ANGIOTOMOGRAPHY IN THE VASCULAR ASSESSMENT OF THE RECIPIENT BEFORE RENAL TRANSPLANTATION: LITERATURE REVIEW

Angiotomografia na avaliação vascular do receptor antes do transplante renal: revisão de literatura

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ABSTRACT

Arterial calcification and atherosclerotic lesions, which have a high incidence in chronic renal patients are important risk factors for immediate and late postoperative complications after renal transplantation. Computed tomography angiography of the iliac arteries can accurately show arterial diseases, including the location and extent of arterial calcification, as well as arterial caliber, which would allow better surgical planning of the site of renal implantation. **Purpose**: This literature review aimed to verify the value of this exam as a diagnostic method for arterial atheromatous disease in the iliac vessels region in patients who are candidates for renal replacement therapy by analyzing primary studies of patients submitted to this exam. **Methods**: The methodology used was a literary search in electronic databases (PubMed, LILACS, Google Scholar and Cochrane Library), dating from 2003 to 2018. **Results**: The literature search resulted in a total of 100 articles, 29 of which pre-selected based on title and abstract, and of those, only 6 met the inclusion criteria. CTA allowed high accuracy in the diagnosis of calcification, with sensitivity ranging from 71% to 100%, and specificity ranging from 73% to 92%. Computed tomography angiography was used for surgical planning based on the degree of calcification, and showed that there were anastomosis site changes or vascular procedures before transplantation in 25.2%, cancellation of transplantation due to the degree of arterial calcification in 7,6%, graft loss in 6.8% and death in 3.9% of the cases. **Conclusion**: Computed tomography angiography has a significant value in detecting vascular calcifications, allowing better surgical planning.

Keywords: Computed Tomography Angiography; Plaque, Atherosclerotic; Kidney Transplantation.

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INTRODUCTION

Atherosclerosis is an inflammation with the formation of plaques of fat, calcium and other elements in the middle and intimate layer of artery walls in the human body, either in diffuse or localized form. It is characterized by the narrowing and hardening of arteries due to the accumulation of fat in its walls, known as atheroma.[1] Over the years, the growth of plaques causes the narrowing of the vessel, which may reach complete obstruction, restricting blood flow in the region. It increases considerably in patients with chronic renal failure due to mechanisms such as oxidative stress, inflammation, hyperphosphatemia, hypercalcemia by parathyroid hormone elevation and low HDL-cholesterol fraction,[2,3] as well as classic factors such as hypertension, diabetes

mellitus, dyslipidemia and smoking. It is a common cause of renal artery graft stenosis, one of the main post-kidney transplant complications,[4] besides other conditions, such as graft dysfunction, renal vessel thrombosis, and the onset of other cardiovascular diseases following replacement therapy. The arterial vessel seriously affected by atherosclerosis constitutes an important technical difficulty for renal artery anastomosis, increasing the risk of immediate bleeding and vessel thrombosis, leading to implant loss.

The possibility to choose the best site for the vascular anastomosis implant preceding kidney transplantation would improve the chances of a successful procedure and exclude patients without a satisfactory vascular bed.[5]

Angiography by helical computed tomography or CT angiography (CTA), a noninvasive method used for studying anatomical tomographic images has been used for vascular analysis, with records since 1991 in aneurysms, stenosis and occlusions,[6] being widely used also in coronary arteries to predict cardiovascular risks by calcification of these arteries.[3,7]

These applications of CTA are due to its ability to accurately portray arterial diseases, including the location and extent of arterial calcification, as well as arterial caliber, as they allow the visualization of reformattable three-dimensional images, enabling a radiological analysis of both the lumen and the arterial wall.[8,9]

The short time required to analyze the results, the three-dimensional detailing and the absence of the risks of invasive exams [9] are significant advantages over other diagnostic methods for verifying atherosclerosis and degree of arterial calcification such as Adragao score, puncture arteriography, ultrasound (US) and magnetic resonance arteriography.

Compared to US, CTA allows a better three-dimensional mapping of the vasculature, as well as faster examination. Unlike US, CTA is able to differentiate between internal and medial vessel calcification, showing the intensity of vascular pathology. It is also superior to magnetic resonance imaging, which in addition to the higher cost has limitations in the assessment of vascular calcification and a risk of an adverse event known as nephrogenic systemic fibrosis in patients with impaired renal function.[5,10-12]

Considering the Adragao method, a semi-quantitative method used for simple radiographic diagnosis has a limited ability to distinguish between the extent and severity of calcification.[13]

Digital subtraction angiography (DSA) remains the gold standard exam for vascular luminal imaging.[5,8]

Compared to DSA, CTA has the advantage of being noninvasive and using less contrast media, besides the three-dimensional visualization from any angle and in any direction.[14] In a comparative study, Catalano et al.[14] showed that there is a statistically significant difference (p <0.05) between CTA and DSA in the lower degrees of calcification, better detected by CTA. The main limitation of arteriography is the inability to scan the entire vascular tree.[14,15]
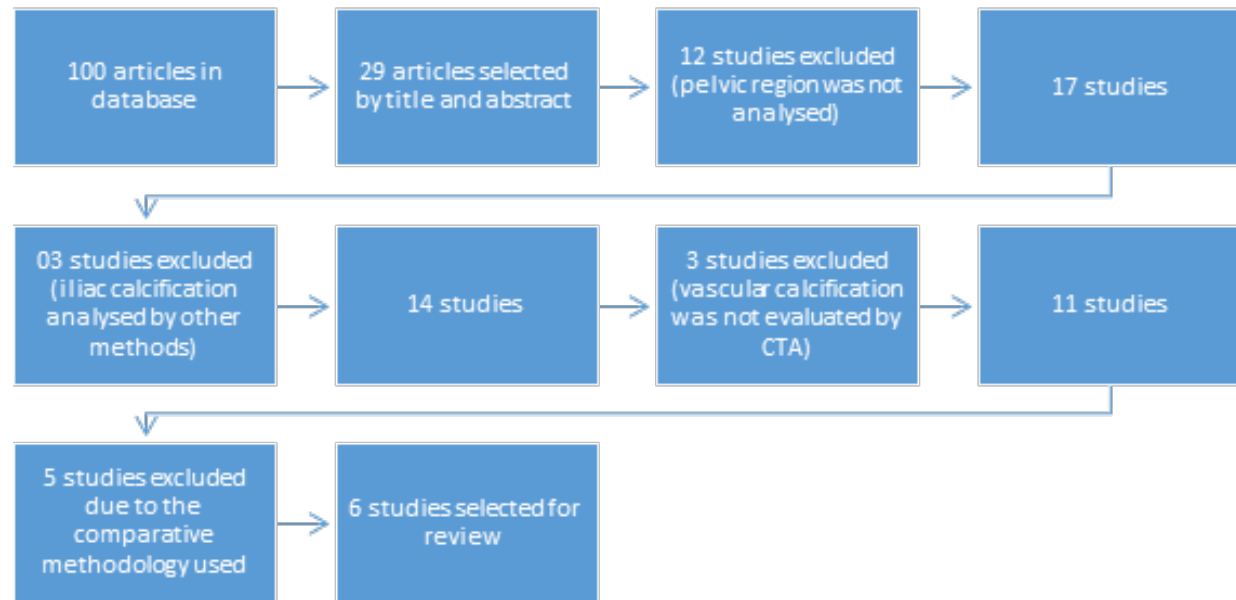
METHODS

Scientific literature search was performed by three authors of the study (G.A., R.J.R. and H.C.L.L), with supervision and selection of the most appropriate studies that met the inclusion criteria (described as follows) performed by the others. The electronic databases searched were PubMed, LILACS, Google Scholar and Cochrane Library, from 2003 to 2018. The strategy consisted of searching the following terms in the Medical Subject Heading (MeSH): "renal transplant recipients", "computed tomography arteriography", "iliac artery calcification" and "peripheral atherosclerosis". This search included studies on the diagnostic and prognostic value of CTA in peripheral arterial disease and vascular bed assessment in renal transplant candidates. Only studies written in English and Portuguese were eligible. The studies that met the inclusion criteria were: a) primary studies; b) performed in a serial manner; c) analyzed the vascular bed of the pelvic region of patients eligible for kidney transplant; and d) performed in the last 15 years.

Data Extraction: Data extraction included characteristics of the studied population (age, gender, body mass index, donor type), intervention characteristics (64-channel computed tomography), outcomes, and outcome data.

RESULTS

Results Data: The literature search resulted in a total of 100 articles, 29 of which pre-selected based on title and abstract, and of those, only 6 met the inclusion criteria (Figure 1). Causes of exclusion were: analysis of other vascular segments, such as coronary arteries (10 articles) and other peripheral segments (2 articles) for risk assessment prior to renal transplantation, use of other imaging techniques for assessment of iliac calcification (3 articles), comparison of techniques without detailed description of iliac vessels in CTA (5 articles) and those that used CTA in the analysis of other pathologies (3 articles), considering that they could not be appropriate if the vascular segment of interest (iliac vessels) was not adequately examined.

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***Figure 1** - Studies inclusion process flowchart.*

A total of 802 patients submitted to CTA were included, with a mean age of 56 years, 63% being males (considering the studies with gender distinction). Studies were conducted on patients in the kidney transplant waiting list.

The main comorbidities evaluated were diabetes mellitus, hypertension and smoking. Although all studies assessed comorbidities in clinical history, not all studies used them as inclusion criteria. Table 1 shows the primary studies and characteristics of the studied patients.

The association of vascular calcification with age occurred in the studies by Kahn et al.[10], Davis et al.,[16] and Aitken et al.[17] and this has been considered the most important independent risk factor in multivariate analysis.

Aitken et al.[17] showed that individuals with moderate to severe calcification were older when compared to those without calcification (59.1 +/- 8.6 years versus 48.4 +/- 8.7; p <0.01). Davis et al.[16] disclosed the relationship between age and calcification separately for calcification length (p <0.05), circumference (p <0.079) and morphology (p <0.004) and Kahn et al.[10] indicated age as the most relevant risk factor (p <0.001).

None of the studies disclosed significant differences between calcification scores and gender, although male gender was prevalent in all cohorts studied.

CTA was performed from one day to one year before surgery. Smith et al.[11] stated that living donor recipients have the advantage of having the most up-to-date examination, since it can be performed weeks and days before surgery, whereas in deceased donors the transplant schedule has uncertain variations.

The ways of quantifying calcification differed between studies. Chavent et al.[18] used a score adapted from Agatston's methodology, which considers calcification surfaces above 1 mm² in which the attenuation value is higher than 130HU. Calcifications were analyzed in a localized and circumferential manner when above this density. Davis et al.[16] used a calcification scoring system to assess the degree and distribution of iliac artery calcifications based on morphology, circumference, and extent of involvement. A numerical score was given for calcification morphology on a scale of 0-3 (ranging from none to worst). Circumference and length scores were assigned based on circumferential impairment and maximum length, respectively, within a segment analyzed on a scale from 0 to 4 (ranging from none to worst). Only axial images obtained with a thickness of 5mm were reviewed. Kahn et al.[10] used a standardized degree of calcification at 0.5-degree intervals, with grade 0 = no visible calcification, grade 1 = deposits calcified within one third of the arterial circumference, grade 2 = calcification up to 2/3 of the circumference, and degree 3 = highest/circular calcification. The other primary studies stated only the CTA technique used, without specifying the way calcification was quantified. CTA allowed high accuracy in the diagnosis of calcification, with sensitivity ranging from 71% to 100% and specificity ranging from 73% to 92%.

The outcomes analyzed [16-18] were: patient and graft survival; change in the anastomosis site or pre-transplant

Table 1: *Primary studies and their characteristics.*

Study	Number of Patients	Average age	Gender	Criteria / Comorbidities	Type of donor
Kahn et al.[10]	205	53.9 +-11.7 years old	146 male 59 female	Comorbidities: diabetes, nephropathies, smoking; Assessed: BMI, diagnosis, and time of dialysis, previous transplant.	Not specified
Smith et al.[11]	179	51 years old	106 male 73 female	Criteria: total duration of dialysis over 4 years; diabetes mellitus type 1, carotid arterial disease, chronic infection	126 living donors
Andres et al.[15]	114	over 55 years old	Not specified	Criteria: a) over 55 years old, b) atheromatosis risk factors (diabetes included), c) candidates to a second kidney transplant, d) vascular calcifications visible in simple abdominal radiographies	Not specified
Davis et al.[16]	131	52 years old	75 male 56 female	Comorbidities: hypertension (88%, n=115), diabetes mellitus (52%, n=68), smoking (21%, n=27) and dyslipidemia (51%, n=67)	Living donor: 30 patients Deceased donor: 131 patients
Aitken et al.[17]	187	58.3+-6.2 years old	92 male 95 female	Comorbidities: smoking, diabetes mellitus, hypertension, lipid profile, and BMI Criteria: calcification seen in pelvic radiography	Deceased donors
Chavent et al.[18]	100	65 years old	Not specified	Analyzed correlation between diabetes and duration of dialysis	Not specified

BMI = body mass index.

treatment, such as interventional vascular procedures due to CTA findings, which directly influenced the survival rates mentioned and need for dialysis in the first week after transplantation.

Patients were followed up from 14 to 66 months, and the studies by Smith et al.[11] and Andres et al.[15] did not specify the time after transplant included in the total study time.

In all studies, CTA was used for better surgical planning based on the degree of calcification. Kahn et al.[10], Smith et al.[11], Davis et al.[16], Aitken et al.[17] and Chavent et al.[18] reported anastomotic site changes or procedures such as iliac artery angioplasty, iliac stents, and endovascular repairs.

In the studies by Kahn et al.[10], Smith et al.[11], Andres et al.[15] and Aitken et al.[17] there was a description that transplant was cancelled due to the degree of calcification.

Regarding deaths after substitution therapy, only in Davis et al.[16] and Aitken et al.[17] showed that calcification was involved, but Davis et al.[16] stated a relationship exclusively in the analysis of the entire common and external iliac system (p = 0.045), whereas in the univariated analysis there was no correlation between the iliac artery segment calcification scores used

for anastomosis and deaths. Aitken et al.[17] showed a higher mortality rate in patients with moderate to severe calcification compared to those with minimal calcification (30.1% versus 16.6%, p = 0.02). Among the deaths by graft loss was also reported a relation to the calcification degree (1.6% mild calcification and 2.7% moderate to severe).

Graft loss was verified in Kahn et al.[10], Andres et al.[15], Davis et al.[16], Aitken et al.[17] and Chavent et al.[18]. The highest index was verified by Aitken et al.[17], with 28.1% related to moderate to severe calcification and 3.4% related to mild calcification (p = 0.01). Chavent et al.[18] states that there was no significant difference between the deaths and graft losses, which was reported as 13%, with the degree of vascular calcification.

Table 2 shows the comparison of outcomes (graft loss, death, transplant suspension, alteration of anastomotic site / vascular treatment, and change in renal function) and follow-up period.

DISCUSSION

In Brazil, the indication for CTA is restricted to patients with significant diabetes mellitus and/or over 50 years of age and history of ischemic strokes. Some of the articles in this review used similar selection criteria. Andres et al.[15]

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Table 2: *Primary studies outcomes.*

Study	N	Transplant cancelled	Post-transplant follow up period	Death	Graft loss	Changes in the anastomosis site and treatment
Kahn et al.[10]	205	7 (3.4%)	37 – 66 months	4 (2%) *	7 (3.4%)	100 (49%)
Smith et al.[11]	179	5 (2.7%)	6 months	NA	NA	41 (22.9%)
Andres et al.[15]	114	33 (29%)	36 months	NA	3 (3.4%)	NA
Davis et al.[16]	131	NA	14.1 – 51.6 months	21 (16%)	14 (10.6%)	23 (18%)
Aitken et al.[17]	93	16 (21.9%)	60 months	3 (4.3%)	22 (31.6%)	18 (24.3%)
Chavent et al.[18]	100	NA	50.16 months (+- 19.68)	4%	9 (9%)	20 (20%)

N – number of patients;   NA - not applicable

selected individuals over 55 years old, with diabetes and a history of previous renal transplantation and calcifications in abdominal radiography. The study by Aitken et al.[17] selected only patients who showed calcifications in plain radiography. Such selections could underestimate the degree of calcification detected in transplant candidates. However, in our review, we found studies that did not use criteria other than chronic renal failure.

Kahn et al.[10] included all patients on the "EUROTRANSPLANT" waiting list. During 4 years, 205 patients were assessed, and total iliac segment calcification was verified in 142 men and 56 women (p = 0.003). Smith et al.[11] used CTA for all of 179 transplant candidates. In 65 (36.3%), moderate to severe aortoiliac disease was found. In 36 (20.1%) patients, significant atherosclerosis of the external iliac artery was found, with 8 (4.5%) of them showing significant stenosis in this vessel.

Longer review studies that followed up patients diclosed that transplantation was beneficial even for those with moderate/severe calcifications. Aitken et al.[17] and Chavent et al.[18] stated that the mortality rate of patients with calcification who had been submitted to surgery was lower when compared to those who remained on the waiting list. CTA was used in these studies for better surgical planning that included transplants above the iliac vessels, endovascular clamping18, iliac stents and laterality change.[17]

All articles revealed the importance of CTA in identifying the best site for anastomosis and the side with the vessel to be anastomosed, identifying the need for pre-surgical intervention such as endoarterectomy, as well as the possibility to predict surgical complexity (p <0.001 for all calcification scores), as reported by Davis et al.,[16] allowing better preparation and awareness of operative risk for patients and surgeons.

This study is limited to the descriptors and databases used. After applying the inclusion criteria, we selected a small number of primary studies conducted before kidney transplantation, which could have limited the sample and made it difficult to select the most homogeneous ones, highlighting the importance of more practical studies using CTA in the pre-transplantation assessment.

We believe that the main limitation of this study was that the literature search resulted only in retrospective studies based only on the evolution of transplanted patients. There were no prospective studies comparing patients with similar clinical characteristics including only iliac vascular conditions as the main variable studied.

CONCLUSION

The present literature review demonstrates that the use of CTA in the assessment of renal transplant candidates showed a significant value in the detection of arterial calcification in the pelvic region. This allowed the identification of the best vessels for graft implantation and helped selecting the cases in which vascular procedures were needed before renal transplantation, avoiding complications after substitution therapy.

RESUMO

Calcificações arteriais e lesões ateroscleróticas, que apresentam alta incidência em pacientes renais crônicos, são importantes fatores de risco para complicações pós-operatórias imediatas e tardias após transplante renal. A angiotomografia computadorizada das artérias ilíacas pode demonstrar com precisão doenças arteriais, incluindo a localização e extensão da calcificação arterial, assim como o calibre arterial, o que permitiria melhor planejamento cirúrgico do local de implantação renal. **Objetivo**: Essa revisão de literatura teve como objetivo verificar o papel desse exame como método diagnóstico de doença arterial ateromatosa na região dos vasos ilíacos em pacientes candidatos à terapia renal substitutiva, por meio da análise de estudos primários de pacientes submetidos a esse exame. **Métodos**: A metodologia utilizada foi uma busca literária em bases de dados eletrônicas (PubMed, LILACS, Google Acadêmico e Cochrane Library), datando de 2003 a 2018. **Resultados**: A busca literária resultou em um total de 100 artigos, com 29 deles selecionados baseados no título e resumo, e destes, somente 6 estavam de acordo com os critérios de inclusão. A angiotomografia computadorizada permitiu alta acurácia no diagnóstico de calcificação, com sensibilidade variando de 71% a 100% e especificidade variando de 73% a 92%. A CTA foi utilizada para planejamento cirúrgico com base no grau de calcificação e mostrou que houve alteração do local da anastomose ou procedimentos vasculares antes do transplante em 25,2%, cancelamento do transplante devido ao grau de calcificação arterial em 7,6%, perda do enxerto em 6,8% e óbito em 3,9% dos casos. **Conclusão**: A angiotomografia computadorizada tem papel significativo na detecção de calcificações vasculares, permitindo melhor planejamento cirúrgico.

Descritores: Angiografia por Tomografia Computadorizada; Placa Aterosclerótica; Transplante de Rim.

REFERÊNCIAS

1. Camacho CRC, Dias-Melicio LA, Soares AMVC. Aterosclerose, uma resposta inflamatória. Arq Ciênc Saúde. 2007;14:41-8.

2. Canziani MEF, Moysés RMA. Calcificação Vascular na DRC. J Bras Nefrol. 2011;33:216-20.

3. Amann K, Ritz C, Adamczak M, Ritz E. Why is coronary heart disease of uremic patients so frequent and so devastating? Nephrol Dial Transplant. 2003;18:631-40.

4. Abreu-Silva EO, Souza RA, Furini FR, Barbosa AHP, Alves CMR, Lima VC. Dissecção causando estenose de artéria de rim transplantado: diagnóstico por angiografia rotacional tridimensional. Rev Bras Cardiol Invasiva. 2011;19:445-7.

5. Catalá V, Martí T, Diaz JM, Cordeiro E, Samaniego J, Rosales A, et al. Use of multidetector CT in presurgical evaluation of potential kidney transplant recipients. Radiographics. 2010;30:517-31.

6. Ofer Amos, Nitecki Sami S, Linn Shai, Epelman Monica, Fischer Doron, Karram Toni, et al. Multidetector CT angiography of peripheral vascular disease: a prospective comparison with intraarterial digital subtraction angiography. AJR Am J Roentgenol. 2003;180:719–24.

7. Azevedo CF, Rochitte CE, Lima JAC. Escore de cálcio e angiotomografia coronariana na estratificação do risco cardiovascular. Arq Bras Cardiol. 2012;98:559-68.

8. Urban B, Ratner LE, Fishman EK. Three-dimensional volume-rendered CT angiography of the renal arteries and veins: Normal anatomy, variants, and clinical applications. Radiographics. 2001;21:373-86

9. Mello Júnior CF, Araujo Neto SA, Carvalho Junior AM, Rebouças RB, Negromonte GRP, Oliveira CD. Angiotomografia computadorizada por multidetectores das artérias renais: anatomia normal e suas variações. Radiol Bras. 2016;49:190-5.

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Marilda Mazzali, Marcelo Lopes de Lima

10. Kahn J, Ram LM, Eberhard K, Groselj-Strele A, Obermayer-Pietsch B, Müller H. Calcification score evaluation in patients listed for renal transplantation. Clin Transplant. 2017;31(3).

11. Smith D, Chudgar A, Daly B, Cooper M. Evaluation of potential renal transplant recipients with computed tomography angiography. Arch Surg. 2012;147:1114–22.

12. Winship B, Ramakrishnan S, Evans J, Lurie C, Martin D, Pearson Tb, et al. A single center analysis of abdominal imaging in the evaluation of kidney transplant recipients. Clin Transplant. 2013;27:701-9.

13. Oliveira RB, Okazaki H, Stinghen AEM, Drüeke TB, Massy ZA, Jorgetti V. Calcificação vascular em doença renal crônica: uma revisão. J Bras Nefrol. 2013;35:147-61.

14. Catalano C, Fraioli F, Laghi A, Napoli A, Bezzi M, Pediconi F, et al. Infrarenal Aortic and Lower-Extremity Arterial Disease: Diagnostic Performance of Multi-Detector Row CT Angiography. Radiology. 2004;231:555-63.

15. Andres A, Revilla Y, Ramos A, Gonzalez E, Vereda MS, Praga M, et al. Helical computed tomography angiography is the most efficient test to assess vascular calcifications in the iliac arterial sector in renal transplant candidates. Transplant Proc 2003;35:1682–3.

16. Davis B, Marin D, Hurwitz LM, James R, Ellis MJ, Ravindra KV, et al. Application of a novel CT-based iliac artery calcification scoring system for predicting renal transplant outcomes. AJR Am J Roentgenol. 2016;206:436-41.

17. Aitken E, Ramjug S, Buist L, Kingsmore D. The prognostic significance of iliac Vessel calcification in renal transplantation. Transplant Proc. 2012;44:2925–31.

18. Chavent B, Maillard N, Boutet C, Albertini JN, Duprey A, Favre JP. Prognostic value of aortoiliac calcification score in kidney transplantation recipients. Ann Vasc Surg. 2017;44:245-52.