CT og MR angiografi ved diagnostik af perifer arteriel iskæmisk sygdom (PAD)

- litteraturstudie -

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Baggrund

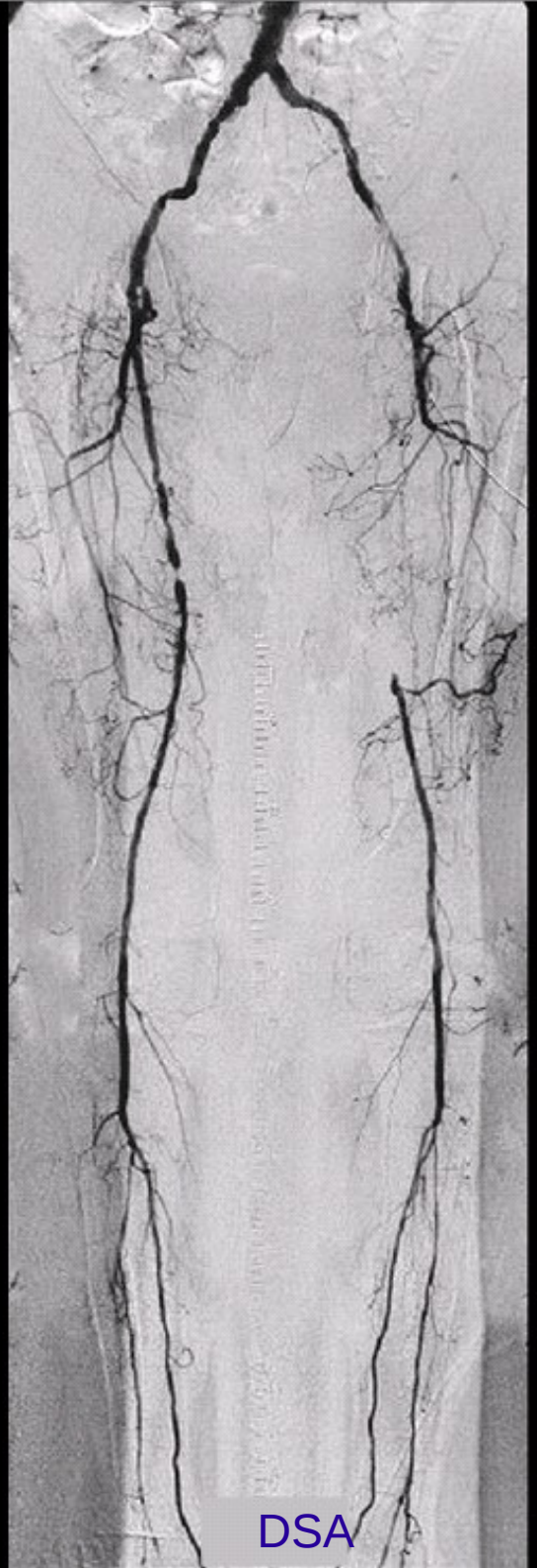
Digital substraktions angiografi (DSA) har været ”gold standard” billeddiagnostiske undersøgelse hos patienter med perifer arteriel iskæmisk sygdom (PAD).

Indenfor de sidste 5-10 år er CT-angiografi (CTA) og MR-angiografi (MRA) i stigende grad blevet anvendt til primær diagnostik af PAD, i stedet for DSA.

Derfor vil vi undersøge om CT-angiografi og MR-angiografi kan erstatte DSA til primær diagnostik af PAD.


CTA-VR


MRA-MIP


DSA

Formål

1. At undersøge om CTA har samme diagnostiske sensitivitet og specificitet som DSA ved diagnose af PAD i underekstremiteterne ?

2. At undersøge om MRA har samme diagnostiske sensitivitet og specificitet som DSA ved diagnose af PAD i underekstremiteterne ?

Metode: PubMed og Cochrane søgning.

Limits: Publiceret efter marts 2007, engelsk

Søgeord:

- tomography, X-ray computed [MeSH]/ magnetic resonance angiography [MeSH]
- digital substraction angiography [MeSH]
- lower extremity [MeSH], peripheral arterial disease [MeSH], arterial occlusive disease [MeSH]

Kombineret søgninger af disse [MeSH] terms med AND.

Fritekst søgninger på CT angiography, MR angiography, critical limb ischemia.

Related citations og artikel referencer.

Inklusionskriterier: DSA reference test, hele underekstremitetens arterier skal være undersøgt

Eksklusionskriterier: Dual-energy CTA, < 20 pt.

CTA vs DSA

Nr	Studie	År	Type	Pt.	MDCT
1	Hingorani et al.	2007		36	16
2	Albrecht et al.	2007		50	16
3	Heijenbrok-Kal MH et al.	2007 (00-06)	Meta (12 st.)	16-50/st	2-16
4	Laswed T et al.	2007		34	16
5	Collins R et al.	2007	Syst. rev.	6 st	4
6	Schernthaner R et al.	2008		50	16
7	Cernic S et al.	2009		53	64
8	Met R et al.	2009	Meta (20 st)	16-279/st	2-64
9	Shareghi S et al.	2010		28	64
10	Fotiadis N et al.	2011		41	64
11	Napoli et al.	2011		212	64
12	Iezzi R et al.	2012		60	64

Ekskluderede studier

1. Hingorani A. et al. - undersøger en høj selekteret population, mhp. behandlings konsekvens

2. Albrecht T. et al., Laswed T. et al., Schernthaner R. et al. – indgår i efterfølgende metaanalyser.

3. Iezzi R. et al. – undersøger effekten af stråledosis ved 3 forskellige CTA protokoller i forhold til DSA.

4. Collins R. et al. (MRA, CTA og Duplex UL vs. DSA) – er med i den nyeste metaanalyse (Met R. et al.).

Heijenbrok-Kal MH et al. 2007

- Studier fra 2000 - 2006 fra Medline, Embase og Cochrane.
- ≥2 slice MDCT vs. DSA
- Claudikanter eller kritisk iskæmi (75% claudikanter)
- 12 studier inkluderet (436 patienter), 16-50 pt/studie
- Stenose ≥50%

Table 1

Selected Characteristics of Included Studies

Study and Year	No. of Sections	Section Thickness (mm)	Sensitivity (%)†	Specificity (%)†
Puls et al, 2001 (16)	4	2.5	89 (56/63)	86 (106/123)
Ofer et al, 2003 (5)	4	3.2	91 (110/121)	92 (267/289)
Heuschmid et al, 2003 (17)	4	3	91 (136/149)	90 (379/419)
Martin et al, 2003 (6)	4	5	90 (327/365)	94 (886/947)
Catalano et al, 2004 (18)	4	3	99 (251/254)	97 (860/883)
Mesurolle et al, 2004 (19)	2	5	91 (52/57)	93 (103/111)
Ota et al, 2004 (20)	4	2	99 (121/122)	99 (345/348)
Portugaller et al, 2004 (21)	4	NR	92 (240/261)	83 (399/479)
Bui et al, 2005 (22)	4	2	90 (159/177)	86 (466/541)
Edwards et al, 2005 (23)	4	3.2	79 (213/270)	93 (721/772)
Fraioli et al, 2005 (24)	4	3	93 (55/59)	94 (393/416)
	4	3	94 (47/50)	95 (405/425)
	4	3	91 (60/66)	96 (392/409)
Willmann et al, 2005 (25)	16	0.75	96 (350/363)	96 (960/1002)

Samlet

Sensitivitet 92%

Specificitet 93%

Heijenbrok-Kal MH et al. 2007 - metaanalyse

3 studier havde data hvor underekstremitetsarterierne er inddelt i regioner

Table 2

Pooled Estimates of Sensitivity and Specificity for Subdivisions of Arterial Tract of Lower Extremities

Study and Year	Tract	Sensitivity (%)	Specificity (%)
Mesurolle et al, 2004 (19)	Aortoiliac	100 (18/18)	97 (29/30)
Portugaller et al, 2004 (21)	Aortoiliac	92 (24/26)	95 (212/224)
Willmann et al, 2005 (25)	Aortoiliac	95 (74/78)	98 (267/273)
Pooled results*		96 (92, 100)	97 (94, 99)
Mesurolle et al, 2004 (19)	Femoropopliteal	97 (31/32)	93 (55/59)
Portugaller et al, 2004 (21)	Femoropopliteal	98 (62/63)	70 (26/37)
Willmann et al, 2005 (25)	Femoral	98 (99/101)	94 (199/211)
Pooled results*		98 (96, 100)	89 (80, 98)
Mesurolle et al, 2004 (19)	Infrapopliteal	43 (3/7)	86 (19/22)
Portugaller et al, 2004 (21)	Infrapopliteal	90 (154/172)	74 (161/218)
Willmann et al, 2005 (25)	Popliteocrural	96 (177/184)	95 (494/518)
Pooled results*		90 (81, 99)	85 (69, 100)

Met R et al. 2009 - metaanalyse

- Studier fra Medline (1966-2008), Embase (1980-2008) og Database of Abstract of Reviews of Effectiveness .
- ≥10 patienter
- MDCT vs. DSA
- Claudikanter eller kristisk iskæmi (68% claudikanter)
- Stenose ≥50%
- 909 studier, 20 er inkluderet (957 patienter), 16-279 patienter/studie

Source	No. of Patients	Slices
Puls et al,[31] 2002	31	4
Heuschmid et al,[23] 2003	23	4
Martin et al,[26] 2003	41	4
Ofer et al,[28] 2003	18	4
Catalano et al,[20] 2004	50	4
Mesurolle et al,[27] 2004	16	2
Ota et al,[29] 2004	24	4
Portugaller et al,[30] 2004	50	4
Bui et al,[18] 2005	25	4
Edwards et al,[21] 2005[d]	44	4
Schertler et al,[32] 2005[e]	17	16
Willmann et al,[33] 2005[d]	39	16
Fraioli et al,[22] 2006[f]	75	4
Zhang et al,[34] 2006	30	16
Albrecht et al,[17] 2007[d]	50	16
Cai et al,[19] 2007	279	16
Li et al,[25] 2007	30	64
Laswed et al,[4] 2008	34	16
Li et al,[24] 2008[g]	31	64
Schernthaner et al,[5] 2008	50	16

Met R et al. 2009 – metaanalyse

- resultater -

Samlet sensitivitet 95% og specificitet 96%

Table 4. Subgroup Analyses Based on Execution of CTA (Number of Slices), Patient Population, Study Design, and Study Quality[a]

Characteristic	Sensitivity, % (95% CI)	*P* Value	Specificity, % (95% CI)	*P* Value
CTA				
2- to 4-slice CT	92 (88-96)	.03	93 (89-96)	.002
16- to 64-slice CT	97 (95-98)		98 (96-99)	
Patient population, %				
≥70 Fontaine II	94 (88-97)	.37	94 (89-97)	.71
<70 Fontaine II	90 (79-96)		93 (87-97)	
Study design				
Prospective	94 (90-97)	.34	96 (92-98)	.81
Retrospective	96 (93-98)		95 (91-98)	
Study quality 1				
High (>11 points)	93 (87-96)	.14	94 (91-96)	.28
Low (≤11 points)	96 (94-98)		96 (93-98)	
Study quality 2				
High (>10 points)	95 (91-97)	.81	96 (93-97)	.82
Low (≤10 points)	95 (91-98)		95 (90-98)	

Source, by Vessels	Sensitivity	Specificity
Aortoiliac arteries		
Mesurolle et al,[27] 2004	100	97
Portugaller et al,[30] 2004	92	95
Willmann et al,[33] 2005[b]	96	98
Laswed et al,[4] 2008	95	100
Schernthaner et al,[5] 2008	95	98
Summary estimates (95% CI)	96 (91-99)	98 (95-99)
Femoropopliteal arteries		
Mesurolle et al,[27] 2004	97	93
Portugaller et al,[30] 2004	98	70
Willmann et al,[33] 2005[b]	97	95
Laswed et al,[4] 2008	93	95
Schernthaner et al,[5] 2008	99	99
Summary estimates (95% CI)	97 (95-99)	94 (85-99)
Tibial arteries		
Mesurolle et al,[27] 2004	43	86
Portugaller et al,[30] 2004	90	74
Schertler et al,[32] 2005	95	85
Willmann et al,[33] 2005[b]	96	96
Laswed et al,[4] 2008	98	91
Schernthaner et al,[5] 2008	100	99
Summary estimates (95% CI)	95 (85-99)	91 (79-97)
Femoropopliteal-tibial arteries		
Li et al,[24] 2008	98	96

6 studier havde data hvor underekstremitetsarterierne er inddelt i regioner

Studier publicerede efter metaanalyserne

	Studie	Pt	CT	Iskæmi grad	Se	Sp	PPV	NPV	Diagnostic accuracy	CTA protokol
1	Cernic S et al. 2009	53 retro	64	Ikke defineret	97	97	92	99	97	4 ml/s, 80-120 ml Iomeron 350/400, >50% stenose
2	Shareghi S et al. 2010	28 prosp	64	II	99	98	-	-	98	4 ml/s, 80-100 ml, Omnipaque 350, >50% stenose
3	Fotiadis N et al. 2011	41 retro	64	IIb/III/IV	99	98	97	99	98	5 ml/s, 100 ml Visipaque 270, >50% stenose
4	Napoli A et al. 2011	212 prosp	64	IIa/IIb/III/IV	99	97	96	99	98	4 ml/s, 130 ml Iomeron 400, >70% stenose

Resultater opdelt på karregion

	Studie	Se			Sp		
		Aortoiliac	Fem-pop	Infrapop	Aortoiliac	Fem-pop	Infrapop
1	Shareghi S et al. 2010	100	97	97	99	99	98
2	Fotiadis N et al. 2011	100	100	98	100	97	97

I forhold til tidligere studier (2-16 slice MDCT) er der nu tilnærmelsesvis samme Se og Sp over og under knæet.

Samlet konklusion CTA vs. DSA

1. Er at undersøge om CTA har samme diagnostiske sensitivitet og specificitet som DSA ved diagnose af PAD i underekstremiteterne ?

- CTA og DSA har tilnærmelsesvis ens Se, Sp, PPV og NPV.

- CTA kan erstatte DSA ved primær diagnostik af PAD - både ved patienter med claudicatio og svær iskæmi, og i samtlige arterielle segmenter i underekstremiteten.

MRA vs DSA

	Studie	År	MRA	Pt	Protokol
1	Berg F. et al.	2007	3 T	21	Hybrid CE-MRA
2	Thurnher S. et al.	2007	1,5T	272	ToF NC-MRA og CE-MRA
3	Vahl AC. et al.	2007	1,5T	197	ToF CE-MRA
4	Collins R et al.	2007	-	681	+/- kontrast, systematisk review
5	Hadizadeh DR. et al.	2008	1,5T	27	First-pass og steady-state CE-MRA
6	Berg F. et al.	2008	3T	30	Hybrid CE-MRA
7	Poschenrieder F. et al.	2009	1,5T	20	IA og IV CE-MRA
8	Owen AR. et al.	2009	1,5T	30	Hybrid CE-MRA
9	Grijalba FU. et al.	2009	1,5T	30	CE-MRA
10	Menke J. et al.	2010	1-3T	32st	CE-MRA, 1998-2009, metaanalyse
11	Bonel HM. et al.	2009	3T	20	CE-MRA blood-pool
12	Attenberger UI. et al.	2010	3T	30	Low dose CE-MRA TWIST, >70% st
13	Bui BT. et al.	2010	1,5T	333	CE-MRA og NC-MRA
14	Bueno A. et al.	2010	1,5T	40	Hybrid CE-MRA
15	Wang C. et al.	2010	1,5T	31	Hybrid CE-MRA og TRICKS
16	Gutzeit A. et al.	2011	1,5T	43	EKG - NC-MRA (TRANCE), >70% st

Ekskluderede studier

1. Berg F. et al. 2007 og Bosma J et al. 2011 ekskluderes - < 20 patienter med både MRA og DSA.

2. Vahl AC. et al 2007 - omhandler behandlingsplan/omkostninger efter MRA vs. DSA., ikke alle patienter undersøgt med både MRA og DSA.

3. Grijalba FU. et al. 2009 - angiver ikke Se og Sp, men kun interobserver agreement.

4. Poschenrieder F. et al. 2008, Bui BT. et al. 2010, Gutzeit A. et al, Bonel HM. et al. 2009 - hele arterietræet i underekstremiteten ikke er undersøgt

MRA vs DSA

	Studie	Resultater					
		Se	Sp	PPV	NPV	Accuracy	MRA protokol
1	Thurnher S. et al. 2007	33-63/54-81	59-90/87-95	22-55/57-79	77-85/86-93	55-77/81-87	TOF/CE
2	Collins R. et al. 2007	95	97				+/- kontrast, systematisk review
3	Hadizadeh DR. et al. 2008	82/100	91/100	73/100	93/100		FP / SS CE-MRA
4	Berg F. et al. 2008	95	98				Hybrid CE-MRA
5	Owen AR. et al. 2009	94	91			92	Hybrid CE-MRA
6	Menke J. et al. 2010	95	96				CE-MRA, metaanalyse
7	Attenberger UI. et al. 2010	85-88	75-80	65-68	91-92	80-81	Low dose CE-MRA / +TWIST
8	Bueno A. et al. 2010	St/Ok 91/95	St/Ok 99/98	St/Ok 96/98	St/Ok 97/94		Hybrid CE-MRA
9	Wang C. et al. 2010	90-92	92-97			92-95	Hybrid CE-MRA

Menke J et al. 2010 - metaanalyse

- Studier fra 1998-2009 fra PubMed, Scopus, BIOSIS Previews og Web of Science.
- CE-MRA vs. DSA, stenose ≥50%
- 32 er inkluderet (1022 patienter), 10-76 patienter/studie, kun prospektive

MR protokoller:

- station-by-station (13 st)
- bolus chasing (15 st)
- hybrid (4 st)

- 2 studier 1T MRA, 2 studier 3T MRA, resten 1,5T

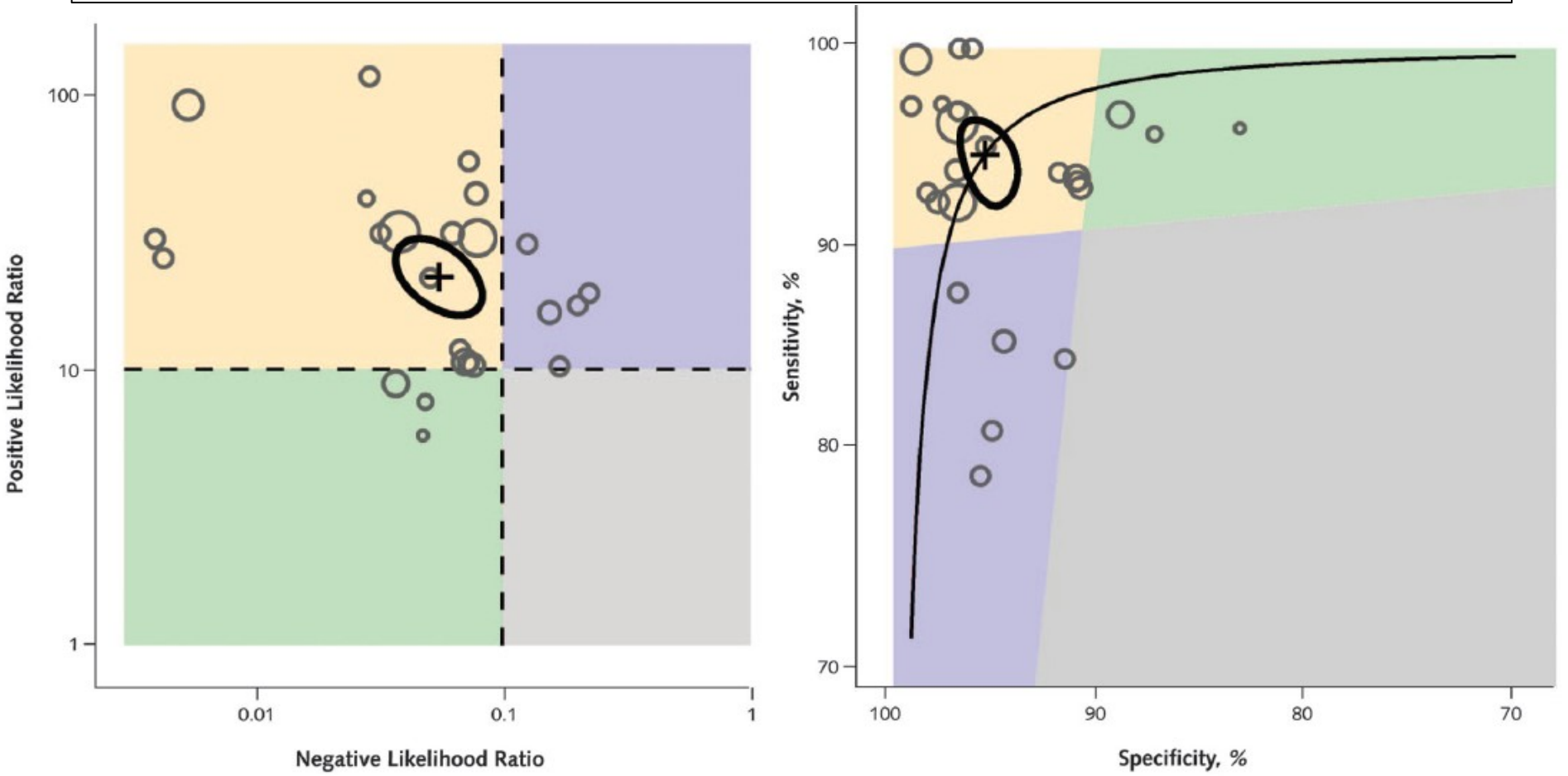
Menke J et al. 2010 - metaanalyse

Resultater opdelt på karregion

Arterial Region	Study Groups, *n*	Sensitivity (95% CI), %	Specificity (95% CI), %
Entire arterial tree	24	94.7 (92.1–96.4)	95.6 (94.0–96.8)
Aortoiliac arteries	24	93.5 (90.5–95.6)	96.3 (94.5–97.6)
Femoropopliteal arteries	20	95.3 (90.6–97.7)	95.6 (93.9–96.8)
Tibiofibular arteries	25	92.2 (89.5–94.4)	93.3 (89.8–95.7)

Se og Sp er lidt lavere for cruskar end for aortoiliaca- og femoropopliteale kar

Positive likelihood ratio – 21.56 Negative likelihood ratio – 0,056



Left Panel Quadrant	Diagnostic Utility of the Index Test	Positive Likelihood Ratio	Negative Likelihood Ratio	Right Panel Area
Left upper	Exclusion and confirmation	≥10	≤0.1	Left upper
Right upper	Confirmation only	≥10	>0.1	Left lower
Left lower	Exclusion only	<10	≤0.1	Right upper
Right lower	No exclusion, no confirmation	<10	>0.1	Right lower

MRA er velegenet både til at be- og afkræfte steno-okklusioner i patienter mistænkt for PAD

Menke J et al. 2010 - metaanalyse

Resultater

MR protokol:

- **Se:** station-by-station (97,2 %) > bolus chase (93,3%) / hybrid (93,2%)
- **Sp:** ingen signifikant forskel afhængig af MR protokol

Gadolinium dosis:

- **Se:** høj dosis single injektion (0,2-0,3 mmol/kg) signifikant lavere Se end standard dosis (0,1-0,2 mmol/kg)
- **Sp:** ingen signifikant forskel afhængig af gadolinium dosis

Iskæmigrad

- Ingen forskel i Se og Sp afhængig af prævalensen af patienter med kritisk iskæmi inkluderet i studierne – MRA er god til alle type PAD patienter

Studier publicerede efter metaanalyserne

	Studie	Pt	MR	Iskæmi grad	Se	Sp	PPV	NPV	Diagnostic accuracy	MRA protokol
1	Attenberger UI. et al. 2010	30	3T	I-IV	85-88	75-79	65-68	91-93	79-81	Low dose CE-MRA/ + TWIST, >70% stenose
2	Wang C. et al. 2010	31	1,5T	III-IV	90-92	92-97	-	-	92-95	Hybrid CE-MRA og TRICKS
3	Bueno A. et al. 2010	43	1,5T	I-II/III/IV	st/ok 91/95	st/ok 99/98	st/ok 97/98	st/ok 98/95	-	Hybrid CE-MRA

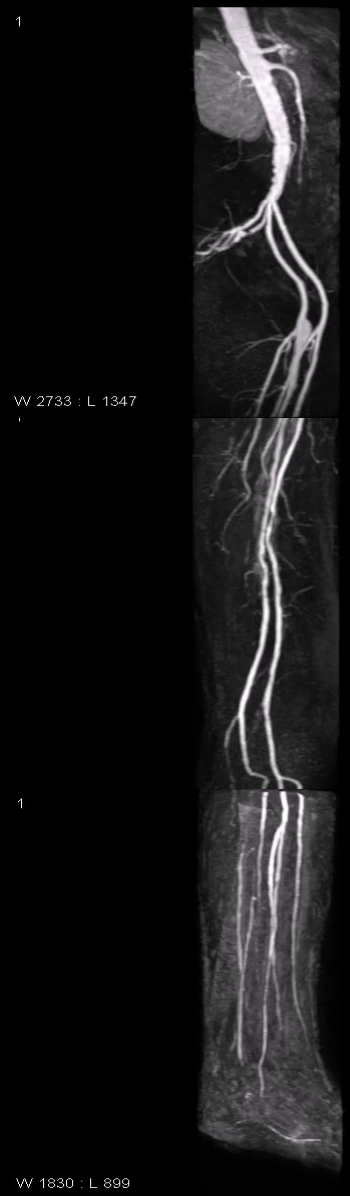
Samlet konklusion MRA vs. DSA

1. Er at undersøge om MRA har samme diagnostiske sensitivitet og specificitet som DSA ved diagnose af PAD i underekstremiteterne ?

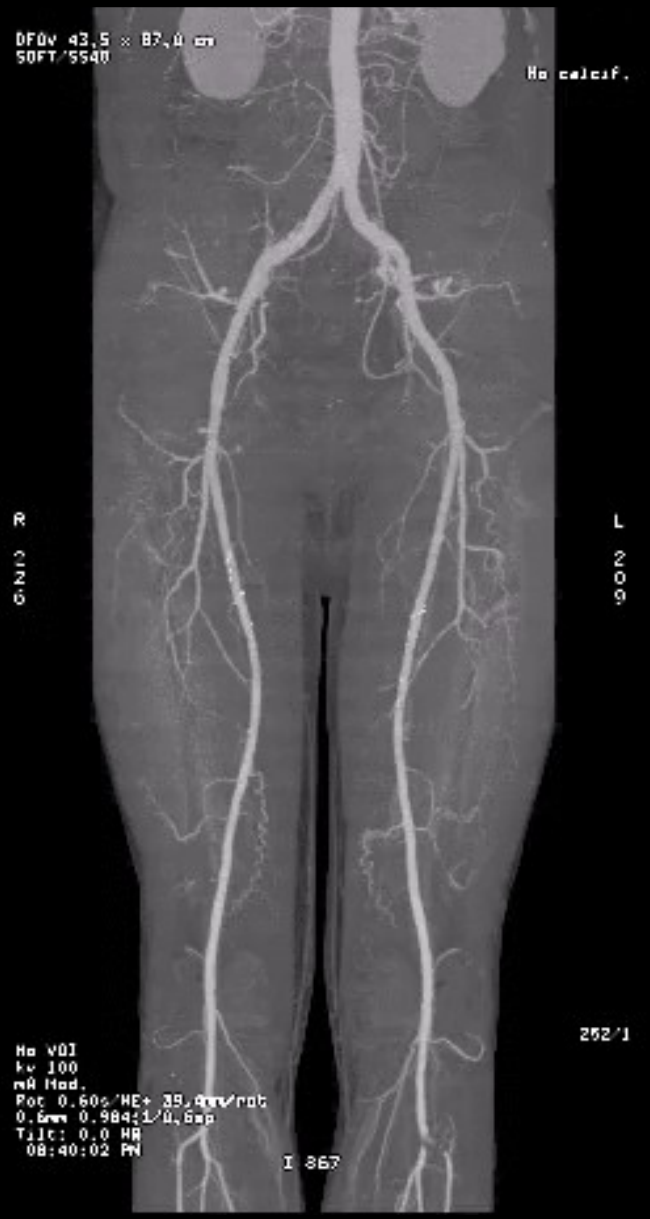
- MRA har en meget høj Se og Sp (ca. 95% i metalysen) sammenlignet med DSA.

- MRA kan erstatte DSA ved primær diagnose af PAD - både ved patienter med claudicatio og svær iskæmi, og i samtlige arterielle segmenter i underekstremiteten.

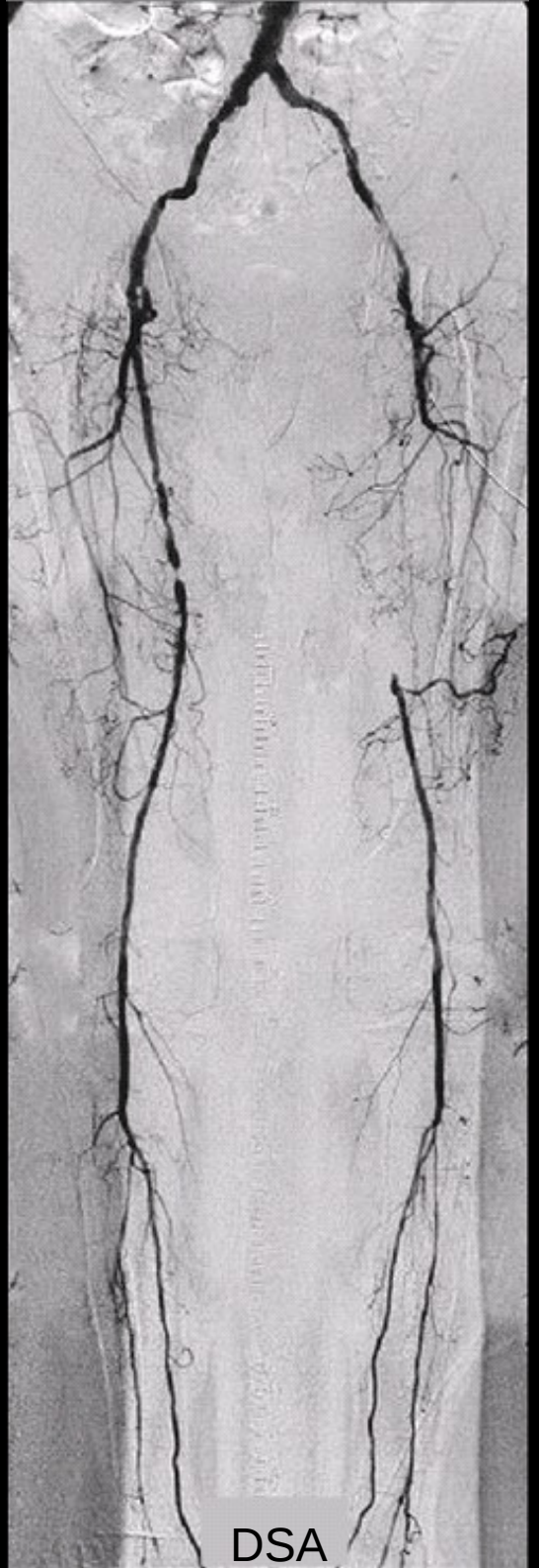
Hvad skal man anvende?



MRA



CTA



DSA

Collins R et al. 2007 systematisk review

Systematisk review – duplex UL, CT angio og MR angio vs. DSA

Formål :

- diagnostik accuracy
- undersøgelsestype effekt på patient outcome og tilfredshed

Metode: - 107 studier indtil april 2005, hvoraf 58 handler om diagnostik accuracy **Konklusion:**

- MRA har **Se 95%** og **Sp 97%**
- CTA har **Se 91%** og **Sp 91%**
- Duplex **UL 88%** og **Sp 96%**

Svagheder:

- inkluderer MRA uden kontrast som har lav Se (78,5-93,5) og Sp (73,9-92,3)

- inkluderer CTA lavet på 4 slice CT – ældre studier

Samlet konklusion

CTA på 64-slice skannere og CE-MRA har tilnærmelsesvis ens diagnostisk høj Se og Sp og begge kan erstatte DSA ved primærdiagnostik af PAD .

De lokale forhold, erfaring, patientkarakteristika og bivirkningsprofil afgør om man vælger MRA, CTA eller DSA i den primære diagnostik af PAD.

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