Review

Kidney and liver transplantation in the elderly

A. I. Sutherland[1,2], J. N. M. IJzermans[1], J. L. R. Forsythe[2] and F. J. M. F. Dor[1]

[1]Division of Hepatopancreatobiliary and Transplant Surgery, Erasmus MC, University Medical Center, Rotterdam, The Netherlands, and [2]Transplant Unit, Royal Infirmary of Edinburgh, Edinburgh, UK

Correspondence to: Dr F. J. M. F. Dor, Division of Hepatopancreatobiliary and Transplant Surgery, Erasmus MC, University Medical Center, Room H-813, PO Box 2040, 3000 CA Rotterdam, The Netherlands (e-mail: f.dor@erasmusmc.nl)

Background: **Transplant surgery is facing a shortage of deceased donor organs. In response, the criteria for organ donation have been extended, and an increasing number of organs from older donors are being used. For recipients, the benefits of transplantation are great, and the growing ageing population has led to increasing numbers of elderly patients being accepted for transplantation.**

Methods: **The literature was reviewed to investigate the impact of age of donors and recipients in abdominal organ transplantation, and to highlight aspects of the fine balance in donor and recipient selection and screening, as well as allocation policies fair to young and old alike.**

Results: **Overall, kidney and liver transplantation from older deceased donors have good outcomes, but are not as good as those from younger donors. Careful donor selection based on risk indices, and potentially biomarkers, special allocation schemes to match elderly donors with elderly recipients, and vigorous recipient selection, allows good outcomes with increasing age of both donors and recipients. The results of live kidney donation have been excellent for donor and recipient, and there is a trend towards inclusion of older donors. Future strategies, including personalized immunosuppression for older recipients as well as machine preservation and reconditioning of donor organs, are promising ways to improve the outcome of transplantation between older donors and older recipients.**

Conclusion: **Kidney and liver transplantation in the elderly is a clinical reality. Outcomes are good, but can be optimized by using strategies that modify donor risk factors and recipient co-morbidities, and personalized approaches to organ allocation and immunosuppression.**

Paper accepted 27 October 2015

Published online 14 December 2015 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.10064

Introduction

Transplantation is one of the greatest success stories in medicine of the 20th century. As in all areas of surgery, the average age of patients receiving transplants has increased. This is mirrored by an increase in the average organ donor age. In transplantation, there is a complex relationship between donor age, recipient age and associated co-morbidities. Organs are affected differentially by age, and all transplant procedures need to be weighed up against the (sometimes very limited) alternative treatments and the scarcity of organs for transplantation. As liver and kidney transplantation has become the mainstay of treatment for end-stage organ disease, this review examines the implications of an ageing population for deceased and live donors in transplantation, and elderly recipients.

Changing demographics of donors

Despite advances in transplantation and many initiatives to increase the number of donors in the UK and Eurotransplant area, there remains a significant disparity between organ availability and clinical need. One strategy to address this shortage is to use organs that would previously have been deemed unsuitable, often referred to as extended criteria organs[1,2]. Although there is not a single definition of such organs, a number of factors are known to have an adverse effect on transplant outcome. Age is a key factor in graft outcome[1–4], and so donors aged 60 years or older, or over 50 years who fulfil certain conditions (at least 2 of the following: history of hypertension, serum creatinine level exceeding 1·5 mg/dl, or stroke as cause of death) are deemed to be extended criteria donors. In the early days of transplantation, no donor aged more than 50 years would be considered[5]. However, the number of deceased donors over 50 years of age, as a fraction of all deceased donor kidney transplants in the USA, increased from 11·6 per cent in 1988 to 30·8 per cent in 2014[6]. Similarly, the median age of donors in the Eurotransplant region has increased from 35 years in 1990 to 53 years in 2014[7]. In the UK, there has been a marked increase in the

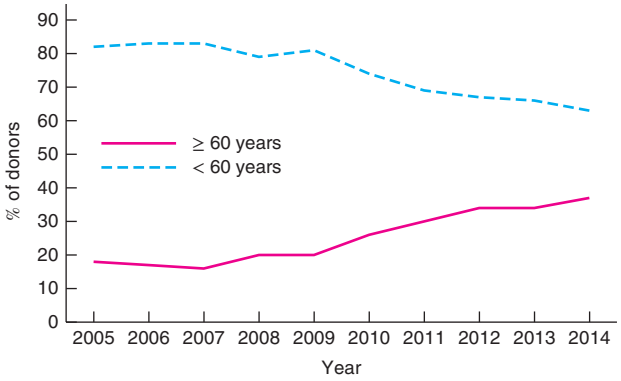

Fig. 1 Percentage of deceased donors aged at least 60 years in the UK (National Health Service Blood and Transplant[8])

age of donors; in 2014, 59 per cent of deceased donors were more than 50 years old and 37 per cent were aged over 60 years[8] (*Fig. 1*).

In addition to the age of donors, the type of organ donor has changed with time. There are three types of donation: live donation, donation after brain death (DBD) and donation after circulatory death (DCD). Among these types, the average age of donors has increased[8]. The number of living donors has increased in both Europe and the USA in recent years, whereas the number of DBD donors has declined[6–8]. This is partly due to improved neurosurgical care and a reduction in the number of deaths following subarachnoid haemorrhages[9], as well as improvement in road safety. DCD can sometimes be a preferred option, rather than waiting for confirmation of brain death. DCD is not used in some countries; however, DCD donor numbers are increasing in Europe and the USA, and make a significant contribution to the potential donor pool[2]. However, DCD donors are associated with poorer outcomes in liver transplantation, and livers from donors aged over 60 years are often not used[10,11]. In renal transplantation, DCD kidneys have similar long-term outcomes to DBD kidneys, albeit with a higher incidence of delayed graft function and reduced 1-year survival[12,13]. There is also evidence that DCD kidneys from donors over the age of 45 years do less well[2]. In both liver and kidney donation there is concern about using organs from elderly DCD donors, and most transplant units have an upper age limit for DCD of between 50 and 70 years.

Given these changes in demographics of donors and the increased demand for organs, the medical community is facing a dilemma for the next decennia: performing fewer transplants, or transplanting more organs from extended criteria donors. Currently, approximately 10–20 per cent of older livers and kidneys are being discarded worldwide[14–16]. These donors represent an important potential source of additional organs.

Renal transplantation

Older kidneys and older recipients

The average life expectancy in the last century increased from 45–50 to over 80 years[17]. Concurrent with this rise has been an increase in the number of older people with end-stage renal disease. In the USA, the number of patients on the kidney transplant list who are older than 65 years has more than tripled since 2000[6]. Despite this steep increase, only a relatively small number of elderly people have been added to the transplant waiting list and, of those listed, only a few go on to transplantation.

Kidney transplantation offers the potential for improved quality and length of life in elderly patients[18–20], and good outcomes have been demonstrated for selected patients[21,22]. In a registry study, Wolfe and colleagues[19] demonstrated that elderly kidney recipients (aged 60–74 years) had a life expectancy of 10 years, compared with 6 years for those who did not receive a transplant. Furthermore, Rao *et al.*[20] showed that even patients older than 70 years had a survival benefit from transplantation. Eighteen months after transplant, the relative risk of death was 56 per cent lower for patients who received a transplant compared with that in those remaining on the waiting list.

Kidneys from younger and healthier deceased donors are associated with lower death rates, but recipients require longer waiting times, especially as matching schemes select against older patients receiving younger kidneys[23]. Registry data from the USA have shown that 46 per cent of patients aged over 60 years on the waiting list are expected to die before receiving a transplant[24]. Thus, transplant candidates over 60 years of age are at significant risk of not surviving to receive a transplant, and a key question is whether older patients would benefit from earlier receipt of an extended criteria organ. Ojo and co-workers[25] examined whether patients would benefit from earlier transplant with extended criteria donor kidneys rather than waiting for a better-quality organ. For patients aged over 65 years, the life expectancy for extended criteria kidney recipients with 2 years on dialysis was 5·6 years, comparable to that of patients who received organs from either standard criteria donors (5·3 years) or living donors (5·5 years) after 4 years of pretransplant dialysis. This study emphasized the importance of early transplantation in this age group, even if older donors are used.

The importance of reducing waiting times by using older organs has been recognized in Europe where a

specific Eurotransplant Senior Programme was established in 1999, with the aim of matching kidneys from deceased donors aged over 65 years with recipients in the same age group[22–28]. Frei and colleagues[27] analysed 5-year outcomes following initiation of the programme, and showed that graft and patient survival were not affected negatively by the Eurotransplant Senior Programme; the availability of older donors doubled and the waiting time for elderly patients decreased. The local allocation scheme led to significantly shorter cold ischaemia times and less delayed graft functioning. Even older donors (aged more than 75 years) were shown in a single-centre study[29] to have acceptable graft outcomes. In Frei and colleagues' study, however, there was a higher incidence of acute rejection in patients within the Eurotransplant Senior Programme.

In all studies of transplantation in the elderly, 'death with functioning graft' is the main reason for graft loss[30,31]. In fact, death-censored graft survival is higher in elderly recipients than younger recipients[31]. Although overall survival in transplant recipients is higher than in patients on dialysis, post-transplant mortality is increased in the initial 12–18 months, and the survival benefit for older recipients is not realized until 1·5 years after transplantation[19]. Clearly, it is important to select appropriate older recipients and optimize any modifiable risk factors. Certainly, biological age is considered more important than chronological age. However, it is difficult to define and measure biological age. Several authors[32–34] have developed clinical risk assessment tools to measure the physiological reserve of recipients. However, despite these measures being independent predictors of mortality, it is difficult to see how an arbitrary cut-off can be found to decide when to list and when not to list elderly patients.

As well as trying to stratify the risk for recipients, a number of groups have tried to develop systems for stratifying the risk from older donors. The most comprehensive of these is the Kidney Donor Risk Index, which was validated on US data[35]. This donor index is based on 14 independent predictive variables that include donor variables as well as factors such as cold ischaemia time and human leucocyte antibody mismatch. A simpler donor risk index based on UK registry data was developed by Watson and co-workers[36]; this relied on five donor variables: age, history of hypertension, body mass index, length of hospital stay and use of adrenaline (epinephrine). Both of these scoring systems can be used to guide the surgeon in deciding whether to use an organ, and also to aid informed consent. Remuzzi and colleagues[37] have concentrated on preimplantation biopsies to guide decisions on whether to transplant a single kidney, both kidneys in a single recipient, or not to transplant the kidneys. However, other studies[29,38] reported that donor glomerular filtration rate, cold ischaemia time and presence of donor-specific antigen were sufficient to predict function, whereas preimplantation biopsies did not. Furthermore, histological scoring may increase cold ischaemia times, adversely affecting graft function[38].

Older living donors

Living donor transplantation remains the best option for elderly renal transplant recipients. Timely transplantation with no or minimal time on dialysis has been shown to increase long-term graft and patient survival for all ages[39], and this is particularly true for elderly patients[25]. There is, however, a dichotomy between the need for early transplants in the elderly population and longer deceased donor waiting times. Having a living donor available can facilitate early transplantation, ideally pre-emptively. Many older recipients are reluctant to accept organs from younger donors; therefore, with the increase in older patients with end-stage renal disease, a parallel increase in the number of older donors has been observed. Most guidelines do not state an upper age limit for kidney donors *per se*[40–42], but there is sometimes a reluctance to accept older donors as they are deemed at higher risk of postoperative complications[42]. As well as presenting an unacceptable risk for the donor, this may also negatively impact a whole donor programme in the event of an operative death. Nevertheless, living donation from donors up to the age of 90 years has been reported in the literature[43].

Ahmadi and colleagues[44] systematically reviewed the evidence for the effect of age on postoperative complications and mortality in living donor nephrectomies. The most comprehensive study to date is a registry study by Segev *et al.*[45], who examined mortality in a registry of more than 80 000 living donors, and found no significant differences in perioperative surgical mortality in those aged over 60 years compared with younger donors. Although long-term mortality was higher in the older donors than younger one, there was no difference in survival compared with that of a matched healthy non-donor control group. Other studies[46,47] have also examined the incidence of postoperative complications and reported no differences between age groups. Interestingly, when quality of life was examined, elderly donors scored higher than younger patients at 1 and 3 months after surgery[48], and were more satisfied with the cosmetic outcome than younger donors[49]. Overall, there is no evidence at the moment that precludes kidney donation over the age of 60 or even 70 years[50].

Clearly it is important to assess living donors thoroughly to exclude co-existing risk factors such as hypertension, diabetes and ischaemic heart disease.

Outcomes following transplant of organs from older donors are excellent, but remain inferior to transplantation from younger donors[50–52]. Kerr and colleagues[51] conducted a univariable analysis of 1126 consecutive transplants, and demonstrated that graft survival of kidneys from older living donors, although inferior to that of organs from younger living donors, was better than survival of deceased donor kidneys from older donors, and comparable to that of kidneys from deceased younger donors. Interestingly, in one study[52] the incidence of acute rejection was significantly higher in recipients of grafts from living donors over 65 years old; however, if recipients did not experience an incidence of acute rejection, graft survival was not affected by donor age.

Immunosuppression in the elderly

For all transplant recipients, immunosuppression is a balance of preventing rejection while minimizing the increased risks of infection and malignancy. It has long been recognized that elderly patients are relatively immunocompromised and therefore may need less immunosuppression[53]. It has also been shown that elderly recipients have lower rates of acute rejection and also have a higher incidence of infection after transplantation[54]. It has therefore been suggested that reduced immunosuppression in the elderly may be appropriate, especially as they have a higher risk of malignancy[55].

Ageing causes a decline in the function of cellular components of the adaptive immune system, and animal studies have shown reduced adaptive immune responses with age[56,57]. The elderly have reduced T and B cell responses to new antigens, as demonstrated by reduced responses to vaccination[58,59]. However, although a number of large registry studies[60–62] have shown a reduction in acute rejection in elderly recipients, other studies[27,63,64] have contradicted this. In particular, when elderly donors receive an elderly kidney, as in the Eurotransplant Senior Programme, there is a higher incidence of acute rejection[27]. Certainly, experimental evidence suggests that alloreactive T cell responses are enhanced against older grafts compared with younger and better preserved grafts[65]. It is, therefore, not possible to have a generic protocol that reduces immunosuppression for all elderly recipients. However, tailoring and reducing immunosuppression in the elderly over time will reduce the incidence of infection and malignancy, and potentially increase patient survival.

Liver transplantation

Donation after brain death

In contrast to end-stage renal disease, where dialysis offers an alternative to transplantation, liver transplant remains the only treatment option for patients with end-stage liver disease. The increasing age in donors worldwide has led to the use of increasingly elderly donor livers. Whereas there is a clear measurable decline in the glomerular filtration rate in elderly kidneys[66], the decline in function in elderly livers is less clear. It is known that liver weight decreases with age[67]. However, elderly livers maintain their functional reserve and regenerative capacity[68,69]. Although there may be a reduction in the rate of regeneration, the aged liver retains the capacity to restore itself to its original size[70]. Livers from donors aged over 70 years are much more likely to be discarded[71,72]. However, a number of registry analyses and case series have now shown acceptable outcomes with livers from donors over 70 years old and from donors aged more than 80 years[69,73–83] (*Table 1*). Some of these studies have reported results equivalent to those obtained using standard criteria livers. The key to achieving good results with older livers is minimization of other risk factors. Donor risk factors that can be controlled include cold ischaemia time, body mass index and steatosis. Although there is experimental evidence suggesting that elderly livers are not more susceptible to ischaemia–reperfusion injury[84], some studies[78,81] have shown that older livers have a greater incidence of ischaemic-type injuries such cholangiopathy. Furthermore, use of livers with cold ischaemia times of more than 12 h is associated with poorer outcomes[85]. Therefore, if cold ischaemia times can be minimized, outcomes for older donor livers can be improved. Indeed, in all the case series that used donors aged over 70 and 80 years, cold ischaemia times were kept low (5–9 h)[69,72–83]. Steatotic livers are also much more susceptible to ischaemia–reperfusion injury[86], and there is a higher incidence of steatosis in elderly livers[87]. Therefore, it is important to avoid older donor livers in patients with a high body mass index and macroscopic steatosis. There are also recipient factors that affect outcome with older livers. Patients with hepatitis C transplanted with older livers do poorly[88,89], and, in contrast with renal transplantation where 'old for old' programmes have been initiated, old livers in old recipients are associated with inferior outcomes[84]. Equally, older livers are not suitable for very young recipients. Segev and colleagues[73] demonstrated that modification of recipient factors can determine outcome in extended criteria donor liver transplantation. There were no differences in graft outcome whether

Table 1 Outcomes following liver transplantation with donors aged over 70 years

Reference	No. of patients	Donor age (years)*	Primary non-function (%)	Graft survival (%)			Patient survival (%)		
				1 year	3 years	5 years	1 year	3 years	5 years
Kim *et al.*[74]	25	74	8	83	72	–	95	90	–
Lai *et al.*[77]	28	74	3·6	41	–	–	47	–	–
Gastaca *et al.*[78]	55	> 70	0	93	90	–	94	91	–
Borchert *et al.*[79]	41	73·4	2·4	86	81	75	91	83	77
Segev *et al.*[73]	1043	74·8	–	–	74·9	–	–	81·2	–
Darius *et al.*[82]	58	77	0	88	–	79	90	–	84
Jiménez Romero *et al.*[69]	50	75·7	0	74	65	58	76	–	63
Ghinolfi *et al.*[83]	233	70–79	3	87·6	78·9	75·1	91	82·8	79
Cescon *et al.*[76]	111	70–79	7	–	62	62	–	68	66
Nardo *et al.*[81]	30	82·3	0	77	–	–	80	–	–
Ghinolfi *et al.*[83]	85	> 80	0	85	77	77	86	78	78
Cescon *et al.*[76]	41	> 80	0	–	81	81	–	86	86
Singhal *et al.*[75]	197	> 80	–	75·5	61·2	–	81	69·1	–

*Values are mean or range.

patients received livers from donors over 70 years old or aged less than 39 years, when the following criteria were met: no acute liver failure or hepatitis C, first transplant, age less than 45 years, body mass index below 35 kg/m^2 and cold ischaemia time less than 8 h.

Donation after circulatory death

Although DCD livers are not available in all countries, they have become a valuable source of additional organs, especially in places such as the Netherlands and the UK, where DCD donation represents nearly 50 per cent of all deceased donation; similar figures are seen in other European countries[7,8]. In the USA, there are fewer DCD donors (21 per cent) but the number is likely to increase[6]. Whereas 83 per cent of DBD livers retrieved are subsequently transplanted, only 27 per cent of livers recovered from DCD donors are transplanted in the UK[8]. Allografts obtained from DCD donors are known to have poorer outcomes than those from DBD donors[90]. This is due to the initial exposure to warm ischaemia, which is known to aggravate organ injury[91]. De Vera and co-workers[92] reported that 1-, 5- and 10-year graft survival rates were significantly lower in DCD (69, 56 and 44 per cent respectively) than DBD (82, 73 and 63 per cent) liver recipients. Primary non-function and biliary complications were more common in those who received DCD organs, accounting for 67 per cent of early graft failures. Importantly, donor age above 60 years was associated with poorer DCD outcomes, along with donor warm and cold ischaemia times. UK guidelines[93] currently recommend that the ideal age for DCD donors is less than 50 years. This guideline is supported by a Dutch multicentre study[94], which used restricted criteria of donors age less than 50 years. One- and 3-year patient survival rates were similar for DCD (85 and 80 per cent) and DBD (86·3 and 80·8 per cent) transplants, as were graft survival rates (74 and 68 per cent *versus* 80·4 and 74·5 per cent). In a series of 70 DCD liver transplants, Detry *et al.*[95] found no difference in graft survival or complications in recipients of livers from DCD donors aged 70 years or over *versus* younger donors. They attributed the successful outcome in older DCD donors to the short initial warm ischaemia time and short cold ischaemia times. These results suggest, as with DBD donors, that good function can be gained from older donor livers if other risk factors are minimized.

Living donation

Living donor liver transplantation, an alternative to deceased donor liver transplantation, has become the mainstream treatment in Asia because there are very few deceased donor liver grafts[96]. The use of older living donors has increased, but the numbers of donors aged over 60 years remains very limited[97,98]. The use of elderly donors is controversial because of increased risk to the donors as well as the potential poorer recipient outcomes. Although some studies[99,100] have shown satisfactory results using older live donors, others[98,101,102] have reported primary non-function and low graft survival rates. Furthermore, older donors are at higher risk of major complications[102]. Although around the world there have been isolated reports of live donors over 70 years old[103], this is not common practice, and in the USA donor age is limited to under 60 years[102].

Older liver recipients

A number of publications[104–108] have examined liver transplantation in elderly recipients. Although some have

reported very poor outcomes[105], others have noted excellent outcomes[107]. There is now a greater recognition that age in itself is not a good measure of suitability for a liver transplant recipient. Physiological age, as far as one can measure it, is more relevant. A relatively fit 65-year-old can expect to live for another 15–20 years and so liver transplantation is a viable option. Furthermore, vigorous assessment of liver transplant recipients, using cardiovascular screening, precludes a number of unsuitable elderly recipients[106]. Using this approach, outcomes are similar between older and younger recipients. Cross and colleagues[109] compared the outcomes of recipients aged 60–64 years, at least 65 years and less than 60 years at the time of transplantation, and found no difference in graft and patient survival for all three groups at 30 days, 1 year and 5 years after transplantation. However, it should be noted that the Model for End-stage Liver Disease (MELD) scores were lower for patients aged over 65 years, and there were fewer patients with hepatitis C and more patients with primary biliary cirrhosis; these factors are known to be associated with improved outcomes. Another study[110] demonstrated that, with appropriately screened older recipients, there was no difference in 10-year survival between transplant recipients aged over 70 years and a cohort of younger patients. The authors also proposed that measures of physiological age and risk of complications should be used in the evaluation process of elderly transplant candidates, and that age by itself should not be a limitation to liver transplantation.

Ethical considerations for using extended criteria donor organs

For each organ offer there is a balance between the risks and benefits of remaining on the transplant waiting list compared with those of accepting that particular donor organ. Although allocation schemes offer an organ to a particular recipient, ultimately the decision to accept an organ is made by the transplant physician and surgeon. Currently, allocation schemes do not formally take into account the wishes of the potential recipient. One of the only studies to examine this found that patients disagreed with a number of aspects of current allocation systems, as they do not factor in individual preferences[111]. The authors also considered that the patients received very little information on donor characteristics. Current best practice is to obtain consent from patients at the time of listing, update this on an annual basis, and confirm consent at time of transplantation[112]. At the time of listing it is possible to gain consent from patients for potential extended criteria donor organs, and a number of units do this in order to avoid accepting an organ that a patient may not consent to being transplanted. A European study[113] found that 23 of 28 centres that accepted extended criteria livers specifically informed the recipients of the increased risks. Of those that did, 43 per cent obtained consent at listing, 14 per cent at the time of surgery, and 43 per cent at listing and at the time of surgery.

As the number of older donors increases, patient preferences may need to be incorporated into allocation systems[111] to avoid the acceptance and subsequent decline of organs, which may lead to organ wastage. To give valid consent, the potential transplant recipient needs to be informed of the risks and benefits of receiving an older donor organ, as outlined in this review. Consent may also be aided by the use of objective donor risk indices[35,36].

Future developments

The increasing use of older donor organs has led the transplant community to examine strategies for improving organ quality, and improving short- and long-term function, allowing more organs to be transplanted. Machine perfusion of donor organs is being explored as a means of both assessing organ viability and potentially improving organ function. Machine perfusion of donor organs is not a new technology; extracorporeal machine perfusion was first used by Marchioro and colleagues[114] in 1963. However, at that time these machines were expensive and cumbersome. With the advent of better and cheaper storage solutions, such as University of Wisconsin fluid, static cold storage became the universal preservation technique. The use of machine perfusion is now being re-evaluated, with a view to expanding the donor pool in the future by using more extended criteria organs and organs procured from DCD donors.

Cold machine perfusion has been used in clinical practice for preservation of kidneys for some time, and has been shown to improve outcomes in DBD and DCD donor kidneys[115]. However, it has been postulated that hypothermic oxygenated perfusion may confer superior protection and this is currently being evaluated as part of a randomized clinic trial[116]. Hypothermic oxygenated perfusion has also been demonstrated to recondition livers in the experimental setting[117].

Normothermic regional perfusion in DCD donors uses an extracorporeal circuit to recirculate warm oxygenated blood for a period after circulatory arrest. Early clinical experience using this technique in DCD suggests an increase in the recovery rates of extra-renal organs, with good initial function and a reduction in delayed graft function in kidneys[118].

Normothermic machine perfusion of individual organs with warm oxygenated blood has been shown in the experimental setting to resuscitate and improve function of both kidneys and livers, and early clinical results have been encouraging[119–121]. Machine perfusion of an organ also has the potential to include other therapies such as immune therapies, pharmacological treatments[122] and stem cell therapies[123].

All of these machine perfusion techniques are now the subject of randomized trials to evaluate the optimal methods for preserving and reconditioning donor organs. Indeed, the landscape of organ retrieval, organ preservation and transplantation is changing rapidly and, as the number of elderly donors increases, the use of machine perfusion for organ preservation is likely to become common practice.

In addition to strategies for reconditioning of donor organs using machine perfusion, other innovations to combat ischaemia–reperfusion injury are currently being evaluated in randomized clinical trials, such as ischaemic conditioning[124,125], pharmacological conditioning (using complement regulatory drugs or calcineurin inhibitors) and cell-based therapies in recipients (ONE study)[126].

Older donors and older recipients have become a clinical reality in transplantation. In live donor kidney transplantation, good results can be obtained for older donors as well as older recipients. For deceased donor liver and kidney transplantation, translational studies have led to innovative ways to recondition organs from older donors, as well as to improve the suitability of 'marginal' recipients. Allocation schemes have been developed to determine the best combination of older donor organs for older transplant recipients. The future is bright for reconditioning and regenerative approaches in clinical transplantation, especially in the era of an ageing population.

Disclosure

The authors declare no conflict of interest.

References

1 Port FK, Bragg-Gresham JL, Metzger RA, Dykstra DM, Gillespie BW, Young EW *et al*. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. *Transplantation* 2002; **74**: 1281–1286.

2 Wadei HM, Heckman MG, Rawal B, Burcin Taner C, Farahat W, Nur L *et al*. Comparison of kidney function between donation after cardiac death and donation after brain death kidney transplantation. *Transplantation* 2013; **96**: 274–281.

3 Busuttil RW, Tanaka K. The utility of marginal donors in liver transplantation. *Liver Transpl* 2003; **9**: 651–663.

4 Amin MG, Wolf MP, TenBrook JA Jr, Freeman RB Jr, Cheng SJ, Pratt DS *et al*. Expanded criteria donor grafts for deceased donor liver transplantation under the MELD system: a decision analysis. *Liver Transpl* 2004; **10**: 1468–1475.

5 Van der Vliet JA, Persijn GG, Kootstra G. Should the upper age limit for cadaveric kidney donors be changed? *Proc Eur Dial Transplant Assoc* 1981; **18**: 439–445.

6 US Department of Health and Human Services. *Organ Procurement and Transplantation Network. Data.* http://optn.transplant.hrsa.gov/converge/latestData/rptData.asp [accessed 12 November 2015].

7 Eurotransplant. *Statistics Report Library*. http://statistics.eurotransplant.org/ [accessed 1 October 2015].

8 NHS Blood and Transplant. Annual Activity Report. http://www.odt.nhs.uk/uk-transplant-registry/annual-activity-report/ [accessed 12 November 2015].

9 Neugebauer H, Heuschmann PU, Jüttler E. DEcompressive Surgery for the Treatment of malignant INfarction of the middle cerebral arterY – Registry (DESTINY-R): design and protocols. *BMC Neurol* 2012; **12**: 115.

10 Casavilla A, Ramirez C, Shapiro R, Nghiem D, Miracle K, Bronsther O *et al*. Experience with liver and kidney allografts from non-heart-beating donors. *Transplantation* 1995; **59**: 197–203.

11 Selck FW, Grossman EB, Ratner LE, Renz JF. Utilization, outcomes, and retransplantation of liver allografts from donation after cardiac death: implications for further expansion of the deceased-donor pool. *Ann Surg* 2008; **248**: 599–607.

12 Moers C, Leuvenink HG, Ploeg RJ. Non-heart beating organ donation: overview and future perspectives. *Transpl Int* 2007; **20**: 567–575.

13 Snoeijs MG, Schaefer S, Christiaans MH, van Hooff JP, van den Berg-Loonen PM, Peutz-Kootstra CJ *et al*. Kidney transplantation using elderly non-heart-beating donors: a single-center experience. *Am J Transplant* 2006; **6**: 1066–1071.

14 Escartin A, Castro E, Dopazo C, Bueno J, Bilbao I, Margarit C. Analysis of discarded livers for transplantation. *Transplant Proc* 2005; **37**: 3859–3860.

15 Sayuk GS, Leet TL, Schnitzler MA, Hayashi PH. Nontransplantation of livers from deceased donors who are able to donate another solid organ: how often and why it happens. *Am J Transplant* 2007; **7**: 151–160.

16 Remuzzi G, Cravedi P, Perna A, Dimitrov BD, Turturro M, Locatelli G *et al*. Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006; **354**: 343–352.

17 www.parliament.uk. *A Century of Change: Trends in UK Statistics Since 1900.* House of Commons Library Research Paper 99/111. http://researchbriefings.parliament.uk/

ResearchBriefing/Summary/RP99-111#fullreport [accessed 12 November 2015].
18 Hariharan S, Johnson C, Bresnahan B, Taranto SE, McIntosh MJ, Stablein D *et al*. Improved graft survival after renal transplantation in the United States, 1988 to 1996. *N Engl J Med* 2000; **342**: 605–612.
19 Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY *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.
20 Rao PS, Merion RM, Ashby VB, Port FK, Wolfe RA, Kayler LK. Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007; **83**: 1069–1074.
21 Dempster NJ, Ceresa CD, Aitken E, Kingsmore D. Outcomes following renal transplantation in older people: a retrospective cohort study. *BMC Geriatr* 2013; **13**: 79.
22 Oniscu GC, Brown H, Forsythe JLR. How great is the survival advantage of transplantation over dialysis in elderly patients? *Nephrol Dial Transplant* 2004; **19**: 945–951.
23 Morris PJ, Johnson RJ, Fuggle SV, Belger MA, Briggs JD. Analysis of factors that affect outcome of primary cadaveric renal transplantation in the UK. *Lancet* 1999; **354**: 1147–1152.
24 Schold JD, Srinivas TR, Sehgal AR, Meier-Kriesche HU. Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. *Clin J Am Soc Nephrol* 2009; **4**: 1239–1245.
25 Ojo AO, Hanson JA, Meier-Kriesche H, Okechukwu CN, Wolfe RA, Leichtman AB *et al*. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001; **12**: 589–597.
26 De Fijter JW. An old virtue to improve senior programs. *Transpl Int* 2009; **22**: 259–268.
27 Frei U, Noeldeke J, Machold-Fabrizii V, Arbogast H, Margreiter R, Fricke L *et al*. Prospective age-matching in elderly kidney transplant recipients – a 5-year analysis of the Eurotransplant Senior Program. *Am J Transplant* 2008; **8**: 50–57.
28 Fabrizii V, Kovarik J, Bodingbauer M, Kramar R, Hörl WH, Winkelmayer WC. Long-term patient and graft survival in the Eurotransplant Senior Program: a single center experience. *Transplantation* 2005; **80**: 582–589.
29 Giessing M, Fuller TF, Friedersdorff F, Deger S, Wille A, Neumayer HH *et al*. Outcomes of transplanting deceased-donor kidneys between elderly donors and recipients. *J Am Soc Nephrol* 2009; **20**: 37–40.
30 Boesmueller C, Biebl M, Scheidl S, Oellinger R, Margreiter C, Pratschke J *et al*. Long-term outcome in kidney transplant recipients over 70 years in the Eurotransplant Senior Kidney Transplant Program: a single center experience. *Transplantation* 2011; **92**: 210–216.
31 Sener A, Schweitzer EJ, Munivenkatappa R, Cooper M, Bartlett ST, Philosophe B *et al*. Deceased-donor renal transplantation in the geriatric population demonstrates equal graft survival compared with younger recipients. *Transplantation* 2009; **87**: 1549–1554.
32 Dusseux E, Albano L, Fafin C, Hourmant M, Guérin O, Couchoud C *et al*. A simple clinical tool to inform the decision-making process to refer elderly incident dialysis patients for kidney transplant evaluation. *Kidney Int* 2015; **88**: 121–129.
33 McAdams-DeMarco MA, Law A, Salter ML, Chow E, Grams M, Walston J *et al*. Frailty and early hospital readmission after kidney transplantation. *Am J Transplant* 2013; **13**: 2091–2095.
34 Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J *et al*. Frailty in older adults: evidence for a phenotype. *J Gerontol A* 2001; **56**: M146–M156.
35 Rao PS, Schaubel DE, Guidinger MK, Andreoni KA, Wolfe RA, Merion RM *et al*. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. *Transplantation* 2009; **88**: 231–236.
36 Watson CJE, Johnson RJ, Birch R, Collett D, Bradley JA. A simplified donor risk index for predicting outcome after deceased donor kidney transplantation. *Transplantation* 2012; **93**: 314–318.
37 Remuzzi G, Cravedi P, Perna A, Dimitrov BD, Turturro M, Locatelli G *et al*. Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006; **354**: 343–352.
38 Aubert O, Kamar N, Vernerey D, Viglietti D, Martinez F, Duong-Van-Huyen JP *et al*. Long term outcomes of transplantation using kidneys from expanded criteria donors: prospective, population based cohort study. *BMJ* 2015; **351**: h3557.
39 Mange KC, Joffe MM, Feldman HI. Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. *N Engl J Med* 2001; **344**: 726–731.
40 Lennerling A, Lovén C, Dor FJ, Ambagtsheer F, Duerinckx N, Frunza M *et al*. Living organ donation practices in Europe – results from an online survey. *Transpl Int* 2012; **26**: 145–153.
41 Klop KW, Dols LF, Kok NF, Weimar W, Ijzermans JN. Attitudes among surgeons towards live-donor nephrectomy: a European update. *Transplantation* 2012; **94**: 263–268.
42 Andrews PA, Burnapp L, Manas D, Bradley JA, Dudley C; British Transplantation Society; Renal Association. Summary of the British Transplantation Society/Renal Association UK guidelines for living donor kidney transplantation. *Transplantation* 2012; **93**: 666–673.
43 Dols LF, Kok NF, Roodnat JI, Tran TC, Terkivatan T, Zuidema WC *et al*. Living kidney donors: impact of age on long-term safety. *Am J Transplant* 2011; **11**: 737–742.

44 Ahmadi AR, Lafranca JA, Claessens LA, Imamdi RM, IJzermans JN, Betjes MG *et al.* Shifting paradigms in eligibility criteria for live kidney donation: a systematic review. *Kidney Int* 2015; **87**: 31–45.

45 Segev DL, Muzaale AD, Caffo BS, Mehta SH, Singer AL, Taranto SE *et al.* Perioperative mortality and long-term survival following live kidney donation. *JAMA* 2010; **303**: 959–966.

46 O'Brien B, Mastoridis S, Sabharwal A, Hakim N, Taube D, Papalois V *et al*. Expanding the donor pool: living donor nephrectomy in the elderly and the overweight. *Transplantation* 2012; **93**: 1158–1165.

47 Jacobs SC, Ramey JR, Sklar GN, Bartlett ST. Laparoscopic kidney donation from patients older than 60 years. *J Am Coll Surg* 2004; **198**: 892–897.

48 Klop KW, Dols LF, Weimar W, Dooper IM, IJzermans JN, Kok NF. Quality of life of elderly live kidney donors. *Transplantation* 2013; **96**: 644–648.

49 Klop KW, Hussain F, Karatepe O, Kok NF, Ijzermans JN, Dor FJ. Incision-related outcome after live donor nephrectomy: a single-center experience. *Surg Endosc* 2013; **27**: 2801–2806.

50 Berger JC, Muzaale AD, James N, Hoque M, Wang JM, Montgomery RA *et al*. Living kidney donors ages 70 and older: recipient and donor outcomes. *Clin J Am Soc Nephrol* 2011; **6**: 2887–2893.

51 Kerr SR, Gillingham KJ, Johnson EM, Matas AJ. Living donors > 55 years: to use or not to use? *Transplantation* 1999; **67**: 999–1004.

52 Øien CM, Reisæter AV, Leivestad T, Dekker FW, Line PD, Os I. Living donor kidney transplantation: the effects of donor age and gender on short- and long-term outcomes. *Transplantation* 2007; **83**: 600–606.

53 Ismail N, Hakim RM, Helderman JH. Renal replacement therapies in the elderly: Part II. *Renal transplantation. Am J Kidney Dis* 1994; **23**: 1–15.

54 Hestin D, Frimat L, Hubert J, Renoult E, Huu TC, Kessler M. Renal transplantation in patients over sixty years of age. *Clin Nephrol* 1994; **42**: 232–236.

55 Bachireddy P, Rakhra K, Felsher DW. Immunology in the clinic review series; focus on cancer: multiple roles for the immune system in oncogene addiction. *Clin Exp Immunol* 2012; **167**: 188–194.

56 Koch S, Larbi A, Derhovanessian E, Ozcelik D, Naumova E, Pawelec G. Multiparameter flow cytometric analysis of CD4 and CD8 T cell subsets in young and old people. *Immun Ageing* 2008; **5**: 6.

57 Yager EJ, Ahmed M, Lanzer K, Randall TD, Woodland DL, Blackman MA. Age-associated decline in T cell repertoire diversity leads to holes in the repertoire and impaired immunity to influenza virus. *J Exp Med* 2008; **205**: 711–723.

58 Frasca D, Blomberg BB. Effects of aging on B cell function. *Curr Opin Immunol* 2009; **21**: 425–430.

59 Larbi A, Pawelec G, Wong SC, Goldeck D, Tai JJ, Fulop T. Impact of age on T cell signaling: a general defect or specific alterations? *Ageing Res Rev* 2011; **10**: 370–378.

60 Tullius SG, Milford E. Kidney allocation and the aging immune response. *N Engl J Med* 2011; **364**: 1369–1370.

61 Tullius SG, Tran H, Guleria I, Malek SK, Tilney NL, Milford E *et al.* The combination of donor and recipient age is critical in determining host immunoresponsiveness and renal transplant outcome. *Ann Surg* 2010; **252**: 662–674.

62 Cecka JM. The OPTN/UNOS renal transplant registry. *Clin Transpl* 2005: **1–16**.

63 Pratschke J, Merk V, Reutzel-Selke A, Pascher A, Denecke C, Lun A *et al*. Potent early immune response after kidney transplantation in patients of the European senior transplant program. *Transplantation* 2009; **87**: 992–1000.

64 Lim WH, Dogra G, Chadban SJ, Campbell SB, Clayton P, Cohney S *et al*. Lack of impact of donor age on patient survival for renal transplant recipients ≥ 60 years. *Transpl Int* 2012; **25**: 401–408.

65 Slegtenhorst BR, Dor FJ, Elkhal A, Rodriguez H, Yang X, Edtinger K *et al*. Mechanisms and consequences of injury and repair in older organ transplants. *Transplantation* 2014; **97**: 1091–1099.

66 Wetzels JF, Kiemeney LA, Swinkels DW, Willems HL, den Heijer M. Age- and gender-specific reference values of estimated GFR in Caucasians: the Nijmegen Biomedical Study. *Kidney Int* 2007; **72**: 632–637.

67 James OF. Gastrointestinal and liver function of old age. *Clin Gastroenterol* 1983; **12**: 671–691.

68 Wynne HA, James OF. The ageing liver. *Age Ageing* 1990; **19**: 1–3.

69 Jiménez Romero C, Moreno González E, Colina Ruíz F, Palma Carazo F, Loinaz Segurola C, Rodríguez González F *et al*. Use of octogenarian livers safely expands the donor pool. *Transplantation* 1999; **68**: 572–575.

70 Schmucker DL, Sanchez H. Liver regeneration and aging: a current perspective. *Curr Gerontol Geriatr Res* 2011; **2011**: 526379.

71 Escartin A, Castro E, Dopazo C, Bueno J, Bilbao I, Margarit C. Analysis of discarded livers for transplantation. *Transplant Proc* 2005; **37**: 3859–3860.

72 Sayuk GS, Leet TL, Schnitzler MA, Hayashi PH. Nontransplantation of livers from deceased donors who are able to donate another solid organ: how often and why it happens. *Am J Transplant* 2007; **7**: 151–160.

73 Segev DL, Maley WR, Simpkins CE, Locke JE, Nguyen GC, Montgomery RA *et al*. Minimizing risk associated with elderly liver donors by matching to preferred recipients. *Hepatology* 2007; **46**: 1907–1918.

74 Kim DY, Cauduro SP, Bohorquez HE, Ishitani MB, Nyberg SL, Rosen CB. Routine use of livers from deceased donors older than 70: is it justified? *Transpl Int* 2005; **18**: 73–77.

75 Singhal A, Sezginsoy B, Ghuloom AE, Hutchinson IV, Cho YW, Jabbour N. Orthotopic liver transplant using

allografts from geriatric population in the United States: is there any age limit? *Exp Clin Transplant* 2010; **8**: 196–201.
76 Cescon M, Grazi GL, Cucchetti A, Ravaioli M, Ercolani G, Vivarelli M *et al*. Improving the outcome of liver transplantation with very old donors with updated selection and management criteria. *Liver Transpl* 2008; **14**: 672–679.
77 Lai Q, Melandro F, Levi Sandri GB, Mennini G, Corradini SG, Merli M *et al*. Use of elderly donors for liver transplantation: has the limit been reached? *J Gastrointest Liver Dis* 2011; **20**: 383–387.
78 Gastaca M, Valdivieso A, Pijoan J, Errazti G, Hernandez M, Gonzalez J *et al*. Donors older than 70 years in liver transplantation. *Transplant Proc* 2005; **37**: 3851–3854.
79 Borchert D, Glanemann M, Mogl M, Langrehr JM, Neuhaus P. Older liver graft transplantation, cholestasis and synthetic graft function. *Transpl Int* 2005; **18**: 709–715.
80 Borchert DH, Glanemann M, Mogl M, Langrehr J, Neuhaus P. Adult liver transplantation using liver grafts from donors over 70 years of age. *Transplant Proc* 2005; **37**: 1186–1187.
81 Nardo B, Masetti M, Urbani L, Caraceni P, Montalti R, Filipponi F *et al*. Liver transplantation from donors aged 80 years and over: pushing the limit. *Am J Transplant* 2004; **4**: 1139–1147.
82 Darius T, Monbaliu D, Jochmans I, Meurisse N, Desschans B, Coosemans W *et al*. Septuagenarian and octogenarian donors provide excellent liver grafts for transplantation. *Transplant Proc* 2012; **44**: 2861–2867.
83 Ghinolfi D, Marti J, De Simone P, Lai Q, Pezzati D, Coletti L *et al*. Use of octogenarian donors for liver transplantation: a survival analysis. *Am J Transplant* 2014; **14**: 2062–2071.
84 Le Couteur DG, Rivory LP, Pond SM. The effects of aging and nutritional state on hypoxia–reoxygenation injury in the perfused rat liver. *Transplantation* 1994; **58**: 531–536.
85 Cassuto JR, Patel SA, Tsoulfas G, Orloff MS, Abt PL. The cumulative effects of cold ischemic time and older donor age on liver graft survival. *J Surg Res* 2008; **148**: 38–44.
86 Garcia Ureña MA, Colina Ruiz-Delgado F, Moreno González E, Jiménez Romero C, García García I, Loinzaz Segurola C *et al*. Hepatic steatosis in liver transplant donors: common feature of donor population? *World J Surg* 1998; **22**: 837–844.
87 D'Alessandro AM, Kalayoglu M, Sollinger HW, Hoffmann RM, Reed A, Knechtle SJ *et al*. The predictive value of donor liver biopsies for the development of primary non-function after orthotopic liver transplantation. *Transplantation* 1991; **51**: 157–163.
88 Berenguer M, Prieto M, San Juan F, Rayón JM, Martinez F, Carrasco D *et al*. Contribution of donor age to the recent decrease in patient survival among HCV-infected liver transplant recipients. *Hepatology* 2002; **36**: 202–210.
89 Wali M, Harrison RF, Gow PJ, Mutimer D. Advancing donor liver age and rapid fibrosis progression following transplantation for hepatitis C. *Gut* 2002; **51**: 248–252.
90 Casavilla A, Ramirez C, Shapiro R, Nghiem D, Miracle K, Bronsther O *et al*. Experience with liver and kidney allografts from non-heart-beating donors. *Transplantation* 1995; **59**: 197–203.
91 Reddy SP, Bhattacharjya S, Maniakin N, Greenwood J, Guerreiro D, Hughes D *et al*. Preservation of porcine non-heart-beating donor livers by sequential cold storage and warm perfusion. *Transplantation* 2004; **77**: 1328–1332.
92 de Vera ME, Lopez-Solis R, Dvorchik I, Campos S, Morris W, Demetris AJ *et al.* Liver transplantation using donation after cardiac death donors: long-term follow-up from a single center. *Am J Transplant* 2009; **9**: 773–781.
93 British Transplantation Society. *United Kingdom Guidelines: Transplantation From Donors After Deceased Circulatory Death*. http://www.bts.org.uk/Documents/FINAL%20July%202013%20DCD%20guidelines.pdf [accessed 12 November 2015].
94 Dubbeld J, Hoekstra H, Farid W, Ringers J, Porte RJ, Metselaar HJ *et al*. Similar liver transplantation survival with selected cardiac death donors and brain death donors. *Br J Surg* 2010; **97**: 744–753.
95 Detry O, Deroover A, Meurisse N, Hans MF, Delwaide J, Lauwick S *et al*. Donor age as a risk factor in donation after circulatory death liver transplantation in a controlled withdrawal protocol programme. *Br J Surg* 2014; **101**: 784–792.
96 Han JH, You YK, Na GH, Kim EY, Lee SH, Hong TH *et al*. Outcomes of living donor liver transplantation using elderly donors. *Ann Surg Treat Res* 2014; **86**: 184–191.
97 Li C, Wen TF, Yan LN, Li B, Yang JY, Xu MQ *et al*. Safety of living donor liver transplantation using older donors. *J Surg Res* 2012; **178**: 982–987.
98 Yoshizumi T, Shirabe K, Soejima Y, Taketomi A, Yamashita N, Ikegami T *et al*. Living donor liver transplantation in patients older than 60 years. *Transplantation* 2010; **90**: 433–437.
99 Ikegami T, Nishizaki T, Yanaga K, Shimada M, Kishikawa K, Nomoto K *et al*. The impact of donor age on living donor liver transplantation. *Transplantation* 2000; **70**: 1703–1707.
100 Grazi GL, Ravaioli M, Zanello M, Ercolani G, Cescon M, Varotti G *et al*. Using elderly donors in liver transplantation. *Transplant Proc* 2005; **37**: 2582–2583.
101 Kuramitsu K, Egawa H, Keeffe EB, Kasahara M, Ito T, Sakamoto S *et al*. Impact of age older than 60 years in living donor liver transplantation. *Transplantation* 2007; **84**: 166–172.
102 Patel S, Orloff M, Tsoulfas G, Kashyap R, Jain A, Bozorgzadeh A *et al*. Living-donor liver transplantation in the United States: identifying donors at risk for perioperative complications. *Am J Transplant* 2007; **7**: 2344–2349.
103 Kim SH, Kim YK, Lee SD, Park SJ. Successful living donor liver transplantation between septuagenarians. *Am J Transplant* 2015; **15**: 274–277.

104 Garcia CE, Garcia RF, Mayer AD, Neuberger J. Liver transplantation in patients over sixty years of age. *Transplantation* 2001; **72**: 679–684.
105 Collins BH, Pirsch JD, Becker YT, Hanaway MJ, Van der Werf WJ, D'Alessandro AM *et al*. Long-term results of liver transplantation in older patients 60 years of age and older. *Transplantation* 2000; **70**: 780–783.
106 Bromley PN, Hilmi I, Tan KC, Williams R, Potter D. Orthotopic liver transplantation in patients over 60 years old. *Transplantation* 1994; **58**: 800–803.
107 Emre S, Mor E, Schwartz ME, Katz E, Acarli K, Fukuzawa K *et al*. Liver transplantation in patients beyond age 60. *Transplant Proc* 1993; **25**: 1075–1076.
108 Sonny A, Kelly D, Hammel JP, Albeldawi M, Zein N, Cywinski JB. Predictors of poor outcome among older liver transplant recipients. *Clin Transplant* 2015; **29**: 197–203.
109 Cross TJ, Antoniades CG, Muiesan P, Al-Chalabi T, Aluvihare V, Agarwal K *et al*. Liver transplantation in patients over 60 and 65 years: an evaluation of long-term outcomes and survival. *Liver Transpl* 2007; **13**: 1382.
110 Lipshutz GS, Hiatt J, Ghobrial RM, Farmer DG, Martinez MM, Yersiz H *et al.* Outcome of liver transplantation in septuagenarians: a single-center experience. *Arch Surg* 2007; **142**: 775–781.
111 Su X, Zenios SA, Chertow GM. Incorporating recipient choice in kidney transplantation. *J Am Soc Nephrol* 2004; **15**: 1656–1663.
112 Bruzzone P. A preliminary European study on extended-criteria liver donation and transplant recipient consent. *Transplant Proc* 2012; **44**: 1857–1858.
113 NHS Blood and Transplant/British Transplant Society. *Guidelines for Consent for Solid Organ Transplantation in Adults*; 2013. http://www.bts.org.uk/Documents/Consent%20Guidance%201%20April%202013.PDF [accessed 12 November 2015].
114 Marchioro TL, Huntley RT, Waddell WR, Starzl TE. Extracorporeal perfusion for obtaining post mortem grafts. *Surgery* 1963; **54**: 900–911.
115 Moers C, Smits JM, Maathuis MH, Treckmann J, van Gelder F, Napieralski BP *et al*. Machine perfusion or cold storage in deceased-donor kidney transplantation. *N Engl J Med* 2009; **360**: 7–19.
116 Minor T, Paul A, Efferz P, Wohlschlaeger J, Rauen U, Gallinat A. Kidney transplantation after oxygenated machine perfusion preservation with Custodiol-N solution. *Transpl Int* 2015; **28**: 1102–1108.
117 Dutkowski P, Schlegel A, de Oliveira M, Müllhaupt B, Neff F, Clavien P-A. HOPE for human liver grafts obtained from donors after cardiac death. *J Hepatol* 2014; **60**: 765–772.
118 Oniscu GC, Randle LV, Muiesan P, Butler AJ, Currie IS, Perera MT *et al*. *In situ* normothermic regional perfusion for controlled donation after circulatory death – the United Kingdom experience. *Am J Transplant* 2014; **14**: 2846–2854.
119 Nicholson ML, Hosgood SA. Renal transplantation after *ex vivo* normothermic perfusion: the first clinical study. *Am J Transplant* 2013; **13**: 1246–1252.
120 Brockmann J, Reddy S, Coussios C, Pigott D, Guirriero D, Hughes D *et al*. Normothermic perfusion: a new paradigm for organ preservation. *Ann Surg* 2009; **250**: 1–6.
121 Ravikumar R, Friend PJ. Human liver transplantation using normothermic machine preservation. *Liver Transplantation* 2014; **20**(Suppl S1): S103.
122 Vogel T, Brockmann JG, Friend PJ. *Ex-vivo* normthermic perfusion: an update. *Curr Opin Organ Transplant* 2010; **15**: 167–172.
123 Van Raemdonck D, Neyrinck A, Rega F, Devos T, Pirenne J. Machine perfusion in organ transplantation: a tool *for ex-vivo* graft conditioning with mesenchymal stem cells? *Curr Opin Organ Transplant* 2013; **18**: 24–33.
124 Krogstrup NV, Oltean M, Bibby BM, Nieuwenhuijs-Moeke GJ, Dor FJ, Birn H *et al*. Remote ischaemic conditioning on recipients of deceased renal transplants, effect on immediate and extended kidney graft function: a multicentre, randomised controlled trial protocol. *BMJ Open* 2015; **5**: e007941.
125 Kierulf-Lassen C, Nieuwenhuijs-Moeke GJ, Krogstrup NV, Oltean M, Jespersen B, Dor FJ. Molecular mechanisms of renal ischemic conditioning strategies. *Eur Surg Res* 2015; **55**: 151–183.
126 Geissler EK. The ONE Study compares cell therapy products in organ transplantation: introduction to a review series on suppressive monocyte-derived cells. *Transplant Res* 2012; **1**: 11.