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The Association Between Macroscopic Arteriosclerosis of the Renal Artery, Microscopic Arteriosclerosis, Organ Discard, and Kidney Transplant Outcome

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Background. During organ retrieval, surgeons estimate the degree of arteriosclerosis and this plays an important role in decisions on organ acceptance. Our study aimed to elucidate the association between macroscopic renal artery arteriosclerosis, donor kidney discard, and transplant outcome. **Methods.** We selected all transplanted and discarded kidneys in the Netherlands between January 1, 2000, and December 31, 2015, from deceased donors aged 50 y and older, for which data on renal artery arteriosclerosis were available (n = 2610). The association between arteriosclerosis and kidney discard, the relation between arteriosclerosis and outcome, and the correlation between macroscopic and microscopic arteriosclerosis were explored. **Results.** Macroscopic arteriosclerosis was independently associated with kidney discard (odds ratio [OR], 1.36; 95% confidence interval [CI], 1.02-1.80; $P = 0.03$). Arteriosclerosis (any degree) was not significantly associated with delayed graft function (OR, 1.16; 95% CI, 0.94-1.43; $P = 0.16$), estimated glomerular filtration rate 1-y posttransplant (B, 0.58; 95% CI, –2.07 to 3.22; $P = 0.67$), and long-term graft survival (hazard ratio, 1.07; 95% CI, 0.86-1.33; $P = 0.55$). There was a significant association between mild arteriosclerosis and primary nonfunction (OR, 2.14; 95% CI, 1.19-3.84; $P = 0.01$). We found no correlation between macroscopic and histological arteriosclerosis, nor between histological arteriosclerosis and transplant outcome. **Conclusions.** Macroscopic arteriosclerosis of the renal artery was independently associated with kidney discard and somewhat associated with primary nonfunction posttransplant. However, there was no effect of arteriosclerosis on delayed graft function, estimated glomerular filtration rate at 1 y, or long-term graft survival. Our results are valid only after inevitable exclusion of discarded kidneys that had on average more arteriosclerosis. Hence, conclusions should be interpreted in the light of this potential bias.

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INTRODUCTION

The past few decades have seen a steady increase in the average deceased donor age.[1] A typical donor today is over 50 years old and is likely to have several relevant comorbidities.[2] Indeed, the once called "expanded criteria" donor has gradually become our standard donor. With rising donor age and associated medical conditions, it will be more likely that a substantial amount of arteriosclerosis is

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encountered during organ retrieval. Arteriosclerosis of the renal artery may cause technical challenges to construct an arterial anastomosis in the recipient. Also, the condition is often believed to be associated with worse renal transplant outcome, either in the short term because of technical/thrombotic vascular complications, or in the long term as a result of a presumed lower functional capacity of the graft.[3]

At organ retrieval, the surgical team estimate the degree of macroscopic arteriosclerosis of the renal artery and this information is communicated to the designated recipient center, along with other donor and organ procurement data. The transplant center's medical team will base their initial decision to accept or decline a kidney offer mainly on these parameters. The aforementioned macroscopic arteriosclerosis grading is a mandatory organ quality parameter in the whole Eurotransplant procurement region (8 European countries, among which the Netherlands) and entirely depends on the subjective opinion of individual retrieval surgeons. Surgeons receive no specific training or protocol for scoring the degree of renal artery arteriosclerosis.

The aim of this study was to investigate whether kidney grafts with macroscopic arteriosclerosis were discarded more often than those with unaffected renal arteries. In addition, we studied the association between macroscopic renal artery arteriosclerosis and outcome of those kidneys that were transplanted and whether macroscopic surgical assessment of the renal artery correlated with histological signs of arteriosclerosis.

MATERIALS AND METHODS

Data Retrieval

We utilized data from the Dutch Organ Transplantation Registry (NOTR) and from Eurotransplant to perform a retrospective cohort study. The NOTR data management committee approved anonymized data usage for this study. No Institutional Review Board approval was required. All kidneys initially offered for transplantation between January 1, 2000, and December 31, 2015, from deceased donors aged 50 years and older, carried out in any of the 8 transplant centers in the Netherlands, were selected. We only included kidneys of those retrieval procedures that were actually commenced and for which data on the macroscopic degree of renal artery arteriosclerosis were available. Baseline demographic variables of the donor, recipient, and organ preservation, as well as relevant posttransplant outcome measures, were collected (Table 1). For occasional missing values (variable <5% incomplete), the overall median was imputed in case of continuous variables, or a negative value ("none"/"no"/"absent") was imputed in case of binary variables. The database was thoroughly checked for inconsistencies and any errors encountered were corrected after consultation of the NOTR data managers.

Macroscopic Arteriosclerosis

In Eurotransplant, the procurement surgeon is required to estimate the degree of macroscopic renal artery arteriosclerosis immediately after organ retrieval. Along with other macroscopic organ characteristics, this assessment is digitally stored and made available to the designated recipient's medical team when a kidney is offered for transplantation. The presence of macroscopic renal artery arteriosclerosis can be scored as "none," "mild," "moderate," or "massive." We utilized this score as the variable which conveys the subjective assessment of macroscopic renal artery arteriosclerosis by the procurement surgeon.

Histological Degree of Arteriosclerosis

In a subcohort of kidneys that were transplanted in the University Medical Center Groningen and for which a preimplantation renal needle biopsy was available, an experienced renal pathologist reread all histological slides on light microscopy and, specifically for this study, scored the degree of vascular fibrous intimal thickening (*cv*) and arteriolar hyalinosis (*ah*). Both could be either 0, 1, 2, or 3, based on the *cv* and *ah* chronicity parameters of the Banff scoring system for renal allografts.[4-6] These 2 Banff subscores are generally considered to be histological indicators of intrarenal arteriosclerosis.

Statistical Analysis

Differences between baseline characteristics of transplanted and discarded kidneys were characterized by means of Mann-Whitney *U* tests and Pearson chi-square tests, wherever appropriate.

First, we explored the association between macroscopic renal artery arteriosclerosis and kidney discard. Univariable analysis consisted of a Pearson chi-square test. In multivariable logistic regression models, we tested whether (degree of) macroscopic arteriosclerosis was an independent risk factor for organ discard. The choice of other covariates in these models was based on literature and presumed clinical relevance. No further selection was applied; hence, all covariates were left in the models, regardless of their significance level. Full models, including all covariates, are listed in the supplementary appendix.

Second, we investigated the relation between macroscopic renal artery arteriosclerosis and delayed graft function (DGF), primary nonfunction (PNF), the (Chronic Kidney Disease Epidemiology Collaboration) estimated glomerular filtration rate (eGFR) at 1 year after transplantation, and death-censored graft survival up to 10 year posttransplant. DGF was defined as any dialysis requirement in the first week after transplantation. Univariable analyses of the association between arteriosclerosis and the incidence of DGF and PNF were performed with Pearson chi-square tests. Univariable analyses for eGFR consisted of a 1-way ANOVA. Univariable analysis of graft survival was performed with a log-rank test. We also conducted multivariable logistic, linear, or Cox regression analyses to explore whether renal artery arteriosclerosis was an independent risk factor for DGF, PNF, a lower eGFR at 1 year, and death-censored graft failure. Selection of covariates for these regression models was done as described in the previous paragraph. Full models are listed in the supplementary appendix.

Third, we studied how well the subjective surgical assessment of macroscopic renal artery arteriosclerosis correlated with Banff histological surrogates for arteriosclerosis in the subgroup of transplanted kidneys for which such data were available. These associations were quantified as Spearman rank correlation coefficients and by

TABLE 1.

Donor, organ, recipient, and transplant demographics for the whole study cohort for which data on macroscopic arteriosclerosis were available (n = 2610 deceased donor kidneys offered, of which 2239 were transplanted and 371 were discarded)

Donor demographics	Transplanted kidneys	Discarded kidneys	*P*
Donor age,[a] y	59 (50–86)	61 (50–85)	0.001
DCD donor (%)	59	74	<0.0005
Donor BMI,[a] kg/m^2	25 (15–67)	26 (14–53)	<0.0005
Traumatic cause of death (%)	14	11	0.001
Donor history of hypertension (%)	33	33	0.47
Donor history of diabetes mellitus (%)	6	13	<0.0005
Donor terminal serum creatinine,[a] μmol/L	69 (24–1185)	79 (24–566)	<0.0005
Organ demographics (%)			
Left kidney	51	51	0.96
No macroscopic arteriosclerosis	31	22	<0.0005
Mild macroscopic arteriosclerosis	9	13	0.02
Moderate macroscopic arteriosclerosis	46	31	<0.0005
Massive macroscopic arteriosclerosis	13	35	<0.0005
Recipient demographics			
Recipient age,[a] y	60 (3–85)		
Recipient BMI,[a] kg/m^2	26 (11–45)		
Total time spent on the waiting list,[a] y	3.6 (0–20)		
Previous transplants ≥1 (%)	10		
PRA level >5% (%)	6		
Transplant demographics			
HLA mismatches (% of 0 mismatches)	3		
Cold ischemic time,[a] h	16 (1–47)		

[a]Median (range).
BMI, body mass index; DCD, donation after circulatory death; PRA, panel reactive antibodies.

TABLE 2.

Timing of and reasons for discard of those 371 kidneys that were discarded during or after organ retrieval and for which data on macroscopic renal artery arteriosclerosis were available

Variable	No. of kidneys, n (%)
Timing of discard	
Discarded before being offered (organ not offered)	13 (3.5)
Discarded after being offered (organ offer not accepted anywhere)	193 (52)
Discarded after initial acceptance	165 (44.5)
Reasons for discard (reported by retrieval team, recipient center, or Eurotransplant)	
Reasons related to presumed inferior organ quality	350 (94.3)
Recipient related medical problems	8 (2.2)
No suitable recipients found	4 (1.1)
Logistical problems	1 (0.6)
Other reasons	8 (2.2)

There was no database field specific for arteriosclerosis-related discard.

TABLE 3.

Logistic regression analysis for the risk of deceased donor kidney discard

Variable	Odds ratio (95% CI)	*P*
Risk of kidney discard (arteriosclerosis as binary variable)		
Any macroscopic renal artery arteriosclerosis	1.36 (1.02-1.80)	<0.0005
Risk of kidney discard (arteriosclerosis as categorical variable with 4 levels)		
Any macroscopic renal artery arteriosclerosis		<0.0005
Mild vs no renal artery atherosclerosis	1.72 (1.13-2.60)	0.01
Moderate vs no renal artery atherosclerosis	0.79 (0.57-1.08)	0.14
Massive vs no renal artery atherosclerosis	3.50 (2.48-4.93)	<0.0005

Full models, listing all covariates and their respective odds ratios, can be found in **Table S1** (**SDC**, http://links.lww.com/TP/B886) of the supplementary appendix.
CI, confidence interval.

means of Pearson chi-square tests, with associated *P*. In addition, we investigated whether in this subcohort Banff *ah* and *cv* scores were associated with DGF, PNF, eGFR at 1 y, and 10-y graft survival, utilizing univariable logistic, linear, and Cox regression.

For all statistical tests and models, a 2-sided $P < 0.05$ was assumed to indicate a statistically significant association.

RESULTS

Between January 1, 2000, and December 31, 2015, 4034 kidneys from deceased donors aged 50 y and older were offered for transplantation in the Netherlands, of which 3505 (87%) were transplanted and 529 (13%) were discarded during or after organ retrieval. For 2610 kidneys that were considered for a transplant, data on macroscopic arteriosclerosis of the renal artery were available. In this subset, the division between actually transplanted and discarded kidneys was comparable to that of the whole group: 2239 (86%) versus 371 (14%). In 70% of all 50+ deceased donor kidneys transplanted in the Netherlands, both kidneys of a pair were transplanted nationally (in 2 different recipients), and thus, both kidneys of those pairs were available in the NOTR database. For 96% of those pairs, macroscopic arteriosclerosis scores of the left and the right kidney were identical. **Table S1** (**SDC**, http://links.lww.com/TP/B886) presents details of this pairwise comparison of arteriosclerosis grading. Demographics of transplanted and discarded kidneys are provided in Table 1. Table 2 shows an overview of the time point in the donor-to-recipient cascade at which kidneys were discarded, as well as grouped reasons for discard. Presumed inferior organ quality was by far the most abundant reason for discard (94.3% of cases). The database did not specifically record when renal artery arteriosclerosis had been the main reason for organ discard. Hence, we could only indirectly determine the extent to which arteriosclerosis might have played a role in the decision to discard a kidney by means of univariable and multivariable regression analysis

exploring risk factors for organ discard. This analysis is presented in the next paragraph.

The Association Between Macroscopic Renal Artery Arteriosclerosis and Kidney Discard

Sixteen percent of kidneys with any degree of macroscopic arteriosclerosis were discarded, compared to 10% of kidneys without arteriosclerosis ($P < 0.0005$). In a multivariable logistic regression model, any macroscopic arteriosclerosis was independently associated with more discard (odds ratio [OR], 1.36; 95% confidence interval [CI], 1.02-1.80; $P = 0.03$; Table 3). When the degree of arteriosclerosis was also modeled, mild arteriosclerosis was significantly associated with discard (OR, 1.72; 95% CI, 1.13-2.60; $P < 0.0005$; Table 3) and massive arteriosclerosis had an even stronger independent association with discard (OR, 3.50; 95% CI, 2.48-4.93; $P < 0.0005$; Table 3) (see **Table S2** for full models, **SDC**, http://links.lww.com/TP/B886).

Of transplanted kidneys, 31% had no macroscopic arteriosclerosis, 9% had mild, 46% moderate, and 13% massive arteriosclerosis. Of discarded kidneys, 22% had no macroscopic arteriosclerosis, 13% had mild, 31% moderate, and 35% massive arteriosclerosis (Table 1).

The Relation Between Macroscopic Renal Artery Arteriosclerosis and Posttransplant Outcome

Of transplanted kidneys without macroscopic arteriosclerosis, 46% developed DGF, and in kidneys with any degree of arteriosclerosis, the incidence of DGF was 50%. In a univariable analysis, this difference was not statistically significant ($P = 0.19$). In a multivariable logistic regression model, macroscopic arteriosclerosis was also not significantly associated with the occurrence of DGF (OR, 1.18; 95% CI, 0.96-1.46; $P = 0.12$; Table 4).

Of transplanted kidneys without macroscopic arteriosclerosis, 5.3% developed PNF and in kidneys with any degree of arteriosclerosis, the incidence of PNF was 7.3%. In a univariable analysis, this difference was not statistically significant ($P = 0.08$). In a multivariable logistic regression model, any degree of macroscopic arteriosclerosis was significantly associated with the occurrence of PNF (OR, 1.53; 95% CI, 1.01-2.32; $P = 0.04$; Table 4). However, when the various degrees of arteriosclerosis were tested in a multivariable logistic regression model, only kidneys with mild arteriosclerosis had significantly more PNF than grafts with unaffected renal arteries. Moderate or massive arteriosclerosis were not associated with more PNF (Table 4). In addition, we explored whether PNF in kidneys with renal artery arteriosclerosis was more often related to perioperative or postoperative vascular/thrombotic complications, compared to kidneys without macroscopic arteriosclerosis. However, this was not the case: In kidneys without arteriosclerosis, 32% of PNF cases were related to vascular or thrombotic complications, whereas in kidneys with any macroscopic arteriosclerosis, this percentage was even lower: 24%.

Chronic Kidney Disease Epidemiology Collaboration calculated eGFR values at 1-year posttransplant (Figure 1) were comparable for kidneys with none, mild, moderate, and massive arteriosclerosis (1-way ANOVA; $P = 0.28$). In a multivariable linear regression model, arteriosclerosis was also not significantly associated with eGFR 1 y after transplantation (B, 0.02; 95% CI, –1.49 to 3.69; $P = 0.40$; Table 4).

Death-censored graft survival (Figure 2) was similar for kidneys with none, mild, moderate, and massive arteriosclerosis (log-rank test; $P = 0.27$). In a multivariable Cox proportional hazards model, arteriosclerosis was also not significantly associated with the risk of graft failure after transplantation (hazard ratio, 1.08; 95% CI, 0.86-1.36; $P = 0.49$; Table 4).

Full models, listing all covariates and their respective odds/hazard ratios and regression coefficients, can be found in **Table S3** (**SDC**, http://links.lww.com/TP/B886) of the supplementary appendix.

TABLE 4.

Multivariable risk analysis[a] for delayed graft function, primary nonfunction, eGFR at 1 y posttransplant, and death-censored graft failure

Variable	Odds ratio/linear regression coefficient/hazard ratio (95% CI)[b]	P
Risk of delayed graft function		
Any macroscopic renal artery arteriosclerosis	1.18 (0.96-1.46)	0.12
Risk of primary nonfunction (arteriosclerosis as binary variable)		
Any macroscopic renal artery arteriosclerosis	1.53 (1.01-2.32)	0.04
Risk of primary nonfunction (arteriosclerosis as categorical variable with 4 levels)		
Any macroscopic renal artery arteriosclerosis		0.09
Mild vs no renal artery atherosclerosis	2.14 (1.19-3.84)	0.01
Moderate vs no renal artery atherosclerosis	1.41 (0.91-2.20)	0.13
Massive vs no renal artery atherosclerosis	1.46 (0.80-2.65)	0.22
Influence on eGFR (CKD-EPI) at 1 y posttransplant		
Any macroscopic renal artery arteriosclerosis	0.02 (–1.49 to 3.69)	0.40
Risk of death-censored graft failure		
Any macroscopic renal artery arteriosclerosis	1.08 (0.86-1.36)	0.49

Full models, listing all covariates and their respective odds/hazard ratios and regression coefficients, can be found in **Table S2** (**SDC**, http://links.lww.com/TP/B886) of the supplementary appendix.

[a]Logistic regression models for delayed graft function and for primary nonfunction, linear regression model for eGFR at 1 y posttransplant, and Cox proportional hazards model for death-censored graft failure.

[b]Odds ratios apply to the logistic regression models, linear regression coefficients apply to the linear regression model and hazard ratios apply to the Cox proportional hazards models.

CI, confidence interval; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate.

The Correlation Between Macroscopic Renal Artery Arteriosclerosis and Histological Surrogates for Intrarenal Arteriosclerosis

For a total of 129 transplanted kidneys, pretransplant biopsies were available. For 109 of these kidneys, macroscopic renal artery arteriosclerosis scores were also available. Table 5 presents an overview of how macroscopic scores correlated with renal histology. The Spearman

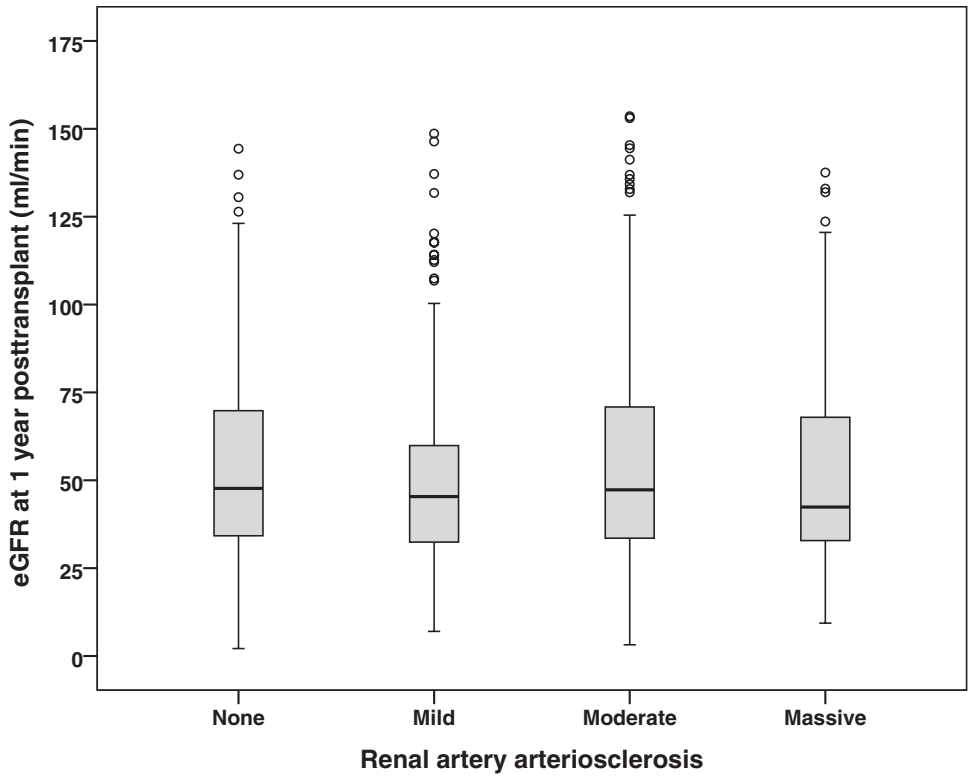

FIGURE 1. Estimated glomerular filtration rate (eGFR) (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula) at 1 y posttransplant for kidneys with various estimated degrees of renal artery arteriosclerosis (medians, interquartile, and full ranges).

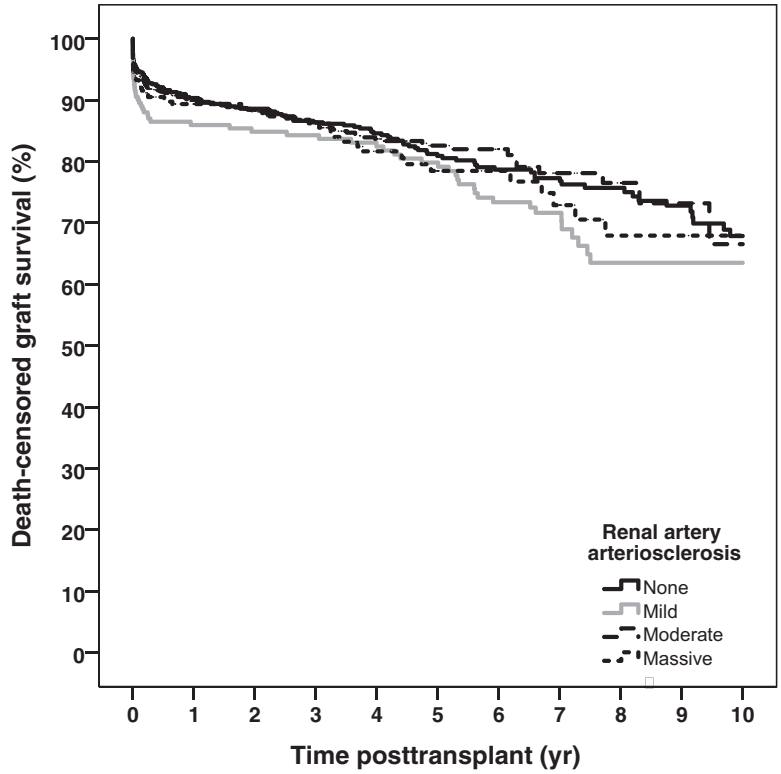

FIGURE 2. Death-censored graft survival of transplanted kidneys with various estimated degrees of renal artery arteriosclerosis.

correlation between macroscopic assessment of arteriosclerosis and Banff microscopic *cv* score was –0.02 ($P = 0.82$), and the Spearman correlation between macroscopic arteriosclerosis and Banff microscopic *ah* score was –0.07 ($P = 0.50$). In addition, any macroscopic arteriosclerosis was not significantly associated with any positive score on the Banff *cv* and *ah* scales (Pearson chi-square test $P = 0.80$ and $P = 0.54$). These results indicate that there was

TABLE 5.

Cross-tabulation of macroscopic renal arteriosclerosis score estimated by the procurement surgeon and histological surrogates of intrarenal microvascular arteriosclerosis, scored by an experienced renal pathologist

Histology score	Macroscopic renal artery arteriosclerosis				
	None	Mild	Moderate	Massive	Total
Vascular fibrous intimal thickening (*cv*-score)					
0	5	0	10	0	15
1	20	0	50	11	81
2	7	0	3	2	12
3	0	0	1	0	1
Arteriolar hyaline thickening (*ah*-score)					
0	28	0	59	12	99
1	3	0	5	0	8
2	1	0	0	1	2
3	0	0	0	0	0
Total	32	0	64	13	109

Values represent the number of kidneys with the respective scores in our local (single-center) subcohort of 109 allografts for which a preimplantation biopsy was available.
ah, arteriolar hyalinosis; *cv*, vascular fibrous intimal thickening.

no sign of any relation between macroscopically observed renal artery arteriosclerosis and histological indicators of intragraft arteriosclerosis. In addition, univariable regression analyses indicated that, in this n = 129 subcohort, there was no statistically significant association between *cv* or *ah* scores and DGF, PNF, 1-year eGFR, and 10-year graft survival.

DISCUSSION

The present study clearly shows that in the Netherlands, the decision to accept or discard a deceased donor kidney is independently influenced by the reported macroscopic degree of arteriosclerosis of the renal artery. This is interesting, as no traceable literature exists on how macroscopic arteriosclerosis affects graft quality and transplant outcome. Neither do any guidelines exist on how to accurately visually assess the degree of renal artery arteriosclerosis. Intuitively, the practice seems wise, as arteriosclerosis could theoretically lead to a variety of intraoperative and posttransplant complications. First, the vascular anastomosis may be technically challenging, potentially resulting in a higher risk of bleeding or thrombosis, which in turn could compromise transplant outcome. Second, macroscopic arteriosclerosis may also be bad news for overall graft quality. In the past, it has been assumed that if the main renal artery is affected, smaller intrarenal vessels may be diseased as well and this could result in inferior posttransplant function and graft survival. The latter has been shown to some extent in small histopathologic series, in which variations of the Banff *ah* score were associated with outcome.[3,7] However, our data showed no correlation whatsoever between histological analogs of arteriosclerosis and reported macroscopic renal artery arteriosclerosis. Although this was done in a small subseries of our main data set, there was not even a trend towards a relevant correlation in these results. Our findings suggest that macroscopic renal artery arteriosclerosis, at least the way it is assessed within Eurotransplant, does not reflect microscopic graft arteriosclerosis in any way. Hence, macroscopic arteriosclerosis cannot be regarded as a surrogate marker for microscopic arteriosclerosis, which is sometimes associated with transplant outcome. This might be explained by the fact that the main renal artery is very different from and quite distant to smaller intrarenal vessels. It seems plausible that intrarenal vascular lesions contribute more to allograft dysfunction than extrarenal arteriosclerotic disease. In addition, an in our experience common—albeit undocumented—observation is that donor surgeons tend to score the degree of renal artery arteriosclerosis looking at the aspect of the aortic patch near the ostium of the renal artery. It is our consistent observation that the patch often has a much higher degree of visible arteriosclerosis than the renal artery itself. An arteriosclerotic patch can easily be removed, which leaves the kidney with an often pristine renal artery that can be anastomosed end-to-side to the recipient iliac artery in a similar fashion as commonly performed for renal grafts retrieved from living donors. Perhaps, if donor surgeons would consistently report only macroscopic arteriosclerosis, which is inside the renal artery itself, a different picture could emerge about the occurrence of macroscopic arteriosclerosis and also of its association with transplant outcome. Nevertheless, in our current study, we also did not find significant associations between histopathologic analogs of intragraft arteriosclerosis and posttransplant outcome. However, this could be due to the limited sample size in this subcohort, which may not have provided adequate power to detect relatively subtle effects of microscopic arteriosclerosis on outcome. In addition, discarded kidneys are likely to have on average more microscopic arteriosclerosis than organs that were transplanted. An inherent shortcoming of analyses such as the present one is that it remains unknown what posttransplant outcome of discarded allografts would have been and, consequently, relevant bias could be introduced in conclusions on the influence of arteriosclerosis on outcome.

In Eurotransplant, no standardized scoring system, protocol, or guideline for the assessment of macroscopic arteriosclerosis of the renal artery is implemented. It is left to the individual retrieval surgeon to grade and report on the extent of arteriosclerosis per organ. Yet, this very subjective assessment is a compulsory field in the organ report that is passed on to the potential recipient center at organ offer. Our study suggests that recipient centers do take this score into serious account when judging an organ offer. Given the fact that the current subjective scoring system did not show a relevant association with transplant outcome, our results could stimulate the development of a more standardized and objective assessment methodology, which might perhaps have a predictive value for aspects of renal posttransplant results.

Within the current Eurotransplant context of how donor surgeons score arteriosclerosis and keeping in mind potential selection bias as described before, our data largely contradict the existence of an association between macroscopic renal artery arteriosclerosis and transplant outcome. The only significant association we could find was that transplanted kidneys with mild arteriosclerosis had more PNF. It is tempting to hypothesize that this may

indeed be due to more technical complications following a suboptimal arterial anastomosis, leading to graft failure as a result of bleeding or thrombosis. However, vascular reasons for graft failure were even less frequent in those kidneys with PNF and arteriosclerosis, compared to grafts with PNF that had unaffected renal arteries. Moreover, more severe degrees of renal artery arteriosclerosis were not associated with an elevated risk of PNF. This finding cannot be attributed to a too small number of cases in the higher degree of arteriosclerosis subgroups. To the contrary: The subgroup with "mild" arteriosclerosis was the smallest of all 4 categories, comprising only 9% of all transplants. Each of the other 3 subgroups consisted of substantially more cases.

The apparent misconception among transplant clinicians that subjectively graded macroscopic arteriosclerosis of the renal artery would have a relevant influence on outcome could originate from common observations in nephrology. After all, many studies have reported a clear relationship between chronic native or graft renal artery stenosis and the development of progressive renal (graft) failure.[8-11] Our present study carefully suggests that this mechanism does not seem to play an important role in kidney grafts accepted for transplantation that have various degrees of renal artery arteriosclerosis already before implantation.

We feel that it is no great surprise that retrieval surgeons' eyes, superficially examining the renal artery, are not the most reliable tool to judge the real condition of the renal graft's (micro)vasculature. Apart from the fact that such macroscopic judgment is very subjective, with likely relevant interobserver variability, reliable vascular quality assessment calls for more advanced diagnostic tools. As mentioned before, histological surrogates for intragraft arteriosclerosis might offer a more predictive pretransplant scoring instrument, but this will have to be demonstrated in a larger cohort with systematically scored preimplantation biopsies. Also, estimating the degree of luminal narrowing in renal arteries on computed tomography-angiographies that deceased donors often routinely undergo could contribute to a more objective rating of actual arteriosclerotic disease, as has been established for coronary artery imaging.[12] Moreover, such an assessment can be done noninvasively and well in advance of a retrieval procedure. The latter would allow the clinical team more time to decide whether kidneys will be procured for transplantation. However, more studies into the relation between radiological scoring of arteriosclerosis and transplant outcome are required before routine donor computed tomography scans can become part of the pretransplant decision-making process.

Our current study has several important limitations. First, our analysis is based on retrospectively collected data. We did not have data on the macroscopic degree of renal artery arteriosclerosis for all transplanted renal grafts in the time period studied and this could have caused bias. Second, this study was only performed on data from transplant centers in the Netherlands. In other countries, scoring, reporting, and subsequently interpreting the macroscopic degree of arteriosclerosis could be different. Third, our series of histologically scored preimplantation biopsies was single-center and quite small. Therefore, we could not reliably determine whether in those biopsies, histopathologic scores for intragraft arteriosclerosis did correlate significantly with posttransplant outcome, as other studies have suggested. Finally, many kidneys with a "massive" arteriosclerosis score were discarded, and we do not know what the outcome would have been when these organs had been transplanted. This may have introduced a bias in our data. Therefore, it is important to note that our results are valid only after inevitable exclusion of discarded kidneys that had on average more arteriosclerosis than those that were transplanted. Conclusions should be interpreted in the light of this potential bias. There was still a considerable number of "massively" arteriosclerotic kidneys that were transplanted (509, 13%). Such a large number should have enabled us to pick up a relevant negative effect of massive arteriosclerosis on transplant outcome. Nevertheless, we cannot entirely rule out that "massively" arteriosclerotic kidneys that were discarded had on average even more severe arteriosclerosis than those that were scored "massive" and transplanted.

In conclusion, our large multicenter retrospective study found that transplant clinicians are much more inclined to discard a 50+ deceased donor kidney when any degree of macroscopic arteriosclerosis of the renal artery is reported by the retrieval team. Subjectively graded macroscopic arteriosclerosis was somewhat associated with PNF, but there was no effect on DGF, eGFR at 1 year, or long-term graft survival. Our analyses also suggest that subjective and nonprotocolled macroscopic assessment of arteriosclerosis is not a good measure of intragraft microscopic arteriosclerosis. Given these data, we feel that kidney discard based on a very subjective macroscopic assessment of renal artery arteriosclerosis—which is currently the only documented and communicated assessment of arteriosclerosis in Eurotransplant—should be discouraged. The implementation of a more structured and objective macroscopic assessment method of renal artery arteriosclerosis could be an opportunity to improve its predictive capacity for renal transplant outcome.

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