Outcome of renal replacement therapy in autosomal dominant polycystic kidney disease

Y. Pirson, J. L. Christophe and E. Goffin

Service de Néphrologie, Cliniques Universitaires St Luc, avenue Hippocrate 10, 1200 Brussels, Belgium

Abstract. We review our own experience as well as pertinent literature on the outcome of renal replacement therapy (RRT) in autosomal dominant polycystic kidney disease (ADPKD). Due to the virtual absence of data on peritoneal dialysis in ADPKD, we deal only with haemodialysis (HD) and renal transplantation (TP). Special attention is paid to the renal and extrarenal complications of ADPKD. On HD, 5 year survival is 10–15% greater in ADPKD than in non-ADPKD patients, probably because of a lower cardiac mortality of ADPKD patients. After TP, patient as well as graft survival rates of ADPKD patients are similar to those of non-ADPKD patients. On HD, the prevalence of renal pain, gross haematuria and renal infection is significantly greater in ADPKD (36, 36 and 16% respectively) than in non-ADPKD patients (2, 16 and 2% respectively), but these complications are rarely severe. Other than preparation for TP, nephrectomy is required in only 4% of ADPKD patients on HD. With a policy of selective removal of problematic kidneys before TP, complications due to native polycystic kidneys do not frequently occur after TP, leading to post-TP nephrectomy in only 7% of ADPKD patients. There is a mild excess of stroke among ADPKD patients undergoing RRT, the contribution of intracranial aneurysm rupture not being clearly defined. Symptoms related to hepatic cysts are rare and to cardiac valvular abnormalities very rare. In conclusion, RRT is at least as successful in ADPKD as in non-ADPKD patients. Renal complications are frequent but rarely severe. Extrarenal complications are not frequent.

Key words: ADPKD; polycystic kidney disease; renal replacement therapy

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) accounts for 3–10% of all patients currently treated for end-stage renal disease (ESRD) in Western countries [1–3]. In this article we review the outcome of ADPKD patients reaching ESRD, with the focus on the question of what extent cystic kidneys and extrarenal complications of ADPKD contribute to mortality and morbidity during renal replacement therapy (RRT). In this paper we will frequently refer to two retrospective studies we have recently performed. In the first, presented at the last meeting of this Concerted Action (Heidelberg, September 1995), we compare the course of haemodialysis (HD) of 50 ADPKD patients with that of 50 properly matched patients with ESRD due to another primary nephropathy who started HD at the same time, between 1981 and 1990 [1]. In the second study, presented in part at the second meeting of this Concerted Action (Paris, June 1990) and recently updated (Heidelberg, September 1995), we compare the fate of 106 ADPKD patients transplanted with a first kidney graft between 1967 and 1993 to that of a control group of 106 patients transplanted for another nephropathy and matched for age, gender, date of transplantation, source of graft and type of immunosuppressive regimen [E. Goffin et al., manuscript in preparation].

Selection of RRT modality

HD was once recommended as the best RRT for ADPKD patients in ESRD [4]: TP was believed to be too risky at the relatively advanced age at which most ADPKD patients reach this stage, whereas HD was particularly well tolerated in these patients because they were less anaemic than other ESRD patients. This attitude has progressively changed as advances, both in immunosuppressive therapy and recipient management, have made TP more successful and safer for older patients. As TP also provides a better quality of life, this modality is nowadays considered in any ADPKD
Renal replacement therapy in ADPKD

Life expectancy < 5 yrs or contraindication to surgery or to immunosuppressants

Yes

No

Pre-TP work-up, including echocardiogram myocardial stress scintigraphy aorto-iliac angiogram

Remove kidney(s) if history of cyst infection recurrent gross haematuria

Eligible for TP

Not eligible for TP

Very large kidneys or Diverticulosis or Abdominal hernia

No

Yes

TP PD HD

Fig. 1. How to select RRT modality in ADPKD patients.

Survival

In our experience, ADPKD does not affect survival on HD: 1 and 5 year survival rates of 50 ADPKD patients (mean age at onset of HD: 55 years) were 92 and 69% respectively, compared with 92 and 66% respectively for the control group. Large surveys have shown that survival is even better for ADPKD patients than for patients with other primary renal diseases. In the USA, 5 year survival rates of patients aged 55–64 at onset of RRT were 49% in patients with ADPKD versus 36% in patients with chronic glomerulonephritis [11]. In the EDTA Registry, 5 year survival rates of male patients with ADPKD in RRT (most of them on HD as first treatment) were 73% in patients aged 45–59 and 51% in those aged >60, compared with 58 and 38% respectively in patients with standard primary renal diseases [12] (Figure 2). This better survival was ascribed to a lower cardiac mortality (which is the leading cause of death on HD) among ADPKD patients [12]. This contrasts with an increased mortality of dialysed ADPKD patients from cerebrovascular accident, a finding observed both in the EDTA and Toronto Registries [12,13].

After TP, the 5 year patient survival of ADPKD patients with a history of renal cyst infections, particularly if the infections were recent, recurrent or severe [8]. Other indications are recurrent gross haematuria and physical interference with graft placement. The decision to undertake binephrectomy is now facilitated by the availability of erythropoietin therapy.

Living-related donor transplantation may be considered, provided ADPKD has been formally excluded in the donor by either ultrasonography/computed tomography (sufficient in donors >30 years old) or genetic analysis (to be advised in donors <30 years old).

When TP is contraindicated, patients may opt for either HD or peritoneal dialysis (PD) [9]. Kidney size is rarely an impediment to PD, but PD is probably less advisable in patients with very large polycystic kidneys because their volume may reduce both the exchangeable surface area and tolerance to abdominal distension. The latter is especially relevant for larger-framed individuals, in whom increased volumes of dialysis solutions are required [10]. HD should also be preferred to PD in patients with colonic diverticula or abdominal hernia (Figure 1).

Though PD was the first RRT therapy for 16% of ADPKD patients recorded at the EDTA Registry, there is very little information about the outcome to this type of therapy. Twenty-two per cent of the ADPKD patients in ESRD reported by Singh and Hariharan [9] were initially treated by PD, but more than half of them subsequently had to be transferred to HD. The reasons for transfer were not provided. The authors only mention that the peritonitis rate in ADPKD patients was not increased compared with that of patients with another nephropathy.

Patient in ESRD with a reasonable life expectancy and in whom no contraindication to surgery or immunosuppressive treatment is present (Figure 1).

A careful evaluation of TP candidates should obviously be made, paying special attention to both the cardiovascular risk (related to age and previous hypertension) and the existence of ADPKD-associated abnormalities. Taking into account the rarity of intracranial aneurysm (ICA) rupture in RRT (see below) on the one hand and the risk of ICA surgery in dialysis patients on the other, we have not yet included routine screening for ICA in our pre-TP work-up. This attitude might have to be revised with further information on both the natural history of ICA and the success of newer endovascular treatments of ICA [5]. Despite a possible increased prevalence of colonic diverticula in ADPKD [6], we do not screen our patients for diverticular disease before TP, since post-TP diverticulitis does not have an increased incidence among ADPKD patients and is not predicted by the existence of diverticula before TP [7].

It is now agreed that ADPKD patients awaiting TP should not be subjected to routine binephrectomy: removal of polycystic kidneys is not a benign operation and the anephric state has some known disadvantages. By contrast, pre-TP nephrectomy should be advised in
Renal complications

Disagreement on the changes in kidney size of ADPKD patients on maintenance HD [19,20] could reflect different durations of HD treatment among the patients investigated. Indeed, a longitudinal study with CT scanning showed a reduction of kidney size within the first 2 years after starting HD, which was followed by a slow enlargement during the next 3 years. This enlargement was attributed to the superimposed development of acquired cystic disease, as in other chronic kidney diseases [21]. The kidneys of ADPKD patients on HD may occasionally become so massive that they cause symptoms requiring nephrectomy [22]. After successful TP, renal volume gradually decreases, the reduction of size averaging ~1% per month [20].

Not unexpectedly, ADPKD patients have an increased frequency of renal complications during HD. In our study the prevalence as well as the number of episodes of renal pain (defined by acute renal pain requiring medical advice and/or analgesics), gross haematuria and renal infection is significantly greater in ADPKD patients than in controls (Figure 3). At 1, 3 and 5 years after starting HD the actuarial risk was 14, 36 and 57% for renal pain, 18, 41 and 51% for haematuria, and 9, 12 and 12% for renal infection respectively [1]. Both gross haematuria and renal infection occur more frequently on HD among patients with such a history before HD than among those without [23]. As in non-dialysed ADPKD patients, rest is the best management for gross haematuria, which rarely lasts for >1 week [24]. Nephrectomy is rarely required during HD outside preparation for TP: out of 50 patients on HD, unilateral nephrectomy was performed in one patient for severe haematuria, in one patient for suspected—but unconfirmed—renal cancer and in four patients in preparation for TP (two recurrent haematuria, one recurrent renal infection and one very large kidney size) [1]. In contrast with older studies [23], we found that renal infections were rarely severe and never fatal. This most probably reflects the easier control of renal infection by presently available lipophilic antibiotics, such as quinolones, reaching high concentrations in cyst fluid despite the loss of renal function [25].

With a policy of pre-TP removal of problematic kidneys (see above), complications due to native kidneys do not frequently occur after TP. In our experience in 83 ADPKD patients retaining at least one native kidney at the time of TP, gross haematuria and renal infection were observed in only three and four patients respectively; nephrectomy was performed in six patients (four for urinary tract infection, one for pain and one for hypertension), i.e. a rate similar to that observed in the control group [E. Goffin et al., manuscript in preparation].

Importantly, no case of renal cancer was observed in our HD and TP patients, confirming the rarity of this complication in ADPKD, even after years of immunosuppression. Renal cancer was the cause of death in none out of 99 ADPKD patients who died during RRT (25 were transplanted) [26]. Reviewing all published cases of renal cancer in ADPKD, Keith et al. [27] recorded only four patients who were on RRT.

Extrarenal complications

Cardiac

In our HD population the frequency of coronary events (acute myocardial infarction and need for myocardial revascularization) tended to be lower in ADPKD than in control patients [1]. This is in agreement with the above-mentioned lower cardiac mortality recorded at the EDTA Registry [12]. Interestingly, those observations would not have been predicted from post-mortem examination studies, which have disclosed a rather greater prevalence of severe coronary atherosclerosis in

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<th>Modality</th>
<th>Age</th>
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<th>Survival (%)</th>
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<tr>
<td>RRT</td>
<td>45-59</td>
<td>6003</td>
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<td></td>
<td>&gt;60</td>
<td>2627</td>
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<tr>
<td>TP</td>
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<td>590</td>
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<tr>
<td></td>
<td>75-84</td>
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Fig. 2. Five year survival of ADPKD patients (■), as compared with patients with standard primary renal disease (○) recorded at the EDTA Registry. RRT: survival calculated from the onset of all forms of first RRT (haemodialysis in >80% of patients). TP survival was calculated from the first cadaver graft, 1979-1982.
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ADPKD than in control patients [12,26]. The paradoxical lower coronary mortality of ADPKD patients on HD has been tentatively related to a haematocrit which could provide some protection against ischaemic heart disease [12].

We [E. Goffin et al., manuscript in preparation] and others [15] have found that after TP there is a similar prevalence of coronary events in ADPKD and control patients. By contrast, Florijn et al. reported an increased risk for cardiovascular disease in ADPKD patients treated by azathioprine–prednisone but not in those treated by cyclosporin–prednisone [17].

Despite the (still debated) increased prevalence of cardiac valvular disease (mainly mitral valve prolapse) in ADPKD [28], valvular abnormalities did not contribute significantly to cardiac morbidity and mortality in RRT. Out of 50 ADPKD patients on HD, only one underwent valvular replacement (for calcified aortic valve stenosis probably not related to ADPKD) and another was successfully treated with antibiotics for Staphylococcus aureus mitral endocarditis [1]. Of 160 ADPKD transplanted patients (Mayo Clinic and our own series pooled) none required valve replacement, and endocarditis did not occur [15; E. Goffin et al., manuscript in preparation]. This is in keeping with a recent post-mortem study of 99 ADPKD patients in RRT, in which cardiac valvular disease did not contribute to death [26].

Cerebrovascular

Because of the 8% prevalence of intracranial aneurysms (ICAs) in ADPKD [5], an increased risk of stroke may be expected in RRT. In our limited series of HD patients, an equal number of ADPKD and control patients experienced a cerebrovascular accident. As previously mentioned, an increased mortality from cerebrovascular accident has, however, been recorded in large surveys among ADPKD patients in RRT [12,13]. To what extent ICA rupture accounts for this is not clear because the cause of the cerebrovascular accidents reported in those surveys is not known. It should be remembered in this regard that only 25–50% of strokes occurring in ADPKD result from ICA rupture [26,29]. Out of 106 transplanted patients, stroke occurred in four ADPKD patients late (mean 101 months) after TP [E. Goffin et al., manuscript in preparation] and was fatal in two of them; aneurysm rupture was proven in only one patient. Interestingly, five other ADPKD patients with a pre-TP history of stroke (aneurysm rupture proven in two) had no recurrence of stroke 8–166 months after TP [E. Goffin et al., manuscript in preparation].

Hepatic

Liver cysts are rarely symptomatic in ADPKD patients in general [25]. This is also true in RRT. In our experience, pain due to liver cyst occurs in <5% of ADPKD patients in RRT [1; E. Goffin et al., manuscript in preparation]. Complications related to massive polycystic liver disease may occasionally be manifest in RRT [30].

Liver cysts became infected in 3% of 229 ESRD patients with ADPKD (mostly on HD) [31] and 1% of 160 TP patients [15; E. Goffin et al., manuscript in preparation]. Special attention should be paid to the rare ADPKD patient with Caroli’s disease receiving immunosuppressive therapy.

Others

Neither diverticulitis nor colon perforation was more frequent in ADPKD patients than in controls either on HD or after TP [1,15; E. Goffin et al., manuscript in preparation]. It is noteworthy that the association of ADPKD with colonic diverticula [6] is now being questioned [26].

None of the other rare extrarenal lesions associated with ADPKD [25] were reported in the studies reviewed in this paper.
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References


