Living Renal Donors: Optimizing the Imaging Strategy—Decision- and Cost-effectiveness Analysis[1]

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Abbreviations:
CAPD = continuous ambulatory peritoneal dialysis
DSA = digital subtraction angiography
QALY = quality-adjusted life-year

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PURPOSE: To determine the most cost-effective strategy for preoperative imaging performed in potential living renal donors.

MATERIALS AND METHODS: In a decision-analytic model, the societal cost-effectiveness of digital subtraction angiography (DSA), gadolinium-enhanced magnetic resonance (MR) angiography, contrast material–enhanced spiral computed tomographic (CT) angiography, and combinations of these imaging techniques was evaluated. Outcome measures included lifetime cost, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios. A base-case analysis was performed with a 40-year-old female donor and a 40-year-old female recipient.

RESULTS: For the donor, MR angiography (24.05 QALYs and $9,000) dominated all strategies except for MR angiography with CT angiography, which had an incremental ratio of $245,000 per QALY. For the recipient, DSA and DSA with MR angiography yielded similar results (10.46 QALYs and $179,000) and dominated all other strategies. When results for donor and recipient were combined, DSA dominated all other strategies (34.51 QALYs and $188,000). If DSA was associated with a 99% specificity or less for detection of renal disease, MR angiography with CT angiography was superior (34.47 QALYs and $190,000).

CONCLUSION: For preoperative imaging in a potential renal donor, DSA is the most cost-effective strategy if it has a specificity greater than 99% for detection of renal disease; otherwise, MR angiography with CT angiography is the most cost-effective strategy.

Before a potential living renal donor donates a kidney, he or she undergoes an extensive work-up that includes an interview, physical examination, laboratory tests, and ultrasonography (US). A detailed radiologic examination of the kidneys concludes this work-up (1–6). The purpose of the radiologic examination is to determine the number, location, and length of the renal arteries and to detect anomalies or diseases of the renal vasculature. In addition, it is used to screen for renal disease that may have escaped detection during an earlier examination (1,3,6–8). The transplantation team uses this information to decide whether or not it is safe for the potential donor to undergo removal of one kidney. Furthermore, the team can decide which kidney to use, on the basis of findings in regard to the renal vasculature and on the basis of the presence of abnormalities (9–12).

At present, imaging at Erasmus MC Rotterdam, the Netherlands, includes intraarterial digital subtraction angiography (DSA) for the examination of the renal arteries, and immediately after, urography is performed for screening the urinary system. DSA with urography is known to be an accurate method, but it requires catheterization, the use of iodine-containing contrast material, and exposure of the patient to ionizing radiation (13,14). Furthermore, DSA is an expensive technique (15), and with the current strategy, only limited information about the venous anatomy is obtained. This information could be important, especially if nephrectomy is performed laparoscopically.

To overcome the drawbacks of the presently used imaging, other techniques have been proposed to replace it. Researchers in a number of studies have assessed the accuracy and

feasibility of alternative techniques, such as gadolinium-enhanced magnetic resonance (MR) angiography (7,16–19) or computed tomographic (CT) angiography (20–27). These techniques can depict both the arterial and venous vasculature and the collecting system and parenchyma. MR angiography accurately depicts the anatomy of the vasculature, but mild forms of fibromuscular dysplasia may be missed (7). CT angiography has capabilities similar to those of MR angiography, but CT angiography has a higher resolution than does MR angiography and is, furthermore, technically more robust. The disadvantages of CT angiography, however, are that the patient is exposed to ionizing radiation and that iodinated contrast material is needed. Nonetheless, both MR angiography and CT angiography are less expensive than DSA (19).

To our knowledge, only two studies were conducted in which CT angiography and gadolinium-enhanced MR angiography were compared (28,29). In these studies, however, the techniques were compared in regard to the depiction of only arterial and venous anatomy. Furthermore, the currently used imaging strategies vary among centers at which transplantation is performed (4). This variation in the use of imaging strategies indicates the prevailing uncertainty as to what the optimal strategy is and, thus, emphasizes the need for further investigation of those that are available. Thus, the purpose of our study was to determine the most cost-effective strategy for preoperative imaging performed in potential living renal donors.

TABLE 1
Strategies Considered for the Study

Strategy	Protocol
DSA*	Current imaging strategy, DSA with urography, was performed
MR angiography†	Performed with enhancement with gadolinium-based contrast material
Spiral CT angiography†	Performed with contrast enhancement
DSA with MR angiography‡	Current imaging strategy, performed first, and MR angiography were performed during one visit
MR angiography, DSA†‡	If results of MR angiography were inconclusive, the current imaging strategy was performed during second visit
MR angiography with CT angiography§	MR angiography, performed first, and CT angiography were performed during one visit
No test, always transplantation‖	No test, and transplantation was always performed
No test, no transplantation‖	No test, and transplantation was not performed

* Standard of reference for detection of renal disease; we assumed DSA did not fail technically.

† If the donor had any contraindications to MR angiography (eg, claustrophobia, metal implants) or if MR angiography or CT angiography failed technically, the donor underwent the current imaging strategy.

‡ If both MR angiography and DSA were performed but MR angiography failed technically, results of only DSA were considered.

§ If MR angiography was contraindicated, only CT angiography was performed, and when the latter failed technically, DSA was performed. When both MR angiography and CT angiography were performed, but one failed technically, it was assumed that the transplantation team relied on the results of the successful imaging strategy. If both failed, DSA was performed.

‖ Reference strategy.

MATERIALS AND METHODS

Model

A decision model comparing various strategies used for screening potential renal donors was developed from the societal perspective to evaluate the morbidity, mortality, and costs to both renal donors and renal recipients (30). The strategies we considered (Table 1) were DSA with urography (ie, the current strategy), MR angiography, spiral CT angiography, and combinations of these imaging techniques.

To compare these imaging strategies, we modeled the prevalence of vascular anomalies and kidney disease, the probability of detection of anomalies and disease, and long-term outcomes. We (Y.S.L., K.V., M.G.M.H.) developed a Markov process model to estimate the quality-adjusted life expectancy and lifetime cost for both renal donors and recipients. Figure 1 shows a schematic representation of the decision model. The model starts with imaging performed in the donor, when the donor has already undergone the first phases of the work-up, which included the interview, physical examination, laboratory tests, and US.

A diagnosis of renal disease was determined when an abnormality in the renovascular system, the kidney, or the collecting system and distal urinary tract was seen on the image. Renovascular anomalies and abnormalities that do not have a major effect on the prognosis of the patient, such as unilateral cysts, calculi, and parenchymatous lesions, were excluded from our determination of the diagnosis of renal disease. If imaging findings suggested renal disease, no transplantation was performed. However, because of inaccuracy, renal disease may not have been present, which constituted a missed opportunity. If imaging findings did not reveal renal disease, transplantation was performed, with its associated morbidity and mortality for both donor and recipient. If unilateral renal disease was not detected during imaging performed in the donor, the donor may have one diseased kidney after transplantation, or the recipient may receive a diseased transplant. In the case of bilateral renal disease, both the donor and the recipient have a diseased kidney after transplantation.

With the model, we considered that the presence of renovascular anomalies (ie, multiple renal arteries or veins, early arterial branching) influences the choice of which kidney to transplant and increases the duration of the surgery, which results in higher costs.

Furthermore, we also considered that a donor with renal disease diagnosed during the radiologic examination will be treated and may need dialysis later in life. A donor who has one diseased kidney after transplantation and a recipient who receives a diseased kidney will develop clinical renal disease at a later point in life and may require dialysis. A potential recipient whose donor received—correctly or incorrectly—a diagnosis of renal disease will continue to receive treatment with dialysis. A recipient whose transplant fails returns to dialysis.

Data Sources and Assumptions

Background information.—A systematic review of the literature pertaining to living renal donor transplantation was performed. The search strategy we used to retrieve the literature-based information was as follows: living donors AND kidney NOT cadaver NOT developing countries NOT DNA NOT Histocompatibility testing NOT reoperation NOT Kidney/*histology NOT Kidney Calculi/*etiology NOT liver NOT drug therapy NOT pancreas transplantation NOT antibodies. Additional data were obtained from our

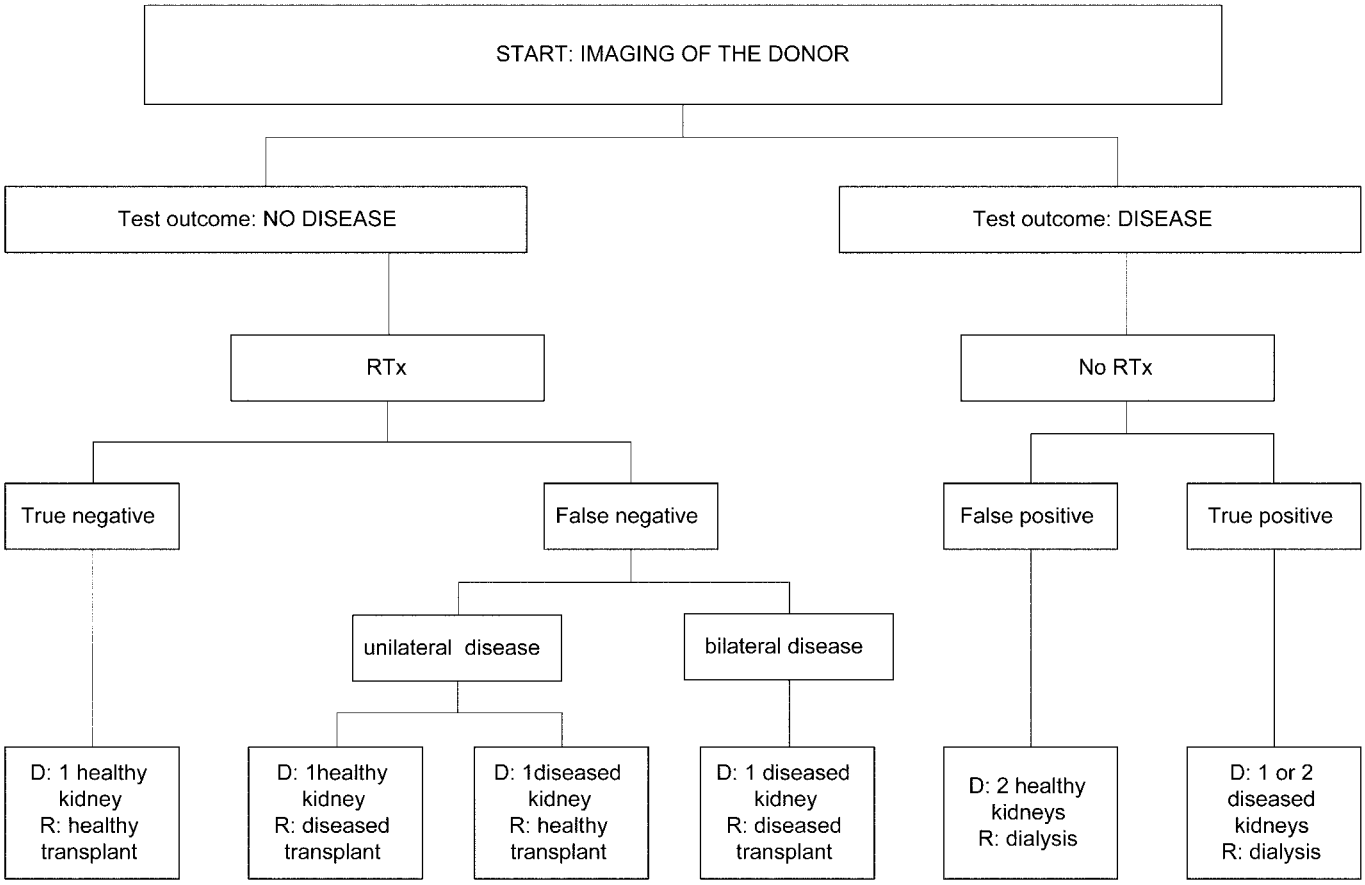

Figure 1. Schematic representation of the structure of the model. *RTx* = renal transplantation, *D* = donor, *R* = recipient.

own clinical data and from the Dutch statistics. We (Y.S.L., M.C.J.M.K.) performed a cost analysis for the local setting. Tables 2–4 present the parameters of the model, with the values used in the base-case analysis and the ranges over which these values were varied in the sensitivity analyses. (More detail on the computation of the test characteristics, probabilities, and costs is available on request.)

Tests and test characteristics of the various strategies.—Published reports were reviewed by the first author (Y.S.L.) concerning DSA performed with a low-osmolar contrast agent administered through intraarterial injection into the femoral artery, MR angiography performed with an intravenously administered gadolinium-based contrast agent, or CT angiography performed with an intravenously administered low-osmolar contrast agent. Studies of researchers were included in this review if they reported sensitivity and specificity for renal disease or renal anomalies.

We considered the currently used strategy (ie, DSA with urography) as the reference standard for detection of renal disease and surgery as the reference standard for detection of renovascular anomalies. Even though the sensitivity and specificity of DSA for detection of renal disease are probably not 100%, DSA is at present the best possible reference standard since disease cannot be detected during surgery. For detection of anomalies, we considered surgery as the reference standard. A disadvantage of choosing surgery as the reference standard is, however, that only one of the two kidneys is seen during surgery, which is most likely the one with the least complicated anatomy.

We (Y.S.L., M.G.M.H.) estimated the sensitivity and specificity for detecting renal disease and the sensitivity for detecting anomalies associated with gadolinium-enhanced MR angiography and contrast-enhanced spiral CT angiography on the basis of data from published studies (18,19,33,34). The specificity for detection of anomalies was not used, because false-positive test results have no consequences since costs are incurred only if anomalies are present. Imaging characteristics are presented in Table 2.

Prevalence of anomalies and kidney disease.—On the basis of data from large studies in regard to the preoperative examination of renal donors (13,26,36–38), we (Y.S.L., M.G.M.H.) estimated the prevalence of renal anomalies and renal disease in potential living renal donors (Table 3).

Donor risks.—We (Y.S.L., M.G.M.H.) estimated the morbidity and mortality associated with various strategies (31,32,35) and the morbidity associated with laparoscopic nephrectomy (39) on the basis of data from the literature. Since a reliable estimate for mortality associated with laparoscopic donor nephrectomy was not available, it was assumed to be the mortality associated with open nephrectomy (6). Long-term survival among renal donors was estimated on the basis of Dutch mortality statistics (55), since on the basis of data in the literature, we determined that this is the same as or better than the survival of the general population (42).

If, however, a renal donor has a diseased kidney after transplantation, and this diseased kidney has escaped detection during the diagnostic work-up, we

TABLE 2
Estimates for Model Variables: Characteristics of Imaging Examinations

Variable	Baseline Value	Range	Reference No. or Other Source
DSA			
Sensitivity for renal disease	100	82–100	. . .*
Specificity for renal disease	100	95–100	. . .*
Sensitivity for renal anomalies	82	75–91	13, 15
Complication rate	1.7	0.5–3.0	31, 32
Mortality rate	0.033	0.029–0.162	31, 32
Technical failures	0	Not available	Expert opinion (M.G.M.H.)
MR angiography			
Sensitivity for renal disease	93	90–100	33
Specificity for renal disease	90	88–100	33
Sensitivity for renal anomalies	82	71–100	18, 19
Complication rate	0	0–0.031	. . .†
Mortality rate	0	0–0.0009	. . .†
Contraindication for MR angiography	6.7	3.0–10.0	. . .‡
Technical failures	2.5	1.0–4.0	16, 19
CT angiography			
Sensitivity for renal disease	95	90–100	23, 34
Specificity for renal disease	98	97–100	23, 34
Sensitivity for renal anomalies	83	65–99	21, 22, 24, 26
Complication rate	0.031	0.002–0.062	35
Mortality rate	0.0009	0.0003–0.0026	35
Technical failures	1.9	0.5–3.5	25
DSA with MR angiography			
Sensitivity for renal disease	100	82–100	. . .§
Specificity for renal disease	100	95–100	. . .§
Sensitivity for renal anomalies	82	82–95	. . .‖
Complication rate	1.7	0.5–3.0	. . .#
Mortality rate	0.033	0.029–0.162	. . .**
Contraindication for MR angiography	6.7	3.0–10.0	. . .‡
Technical failures	2.5	1.0–4.0	16, 19
MR angiography, DSA if MR angiography results inconclusive			
Sensitivity of MR angiography for renal disease	95	90–99	. . .††
Specificity of MR angiography for renal disease	95	90–99	. . .††
Sensitivity of MR angiography for renal anomalies	82	82–95	. . .‡‡
Complication rate when only MR angiography was performed	0	0–0.031	. . .†
Mortality rate when only MR angiography was performed	0	0–0.0009	. . .†
Contraindication for MR angiography	6.7	3.0–10.0	. . .‡
Technical failures of MR angiography	2.5	1.0–4.0	16, 19
Inconclusive results of MR angiography	30	10–50	. . .§§
Sensitivity of DSA with MR angiography for renal disease	100	82–100	. . .‖ ‖
Specificity of DSA with MR angiography for renal disease	100	95–100	. . .‖ ‖
Sensitivity of DSA with MR angiography for renal anomalies	82	82–95	. . .‖ ‖
Complication rate	1.7	0.5–3.0	. . .#
Mortality rate	0.033	0.029–0.162	. . .**
MR angiography with CT angiography##			
Sensitivity for renal disease	100***	Not available†††	23, 33, 34
Specificity for renal disease	100***	Not available†††	23, 33, 34
Sensitivity for renal anomalies‡‡‡	83	65–99	21, 22, 24, 26
Complication rate	0.031	0.002–0.062	. . .#
Mortality rate	0.0009	0.0003–0.0026	. . .**
Contraindication for MR angiography	6.7	3.0–10.0	. . .‡

Note.—All data are percentages.

* DSA was assumed to be the reference standard.

† It was assumed that MR angiography did not involve any risks.

‡ Paul Nederkoom, MD, written communication, August 2000.

§ The sensitivity and specificity of DSA were used.

‖ The sensitivity for the detection of anomalies with MR angiography was used; however, since MR angiography can depict venous anomalies, the sensitivity for detection of anomalies with this strategy was expected to be higher than that of DSA. Therefore, a sensitivity analysis was performed with the baseline estimate as the lower value and an estimated value of 95% as the upper value.

Complication rates of the combination of strategies were computed by summing the complication rates of each strategy.

** Mortality rates of the combination of strategies were computed as follows: mortality of the first imaging examination performed + (1 − mortality of the first imaging examination performed) × mortality of the second imaging examination performed.

†† No data were available. Estimates were determined on the basis of the assumption that these values were higher than those of the characteristics of MR angiography.

‡‡ The sensitivity of MR angiography was used.

§§ Because of inconclusive results of MR angiography, DSA was performed.

‖ ‖ The values of the characteristics (baseline and sensitivity analysis estimates) of DSA with MR angiography were used.

Data are those that apply when both MR angiography and CT angiography were technically successful.

*** Technically, these values were between 99% and 100%, but when rounded, they were 100%.

††† Values of characteristics of MR angiography and CT angiography were varied separately. Because the same variables were used with MR angiography with CT angiography, the values of the characteristics of this strategy were also varied over a plausible range.

‡‡‡ The sensitivity for depiction of anomalies with CT angiography was used.

TABLE 3
Estimates for Model Variables: Prevalences and Risks

Variable	Baseline Value	Range	Reference No. or Other Source
Prevalence among donors			
Renal anomalies (%)*	44.7	41.5–49.4	13, 26, 36
Unilateral anomalies (% of all anomalies)	75	70–79	36–38
Venous anomalies (% of all anomalies)	25	15–35	26
Renal disease (%)	6.3	3.2–10.6	13, 26, 36, present study
Unilateral disease (% of all diseases)	80	70–90	36
Donor risks			
At surgical operation			
Morbidity (% of complications)	14	5–20	39
Mortality (%)	0.03	0.00–0.05	39, 40, 41
In the long term			
Relative risk of mortality compared with that of general population	1	0.39–1.50	42
Dialysis-free survival if renal disease was present	15	10–20	. . .†
Proportion of donors developing end-stage renal disease in whom disease was not detected (%)‡	25	0–100	. . .‡
Proportion of donors developing end-stage renal disease in whom disease was detected (%)	5.3	0–10	Expert opinion (W.W.)
Recipient risks			
At surgical operation			
Morbidity (% of complications)	33	10–50	Expert opinion (J.N.M.I.)
Mortality (%)	1	0.5–3.0	Expert opinion (J.N.M.I.)
In the long term			
Relative risk of mortality of renal transplant recipient after transplantation, compared with that of general population			
1 y	9.7	7.5–35.5	43–46
3 y	3.6	Not available	43–46
5 y	5.0	4.8–8.7	43–46
Relative risk of mortality of patient receiving CAPD, compared with that of general population	14	11–16	47
Relative risk of mortality of patient receiving hemodialysis, compared with that of general population	21	18–24	47
Proportion of patients receiving CAPD among total of those receiving dialysis (%)	28	10–50	48
Graft failure rate after transplantation			
1 y	0.072	0.020–0.092	43–45, 49, 50
3 y	0.050	0.026–0.044	43–45, 49, 50
5 y	0.034	0.039–0.048	43–45, 49, 50

Note.—CAPD = continuous ambulatory peritoneal dialysis.

* Renal anomalies include multiple renal arteries, early arterial branching, and multiple renal veins.

† Dialysis-free survival for a donor was assumed to be 15 years.

‡ Since the probability that dialysis was needed in donors with undetected disease was unknown, it was assumed to be 25%, and it was varied over a wide range.

assumed a 25% chance that the donor would need renal replacement therapy after 15 years. If a donor receives a diagnosis of renal disease during the work-up, the donor is treated for the disease. On the basis of our own clinical data, we estimated that 5% (one of 19) of these donors who receive a diagnosis of disease and are treated would require dialysis after 15 years because of untreatable or recurrent disease. The survival rate for a donor who requires dialysis after 15 years was assumed to be the same as that of the general population for the first 15 years and to be the same as that of patients receiving dialysis after this period. Data regarding donor risks are presented in Table 3.

Recipient risks.—Morbidity associated with renal implantation was estimated on the basis of our own clinical data. We (Y.S.L., J.N.M.I.) estimated surgical mortality to be 1%. Relative risks of mortality for recipients of a renal transplant (43–46) and for patients receiving both CAPD and hemodialysis (47) compared with the mortality of the general Dutch population (55) were computed on the basis of data from the literature (43–47). To determine a relative risk of mortality for dialysis, the relative risks of CAPD and hemodialysis were averaged according to the prevalences of both methods among patients receiving dialysis in the Netherlands (48). We also computed transplant failure rates on the basis of data from the literature in regard to graft survival (43–45,49,50). We assumed that recipients who received a diseased transplant had a survival rate that was the same as that of recipients of a nondiseased transplant for the first 10 years, and we assumed that they would need dialysis after this period. Table 3 includes the data on recipient risks.

Quality weights.—Because renal donors are healthy individuals, their quality-of-life estimate was considered to be 1. However, for donors who need dialysis after 15 years, the estimate was assumed to be 1 for the first 15 years and the same as the estimate for patients receiving dialysis after this period. The quality-of-life estimates for transplant recipients and patients receiving dialysis were obtained from the literature (51,52) (Table 4). We assumed that the quality weight of a recipient who received a diseased transplant was the same as the quality weight of a transplant recipient for the first 10 years and the same as the quality weight associated with dialysis after this period.

Costs.—To compute costs of imaging and transplantation, the Dutch guidelines for computing costs in health care were used (56). Costs were determined from the societal perspective and included both medical and nonmedical costs (Table 4).

Direct medical costs included costs for personnel, materials, equipment, supporting departments, housing and overhead, and hospitalization and consultations. For the computations, we obtained data from the Departments of Radiology and of Surgery and the Finance Department of our center. For the computation of equipment costs, we used the annuitization method, with a discount rate of 3% (30). Costs for hospitalization and consultations were computed by using prices from the Dutch guidelines and data from our center.

Furthermore, we (Y.S.L., M.C.J.M.K.) computed direct nonmedical costs of the imaging strategies and of surgery of both donor and recipient, which included travel expenses and time costs. On the basis of the Dutch guidelines, travel expenses were calculated as travel distance

TABLE 4
Estimates for Model Variables: Quality-of-Life and Cost Estimates

Variable	Baseline Value	Range	Reference No. or Other Source
Quality-of-life estimates			
Donor	1	0.9–1.0	. . .*
Renal transplant recipient†	0.84	0.84–0.94	51, 52
Patient receiving CAPD†	0.56	0.56–0.79	51, 52
Patient receiving hemodialysis†	0.43	0.43–0.63	51, 52
Cost estimates for year 2000 ($)			
Mortality	2,152	1,076–3,228	. . .‡
Imaging			
Current strategy, DSA with urography	440	362–597	Present study
MR angiography	469	333–604	Present study
CT angiography	232	168–299	Present study
Complications§	627	313–940	Present study
Transplantation			
Donor nephrectomy	6,104	5,647–6,563	Present study
Extra costs per surgical operation when anomalies were present and detected during imaging‖	88	44–152	Present study
Extra costs per surgical operation when anomalies were present but not detected during imaging‖	220	111–379	Present study
Complications of donor nephrectomy#	1,567	940–2,194	Present study
Recipient implantation	6,412	5,954–6,871	Present study
Complications of recipient implantation**	3,133	1,567–4,701	Present study
Costs per year of life			
Donor who has donated	84	57–149	. . .††
Patient receiving CAPD	25,327	16,802–33,520	53, 54
Patient receiving hemodialysis	40,401	27,933–53,009	53
Renal transplant recipient, 1st year after transplantation	3,843	1,374–5,553	53, expert opinion (W.W.)
Renal transplant recipient, subsequent years after transplantation as long as donor is alive without dialysis	2,866	1,288–5,466	53, expert opinion (W.W.)

Note.—CAPD = continuous ambulatory peritoneal dialysis.
* Donors were assumed to be in perfect health.
† Quality estimates were obtained from the patient populations by using the time trade-off technique.
‡ It was assumed that mortality resulted within 2 days of hospitalization in the intensive care unit prior to death.
§ It was assumed that complications required 2 days of hospitalization.
‖ Costs were computed by considering the prevalences of unilateral and bilateral disease.
It was assumed that complications required 5 days of hospitalization.
** It was assumed that complications required 10 days of hospitalization.
†† It was assumed that donor check-up costs were similar to costs of a visit to the outpatient clinic of a university hospital.

multiplied by a fixed cost per kilometer. Time costs were computed by using the estimated time required to undergo the imaging and the surgery and the average sex- and age-specific wage rates (57). We obtained wage rates from the Central Bureau of Statistics, Voorburg/Heerlen, the Netherlands.

We assumed that annual direct medical costs for a donor after transplantation were the same as the costs of an outpatient visit (56). Annual direct medical costs of receiving a renal transplant and yearly costs of CAPD and hemodialysis were computed on the basis of data from the literature (53,54). For the annual direct nonmedical costs, we computed travel expenses and time costs in the same manner as we computed these costs for the imaging and the surgery. All costs were standardized to Dutch guilders for the year 2000 and subsequently were converted to U.S. dollars for the year 2000 (exchange rate: 10,000 Dutch guilders = $4,186 = 4,545 euros).

Indirect costs were not considered in the computation of costs. Production loss for a donor does not occur because the general health of a donor was assumed to be the same before and after donation. For the recipient, production loss was assumed to be negligible, since recipients' pre- and posttransplantation employment rates did not differ significantly (58).

Analyses

The lifetime costs and quality-adjusted life-years (QALYs) gained were calculated for each strategy. First, these data were calculated for the donor and recipient separately, and subsequently, the total lifetime cost and total QALYs were calculated for each strategy for donor and recipient combined. Both QALYs and costs were discounted at 3% (range, 0%–10%) per year. On the basis of costs and QALYs for donor and recipient considered separately, we computed incremental cost-effectiveness ratios. To enable decision making for both donor and recipient combined, we summed the costs for the recipient and donor, summed their respective QALYs, and calculated the corresponding incremental cost-effectiveness ratios.

Strategies that were dominated or extended dominated were eliminated from further consideration. A strategy was considered to be dominated by another strategy if costs were higher, whereas QALYs were lower than they were for the other strategy. A strategy was considered to be extended dominated by another strategy if it had a higher incremental cost-effectiveness ratio and lower QALYs. A strategy that was both more costly and more effective was considered to be cost effective if its incremental cost-effectiveness ratio did not exceed the threshold of society's willingness to pay for gaining 1 QALY *(R)* (59). A recently published article indicated that *R* was $25,000–$400,000 (60).

Since the purchasing power of $1 in the United States was about the same as that of 1 Dutch guilder in the Nether-

TABLE 5
QALYs, Cost, and Incremental Cost-Effectiveness Ratios

Strategy*	QALYs†	Cost ($)	Incremental Cost-Effectiveness Ratio ($ per QALY)‡
Donor			
No test, always transplantation	23.98	11,100	Reference strategy
DSA	24.05	9,600	Dominated
DSA with MR angiography	24.05	9,900	Dominated
MR angiography	24.05	9,000	. . .§
MR angiography, DSA if MR angiography results inconclusive	24.05	9,500	Dominated
CT angiography	24.06	9,300	Extended dominated
MR angiography with CT angiography	24.06	9,800	245,000
No test, no transplantation	24.07	1,200	Reference strategy
Recipient			
No test, no transplantation	5.16	425,000	Reference strategy
MR angiography	9.99	200,000	Dominated
MR angiography, DSA if MR angiography results inconclusive	10.29	186,000	Dominated
CT angiography	10.36	183,000	Dominated
MR angiography with CT angiography	10.42	180,000	Dominated
DSA	10.46	179,000	. . .§
DSA with MR angiography	10.46	179,000	. . .§
No test, always transplantation	10.62	165,000	Reference strategy

* Strategies are listed according to increasing QALYs.
† QALYs were rounded off and may falsely seem similar.
‡ Computed without considering the "no test, no transplantation" strategy and the "no test, always transplantation" strategy.
§ Strategy associated with lowest cost was used as a reference strategy to compute incremental cost-effectiveness ratios.

TABLE 6
Cost, QALYs, and Incremental Cost-Effectiveness Ratios for Donor and Recipient Combined

Strategy*	QALYs†	Cost ($)†	Incremental Cost-Effectiveness Ratio ($ per QALY)‡
No test, no transplantation	29.23	426,000	Reference strategy
MR angiography	34.04	209,000	Dominated
MR angiography, DSA if results inconclusive	34.35	196,000	Dominated
CT angiography	34.42	192,000	Dominated
MR angiography with CT angiography	34.48	190,000	Dominated
DSA	34.51	188,000	. . .§
DSA with MR angiography	34.51	189,000	Dominated
No test, always transplantation	34.60	176,000	Reference strategy

* Strategies are listed according to increasing QALYs.
† Numbers are based on data from the base-case analysis and therefore may differ from those of the sensitivity analysis.
‡ Computed without considering the "no test, no transplantation" strategy and the "no test, always transplantation" strategy.
§ Strategy associated with lowest cost was used as a reference strategy to compute incremental cost-effectiveness ratios.

lands in the year 2000, we used an *R* of 100,000 Dutch guilders ($41,000) as our baseline estimate and varied *R* from 25,000 to 400,000 Dutch guilders ($10,000–$168,000) in our sensitivity analyses. All analyses were performed with statistical software (DATA 3.5.7; TreeAge Software, Williamstown, Mass). A base-case analysis was performed with a 40-year-old female donor and a 40-year-old female recipient. We performed one-way sensitivity analyses to test if our baseline results were sensitive to varying all estimates over plausible ranges. In addition, we performed several two-way sensitivity analyses.

RESULTS

Base-Case Analysis

The lifetime costs, QALYs, and incremental cost-effectiveness ratios in regard to the donor and recipient considered separately are shown in Table 5 for our base-case analysis. With respect to the donor, QALYs differed very little among the imaging strategies. The "no test, no transplantation" reference strategy dominated all other strategies, but since the donor desires to donate his or her kidney, we assumed this strategy would not be an option for the donor. The "no test, no transplantation" strategy is presented for comparison purposes only. Of the strategies, MR angiography was associated with the lowest cost. MR angiography with CT angiography yielded more QALYs but at $245,000 per QALY. In regard to the recipient, the QALYs varied more among the strategies, and the costs were much higher. From the recipient's perspective, the "no test, always transplantation" strategy dominated all other strategies, but it would be unethical not to test donors at all (this strategy is also presented for comparison purposes only). Of the strategies, DSA and DSA with MR angiography dominated all other strategies. Costs and QALYs for these strategies were the same, since additionally performing MR angiography would affect only donor costs of the imaging and the surgery.

Summation of costs and QALYs of donor and recipient and computation of incremental cost-effectiveness ratios (Table 6) showed that DSA (34.51 QALYs and $188,000) dominated all other strategies.

Sensitivity Analyses

The results of application of the model were not sensitive to varying parameters over a plausible range except for two of the one-way sensitivity analyses. In one analysis, in which specificity of DSA was 99% or less, MR angiography with CT angiography was the most cost effective from the combined perspective of donor and recipient (34.47 QALYs and $190,000). In another analysis, the model proved to be sensitive to the specificity of CT angiography for detection of renal disease: if specificity was 100%, CT angiography would be the most cost-effective strategy (34.52 QALYs and $187,000).

In two-way sensitivity analyses, we varied both the prevalence of disease and sensitivity or specificity of MR angiography or CT angiography for detection of renal disease. The analysis for the optimal decision from the combined perspective of donor and recipient, when sensitivity of MR angiography and prevalence of disease were varied, is shown in Figure 2. At low prevalences of disease, DSA is

the most cost effective. When prevalence is slightly higher, MR angiography with CT angiography is superior. Contrary to what we would have expected, at high prevalence of disease, MR angiography is the most cost effective when its sensitivity for detection of renal disease is low, and CT angiography is the most cost effective when sensitivity of MR angiography for disease is high.

When both prevalence of disease and the sensitivity of MR angiography are varied in determining the most cost-effective strategy from the perspective of the donor (Fig 3), MR angiography is most cost effective at low prevalence of disease. When prevalence is slightly higher, CT angiography is superior, and if prevalence of disease is high, DSA is most cost effective. However, if the sensitivity of MR angiography is high, MR angiography is superior (unless the prevalence of disease is 100%).

Age was also varied from 25 to 75 years for both donor and recipient in a two-way sensitivity analysis. The DSA strategy was most cost effective over the entire age range.

DISCUSSION

The objective of our study was to identify the most cost-effective strategy for the preoperative evaluation of living, related, potential renal donors. On the basis of a decision- and cost-effectiveness analysis, we conclude that from the perspective of the donor, MR angiography is the most cost-effective strategy, whereas from the combined perspective of donor and recipient, DSA is the most cost-effective strategy. If, however, specificity of DSA for the detection of renal disease is 99% or less, MR angiography with CT angiography is most cost effective from the combined perspective of donor and recipient.

Several general limitations to our study should be mentioned. First, the model was based on multiple data sources. Second, much of the information used in this study was obtained from the literature and, thus, may be subject to publication bias. Furthermore, generalizability is limited because cost data were obtained from only our own center. In addition, imaging protocols for each of the techniques, characteristics of both the donor and recipient population, and expertise may vary among transplantation centers.

Limitations more specifically related to our model included limited availability of data. No literature data were available concerning survival with renal disease. Pozniak and colleagues (26) argued that fibromuscular dysplasia is relatively stable in patients older than 40 years and that most donors are approximately 40 years of age. However, arterial stenosis is known to progress. Thus, we took into account the possibility that donors would need dialysis after a number of years and varied the estimates over a wide range to assess possible changes in results. Also, few data have been published that can be used to quantify the quality of life of renal donors. On the basis of the available qualitative literature (61), we assumed the donors were perfectly healthy. Further research into the quality of life of renal donors is necessary, however, because preserving the quality of life of the donor is a high priority.

Information concerning the test characteristics of the imaging strategies for detection of renal disease is also lacking. Most studies report characteristics for detection of arterial anomalies, such as multiple renal arteries and early arterial branching. These anomalies, however, only influence the costs of the surgery that the donor undergoes because the length of the surgery is increased. More important for the radiologic examination are the sensitivity and specificity with respect to detection of renal disease, since these influence both costs and QALYs in regard to both donor and recipient. Therefore, researchers in future studies should focus on test characteristics of imaging strategies for the detection of renal disease rather than on test characteristics of those for the detection of renal anomalies.

Several technical implications of our analyses can be mentioned. First, some of our results were counterintuitive but, on reflection, could be explained and helped us obtain insight into how various factors could and should contribute to the decision. For example, counter to our intuition, we found that DSA is the most cost-effective option at low prevalence of disease (Fig 2). This can be explained by the fact that, at low prevalence of disease, specificity is more influential. A high transplantation rate is more cost effective from the combined perspective of both donor and recipient because of the benefits to the recipient. Because false-positive results imply no transplantation, a high specificity is required, and DSA has the greatest specificity of 100%. At higher prevalence of disease, sensitivity becomes more important, and for the transplantation rate to be high, a high false-negative rate (implying transplantation), and thus low sensitivity, is required. This explains why MR angiography is the most cost-effective option when prevalence of disease is high and sensitivity for detection of disease is low.

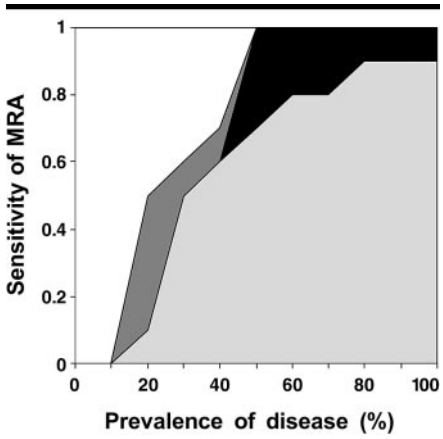

Figure 2. Two-way sensitivity analysis with varying prevalence of disease and sensitivity of MR angiography (light gray area) for detection of disease from the combined perspective of donor and recipient. On the x axis, prevalence of renal disease is represented, and on the y axis, sensitivity of MR angiography for detection of renal disease is represented. Both were varied 0%–100%. The areas in the plot represent the ranges over which a certain strategy is most cost effective from the combined perspective of donor and recipient, when the "no test, always transplantation" strategy was left out of the analysis. At low prevalence of disease, DSA (white area) was the most cost effective. MR angiography with CT angiography (dark gray area) was superior if the prevalence was slightly higher. For high prevalence of disease, either CT angiography (black area) or MR angiography was superior depending on the sensitivity of MR angiography.

With consideration of only the donor's results (Fig 3), it can be seen that the counterintuitive results from the combined perspective are indeed caused by the benefit to the recipient (both in terms of QALY gains and cost savings) through a higher transplantation rate.

Second, a one-way sensitivity analysis showed that CT angiography is most cost effective if its specificity is 100%. Since results in studies in the literature are contradictory as to the ability of CT angiography to depict or exclude fibromuscular dysplasia (22,26,34,62–64), one can argue that a specificity of 100% will not be attainable. However, researchers in all studies used single–detector row spiral CT angiographic equipment, and one might argue that with multi–detector row spiral CT angiography, a higher specificity of CT angiography could be deter-

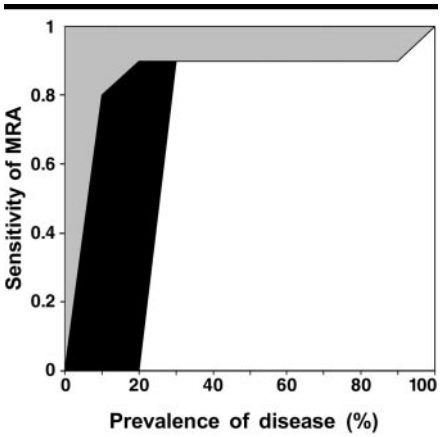

Figure 3. Two-way sensitivity analysis with varying prevalence of disease and sensitivity of MR angiography (gray area) for detection of disease from the perspective of the donor only. On the x axis, prevalence of renal disease is represented, and on the y axis, sensitivity of MR angiography for detection of renal disease is represented. Both were varied 0%–100%. The areas in the plot represent the ranges over which a certain strategy is most cost effective from the perspective of the donor, when the "no test, always transplantation" strategy was left out of the analysis. MR angiography was superior if it was associated with a high sensitivity. For the combination of a low prevalence of disease and low-to-moderate sensitivity of MR angiography, CT angiography (black area) was superior. In all other cases DSA (white area) was superior.

mined. Even if 100% specificity can be determined, the harmful effects of radiation exposure should also be considered.

Furthermore, although some authors advocate the use of MR angiography in addition to DSA to depict venous anomalies, the addition of MR angiography to the imaging strategy cannot be cost effective, because the additional costs that result from having to deal with anomalies during the surgery are less than the cost of MR angiography. However, in our analysis we did not take into account the confidence of the surgeon who performed the transplantation. One would expect that having imaging data prior to surgery would enhance the surgeon's confidence. Quantification of this increased confidence could translate into an increase in the surgeon's quality of life. If an analysis is performed from the societal perspective, this should also be considered. We believed, however, that including the surgeon's quality of life would be extending the analysis too far.

Finally, in the analyses, the "no test, always transplantation" reference strategy appeared to be the most cost effective option for the combined perspective of the donor and the recipient. As has been stated, however, performing no test at all in donors would be unethical, since the transplantation team relies on the findings on the images in planning and performing the surgery (28) and because the team should not compromise its care for the safety of the donors (22).

In the analysis of the clinical implications of our results, we should emphasize the importance of the perspective used. If costs and effectiveness of only the donor were considered, MR angiography would be best because it is associated with a lower transplantation rate. To optimize the recipient's outcome, it would be best if the donor underwent DSA or DSA with MR angiography. When the combined perspective of donor and recipient was considered, DSA was the most cost effective. The outcomes of the recipient may outweigh those of the donor in this combined result, because, for the recipient, the difference in QALYs gained varies more among the strategies.

The choice of how to combine the outcomes of two subjects, in this case, the donor and the recipient, is not as straightforward as it may seem. According to Hippocrates's principle of "first do no harm," we may believe that the donor's survival and quality of life should weigh more in the overall analysis. According to the utility theory applied in the context of cost-effectiveness analysis of health care, all QALYs are considered the same, regardless of who benefits from the gained QALYs (57). In accordance with this theory, we valued a QALY of a donor the same as a QALY of the recipient. It may, however, be argued, that a QALY of the donor should be weighed more heavily than a QALY of the recipient, because the donor gives up QALYs for the benefit of the recipient. Such an argument would be based on the notion that "losses loom larger than gains" (65). Altruistic motives of the donor were not considered in this model, since the desire to donate is extremely difficult, if not impossible, to quantify.

In conclusion, for the preoperative radiologic examination performed in potential living renal donors, DSA is the most cost-effective strategy when it is considered as the reference standard, but if the specificity of DSA for the detection of disease is 99% or less, which is probable, MR angiography with CT angiography is the most cost-effective strategy.

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