Shifting paradigms in eligibility criteria for live kidney donation: a systematic review

Ali R. Ahmadi[1,3], Jeffrey A. Lafranca[1,3], Laura A. Claessens[1], Raoul M.S. Imamdi[1], Jan N.M. IJzermans[1], Michiel G.H. Betjes[2] and Frank J.M.F. Dor[1]

[1]Division of Transplant Surgery, Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands and [2]Division of Nephrology, Department of Internal Medicine, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

As the organ shortage increases, inherently the demand for donor kidneys continues to rise. Thus, live kidney donation is essential for increasing the donor pool. In order to create successful expansion, extended criteria live kidney donors should be considered. This review combines current guidelines with all available literature in this field, trying to seek and establish the optimal extended criteria. Comprehensive searches were carried out in major databases until November 2013 to search for articles regarding older age, overweight and obesity, hypertension, vascular anomalies/multiplicity, nulliparous women, and minors as donors. Of the 2079 articles found, 152 fell within the scope of the review. Five major guidelines were included and reviewed. Based on the literature search, live kidney donation in older donors (up to 70 years of age) seems to be safe as outcome is comparable to younger donors. Obese donors have comparable outcome to lean donors, in short- and mid-term follow-up. Since little literature is available proving the safety of donation of hypertensive donors, caution is advised. Vascular multiplicity poses no direct danger to the donor and women of childbearing age can be safely included as donors. Although outcome after donation in minors is shown to be comparable to adult donors, they should only be considered if no other options exist. We conclude that the analyzed factors above should not be considered as absolute contraindications for donation.

Kidney International (2015) **87,** 31–45; doi:10.1038/ki.2014.118; published online 30 April 2014

KEYWORDS: eligibility; extended criteria; live kidney donation; systematic review

Correspondence: *Frank J.M.F. Dor, Division of Transplant Surgery, Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Room H-903, PO BOX 2040, Rotterdam 3000 CA, The Netherlands. E-mail: f.dor@erasmusmc.nl*

[3]These authors are joint first authors.

Received 29 November 2013; revised 6 February 2014; accepted 20 February 2014; published online 30 April 2014

The incidence and prevalence of end-stage renal disease (ESRD) is rising globally as a result of an increased prevalence of hypertension, diabetes, obesity, older age, and other risk factors.[1] The best therapy for patients with ESRD is kidney transplantation. Not only does kidney transplantation reduce the risk of morbidity and mortality, it also improves the quality of life compared with other forms of renal replacement therapy.[2,3] However, the number of deceased donor organs cannot meet the increasing demand.[4] Therefore, live kidney donation has become increasingly important to enlarge the donor pool. Live donor kidney transplantation has superior graft outcome compared with deceased donor kidney transplantation, and is therefore the preferred therapeutic option for ESRD.[5] However, organ shortage remains, as not all transplant candidates have the luxury of a live donor.[4] Since the start of live kidney transplantation in the 1950s, the eligibility criteria for donation have been very strict and many risk factors, such as older age, overweight, obesity, hypertension, and vascular anomalies, were absolute contraindications for donation. During the past decades, there have been enormous developments in kidney donation. Experience with the assessment and evaluation of (potential) donors and technical aspects in this field has increased widely.[6–8] The outcome in donors and in recipients has proven to be excellent, leading to an extension of donor criteria in several transplant centers. Still, the local criteria for accepting live kidney donors vary greatly between transplant centers.[9] Furthermore, considerable variation is observed in the organization of live kidney donor evaluation and the methods of assessment used. With the increasing presence of certain risk factors and the shortage of kidney donors, the transplant community has made efforts to extend donor eligibility criteria to increase the live kidney donor pool. Hence, a shift has occurred in relative and absolute contraindications for live kidney donation.[10] Some contraindications for live donations are indisputable; however, controversy remains on some of the contraindications. The criteria for live kidney donation are elusive and differ worldwide, as well as nationally.[9] Thus, it is up to the transplant community, and the transplant teams in particular, to calculate the individual risk in each potential

live kidney donor and set limits. However, as a consequence, many willing potential kidney donors with comorbidity, so-called 'marginal live kidney donors', or 'extended criteria live kidney donors' are excluded in many transplant centers.

In this review, we searched for available guidelines and combined these to draw conclusions regarding the current attitudes on live kidney donor criteria. Furthermore, we examined available literature and evidence on extended living donor criteria regarding the controversial contraindications, such as older age, overweight and obesity, hypertension, vascular anomalies/multiplicity, women of childbearing age, and minors as donors. However, one must bear in mind that a live kidney donor should not become a patient. Even though technically a donation and successive transplantation might surgically not be a problem, the health of a donor must be the main priority at all times, surgical risks should be avoided at all costs, and good long-term outcome should be warranted.

RESULTS

We included five major available guidelines that are currently available in the field: the consensus statement of the Amsterdam Forum on the Care of the Live Kidney Donor,[11] the Summary of the British Transplantation Society/Renal Association UK guidelines for living donor kidney transplantation,[12] consensus guidelines on eligibility for kidney transplantation of the Canadian Society of Transplantation,[13] the Guidelines on Renal Transplantation by the European Association of Urology,[14] and the living kidney donors guideline Caring for Australasians with Renal Impairment (CARI) on obesity and hypertension were included.[15,16]

We also performed an extensive systematic literature search. Of the 2079 papers found after the initial search, 124 fell within the scope of the review. No additional studies were included after manually scrutinizing the reference lists. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for systematic reviews is presented in Figure 1. The assessment of the quality of the available evidence using the GRADE tool is presented in Figure 2.

Older donor age

Guidelines. No guidelines regarding maximum age for donation are available, nor are these included in the Amsterdam forum consensus in 2004,[11] the Canadian consensus guidelines,[13] and the CARI guidelines.[17] The British guideline states that older age alone is not an absolute contraindication for donation, but that the medical work-up of older donors must be particularly rigorous to ensure suitability. Donors older than 60 years should have a corrected glomerular filtration rate (GFR) of at least 68. This guideline also states that the older donor may have a greater risk of developing perioperative complications. This is particularly true for donors >60 years of age.[12] The Guidelines on Renal Transplantation by the European Association of Urology mention that age limits for organ donation are not currently fixed, but lacks a recommendation for the maximum age for donation.[14]

Literature. Life expectancy in the western population is rapidly increasing. In 2008, 17% of the European Union residents were 65 years or older. It is estimated that the population living in the European Union aged 65 years and older will increase by 70% in 2050, and the number of octogenarians is expected to increase by 170%.[18] This trend will lead to an increase in the incidence and prevalence of ESRD. At the same time, this age group may also be considered a source for live donor kidney transplantation. Raising the maximum age for live kidney donation will result in more donors, but using older donors for live kidney transplantation still remains controversial.

Donors aged 60–70 years

Segev *et al.*[19] observed no significant difference in perioperative mortality for different live kidney donor age groups. Donors aged 50–59 years (hazard ratio (HR) 3.3; 95% confidence interval (CI) 2.6–4.1) and donors aged 60 years or older (HR 9.4; 95% CI 7.3–12.1) were associated with a greater 12-year mortality rate when compared with donors aged 18–39 years (HR 1). However, long-term mortality was similar or lower for live kidney donors in comparison with the healthy matched nondonor control cohort throughout the 12-year follow-up period (1.5 vs. 2.9%; $P<0.001$). Thus, no evidence was found that live kidney donors older than 50 years have an increased risk of mortality after donation. O'Brien *et al.*[20] determined whether acceptance of elderly and obese living kidney donors was associated with a greater perioperative risk and long-term complications. Therefore, kidney donors were divided into groups, consisting of elderly donors, obese donors, elderly and obese donors, and a reference group. O'Brien *et al.* demonstrated no significant differences in operative time, length of hospital stay, estimated blood loss, and rate of early postoperative complications between two groups of older live kidney donors (62.0 ± 1.5 and 68.2 ± 2.6 years) and a reference group of younger live kidney donors (42.3 ± 10.4 years). Renal function parameters showed a significant decrease after donation, but variation between the groups was not significant when compared with the reference group ($P>0.28$). Major complications and mortality rates were absent in the groups. Jacobs *et al.*[21] demonstrated that donor nephrectomy may be performed safely in live kidney donors older than 60 years of age. There were no significant differences between the older (>60 years) and younger (<40 years) live kidney donors with regard to operative time (210.2 ± 51.2 and 201.7 ± 55.1 min, respectively), warm ischemia time (195.6 ± 99.8 and 170.3 ± 95.9 s, respectively), and estimated blood loss (157 ± 266 and 112 ± 121 ml, respectively). Intraoperative and postoperative complication rates were also equivalent between older and younger live kidney donors. In all, 9.5% of donors older than 60 years experienced intraoperative complications, a similar rate as in donors younger than 40 years, according to the authors (21%).

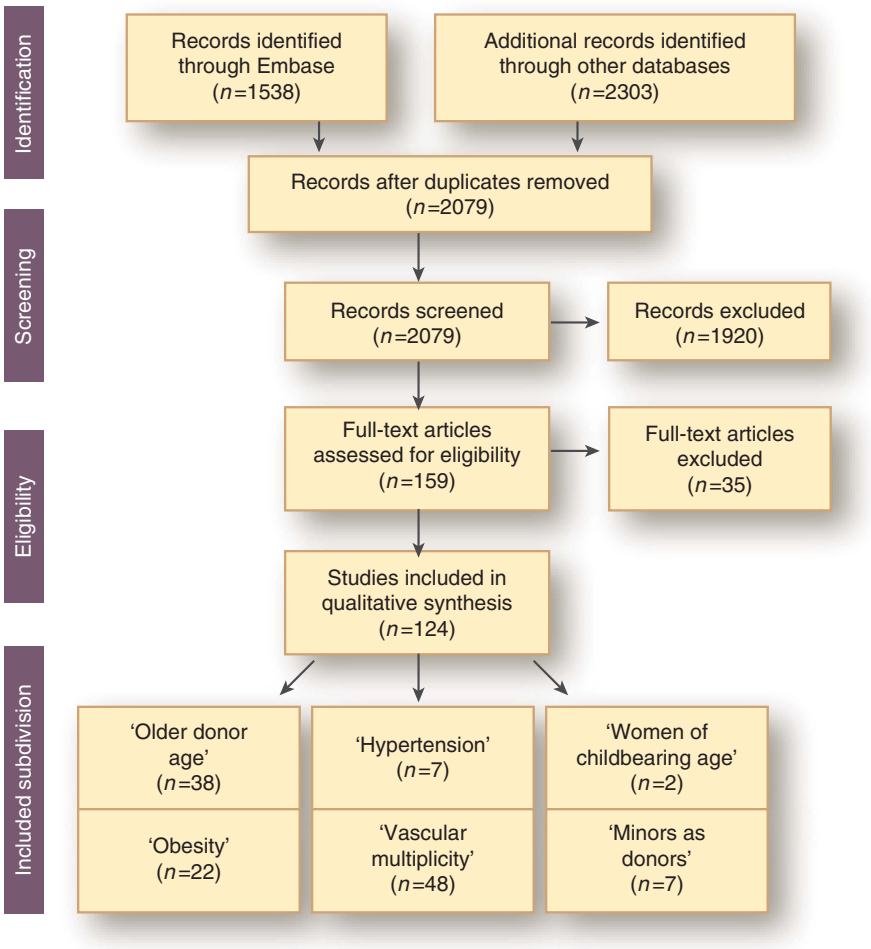

Figure 1 | PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the systematic literature search.

Postoperative complications occurred in 21% of the elderly donors and in 11.9% of the younger donors, respectively. Furthermore, there was no increased length of hospital stay for the older live kidney donors, and serum creatinine levels during the postoperative hospital stay were identical. In a systematic review by Young *et al.*[22], no significant differences were found between the younger and older donors, most commonly defined as older than 60 years, when comparing operative time ($P = 0.11$), blood loss ($P = 0.90$), and length of hospital stay ($P = 0.83$). Klop *et al.* quantified the effect of the surgical procedure on the quality of life of elderly donors $\geqslant$60 years compared with younger donors. Their findings demonstrate that elderly donors recover relatively fast. In a different study, Klop *et al.*[23] also demonstrated that the prevalence of incisional hernias after live donor nephrectomy is very low, and body image and cosmetic scores are excellent. The mean age in the elderly group was 66 years, as compared with 45 years in the younger group. Body mass index (BMI) (mean 26 kg/m^2 in both groups), type of operation (open in 25% vs. 23%), postoperative complication rate (10% and 9%), and length of hospital stay (median 3 days in both groups) did not differ between groups. One month postoperatively, inter-group analysis showed a significant advantage in the quality of life in favor of the elderly group regarding the SF-36 dimensions 'bodily pain', 'role physical', and 'vitality'. At 3 months, 'bodily pain' and 'role physical' were still in favor of the older group. At 6 and 12 months, 'physical function' was in favor of the younger group.[24] Dols *et al.*[25] demonstrated that median estimated blood loss was significantly higher (230 (0–1285) vs. 180 (0–3000) ml; $P = 0.011$) and median warm ischemia time was significantly shorter (4 (1–13) vs. 5 (1–20) min; $P = 0.024$) in live kidney donors $\geqslant$60 years, when compared with donors $<$60 years. Moreover, live kidney donors in the older group had a significantly longer median length of hospital stay (4 (2–15) vs. 3 (1–31) days; $P = 0.012$). The rates of minor and major intraoperative and postoperative complications did not differ significantly between the two groups. The older live kidney donors had a lower GFR before donation, but there were no significant differences in GFR decline between the two groups. Five years after donation, significantly more of the older live kidney donors had a GFR $<$60 ml/min compared with the younger live kidney donors (131 (80%) vs. 94 (31%); $P < 0.001$), but renal function was stable and no GFR

Live kidney donation of extended criteria live kidney donors

Patient or population: extended criteria live kidney donors
Settings: several extended criteria as listed below
Intervention: live kidney donation

Outcomes	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
Women of childbearing age Questionnaires Timing of exposure: 0–40 years[1]	23,325 (2 studies[2])	⊕⊖⊖⊖ Very low[3,4]	1814 cases and 22,015 controls in case–control studies
Hypertension Follow-up: 1–20 years[5]	81,497 (7 studies[6])	⊕⊕⊖⊖ Low	
Obesity Follow-up: 0–5 years[7]	5924 (22 studies[8])	⊕⊕⊖⊖ Low	
Older donor age Follow-up: 0–10 years[9]	90,027 (38 studies[10])	⊕⊕⊖⊖ Low	
Vascular multiplicity Follow-up: 0–10 years[11]	14,878 (48 studies[12])	⊕⊕⊖⊖ Low	
Minors as donors Follow-up: 40 years	347 (7 studies[13])	⊕⊖⊖⊖ Very low	

GRADE Working group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

[1] Mean time of exposure of the two studies.
[2] Two case-control studies.
[3] Control groups consist of the general population.
[4] Some comparisons were made with the general population.
[5] Median follow-up of 5 years.
[6] Four retrospective cohort studies, two case studies, one review.
[7] Median follow-up of 12 months.
[8] Prospective cohort studies, nine retrospective cohort studies, two case-control studies, two systematic reviews.
[9] Median follow-up of 4.6 years.
[10] Prospective cohort studies, 16 retrospective cohort studies, five case-control studies, four case-series, one review.
[11] Median follow-up of 1.1 year.
[12] Prospective cohort studies, 43 retrospective cohort studies, one discussion.
[13] Retrospective cohort study, one case-series study, one case–control study, two surveys, two reviews.

Figure 2 | Summary of findings table of extended criteria in live kidney donation generated by the GRADE tool.

of less than 30 ml/min was observed. Some other studies also recommend that healthy older-aged donors should not be turned down because they do not seem to have a greater risk of intraoperative and postoperative complications. Furthermore, long-term follow-up data show good outcomes for donors of older age.[26–53] Thus, live kidney donation by older donors may be considered safe, as the complications after donation are limited and GFR does not progressively decline, at least not during relatively short-term follow-up (median follow-up: 5.5 years). Multiple other, smaller studies showed similar results.[54–56] Recently, Hourmant *et al.*[57] published that despite reduced renal function of an old kidney, the results of transplantation from an old living donor appeared to be equivalent to deceased transplantation from a younger donor. Finally, transplantation from an old living donor appeared to be a reasonably safe procedure for both the donor and the recipient, and age alone is certainly not a contraindication for donation.

Donors over 70 years of age

The majority of elderly donors described in the aforementioned studies are between 50 and 70 years old. Older age has

a wide age range. A subdivision in these older-age categories will provide a clear overview of the currently available data concerning the safety of donation in these specific age populations. Berger *et al.*[56] studied the outcome of living kidney donors aged 70 years and older. A total of 219 healthy adults aged older than or equal to 70 years donated a kidney. Competing risk models with matched controls were used to study the independent association between older donor age and donor survival. Survival among live donors aged 70 years was 95.8% (95% CI 91.4–98.1%) at 5 years and 90.0% (95% CI 83.5–94.0%) at 10 years. Among matched nondonor controls from the general population, survival was 91.8% (95% CI 87.3–94.7%) at 5 years and 73.0% (95% CI 65.6–79.0%) at 10 years. Mortality among live kidney donors aged 70 years and older was no higher than that in healthy matched controls drawn from the National Health and Nutrition Examination Survey III (NHANES-III) cohort; in fact, mortality rates were lower, probably reflecting greater selectivity among older live donors than could be captured in NHANES-III (HR 0.37, 95% CI 0.21–0.65, $P<0.001$). These findings support that live donation among donors aged above 70 years is safe. The study of Dols *et al.*,[25] as mentioned before, included 25 (5%) donors aged 70 years or older. The mean age in this group was 74 (74–90) years. No significant differences in operative time, complications, conversions, or development of hypertension were observed in comparison with the group younger than 70 years. However, hospital stay was significantly longer for donors aged 70 years or older (5 vs. 4 days, $P<0.001$), possibly explained by the social conditions needed to offer these donors adequate care in their home situation. Ivanovski *et al.*[44] presented their 20-year experience with 230 living donor renal transplantations using elderly individuals, with 90 of them being older than 65 years, and a mean age of 68 ± 4.5; (range 65–86 years). There were no significant surgical complications among the kidney donors. Their findings confirmed that donor nephrectomy is a safe procedure even in donors over 65 years of age.

Little data are available related to live kidney donation in donors older than 70 and 80 years. This is due to the fact that many previous studies generalized 'older donors' as donors over 60 years, and a subdivision in older ages is generally not made. Moreover, some transplant centers are reluctant selecting donors over 70 years or even 80 years of age.[9] Another limitation for excluding donors older than 70 years is fear of delayed graft function by transplant physicians.[58,59]

Recommendation. We conclude that an older age (at least up to the age of 70) is no contraindication for living kidney donation. Little data are available about live kidney donors aged over 70 or 80 years. However, data that are available for these specific donors show that donor nephrectomy is a safe procedure and survival of donors is comparable to that of general populations. Besides the fact that older age does not seem to have a negative impact on the outcome after donor nephrectomy, it is not necessarily actual age itself, but renal function, the presence of other comorbidities, and overall health that will determine whether an older live kidney donor should be included or excluded. In other words, biological age rather than actual age seems to be important. A current view is that a possible impaired renal function and health after donor nephrectomy may be considered more acceptable for older live kidney donors than for younger live kidney donors. The largest prospective follow-up study reporting on the quality of life of the donor was conducted by Klop *et al.*[60] It demonstrates that the elderly donor had an advantage in three of the four end points during the follow-up and that the quality of life is comparable between donor groups. This perspective of excellent postoperative quality of life may actually convince older people to donate.[60]

Level of evidence for this extended criterion:

Level 1: 2%	Level 4: 2%
Level 2: 23%	Level 5: 0%
Level 3: 74%	Grade of recommendation: B

Obesity

Guidelines. The British guidelines recommend that otherwise healthy overweight individuals (BMI 25–30 kg/m^2) may safely proceed to kidney donation. Moderately obese individuals (BMI 30–35 kg/m^2) should undergo careful preoperative evaluation to exclude cardiovascular, respiratory, and kidney disease. The guidelines also suggest that as data on the safety of kidney donation in the very obese (BMI >35 kg/m^2) are limited, such individuals should be discouraged from donating.[12] The CARI guidelines consider obesity (BMI >30 kg/m^2) a relative contraindication to donation.[15] In addition, potential donors who are obese should be very carefully assessed for risk factors associated with chronic kidney disease. These include impaired glucose tolerance, hypertension, and proteinuria. The presence of obesity and a second risk factor should be considered a contraindication to donation. The Canadian guideline does not provide any recommendations concerning obese donors, neither does the European Association of Urology.[13,14]

Literature. A BMI >35 kg/m^2 is considered a relative contraindication for live kidney donation.[9] In the general population, obesity is associated with proteinuria and hypertension, and may lead to ESRD.[10,61] Praga *et al.*[62] studied obesity as a potential risk factor for renal insufficiency after nephrectomy for reasons other than donation. Long-term follow-up demonstrated a correlation between the development of proteinuria and some level of renal insufficiency with a BMI >30 kg/m^2. The question remains whether this is also applicable to donors with obesity. The following consensus guidelines regarding obesity were adopted at the International Forum for the Care of the Live Kidney Donor held in Amsterdam in 2004:[11]

- Individuals with a BMI >35 kg/m^2 should be discouraged from donating, especially when other comorbidities are present.
- Obese individuals should be encouraged to lose weight before kidney donation and should be advised not to donate if they have other associated comorbidities.

- Obese individuals should be informed of both acute and long-term risks, especially when other comorbidities are present.

Healthy lifestyle education should be available to all living donors. A recent survey in the UK showed that there is an inconsistency in accepting donors with a BMI $>30\,kg/m^2$.[63]

Tavakol *et al.*[64] showed that obese live kidney donors (BMI $\geqslant 30\,kg/m^2$) have no increased risk of reduced renal function after donation when compared with nonobese live kidney donors (BMI $<30\,kg/m^2$), but that there is an increased risk of developing hypertension (odds ratio 4.02; 95% CI 1.20–13.00; $P=0.021$) and other risk factors for cardiovascular disease, such as abnormal high-density lipid cholesterol levels (odds ratio 4.5; 95% CI 1.3–15.0; $P=0.015$), at a mean follow-up of 11 years. However, when donors were compared with BMI-matched two-kidney control subjects to determine whether this increase was due to nephrectomy, obesity, or a combination of both, the rates of hypertension and lipid abnormalities in obese donors were similar to the rates observed in the obese two-kidney control subjects. Two-kidney control subjects were matched with donors for current BMI, current age, race, gender, diabetes, and smoking history. Individuals with known renal disease and other significant medical comorbidities, with the exception of hypertension and dyslipidemias, were excluded. This suggests that the increased risks were attributable to obesity rather than the nephrectomy itself. O'Brien *et al.*[20] showed that operative time, estimated blood loss, and length of hospital stay were not significantly increased in obese live kidney donors (BMI 31.9 ± 1.2 and $38.0 \pm 3.4\,kg/m^2$) in comparison with nonobese live kidney donors (BMI $24.9 \pm 2.8\,kg/m^2$). Early postoperative complication rates were not significantly different, although subgroup analysis demonstrated a higher incidence of respiratory complications at the extremes of obesity (BMI $\geqslant 40\,kg/m^2$), with 57% of these donors requiring antibiotic therapy for suspected pneumonia ($P<0.01$). On follow-up, renal function parameters showed significant changes post-nephrectomy, but variation between all groups was not significant when compared with the reference group ($P>0.28$). Heimbach *et al.*[65] found an increased risk of minor surgical complications, especially wound complications, in obese live kidney donors (BMI 30–34.9 and BMI $\geqslant 35\,kg/m^2$) when compared with nonobese live kidney donors (BMI $<25\,kg/m^2$) (11 (10%), 5 (9%), and 4 (2%) donors, respectively ($P<0.05$)). The rate of major surgical complications was low and comparable in all groups of live kidney donors, and a similar length of hospital stay was observed. Operative times were significantly longer for obese live kidney donors. At 6 to 12 months after donation, renal function and microalbuminuria did not differ according to BMI. Reese *et al.*[66] reported that live kidney donors with an increased BMI have higher mean blood pressures at baseline and after nephrectomy, but that changes in blood pressure were not related to BMI. Higher donor BMI at baseline did not increase the risk of reoperation, readmission, vascular or other complications, or increase the length of hospital stay. At six months follow-up, the relative changes in donor serum creatinine and GFR were similar across BMI groups ($P=0.62$). Differences in mean absolute estimated GFR across BMI groups, although statistically significant, were not clinically important (62.0 ml/min per $1.73\,m^2$ for normal-weight donors (BMI $<25\,kg/m^2$) vs. 59.9 for overweight donors ($25 \leqslant$ BMI $<30\,kg/m^2$), 60.6 for obese donors ($30 \leqslant$ BMI $<35\,kg/m^2$), and 62.7 for very obese donors (BMI $\geqslant 35\,kg/m^2$); $P<0.01$) and did not rise consistently across BMI categories ($P=0.62$). Young *et al.*[22] showed that intraoperative outcomes including operative time and estimated blood loss were marginally increased in obese groups, where the pooled estimate of the mean increase in blood loss amounted to 57 ml and that of operative time to 20 min. Recently, we published a systematic review and meta-analysis of the aforementioned studies and the current literature regarding perioperative outcome of live donor nephrectomy between high and low BMI donors ($\geqslant 30$ vs. $\leqslant 29.9\,kg/m^2$).[67] Significant differences were found in favor of low-BMI donors ($\leqslant 29.9\,kg/m^2$): a difference in mean operation duration of 16.9 min (CI 9.1–24.8; $P<0.0001$), a difference in mean rise in serum creatinine of 0.05 mg/dl (CI 0.01–0.009; $P=0.02$), and a risk ratio for conversion of 1.69 (CI 1.12–2.56; $P=0.01$). No significant difference in warm ischemia time, blood loss, length of hospital stay, the number of perioperative complications (such as bleeding, conversion, wound complications, urinary tract infections, readmission, and reoperation), and change in GFR were found. In a subanalysis, no significant differences in aforementioned outcome measures were found between kidney donors with a BMI of 30–34.9 kg/m^2 compared with those with a BMI of $35\,kg/m^2$ and higher. The authors conclude that regarding short-term outcome a high BMI itself should not be a contraindication for live kidney donation. Various other studies have reported on the feasibility of live kidney donation from obese donors.[33,68–79]

Recommendation. On the basis of the available literature, we conclude that the selection of potential kidney donors should not be based on BMI alone. A high BMI, irrespective of its actual value, should not be considered as an absolute contraindication for living kidney donation. The transplant community should carefully screen each individual obese donor for other comorbidities and make a selection based on those results. Donation in obese living kidney donors appears to be safe. However, the selection for donation by an obese potential donor should be a careful individualized process, where all possible comorbidities must be carefully interpreted. The most important factor is the pretransplant renal function and, obviously, the reserve capacity of the remaining kidney. The donors' health should always be prioritized, especially in this selective group, as data on long-term renal function of obese donors are scarce. In addition, counseling should be provided to control weight, and appropriate medical follow-up should be maintained

after donation. Worldwide consensus is that all individuals with a BMI > 40 kg/m^2 (regardless of a wish for donation) should be considered to undergo bariatric surgery.[80] Furthermore, we advocate bariatric surgery for all potential donors with a BMI > 40 kg/m^2, in which standard dietary restriction results in insufficient weight loss. One must bear in mind that long-term follow-up of obese renal donors is limited, as obesity has been considered a relative contraindication to donation until now. Therefore, little evidence is available regarding obese individuals with comorbidities such as hypertension or older age, who have donated their kidney.

Level of evidence for this extended criterion:

Level 1: 10%	Level 4: 10%
Level 2: 5%	Level 5: 0%
Level 3: 75%	Grade of recommendation: B

Hypertension

Guidelines. Hypertension (defined as blood pressure > 140/90 mm Hg)[81] has been considered to be a contraindication for live kidney donation, but the exact risk for donors with a raised blood pressure has not yet been determined. Guidelines regarding hypertensive donors were adopted at the aforementioned forum in Amsterdam in 2004.[11] These guidelines recommend the following: Patients with a blood pressure > 140/90 by ambulatory blood pressure monitoring (ABPM) should generally not be accepted as donors; blood pressure should preferably be measured by ABPM, particularly among older donors (> 50 years) and/or those with high office blood pressure readings; some patients with easily controlled hypertension who meet other defined criteria (e.g., > 50 years of age, GFR > 80 ml/min, and urinary albumin excretion < 30 mg/day) may represent a low-risk group for the development of kidney disease after donation and may be acceptable as kidney donors; donors with hypertension should be regularly followed up by a physician. The British guidelines recommend that potential donors with blood pressure < 140/90 mm Hg should be considered as normotensive and therefore suitable for donation on the basis of blood pressure. The presence of mild–moderate hypertension that is controlled with 1–2 antihypertensive agents is not a contraindication to donation, provided that significant end-organ damage has been excluded. Last, they recommend that evidence of hypertensive end-organ damage, poorly controlled hypertension, or hypertension that requires more than two drugs to achieve adequate control are relative contraindications to donor nephrectomy.[12] The CARI guidelines consider elevated blood pressure above 140/90 mm Hg as a relative contraindication for donation.[16] Donors with evidence of end-organ damage related to hypertension, for example, retinopathy, left ventricular hypertrophy, proteinuria, or poorly controlled hypertension (requiring more than two agents), should not be considered for donation. The Canadian guidelines do not include recommendations regarding hypertensive donors.[13] The European Association of Urology only states that uncontrolled hypertension is an absolute exclusion criterion of these potential living kidney donors.[14]

Literature. To date, few articles have been published regarding the outcome of accepting hypertensive live kidney donors for donation. Segev *et al.*[19] showed that hypertension in live kidney donors was associated with an increased mortality rate within 3 and 12 months after donor nephrectomy (risk ratio 27.4; 95% CI 5.0–149.5; $P < 0.001$), although this was solely based on a small number of donors among the total donor population with hypertension. Therefore, the magnitude of the excess risk remained uncertain. In addition, a systolic blood pressure of 120–139 or ⩾140 mm Hg was associated with higher 9-year mortality rates when compared with a systolic blood pressure of less than 120 mm Hg (HR 1.2, 95% CI 0.8–1.6; HR 1.7, 95% CI 1.1–2.9, respectively). Long-term risk of mortality was not higher for live kidney donors than for a healthy matched nondonor control cohort throughout the 12-year follow-up period (1.5 vs. 2.9%; $P < 0.001$). Textor *et al.*[82] showed that hypertension in live kidney donors (awake ABPM 142 ± 3/85 ± 2 mm Hg, clinic blood pressure 155 ± 3/88 ± 2 mm Hg and nurse blood pressure 136 ± 3/78 ± 2 mm Hg) with otherwise normal GFR and protein excretion has no measurable adverse effects on the donor during the first year after nephrectomy regarding blood pressure, GFR, serum creatinine, urinary protein excretion, and urinary microalbumin. Tent *et al.*[83] demonstrated that hypertensive live kidney donors (awake ABPM 139 ± 16/82 ± 10 mm Hg) show a similar course in postdonation renal function and blood pressure when compared with normotensive donors (awake ABPM 129 ± 12/77 ± 8 mm Hg), and that hypertensive donors do not have an increased risk of renal function loss up to 5 years after donation. Young *et al.*[22] compared live kidney donors with hypertension with donors without hypertension. The results regarding the decrement in GFR after donor nephrectomy were conflicted, substantially heterogeneous, and not pooled (a mean difference in GFR decrement between hypertensive and normotensive donors of 4 ml/min per 1.73 m^2 (95% CI −1 to 10) vs. a mean difference of −8 (95% CI −12 to −4)). Hypertension in live kidney donors was also not associated with a greater increase in blood pressure after donor nephrectomy. Rather, blood pressure appeared to decrease more in hypertensive than in normotensive donors after donation. Some other studies reported positive outcome on including hypertensive donors.[38,84–86]

Recommendation. Hypertension should remain a relative contraindication for live kidney donation. Hypertensive live kidney donors with a blood pressure of approximately 140/90 mm Hg, established by 24-h ambulatory blood pressure measurement (ABPM) and normal renal function, show similar postdonation blood pressure and renal function as normotensive living kidney donors. However, based on the evidence available, the exact degree of hypertension and renal function has not yet been established. In general, the

manageability of the hypertension, the presence of other comorbidities, and overall health determine whether individuals with hypertension should be included or excluded as live kidney donors. These conclusions are also in accordance with the consensus guidelines that were adopted at the Amsterdam Forum in 2004, further stressing the importance of observing these guidelines among transplant centers.[11]

Level of evidence for this extended criterion:

Level 1: 12.5%	Level 4: 12.5%
Level 2: 0%	Level 5: 0%
Level 3: 75%	Grade of recommendation: B

Vascular multiplicity

Guidelines. Surprisingly, no guidelines regarding live kidney donors with multiple renal arteries or veins are available and stated in the consensus of the Amsterdam Forum in 2004, whereas some centers repeatedly exclude live donor kidneys with more than one artery.[87] With regard to this matter, the British guidelines state that multiple renal arteries or kidneys with anatomical anomalies are not absolute contraindications to donation. Decisions should be made on an individual basis as part of a multidisciplinary team meeting.[12] They also state that multiple renal arteries are associated with an increased incidence of complications in the recipient. Again, the Canadian guidelines, the guidelines of the European Association of Urology, and the CARI guidelines do not propose any recommendations concerning arterial or venous multiplicity.[13,14,16]

Literature. Kidneys with multiple arteries are common in the general population and thus in potential live donors. Autopsy studies have suggested a prevalence of 18%–30% for multiple renal arteries, with 15% being bilateral.[88,89] The presence of multiple renal arteries presents a challenge, because it may affect both donor safety and recipient outcome. This is because having multiple renal arteries may lead to intraoperative technical difficulties and complications, such as increased operative time, complicated dissection, or bleeding. Furthermore, either (arterial) reconstructions need to be created after extraction of the kidney or multiple arterial anastomoses are needed in the recipient, both associated with an increased risk for complications.[90] One other study reported on ureteral complications in recipients after donor nephrectomy of kidneys with multiple vessels.[91] Ureteral complications occurred in 6 of 36 (17%) recipients of kidneys with reimplanted accessory arteries compared with 10 of 312 (3%) control recipients and 1 of 13 (8%) recipients of kidneys with ligated accessory arteries ($P = 0.0013$). Kok *et al.*[92] showed that accessory arteries to the lower pole correlated with an increased rate of ureteral complications ($P = 0.01$). These complications consisted of one distal ureteral necrosis because of thrombosis of the inferior pole accessory vessel, and one other patient developed an ureteral stricture 10 days following transplantation. Several studies have been conducted in the past decade regarding the outcome of renal artery multiplicity in live donors.[93–98] Desai *et al.* observed that, when compared with live donors with a single renal artery, live donors with two renal arteries and donors with early branching had a significantly longer graft retrieval time (3.9 ± 1.4 and 3.9 ± 0.8, respectively, vs. 3.5 ± 1.0 min; $P = 0.03$ and $P = 0.01$, respectively) and longer operative time (166.3 ± 49.1 and 162.4 ± 41.5, respectively, vs. 147.6 ± 44.1 min; $P = 0.02$ and $P = 0.04$, respectively).[93] However, all donors were equivalent in terms of postoperative analgesia use and length of hospital stay. Intraoperative and postoperative complications did occur, but none of the complications were related to the number of vessels. In addition, no bleeding complications were observed in donors with multiple vessels. Although the serum creatinine level was higher in the multiple-vessel group at 1 day, at 1 month and 1 year, the difference was not statistically significant. Moreover, the overall graft outcome was similar in all groups, implying low clinical relevance. Paragi *et al.*[98] observed no significant difference in postoperative serum creatinine ($P < 0.31$), mean estimated blood loss ($P < 0.75$), complication rate ($P > 0.99$), or length of hospital stay ($P < 0.28$) between single and multiple-artery donor kidneys. Only operative time was significantly different between the two groups in favor of the donors with a single artery (119 ± 43 vs. 128 ± 40 min; $P < 0.01$). On the contrary, Hsu *et al.*[99] showed that the presence of multiple renal arteries was not associated with a significantly longer operative time: the comparison between donors with one and two renal arteries showed no significant difference in mean total operative time ($P = 0.14$), as well as the comparison between donors with one and three renal arteries ($P = 0.65$) and two and three renal arteries ($P = 0.74$). Moreover, no relation was found between the number of renal arteries and estimated blood loss, complication rate, and length of hospital stay. In addition, more studies demonstrate that arterial multiplicity is not a contraindication to donation.[87,93,94,100–133] Besides renal artery multiplicity, vascular anomalies may also concern venous anomalies. Whereas most studies concern the impact of multiple renal arteries only, in 2008 Fettouh *et al.*[97] also included donors with venous anomalies. They demonstrated that when comparing the results of live kidney donors with vascular anomalies with donors without vascular anomalies, only operative time was significantly increased in donors with vascular anomalies (161 ± 35 vs. 131 ± 26 min; $P < 0.05$). No significant differences were observed in estimated blood loss, hospital stay, and readmission.

Recommendation. Vascular anomalies (in particular, arterial multiplicity up to 3 renal arteries) should not be a contraindication for live kidney donation. The presence of multiple renal arteries or veins may present a challenge to the donor's surgeon, but inherent longer operative times have no negative impact on outcome of the donor after living donor nephrectomy. With modern surgical techniques and high surgical skills, neither renal artery multiplicity nor venous anomalies seem to pose any significant danger to the living kidney donor. With the optimization of the preoperative

imaging nowadays (specifically CT scans), we are able to meticulously define the anatomy and therefore can choose the kidney with the least complex vascular anatomy. During the early years of the donor nephrectomy, preoperative angiography was used. In the following years, MRI was introduced; however, both were considered suboptimal in the more complex anatomical cases.[92] Nowadays, in most centers, the CT scan is a gold standard and is considered to be more sensitive in correctly assessing the complex vascular anatomy.[134–136]

A small accessory artery that supplies a minor part of the upper pole (subjectively assessed using predonation CT scans) can be safely sacrificed.[137] However, an accessory artery that vascularizes the lower pole and inherently the proximal part of the ureter must be saved and reconstructed after nephrectomy. Ali-El-Dein *et al.*[119] proved that bench surgery is as effective as intracorporeal reconstruction of the anastomosis of multiple renal arteries, with no increase in the incidence of relevant complications for the recipient.

Nevertheless, it should be noted that most living donors with multiple renal arteries in the reported studies were donors with a maximum of three renal arteries.[47,92,93,95–99,111–113,115,116,118–123,126,128,129,131] Only a minority of the donors with multiple renal arteries had four or more renal arteries.[92,93,95,98,112,113,119,121–123] Moreover, as no literature is available on donors with more than four renal arteries, we cannot draw any definitive conclusions in this regard. Thus, the results from these studies are probably best applied to living donors with up to three renal arteries.

Level of evidence for this extended criterion:

Level 1: 0%	Level 4: 5%
Level 2: 2%	Level 5: 0%
Level 3: 93%	Grade of recommendation: B

Women of childbearing age as potential donors

Guidelines. The Amsterdam Forum Guidelines state that donor nephrectomy is not detrimental to the prenatal course or outcome of future pregnancies. It is recommended, however, to delay pregnancy until at least 2 months after nephrectomy to assess renal compensation before conception, with evaluation including blood pressure, GFR, and assessment for microalbuminuria. The British Guidelines state that the presence of a solitary kidney does not appear to pose a significant risk during the course of a normal pregnancy, and outcomes for pregnant kidney donors are considered comparable to those in the general population. Other guidelines give no statements regarding this subject.

Literature. Ibrahim *et al.*[138] published a large survey in 2009 of 2102 women who had donated a kidney, in which fetal and maternal outcomes and pregnancy outcomes after kidney donation were similar to those reported in the general population. However, postdonation pregnancies were associated with a lower likelihood of full-term deliveries compared with predonation pregnancies (73.7% vs. 84.6%, $P = 0.0004$) and a higher likelihood of fetal loss (19.2% vs. 11.3%, $P < 0.0001$). Furthermore, postdonation pregnancies were also associated with a higher risk of gestational diabetes, gestational hypertension, proteinuria, and preeclampsia (all $P < 0.0001$). In 2009, Reisaeter *et al.*[139] published that in 326 donors the occurrence of preeclampsia was more common in pregnancies after donation (5.7% vs. 2.6%, $P = 0.026$). No differences were observed in the occurrence of adverse pregnancy outcome in kidney donors compared with the general population.

Recommendation. On the basis of the literature that is available on this topic, there is no evidence to conclude that women of childbearing age should be declined as potential kidney donors. However, one must bear in mind that comparison with the general population may be prone to confounding, because live kidney donors are generally considered to be in better health. Most importantly, the effects of donation on maternal and fetal outcomes should be part of the routine discussion about the risks of donation during the informed consent procedure.

Level of evidence for this extended criterion:

Level 1: 0%	Level 4: 100%
Level 2: 0%	Level 5: 0%
Level 3: 0%	Grade of recommendation: C

Minors as kidney donors

Guidelines. The Amsterdam Forum Guidelines state that with the excellent outcome of specified live donor kidney transplantation using adult donors that are genetically unrelated, minors less than 18 years of age should not be used as living kidney donors. The British Guidelines state that the moral arguments for not subjecting young people, under the age of 18 years, to the rigors of living kidney donation are compelling and minors should rarely, if ever, be considered as potential living donors. However, some regard the use of an identical twin as an acceptable child donor, on the basis that the outcome for the recipient twin is exceptional and because the relationship between identical twins is so close that restoring the health of the recipient confers major psychological benefit for the donor.[140] This view is highly controversial and has been challenged.[141,142]

Literature. In 1997, Spatel *et al.*[143] performed a survey amongst 117 US transplant centers. The great majority of responding centers (68%) required living donors to be at least 18 years old. They state that in unusual circumstances in which no other suitable donor is available, consenting mature minors, and even rare immature minors who are highly likely to benefit from donating, may be ethically acceptable. In 2002, Delmonico *et al.*[144] performed an analysis of the UNOS database and concluded that a minor may ethically act as a live organ donor when the potential donor and recipient are both highly likely to benefit (as in the case of identical twins); when the surgical risk for the donor is extremely low; when all other opportunities for transplantation have been exhausted; when no potential adult living donor is available, and timely and/or effective transplantation from a

cadaver donor is unlikely; and when the minor freely agrees to donate without coercion (established by the independent donor advocate). Recently, Thys *et al.*[145] published a systematic review about this topic, combining all available guidelines, publications, and reports. They conclude that 27 out of 39 'guidelines' endorse a prohibition of living kidney donation by minors. In contrast, 12 guidelines exceptionally allow living kidney donation by minors, provided that adequate safeguarding mechanisms are present. These include an assessment of the minor's decision-making capacity and best interests by an independent competent body. MacDonald *et al.*[146] recently showed that, during long-term follow-up (mean 31.6 years), pediatric donors do not have a greater risk of developing hypertension or diabetes and have a significantly lower risk of developing an estimated GFR <60.

Recommendation. We recommend that minors (aged <18 years) should not be considered as kidney donors, except in rare cases where no other options are available for the recipient.

Level of evidence for this extended criterion:

Level 1: 0%	Level 4: 87.5%
Level 2: 12.5%	Level 5: 0%
Level 3: 0%	Grade of recommendation: C

General conclusions. The transplant community's attempt to extend donor eligibility criteria has led to a shift in accepting live kidney donors with more comorbidities over the years. The main concern with this trend is the safety of the potential live kidney donor and the outcome of the recipient. Furthermore, there is a lack of international consensus. This accounts for the (in some cases major) differences in donor criteria between transplant centers. Four of the most common comorbidities discussed in our review are considered to be a contraindication for donation.

As pointed out before, the most important aspect in selecting possible live kidney donors is their safety. A live kidney donor is generally in good health. The transplant community should be aware of this fact and realize that the donor should not become a patient. Moreover, because donors do not directly benefit from the procedure, especially this particular group should be treated with the best medical attention. In the current era, in which efforts are made to increase the donor pool by increasingly accepting extended criteria donors, we should be extremely careful in the selection process.

Few similar studies are conducted regarding these comorbidities to live kidney donation. The United Kingdom has established guidelines regarding the majority of comorbidities to live kidney donation in May 2011.[12] The UK guidelines are in concordance with the findings of this review regarding older age, overweight/obesity, hypertension, and vascular anomalies. Serur *et al.*[147] conducted a similar study on the available data on high-risk donors and the appropriateness of accepting them as live kidney donors. However, in this review, we focused on the most controversial donor criteria for acceptance. We performed a systematic review, including all available literature, and thereby studied the outcome in a comprehensive donor population with an extensive follow-up duration, aiming to establish the optimal criteria for safe live kidney donation regarding these extended donor criteria.

Limitations. Even though our findings support the inclusion of donors with older age, obesity, hypertension, vascular anomalies, and women of childbearing age for live

Figure 3 | Oxford Centre for Evidence-based Medicine—Levels of Evidence. (**a**) Oxford Centre for Evidence-based Medicine Levels of Evidence Scales. (**b**) Oxford Centre for Evidence-based Medicine Grades of Recommendation. CDR, clinical decision rule; RCT, randomized controlled trials; SR, systematic review.*, By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level. †, Clinical Decision Rule. (These are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category.) ‡, See note above for advice on how to understand, rate, and use trials or other studies with wide confidence intervals. §, Met when all patients died before the Rx became available, but some now survive on it, or when some patients died before the Rx became available, but none now die while on it. §§, A poor-quality cohort study is one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded) objective way in both exposed and nonexposed individuals, and/or failed to identify or appropriately control known confounders, and/or failed to carry out a sufficiently long and complete follow-up of patients. A poor-quality case–control study is one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded) objective way in both cases and controls and/or failed to identify or appropriately control known confounders. §§§, Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into derivation and validation samples. ††, An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis. †††, Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but are still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study. ††††, Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive. **, Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g., using a regression analysis) to find which factors are 'significant'. ***, A poor quality prognostic cohort study is one in which sampling was biased in favor of patients who already had the target outcome, or the measurement of outcomes was accomplished in $<80\%$ of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors. ****, Good follow-up in a differential diagnosis study is $>80\%$, with adequate time for alternative diagnoses to emerge (for example 1–6 months acute, 1–5 years chronic).

kidney donation, one needs to bear in mind that the long-term outcome (longer than 20 years) for these donors has yet to be established. Moreover, some of the studies that concern the outcome of extended eligibility criteria for the live kidney donor have limitations, such as single-center experience, retrospective study design, small sample sizes, and non-matched

a

Level	Therapy/prevention, Etiology/harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of level 1 diagnostic studies; CDR† with 1b studies from different clinical centers	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of level 1 economic studies
1b	Individual RCT (with narrow confidence interval‡)	Individual inception cohort study with > 80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical center	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case series	Absolute SpPins and SnNouts††	All or none case series	Absolute better-value or worse-value analyses††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of level>2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of level>2 economic studies
2b	Individual cohort study (including low quality RCT; e.g. <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; derivation of CDR† or validated on split sample§§§ only	Exploratory**cohort study with good††† reference standards; CDR† after derivation, or validation only on split sample§§§ or databases	Retrospective cohort study or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses.
2c	'Outcomes' research; ecological studies	'Outcomes' research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case–control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual case–control		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor-quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations
4	Case series (and poor-quality cohort and case-control studies§§	Case series (and poor-quality prognostic cohort studies***)	Case–control study, poor or non-independent reference standard	Case series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or 'first principles'	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or 'first principles'	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or 'first principles'	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or 'first principles'	Expert opinion without explicit critical appraisal, or based on economic theory, or 'first principles'

b

a	Consistent level 1 studies
b	Consistent level 2 or 3 studies or extrapolations from level 1 studies
c	Level 4 studies or extrapolations from level 2 or 3 studies
d	Level 5 evidence or troublingly inconsistent or inconclusive studies of any level

cohorts. It is important to remain cautious when drawing hard conclusions from these studies regarding the extended live kidney donor criteria. In this respect, again, we also like to emphasize the importance of long-term follow-up. Furthermore, regarding older donors, little data are available regarding the age groups of older than 70 or even 80 years. Although we conclude that older age in itself is no contraindication, careful consideration is warranted regarding the upper age ranges.

In this systematic review, we have assessed a number of individual extended criteria. However, the transplant community should be aware that in the future an increasing number of potential donors will have more than one extended criterion. Although one specific criterion can be harmless, a combination of several criteria could pose a problem regarding donor safety, both in short-term and long-term consequences. By conducting this review, we did not create any insight in this important issue.

Another important point is the scoring of the evidence. Although the GRADE method is a great tool to score the level of evidence, regarding our extended criteria, no randomized controlled trials can be performed. Thus, all available literature are observational studies, automatically resulting in a lower evidence scale. This is one of the reasons why also the Oxford Level of Evidence scale is included.

Despite the limitations in currently available literature, we conclude that older age, obesity, hypertension, vascular anomalies, and women of childbearing age are no absolute contraindications for live kidney donation. Accepting donors with these conditions has great potential in diminishing the kidney donor shortage. With regard to contraindications for live kidney donation, it must be emphasized that every potential donor should be approached individually and that no generalizations should be made. It is of utmost importance, as mentioned above, that potential risks for the donor should be avoided. Another important aspect in our opinion is the experience of the transplant team and inherent center volume. It should be emphasized that, especially in the extended donor criteria donors, the entire 'procedure' of donor selection/screening and informed consent should be performed by a dedicated team, consisting of nephrologists, transplant surgeons, cardiologists, transplant coordinators, social workers, dietitians, and nursing staff, who are recognized for their expertise in this specific field. In relatively low-volume centers, inherently the experience could be less and therefore we feel that extended criteria donors should be referred to a high-volume center.

Altogether, selecting extended criteria live kidney donors has to be a well-considered multidisciplinary decision, and all options should be explored beforehand, as the use of live kidney donors without comorbidities intuitively will remain preferred. However, with the increasing demand for kidney donors and the subsequent changing tendency regarding contraindications for live kidney donation, the future live kidney donor may not be the same as the donor from the past.

MATERIALS AND METHODS

All aspects of the Cochrane Handbook for Interventional Systematic Reviews were followed, and the study was written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[148]

Literature search strategy

Comprehensive searches were carried out in Embase, Medline OvidSP, CENTRAL (the Cochrane Library 2013, issue 10), Web-of-Science, PubMed Publisher, and Google Scholar. The search was performed for articles published until November 2013 using search terms specific to each search engine, provided in the Supplementary Data. In addition, 'related citations' in PubMed and cross-referencing were used to search for relevant articles. We focused on the outcome of the live donor nephrectomy and therefore excluded articles regarding deceased kidney donors and outcome in kidney transplant recipients.

Literature screening

Articles were screened by two independent researchers (ARA, JAL) for relevance and possible inclusion. In case of discrepancy, a third author was consulted (FJMFD). After assessing the results of the systematic literature search, articles regarding older donor age, overweight and obesity, hypertension, vascular anomalies or multiplicity, women of childbearing age (nulliparous women), and minors as potential donors were selected for further screening. All selected articles were screened for relevance, utility, and reliability. Articles were evaluated using the PICO method.[149] Furthermore, we used the Oxford level of evidence table to grade the literature for each extended criterion (Figure 3a).[150] A grade of recommendation (Figure 3b) is given after each extended criterion is summarized. The aim of grading recommendations is to provide transparency between the underlying evidence and the recommendation given. In addition, the GRADE tool was used to further enlarge the transparency of the quality of the available literature.[151] The GRADE approach defines the quality of a body of evidence by consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias.

DISCLOSURE

All the authors declared no competing interests.

ACKNOWLEDGMENTS

We thank WM Bramer for his help with the systematic literature search. Furthermore, we thank MJ Siebelink and K Thys for their input regarding the topic of minors as potential donors.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/ki

REFERENCES

1. USRDS Coordinating Center. Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2012. Available from http://www.usrds.org/adr.aspx.
2. Kasiske BL, Snyder J, Matas A *et al.* The impact of transplantation on survival with kidney failure. *Clin Transpl* 2000; 135–143.
3. Clemens KK, Thiessen-Philbrook H, Parikh CR *et al.* Psychosocial health of living kidney donors: a systematic review. *Am J Transplant* 2006; **6**: 2965–2977.

4. Oosterlee A, Rahmel A. Annual Report: Eurotransplant International Foundation, 2011.
5. Hariharan S, Johnson CP, Bresnahan BA *et al.* Improved graft survival after renal transplantation in the United States, 1988 to 1996. *N Engl J Med* 2000; **342**: 605–612.
6. Dols LF, Kok NF, Ijzermans JN. Surgical aspects of live kidney donation. *Front Biosci* 2009; **14**: 4746–4757.
7. Ibrahim HN, Foley R, Tan L *et al.* Long-term consequences of kidney donation. *N Engl J Med* 2009; **360**: 459–469.
8. Dols LF, Kok NF, Ijzermans JN. Live donor nephrectomy: a review of evidence for surgical techniques. *Transpl Int* 2010; **23**: 121–130.
9. Lennerling A, Loven C, Dor FJ *et al.* Living organ donation practices in Europe—results from an online survey. *Transpl Int* 2012; **26**: 145–153.
10. Klop KW, Dols LF, Kok NF *et al.* Attitudes among surgeons towards live-donor nephrectomy: a European update. *Transplantation* 2012; **94**: 263–268.
11. Ethics Committee of the Transplantation S. The consensus statement of the Amsterdam Forum on the Care of the Live Kidney Donor. *Transplantation* 2004; **78**: 491–492.
12. Andrews PA, Burnapp L, Manas D *et al.* Summary of the British Transplantation Society/Renal Association U.K. guidelines for living donor kidney transplantation. *Transplantation* 2012; **93**: 666–673.
13. Knoll G, Cockfield S, Blydt-Hansen T *et al.* Canadian Society of Transplantation: consensus guidelines on eligibility for kidney transplantation. *CMAJ* 2005; **173**: S1–S25.
14. Kalble T, Lucan M, Nicita G *et al.* EAU guidelines on renal transplantation. *Eur Urol* 2005; **47**: 156–166.
15. Isbel N. The CARI guidelines. Donors at risk: obesity. *Nephrology* 2010; **15**(Suppl 1): S121–S132.
16. Ierino F, Boudville N, Kanellis J *et al.* The CARI guidelines. Donors at risk: hypertension. *Nephrology* 2010; **15**(Suppl 1): S114–S120.
17. The CARI Guidelines: Living Kidney Donors, 2010. Available from www.cari.org.au/Transplantation/transplantation%20living%20donors/transplant_living_donors.html. (accessed 22 January 2014).
18. Health-EU Elderly. European Commission. Available from. http://ec.europa.eu/health/population_groups/elderly/index_en.htm. (accessed 29 July 2013).
19. Segev DL, Muzaale AD, Caffo BS *et al.* Perioperative mortality and long-term survival following live kidney donation. *JAMA* 2010; **303**: 959–966.
20. O'Brien B, Mastoridis S, Sabharwal A *et al.* Expanding the donor pool: living donor nephrectomy in the elderly and the overweight. *Transplantation* 2012; **93**: 1158–1165.
21. Jacobs SC, Ramey JR, Sklar GN *et al.* Laparoscopic kidney donation from patients older than 60 years. *J Am Coll Surg* 2004; **198**: 892–897.
22. Young A, Storsley L, Garg AX *et al.* Health outcomes for living kidney donors with isolated medical abnormalities: a systematic review. *Am J Transplant* 2008; **8**: 1878–1890.
23. Klop KW, Hussain F, Karatepe O *et al.* Incision-related outcome after live donor nephrectomy: a single-center experience. *Surg Endosc* 2013; **27**: 2801–2806.
24. Klop KW, Dols LF, Weimar W *et al.* Quality of life of elderly live kidney donors. *Transplantation* 2013; **96**: 644–648.
25. Dols LF, Kok NF, Roodnat JI *et al.* Living kidney donors: impact of age on long-term safety. *Am J Transplant* 2011; **11**: 737–742.
26. Mastoridis S, O'Brien B, Sabharwal A *et al.* Expanding the envelope: older age and its impact on perioperative and long-term outcomes following living-donor nephrectomy. *Transpl Int* 2011; **24**: 133.
27. Duchene DA, Woodruff DY, Gallagher BL *et al.* Successful outcomes of older donors in laparoscopic donor nephrectomy. *J Endourol* 2010; **24**: 1593–1596.
28. Shrestha SM, Talbot D, Rix D *et al.* Effect of age or obesity on the short-term and long-term outcomes in living kidney donors: a single centre experience (2001–2009). *Am J Transplant* 2011; **11**: 199–200.
29. Brakemeier S, Budde K, Campistol JM *et al.* Kidney transplantation from living donors over 60: donor age does matter. *Transpl Int* 2011; **24**: 283.
30. Johnson SR, Khwaja K, Pavlakis M *et al.* Older living donors provide excellent quality kidneys: a single center experience (older living donors). *Clin Transplant* 2005; **19**: 600–606.
31. Ghazanfar A, Forgacs B, Tavakoli A *et al.* Is donor age a barrier for living renal transplantation? An outcome analysis of renal transplants from above 60 years old donors. *Am J Transplant* 2012; **12**: 333.
32. Balachandran VP, Aull MJ, Charlton M *et al.* Kidneys from older living donors provide excellent intermediate-term outcomes after transplantation. *Transplantation* 2012; **94**: 499–505.
33. Wu X, Moore D, Wansley S *et al.* 3 year comparative outcomes of live kidney donors over age 50 or with a BMI > 30: a single center experience. *Am J Transplant* 2012; **12**: 330.
34. Gallinat A, Sotiropoulos GC, Treckmann J *et al.* Safety and effectiveness of kidney transplantation from living donors (greater-than or equal to) 60 years of age. *Am J Transplant* 2012; **12**: 333.
35. Kumar A, Verma BS, Srivastava A *et al.* Long-term followup of elderly donors in a live related renal transplant program. *J Urol* 2000; **163**: 1654–1658.
36. El-Agroudy AE, Wafa EW, Sabry AA *et al.* The health of elderly living kidney donors after donation. *Ann Transplant* 2009; **14**: 13–19.
37. Cohney S, Van Hardeveld E, Bennett B *et al.* Outcomes for donors and recipients following kidney donation from living donors, 65 years and older. *Immunol Cell Biol* 2010; **88**: A16.
38. Taner T, Iqbal CW, Cosio FG *et al.* Impact of donor age, obesity and hypertension on remaining kidney volume. *Am J Transplant* 2011; **11**: 308.
39. Hsu THS, Su LM, Ratner LE *et al.* Laparoscopic donor nephrectomy in the elderly patient. *Urology* 2002; **60**: 398–401.
40. Facundo C, Guirado L, Diaz JM *et al.* Expanded criteria for live donor nephrectomy. *Transpl Int* 2011; **24**: 26.
41. Minnee RC, Bemelman WA, Polle SW *et al.* Older living kidney donors: surgical outcome and quality of life. *Transplantation* 2008; **86**: 251–256.
42. Kumar A, Kumar RV, Srinadh ES *et al.* Should elderly donors be accepted in a live related renal transplant program? *Clin Transplant* 1994; **8**: 523–526.
43. Dols LFC, Kok NFM, Tran KTC *et al.* Elderly live kidney donors: safety on long-term follow-up. *Am J Transplant* 2010; **10**: 178–179.
44. Ivanovski NI, Masin JG, Kolevski PD *et al.* Use of elderly living kidney donors—20 years experience on the balkans. *Transpl Int* 2011; **24**: 162.
45. Ibrahim HN, Leister E, Matas AJ. Long term medical outcomes and measured GFR in live kidney donors 55 years and older. *Am J Transplant* 2010; **10**: 276.
46. Oien CM, Reisaeter AV, Leivestad T *et al.* Living donor kidney transplantation: the effects of donor age and gender on short- and long-term outcomes. *Transplantation* 2007; **83**: 600–606.
47. Wang K, Qu QS, Miao SZ. Clinical effect analysisis of the elder living kidney donors and relatives kidney transplants. *J Clin Rehab Tissue Eng Res* 2011; **15**: 3395–3397.
48. Askari A, Novick AC, Braun WE *et al.* The older living renal donor: prognosis for the donor and recipient. *J Urol* 1980; **124**: 779–780.
49. Yashi M, Nukui A, Fujiwara T *et al.* Acceptable residual renal function after retroperitoneoscopic kidney donation in elderly donors. *Transplant Proc* 2010; **42**: 3989–3991.
50. Qing-Xiang X, Cong-Xiang H, Li Z *et al.* Living-related donor kidney transplantation in elderly donors: a retrospective case analysis from one institute during 2 years. *J Clin Rehab Tissue Eng Res* 2011; **15**: 5865–5868.
51. Fauchald P, Sodal G, Albrechtsen D *et al.* The use of elderly living donors in renal transplantation. *Transpl Int* 1991; **4**: 51–53.
52. Hoque MM, Berger J, Segev D. Comparing the mortality rate of older adult living kidney donors with matched NHANES controls may increase living kidney donor pool. *J Am Geriatr Soc* 2011; **59**: S175–S176.
53. Hu XP, Yin H, Zhang XD *et al.* Recovery characteristic of donor's and receptor's renal function from age over 55 years living donors donate kidneys. *Zhonghua Yi Xue Za Zhi* 2009; **89**: 2702–2704.
54. Neipp M, Jackobs S, Jaeger M *et al.* Living kidney donors > 60 years of age: is it acceptable for the donor and the recipient? *Transpl Int* 2006; **19**: 213–217.
55. Lezaic V, Djukanovic L, Blagojevic-Lazic R *et al.* Living related kidney donors over 60 years old. *Transpl Int* 1996; **9**: 109–114.
56. Berger JC, Muzaale AD, James N *et al.* Living kidney donors ages 70 and older: recipient and donor outcomes. *Clin J Am Soc Nephrol* 2011; **6**: 2887–2893.
57. Hourmant M, Lerat L, Karam G. Donation from old living donors: how safe is it? *Nephrol Dial Transplant* 2013; **28**: 2010–2014.
58. Ramalho AL, Custodio FB, Tokuda BM *et al.* Clinical and histopathologic comparative analysis between kidney transplant recipients from expanded-criteria donors and standard-criteria donors. *Transplant Proc* 2013; **45**: 3234–3238.
59. Lim WH, Clayton P, Wong G *et al.* Outcomes of kidney transplantation from older living donors. *Transplantation* 2013; **95**: 106–113.
60. Klop KWJ, Dols LFC, Dooper IM *et al.* Live kidney donation at higher age: quality of life. *Am J Transplant* 2012; **12**: 152.
61. Hsu CY, McCulloch CE, Iribarren C *et al.* Body mass index and risk for end-stage renal disease. *Ann Intern Med* 2006; **144**: 21–28.

62. Praga M, Hernandez E, Herrero JC *et al.* Influence of obesity on the appearance of proteinuria and renal insufficiency after unilateral nephrectomy. *Kidney Int* 2000; **58**: 2111–2118.
63. Arunachalam C, Garrues M, Biggins F *et al.* Assessment of living kidney donors and adherence to national live donor guidelines in the UK. *Nephrol Dial Transplant* 2013; **28**: 1952–1960.
64. Tavakol MM, Vincenti FG, Assadi H *et al.* Long-term renal function and cardiovascular disease risk in obese kidney donors. *Clin J Am Soc Nephrol* 2009; **4**: 1230–1238.
65. Heimbach JK, Taler SJ, Prieto M *et al.* Obesity in living kidney donors: clinical characteristics and outcomes in the era of laparoscopic donor nephrectomy. *Am J Transplant* 2005; **5**: 1057–1064.
66. Reese PP, Feldman HI, Asch DA *et al.* Short-term outcomes for obese live kidney donors and their recipients. *Transplantation* 2009; **88**: 662–671.
67. Lafranca JA, Hagen SM, Dols LF *et al.* Systematic review and meta-analysis of the relation between body mass index and short-term donor outcome of laparoscopic donor nephrectomy. *Kidney Int* 2013; **83**: 931–939.
68. Aggarwal N, Porter A, Tang I *et al.* Post-nephrectomy renal outcomes in obese living kidney donors. *Am J Transplant* 2012; **12**: 331.
69. Amin R, Tavakol M, Amirkiai S *et al.* Effect of obesity on renal function and cardiovascular disease risk factors in long-term kidney donors. *Am J Transplant* 2012; **12**: 100.
70. Crane JS, O'Brien B, Mastoridis S *et al.* Feasibility of live kidney transplantation from morbidly obese donors. *Transpl Int* 2011; **24**: 213.
71. Jacobs SC Jr, Cho E, Dunkin BJ *et al.* Laparoscopic nephrectomy in the markedly obese living renal donor. *Urology* 2000; **56**: 926–929.
72. O'Brien B, Mastoridis S, Crane J *et al.* Safety of nephrectomy in morbidly obese donors. *Exp Clin Transplant* 2012; **10**: 579–585.
73. Omoto K, Sawada Y, Miyauchi Y *et al.* Outcome of retroperitoneoscopic living donor nephrectomy in obese donors. *J Endourol* 2011; **25**: A211.
74. Pesavento TE, Henry ML, Falkenhain ME *et al.* Obese living kidney donors: short-term results and possible implications. *Transplantation* 1999; **68**: 1491–1496.
75. Stahler PA, Connaire J, Hill MJ *et al.* Should severely obese donors be excluded from donation or counseled regarding risk of declining renal function? *Am J Transplant* 2012; **12**: 330–331.
76. Tent H, Rook M, Hofker HS *et al.* Long term follow-up of overweight and obese living kidney donors. *Transpl Int* 2011; **24**: 134–135.
77. Afaneh C, Sheth S, Aull MJ *et al.* Laparoendoscopic single-site nephrectomy in obese living renal donors. *J Endourol* 2012; **26**: 140–146.
78. Doublet JD, Belair G. Retroperitoneal laparoscopic nephrectomy is safe and effective in obese patients: a comparative study of 55 procedures. *Urology* 2000; **56**: 63–66.
79. Kuo PC, Plotkin JS, Stevens S *et al.* Outcomes of laparoscopic donor nephrectomy in obese patients. *Transplantation* 2000; **69**: 180–182.
80. Mechanick JI, Kushner RF, Sugerman HJ *et al.* American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. *Obesity (Silver Spring)* 2009; **17**: S72.
81. Chobanian AV, Bakris GL, Black HR *et al.* Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 2003; **42**: 1206–1252.
82. Textor SC, Taler SJ, Driscoll N *et al.* Blood pressure and renal function after kidney donation from hypertensive living donors. *Transplantation* 2004; **78**: 276–282.
83. Tent H, Sanders JS, Rook M *et al.* Effects of preexistent hypertension on blood pressure and residual renal function after donor nephrectomy. *Transplantation* 2012; **93**: 412–417.
84. Tent H, Van Den Berg E, Hofker HS *et al.* Hypertensive kidney donors perform well at short term post-donation follow-up. *Transpl Int* 2011; **24**: 160–161.
85. Okamoto M, Sakai K, Nobori S *et al.* The consequences of hypertensive live kidney donors—analysis of 674 cases for 38 yrs in Japanese single center. *Am J Transplant* 2011; **11**: 86–87.
86. Burgelova M, Slatinska J, Brunullzkova I *et al.* Hypertension in living kidney donors is frequent, well corrected and without markers of damage of the solitary kidney after 5 years. *Kidney Blood Press Res* 2010; **33**: 328.
87. Gurkan A, Kacar S, Basak K *et al.* Do multiple renal arteries restrict laparoscopic donor nephrectomy? *Transplant Proc* 2004; **36**: 105–107.
88. Roza AM, Perloff LJ, Naji A *et al.* Living-related donors with bilateral multiple renal arteries. A twenty-year experience. *Transplantation* 1989; **47**: 397–399.
89. Pollak R, Prusak BF, Mozes MF. Anatomic abnormalities of cadaver kidneys procured for purposes of transplantation. *Am Surg* 1986; **52**: 233–235.
90. Bessede T, Droupy S, Hammoudi Y *et al.* Surgical prevention and management of vascular complications of kidney transplantation. *Transpl Int* 2012; **25**: 994–1001.
91. Carter JT, Freise CE, McTaggart RA *et al.* Laparoscopic procurement of kidneys with multiple renal arteries is associated with increased ureteral complications in the recipient. *Am J Transplant* 2005; **5**: 1312–1318.
92. Kok NF, Dols LF, Hunink MG *et al.* Complex vascular anatomy in live kidney donation: imaging and consequences for clinical outcome. *Transplantation* 2008; **85**: 1760–1765.
93. Desai MR, Ganpule AP, Gupta R *et al.* Outcome of renal transplantation with multiple versus single renal arteries after laparoscopic live donor nephrectomy: a comparative study. *Urology* 2007; **69**: 824–827.
94. Hung CJ, Lin YJ, Chang SS *et al.* Kidney grafts with multiple renal arteries is no longer a relative contraindication with advance in surgical techniques of laparoscopic donor nephrectomy. *Transplant Proc* 2012; **44**: 36–38.
95. Saidi R, Kawai T, Kennealey P *et al.* Living donor kidney transplantation with multiple arteries: recent increase in modern era of laparoscopic donor nephrectomy. *Arch Surg* 2009; **144**: 472–475.
96. Troppmann C, Wiesmann K, McVicar JP *et al.* Increased transplantation of kidneys with multiple renal arteries in the laparoscopic live donor nephrectomy era: surgical technique and surgical and nonsurgical donor and recipient outcomes. *Arch Surg* 2001; **136**: 897–907.
97. Fettouh HA. Laparoscopic donor nephrectomy in the presence of vascular anomalies: evaluation of outcome. *J Endourol* 2008; **22**: 77–81.
98. Paragi PR, Klaassen Z, Fletcher HS *et al.* Vascular constraints in laparoscopic renal allograft: comparative analysis of multiple and single renal arteries in 976 laparoscopic donor nephrectomies. *World J Surg* 2011; **35**: 2159–2166.
99. Hsu TH, Su L, Ratner LE *et al.* Impact of renal artery multiplicity on outcomes of renal donors and recipients in laparoscopic donor nephrectomy. *Urology* 2003; **61**: 323–327.
100. Keller JE, Dolce CJ, Griffin D *et al.* Maximizing the donor pool: use of right kidneys and kidneys with multiple arteries for live donor transplantation. *Surg Endosc* 2009; **23**: 2327–2331.
101. Genc V, Karaca AS, Orozakunov E *et al.* Multiple renal arteries challenge in laparoscopic donor nephrectomy: how far can we go? *J Korean Surg Soc* 2011; **80**: 272–277.
102. Husted TL, Hanaway MJ, Thomas MJ *et al.* Laparoscopic living donor nephrectomy for kidneys with multiple arteries. *Transplant Proc* 2005; **37**: 629–630.
103. Mastoridis S, O'Brien B, Sabharwal A *et al.* Renal vessel multiplicity and its impact on perioperative and long-term donor outcomes following living-donor nephrectomy. *Transpl Int* 2011; **24**: 295.
104. Kuo T, Yip SKH, Ng CF *et al.* Outcome of laparoscopic live donor nephrectomy and impact of double renal arteries: results from two transplant centres. *Asian J Surg* 2010; **33**: 70–75.
105. Kuo T, Cheng C, Yip S. The effect of multiple renal arteries on the outcomes of laparoscopic living donor nephrectomy. *Urology* 2009; **74**: S81–S82.
106. Indrajit B, Vasilaras A, Boulas J *et al.* Single centre experience in laparoscopic donor nephrectomy including laparoscopic right donor nephrectomy and laparoscopic donor nephrectomy with complex vasculature. *BJU Int* 2010; **105**: 10.
107. Giessing M, Deger S, Ebeling V *et al.* Laparoscopic living donor nephrectomy of kidneys with multiple renal vessels. *Urologe Ausg A* 2003; **42**: 225–232.
108. Johnston T, Reddy K, Mastrangelo M *et al.* Multiple renal arteries do not pose an impediment to the routine use of laparoscopic donor nephrectomy. *Clin Transplant* 2001; **15**: 62–65.
109. Choi HW, Jung JW, Jung JU *et al.* Feasibility and safety of performing hand-assisted laparoscopic donor nephrectomy for patients with multiple renal arteries. *Korean J Urol* 2008; **49**: 443–448.
110. Sinescu I, Harza M, Serbanescu B *et al.* Vascular anomalies in kidney transplantation—a surgical challenge? *Eur Urol Suppl* 2010; **9**: 652–653.
111. Omoto K, Sawada Y, Nozaki T *et al.* Outcome of kidney transplantation with right single versus left multiple renal arteries after retroperitoneoscopic donor nephrectomy. *J Endourol* 2011; **25**: A211.
112. Kitada H, Doi A, Nishiki T *et al.* Living donor renal transplantation using grafts with multiple arteries procured by laparoscopic nephrectomy. *Transplant Proc* 2010; **42**: 2427–2429.
113. Ghazanfar A, Tavakoli A, Zaki MR *et al.* The outcomes of living donor renal transplants with multiple renal arteries: a large cohort study

with a mean follow-up period of 10 years. *Transplant Proc* 2010; **42**: 1654–1658.
114. Volpe A, De Lorenzis E, Tarabuzzi R *et al.* Is laparoscopic living donor nephrectomy in patients with vascular anomalies safe and effective? *Urology* 2012; **80**: S169–S170.
115. Disick GIS, Shapiro ME, Miles RA *et al.* Critical analysis of laparoscopic donor nephrectomy in the setting of complex renal vasculature: Initial experience and intermediate outcomes. *J Endourol* 2009; **23**: 451–455.
116. Kapoor A, Lambe S, Kling AL *et al.* Outcomes of laparoscopic donor nephrectomy in the presence of multiple renal arteries. *Urol Ann* 2011; **3**: 62–65.
117. Omoto K, Miyauchi Y, Shimizu T *et al.* Impact and implication of renal artery number on outcomes of renal donors and recipients in retroperitoneoscopic live donor nephrectomy – experience of 500 cases at a single center. *Am J Transplant* 2011; **11**: 459.
118. Bagul A, Frost JH, Mathuram Thiyagarajan U *et al.* Extending anatomic barriers to right laparoscopic live donor nephrectomy. *Urology* 2012; **79**: 465–469.
119. Ali-El-Dein B, Osman Y, Shokeir AA *et al.* Multiple arteries in live donor renal transplantation: surgical aspects and outcomes. *J Urol* 2003; **169**: 2013–2017.
120. Crane C, Lam VWT, Alsakran A *et al.* Are there anatomical barriers to laparoscopic donor nephrectomy? *ANZ J Surg* 2010; **80**: 781–785.
121. Choi JM, Stamatakis L, Sanchez E *et al.* Multiple renal arteries do not adversely affect donor or recipient outcomes following standard laparoscopic or laparoendoscopic single-site (LESS) donor nephrectomy. *J Endourol* 2011; **25**: A85.
122. Cho HJ, Lee JY, Kim JC *et al.* How safe and effective is routine left hand-assisted laparoscopic donor nephrectomy with multiple renal arteries? a high-volume, single-center experience. *Transplant Proc* 2012; **44**: 2913–2917.
123. Cooper M, Kramer A, Nogueira JM *et al.* Recipient outcomes of dual and multiple renal arteries following 1000 consecutive laparoscopic donor nephrectomies at a single institution. *Clin Transplant* 2013.
124. Wang L, He F, Shi M *et al.* Treatment of multiple arteries in renal transplantation from living related donors. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 2008; **22**: 582–585.
125. Abbasi Eslamloo MA, Kamail K. Renal transplantation in allografts with multiple versus single renal arteries. *Eur Urol Suppl* 2011; **10**: 608.
126. Basaran O, Moray G, Emiroglu R *et al.* Graft and patient outcomes among recipients of renal grafts with multiple arteries. *Transplant Proc* 2004; **36**: 102–104.
127. Stamatakis L, Choi JM, Sanchez EJ *et al.* Analysis of perioperative outcomes in donors with multiple renal arteries: is less comparable to conventional laparoscopy? *Am J Transplant* 2012; **12**: 80.
128. Frost JH, Bagul A, Thiagarajan UM *et al.* Extending the anatomical barriers to a right sided laparoscopic live donor nephrectomy (LLDN). *Transpl Int* 2011; **24**: 134.
129. Kamali K, Abbasi MA, Ani A *et al.* Renal transplantation in allografts with multiple versus single renal arteries. *Saudi J Kidney Dis Transpl* 2012; **23**: 246–250.
130. Meyer F, Nichele SA, Adamy A *et al.* Early outcomes of laparoscopic donor nephrectomy with multiple renal arteries. *Int Braz J Urol* 2012; **38**: 496–503.
131. Tyson MD, Castle EP, Ko EY *et al.* Living donor kidney transplantation with multiple renal arteries in the laparoscopic era. *Urology* 2011; **77**: 1116–1121.
132. Gandelman JA, Yoo PS, Kulkarni S. Retrocaval renal artery bifurcation is not a contraindication to laparoscopic right donor nephrectomy. *J Am Coll Surg* 2013; **217**: 406–411.
133. Elramah M, Patil V, Becker Y *et al.* Development of new onset hypertension in living kidney donors: are multiple renal arteries a risk factor? *Am J Transplant* 2013; **13**: 391–392.
134. Turkvatan A, Akinci S, Yildiz S *et al.* Multidetector computed tomography for preoperative evaluation of vascular anatomy in living renal donors. *Surg Radiol Anat* 2009; **31**: 227–235.
135. Arevalo Perez J, Gragera Torres F, Marin Toribio A *et al.* Angio CT assessment of anatomical variants in renal vasculature: its importance in the living donor. *Insights Imaging* 2013; **4**: 199–211.
136. Liefeldt L, Kluner C, Glander P *et al.* Non-invasive imaging of living kidney donors: intraindividual comparison of multislice computed tomography angiography with magnetic resonance angiography. *Clin Transplant* 2012; **26**: E412–E417.
137. Carter JT, Posselt AM, McTaggart RA *et al.* Laparoscopic procurement of donor kidneys with multiple renal arteries does not compromise donor outcome but is associated with increased ureteral complications in the recipient. *Am J Transplant* 2004; **4**: 486.
138. Ibrahim HN, Akkina SK, Leister E *et al.* Pregnancy outcomes after kidney donation. *Am J Transplant* 2009; **9**: 825–834.
139. Reisaeter AV, Roislien J, Henriksen T *et al.* Pregnancy and birth after kidney donation: the Norwegian experience. *Am J Transplant* 2009; **9**: 820–824.
140. World Health O. WHO guiding principles on human cell, tissue and organ transplantation. *Transplantation* 2010; **90**: 229–233.
141. Curran WJ. Kidney transplantation in identical twin minors–justice is done in Connecticut. *N Engl J Med* 1972; **287**: 26–27.
142. Hollenberg NK. Altruism and coercion: should children serve as kidney donors. *N Engl J Med* 1977; **296**: 390–391.
143. Spital A. Should children ever donate kidneys?: Views of U.S. transplant centers. *Transplantation* 1997; **64**: 232–236.
144. Delmonico FL, Harmon WE. The use of a minor as a live kidney donor. *Am J Transplant* 2002; **2**: 333–336.
145. Thys K, Van Assche K, Nobile H *et al.* Could minors be living kidney donors? A systematic review of guidelines, position papers and reports. *Transplant Int* 2013; **26**: 949–960.
146. MacDonald D, Jackson S, Matas A *et al.* Long term outcomes of young (<18 years) kidney donors: a matched cohort analysis. *Am J Transplant* 2013; **13**: 92.
147. Serur D, Charlton M. Expanded criteria living donors: how far can we go? *Prog Transplant* 2012; **22**: 129–132.
148. Moher D, Liberati A, Tetzlaff J *et al.* Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339**: b2535.
149. Huang X, Lin J, Demner-Fushman D. Evaluation of PICO as a knowledge representation for clinical questions. *AMIA Annu Symp Proc* 2006; 359–363.
150. The Oxford Levels of Evidence 2. Oxford Centre for Evidence-Based Medicine, 2011. Available from http://www.cebm.net/index.aspx?o=5653.
151. Brozek J, Oxman A, Schünemann H. GRADEpro Computer Program 3.6 for Windows ed, 2011.