Research Article

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Nutritional status and survival of End-Stage Renal Disease patients treated with continuous ambulatory peritoneal dialysis

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Abstract. The objective of the work was to study the survival peculiarities of end-stage renal disease patients treated with continuous ambulatory peritoneal dialysis (CAPD) depending on the nutritional status and informative markers associated with it.

Methods. 105 ESRD patients who received CAPD treatment during 2012 - 2017 years at the Kyiv Scientific and Practical Center of Nephrology and Dialysis, which is the clinical base of the State Institution “Institute of Nephrology National Academy of Medical Sciences of Ukraine” were included in the cohort prospective open study.

The survival analysis was carried out both in the studied population as a whole and in groups depending on the nutritional status (NS) indicators defined basing on the calculation of the subjective global assessment (SGA) points: the first group (n = 51) consisted of patients without malnutrition, the second group (n = 30) - patients with a mild degree of malnutrition, the third group (n = 13) - patients with a moderate degree of malnutrition, and the fourth group (n = 11) - patients with a severe degree of malnutrition. The survival analysis was conducted both in the groups in compliance with NS, and depending on the informational markers associated with NS, in particular, albumin, body mass index (BMI), residual renal function (RRF).

Survival were calculated using the Kaplan-Meier method, and the difference between survival rates was analyzed using the log-rank test and $\chi^2$. The starting date of peritoneal dialysis treatment was considered as the starting point of the monitoring. The difference was considered to be accurate at $p < 0.05$. Analyzed cases were included till January 7, 2019. The event risk assessment was carried out with the probability of relative risk (RR) values calculating their confidence intervals (95% CI).

Results. Forty-three (40.95%) patients died during the current analysis, 17 patients were switched to the hemodialysis (HD), 4 patients had undergone kidney transplantsations, Cardiovascular disease was the leading cause of death (41.9%), the second cause of death by frequency was bacterial infections (20.9%).

Longer monitoring periods death rate was significantly higher in patients of group with an average (1/14; 8.6% vs 1/64.1; 1.5% p < 0.0001; RR - 3.08; 95% CI: 1.8 - 5.19) and mild degree of nutritional disorders (ND) (1/14; 7.1% vs 1/64.6; 1.6% p = 0.0018; RR - 2.3, 95% CI: 1.36-3.89) compared with normal NS. Similarly, the percentage of died patients with a severe ND degree was significantly higher than those with a normal nutritional status (7/63.6% vs. 14/27.45%, p = 0.0094, RR - 2.31, 95% CI: 1.23 - 4.33).

The cumulative survival during the 1- year amounted to 90% of patients for 3 and 5 years - 64% and 41%, respectively. It was found that the survival rate of PD patients is credibly higher in groups with normal NS or mild ND degree than patients of group with a moderate or severe degree of nutritional disorders ($\chi^2 = 22.9$; df = 3; $p = 0.00004$). The cumulative survival for 1 and 3 years was 97%, 98%, 70%, 81% and 76%, 70%, 24%, 36% in groups of patients without nutritional disorder, with mild nutritional disorders, moderate and severe disorders, respectively.

Conclusions. Thus, our study found that serum albumin level, BMI and RRF magnitude are the markers for the survival of ESRD patients treated with PD. Veritable difference between the survival of patients depending on the nutritional status was stated. Three-year cumulative survival with mild degree of malnutrition group was twice as high as in severe nutritional disorders and it was 70% vs 36% (p < 0.001). The relative risk of death from all causes increases by 3.1 and 2.32 times for moderate and severe nutritional disorders patients compared to the patients group with normal NS.

Keywords: end-stage renal disease, peritoneal dialysis, mortality, survival, nutritional status, subjective global assessment, residual renal function, body mass index, serum albumin.

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Нутритивний статус та виживання хворих на хронічну хворобу нирок VД стадії, які лікуються постійним амбулаторним перитонеальним діалізом

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Резюме. Метою роботи було вивчити особливості виживання хворих на хронічну хворобу нирок VД стадії, які лікуються ПАПД в залежності від нутритивного статусу та його інформативних маркерів.

Методи. До когортного проспективного відкритого дослідження було включено 105 хворих на ХХН VД ст., які отримували лікування ПАПД в Київському міському науково-практичному центрі нефрології та діалізу, що є клінічною базою Державної установи «Інститут нефрології НАМН України», протягом 2012 - 2017 років. Аналіз виживання проводився як у досліджуваній популяції в цілому, так і в групах в залежності від показників НС, визначеного на підставі обчислення балів СГО: першу групу (n=51) склали хворі без порушення харчування, другу групу (n=30) - хворі з легким ступенем порушення харчування, третю (n=13) – з середнім ступенем, та четверту групу (n=11) - хворі з важким ступенем. Аналіз виживання проводився, як в групах відповідно НС, так і в залежності від інформативних маркерів НС, зокрема альбуміну, індексу маси тіла.

Висновки. Таким чином за результатами проведеного дослідження встановлено, що рівень сироваткового альбуміну, показник ІМТ та величина ЗФН є маркерами виживання хворих на ХХН VД стадії, які лікуються ПАПД.

Ключові слова: хронічна хвороба нирок, перitoneальний діаліз, смертність, виживання, нутритивний статус, суб'єктивна глобальна оцінка, залишкова функція нирок, ІМТ, сироватковий альбумін.
dicators. At the same time, the three-year survival rate of ESRD patients is only 54% and 65% during the treatment with hemodialysis and peritoneal dialysis (PD), respectively. The anticipated life expectancy for ESRD patients is less than one-third of the life expectancy for the individuals of the general population in comparable age and gender groups [1].

At the moment there is no single point of view regarding the benefits for patients’ survival depending on the dialysis modality of renal replacement therapy (RRT). Thus Garcia-Cant n C. and co-authors have concluded that PD patients have better survival rate than patients treated with hemodialysis (HD) using a central venous catheter as vascular access [2]. However, after the formation of continuous vascular access, the difference in the survival rate of HD and PD patients was not investigated. Stanley M. in her multicenter study with the main objective to compare survival rate and life quality of patients treated with HD and PD has concluded that the survival rate of PD patients during the first two years of treatment is better than that of HD patients especially with the preserved residual renal function [3]. Nevertheless, over time (after 3 - 4 years of treatment with RRT methods) the survival rate of HD patients compared to PD patients is better. Therefore, according to this study survival rate for patients of HD treatment is better than for patients of PD treatment with long-term treatment [3]. J. Pedro Teixeira and co-authors basing on the meta-analysis of survival for patients who are treated by continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD) have not determined a significant difference between these groups of patients [4]. The results of the study conducted in Colorado allowed stating that the survival rate of PD patients significantly reduces in the course of time. The main cause of patient’s death according to the study is cardiovascular disease (CVD) [5]. Nowadays it is well-known that the residual renal function (RRF) has a significant effect on both the frequency of fatal cardiovascular episodes and the nutritional status of patients treated with RRT dialysis methods. In particular, RRF loss is accompanied by an increase in the proportion of nutritional disorders and cardiovascular mortality in the population of ESRD patients treated with PD [6].

A. Chandrahashekarzi and co-authors count a number of factors including low serum albumin level as the reasons that have a negative effect on survival. The authors emphasize that the correction of nutritional disorders can improve survival [7]. A group of authors from Turkey in their study during the examination of 58 PD patients have received similar data. In particular, the factors that aggravate the survival rate of patients treated with CAPD according to the results of this study are low serum albumin level and loss of residual renal function at the time of PD initiation [8].

It is known simultaneously that nutritional disorders (ND) are quite common among patients treated with RRT methods. Many studies have shown that namely nutritional disorders are one of the reasons for life quality deterioration, mortality increase and accordingly have a negative impact on the survival of patients in this category. Researchers from the United States have got similar data. Monitoring of 177 PD patients state allowed to determine that significant disorders of nutritional status are the factor that aggravates survival and increases mortality among the studied population. The authors have proved that normal values of such nutritional markers as pre-albumin, albumin and creatinine serum are associated with lower mortality rates [9]. Dombros A. in another study examining patients treated with PD in Greece has come to a similar conclusion. According to the data obtained by the researcher, the presence of protein-energy insufficiency is associated with an increase of fatal cardiovascular complications number [10].

In another study basing on the monitoring of 199 PD treated patients in Brazil, the researchers have stated that serum albumin level decrease, the level of subjective global assessment (SGA), and the number of calories taken according to dietary diaries were the main parameters of nutrition decrease associated with higher mortality. At the same time, it has been proved that higher values of body mass index are associated with a better survival rate of patients within the dialysis population [11]. The latter in its turn relates to the phenomenon of “reverse epidemiology” which was described in the works of Kalantar-Zadeh K. with co-authors [12]. However, in a series of studies, there was no link proved between low BMI and mortality rate [13, 14].

Another interesting study according to which NS was evaluated among 106 PD patients was conducted in Poland with the administration of laboratory, functional and anthropometric methods. The results of this study have once again confirmed that ND is a fairly widespread problem and has a negative impact on the mortality and survival rates for ESRD patients treated with PD. The authors of the work determine the serum albumin decrease, total cholesterol increase and low index of arm muscle circumference as the main NS parameters which affect mortality [15].

In the meantime, Sung Hee Chung with co-authors basing on the analysis of 153 ESRD patients treated with PD has received a bit different result. On the one hand, the authors have confirmed the available data concerning the high frequency of ND among PD patients (41.8% of the examined), on the other hand, they have stated that the effect of nutritional status disorders on survival is manifested only in combination with comorbid diseases. Summarizing the authors note that in compliance with the results of the conducted study, the presence of only ND is not a reason for reducing the survival rate in this category of patients. However, according to the authors’ ideas this conclusion requires further study [16].

In conclusion, it is worth mentioning one more study that was conducted at the State University of the New York Downstate Medical Center, USA. The re-
searchers confirmed the relationship between the parameters of NS and mortality of patients treated with PD. According to the results of this study, robust laboratory parameters of NS that affect the survival of patients in this population are serum albumin, creatinine and standardized protein equivalent of nitrogen excretion [17].

Consequently, considering the above mentioned, it can be assuredly asserted that the problem of survival for ESRD patients treated with RRT methods and their mortality rate decrease does not lose its relevance. Simultaneously despite the importance and clinical significance of this problem data concerning the survival rate of patients treated with PD both in general and depending on the nutritional status are rather controversial. Data related to the survival rate of ESRD patients treated with PD in Ukraine are absent.

**Objectives.** To study the survival rate for ESRD patients treated with CAPD depending on nutritional status and informational markers associated with it.

**Materials and methods.** 105 ESRD patients were included in the cohort prospective open study who received CAPD treatment during 2012 - 2017 years at the Kyiv Scientific and Practical Center of Nephrology and Dialysis, the clinical base of the State Institution «Institute of Nephrology National Academy of Medical Sciences of Ukraine».

Patients were selected after signing the Informed consent to participate in the study. The rules of patient safety were followed during the research, the rights and canons of human dignity were kept as well as moral and ethical standards in accordance with the main provisions of the GCP (1996), the Council of Europe conventions on human rights and biomedicine (dated 04.04.1997) Helsinki Declaration of the World Medical Association on the Ethical Principles of Scientific Medical Research with Human Participation (1964 - 2008) and the Order of the Ministry of Health of Ukraine No. 690 dated September 23, 2009 (as amended in accordance with the Order of the Ministry of Health of Ukraine No. 523 dated July 12, 2012), the Ethical code of the scientist of Ukraine (2009).

The criteria for inclusion of patients in the study were age over 18 years old, the CAPD treatment method, provision of patient’s informed consent to participate in the research, the availability of functional, laboratory and anthropometric research results of nutritional status assess determined 6 months after starting PD treatment, the capacity for adequate cooperation during research process. The criteria for exclusion from the study were patient’s denial, acute or exacerbation of chronic infectious diseases of bacterial and viral genesis (PD-associated peritonitis, infection of the catheter exit place, pneumonia) within one month prior to the patient inclusion in the study, duration of PD treatment for less than 6 months, maldigestion and malabsorption symptoms, mental disorders.

**Clinical and laboratory characteristics of study population at baseline are providing in Table 1.**

**Patient characteristics for the study population**

<table>
<thead>
<tr>
<th>Characteristics (n =105)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Age ( years, M ± SD)</td>
<td>55.9 ± 14.6</td>
</tr>
<tr>
<td>Male gender (n / %)</td>
<td>53 / 50.5%</td>
</tr>
<tr>
<td><strong>Cause of ESRD, (n / %)</strong></td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>63/60.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>24/22.86</td>
</tr>
<tr>
<td>Urolithiasis</td>
<td>9/8.57</td>
</tr>
<tr>
<td>Other</td>
<td>9/8.57</td>
</tr>
<tr>
<td><strong>Nutrition markers</strong></td>
<td></td>
</tr>
<tr>
<td>Serum albumin (g/l)</td>
<td>32.97 ± 5.7</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>21.99 ± 6.11</td>
</tr>
<tr>
<td>SGA (points, M ± SD)</td>
<td>5.39 ± 1.82</td>
</tr>
<tr>
<td><strong>Dialysis parameters</strong></td>
<td></td>
</tr>
<tr>
<td>PD duration (months, M ± SD)</td>
<td>34.24 ± 20.6</td>
</tr>
<tr>
<td>Weekly urea clearance (Kt/V)</td>
<td>1.98 ± 0.56</td>
</tr>
<tr>
<td>RRF ≥ 500 ml (n / %)</td>
<td>45/43%</td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m2, (M ± SD)</td>
<td>3.27 ± 2.92</td>
</tr>
</tbody>
</table>

For further analysis, the patients were divided into four groups according to the nutritional status defined basing on the calculation of the SGA points [8]. The first group (I group, n = 51) consisted of patients without malnutrition, the second group (II group, n = 30) - patients with a mild degree of malnutrition, the third (III group, n = 13) - patients with an average degree of malnutrition, and the fourth group (IV group, n = 11) - patients with a severe degree of malnutrition. The features of the NS informational markers and the RRF value in the monitoring groups are presented in Table 2.

**Nutritional parameters in ESRD studied groups**

<table>
<thead>
<tr>
<th>Patient groups</th>
<th>Markers (M ± SD)</th>
<th>RRF (ml/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SGA (points)</td>
<td>Serum albumin (g/l)</td>
</tr>
<tr>
<td>Group 1</td>
<td>6,2±0,72</td>
<td>41,±2,5</td>
</tr>
<tr>
<td>Group 2</td>
<td>4,44±1,31</td>
<td>33,84±0,64</td>
</tr>
<tr>
<td>Group 3</td>
<td>3,45±1,21</td>
<td>27,2±1,48</td>
</tr>
<tr>
<td>Group 4</td>
<td>1,3±0,56</td>
<td>20,7±1,4</td>
</tr>
</tbody>
</table>
The study of the survival peculiarities of ESRD patients treated with PD depending on the NS was conducted in the monitoring groups. The survival analysis was conducted both in the groups in general and depending on the informational markers which is associated with NS (albumin, BMI, RRF). Survival analysis depending on serum albumin contents and BMI was conducted considering the available recommendations: serum albumin level > 35 g/l vs ≤ 35 g/l and BMI > 24 kg/m² vs ≤ 24 kg/m² [18]. The survival analysis depending on RRF was conducted considering its value, namely < 2 ml/min/1.73 m²; 2.0-5.0 ml/min/1.73 m²; >5.0 ml/min/1.73 m². Survival was determined by Kaplan-Mayer method, log-rank test and $\chi^2$ were analyzed. The starting date of peritoneal dialysis treatment was considered the starting point of the monitoring. The primary endpoint was death for any reason. A $P$ value <0.05 was considered to be statistically significant in this study. Analyzed cases were included to January 7, 2019. Statistical processing and mathematical analysis of the study results were carried out by calculating relative and average values, criteria of their reliability. Average value (M) and standard deviation (SD) were determined. The reliability of the differences was estimated according to the generally accepted in variation statistics Student, $\chi^2$. The difference was considered to be reliable when the significance level was $p <0.05$. Significant effect of risk factor associated with nutritional status was measured as relative risk (RR), with the confidence interval (95% CI). All received digital data were processed using modern methods of variation statistics by means of the statistical software package STATISTIKA for Windows 10.0.

Results: During follow up periods 43 (40.95%) cases of death were registered, 17 patients were switched to the hemodialysis (HD), 4 patients had kidney transplantations. Cardiovascular disease was the leading cause of death (41.9%), the second cause of death by frequency was bacterial infections (20.9%) and 11.6% - cerebrovascular diseases. Other causes of death were registered among 14.0% of patients and 11.6% of cases the cause of death is unknown.

The proportion of deceased patients during the monitoring period was apparently higher in the group of patients with an average degree of nutritional disorders (ND) in comparison with normal NS (11/84.6% vs 14/27.45%, $p < 0.0001$; RR - 3.08; 95% CI: 1.86 - 5.09) and a mild degree of disorders (11/84.6% vs 11/36.7%, $p = 0.0018$, RR - 2.3, 95% CI: 1.36-3.89). Similar data were obtained by analyzing the proportion of deceased patients with severe ND and normal nutritional status (7/63.6% vs 14/27.45%, $p = 0.0091$, RR - 2.3, 95% CI: 1.23 - 4.35).

The one-, three- and five-years cumulative survival rates in study population were 90%, 64% and 41%, respectively (Fig. 1)
Further analysis of PD patients’ survival peculiarities depending on the laboratory and anthropometric parameters of NS allowed to state that serum albumin level, BMI and the magnitude of RRF are not only informational markers which is associated with NS but also survival markers in the specified population. The cumulative survival in the group of patients with serum albumin level < 35 g/l and in the group of patients with serum albumin level ≥ 35 g/l in 1 and 3 years was 73% vs 96% and 37% vs 74%, respectively (Fig. 3; p = 0.00005, log-rank test).

Similar data were obtained in the study of survival rate based on BMI (Fig. 4).

In particular, the cumulative survival in 1 and 3 years in the group of patients with BMI > 24 kg/m² was 94% vs 86% and 79% vs 47%, respectively (p = 0.00321, log-rank test).

Study of ESRD patients’ survival depending on the RRF (Fig. 5) allowed stating that the cumulative survival was authentically lower among patients with RRF < 2 ml/min/1.73 m² and in the group of patients with serum albumin level ≥ 35 g/l and in 1 and 3 years was 73% vs 96% and 37% vs 74%, respectively (Fig. 3; p = 0.00005, log-rank test).

**Discussion.** It is well-known currently that despite the continuous improvement of dialysis technologies, ESRD patient’s mortality rate remains unsatisfactory [1]. Disorders of nutritional status according to available researches is one of the most studied factors that increases the mortality rate of ESRD patients treated with CAPD [7-10]. This way Kendrick J. with co-authors stated that long-term survival of PD patients remains low. The most common cause of death in the population of ESRD patients is cardiovascular diseases (CVD) [5, 19]. Data from genuine study coincide with the data received by the researchers from the Colorado Health Sciences Center, USA. In particular, the proportion of CVD in the causes of death structure in the study population was almost 42%.

The results of studies concerning the impact of certain markers of nutritional status on PD patient’s survival are rather contradictory [8-10, 13, 14]. Accordingly, in the work of Tamer Sakaci and co-authors it has been shown that low serum albumin level and RRF loss at the time of PD initiation are factors that aggravate the survival rate of CAPD [8]. Avram M. and co-authors basing on a 177 ESRD patients study being treated PD in the USA have determined that malnutrition and inflammatory processes are factors that aggravate survival rate and increase mortality among patients of the specified population [9]. Similar data have been obtained by researchers from Greece [10]. Malgorzewicz S. and co-authors also determine serum albumin decrease, total cholesterol increase, and a low index of arm muscle circumference are the main NS parameters that have a negative effect on survival [15]. Leining C. and co-authors in their work have determined that higher body mass index contributes to better survival of patients of dialysis patients’ population [11]. Namely, this phenomenon of “reverse epidemiology” has been described in the works of Kalantar-Zadeh [12]. At the same time, a number of studies have not stated the negative effects of low BMI on survival and mortality rates [13, 14]. According to the results of genuine research it has been proved that RRF indicator shows a strong
The results of work carried out by Brazil researchers turned out to be interesting. Basing on an examination of 199 PD patients, the authors stated that low serum albumin level, subjective global assessment (SGA), and an insufficient amount of calories taken according to dietary diaries are the main markers of nutritional disorders associated with a veritable increase of mortality and survival rates [11]. Basing on laboratory, functional and anthropometric methods of NS assessment researchers have confirmed the available data concerning the prevalence of ND and their negative impact on the survival of ESRD patients treated with PD [15]. The received data show that the PD treated patients’ survival rate is apparently higher in groups with normal NS or a light degree of ND (χ² = 22.9; df = 3; p = 0.00004). Existence of nutritional disorders of moderate or severe degrees is associated with an increase of mortality and accordingly a decrease in PD patients’ survival rate.

Conclusions: Thus, according to the results of the study it was found that serum albumin level, BMI and RRF magnitude are the markers of survival for ESRD patients treated with PD. Veritable difference between the survival of patients depending on the nutrition status was stated. Three-year cumulative survival with mild degree of malnutrition group was twice as high as in severe nutritional disorders and it was 70% vs 36% (p < 0.001). There was no difference between the survival analysis for 1 - years (has not allowed determining an accurate difference) in cumulative frequencies, depending on the nutritional status of patients of the study population.

The relative risk of death from all causes increases by 3.1 and 2.32 times for moderate and severe nutritional disorders patients compared to the patients group with normal NS (p <0.001).

The discovered differences in the survival rate of ESRD patients treated with CAPD depending on nutritional status once again demonstrate the necessity for continuous monitoring of its informational markers in order to timely detect violations in time.

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Authors’ contributions. 
Anna Shimova: idea of the research, analyzed and interpreted the patient data, a major contributor in collating the manuscript.
Irina Shifris: designed study, consultation of patients, statistic analyzed and interpreted the patient data, preparation of the manuscript.
Iryna Dudar: management of the research.

References:


