Costs of Long-Term Post-Transplantation Care in Kidney Transplant Recipients

Background: Solid organ transplantations lead to improvements in patient survival and patient quality of life, as well as health care system economic benefits. However, over time, health problems can accumulate post-transplantation. Therefore, we hypothesized that in the late post-transplantation period, the costs of patient care increase.

Material/Methods: We retrospectively calculated costs of patient care in 306 randomly selected kidney transplant recipients who had different follow-up time periods after kidney transplantation (between 1 year and 25 years). Direct costs of inpatient care as well as outpatient care, from the perspective of a transplant center, were considered.

Results: The mean costs, as well as median costs of post-transplantation care were the highest in the first post-transplantation year. Afterwards, the mean costs and median costs decreased, without an increase in costs of care in the late post-transplantation periods.

Conclusions: From the perspective of a transplant center, costs of long-term post-kidney transplantation care did not increase in the late period, even as long as 25 years after transplantation. Our results confirmed that kidney transplantation is a modality of renal replacement therapy that can be associated with economic benefits even when considering long-term post-transplantation care.

MeSH Keywords: Economics, Medical • Kidney Transplantation • Long-Term Care

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Background

Solid organ transplantations lead to improvements in both patient survival and patient quality of life [1,2]. In cases where alternative therapies are available, for example in patients with end stage renal disease (ESRD) when a patient might be treated with dialysis instead of transplantation, transplantations are still connected with economical health care benefits [3]. This is of special importance because the costs of ESRD treatment have increased worldwide; for example, in the United States (US), the total Medicare expenditures connected to ESRD treatment almost doubled in value between 2004 and 2016. Kidney transplantation remains the least expensive modality of renal replacement therapy; in the US, the annual costs per patient connected to kidney transplantation were approximately 2.5 times less compared to the costs connected to peritoneal dialysis, and 3 times less compared to the costs of treatment with hemodialysis [4].

However, over time, after kidney transplantation, health problems connected with aging as well as complications of immunosuppression can accumulate, including cardio-vascular diseases, neoplastic diseases, and infections [5–7]. These health problems are connected with substantial costs. Therefore, we hypothesized that in the late post-transplantation period, costs of care might increase, and this might lead to increased economic burden connected with kidney transplantations. To verify this hypothesis, costs of post-transplantation care in kidney transplant recipients who were in different post-transplantation periods were calculated.

Material and Methods

In 2018, 2571 kidney transplant recipients were treated in the outpatient department of the Department of Immunology, Transplant Medicine, and Internal Diseases of the Medical University of Warsaw. From this population, a study group was randomly selected. The study group consisted of kidney transplant recipients in different post-transplantation follow-up periods (1 year to 25 years after transplantation). Subsequently, the costs of 1-year of care incurred in 2017 by our Transplant Center in individual post-transplantation years were retrospectively calculated, based on case records. Direct costs of hospitalizations as well as outpatient care, including laboratory diagnostics, imaging, and treatment, were considered. However, the costs of the first hospitalization in the surgical ward that were connected to the transplantation procedure were omitted. Similarly, we did not include in our analysis costs of immunosuppression used outside the hospital, as in our health care system they are not covered by a transplant center. Additionally, costs of diagnostics and treatments provided by general practitioners and other specialty centers were not included in our analysis. Mainly due to the fact that in our center the care of kidney transplant recipients starts at different time points after the transplantation procedure, the calculated costs were divided by the number of months a patient was actually under care at our center. That is why results of our calculations are expressed as the mean costs of 1-month care in the particular post-transplantation year. Additionally, we present the medians of these costs, as the distribution of data was not always normal, and thus, the means did not always reflect real patient scenarios.

Calculated costs are presented in Polish Zloty (PLN) local currency (1 PLN~0.23 EUR).

The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the design of our study, the approval of the Ethics Committee, as well as informed consent of each participant, were not necessary.

Statistical analysis was performed using Statistica 13.1 software. Descriptive statistics, one-way analysis of variance (ANOVA), and Tukey’s post hoc test were used when appropriate. A P value of <0.05 was considered statistically significant.

Results

There were 306 kidney transplant recipients included in our study, including 174 male patients and 132 female patients. The mean age was 55 years. All of the patients were Caucasians. Kidney transplantations were performed at 1 to 25 years before the patient was included in the study. Table 1 summarizes demographic data of study participants.

The mean costs of 1-month post-transplantation care was the highest in the first post-transplantation year (1974.69 PLN). Afterwards, mean costs of 1-month post-transplantation care decreased; between the second and the ninth post-transplantation year, the costs were between 213.87 PLN and 1111.22 PLN. In years 10 to 25, the costs were below 559 PLN per 1-month of care. Results are presented in Figure 1 and Table 2. The differences between the means and medians of costs reflected considerable diversity in costs of care between cases. In years 1 to 16, the mean costs of inpatient care were higher compared to the mean costs of outpatient care, while in years 17 to 25, this situation reversed. In the outpatient settings, it was laboratory diagnostics, including monitoring of immunosuppressants levels, that were the main source of costs of care. In hospitalized patients, the main sources of care were differentiated by years of care; in the first 12 years post-transplantation, in the majority of years, including the first post-transplantation year, the most important specific source of costs were pharmaceuticals, while between year 16 and year
25 post-transplantation, in the majority of years the dominate costs were for laboratory diagnostics. The costs of immunosuppressive medicines in the Polish health care system are not a burden of a transplant center in the outpatient settings, while in the inpatient settings these costs are categorized as pharmaceutical costs. However, our further analysis showed that the post-transplantation immunosuppressive medicines were not a major source of costs of pharmaceuticals.

Table 1. Demographic data of study participants.

| Year post-transplant | Number of patients | Male/Female (n, %) | Mean age (range) in years | Number of renal transplant: 1\textsuperscript{st}/2\textsuperscript{nd}/3\textsuperscript{rd} (n, %) |
|----------------------|-------------------|-------------------|--------------------------|-------------------------------------------------|
| 1                    | 16                | 11 (69)           | 50 (26–780)              | 16 (100)                                         |
| 2                    | 13                | 7 (54)            | 54 (35–72)               | 11 (85)                                           |
| 3                    | 25                | 15 (60)           | 51 (20–75)               | 22 (88)                                           |
| 4                    | 27                | 16 (59)           | 53 (30–72)               | 23 (85)                                           |
| 5                    | 14                | 6 (43)            | 55 (39–74)               | 12 (86)                                           |
| 6                    | 21                | 11 (52)           | 58 (13–79)               | 21 (100)                                          |
| 7                    | 17                | 11 (65)           | 56 (33–77)               | 15 (88)                                           |
| 8                    | 15                | 6 (40)            | 53 (35–79)               | 14 (93)                                           |
| 9                    | 13                | 7 (54)            | 63 (47–81)               | 12 (92)                                           |
| 10                   | 11                | 5 (45)            | 52 (35–76)               | 11 (100)                                          |
| 11                   | 9                 | 5 (63)            | 45 (24–66)               | 8 (100)                                           |
| 12                   | 12                | 7 (58)            | 57 (34–69)               | 11 (92)                                           |
| 13                   | 14                | 5 (36)            | 57 (37–76)               | 14 (100)                                          |
| 14                   | 11                | 7 (64)            | 54 (40–71)               | 11 (100)                                          |
| 15                   | 10                | 7 (70)            | 57 (40–67)               | 8 (80)                                            |
| 16                   | 10                | 8 (80)            | 57 (42–69)               | 10 (100)                                          |
| 17                   | 12                | 7 (58)            | 52 (37–69)               | 11 (92)                                           |
| 18                   | 7                 | 4 (57)            | 49 (35–56)               | 7 (100)                                           |
| 19                   | 8                 | 4 (50)            | 56 (42–73)               | 8 (100)                                           |
| 20                   | 13                | 8 (62)            | 61 (43–77)               | 12 (92)                                           |
| 21                   | 11                | 8 (73)            | 54 (33–74)               | 10 (90)                                           |
| 22                   | 5                 | 1 (20)            | 55 (38–69)               | 4 (80)                                            |
| 23                   | 3                 | 1 (33)            | 55 (52–58)               | 3 (100)                                           |
| 24                   | 5                 | 3 (60)            | 65 (58–72)               | 5 (100)                                           |
| 25                   | 5                 | 4 (80)            | 55 (43–72)               | 5 (100)                                           |

Figure 1. Mean 1-month costs of post-transplantation care in particular years after kidney transplantation.

25 post-transplantation, in the majority of years the dominate costs were for laboratory diagnostics. The costs of immunosuppressive medicines in the Polish health care system are not a burden of a transplant center in the outpatient settings, while in the inpatient settings these costs are categorized as pharmaceutical costs. However, our further analysis showed that the post-transplantation immunosuppressive medicines were not a major source of costs of pharmaceuticals.
| Year post-transplant | Total costs | Costs of inpatient care | Costs of outpatient care |
|---------------------|-------------|-------------------------|-------------------------|
|                     | Mean 1-month cost in PLN | Median (Q25–Q75) of 1-month cost in PLN | Laboratory diagnostic (Mean, Minimum-Maximum) | Imaging (Mean, Minimum-Maximum) | Pharmacuticals (Mean, Minimum-Maximum) | Others (Mean, Minimum-Maximum) | HD (Mean, Minimum-Maximum) | Laboratory diagnostics (Mean, Minimum-Maximum) | Imaging (Mean, Minimum-Maximum) | Others (Mean, Minimum-Maximum) |
| 1                   | 1974.69     | 305.6 (217.0–1969.6)     | 153.88                   | 36.60                        | 314.51                        | 1178.72                        | 34.09                        | 150.74                        | 7.96                        | 98.10                        |
| 2                   | 358.72      | 120.1 (99.0–198.1)       | 20.60                    | 11.87                        | 14.75                        | 185.49                        | 0.00                         | 71.76                         | 6.76                         | 47.43                        |
| 3                   | 853.80      | 111.2 (89.7–301.9)       | 51.55                    | 11.80                        | 190.07                        | 464.88                        | 8.33                         | 65.67                         | 10.12                        | 48.00                        |
| 4                   | 516.04      | 140.7 (94.7–663.3)       | 42.18                    | 16.29                        | 33.59                        | 322.33                        | 12.35                        | 47.58                         | 4.52                         | 36.42                        |
| 5                   | 1111.22     | 188.6 (89.8–652.3)       | 82.49                    | 25.83                        | 449.54                        | 394.70                        | 20.83                        | 61.90                         | 3.99                         | 58.93                        |
| 6                   | 213.87      | 91.5 (67.2–133.7)        | 20.10                    | 9.47                         | 1.27                         | 85.87                         | 0.00                         | 51.89                         | 5.21                         | 40.08                        |
| 7                   | 712.78      | 85.6 (79.3–97.8)         | 32.26                    | 5.71                         | 343.77                        | 224.58                        | 14.71                        | 50.98                         | 4.47                         | 33.82                        |
| 8                   | 667.78      | 101.8 (55.0–195.9)       | 9.73                     | 2.26                         | 392.82                        | 96.44                         | 19.44                        | 54.22                         | 6.96                         | 41.67                        |
| 9                   | 995.37      | 77.6 (62.3–101.2)        | 43.16                    | 0.00                         | 211.18                        | 465.51                        | 125.00                       | 41.38                         | 5.31                         | 28.21                        |
| 10                  | 245.09      | 80.1 (63.8–119.7)        | 10.95                    | 0.00                         | 22.07                         | 102.98                        | 4.71                         | 49.03                         | 5.65                         | 31.82                        |
| 11                  | 507.71      | 101.9 (87.7–658.0)       | 27.23                    | 0.00                         | 75.31                         | 270.10                        | 0.00                         | 56.08                         | 5.70                         | 38.54                        |
| 12                  | 408.65      | 75.7 (60.1–116.6)        | 17.39                    | 0.00                         | 81.13                         | 205.32                        | 0.00                         | 43.99                         | 3.75                         | 30.56                        |
| 13                  | 332.35      | 91.2 (78.0–149.6)        | 12.25                    | 0.00                         | 3.88                          | 180.39                        | 0.00                         | 50.49                         | 7.71                         | 35.12                        |
| 14                  | 558.62      | 88.7 (59.9–165.4)        | 19.94                    | 0.00                         | 137.97                        | 246.30                        | 15.00                       | 47.45                         | 2.88                         | 42.42                        |
| 15                  | 393.40      | 105.5 (61.4–156.8)       | 16.75                    | 0.00                         | 11.87                         | 216.43                        | 41.67                        | 45.49                         | 5.03                         | 39.17                        |
Table 2 continued. Structure of costs of post-transplant care in particular years after renal transplantation.

| Year post-transplant | Mean 1-month cost in PLN (Q25–Q75) | Median Laboratory of 1-month cost in PLN (Mean, diagnostic (Mean, Imaging (Mean, Laboratory) | Costs of inpatient care | Costs of outpatient care |
|----------------------|--------------------------------------|-----------------------------------------------|-------------------------|--------------------------|
|                      | Mean, Median (Q25–Q75) | Imaging | Pharmaceticals | Others | HD | Imaging | Others |
|                      | (Mean, Minimum–Maximum) | (Mean, Minimum–Maximum) | (Mean, Minimum–Maximum) | (Mean, Minimum–Maximum) | (Mean, Minimum–Maximum) | (Mean, Minimum–Maximum) | (Mean, Minimum–Maximum) |
| 16                   | 384.56 (63.6–163.9) | 17.04 (0.00–160.78) | 6.56 (0.00–57.84) | 237.11 (3.01–2247.35) | 0.00 (14.60–144.0) | 52.03 (0.00–116.60) | 5.33 (0.00–116.60) |
| 17                   | 123.59 (71.5–173.6) | 11.18 (0.00–14.60) | 0.00 (0.00–14.70) | 31.59 (147.78) | 0.00 (0.00–16.13) | 38.33 (0.00–16.13) | 8.22 (0.00–16.13) |
| 18                   | 82.08 (52.1–105.7) | 0.00 (0.00–6.22) | 0.00 (0.00–125.20) | 0.00 (0.00–19.10) | 96.98 (0.00–191.00) | 6.83 (0.00–191.00) | 33.33 (0.00–191.00) |
| 19                   | 314.00 (72.9–143.2) | 79.39 (0.00–631.56) | 0.00 (0.00–1248.55) | 0.00 (0.00–1248.55) | 0.00 (0.00–631.56) | 0.00 (0.00–1248.55) | 0.00 (0.00–631.56) |
| 20                   | 119.77 (74.0–122.2) | 0.48 (0.00–6.22) | 0.00 (0.00–125.20) | 0.00 (0.00–19.10) | 0.00 (0.00–106.07) | 54.98 (0.00–106.07) | 0.00 (0.00–106.07) |
| 21                   | 184.92 (70.1–171.6) | 3.59 (0.00–31.49) | 0.00 (0.00–681.64) | 0.00 (0.00–92.87) | 0.00 (0.00–20.55) | 46.09 (0.00–29.87) | 5.86 (0.00–20.55) |
| 22                   | 177.31 (49.2–103.8) | 3.18 (0.00–15.90) | 0.00 (0.00–371.41) | 0.00 (0.00–71.92) | 0.00 (0.00–34.35) | 0.00 (0.00–71.92) | 7.78 (0.00–34.35) |
| 23                   | 87.89 (77.9–103.1) | 0.00 (0.00–0.00) | 0.00 (0.00–71.52) | 0.00 (0.00–71.52) | 0.00 (0.00–34.35) | 46.78 (0.00–71.52) | 7.78 (0.00–71.52) |
| 24                   | 133.84 (56.3–93.8) | 0.00 (0.00–0.00) | 0.00 (0.00–71.52) | 0.00 (0.00–71.52) | 0.00 (0.00–34.35) | 46.78 (0.00–71.52) | 7.78 (0.00–71.52) |
| 25                   | 162.36 (55.9–115.7) | 2.39 (0.00–11.94) | 0.00 (0.00–304.50) | 0.00 (0.00–68.82) | 0.00 (0.00–18.67) | 42.83 (0.00–68.82) | 3.73 (0.00–18.67) |

Subsequently, assessments with ANOVA and Tukey’s post hoc test were done. Data from the first post-transplantation year were omitted in these analyses due to the fact that the distribution of these data was not normal, and we were interested mainly in the late post-transplantation period. Therefore, 3 subgroups were used for analyses: subgroup I was 2 years to 9 years post-transplantation, subgroup II was 10 years to 16 years post-transplantation, and subgroup III was 17 years to 25 years post-transplantation. This division into 3 subgroups was due to the fact that mean costs were relatively similar within subgroups, and the number of cases in each subgroup (n=145, n=76, and n=69 in groups I, II, and III, respectively) enabled application of chosen statistical methods. In effect, statistically significant differences were observed between the 3 subgroups, especially in costs of inpatient care (Table 3).

**Discussion**

The economic burden of kidney disease, especially ESRD, has increased worldwide [4,8,9]. Kidney transplantation is considered an optimal method of renal replacement therapy both due to clinical effects [10] and financial considerations [4,11,12]. However, data from the literature on the economic aspects of kidney transplantation are limited mainly to the early post-transplantation period. As far as we know, this is the first study in which real costs of post-transplantation care in the late...
post-transplantation period have been calculated. It might be speculated that, at least in part, the economic benefits of early post-transplantation years are connected to the fact that only relatively healthy patients get on waiting lists, while those with serious comorbidities, which generate higher expenditures, are not placed on transplant waiting lists. Additionally, diagnostic workup preceding transplantation makes numerous diagnostic procedures unnecessary during this period. However, with the passage of time after transplantation, new health problems might appear, such as health problems associated with aging as well as with chronic complications of immunosuppressive therapy. It might, therefore, be presumed that costs of post-transplantation care would increase in the late post-transplantation period. Surprisingly, our results showed that the economic burden for the transplant center associated with post-kidney transplantation care systematically decreased, even in the period of 25 years. However, it should be noted that although the proportion of costs connected to inpatient and outpatient care changed with time, the mean costs of outpatient care remained quite stable in years 2 to 25 (the costs in the first year were obviously higher due to the frequency of visits). Meanwhile, the mean costs of inpatient care decreased with time; in the first 16 years post-transplantation, the costs were higher, and starting from year 17 post-transplantation, the costs were smaller compared to outpatient care, and the costs of laboratory diagnostics were the most important source of costs. This might be explained by the fact that comorbidities that appear in the late post-transplantation period are in a large part diagnosed and treated by other health care centers. In fact, this is not a difference compared to the non-transplantation population.

In 2015, the costs of 1 hemodialysis session in Poland averaged between 400 PLN and 500 PLN, depending on the dialysis center [13]. Similarly, in 2018, the costs of 1 hemodialysis session in our hospital was 500 PLN. Therefore, in Poland, the 1-month costs of therapy in patients on maintenance hemodialysis was approximately 6500.00 PLN in the analyzed period. Hence, our results confirmed that kidney transplantation is a modality of renal replacement therapy that is economically justified even over long periods of patient care. Moreover, it should be stated that the economic benefits compared to chronic dialysis, increased with time. In general, our results agreed with data from the literature, e.g., in Sweden, kidney transplantation was reported to lead to substantial cost savings compared to dialysis [14]. The costs of post-transplantation care were the highest in the first post-transplantation year, while starting from the second-year post-transplantation, the costs decreased and remained quite stable for at least 5 years [15]. However, a detailed comparison of Swedish data with our results was impossible due to differences in methodology; in the cited papers, the analyses were performed from the perspective of health care system, while our analysis was performed

### Table 3. Comparison of mean 1-month costs (in PLN) of post-transplant care in subgroups.

| Subgroup | I (2–9 years post-transplant) n=145 | II (10–16 years post-transplant) n=76 | III (17–25 years post-transplant) n=69 | Total n=290 | p |
|----------|-----------------------------------|---------------------------------------|---------------------------------------|-------------|---|
| **Inpatient care** | | | | | |
| Laboratory diagnostics | 38.1 | 16.8* | 3.9* | 24.4 | 0.005 |
| Imaging | 10.9 | 0.0* | 2.5* | 6.1 | <0.001 |
| Pharmaceuticals | 184.8 | 47.0 | 10.5 | 107.2 | 0.150 |
| Others | 285.4 | 204.3 | 48.5* | 207.8 | 0.039 |
| Dialysis | 20.7 | 7.7 | 0.0 | 12.4 | 0.314 |
| **Outpatient care** | | | | | |
| Laboratory diagnostics | 55.4 | 48.9 | 47.1 | 51.7 | 0.066 |
| Imaging | 6.1 | 5.2 | 5.4 | 5.7 | 0.577 |
| Others | 41.6 | 35.5 | 36.1 | 38.7 | 0.058 |
| Total | 642.9 | 365.5 | 154.1 | 453.9 | 0.036 |

* p<0.05 vs. group I (Post hoc Anova).
from the perspective of a health care provider, and some costs were, therefore, omitted in our study, such as the costs of immunosuppressive drugs in the outpatient settings, which are covered by the National Health Fund, and not by a transplant center. The perspective of analysis is an important factor to consider; if we had used the perspective of a health care system rather than a health care provide, most probably, the costs of immunosuppressive drugs would have been a substantial part of post-transplantation expenditures.

The analysis of our data showed substantial differences between the mean and the median 1-month costs of care in the majority of post-transplantation years. This was due to the fact that there were considerable differences in costs of care in individual cases, with a small number of patients who had costs of care that was considerably higher compared to the majority of cases. This fact might also explain the differences in mean 1-month costs of care in particular post-transplantation years, especially between the second and the ninth post-transplantation year. The most expensive procedures included procedures connected to diagnosis, treatment of antibody-mediated rejection (AMR) of the kidney graft, and some infections. These costs were significantly over the mean costs in some years, for example in the fifth and the ninth year. Despite the fact that universal standards of AMR management are lacking, it is a clinical entity that is connected with high costs for diagnostics and therapy. Although costs of care of patients with AMR were significantly higher compared to non-AMR cases, we included them in the current analysis as we wanted data that were as close as possible to clinical reality. However, a separate analysis concerning only patients with AMR would be of interest. Nevertheless, analysis of medians of costs of 1-month care also showed that the costs do not increase in the late post-transplantation period.

Our study had several limitations. First, it was a perspective of a transplant center that was used for the assessment. Thus, our results might be of great interest and importance for the management of transplant centers; however, the results do not reflect total costs of health care of the studied population. Costs of primary health care and care received at other specialty centers, as well as refunds of pharmaceuticals by the National Health Fund, including outpatient use of immunosuppressive, anti-infectious, anti-hypertensive, lipid-lowering agents, etc., were omitted in our study. This was, at least partially, caused by the fact that these costs are not a burden for a transplant center in a Polish system, and complete data on these subjects was not available to us. However, a large proportion of these expenditures would also not be considered a part of ESRD treatment, as they are connected, at least in part, to aging, and involve the general population as well. Second, due to the retrospective design of the analysis, some patients might have been omitted, including those who lost their graft; and in the end-stage phase of graft function some significant costs might appear, e.g., vascular access for hemodialysis must be done. Third, due to the differences in health care models, and structure of costs, our results might not reflect the situation in other countries.

Conclusions

From the perspective of a transplant center, the costs of long-term post-kidney transplantation care did not increase in the later periods, even as long as 25 years post-transplantation. Starting from the second post-transplantation year, the mean costs of outpatient care remained quite stable, while the mean costs of inpatient care decreased with time. Our results confirmed that kidney transplantation is a modality of renal replacement therapy that is associated with economic benefits even over a long period of post-transplantation patient care.

Conflict of interest

None.

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