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MESTRADO INTEGRADO EM MEDICINA

# Association of the calcification score of the abdominal aorta, common iliac and renal arteries with outcomes in kidney donors

Luís Miguel da Costa Ribeiro

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## Artigo Original

Dissertação de Mestrado Integrado em Medicina

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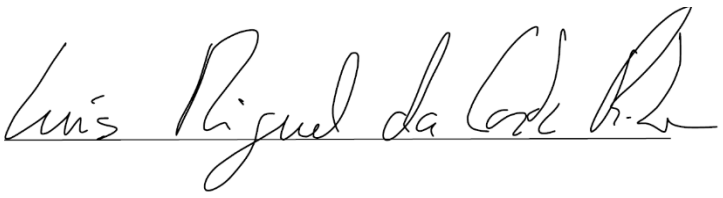
## Artigo Original

This study was approved by the Ethics Committee of Centro Hospitalar Universitário do Porto. Reference number: 2021-300(246-DEFI/254-CE).

**Estudante:**



(Luís Miguel da Costa Ribeiro)

**Orientador:**

(Miguel Silva Ramos)

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## Abstract

**Introduction:** The increasing demand for kidney transplants has led to the use of expanded criteria donors, which in living donors might carry some increased risk, as their prognosis are less established. This expansion of selection criteria renders vascular calcification an ever more common finding in protocoled pre-transplant imaging. The purpose of the present study was to explore whether a connection can be found between Agatston calcification score of the abdominal, common iliac and renal vessels, prior to kidney donation, and post donation renal function.

**Methods:** This is a retrospective analysis of 156 living kidney donors who underwent living donor nephrectomy between January 2010 and December 2016. We analyzed donor's multi-slice computed topographies and quantified the Total Calcification Score (TCaScore), by calculating the Agatston score for each vessel, aorta, common iliac and renal arteries. Donors were placed into two different groups based on their TCaScore: minimal calcification group, <100 TCaScore, and moderate to severe calcification group, ≥100 TCaScore. The relationship between TCaScore, 1-year eGFR, proteinuria and risk of one measurement of decreased renal function (eGFR <60 ml/min/1.73m$^2$) over 5 years of follow-up were investigated.

**Results:** The ≥100 TCaScore group consisted of 29 (19%) donors with a median (interquartile range) calcification score of 164 (117-358). This group was significantly older, 56.7 ± 6.9 vs 45.5 ± 10.6 (*P* <0.001), had a higher average BMI (*P* <0.019), a higher prevalence of comorbidities and a lower preoperative eGFR (*P*<0.014). 1-year eGFR was diminished in the ≥100 TCaScore group, 69.9 ± 15.7mL/min/1.73m$^2$ vs 76.3 ± 15.5mL/min/1.73m$^2$ (*P*<0.048), while also having increased risk for a measurement of decreased renal function over the 5-year follow-up, 22% vs 48% (*P*<0.007). Multivariable analysis of either 1-year eGFR and risk of a measurement of decreased renal function in 5 years, did not reveal any statistically relevant differences.

**Conclusion:** Our study, through univariate analyses, found that donors with >100 TCaScore were at risk of lower 1-year eGFR and one measurement of decreased renal function in 5 years. However, a higher-than-expected vascular calcification, found during the screening process, should not be an excluding factor in donors, although they may require closer monitoring during follow-up.



**Keywords:** kidney transplantation; vascular calcification; Agatston score; donor outcomes; expanded criteria donors.

# Resumo

**Introdução:** A crescente necessidade de transplantes renais leva uma maior utilização de dadores com critérios expandidos, o que, no caso dos dadores vivos, pode comportar algum risco acrescido, uma vez que o seu prognóstico é menos estudado e conhecido. Esta expansão dos critérios de seleção torna a calcificação vascular um achado radiográfico cada vez mais comum na imagiologia pré-transplante. O objetivo do presente estudo foi explorar a possível ligação entre o score de calcificação de Agatston na aorta abdominal, ilíacas comuns e artérias renais, antes da nefrectomia, e a função renal pós-doação.

**Métodos:** Este é um estudo retrospetivo de 156 dadores que foram submetidos a nefrectomia entre janeiro de 2010 e dezembro de 2016. A análise das topografias computorizadas pré transplante permitiu o cálculo do *Score de Calcificação Total* (TCaScore) através da aplicação do score de Agatston para cada vaso, aorta, ilíacas comuns e artérias renais. Os doadores foram colocados em dois grupos diferentes com base no seu TCaScore, um grupo com calcificação mínima, <100 TCaScore, e outro grupo com calcificação moderada a grave, ≥100 TCaScore. Foi investigada a relação entre TCaScore, taxa de filtração glomerular (TFG) ao 1 ano, proteinúria e risco de uma medição com função renal diminuída (TGF <60 ml/min/1,73m$^2$) ao longo de 5 anos de seguimento.

**Resultados:** O grupo com ≥100 TCaScore consistia em 29 (19%) doadores com uma valor médio de calcificação (intervalo interquartil) de 164 (117-358). Este grupo era significativamente mais idoso, 56,7 ± 6,9 vs. 45,5 ± 10,6 (P<0,001), tinha um IMC médio mais elevado (P<0,019), uma maior prevalência de comorbilidades e uma menor TFG pré-operatória (P<0,014). A TFG ao 1 ano estava diminuída no grupo com ≥100 TCaScore, 69,9 ± 15,7mL/min/1,73m2 vs. 76,3 ± 15,5mL/min/1,73m2 (P<0,048), assim como tinham um risco aumentado para uma medição com função renal diminuída durante o seguimento de 5 anos, 22% vs. 48% (P<0,007). A análise multivariável da TFG ao 1 ano e o risco de uma medição da função renal diminuída em 5 anos não revelou quaisquer diferenças estatisticamente relevantes.

**Conclusão:** O nosso estudo, através de análise univariada, concluiu que os doadores com >100 TCaScore correm o risco de apresentarem uma TFG inferior ao 1 ano e uma medição com diminuição da função renal em 5 anos. No entanto, uma calcificação vascular superior à esperada não deve ser um fator de exclusão nos dadores, apesar destes poderem vir a necessitar de um seguimento mais apertado.



**Palavras-chave**: transplante renal; calcificação vascular; score de Agatston; desfechos dos dadores; dadores com critérios expandidos.

# Abbreviations and Acronyms List

| | |
|---|---|
| **BMI** | Body Mass Index |
| **CaScore** | Calcification Score |
| **CHUP** | Centro Hospitalar Universitário Do Porto |
| **CKD** | Chronic Kidney Disease |
| **CT** | Computer Tomography |
| **ECD** | Expanded Criteria Donors |
| **eGFR** | Estimated Glomerular Filtration Rate |
| **ESRD** | End-Stage Renal Disease |
| **GFR** | Glomerular Filtration Rate |
| **HU** | Hounsfield Units |
| **HDL** | High-Density Lipoprotein |
| **ICBAS** | Instituto De Ciências Biomédicas Abel Salazar |
| **LDL** | Low-Density Lipoprotein |
| **SD** | Standard Deviation |
| **TCaScore** | Total Calcification Score |

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# Introduction

Studies estimate that 1 in 10 people suffer from chronic kidney disease (CKD) in highly developed nations. Its diagnosis and treatment, especially in the more advanced stages of the disease, can have a severe impact on the expectancy and quality of life. [1] This is the reality of more than 20,000 Portuguese patients in end-stage renal disease (ESRD), where kidney transplantation has been proven to be the best therapy, since the average life expectancy and quality of life of those who undergo kidney transplantation is higher than those who remain on dialysis.[2] After transplantation, estimates point to an increase of 10 years in overall life span, which varies between 3 to 17 years according to patient group, with older patients having less benefit than younger recipients, although they still positively gain from the procedure.[3–5]

Despite the increase in the number of kidney transplants performed annually, the waiting lists continue to grow, with the number of patients waiting for a kidney transplant increasing all around the globe. This increasing demand for grafts has led to the use of expanded criteria donors (ECD), which can be defined as any brain-dead donor aged > 60 years or a donor aged >50 years with 2 of the following features: history of hypertension, death resulting from a cerebrovascular accident, or terminal serum creatinine level ≥ 1.5 mg/dL.[4,6] These ECD kidneys have demonstrated to have similar short- and long-term outcomes to standard criteria donors for the recipients, despite a slight decrease in 1- to 15-year patient and graft survival rates after kidney transplantation using ECD kidneys in some multicenter and single center studies.[6–8] Although it should be highlighted that there is a clear decrease in mortality in these recipients when compared to patients who stayed on dialysis.[5]

Parallelly, an expansion of selection criteria for living transplantation has started to occur, which has the potential to further diminish the number of end-stage renal disease on waiting lists.[9] Furthermore, with a society becoming progressively older and obese, with all associated health problems, the need to consider these donors is vital.[10,11] This expansion of selection criteria, even though living kidney donation has been performed for the better part of 8 decades, with minimal short-and long-term risk to the donor, might carry some increased peril to the donors, as their predicted medical futures are less precise than in the past. Thus, a thorough evaluation of these risk factors and comorbidities is therefore essential to maintain donor safety.[10,12]

One age-associated comorbidity, relevant to this population, is atherosclerosis. Atherosclerosis is a representative lifestyle disease, where two of the central factors of cardiovascular ageing are arterial calcification and its associated arterial stiffening. The acceleration of arterial calcification is known to be strongly related with age, loss of kidney function, smoking, glucose

resistance, dyslipidemia, hypertension and mineral/bone parameter disorders.[13,14] In spite of not being as well established as the coronary artery calcification, a well-studied predictor of cardiovascular events, abdominal aortic calcification has been able to predict both cardiovascular events and all-cause mortality in recipients, while also being associated with lower glomerular filtration rate (GFR) and cardiac structural changes in specific population of CKD patients.[15–18] In donors, a seemingly healthy population, abdominal aortic calcification has been less researched, though Tanaka et al. claimed that aortic calcification might be an independent risk factor for pre-existing histopathological injuries in the allograft.[19]

In order to further advance the research into donors' selection and risk assessment parameters, this study aims to analyze the abdominal aortic, common iliac and renal calcification in pre-nephrectomy living donors and its relationship with GFR, GFR trajectory and proteinuria development, since ESKD, cardiovascular events and mortality after donation are such rare outcomes for a 5-year follow-up study. The quantification of calcification in the arteries is calculated through the Agatston score, which is based on the size of lesions positively weighted by a categorical factor of the calcium density, on abdominal and pelvic CT imaging taken prior to kidney transplantation, which are primarily performed for surgical planning. As the imaging data are available, non-contrast enhanced CT-based quantification of aortic, iliac, and renal calcification can be used for risk stratification of patients screened for kidney transplantation, without the need for additional procedures [20,21]

## Materials and Methods

### Subjects and Study Design

This is a retrospective study of a single transplant centre, reviewing the clinical records of living kidney donors, with nephrectomies performed at *Centro Hospitalar Universitário do Porto* (CHUP) between January 2010 and December 2016. The study was approved by the Ethics Committee and Department for Education, Training and Research of CHUP/ICBAS, as the data for the study was retrieved from the patients' electronic and paper medical records, always maintaining their anonymity. Out of the total 169 donor nephrectomies performed in this 6-year timeframe, 9 patients were excluded as their CT scans were unavailable for examination and another 4 patients were additionally excluded due to not having evaluation of pre-operative eGFR or eGFR at 1-year. Thus, the remaining 156 donors defined our study cohort

Donor characteristics regarding demographic information, anthropometric measurements, prior or current diagnosis or treatment for hypertension, diabetes mellitus and dyslipidemia, laboratory data and imaging before nephrectomy were recorded, as well as during the 5-year

follow-up period. The CT scans, performed according to the pre-transplant screening protocol, with one of two multidetector-row CT scans available at our institution (a 64-detector GE VCT LightSpeed® or a 16-detector GE Brightspeed® ), were examined using the 3D Slicer software, version 4.11, which allows for the calculation of the calcification score of the abdominal aorta, from the branch of the celiac trunk to the branch of the common iliac artery, and of the common iliac and renal arteries, along their entire length. The calcification scores were calculated through the Agatston method, using a 5 mm CT slice thickness and detection threshold ≥130 Hounsfield units involving ≥1 $mm^2$ area or three adjacent pixels. The individual Agatston scores were calculated by multiplying each area of interest by a weighted score assigned to the highest density of calcification (1 for 130-199 HU, 2 for 200-299 HU, 3 for 300-399 HU and 4 for >400 HU) within the individual area. The total calcification score (TCaScore) was the cumulative sum of the Agatston scores of all calculated areas and vessels (CaScore).[20,21]

Outcome Parameters

The parameter of interest was the total calcification score (TCaScore) at donation. Donors were stratified into two different groups by their baseline TCaScore, either absent to minimal calcification, <100 TCaScore, and moderate to severe calcification, ≥100 TCaScore. The glomerular filtration rate (eGFR) was estimated employing the 2021 Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI). A postdonation eGFR <60 ml/min per 1.73$m^2$ was considered to be decreased, and was evaluated on a yearly basis during follow-up, in addition to being used as a main endpoint. In terms of other relevant medical conditions, postdonation Diabetes Mellitus was defined as fasting glycemia ≥126 mg/dl or the use of insulin and/or other hypoglycemic agents. Hypertension was classified as a prescription of antihypertensive medications or a registered blood pressure ≥ 140/90 mmHg during visits. Dyslipidemia, before or after nephrectomy, was considered present when donors either used hypolipidemic agents, had total cholesterol >200 mg/ dL, LDL >130 mg/dL, triglycerides >150 mg/dL or HDL <40 mg/dL. On urinary analysis, proteinuria was defined by the presence of urine random protein >15 mg/dl or 24-hour protein >300 mg/day.

Statistical Analysis

Continuous variables are reported as mean + standard deviation (SD) or median (interquartile range [IQR]), and categorical variables are presented as frequency and percentage. Categorical data including were compared using Pearson chi-square test or Fisher exact test, and continuous variables were compared with Student's t test or Mann–Whitney U-test, as appropriate.

Correlations between eGFR values, at donation as well as at 1 year of follow-up, and total calcification scores (TCaScore) were assessed by Spearman's correlation test.

Linear prediction of eGFR at 1 year of follow-up were analysed through a univariate and multivariable linear regression model, and risk factors for an eGFR < 60 ml/min per 1.73m$^2$ at 1 year were calculated through a univariate multivariable logistic regression. In order to establish comparisons between covariates regarding strength of association, the increment in continuous variables was assessed per standard deviation.

Recipient eGFR slope between 1 and 5 years after transplant was assessed by univariate and multivariable linear mixed regression model that imputed subject specific random effects (intercept and slope defined as eGFR at 1 year and time in years, respectively) on an unstructured covariance matrix. The dependent variable was all eGFR measurements, and the independent variables were entered as 2-way interaction terms between them and the time (in years) variable. All 156 donors were studied, and a median of 3 (IQR: 2–4) annual measurements of eGFR were available. All multivariable models were constructed by including variables with a univariate P-value < 0.150.

Risk predictors of first measurement with an eGFR < 60 ml/min/1.73m$^2$ or first proteinuria (as defined above) was analyzed by, using univariate and multivariate Cox regression model. Previous outcomes-free survival curves, between donors with TCaScore <100 and TCaScore ≥100, were depicted by Kaplan-Meier curves and comparisons were made by log-rank test.

Statistical analysis was performed using STATA/MP®, version 15.1 (Stata Corp, College Station,TX). A 2-sided P-value < 0.05 was considered as statistically significant.

## Results

Of total 156 donors present in this cohort, 29 (19%) presented with a total calcification score (TCaScore) ≥100, based on their pre-transplant CT scans. The majority of donors were female (71%), presented with an average body mass index (BMI) at donation of 25.1 ± 3.5kg/m$^2$, with Body Mass Index (BMI) between groups being 24.8 ± 3.5kg/m$^2$ vs 26.4 ± 2.9kg/m$^2$ in the TCaScore <100 and TCaScore ≥100, respectively (*P* <0.019). On the whole, the average donor age was 47.6 ± 10.9, the mean preoperative glomerular filtration rate (GFR) was 105.3 ± 13.6 mL/min/1.73m$^2$ and there were only 20 active smokers, at the time of donation.

The median (interquartile range) total calcification score was 0 (0-50), including the TCaScore ≥100 group with median (interquartile range) calcification of 164 (117-358). There were notary differences between the TCaScore groups, regarding age the TCaScore<100 group presented

with 45.5 ± 10.6, contrasting with the mean age of 56.7 ± 6.9 in the TCaScore ≥100 group (*P* <0.001). Dyslipidemia was more commonly found in TCaScore ≥100 donors, with 21 (75%; *P* < .027), along with a higher likelihood of hypertension history, 26 donors (17%) overall, 10 (34%) of which in the TCaScore ≥100 group (*P* <0.004). Regarding, the TCaScore ≥100 group had lower preoperative eGFR values, 106.6 ± 13.4mL/min/1.73m$^2$ vs 99.7 ± 13.5mL/min/1.73m$^2$ (*P*<0.014) (Table I).

At the first year of postoperative follow-up the mean eGFR was 75.1 ± 15.7mL/min/1.73m$^2$, although when analysing each group separately the TCaScore ≥100 group more frequently had delayed renal function recovery, 69.9 ± 15.7mL/min/1.73m$^2$ vs 76.3 ± 15.5mL/min/1.73m$^2$ (*P*<0.048). The same group of donors also showed an increase in the probability of postdonation eGFR <60 mL/min/1.73m$^2$ at 1 year of follow-up, with 8 donors (28%) vs 16 donors (13%; *P*<0.044) (Table II). Linear and logistic regression analysis for eGFR and eGFR <60 mL/min/1.73m$^2$, respectively, showed a univariate statistically significance for both, (*P*<0.048; *P*<0.049), although the same cannot be said when a multivariable analysis, adjusted for age, sex, hypertension, BMI and eGFR at donation, was performed (*P*<0.887; *P*<0.651). Estimated eGFR slope from 1 to 5-years of postdonation follow-up was assessed by univariate and multivariable linear mixed regression model but wielded no statistically significant results.

Risk of one measurement of decreased eGFR, < 60 mL/min/1.73m$^2$, over the course of the 5-year of follow-up was 27% for the entire donor pool, along with 22% for the TCaScore <100 group and 48% for the TCaScore ≥100 group (Univariate = *P*<0.007; Graph. I). Moreover, risk of proteinuria in the same time period was 33% (31% vs 38%; Univariate = *P*<0.433; Multivariate [adjusted for age, sex, hypertension, BMI, eGFR at donation] = *P*<0.136).

## Discussion

In this retrospective single centre study, we analyzed the clinical implication of vascular calcification score, through the Agatston method, and its association with renal function. Regarding the presence of moderate to severe calcification (TCaScore ≥100), compared with minimal to absent calcification of their aorta, iliac and renal arteries (TCaScore <100), we found that higher degrees of vascular calcification was observed significantly more often in older patients, those with higher BMI, hypertension, dyslipidemia and lower eGFR at donation, corroborating the known relationship between these traditional risk factors and arterial calcification. [13,14,16]

At 1-year of follow-up, donors with TCaScore ≥100 exhibit a trend of lower mean eGFR and were at significant risk for decreased renal function (eGFR <60 mL/min/1.73m$^2$); nevertheless, this

trend was parallelly associated with more advanced age and other comorbidities in donors. Thus, after correcting for age difference, sex, the presence of hypertension, BMI and eGFR at donation, there was no difference in predicting eGFR at 1-year or risk eGFR <60 mL/min/1.73m$^2$ between the 2 groups. Several previous studies have evaluated aortic calcification, but relatively few focused on donors and their outcomes. The only one, to our knowledge, is the study of 287 donors by Yoon et al., which arrived at similar findings to ours, a calcification score of the abdominal aorta valued over 100 raised the probability of GFR <60 ml/min per 1.73m$^2$, at 6 months of follow-up, and was associated with histologic findings of nephrosclerosis.[22] Studies featuring abdominal arteries calcification and graft outcomes are more common, with clear similarities and parallels with our findings. Ichii et al. arrived at the statistically independent association between lower eGFR and the quantitative degree of aortic calcification in non-dialysis patients.[17] Moreover, in 2021 Benjamens et al. demonstrated that pre-transplant aorto-iliac calcification is associated with one-year eGFR in univariate linear regression analyses.[23] While Tatami et al. identified trends between abdominal aortic calcifications and cardiovascular events in asymptomatic non-dialysis patients (median eGFR, 43.2 + 17.7 mL/min/1.73 m$^2$).[24]

We further evaluated the effects of TCaScore over a longer period and identified a non-causal inverse association between the two calcification groups and the risk of one measurement of decreased eGFR, < 60 mL/min/1.73m$^2$, over the course of the 5-year of follow-up, in univariate analysis. Donors lose roughly 30% of their pre-donation glomerular filtration rate after they go through compensatory hypertrophy and hyperfiltration, and donor nephrectomy itself does not appear to cause long-term loss of eGFR at a higher rate than what is seen in general population.[25–27] Although certain pre-donation characteristics, for instance arterial calcification, analyzed in this study, pre-donation eGFR and even remaining kidney volume indexed to weight, might put donors at risk of decreased compensatory mechanisms and even future post-donation kidney injury. [26,28]

The screening protocol for renal donors is thorough for any cardiac or kidney disease, diabetes or other comorbidities that might render the transplant a higher than accepted risk for the donor.[10] CT scans are also routinely performed, in order to evaluate the number of renal vessels, kidney volumes, and the presence of renal artery atheroma, which has been associated with graft thrombosis and even mortality.[29] Stands to reason that using the same CT data to further evaluate calcification score of aorta, iliac and renal arteries, will only optimize donor's pre-donation risk assessment, especially in expanded criteria living donors, gaining further safety and information for an ever more common donor profile.

This study has a number of important limitations. Firstly, the retrospective observational nature of the study design, of which the selection of donors depended on the availability of a pre-transplant CT scan, makes the study prone to selection bias and confounding, even though we controlled for important demographic factors, comorbidities, and baseline eGFR. Secondly, the quantification technique for vascular calcification, in this study, was performed by an isolated examiner, although the Agatston method is considered to be a reliable and reproducible method, with reasonable inter-scanner variability.[30] Thirdly, the relative small study cohort of 156 and follow-up period, of 5 years for nearly every donor, which despite being , to our knowledge, the longest of any CT-based studies on vascular calcification, lack when compared to larger registry studies, which are required in order to comprehend the conclusively implications of vascular calcification score in kidney donors outcomes.

## Conclusion

In conclusion, this study proved that pre-transplant vascular calcification score is correlated with a 1-year eGFR and risk of decreased renal function in 5-years in univariate, but not in multivariable linear regression analyses. Increased donor age and lower pre-operative eGFR were found to be significant confounder for this association, not to mention sex, hypertension, and BMI. These results underline that living donors from expanded criteria living donors are safely stratified with current practices of screening, despite the increase of older, overweight, with comorbidities, donors. Even though, based on these findings, living donor with severe calcification on CT scans require close monitoring and follow-up.

# Appendix

**Table I**- Baseline characteristic and calcification scores.

| | **Total N=156** | **TCaScore <100 N=127 (81%)** | **TCaScore ≥100 N=29 (19%)** | ***P*** |
|---|---|---|---|---|
| **Age at donation, mean ± SD** | 47.6±10.9 | 45.5±10.6 | 56.7±6.9 | <0.001 |
| **Female donor, n (%)** | 111 (71) | 94 (74) | 17 (59) | 0.099 |
| **BMI at donation, mean ± SD** | 25.1±3.5 | 24.8±3.5 | 26.4±2.9 | 0.019 |
| **Hypertension at donation, n (%)** | 26 (17) | 16 (13) | 10 (34) | 0.004 |
| **Smoker, n (%)** | 20 (13) | 16 (13) | 4 (14) | 0.768 |
| **Dyslipidemia at donation, n (%) Missing=3** | 86 (56) | 65 (52) | 21 (75) | 0.027 |
| **eGFR at donation, mean ± SD** | 105.3±13.6 | 106.6±13.4 | 99.7±13.5 | 0.014 |
| **TCaScore, median (P25-P75) [P10-P90]** | 0 (0-50) [0-262] | 0 (0-0) [0-35] | 269 (182-564) [125-1276] | <0.001 |
| **CaScore Abdominal Aorta, median (P25-P75) [P10-P90]** | 0 (0-10) [0-151] | 0 (0-0) [0-12] | 164 (117-358) [5-815] | <0.001 |
| **CaScore Renal Artery, median (P25-P75) [P10-P90]** | 0 (0-0) [0-0] | 0 (0-0) [0-0] | 0 (0-0) [0-7] | <0.001 |
| **CaScore Common Iliac Artery, median (P25-P75) [P10-P90]** | 0 (0-0) [0-84] | 0 (0-0) [0-9] | 99 (18-247) [0-610] | <0.001 |

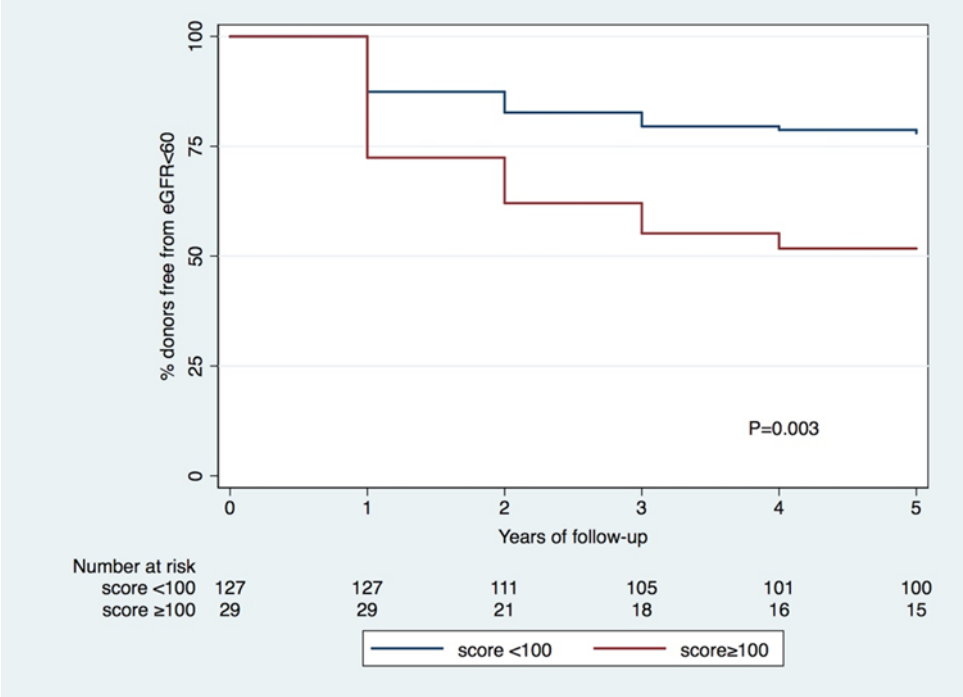
SD, standard deviation; BMI, body mass index, expressed in kg/m$^2$; eGFR, estimated glomerular filtration rate, expressed in ml/min/1.73m$^2$; TCaScore, Total Calcification Score; CaScore, Calcidication Score.

**Table II**- Outcomes 1-year postdonation follow-up.

| | **Total N=156** | **TCaScore <100 N=127 (81%)** | **TCaScore ≥100 N=29 (19%)** | ***P*** |
|---|---|---|---|---|
| **eGFR, mean ± SD** | 75.1±15.7 | 76.3±15.5 | 69.9±15.7 | 0.048 |
| **eGFR <60, n (%)** | 24 (15) | 16 (13) | 8 (28) | 0.044 |
| **Proteinuria, n (%) Missing=25** | 24 (18) | 17 (17) | 7 (25) | 0.303 |
| **Dyslipidemia, n (%) Missing=12** | 89 (62) | 69 (59) | 20 (71) | 0.243 |

SD, standard deviation; eGFR, estimated glomerular filtration rate, expressed in ml/min/1.73m$^2$; TCaScore, Total Calcification Score.

**Graph I**- Risk of one measurement of decreased eGFR, < 60 ml/min/1.73m$^2$, over the course of the 5-year of follow-up in donors with and without moderate to severe abdominal aortic, iliac and renal calcification.




| | Hazard Ratio | 95% CI | P |
|---|---|---|---|
| **Univariate** | | | |
| **Score Agatston≥100** | 2.433 | 1.280; 4.628 | 0.007 |
| **Multivariable*** | | | |
| **Score Agatston≥100** | 1.267 | 0.617; 2.604 | 0.520 |

* Adjusted for Age, Sex, Hypertension, BMI, eGFR at donation

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