CT vs DS Angiography in renal artery fibromuscular dysplasia

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PF Plouin, L. Boyer, E Mousseaux
CTA in fibromuscular dysplasia (FMD) of Renal Arteries (RA)

- FMD is an idiopathic nonatherosclerotic and non-inflammatory vascular disease.

- Characteristics:
  - Distal RA stenosis, thin diaphragms, 2 subtypes:
    - Unifocal
    - Multifocal

- Assessed by:
  - Digital subtraction angiography (DSA): Reference standard, invasive
  - New Multislice computed tomography angiography (MSCTA) with submillimetric slices, non-invasive

Savard, Azarine, Plouin et al. Circulation 2012
Background: prospective study
CTA & MRA vs DSA in RA stenosis

- Few studies available to test CTA accuracy but with old scanners
- Stenosis >50% atherosclerosis and FMD patients
  - Many studies used 1-3mm slice thickness

<table>
<thead>
<tr>
<th></th>
<th>Se</th>
<th>Spe</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTA</td>
<td>64%</td>
<td>92%</td>
<td>0.59-0.60</td>
</tr>
<tr>
<td>MRA</td>
<td>62%</td>
<td>84%</td>
<td>0.40-0.51</td>
</tr>
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</table>
Accuracy of submillimetric MSCTA compared to DSA to assess RA FMD:

- To diagnose renal artery FMD
- To assess stenosis severity
Material and methods
Study design and population

- Dataset from a French Retrospective observational study (ARCADIA) (November 2009 - December 2014)
  - Multicentric study to document phenotypic and genetic traits in patients with renal and/or cervical artery FMD

- Inclusion criteria: submillimetric CTA and DSA within 6 months

- Exclusion criteria: Renal artery angioplasty prior to CTA
### Material and methods

#### Techniques

<table>
<thead>
<tr>
<th><strong>MSCTA</strong></th>
<th><strong>DSA</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40 row MSCT</td>
<td>Seldinger</td>
</tr>
<tr>
<td>Slice thickness: 0.6-1 millimeter</td>
<td>Global and selective catheterization of RA</td>
</tr>
<tr>
<td>Iodine injection:</td>
<td></td>
</tr>
<tr>
<td>- Concentrations 350-370 mg I/mL</td>
<td></td>
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<tr>
<td>- 70-100mL + saline flush</td>
<td></td>
</tr>
<tr>
<td>- Flow rate of 4-5 mL/s</td>
<td></td>
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<tr>
<td>- Bolus Tracking</td>
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</tr>
</tbody>
</table>
Material and methods : 
**Image analysis MSCTA & DSA**

- Two radiologists:
  - A senior
  - A junior radiologist
- Double Blinded
- Evaluation of the main renal arteries and the accessory arteries
- For each renal artery, we noted:
  1. Presence of FMD
     - Main trunk, branches
  2. Subtype FMD unifocal, multifocal
  3. Stenosis severity in % was deduced using minimal/reference diameter measurements

DSA was used as the reference standard (2 expert readers, double blinded)
Discrepancies: a third reader reviewed the image and established a final diagnosis
Diameter measurement in CTA

- Readers only measure min & ref diameters
- Stenosis = 100x(ref-min)/ref
- Calculated afterwards
- muliplanar measurements
- using centerline corrected curved images
FLOW CHART

ARCADIA cohort
n=483 patients

368 patients renal FMD

Eligible population n=91

INCLUDED
n=43 patients

Excluded 115 Exclusively Cerebrovascular form

Excluded 277
-No CTA & DSA (249)
- > 6 months between DSA and CTA (26)
- RA stenting prior to CTA (2)

Excluded 48:
- Section thickness >1mm (16)
- Problems of DICOM archiving files (32)
## Characteristics of the selected patients, n=43

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age +/- SD (range), y</td>
<td>49+-18 (19-89)</td>
</tr>
<tr>
<td>Mean systolic pressure at baseline +/- SD (range), mmHg</td>
<td>136+-21 (149-180)</td>
</tr>
<tr>
<td>Mean diastolic pressure at baseline +/- SD (range), mmHg</td>
<td>81+-12 (56-110)</td>
</tr>
<tr>
<td>Mean body max index +/- SD (range), kg/m2</td>
<td>24+-4 (16-33)</td>
</tr>
<tr>
<td>Mean creatinine concentration +/- SD (range), µmol/L</td>
<td>68+-14 (45-102)</td>
</tr>
<tr>
<td>Women, n(%)</td>
<td>37(86%)</td>
</tr>
<tr>
<td>Smoke, n(%)</td>
<td>13(30%)</td>
</tr>
</tbody>
</table>
Results:

43 patients = 103 RA

- 7 arteries were missed by DSA readers
- 1 by CTA junior reader

Total of renal arteries = 103

1 artery not detected by EC

102 renal arteries detected by the two CTA readers

-7 arteries not detected by FT
- 5 by EM

95 RA analyzed by all readers
Results:
95 RA
55 FMD

Bilateral DFM 42%

Total of renal arteries = 103
- 1 artery not detected by EC
- 7 arteries not detected by FT
  - 5 by EM

102 renal arteries detected by the two CTA readers

95 RA analyzed by all readers

55 FMD

44 multifocal FMD
11 unifocal FMD
55/95 renal arteries had FMD lesions
Multifocal subtype: 44/55 (80%)
55/95 renal arteries had FMD lesions
unifocal subtype : 11/55 (20%)
CTA accuracy for the Diagnosis of Renal Artery Fibromuscular Dysplasia

<table>
<thead>
<tr>
<th>Readers</th>
<th>Se</th>
<th>Spe</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main Troncular Renal Artery</strong> Kappa= 0.788</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA (expert)</td>
<td>87%</td>
<td>98%</td>
<td>98%</td>
<td>85%</td>
</tr>
<tr>
<td>EC (Junior)</td>
<td>93%</td>
<td>90%</td>
<td>93%</td>
<td>90%</td>
</tr>
</tbody>
</table>

AA missed 3 FMD
EC missed 1 FMD
None had significant stenosis (<50%)

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<tbody>
<tr>
<td><strong>RA Branches</strong> Kappa= 0.704</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>74%</td>
<td>91%</td>
<td>67%</td>
<td>93%</td>
</tr>
<tr>
<td>EC</td>
<td>53%</td>
<td>92%</td>
<td>63%</td>
<td>89%</td>
</tr>
</tbody>
</table>
Troncular FMD missed by CTA: artifacts

Diagnostic positif de l’artère tronculaire gauche sur l’artériographie

Pas de diagnostic de DFM de l’artère tronculaire gauche sur le TDM.
Troncular FMD missed by CTA: lack of resolution?

Diagnostic positif DFM de l’artère tronculaire gauche à l’artériographie sélective

DFM non diagnostiqué en TDM
Exclusively RA branches FMD missed by CTA: lack of resolution? Global DSA similar to CTA
Only selective DSA depicts branch FMD
CTA VS DSA: Stenosis severity?
Stenosis severity: B & A between DSA readers

Gold Standard (GS) = (FT + EM) / 2

Graphique de Bland et Altman

ANALYSE de BLAND et ALTMAN:
Biais: -0,068
Erreur standard: 0,135
IC biais (95%): [-0.095; -0.040]
Intervalle de confiance des différences = [-0.332; 0.196]
Stenosis severity: B & A between CTA readers

**Graphique de Bland et Altman**

ANALYSE de BLAND et ALTMAN:
Bias : -0.008
Erreur standard= 0.166
IC bias (95%)= ]-0.024;0.041 [
Intervalle de confiance des différences = ]-0.333 ;0.317[
## Results: severity of truncular stenosis

**MSCTA versus DSA**

<table>
<thead>
<tr>
<th></th>
<th>Readers</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>VPP</th>
<th>VPN</th>
</tr>
</thead>
</table>
| **≥50%**
| *Kappa=0.7    | AA      | 90%         | 90%         | 73% | 97% |
|                | EC      | 76%         | 92%         | 73% | 93% |
| **≥70%**
| *Kappa=0.59   | AA      | 75%         | 90%         | 25% | 99% |
|                | EC      | 75%         | 92%         | 30% | 99% |
Results: Accuracy of MSCT for severe stenosis

Receiver operating characteristic curves for stenosis ≥50%

ROC curves for experimented MSCT reader for stenosis ≥50%
As observed by DSA

Best Cutoff value = 0.537
AUC = 0.965

Se 90.5%  Spe 93.2%
VPP 79.2%  VPN 97.1%
Results: Accuracy of MSCT for severe stenosis

Receiver operating characteristic curves for stenosis ≥70%

ROC curves for experimented MSCT reader for stenosis ≥70%

As observed by DSA

Best Cutoff value = 0.675

AUC = 0.897

Se = 100%

Spe = 87%
Discussion: 115 patients avec CTA et DSA
pas de différence significative avec la population exclue

<table>
<thead>
<tr>
<th>Site :</th>
<th>Population inclue (n=43)</th>
<th>Population exclue (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artère rénale</td>
<td>41(95%) 2(5%)</td>
<td>65(90%) 7(10%) p=0.31</td>
</tr>
<tr>
<td>Artère rénale +TSA</td>
<td>2(5%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sous-type</th>
<th>Population inclue (n=43)</th>
<th>Population exclue (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Multifocal</td>
<td>35(81%) 8(19%)</td>
<td>61(85%) 11(15%) p=0.644</td>
</tr>
<tr>
<td>- Unifocal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grades de sténose par patient :</th>
<th>Population inclue (n=43)</th>
<th>Population exclue (n=72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Moins de 50%</td>
<td>16 (37%) 18 (42%) 9 (21%)</td>
<td>30 (42%) 22 (31%) 20 (28%) p=0.6363 p=0.2202 p=0.4090</td>
</tr>
<tr>
<td>- Entre 50 et 80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- &gt;80%</td>
<td></td>
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</table>
La discussion porte sur le kappa entre les lecteurs «artériographies» vs CTA.

<table>
<thead>
<tr>
<th></th>
<th>Les lecteurs TDM (pour les 95 AR)</th>
<th>Les artériographistes (pour les 95 AR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kappa pour le diagnostic positif de DFM AR tronculaire</td>
<td>0.788 Se=0.063 IC95=0.665-0.911</td>
<td>0.828 Se=0.058 IC95=0.715-0.941</td>
</tr>
<tr>
<td>Kappa pour le diagnostic de sous type de DFM</td>
<td>0.750 Se=0.058 IC95=0.635-0.864</td>
<td>0.767 Se=0.057 IC95=0.665-0.887</td>
</tr>
<tr>
<td>Kappa pour l’atteinte des segmentaires</td>
<td>Se=0.093 IC95=0.517-0.881</td>
<td>Se=0.112 IC95=0.415-0.853</td>
</tr>
<tr>
<td>Kappa pour le diagnostic de sténoses supérieures à 50%</td>
<td>SE of kappa = 0.082 IC95% = 0.561 to 0.882</td>
<td>SE of kappa = 0.086 IC 95% 0.555 to 0.890</td>
</tr>
<tr>
<td>Kappa pour le diagnostic de sténoses supérieures à 70%</td>
<td>SE of kappa = 0.131 IC95% = 0.333 to 0.846</td>
<td>SE of kappa = 0.170 IC95% 0.101 to 0.767</td>
</tr>
</tbody>
</table>
Désaccord sur DFM tronculaire entre lecteurs CTA AA & EC

DFM de l’artère rénale gauche sur l’artériographie

Pas de DFM tronculaire AR sur le TDM pour EC
Discussion: effet de l’âge

chez sujet < 50 ans, performance pour sténose >50%

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<th>Readers</th>
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<td>AA</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>EC</td>
<td>88%</td>
<td>90%</td>
</tr>
</tbody>
</table>
Discussion: effet du surcharge pondéral, sténose >50% chez sujet BMI<25

<table>
<thead>
<tr>
<th>Readers</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>96% (vs 91%)</td>
<td>100%</td>
</tr>
<tr>
<td>EC</td>
<td>90% (vs 76%)</td>
<td>78%</td>
</tr>
</tbody>
</table>
Different class but same severe stenosis

Sténose à 68% en artériographie

AA: sténose à 70% = 1,2mm = 2 pixels

Influence de la résolution spatiale du scanner (0,625mm) sur le degré de sténose:
Si diam ref = 4mm
+1 pixel → Sténose à 55%
-1 pixel → Sténose à 85%
Conclusion: MSCTA for RA FMD

- Very Good Accuracy for the diagnosis of truncular FMD
- Good reproducibility between the junior and the experimented radiologist
- Good Assessment of significant stenosis $\geq 50\%$ much better than before!
  - Experience seems to be required for accurate evaluation of significant stenosis

But... still some difficulties
- Results are good for trunkal arteries, but not for segmental branches
- Selective DSA if needed to better assess significant stenosis
- Severe stenosis: MSCTA seems to underestimate. Lack of spatial resolution to assess thin diaphragms?
- Targeted doppler or 4DFLOW MRI to further evaluate...