

*Invited Editorial***Is Chronic Hemodialysis Really so Inferior to Kidney Transplantation?**

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Introduction

One of the most untouchable paradigms in nephrology is that kidney transplantation is absolutely superior to dialysis in treating patients with end-stage renal disease (ESRD). Even a mild and prudent position saying that »hemodialysis is not so inferior to kidney transplantation« sounds like heresy. The aim of this paper is to put some arguments behind this heresy.

My arguments (dialysis vs. transplantation) will be restricted to adult patients. I will address survival, pregnancy and quality of life. I will pay special attention to living donors and related problems. At the end of my paper, I will summarize the inherent problems and limitations of kidney transplantation and the achievements of hemodialysis.

Why do I believe that a critical analysis and debate on this topic is necessary? As a nephrologist, I had the opportunity and privilege to work and live with both dialysis and transplant patients for 27 years, witnessing the life and death of many of them, and following the problems, progress, false beliefs, and limitations of both therapies. During these years, after coming back from scientific meetings to real patients, I always had the impression that kidney transplantation was idealized and hemodialysis unjustly underestimated as regards its contribution to the well-being of patients with ESRD. This idealization of transplantation (and »condemnation« of hemodialysis) was present both in the scientific and lay communities. The central premise of many transplant meetings I have attended, including the last one in Paris in 2009 (14th ESOT – European Society for Organ Transplantation Congress), was that dialysis equals misery. The consequence of this premise is the approach that every price paid to avoid such misery is justified. I believe that such a premise is wrong and may lead to the unoptimal use of the powerful therapeutic options that we have available. In the case of living donation, such a premise may cause significant collateral damage.

Survival

Does kidney transplantation prolong the survival of hemodialysis patients? Comparing survival between

dialysis and transplant patients is difficult. Younger and healthier patients are selected as candidates for transplantation, put through increasingly more intensive preparation for transplantation [1], which includes extensive diagnostic (and, if needed, aggressive therapeutic) interventions addressing cardiovascular, infective, malignant, immunological and other issues, and after completing (and surviving) all this workup, are enrolled for transplantation. Randomized studies are not possible and we rely on observational studies.

For many years, it was not clear whether transplantation prolongs survival. When I studied my first chapter on transplantation in Brenner's »The Kidney« in the 80-ies, it stated that there is no difference in survival among age and health-matched dialysis and transplant patients. In 1999, Wolfe *et al.* published a study [2] based on USRDS (United States Renal Data System) data, comparing the survival of dialysis patients and patients on the waiting list for transplantation, both transplanted and not transplanted. They found that among patients on the waiting list, those that were transplanted had significantly improved survival, especially if they were younger. For patients from the age group of 20-39 years, they calculated an estimated 17 years of life gain compared to staying on the waiting list.

Wolfe's study had a profound impact in nephrology. From the moment it was published, the survival benefit of kidney transplantation was accepted as unquestionable, supported by the results of some other studies [3]. Excerpts from Wolfe's study are available to the wider community, including Wikipedia [4]). At the same time, UpToDate describes survival on dialysis as only slightly better than survival with lung cancer [5]. Wolfe's study is an excellent and important study. However, like any study, it has some limitations: 1) the patients on the transplant list are not all alike: those on the waiting list who were not transplanted may have reasons for that, so selection bias may play a role; 2) the study refers to US hemodialysis, which is well known for having the highest mortality in the developed world, with three major problems: short dialysis, reuse of dialysers, and nonoptimal vascular access. So, the conclusion that transplantation prolongs survival may work for US hemodialysis patients, but not for others. It should be noted that Wolfe's paper contains a precise

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conclusion starting with »Our analysis of US data demonstrated...«; 3) the data on patients studied were from 1991-1996, so the conclusions that may have been valid for the patients of that time may not be valid for today's patients (hemodialysis has improved, the quality of organs has decreased, today's patients are different). Wolfe also demonstrated that mortality after transplantation is significantly increased in the first 106 days after surgery, compared to staying on dialysis. This important fact is frequently neglected. When we approach a patient and offer him transplantation as a life-extending procedure (as it is described in Wikipedia) [4], it is fair to say: »According to Wolfe's study, you will live longer if you are transplanted, but first you must survive the first 106 days, when the chances of dying are significantly higher than if you stay on dialysis.«

Rao *et al* warned of the significant number of transplant patients who return to dialysis after kidney transplant failure. They have found that mortality among patients on dialysis after primary graft failure increases significantly relative to the mortality among patients still awaiting primary kidney transplantation. To simplify, if someone receives a graft that will not function for very long, he will live for a shorter time than if he stays on dialysis [6]. Faced with the increased use of marginal and extended-criteria donors, this problem may increase in future. This study also raises the question of how death in patients with a failing kidney graft is counted in registry data. Many critically-ill transplant patients need dialysis before death. Their death is usually caused by complications of transplantation and immunosuppressive therapy. However, in registry data such patients may be counted as graft failure and dialysis death.

Recently, a Canadian group published a study demonstrating that survival in nocturnal dialysis is comparable to the survival of transplanted patients (from a deceased donor), emphasizing the fact that practice and quality of dialysis are to be taken into account when comparing survival to kidney transplantation [7]. For the first time, it was stated that nocturnal dialysis may be a suitable alternative to kidney transplantation in the situation of organ shortage. Long (nocturnal) hemodialysis, 3x8 hours a week, became famous because of the Tassin experience [8], and is an increasingly used option in past years (in our hemodialysis centre as well) [9]. The importance of time as an independent factor of dialysis adequacy was demonstrated simply and brilliantly in the experimental study by Eloit *et al* [10]. The patients that benefit the most from long (nocturnal) dialysis are actually those who are candidates for kidney transplantation, and these represent the minority of hemodialysis patients (the majority of incident and prevalent hemodialysis patients are elderly and with significant comorbidities). So, offering long (nocturnal) hemodialysis (either at home or in-centre) to patients who can benefit the most, and who represent the minority of today's hemodialysis patients, may be a task that is realistic.

If kidney transplantation improves survival, it should be reflected in simple statistics like gross mortality rate. The gross mortality rate of Japanese dialysis patients was probably the lowest in the world, 9.2% in 2006 [11] and pretty stable through the years, although these patients are getting older. The major objection to this impressive result was that transplant activity was very low in Japan. Critics argued that the Japanese keep young and healthy patients on dialysis, thus decreasing mortality on dialysis. This bias can easily be overcome if we calculate both dialysis and transplant mortality in other regions. In Slovenia, both dialysis and transplant mortality was 11.4% in 2006, with 25% of RRT (renal replacement therapy) patients having a functioning kidney graft, no preemptive transplantations, and with incident patients day 1 included [12,13]. In the USA, the combined dialysis and transplant mortality was 16.4 % (29.9% of all RRT patients were transplanted, incident patients day 91 included) [14]. The proportion of graft from living donors and preemptive transplant (because of lead-time bias) is also important for the interpretation of data. So, if transplantation significantly (or dramatically, as frequently quoted) improves survival, why is this not reflected in combined dialysis and transplant mortality, and why is this combined mortality not better than Japanese dialysis-only mortality?

Long-term survivors (>30 or even >40 years) are living evidence of the achievements of RRT. The largest cohort of long-term survivors (8275 patients hemodialyzed for more than 25 years, 3.3% of the prevalent hemodialysis population) is reported from Japan, with the longest hemodialysis survival of 39 years [11]. More than 40-year hemodialysis survivors are reported from France (Tassin) and from the USA [15]. A forty-year transplant survivor was reported from the University of Penn [16]. These exciting reports are frequently found in lay and not in scientific literature, and much easier to obtain through Google than through Pubmed. I strongly believe that the long-term survivors of RRT should be one of the focuses of our research – to identify what kind of patients and what kind of therapies are associated with and able to produce long-term survivors. These reports have begun to accumulate in literature in recent years [17-22].

To conclude, the survival benefit of transplantation over dialysis is neither clear nor definite. It is very difficult to assess, and depends on the quality and prescription of hemodialysis and on the practice of transplantation, both varying significantly throughout the world. This relation is dynamic and should be reevaluated constantly. Applying statistics to the very complex issue of an individual patient's decision should be done with utmost care, because, as we can see in clinical practice, many patients may benefit, while others – and these, unfortunately, are not so rare – may be devastated by transplantation, despite careful selection and extensive preparations.

Pregnancy

For several decades, transplantation had a clear advantage over hemodialysis regarding possibility of successful pregnancy. A successful pregnancy in transplanted women was commonplace, while pregnancy during dialysis was a miracle. However, in recent years there seems to be a growing enthusiasm for dialysis pregnancy [23] and an increasing concern regarding pregnancy after kidney transplantation, both for the mother and for the child [24].

Reports on successful pregnancies while being on hemodialysis are accumulating in past years [25-28]. A report by Barua *et al* from Canada describes 7 pregnancies in 5 patients treated by daily nocturnal hemodialysis, with an average gestational age of 36 weeks and an average birth weight of approximately 2400 grams [26]. The prescription of hemodialysis during pregnancy was clarified in recent years, targeting the physiological levels of urea and appropriate anemia management [28,29].

The emerging problems with pregnancy in transplanted patients are emphasized in the most recent guidelines for kidney graft recipient care, which state: » Pregnancy in kidney transplant recipients has a high incidence of complications both for the mother and for the child« [30]. Mycophenolate mophetil, now a part of almost all immunosuppressive protocols, has to be stopped before planning pregnancy. The same is suggested for mTOR inhibitors, as well as ACE inhibitors and angiotensin-2 receptor blockers, a common therapy for kidney graft recipients. There is concern about immunosuppressive influence on the second generation (because of the influence on the fetal germ cells). A recent comprehensive report from the United States (based on Medicare claim data from the first three posttransplant years) has found that the live birth rate in transplanted women was substantially lower than reported in voluntary registries, and that the incidence of pregnancy had significantly decreased from 59 in 1990 to 20 in 2000 per thousand of female transplant recipients, with an increased proportion of pregnancies resulting in unexpected fetal loss [31,32].

Quality of life

A better quality of life after kidney transplantation as compared to hemodialysis is considered unquestionable. A frequently cited study supporting this statement is that of Jofre *et al* [33]. In this study, based on quality of life indicators (Karnofsky Scale and Sickness Impact Profile), patients served as their own controls, assessing their quality of life before and after transplantation. The study found significant improvement in quality of life after transplantation, which, for unclear reasons, was much more pronounced in men than in women. However, being their own controls, the patients may have been biased, because people tend to justify decisions they have already made. In a recent review article, Habwe VQ stressed the problem of changed

appearance caused by immunosuppression, which can have serious psychosocial implications [34], especially in adolescents, probably contributing to noncompliance [35].

Recently, a very sophisticated study was published by Riis *et al* [36], comparing the quality of life in hemodialysis patients and healthy people. In addition to a questionnaire, the authors used a method called »ecological momentary assessment« of mood, assessing mood in real-time and in real life. The authors failed to find evidence that dialysis patients are less happy than healthy nonpatients, suggesting that they have largely, if not completely, adapted to their condition. In a forecasting task, healthy people failed to anticipate this adaptation. That can mean that we as nephrologists may believe our patients are less happy than they really are.

In Slovenia, 17% of hemodialysis patients <65 years refuse to be transplanted [12,13]. At first it may seem that these patients refuse to live longer and better. In a discussion on this topic, some nephrologists argued that these patients are not adequately informed or educated about transplantation. I have talked to some of these patients and was impressed at how deep and broad their knowledge of kidney transplantation is. And I realized this might not be as surprising after all. These patients are fighting for their own lives. They will carry the consequences of their choices, right or wrong. So, why should they refuse transplantation if it is so good?

Kidney transplantation in Slovenia is of high quality. Graft and patient survival rates are higher than the Eurotransplant average [12]. We believe this is due to several reasons: 1) we do not transplant over a positive historical cross-match; 2) our acceptance of marginal donors is limited; 3) the recipients are strictly selected and prepared thoroughly; 4) all recipients are strictly and actively followed after transplantation in one centre, at our Department; 5) our immunosuppressive protocol is relatively »mild« (basiliximab induction, low dose steroids, low dose cyclosporin, diltiazem to diminish cyclosporine nephrotoxicity, and, of course, mycophenolate mophetil). Despite the relatively mild protocol, our incidence of biopsy-proven acute rejection in the first posttransplant year is only 8.3%.

Hence, those dialysis patients who refuse to be transplanted are not refusing because the results of kidney transplantation in Slovenia are bad; on the contrary, they are very good. But for a particular patient who is well-adapted to hemodialysis (dialysing in-centre overnight, 3x8 hours per week, a strategy shown to dramatically improve survival), working full-time, active in a demanding sport, and living a life that is stable and predictable over the decades, transplantation can represent an unacceptable risk. He may gain a great deal (independence of dialysis), but he may lose even more: not being able to walk because of hip problems, Achilles tendon problems, he may lose a significant amount of muscle mass, may no longer be as good-looking as he currently is, not to mention standard complications like infections, increased incidence of malignant diseases, posttransplant diabetes etc. Of

course, many dialysis patients desperately want to be transplanted, and they should be, especially those with vascular access problems, but one size doesn't fit all, and kidney transplantation is not the best treatment for every patient with ESRD who fulfils the criteria for it.

Complications and risks are an unavoidable part of medical practice. Why are complications after kidney transplantation so frustrating not only for patients, but also for nephrologists, especially dialysis doctors? Because we send the best dialysis patients to transplantation. The rest (who are the majority) stay on dialysis. And when it turns out wrong – and it does, unfortunately not so rarely – we are faced with the fact that we have done harm to the patient. For a doctor, it is easier to live with that if the patient really wanted to or insisted on being transplanted. It is much harder if the patient was reluctant or afraid, and we pushed him to get a transplant (promising him he would live many years longer and better).

Living donors and related problems

Owing to the organs shortage, we are being pressured by society to increase the number of all kinds of living donors. In a recent report, it was estimated that approximately 27,000 legal transplantations from living donors were performed worldwide in 2006, representing 39% of all kidney transplantations performed that year [37]. Another argument used to increase the pressure is that kidneys from living donors are better than from deceased donors. All organs from living donors, including the heart, are probably better than organs from the brain-dead. However, emphasizing the better quality of living organs has the unintentional consequence of increasing pressure for donating kidneys from young persons and for organ trading, as described by Nancy Scheper-Hughes [38].

I am not in principle against living organ donation. I would be prepared myself to give a kidney (and not only a kidney) to my child without hesitation. However, the strategy of social pressure on living donors as an increasingly more important or even main source of organs bears and creates many problems we are facing today, and can expect to face in future. I will address the most important among them.

1) *Harm to living donors and the »donor paradox« in nephrology*

As a nephrologist, I've always found it difficult to accept that removing half of the nephron mass is not harmful, even if such conclusion comes from the highest ranked journal [39]. However, this study was retrospective, with only a small proportion of donors (less than 10%) having assessed kidney function. Hyperfiltration is harmful in any setting (diabetes, single kidney from birth, pregnancy, etc.), except if you are a kidney donor. If hyperfiltration is not harmful, then nephropathophysiology should be revised.

A recent prospective study by Prasad *et al* has shown that GFR decreases significantly, by more than 30%, 6

months after donation [40]. The majority of donors were women (another problem of living donation – the majority of living donors are women, except in organ trading), 45 years old on average. Some of them ended up in GFR 35ml/min, close to CKD (chronic kidney disease) stage 4. According to some guidelines [1], these donors are very close to starting to prepare themselves as potential recipients of a kidney graft. However, the conclusion of the main study was that kidney donation is safe in the short term.

This can be referred to as the donor paradox. On the one side, the nephrology community warns the world that CKD kills, and we are nowadays facing a lot of 80+ patients urgently referred to our practice with a stable creatinine of 160-180 micromol/l (CKD 4, close to 5), while on the other side we create CKD in young persons and claim it to be safe.

Two recent studies have warned of the increased risk of eclampsia in living donors who become pregnant after donating a kidney [41-43]. This finding is not surprising, and is in harmony with our classical knowledge of nephropathophysiology.

2) *Tyranny of the gift*

Nancy Scheper-Hughes argues that paid kidney sellers and related donors are often responding to family pressures and a call to sacrifice [38]. She comments on the increase in kidney donation from children and grandchildren to their parents and grand-parents, citing an ethnographic study from UC San Francisco that identified a subtle practice through which children were recruited by transplant professionals to donate a kidney to their elders. She also describes how elderly wealthy Americans sometimes start to feel distaste for organs from deceased donors (which are of increasingly more marginal quality), and prefer to go abroad to get a »fresh« kidney from a young and healthy person. And she concludes: »Ethical solutions are not always palatable. Rather than find new ways to compensate or honour living donors, we need to continue to struggle to increase deceased donation«. I would add: »And we are lucky to have dialysis already«.

Not surprisingly, the above-mentioned paper was heavily criticized in a subsequent issue of the American Journal of Transplantation, but the arguments of Scheper-Hughes sounded more than convincing [44].

Samaritan donors were one of the important topics at the 14th ESOT Congress in Paris 2009, with the awarded presentation describing how happy and fulfilled all these donors are after donation.

However, in an oral presentation by Mazari EM from the UK, entitled »Attitudes of health care professionals and patients towards non-directed donation and commercialisation of live donor kidney transplantation«, it was presented (not surprisingly) that the wisest voice on samaritan donors came from the patients – future recipients. The patients raised 4 issues on this topic: 1) Why should someone submit himself to major surgery without obvious benefit? 2) If someone wants to enjoy the emotion of altruism, why not donate money or other

valuable to the humanitarian organisation or individual in need? 3) Why doesn't the donor preserve his organs for his own family members or friends when they will be in need? 4) A more extensive psychiatric evaluation than is standard should be performed on samaritan donors.

3) *Organ trading*

In 2007, the World Health Organization estimated that organ trafficking accounted for 5-10% of all kidney transplants performed annually throughout the world [45]. The rate may be even higher. The international movement of potential recipients is often arranged or facilitated by intermediaries and health-care providers who make travel arrangements and recruit donors. Several websites offer all-inclusive »transplant packages« featuring wide price ranges. Some US citizens travel to their regions of ethnicity, undergo transplantation, and come back to the US, being taken care of thereafter by US nephrologists [46]. Such a practice is becoming part of our reality.

I do not believe that declarations, consensus conferences and regulations will abort organ trading, a the tragic, unintended consequence of transplantation development in which poor people are serving as spare parts for the rich [47,48]. As long as there is demand and supply, individuals will always find a way to engage in such transactions. The most effective way to win the war on organ trading is the presence of a competitive alternative, such as artificial organs. In the case of ESRD and dialysis, this is a very real option.

4) *Preemptive transplantation, lead-time bias, and other problems*

In preemptive transplantation, the kidney is transplanted into a patient who requires neither dialysis nor transplantation. The indication for transplantation is based on arbitrary criteria, like GFR 20 ml/min, without any real clinical problem requiring the introduction of RRT. The argument given for this is that, besides avoiding dialysis, there is a clear patient survival advantage [49]. However, the papers advocating this did not address the lead-time bias [50] for preemptively transplanted patients. When a kidney is put into a patient with GFR 20 ml/min, survival is counted from the day of transplantation and compared to the survival time of patients who started dialysis at the level of GFR 5 ml/min, or who were transplanted after they began dialysis. It is not surprising that the Kaplan-Meier curve looks nicer with such statistics. It would look even nicer if the kidney were transplanted even earlier, in patients with GFR 30 or 40 ml/min.

The idea of early dialysis and its potentially beneficial influence on survival, fashionable some time ago, was abandoned after addressing lead-time bias [51,52]. Addressing lead-time bias may be very demanding or hardly possible [53]. So, when to start RRT? I believe that every patient has to be closely followed and treated individually (with guidelines serving only as a reminder), and renal replacement therapy (dialysis for the

majority) should be started in order to address any defined clinical problem(s) that may be different in every patient, and much more complex than the GFR level alone.

a) Besides lead time bias, there are other problems with preemptive transplantation.

b) The lifespan of the kidney graft is limited, and in the case of preemptive transplantation, its consumption begins before it is truly needed.

c) The ability of patients to consume toxic immunosuppressive regimens is limited, and serious complications may occur both in the short and long term, reinforcing the point that consumption should not begin before it is truly needed.

d) In an individual patient with GFR 20 ml/min or similar, one cannot predict how long he will live without the need for RRT. He may be well for a long period at the given level of kidney function. In my practice, I have seen such cases. Furthermore, if transplantation turned out to be less than ideal, he might end up in severe CKD, and with a toxic immunosuppression regimen on the top of that; potentially life-threatening antirejection treatment, possibly leading to serious opportunistic infections; the potential for malignancy and other complications in subsequent years. We have recently experienced many of these problems with an adolescent, and have lost some of our initial enthusiasm for preemptive transplantation. And this is not even counting the fact that a patient can simply die of (unnecessary) transplantation.

e) An additional problem in the interpretation of preemptive transplantation outcome is that it is not clear to what extent the native and transplant kidney contributes to the global kidney function after transplantation. On the day of preemptive transplantation, the patient has a significant own kidney function that can remain stable or even improve after immunosuppressive therapy, hydration, diuretics, etc., depending on the original kidney disease. Interventions used to enhance graft function may actually improve the function of the native kidneys. However, a patient's independence of dialysis from the day of preemptive transplantation is attributed completely (entirely) to the transplanted kidney.

Primum non nocere (First, do no harm), taken from the Hippocratic Oath, our most important guideline, still applies today - do no harm to any patient. When performing preemptive interventions, especially such complex and dangerous ones as kidney transplantation, we are in the position of doing serious harm to a patient. I do not believe that the utilitarian approach, in which the benefit for the majority justifies the harm done to an individual, is acceptable in this situation, especially when this supposed benefit is based on statistics that can have many problems, inherent limitations, mispremises and misconclusions.

The main clinical situation which I would consider preemptive transplantation is a patient with a failing kidney graft. Such a patient already receives immunosuppressive therapy and is often very distressed at the thought

of going back to hemodialysis (which may be one of the reasons why such patients start dialysis very late and in bad clinical condition); giving him another kidney will help him to avoid dialysis and the need for transplant nephrectomy (which is a demanding surgical procedure) after stopping immunosuppression.

Cost

An in-depth, comparative cost analysis of dialysis vs. transplantation is beyond the scope of this paper and the expertise of a nephrologist. However, some remarks on cost can nevertheless be made. In past years, the cost (and reimbursement) of kidney transplantation in Slovenia increased significantly, and the cost of dialysis reimbursement decreased. Dialysis patients who cost the most are usually not candidates for transplantation. The majority of transplanted patients are selected from among the “healthiest” dialysis patients, whose dialysis cost is the lowest.

Comparing the costs of both treatments is extremely complex. There are many costs related to transplantation that are not “visible” when calculating the cost of an individual transplanted patient: the workup on many dialysis patients, which is becoming increasingly more complex and expensive, and many of these patients will never be transplanted; the cost of unsuccessful transplantation; immunological and other tests for all patients on the waiting list, many of whom will never be transplanted.

Some of the factors increasing the cost of transplantation are: new immunosuppressive drugs, epoetin therapy prescribed for increasing the number of transplant recipients, expensive and increased monitoring for viral and other infections, antiviral therapy, etc. The relation between dialysis vs. transplantation costs is dynamic and is changing with time, so the cost benefits of one therapy that proved to be valid yesterday may not be valid today or tomorrow.

Inherent problems and limitations of kidney transplantation

Kidney transplantation has significant inherent problems and limitations. Transplanted patients are often not patients with normal kidney function. A significant portion of transplanted patients, in reality 74%, have CKD stage 3-5, while almost one third have advanced CKD stage 4-5 [54]. And there is not only CKD, but also a toxic immunosuppressive regimen on the top of that, as well as many additional drugs for treating complications of immunosuppression. Many patients take more than 10, and some more than 20 different drugs.

The lifespan of a kidney graft is limited. The actual (not actuarial) 10-year survival rate is less than 50% [55]. Why? Because a transplanted patient gets less than one kidney. First he gets only one kidney, and this kidney suffers additional loss of functional nephrons because of cold and warm ischemia, reperfusion injury, acute tubular necrosis, acute and chronic cellular and humoral re-

jection, nephrotoxicity, infections, recurrent original kidney disease, etc. We have already extended this “less-than-one-kidney” survival to its very limits and even further; in reality many patients with a failing graft start dialysis very late and in bad condition, which is reflected in their high mortality thereafter. Because of organ shortage, more marginal and extended-criteria donors are being accepted, resulting in the decreasing quality of organs (both from deceased and living donors). It can therefore be expected that the long-term survival of organs transplanted today will not be better, but may even be worse than it is at present.

The best kidney graft recipients we see today, walking around for more than 30 years after kidney transplantation, are from the azathioprine era. One-year graft survival was poor at that time, but mild protocols allowed for the selection of tolerant individuals who were later exposed to a minimally toxic immunosuppressive regimen. Today, all patients receive much more potent immunosuppression from the start, even those who might do well with much milder immunosuppression. One year-survival is, of course, much better, but we have yet to face the long-term consequences of, for example, mycophenolate mophetil, a very potent drug (as we can see from its side effects in daily practice), and see if therapy with this drug will permit patient survival of 30 years or more.

Lack of individualization and predictability is one of the major problems of immunosuppressive protocols. The majority of patients in one centre receive the same protocol, some tolerate it well, others have minor problems, and still others are devastated by it. We do not have a tool to predict how an individual patient will react to these potent and toxic drugs. Some of our patients who refuse to be transplanted have encountered these drugs during therapy of their original kidney disease, and so they know what to expect.

Achievements of hemodialysis

More than 40-year survival on hemodialysis is a reality. Successful pregnancy while being on dialysis is a reality. Good quality of life, full-time employment or study, and travel around the globe while being on chronic hemodialysis is a reality. The majority of patients who do poorly on hemodialysis are not candidates for transplantation, anyway. The individualization of prescriptions, tailored to the needs and lifestyle of the patient, is possible. Dialysis is increasing all over the world, even in developing countries. The potential for providing supplies for dialysis is practically unlimited. The improvements in technology and our knowledge of dialysis are obvious. With increasing markets and competition, the costs of treatment will probably decrease.

More than 1.5 million people with end-stage kidney disease are currently alive thanks to dialysis [56], and many more have lived thanks to it. Many others have survived acute kidney failure supported by hemodialysis. Although the mortality of critically ill patients with acute kidney failure is high, it would probably be 100%

without dialysis. Hemodialysis is the basis for kidney transplantation: it offers the bulk of patients from whom the best candidates are selected, it offers enough time to prepare them for transplantation, and it is always there as a back-up for acute or chronic graft failure. That is why hemodialysis is one of the most important achievements of medicine in the 20th century, having already saved millions of lives and expecting to save many more.

Conclusions

I do not claim hemodialysis to be better than kidney transplantation, but it is not much worse, either. However, the perception of kidney transplantation in the professional and lay communities is much better than the reality of transplantation is. On the contrary, the perception of hemodialysis is much worse than it really is. I believe that the achievements, limitations and problems of both dialysis and transplantation need to be presented to the professional and lay communities in their full reality and clarity. Transplant professionals should not ignore the achievements and progress made in chronic hemodialysis. At the moment, dialysis and kidney transplantation are not competitors or alternatives, but both very valuable complementary therapies in treating our patients with end-stage renal disease. Nephrologists taking care of these patients should be fully aware of the limitations and achievements of both dialysis and transplantation, closely follow the progress and problems, as well as use and combine both therapies in the best interests of the individual patient in his local environment, fully respecting the patient's choice.

Conflict of interest statement. None declared.

Editorial disclosure. This is solely the author's position.

References

- Bunnapradist S, Danovitch GM. Evaluation of adult kidney transplant candidate. *Am J Kidney Dis* 2007; 50(5): 890-898.
- Wolfe RA, Ashby VB, Milford EL, *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; 341: 1725-1730.
- Post TW, Wella J. Patient survival after renal transplantation. UpToDate, Online 17.2. Available on October 27, 2009 from URL: http://www.uptodate.com/online/content/topic.do?topicKey=renltrn/5586&selectedTitle=3~150&source=search_result#12
- Kidney transplantation. From Wikipedia, the free encyclopedia. Available on October 27, 2009 from URL: http://en.wikipedia.org/wiki/Kidney_transplantation#Prognosis
- Mailloux LU, Henrich WL. Patient survival and maintenance dialysis. UpToDate, Online 17.2. Available on October 27, 2009 from URL: <http://www.uptodate.com/online/content/topic.do?topicKey=dialysis/13376#14>
- Rao PS, Schaubel DE, Jia X, Li S, Port FK, Saran R. Survival on dialysis post-kidney transplant failure: results from the scientific registry of transplant recipients. *Am J Kidney Dis* 2007; 49(2): 294-300.
- Pauly RP, Gill JS, Rose CL, Asad RA, Chery A, Pierratos A, Chan CT. Survival among nocturnal home hemodialysis patients compared to kidney transplant recipients. *Nephrol Dial Transplant* 2009; 24: 2915-2919.
- Charra B, Caemard E, Ruffet M, Chazot C, Terrat JC, Vanel T, Laurent G. Survival as an index of adequacy of dialysis. *Kidney Int* 1992; 41: 1286-1291.
- Buturovic-Ponikvar J, Likar C, Gaber L, *et al.* Regular night shift hemodialysis in dialysis center Zaloska. *Ther Apher Dial* 2009; 13: A16.
- Eloot S, Van Biesen W, Dhondt A, *et al.* Impact of hemodialysis duration of the removal of uremic retention solutes. *Kidney Int* 2008; 73: 765-770.
- Nakai S, Masakane I, Akiba T, *et al.* Overview of regular dialysis treatment in Japan as of 31 December 2006. *Ther Apher Dial* 2008; 12(6): 428-456.
- The Slovenian renal replacement therapy registry: 2006 Annual Report. Available on October 27, 2009, on URL: <http://www.nephroslovenia.si/register2006.pdf>
- Buturović-Ponikvar J, on behalf of the Slovenian Renal Replacement Therapy Registry Group. Slovenian Renal Replacement Therapy Registry: Excerpts from the 2006 Annual Report. *Ther Apher Dial* 2009; 23: 258-263.
- 2008 USRDS Annual Data Report III. Mortality and causes of death. Table H2. Annual mortality rates for ESRD patients. Available of October 27, 2009, from URL: http://www.usrds.org/2008/ref/H_Mortality_&_Causes_of_Death_08.pdf
- Faber RL. Forty years on hemodialysis. Available on October 27, 2009 from URL: http://users.rcn.com/ktda1/Forty_Yrs.pdf
- Penn Honors 1st Transplant at the Hospital of the University of Pennsylvania... And Introduces the Transplant House. Available on October 27, 2009, from URL: http://www.uphs.upenn.edu/news/News_Releases/f eb06/trnshse.htm
- Piccoli GB, Mezza E, Anania P, *et al.* Patients on renal replacement therapy for 20 or more years: a clinical profile. *Nephrol Dial Transplant* 2002; 17: 1440-1449.
- Buturovic-Ponikvar J, Kandus A, Malovrh M, Ponikvar R. Long-term (>30 years) renal replacement therapy survivors in Slovenia. *Ther Apher Dial* 2009; 13(3): A5.

19. Buturović-Ponikvar J, Persic V, Malovrh M, Ponikvar R. Vascular access in patients treated by chronic hemodialysis for 30 years or more. *Ther Apher Dial* 2009; 13: 354-357.
20. Kurkus J, Nykvist M, Lindergard B, Segelmark M. Thirty-five years on hemodialysis: two case reports as a tribute to Nils Alwall. *Am J Kidney Dis* 2007; 49(3): 471-476.
21. Otsubo S, Otsubo K, Sugimoto H, et al. Characteristics of patients on hemodialysis therapy for more than 30 years. *Ther Apher Dial* 2007; 11(4): 274-279.
22. Otsubo S, Kimata N, Okutsu I, et al. Characteristics of dialysis-related amyloidosis in patients on hemodialysis therapy for more than 30 years. *Nephrol Dial Transplant* 2009; 24: 1593-1598.
23. Hou S. Pregnancy in women on dialysis: Is success a matter of time? *Clin J Am Soc Nephrol* 2008; 3: 312-313.
24. McKay DB, Josephson MA. Pregnancy after kidney transplantation. *Clin J Am Soc Nephrol* 2008; S117-S125.
25. Haase M, Morgera S, Bamberg C, et al. A systematic approach to managing pregnant dialysis patients – the importance of an intensified haemodiafiltration protocol. *Nephrol Dial Transplant* 2005; 20: 2537-2542.
26. Barua M, Hladunewich M, Keunen J et al. Successful pregnancies on nocturnal home hemodialysis. *Clin J Am Soc Nephrol* 2008; 3: 392-396.
27. Marn Pernat A, Ponikvar J, Buturović-Ponikvar J. Daily hemodialysis during successful pregnancy in women with end-stage renal disease. *Blood Purif* 2008; 26: 17 (A).
28. Asamiya Y, Otsubo S, Matsuda Y, et al. The importance of low blood urea nitrogen levels in pregnant patients undergoing hemodialysis to optimize birth weight and gestational age. *Kidney Int* 2009; 75: 1217-1222.
29. Subhodhini Reddy A, Holley JL. The importance of increased dialysis and anemia management for infant survival on hemodialysis. *Kidney Int* 2009; 75: 1133-1134.
30. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Working Group. KDIGO clinical practice guideline for care of the kidney transplant recipient. Chapter 25. Sexual activity and fertility. *Am J Transplant* 2009; 9 (Suppl. 3): S106-S109.
31. Gill JS, Zalunardo N, Rose C, Tonelli M. The pregnancy rate and live birth rate in kidney transplant recipients. *Am J Transplant* 2009; 9: 1541-1549.
32. Richards L. Low pregnancy rates in kidney transplant recipients. *Nature Rev Nephrology* 2009; 5: 550.
33. Jofre R, Lopez-Gomez JM, Moreno F, Sanz-Guajardo D, Valderrabano F. Changes in quality of life after renal transplantation. *Am J Kidney Dis* 1998; 32: 93-100.
34. Habwe VQ. Posttransplantation quality of life: more than graft function. *Am J Kidney Dis* 2006; 47 (4): Suppl 2: S98-S110.
35. Buturović-Ponikvar J, Novljan G, Ponikvar R. Cosmetic side effects of immunosuppressive therapy in children and adolescents with renal graft. *Transplant Proc* 2002; 34: 3009-3011.
36. Riis J, Loewenstein G, Baron J, Jepson C, Fagerlin A, Ubel PA. Ignorance of hedonic adaptation to hemodialysis: a study using ecological momentary assessment. *Journal of Experimental Psychology: General* 2005; 134 (1). 3-9.
37. Horvat DL, Shariff SZ, Garg AX, for the Donor Nephrectomy Outcomes Research (DONOR) Network. *Kidney Int* 2009; 75: 1088-1098.
38. Scheper-Hughes N. The tyranny of the gift: sacrificial violence in living donor transplants. *Am J Transplant* 2007; 7: 507-511.
39. Ibrahim HN, Foley R, Tan L, et al. Long-term consequences of living kidney donation. *N Engl J Med* 2009; 360: 459-469.
40. Prasad GVR, Lipszyc E, Huang M, Nash MM, Rapi L. A prospective observational study of changes in renal function and cardiovascular risk following living kidney donation. *Transplantation* 2008; 86: 1315-1318.
41. Ibrahim HN, Akkina SK, Gillingham K et al. Pregnancy outcomes after kidney donation. *Am J Transplant* 2009; 9: 825-834.
42. Reisaeter AV, Roislien J, Henriksen T, Irgens LM, Hartmann A. Pregnancy and birth after kidney donation: the Norwegian experience. *Am J Transplant* 2009; 9: 820-824.
43. Josephson MA. Pregnancy after kidney donation: more questions than answers. *Nature Rev Nephrol* 2009; 5: 495-497.
44. Hipper BE, Taylor JS. In defense of transplantation: a reply to Nancy Scheper-Hughes. *Am J Transplant* 2007; 7: 1695-1697.
45. Shimazono Y. The state of the international organ trade: a provisional picture based on integration of available information. *Bulletin of the World Health Organization* 2007; 85: 955-962.
46. Gill J, Madhira BR, Gjerson D et al. Transplant Tourism in the United States: a single center experience. *Clin J Am Soc Nephrol* 2008; 3: 1820-1828.
47. The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. *Nephrol Dial Transplant* 2008; 23: 3375-3380.
48. The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. *Transplantation* 2008; 86: 1013-1018.
49. Liem YS, Weimar W. Early living-donor kidney transplantation: a review of the associated survival benefit. *Transplantation* 2009; 87: 317-318.
50. Grootendorst DC, Jager KJ, Zoccali C, Dekker FW. Screening: why, when and how. *Kidney Int* 2009; 76: 694-699.

-
51. Korevaar JC, Jansen MA, Dekker FW, *et al.* When to initiate dialysis: effect of proposed US guidelines on survival. *Lancet* 2001; 358: 1046-1050.
 52. Traynor JP, Simpson K, Geddes CC, Deighan CJ, Fox JG. Early initiation of dialysis fails to prolong survival in patients with end-stage renal failure. *J Am Soc Nephrol* 2002; 13: 2125-2132.
 53. Lameire N, Van Biesen W, Vanholder R. Initiation of dialysis – is the problem solved by NECOSAD? *Nephrol Dial Transplant* 2002; 17: 1550-1552.
 54. Gill JS. Potential advantages and limitations of applying the chronic kidney disease classification to kidney transplant recipients. *Am J Transplant* 2006; 6: 2821-2826.
 55. Mattas AJ, Gillingham KJ, Humar A, Kandaswamy R, Sutherland DER, Payne WD, Dunn TB, Najarian JS. 2002 kidney transplant recipients with 10 years of graft function: what happens next? *Am J Transplant* 2008; 8: 2410-2419.
 56. Grasmann A, Gioberge S, Moeller S, Brown G. ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. *Nephrol Dial Transplant* 2005; 20: 2587-2593.