In Denmark kidney transplantation is more cost-effective than dialysis

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ABSTRACT

INTRODUCTION: Approximately 5,000 Danish patients are being treated for end-stage renal disease, for which the two treatment options are dialysis and transplantation. The objective of this study was to estimate the cost-effectiveness of kidney transplantation versus dialysis from a public health-care perspective.

MATERIAL AND METHODS: A cost-utility analysis was conducted using a decision analytic model. The model was designed as a Markov model in which all relevant costs and effects of the two alternative treatments were included. Deterministic data were used alongside the best available evidence from the literature. To estimate the overall uncertainty concerning the incremental cost-effectiveness ratio (ICER), a probabilistic sensitivity analysis with second-order Monte Carlo simulations was carried out on a hypothetical cohort of 10,000 patients.

RESULTS: The cost per quality-adjusted life year (QALY) was 1,032,934 DKK for dialysis compared with 810,516 DKK for transplantation. When comparing kidney transplantation with dialysis, kidney transplantation was cost-saving and resulted in additional QALYs. When taking the overall uncertainty associated with the ICER into account, an incremental cost-effectiveness scatter plot supported that transplantation was dominating and that the results were robust. In addition, a cost-effectiveness acceptability curve showed that transplantation had a 99.93% likelihood of being cost-effective at a willingness-to-pay value of 0 DKK.

CONCLUSION: The cost-effectiveness ratio was favourable for kidney transplantation when compared with dialysis. In view of this, it was concluded that transplantation is preferable to dialysis when treating patients with end-stage renal disease.

FUNDING: not relevant.

TRIAL REGISTRATION: not relevant.

At the end of year 2012, 4,829 patients were being treated for end-stage renal disease (ESRD) in Denmark. Of these, 2,330 patients had received kidney transplantation, whereas the remaining 2,499 patients were in dialysis [1]. Transplantation and dialysis, haemodialysis or peritoneal dialysis, are the two alternative treatments for ESRD.

Multiple studies have shown the positive effects of kidney transplantation on quality of life for patients with ESRD. However, the demand for transplantation is not met by the supply of kidneys with the implication that the waiting list for transplantation is long. Since 2006, an average 489 patients have been on the waiting list for kidney transplantation annually, while 208 patients have received transplantation annually [2].

The objective of this study was to estimate the cost-effectiveness of kidney transplantation versus dialysis. To the knowledge of the authors, no other studies have estimated the cost-effectiveness of kidney transplantation in Denmark in the theoretical framework of a cost-utility analysis (CUA).

MATERIAL AND METHODS

Study design

A CUA was produced to estimate if kidney transplantation is a cost-effective alternative to dialysis. In this type of analysis all relevant costs associated with the two alternative treatments are weighed against the effect of treatment. Economic evaluations such as CUA frequently measure health outcomes in quality-adjusted life years (QALYs), which is a composite measure of health-related quality of life (HRQoL) and life expectancy [3]. Typically, generic HRQoL measures are used, which provide an index score for various health states. An index score is numeric and reflects the preferences of the general population regarding a health state compared with other health states. The EuroQoL-5 Dimension (EQ-5D) questionnaire is an example of a generic index-based HRQoL measure [4, 5].

The result of the CUA is an incremental cost-effectiveness ratio (ICER), which is a measure of the cost-effectiveness of transplantation versus dialysis [3]. To reach the objective of the study, a decision analytic model was constructed using the TreeAge software (Pro 2010, TreeAge Software, Williamstown, MA). This study used a public health-care perspective including direct costs and effects for both dialysis and transplantation.

The model

The decision analytic model was constructed as a decision tree with two Markov models (**Figure 1**). The square decision node represents the choice between the two treatment options, dialysis and transplantation. At the beginning of each of the two arms, there is a circle with

ORIGINAL ARTICLE

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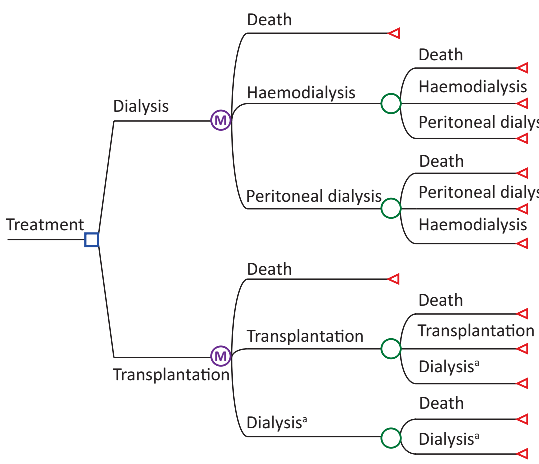
Dan Med J 2014;61(3):A4796

FIGURE 1

Simplified view of the decision tree comparing transplantation with dialysis. At the dialysis arm, patients can either be in haemodialysis or peritoneal dialysis. After one cycle in haemodialysis, it is possible to either transition to peritoneal dialysis or death or to remain in haemodialysis. The same structure is applied for patients starting in peritoneal dialysis. For the transplantation arm, all patients start in transplantation and after one cycle, it is possible to remain in transplantation or transition to dialysis or death in the next cycle.



M = Markov model.
a) Composite state where costs and effects of both haemodialysis and peritoneal dialysis are included.

an M representing that consecutive branches compose a Markov model. One advantage of the Markov model is that it allows patients to move back and forth between different states defined according to the Markov nodes. The circular chance nodes represent allowable transitions to other states. The model is set to run for six cycles each with a duration of one year. As the model thereby captures a six-year period, all costs and effects after the first cycle are discounted by 3.5%.

Probabilities

Most probabilities for the different states in this model are derived from the 2012 annual report from the Danish Nephrology Registry, which has been published since 1990. In Denmark, all centres treating patients with ESRD report data on treatment and other clinical aspects to this register [1]. However, it is not possible to distinguish which dialysis patients are eligible for transplantation based on the reports from the Danish Nephrology Registry. The majority of the probabilities are calculated as a mean and standard deviation for the year 2005 through year 2012.

Included for the dialysis arm are the probabilities of being in either haemodialysis or peritoneal dialysis, changing between the type of dialysis, and the risk of death. In the transplantation arm, the probability of either normal or complicated kidney transplantation is retrieved from eSundhed. Further probabilities include; risk of graft failure, transfer to either haemodialysis or peritoneal dialysis in case of graft failure, and the risk of death [1]. **Table 1** shows the applied probability parameters. For both arms, treatment change is assumed to occur at the end of a cycle.

Costs

All unit costs were identified and valued using the year 2012 currency for DKK. A gross-costing method was used to value all costs related to hospital care for both treatment arms, using tariffs from the Danish case-mix system 2012. Danish diagnose-related groups (DkDRG) tariffs and the Danish ambulatory groups system (DAGS) tariffs represent the average public health-care cost for in-patient treatments and ambulatory visits, respectively [6, 7].

When taking into account only marginal costs, the costs of initiating dialysis are not included in the model as transplantation is assumed to occur in immediate continuation of dialysis. All costs are listed in Table 1.

The majority of patients who receive dialysis are in haemodialysis (78%), either at a hospital (94%) or at home (0.6%) [1]. The cost of haemodialysis at a hospital includes treatment three times a week, while the total cost of home-based haemodialysis includes treatment and bimonthly check-ups. Also included for peritoneal dialysis is the cost of treatment and check-ups every three months [8]. In addition, the costs of changing treatment from haemodialysis to peritoneal dialysis and vice versa are included in the model.

Eligible for transplantation is a kidney from either a deceased or a living donor; the cost profiles of these two kinds of transplantation differ. As a deceased donor on average donates 3.3 organs [2], the cost of removing a kidney is estimated to approximately 30% of the cost of removing organs for donation [6]. Costs associated with transplantation were calculated as the cost for regular or complicated transplantation multiplied by the probability of the type of transplantation. Further costs included for transplantation were the cost of check-ups and immunosuppressive treatment. In the first year after transplantation, patients attend approximately ten check-ups, while check-ups in subsequent years are quarterly. The number of check-ups was estimated by the authors based on information from Rigshospitalet, Copenhagen [9]. Immunosuppressive treatment is a patient-specific triple-drug therapy [10, 11] for which cost estimations were made from defined daily dosage and retail prices from the Danish medical information agency Dansk Lægemiddel Information. Costs were calculated as the average retail price for all relevant immunosuppressive drugs sold within the past five years; data on these costs were collected through the Danish Registry

TABLE 1

Model input.

	Cost/treatment, DKK	Treatments/ year, n	Probability ± SD	Effect/year	Reference
Dialysis					
Haemodialysis:	–	–	0.78 ± 0.003	0.44 ± 0.083	[1, 14]
At hospital	2,296	52 weeks × 3 = 156	0.94 ± 0.002	–	[1, 6, 8]
At home	27,606	12 months/2 = 6	0.06 ± 0.002	–	[1, 6, 8]
Change to peritoneal dialysis	12,939[a]	–	0.03 ± 0.003	–	[1, 6]
Annual mortality	–	–	0.22 ± 0.003	–	[15]
Peritoneal dialysis:	25,972	12 months/3 = 4	0.22 ± 0.003	0.65 ± 0.148	[1, 6, 8, 14]
Change to haemodialysis	17,974[b]	–	0.21 ± 0.018		[1,6]
Annual mortality		–	0.15 ± 0.005		[15]
Transplantation				0.86 ± 0.133	[14]
Deceased donor	10,562	–	0.63 ± 0.012	–	[1, 6]
Living donor	53,505	–	0.37 ± 0.012	–	[1, 6]
Transplantation, normal	180,722	–	0.89 ± 0.015	–	[6]
Transplantation, complicated	511,899	–	0.11 ± 0.015	–	[6]
Check-up	954	10/4[c]	–	–	[6, 9]
Immunosuppressive treatment:					
Group I	132.93 ± 6.33[d]	365	–	–	[12, 13]
Group II	58.47 ± 25.87[d]	365	–	–	[12, 13]
Group III	1.49 ± 0.18[d]	365	–	–	[12, 13]
Self-payment	–3,665[e]	–	–	–	[16]
Rejection	51,021	–	0.18 ± 0.025	–	[6, 7, 9]
Graft failure	51,021	–	0.05/0.2[f]	–	[1, 6, 7]
Change to haemodialysis	17,974[b]	–	0.78 ± 0.058	–	[1, 6]
Change to peritoneal dialysis	12,939[a]	–	0.22 ± 0.058	–	[1, 6]
Mortality	–	–	0.02/0.12[g]	–	[1]

N/A = not applicable; SD = standard deviation.
a) The cost of a peritoneal dialysis catheter is included as well as training in home-based peritoneal dialysis. b) The cost of an arteriovenous fistula and training for the proportion of patients starting home-based haemodialysis is included. c) During the first year post-transplantation, there are 10 check-ups, while there are 4 check-ups in subsequent years. d) Group I: Sandimmun Neoral, Advagraf, Prograf. Group II: Imurel, CellCept. Group III: Prednisolon “DAK”, Prednisolon “DLF”. e) Patient self-payment/year. f) Probability of graft failure after 1 year and after 5 years, SD = N/A. g) Risk of mortality after 1 year and after 5 years, SD = N/A.

of Medical Products Statistics, excluding patients’ self-payment [12, 13].

Despite the immunosuppressive treatment, some patients experience graft rejection, which may lead to further costs associated with reduced graft survival and transition to either haemodialysis or peritoneal dialysis.

Effects

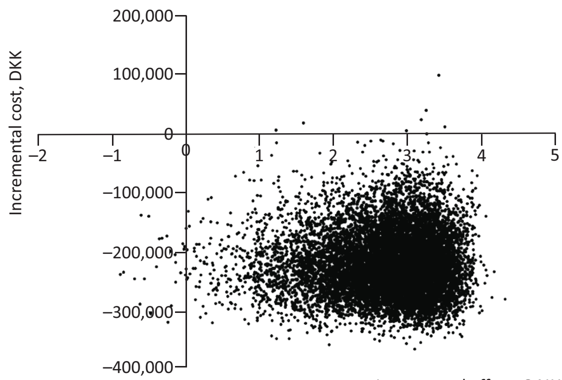
The effect of treatment is measured in QALYs. A systematic review of the literature revealed no Danish studies reporting on the average HRQoL for which reason effect estimates from a study by Sennfält et al were applied. The average HRQoL was measured in a Swedish population and thereby found to be suitable for the decision model in this study. In the study by Sennfält et al, all patients in the South-eastern health-care region who were accepted for transplantation and in either haemodialysis or peritoneal dialysis or alive after kidney transplantation were invited to fill out an EQ-5D questionnaire [14]. The EQ-5D instrument is a health state descriptive system that consists of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme problems. Thus, this system yields 243 possible health states, each of which are assigned an index score, where 1.0 is full health, 0 is death, and negative scores are considered by the general population to be worse than death [5]. Results from the questionnaire are listed in Table 1. Gain in QALY was found by multiplying the number of years by the average HRQoL for the different states in the model. Hereby, QALY incorporates both quality and quantity of life lived.

Sensitivity analysis

Finally, a sensitivity analysis was conducted to evaluate the uncertainty surrounding the ICER. Here, a probabilistic sensitivity analysis (PSA) with second-order Monte Carlo simulations was carried out on a hypothetical cohort of 10,000 patients. By utilising applied distributions, the PSA takes into account all uncertainties of the different parameters in Table 1. As recommend by Briggs et al, cost parameters were assigned a gamma distribution,

FIGURE 2

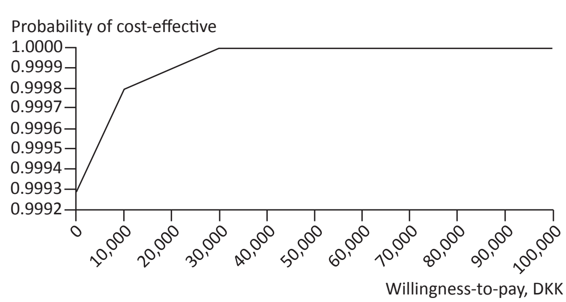
Incremental cost-effectiveness scatter plot. The majority of the simulated incremental cost-effectiveness ratios (ICERs) are found in the lower right quadrant (99.73%), while the remaining ICERs are found in the upper right quadrant (0.07%) and in the lower left quadrant (0.2%).



QALY = quality-adjusted life year.

FIGURE 3

Cost-effectiveness acceptability curve. At a willingness-to-pay value of 0 DKK, transplantation has a 99.93% chance of being cost-effective. The probability of transplantation being cost-effective increases with the willingness-to-pay. Transplantation has a 100% chance of being cost-effective at a willingness-to-pay value of 30,000 DKK.



whereas effect as well as probability parameters were assigned a beta distribution [17].

The results of the PSA are presented in an incremental cost-effectiveness scatter plot and a cost-effectiveness acceptability curve. Hereby, the PSA quantifies the level of confidence of the conclusion of the CUA.

Trial registration: not relevant.

RESULTS

The CUA shows that when comparing the total average costs and effects of the two alternative treatments, transplantation holds a dominant position as it yields both lower costs (810,516 DKK versus 1,032,934 DKK) and higher effects (4.4 QALY versus 1.7 QALY). Over the six-year period the model captures, there is a potential saving of 222,418 DKK through transplantation, with an average additional gain of 2.8 QALY compared with dialysis. Observation of a dominant position negates the need to calculate an ICER.

Sensitivity analysis

When including overall parameter uncertainties, the results of the PSA show that transplantation is still the dominating treatment. This indicates that the result of the CUA is not sensitive to parameter changes. **Figure 2** illustrates the incremental cost-effectiveness scatter plot of the second-order Monte Carlo simulations. More than 95% of the simulated ICERs are located in the lower right quadrant, meaning that transplantation is associated with lower costs and higher effects than dialysis.

The cost-effectiveness acceptability curve (**Figure 3**) indicates that transplantation has a 99.93% likelihood of being cost-effective at a willingness-to-pay value of 0 DKK per QALY.

DISCUSSION

The CUA shows that transplantation is cost-effective compared with dialysis, which supports the results of a systematic literature review by Jarl & Gerdtham [18]. However, there are some limitations to the decision model presented in this paper. In a health economic evaluation, it is desirable to have a societal perspective, in which, among others, productivity losses are included. Sennfält et al found that patients in haemodialysis rarely have paid work; patients in peritoneal dialysis work an average of 37.5% of full-time hours, while patients who have had transplantation work an average of 75% of full-time hours [14]. If this were transferable to a Danish context, including productivity costs would not change the result of the CUA as this would yield a more cost-effective result.

Due to a lack of Danish guidelines on whether or not to perform a nephrectomy after graft failure, nephrectomy is not included in the model. In the model, patients who experience graft failure will remain on immunosuppressive treatment and have check-ups while receiving dialysis, either haemodialysis or peritoneal dialysis. Alternatively, patients could have a nephrectomy and return to dialysis. Messa et al review the different implications of the alternatives and find that remaining on immunosuppressive treatment will sustain any residual effect of the graft. However, in patients on dialysis, this is associated with high rates of infections and an increased risk of malignancy. Furthermore, continuous monitoring is required to diagnose an acute rejection to avoid graft rupture [19].

In the study by Sennfält et al, all patients who were invited to fill out a questionnaire had to be eligible for transplantation as a general measure of health [14]. This criterion could not be met when using data from the Danish Nephrology Registry to assign probabilities for the different states in the model. The probability parameters used in the dialysis arm are, therefore, affected by the fact that patients who are too ill to be considered for transplantation are in the dialysis group. This especially affects the mortality rates for haemodialysis and peritoneal dialysis and thereby affects the average gain in QALYs in the dialysis arm of the model.

According to this analysis, transplantation should be prioritised over dialysis. Currently, the need for transplantation cannot be fulfilled solely by transplantation from deceased donors. For this reason, it may be relevant to promote the possibility of utilising kidneys from living donors as this has shown to increase the length of life of transplantees and to enhance self-esteem and sense of wellbeing among donors. However, organ procurement is associated with a risk of complications for the living donor [20].

CONCLUSION

The cost-utility analysis showed that transplantation is cost-effective compared with dialysis as it yields both lower costs and higher effects. The robustness of the analysis was confirmed through probabilistic sensitivity analysis. Further studies are needed to build a more knowledge-based model as no studies have evaluated the health-related quality of life in a Danish end-stage renal disease population.

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ACCEPTED: 7 January 2014.

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

ACKNOWLEDGEMENTS: The authors would like to thank *Christian Balthazar Møller* from the Department of Health Economics, The North Denmark Region for his help and expertise.

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