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Living kidney donor transplantation – new dimensions

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Abstract The ethical view points concerning living kidney donation are changing in Europe. Objections against emotionally related donation are fading away, whilst ethical arguments around brain death and "true death" are put first in some regions. Emotionally related donation is highly motivated and gives excellent results, despite rather bad HLA matches, but yet remains neglected as large source of kidneys in many centres and countries. Avoiding dialysis by pre-emptive transplantation with living donors is the best treatment of end-stage renal disease in order to maintain quality of life and socioeconomic benefit. The technique of laparoscopic donor nephrectomy will probably spread quickly. The future of cross-over transplantation is unclear as yet, but will probably not be stopped by law since it is ethically and biologically well justified. And, finally, all centres in regions where live donor kidney transplantation is rapidly expanding should prospectively follow up the health of their donors and interact as soon as necessary. An example of such an institution is the Swiss living kidney donor registry which has been following up 181 donors since April 1993.

Key words Living kidney donation · Emotionally related donation · Pre-emptive transplantation · Laparoscopic nephrectomy · Cross-over transplantation

Introduction

Living kidney donor transplantation is the oldest solid organ transplantation. In Europe, after decades of running as a not very popular and rarely performed alternative to cadaveric transplantation (< 5% of all renal transplantations), living kidney donation is experiencing a kind of revival in recent years. Several new dimensions of this very old procedure will be briefly discussed.

Changing ethical view points

In Central Europe, living donor nephrectomy was viewed with much disfavour for more than 20 years. It was thought to be ethically almost unacceptable to damage a healthy donor by nephrectomy, whereas in cadaveric donation the donor is already dead and thus no harm can be done to him or her. In the last 10 years, however, transplant surgeons and nephrologists were rather surprised to find out that professional moral philosophers saw more problems in harvesting organs from cadaveric donors than from voluntary living donors. In the recent debate in the German parliament, the major ethical and psychological obstacle for a transplantation law was the question of whether a brain-dead person is really dead or only dying and whether a dying person should be used for organ retrieval. Emotionally related living donation, however, passed the parliamental hurdle easily, which would have been impossible 10 years ago.

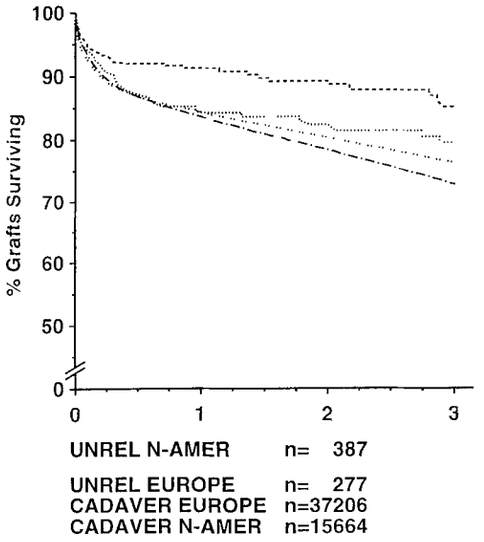

Fig. 1 Collaborative transplant study: the results of renal graft survival of unrelated live donor *(UNREL)* transplantation as compared to first cadaveric renal transplants in North America *(N-AMER)* and Europe (kindly provided by Prof. G. Opelz, Heidelberg)

Emotionally related kidney donation

Emotionally related kidney donation was sporadically performed as early as 1966 in some European centres, for example, Brussels [5]. But as a regular programme, it was started much later: 1983 in Rome (D. Alfani, personal communication) and 1984 in Oslo (A. Jacobsen, personal communication). In other countries, it is still forbidden by law or restricted to extreme life-threatening emergencies. As for Switzerland, emotionally related transplantation was thought to be unethical, until it became evident in the Basel transplant centre, in 1991, that the motivation of spouses to donate a kidney to the partner is the highest apart from parent to child donation and that no real ethical argument speaks against it. Our former refusal was rather based on prejudice. Once we became familiar with emotionally related living donor transplantation, this programme grew rapidly in number and popularity in our centre, but, of course, every single case must be carefully evaluated from all psychological, somatic and immunological aspects. Currently, many other European centres have reconsidered their attitude and also started a programme of emotionally related living kidney donor transplantation.

Besides the high motivation of emotional donors, the data analysis of Terasaki and Eurotransplant brought a strong argument in favour of spousal transplantation. Terasaki's analysis (1995) [6] shows a 3-year outcome of spousal donation in the USA which is better than the outcome of cadaveric kidney transplantation. In August 1997, Paul Terasaki (personal communication) up-dated these results with many more cases, confirming very clearly this earlier report. The analysis of Eurotransplant shows that the 3-year graft survival in spousal donation is nearly identical to zero-mismatched cadaveric kidneys [4].

Gerhard Opelz's interesting, unpublished analysis from the Collaborative Transplant Study (CTS) confirms the excellent results of the North American unrelated live donors, which are doing better than cadaveric kidneys (Fig. 1). In the European centres of the CTS, however, there is little difference between cadaveric and unrelated live donors during the first year. They then move up in parallel with the USA emotional donors, but at about a 5% lower level.

A new approach to renal replacement therapy

The classic old way to approach a patient with chronic progressive renal failure is depicted in Fig. 2. When the creatinine is rising close to terminal uraemia, an arteriovenous bypass is placed and, some weeks to months later, chronic dialysis is started. Little attention is paid to the fact that by now most patients lose their job partially (i.e. a half-time job) or totally. For an active woman or a man planning a career, the start of chronic dialysis therefore means a collapse of their professional dreams and, very often, of their self-esteem as well. There are more socioeconomic aspects: dialysis is expensive, the health insurance has to pay the dialysis costs for years, and the public social security will have to pay invalidity pensions, mostly for ever. Depending on the dialysing physician, the patient will sooner or (years) later be put on a waiting list for cadaveric transplantation and, with some luck, will finally receive a cadaveric kidney 3–6 years later. By this time, the disability of the patient is psychologically fixed and the invalidity pension can barely ever be replaced by a good income. The job was lost in the "dialysis trap".

The new approach (Fig. 3) does not lead into such a trap and is much more favourable for the patient. Approximately 2 years before the expected renal end-stage, the search for a living kidney donor should be started. Additionally, the patient can be put on a waiting list for cadaveric kidneys which, however, is not allowed in many centres before dialysis is started. If the nephrologist is actively searching then, in time, living donors can be motivated more often than anticipated, even after full information about the risks for the donor. The somatic, psychological and immunological donor work-up can be performed without rush. When renal function reaches the end-stage, donor nephrectomy and renal transplantation are performed as a previously planned procedure. By avoiding chronic dialysis using pre-emptive renal transplantation, the majority of patients can

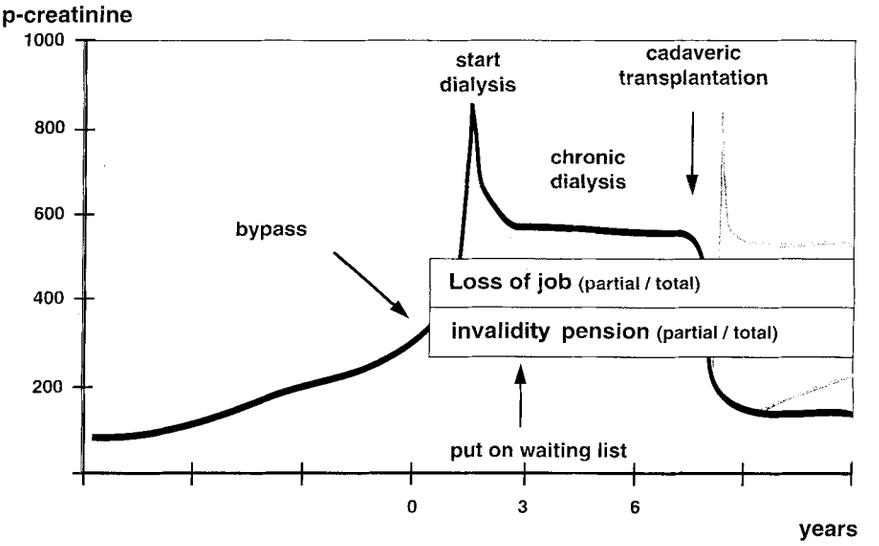

Fig. 2 Renal replacement therapy: the old way. *p* Plasma

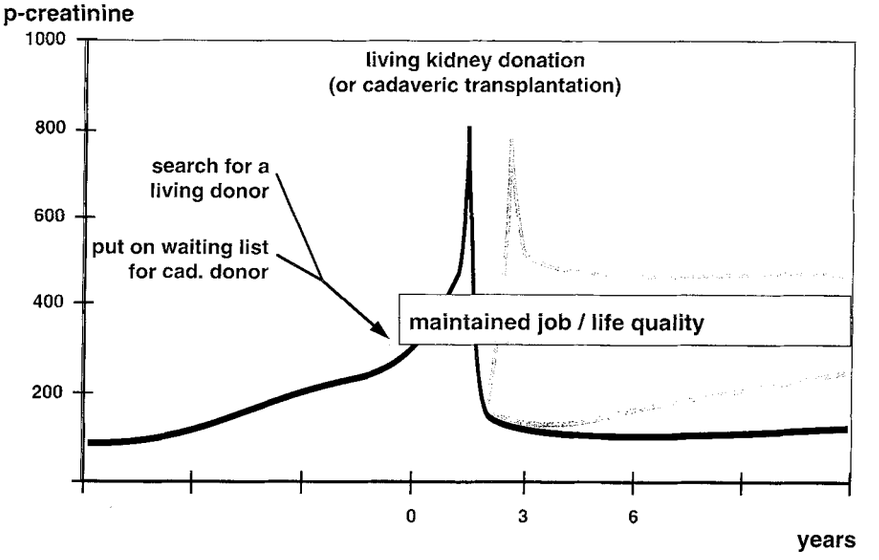

Fig. 3 Renal replacement therapy: the new way of pre-emptive transplantation, planned ahead for 2 years before end-stage renal failure

maintain their job. The treatment time for end-stage renal failure is shortened down to 6–8 weeks, not much longer than a prolonged summer holiday. Health insurances save on the costs of dialysis and the public funding is relieved of paying invalidity pensions.

In our experience, the highest rate of pre-emptive transplantation can be reached with emotionally related donors. Theoretically, pre-emptive transplantation can also be performed with cadaveric kidneys, but in practical terms one will neither succeed often enough to find a kidney at the right time, nor can it easily be accepted ethically to give patients such a benefit when the majority of others stay on a waiting list for years. A recent analysis in our centre showed that only 5% of patients received a cadaveric kidney before starting dialysis (a few AB and B recipients and some diabetics), but pre-emptive transplantation was possible in 26% of related kidney transplantations and 48% of emotionally related donations [1].

All socioeconomic benefits gained by pre-emptive transplantation are accompanied moreover by better quality of life and psychological advantages, unless the graft fails which is the case in about 10–15% of cases. For these 10–15%, the disappointment is very painful, but they are told beforehand about this risk. They have now to begin dialysis as they would have done a year before, without having had the chance of an 85–90% success.

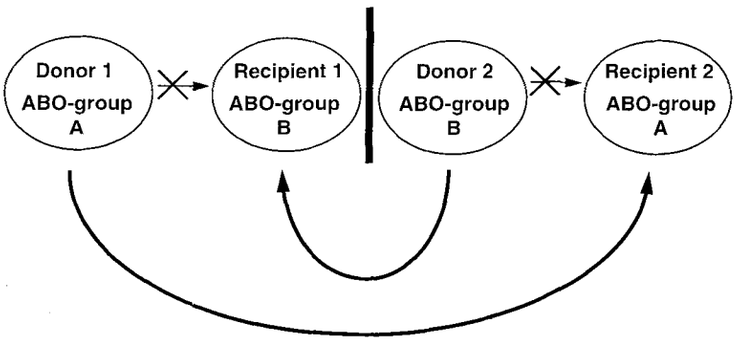

Fig. 4 Cross-over kidney transplantation

The realisation of this concept primarily depends on the motivation of the nephrologist in charge. He has to learn to speak about living donation early during progressive renal disease. Renal patients and their families need time to handle the new situation. If a nephrologist owns a private dialysis unit, he has to overcome his own financial interest in dialysis treatment.

As for the failure of spousal donation, we confront the couple from the beginning in several discussions about living donation, with the possibility of graft failure. Our experience is that couples, in the case of graft failure, are depressed, but prepared. They do not regret it, since the partner has given his or her best for the other and has proven love and solidarity. This gift remains untouched, even in the case of graft failure. The potential for pre-emptive transplantation with genetically or emotionally related donors is much underestimated and underused, at present in most European countries besides Norway.

Laparoscopic living donor nephrectomy

The classic procedure of donor nephrectomy will most probably be superceded in the near future by a laparoscopic-assisted living donor nephrectomy. This method was pioneered by Lloyd Ratner, Louis Kavoussy and colleagues at the John Hopkins University in Baltimore in February 1995 [3]. The main reason for moving away from the classic nephrectomy procedure was the cut of more than 30 cm, leading to permanent scarring, and itching, pain, dysaesthesia and relaxation in about 15% of donors which is less than optimal. The group reports that all potential donors since 1995 chose the laparoscopic operation rather than the open procedure, despite the fact that equivalent safety could not yet be guaranteed. It is interesting that some of the patients would not have agreed to donate a kidney if the laparoscopic operation had not been available to them. Lloyd Ratner has recently founded an international registry on laparoscopic living donor nephrectomy (L. Ratner, Department of Surgery, John Hopkins University School of Medicine, 600 Wolfe Street/Harvey 611, Baltimore, Md., USA 21287-8611). He wrote to us in August 1997 that over 90 institutions have reported to the registry so far.

Cross-over transplantation

The cross-over transplantation or also called paired-kidney exchange programme is designed to solve the AB0 incompatibility problems, if one donor has blood group A and his loved recipient blood group B, by finding another couple with a vice versa A and B incompatibility (Fig. 4). For all other AB0 incompatibilities, this concept makes little sense. The universities of Freiburg im Breisgau and Basel agreed in January this year to start together a kidney cross-over transplantation programme. The ethical committees of both universities accepted it. We agreed on the conditions of simultaneous transplantation in order to avoid the sudden refusal of one donor to donate if the kidney received by his beloved recipient failed a day earlier because of some technical reasons. However, we did not decide whether the donors or rather the removed kidneys have to move to the other university and whether the two couples should remain anonymous. We rather argue against anonymity, since cross-over transplantation is a kind of exchange deal, and it would be only fair if the partners know each other beforehand. This is exactly opposite to the opinion published a few weeks ago by a Chicago transplant group [2].

All our plans have been interrupted by the new German transplantation law which passed the parliamentary hurdle a few months ago. This law wants non-related kidney donation to be based on an emotional relationship and this, of course, is not the case in cross-over transplantation, particularly if the two pairs stay anonymous. In the long run, however, cross-over transplantation will not be stopped simply by law, rather the law will be changed again since the concept is very reasonable and ethically impeccable.

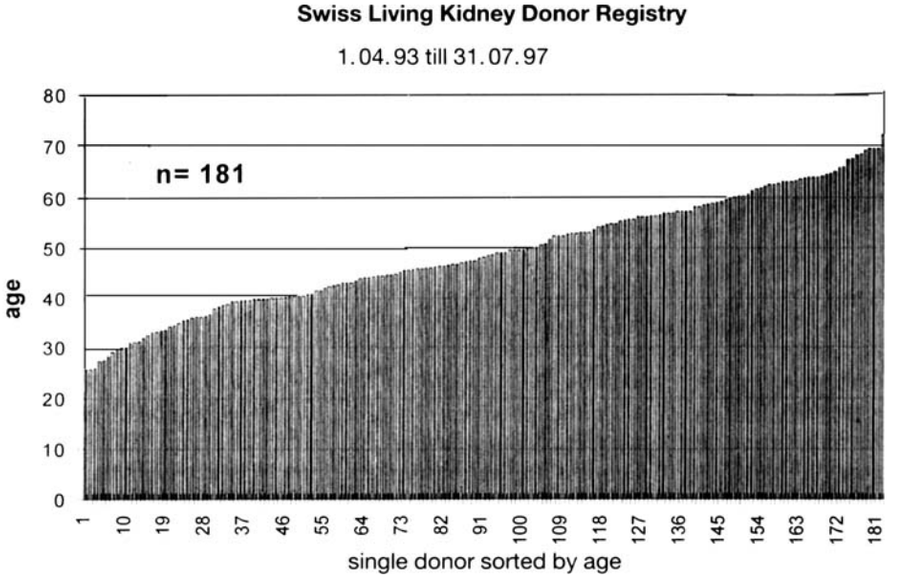

Fig. 5 Swiss living kidney donor registry: living donors sorted by age

The need for living kidney donor health registries

The first world-wide living kidney donor health registry was founded in April 1993 in Switzerland for five reasons: (1) to give transparency over all live donor sources occurring in this country, (2) to perform a prospective survey of complications and their frequency, (3) to collect information for future potential donors, (4) for the recognition of treatable late complications, such as hypertension and proteinuria, in order to intervene in time, and (5) to have control over private clinics and to prevent commercial living transplantation.

From April 1993 to the end of July 1997, 181 living donor transplantations were registered in Switzerland. Figure 5 shows all of them sorted by age. The large majority of donors were between 40 and 60 years old. None was younger than 27 years, which is reasonable. It needs some maturity to decide on donating a kidney. Thirty-two persons above 60 years were willing to donate a kidney. The oldest was a 72-year-old lady for her 70-year-old brother. The source of old people as donors is not used enough. One can argue that one should not give a cadaveric kidney from a young donor to a 70-year-old man, but there is nothing wrong with sharing the kidneys between two old people who love each other. The same argument holds true also for the source of kidneys from grandparents for their uraemic grandchildren.

A nephrologist should make a life-long plan for a young uraemic child, not just think of the next couple of years. A grandparent's kidney is a good option for the start. Many old people are in excellent health. Just think of the jogging grandparents, why should they not

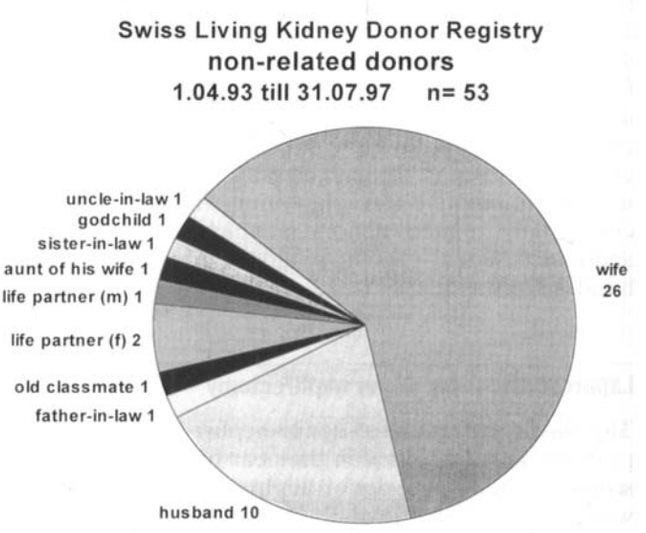

Fig. 6 Swiss living kidney donor registry: donor source in all emotionally related kidney transplantations performed in Switzerland since April 1993

be kidney donors for their uraemic grandchildren? The father and mother of a uraemic child stay in reserve for later, as do the siblings. It is clear that many colleagues will not like this idea. Using the family repeatedly as a stock of organs sounds awful. But I do not agree. There is nothing wrong with sharing the organs in favour of a sick family member. Voluntariness is the condition sine qua non and, if voluntariness is respected, sequential organ donations are the proof of an admirable solidarity within a family. The only concern is an immunological

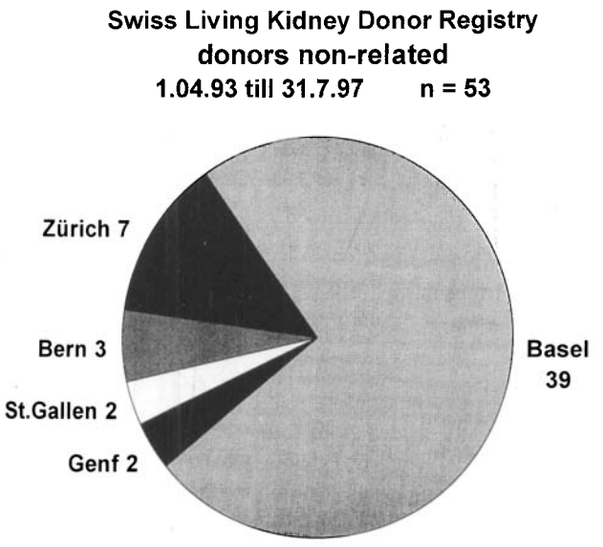

Fig. 7 Swiss living kidney donor registry: Swiss centres participating in emotionally related donor transplantation

Table 1 Mean data gained by prospective follow up of the donors (n = 181). Swiss living kidney donor registry (U_{alb} urinary albumin, U_{creat} urinary creatinine, BP blood pressure)

	Before donation	1 year after donation	3 years after donation
Plasma creatinine	85 ± 14	112 ± 19	113 ± 14
U_{alb}/U_{creat}	1.7 ± 2.6	1.4 ± 2.1	2.3 ± 5.5
BP systolic	125 ± 16	127 ± 17	129 ± 16
BP diastolic	80 ± 10	80 ± 10	81 ± 9

one; the sensitisation against a foreign HLA antigen being present in several members of the family. This potential risk has to be considered and carefully evaluated by cross-matching, eventually after three donor-specific blood transfusions. In return, centres promoting living kidney donation should be actively obliged to follow up the health of their donors. This is one of the functions of a live donor registry. Figure 6 shows the donor source in all emotionally related kidney transplantations performed in Switzerland since April 1983. The dominant source was wives, followed by husbands, and there are many particular cases such as fathers-in-law or an old classmate. Most of the emotionally related donor transplantations were performed in Basel (Fig. 7). This points to the large size of still unused resources existing in the other Swiss centres. Nobody would ever believe that the emotional relations between life partners would be less close in these other centres. The only reason for the difference is the other approach of nephrologists in the use of these donor resources.

Table 1 shows the mean data gained by prospective follow up of the donors concerning the critical parameters: renal function, microalbuminuria and blood pressure. Mean plasma creatinine elevated as expected after donation, but then remained stable for over 3 years. The ratio of urinary albumin to creatinine (which is normal up to 3) and the systolic blood pressure show a tendency to increase, although not significant. However, if a donor health register fulfils its duty the way it should, it is not enough to follow "mean values". The register has to pick up and warn single individuals as soon as measured data become abnormal. Some examples should be mentioned.

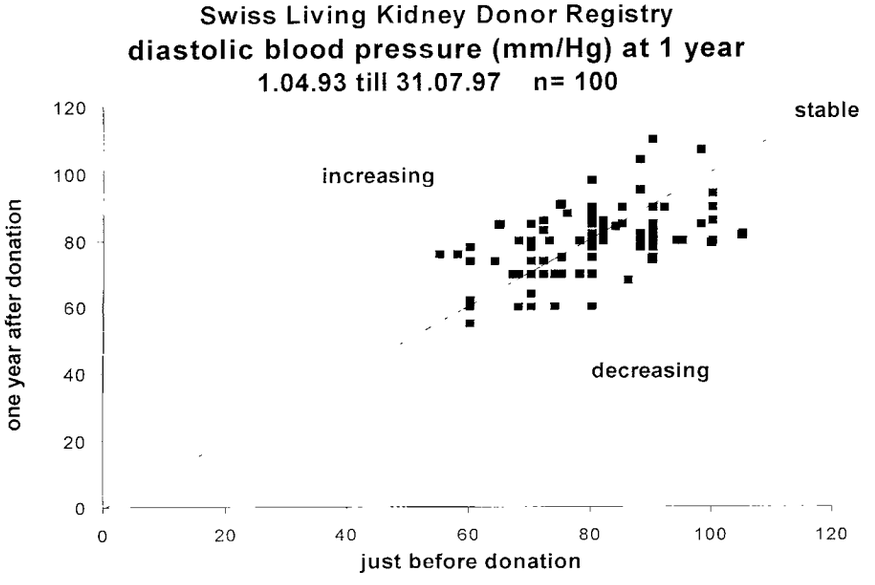

Fig. 8 Swiss living kidney donor registry: 1-year follow up of diastolic blood pressure in living kidney donors

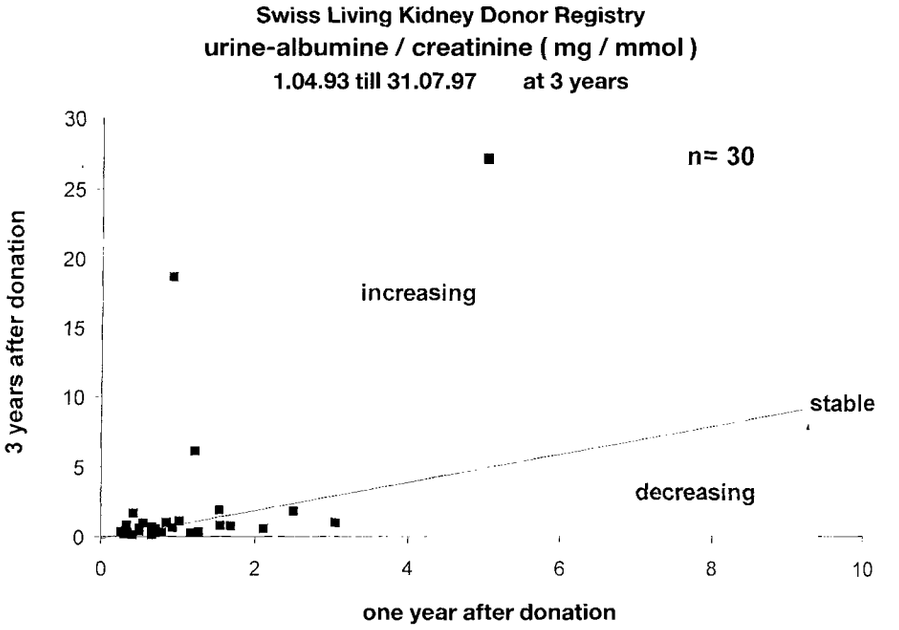

Fig. 9 Swiss living kidney donor registry: 3-year follow up of microalbuminuria in living kidney donors

Figure 8 gives the diastolic blood pressure values. Every point shows the result of every single individual twice, just before donation and 1 year later. One can easily see whether the values are increasing, stable or decreasing. Figure 8 looks in general reassuring, but this is not really the case for four individuals with diastolic blood pressures above 90. All four and their treating physicians, received a letter from the registry with an invitation to treat the hypertension. Figure 9 shows the development of microalbuminuria. Among 32 donors already followed for 3 years, all values of albuminura remained in the normal range below 3, except for 3 donors. One donor, with an initial ratio of 5, rose up to 28 in the 3rd year. He is one of the donors whose hypertension was not treated despite warning. He would profit from an ACE inhibitor. All 3 donors and their physicians received individual letters from the registry.

This is the way, we believe, a donor health registry for living kidney donors should work. We also believe that a kind of donor health registry should be obligatory for all centres with an active live donor programme. Ideally, the registry should cover a region of up to ten centres in order to stay in close contact with the donors and the colleagues running the centre. The risk for large international registries is that they become swamped by too many distant centres and lose control over single centres and single donors. This would then undermine the role of such a registry for solving the five duties mentioned earlier. Live kidney donation and in particular spouse donation will probably experience a dynamic expansion in many European countries over the next decades. This development will bring numerous advantages for patients with chronic renal failure, but has to be flanked by institutions controlling the donor sources, the ethical background, the results and the donor's health.

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