one half years after KTx</th>
<th>Body weight (kg) 10 years after KTx</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Kidney transplant patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (N = 9)</td>
<td>71.20 ± 9.00</td>
<td>75.77 ± 11.24</td>
<td>0.0680</td>
</tr>
<tr>
<td>Female (N = 11)</td>
<td>77.48 ± 22.62</td>
<td>78.59 ± 20.78</td>
<td>0.3166</td>
</tr>
<tr>
<td>Control kidney transplant patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (N = 21)</td>
<td>75.70 ± 11.92</td>
<td>82.14 ± 13.07</td>
<td>0.0016*</td>
</tr>
<tr>
<td>Female (N = 15)</td>
<td>70.95 ± 11.36</td>
<td>77.93 ± 13.55</td>
<td>0.0040*</td>
</tr>
</tbody>
</table>

*P < 0.05; SD, standard deviation; KTx, kidney transplantation.

### Table 2. The results of energy and main nutrient content in 3-day menus in patients 1.5 and 3 years after kidney transplantation.

<table>
<thead>
<tr>
<th>Study groups</th>
<th>1.5 years after KTx (FM)</th>
<th>3.0 years after KTx (FU)</th>
<th>P-value</th>
<th>Estonian reference nutrient intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (N = 12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.8 ± 16.1 (18–70)</td>
<td>173.5 ± 7.6 (164.0–189.3)</td>
<td>0.001*</td>
<td>2700±200</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>174.8 ± 7.4 (166.5–190.0)</td>
<td>83.3 ± 19.9 (61.2–138.1)</td>
<td>0.001*</td>
<td>50–90</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>75.1 ± 20.7 (57.1–134.1)</td>
<td>27.7 ± 6.8 (22.0–47.5)</td>
<td>0.013*</td>
<td>1.0</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.7 ± 7.2 (19.4–46.1)</td>
<td>91.6 ± 10.7 (72.0–107.9)</td>
<td>0.084</td>
<td>50–90</td>
</tr>
<tr>
<td>Total energy (kcal/day)</td>
<td>2689.7 ± 467.5 (2030.4–3675.7)</td>
<td>2424.9 ± 291.4 (1966.4–2910.2)</td>
<td>0.409</td>
<td>250–350</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>106.7 ± 22.4 (74.9–153.1)</td>
<td>88.3 ± 14.6 (62.3–115.1)</td>
<td>0.009*</td>
<td></td>
</tr>
<tr>
<td>% of proteins in food energy</td>
<td>15.9 ± 1.5 (13.6–18.0)</td>
<td>1.1 ± 0.3 (0.6–1.6)</td>
<td>0.013*</td>
<td></td>
</tr>
<tr>
<td>Proteins/body weight (g/kg)</td>
<td>1.5 ± 0.4 (1.0–2.3)</td>
<td>1.5 ± 0.4 (1.0–2.3)</td>
<td>0.283</td>
<td></td>
</tr>
<tr>
<td>Carbohydrate (g/day)</td>
<td>101.3 ± 21.4 (69.2–144.9)</td>
<td>311.8 ± 49.4 (198.5–347.9)</td>
<td>0.052</td>
<td></td>
</tr>
<tr>
<td>Lipid (g/day)</td>
<td>329.3 ± 74.0 (238.3–491.2)</td>
<td>101.3 ± 21.4 (69.2–144.9)</td>
<td>0.003*</td>
<td></td>
</tr>
</tbody>
</table>

Female (N = 16)

| Age (years)           | 47.0 ± 14.9 (31–71)      | 163.5 ± 6.8 (147.3–169.5)| 0.001*  | 2000±150                           |
| Height (cm)           | 164.9 ± 6.5 (150.0–171.5)| 76.6 ± 22.7 (46.2–124.9)| 0.101   | 50–90                              |
| Body weight (kg)      | 74.4 ± 22.3 (40.0–126.5)| 28.5 ± 7.7 (17.2–44.5)   | 0.013*  | 10–15                              |
| Body mass index (kg/m²)| 27.3 ± 7.5 (14.9–43.8)  | 92.2 ± 19.5 (61.6–131.0)| 0.038*  | 1.0                                |
| Total energy (kcal/day)| 2028.0 ± 466.5 (1128.3–2974.3)| 2352.9 ± 487.0 (1380.2–3266.7)| 0.002*  |                                   |
| Protein (g)           | 79.6 ± 19.7 (49.2–123.1)| 89.2 ± 19.5 (61.6–131.0)| 0.084   |                                   |
| % of proteins in food energy | 15.8 ± 2.2 (11.7–20.3) | 15.2 ± 1.7 (12.1–18.1) | 0.013*  |                                   |
| Proteins/body weight (g/kg) | 1.2 ± 0.4 (0.5–2.2) | 1.2 ± 0.4 (0.5–2.2)   | 0.382   |                                   |
| Carbohydrate (g/day)  | 76.0 ± 23.0 (22.1–119.1)| 88.0 ± 27.1 (50.1–162.5)| 0.283   |                                   |
| Lipid (g/day)         | 252.8 ± 58.3 (178.9–362.3)| 293.2 ± 61.0 (166.0–414.1)| 0.052   |                                   |

*P < 0.05; KTx, kidney transplantation; FM, first measurements; FU, follow-up measurements.
questionnaire revealed that patients consumed various types of food (milk and dairy products; meat and fish products; cereal and flour products; vegetables; fruits; sweets) at different frequencies, but there was a tendency towards excessive consumption of food rich in proteins and carbohydrates in both males and females in FM. The following changes in nutrient intake were noticed: at FU, mean daily energy and protein intakes were significantly higher than FM in female patients, and in males, mean daily energy, protein, fat and carbohydrate intakes had a tendency to decrease after FU when compared with FM data. However, mean daily intakes of energy, fat and protein estimated at FM and at FU were adequate in both males and females when compared with the Estonian Dietary Reference Intakes (Table 2). Thus, there was a positive tendency in the change of the content of different macronutrients among all counselled subjects, although the directions in which macronutrient intake changed were not similar in males and females.

Discussion
The impact of obesity and overweight on clinical outcomes after serious disease, have long been the object of research, with contradictory results. In our study, WG was not significant 10 years after KTx in patients who received additional intensive nutritional counselling compared with standard care control KTx patients group.

We conclude that nutritional counselling and guidance is important and should be offered early and regularly after kidney transplantation to maintain body weight and appropriate nutritional state longitudinally. Post-transplant outcomes will be optimized by a team approach for the comprehensive management of the kidney transplantation recipient combined with vigilant surveillance to detect WG in a timely fashion. However, long-term WG data clearly showed that in our KTx patient population, the patients who received intensive individual dietary counselling had much more educated behaviour in the long-term, thereby preventing WG which is a really well-known risk factor for long-term graft failure as well as for cardiovascular complications and mortality. We are awaiting the final results of the Australian researchers with great interest.

Data availability
F1000Research: Dataset 1. Raw data supporting the patients’ long-term body weight gain findings in different study groups. 10.5256/f1000research.10035.d14156

Author contributions
LK conceived of the study, carried out the data collection, participated in the design of the study, was involved in drafting the manuscript and revising it critically for important intellectual content.

MO-R participated in the design of the study and performed the statistical analysis, carried out the data collection, participated in the design of the study and drafted the manuscript.

Both authors read and approved the final manuscript.

Competing interests
No competing interests were disclosed.

Grant information
The study was partly supported by the governmental scientific grants SF0182558s03 (PI Prof. A. Peetsalu, subproject leader Prof. M. Ots-Rosenberg), SF0180081s07 (PI Prof M. Lember), IUT2-8 (PI Prof. M. Lember).

Acknowledgements
The authors thank doctors Mart Lintsi, Ingrid Kull, Siiri Mesikepp, Elviira Seppet for their kind help. The authors thank Viive Saar for proofreading the manuscript.

Supplementary material
Food-frequency questionnaire.
The research of nutritional habits was carried out on the basis of a food-frequency questionnaire (FFQ). A special food questionnaire “The card of nutritional habits” was worked out by the Centre of Physical Anthropology at the University of Tartu and was used for nutritional research. “The card of nutritional habits” was worked out for kidney transplant patients. A FFQ consisted of six parts and 180 variables which covered the questions. Click here to see the questions. An example FFQ with results are available in Kiisk et al.7.

Click here to access the data.

References


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Version 1

Referee Report 07 March 2017

doi: 10.5256/f1000research.10811.r20338

Ieva Ziedina
Transplant Research Laboratory, Riga Stradiņš University, Riga, Latvia

The authors of the article "Intensive nutritional counseling obviates a weight gain in kidney transplant recipients with long-term graft survival in Estonia" focused their attention on important and hardly manageable complication after kidney transplantation - weight gain.

The authors themselves admit that they publish a part of the study in this open access resource, therefore it's possible the aim and methods of study are not completely clear; when exactly did the dietician analyze and give his recommendations to the patients? Did he do it just twice- 18 and 36 months post-transplant? And do the authors believe that it affected patients' weight 8, 5 and 7 years later? For how long has the follow up lasted - 10 years with half-way assessment 3 years post-transplant? Then why do they have the results of energy and nutrient content just 1,5 and 3 year post-transplant and don't have 10 years post-transplant (table 2), but body weight data are reviewed 1,5 and 10 years post-transplant but not 3 years post-transplant?

What about study cohort? There is stated in the methods that 75 patients were included, but in abstract they report only 56 patients? What happened to 19 patients? Have they gained / lost weight?

The authors assessed absolute weight gain (measured in kg), but there is no information about body mass index (except table 2), body composition, lean body mass and/or fat mass. It could be possible that some of patients had malnutrition after dialysis and then they acquired normal body weight. May be all patients had normal body weight (normal nutrition status) and all of them got obese (range of weight at the first assessment was from 57.1! kg till 134.1! kg)? By merging both tables it is possible to follow that men in counseled group had mean weight 75.1 – 83.3 – 75.77 kg at anthropometrical measurement time points but women had mean weight 74.4-76.6-78.59 kg at the same time points. Authors could discuss what was a trigger for weight loss in cohort of men. There is no information about results of energy and nutrient content in standard dietary guidance group. Therefore in my opinion it is not fair to compare groups.

Conclusions could not be made about graft failure, cardiovascular complications and mortality because this information wasn’t stated in the article.

The article could be approved with reservations.
I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

**Competing Interests:** No competing interests were disclosed.

**Referee Report 28 November 2016**

doi:10.5256/f1000research.10811.r17515

**Edita Ziginskiene**
Department of Nephrology, Lithuanian University of Health Sciences, Eiveniu 2, Kaunas, Lithuania

The article "Intensive nutritional counselling obviates a weight gain in kidney transplant recipients with long-term graft survival in Estonia" is an interesting manuscript evaluating impact of intensive nutritional counselling on patients after kidney transplantation in the prevention of post transplant weight gain. Diet is one of the important factors of management of this patients group.

My specific comments:

**Title and abstract.**
The aims of the study must be in the abstract. It must be more clearly described compared groups of patients. Please write the results accurately identifying periods of study.

**Article content.**
There is an error at the title of second column of Table 1 ("Body weight (kg) one half years..." Should be 
"... one and half years..." First study group at the Table 1 should be identified accurately (Kidney transplant patients with intensive nutritional counselling), as both groups of patients are" kidney transplant patients".

Explanation of results of Table 2: “Thus, there was a positive tendency in the change of the content of different macronutrients among all counselled subjects, although the directions in which macronutrients intake changed were not similar in males and females”. In my opinion, differences of males and females should be clarified in the text.

The discussion is quite short. The results must be compared with data from the literature, or at least you need to provide the data, which are found in the literature on the matter. Discussion should be based on both parts of the results.

**Conclusions** should accurately reflect the aims of study and results, so they must include changes in macronutrients intake and body composition in patients after kidney transplantation and long-term impact of intensive nutritional counselling 10 years after kidney transplantation on weight gain. Conclusions should accurately reflect the results of the study.

In my opinion, the article could be indexed after the corrections.
I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

**Competing Interests:** No competing interests were disclosed.