TAKAYASU'S ARTERITIS

PREPARED BY: NURMAGAMBETOV SH. 462 GM

EPIDEMIOLOGY

- More case reports from Japan ,India, South-east Asia, Mexico
- No geographic restriction
- No race – immune
- Incidence-2.6/million/year-N.America/Europe
- The incidence in Asia is 1 case/1000-5000 women.

Age

Mc-2nd & 3rd decade

- May range from infancy to middle age
- Indian studies-age 3- 50 yrs

Gender diff

- Japan-F:M=8-9:1
- India-F:M ratio varies from -1:1 - 3:1

(Padmavati S, Aurora AP, Kasliwal RR Aortoarteritis in India. J Assoc Physicians India 1987)

- India=F:M- 6.4:1 (Panja et al, 1997 JACC)

Genetics

- Japan - HLA-B52 and B39
- Mexican and Colombian patients - HLA-DRB1*1301 and HLA-DRB1*1602
- India- HLA- B 5, -B 21

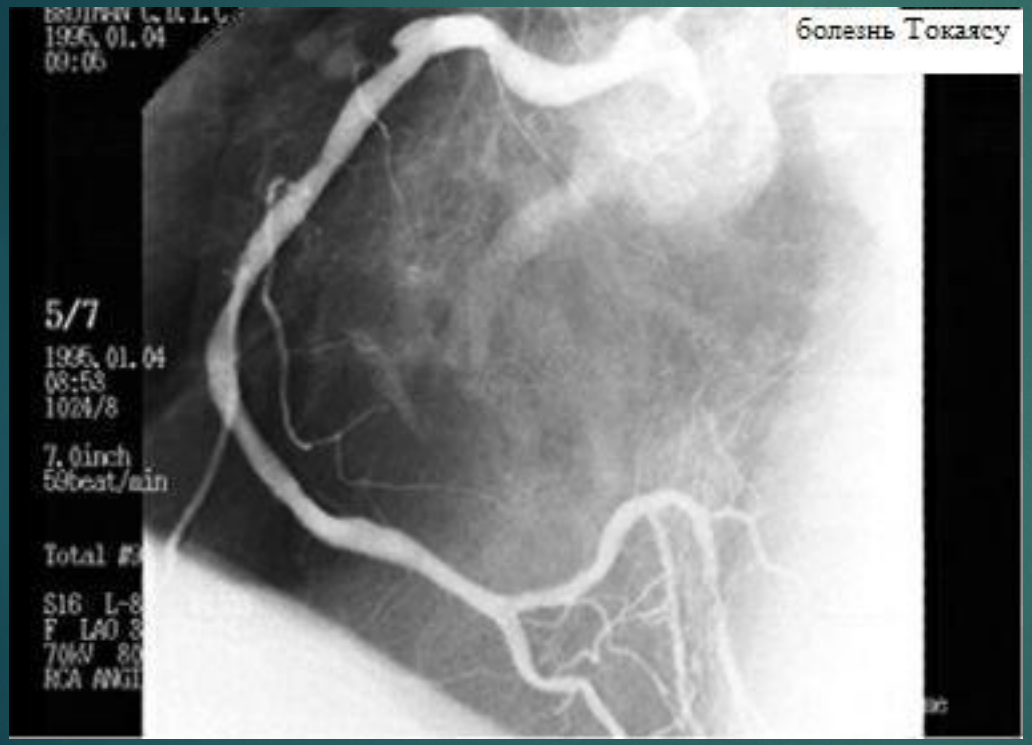
Histopathology

- Idiopathic c/c infla arteritis of elastic arteries resulting in occlusive &/ ectatic changes

- Large vessels, esp, Aorta & its main branches (brachiocephalic, carotid, SCL, vertebral, RA)
- **+**Coronary & PA

- Ao valve –usually not beyond IMA

- Multiple segs with dis & skipped nl areas or diffuse involvement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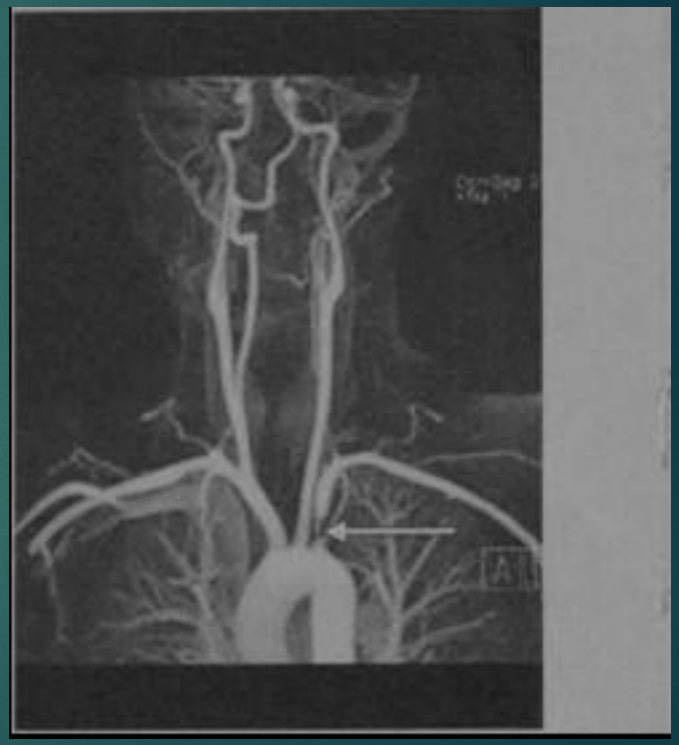


Gross

1) Gelatinous plaques-early
2) White plaques-collagen
3) Diffuse intimal thickening

Superficial– deep scarring

circumferential stenosis

4) Mural thrombus

5) 2^0 atheromatous changes

long standing,

HTN

Histology

Panarteritis-granulomatous lesion with giant cells

1) a/c phase diffuse infil-mono

granulomatous infil

2) c/c phase-coll rich fibrous tissue-adventitia thicker than media

3) Healed phase-no infl cells, vas media scarred

- Wall thickening, Fibrosis, Stenosis, & Thrombus formation →end organ ischaemia
- More a/c inflammation → destroys arterial media → Aneurysm (fibrosis inadequate)
- Stenotic lesions predominate & tend to be B/L
- Nearly all pts with aneurysms also have stenoses

- Associated pathology-TB (LN)-55%
  - Erthema multiforme
  - Bazins disease(eryt induratum)
  - churg strauss synd
  - reteroperitoneal fib
  - PAN,UC,CD etc

Clinical features

Early pre pulseless/gen manif

- Fever,weight loss,headache, fatigue,malaise,night sweats, arthralgia
- +/_ splenomegaly/ cervical, axillary lymphadenopathy
- Disappear partly/ completely in 3 months
- 50% -no h/o acute phase

Late ischemic phase

- Sequel of occl of Ao arch/br

- Diminished/absent pulses (84–96%)
- Bruits (80–94%)
- Hypertension (33–83%)
- RAS(28–75%) &
- CCF(28%)

CVS	**↓/− pulses (84–96%) -claudication & BP Diff ,Bruits (80–94%) -carotids, subcl & abd vess.** **HTN- (33–83%) –Mcc RAS (28–75%),↓Ao capacitance,atyp CoA, barroreceptor reactivity** **CHF-(28%)- HTN, AR, DCM-5%** **AR-(7-24%) Ao root dil > valve inv, annuloaortic ectasia** **Coronary & vascular involvement**
CNS	Cerebral ischemia 2 ^{0} to obliterative arteritis, seizures etc
RENAL	RAS & Ischemic Nephropathy
SKIN	Erythema nodosum, Raynauds disease, leg& hand ulcers
PULMONARY	15-27%, stenosis/ occlusion of lobar/segmental pul art UL>LL, R> L—INDIA (Panja et al 1997)

Coronary involvement in TA

- Occurs in 10～30%
- Often fatal
- Classified into 3 types

Type1:stenosis or occlu of coronary ostia

Type2:diffuse or focal coronary arteritis

Type3:coronary aneurysm

Occular involvement-Amaurosis fugax, pain behind eye, no real visual loss

Hypertensive retinopathy

- Commonest
- Arteriosclerotic –art narrowing, av nipping,silver wiring
- Neuroretinopathy-exudates and papilloedema
- Direct opthalmoscopy

Nonhypertensive retinopathy

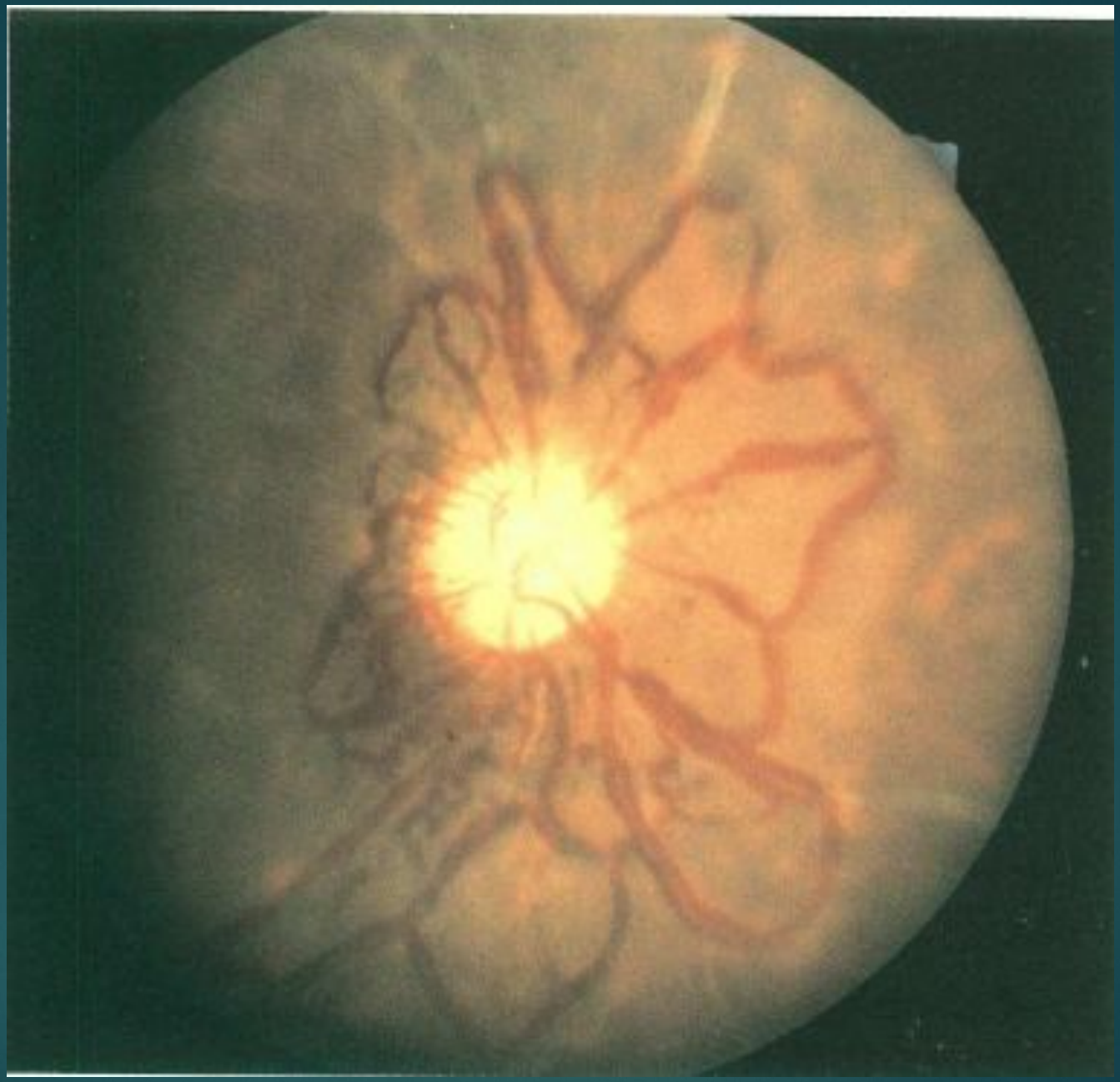
- UYAMA & ASAYAMA CLASS
- stage 1- Dil of small vessels
- stage 2- Microaneurysm
- stage 3- Art-ven anastomoses
- stage 4- Ocular complications

Mild -stage 1

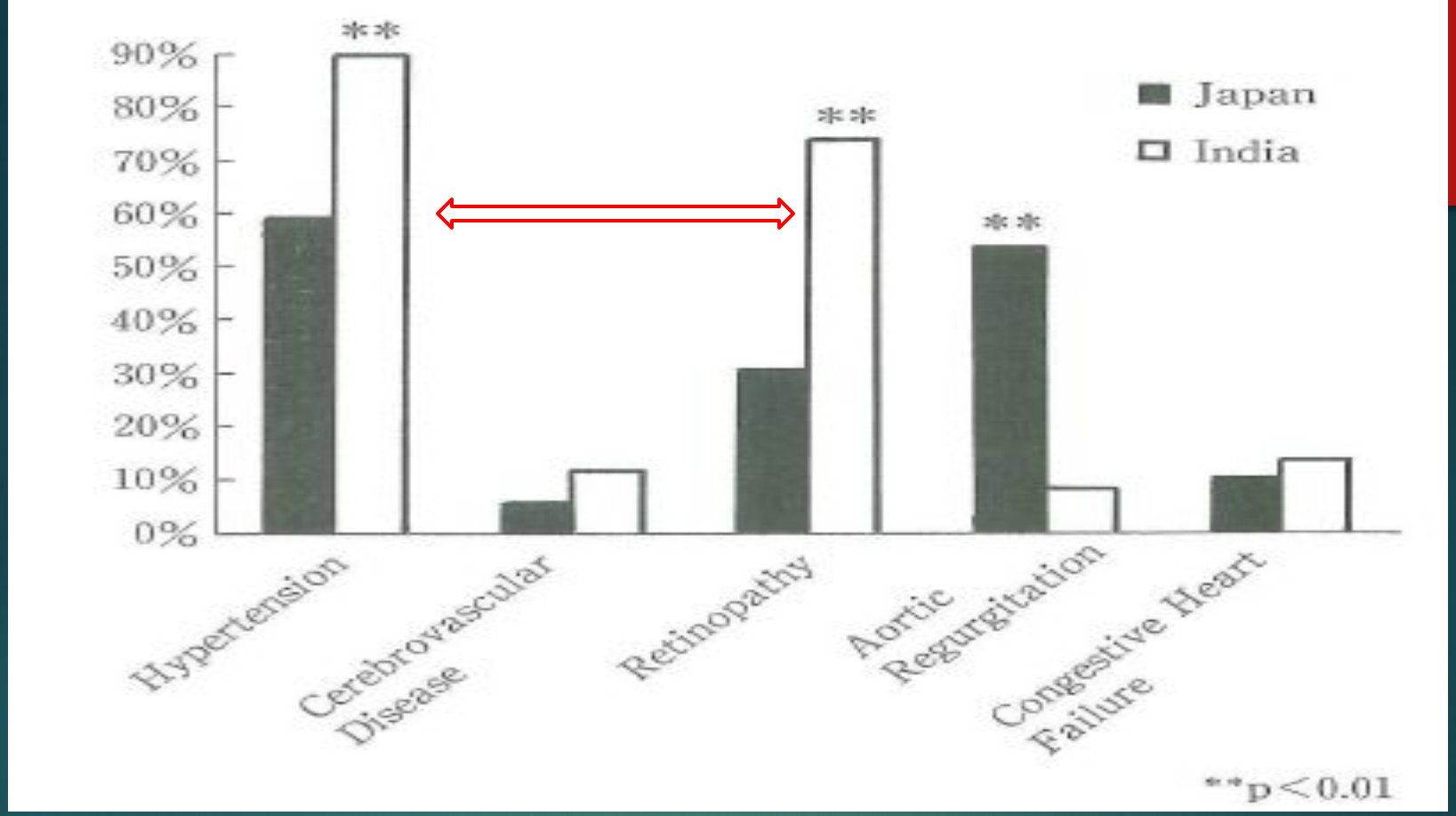
Moderate -stage 2

Severe -stages 3 & 4

Flourescien angio sensitive



Coronary anastomosis of retinal vessels



Frequencies of complicated diseases in Takayasu Arteritis between Japan & India

HTN is the most characteristic manifestation in Indian patients,suggesting a high frequency of lesions in the abdominal aorta, including the renal arteries, leading to renovascular hypertension

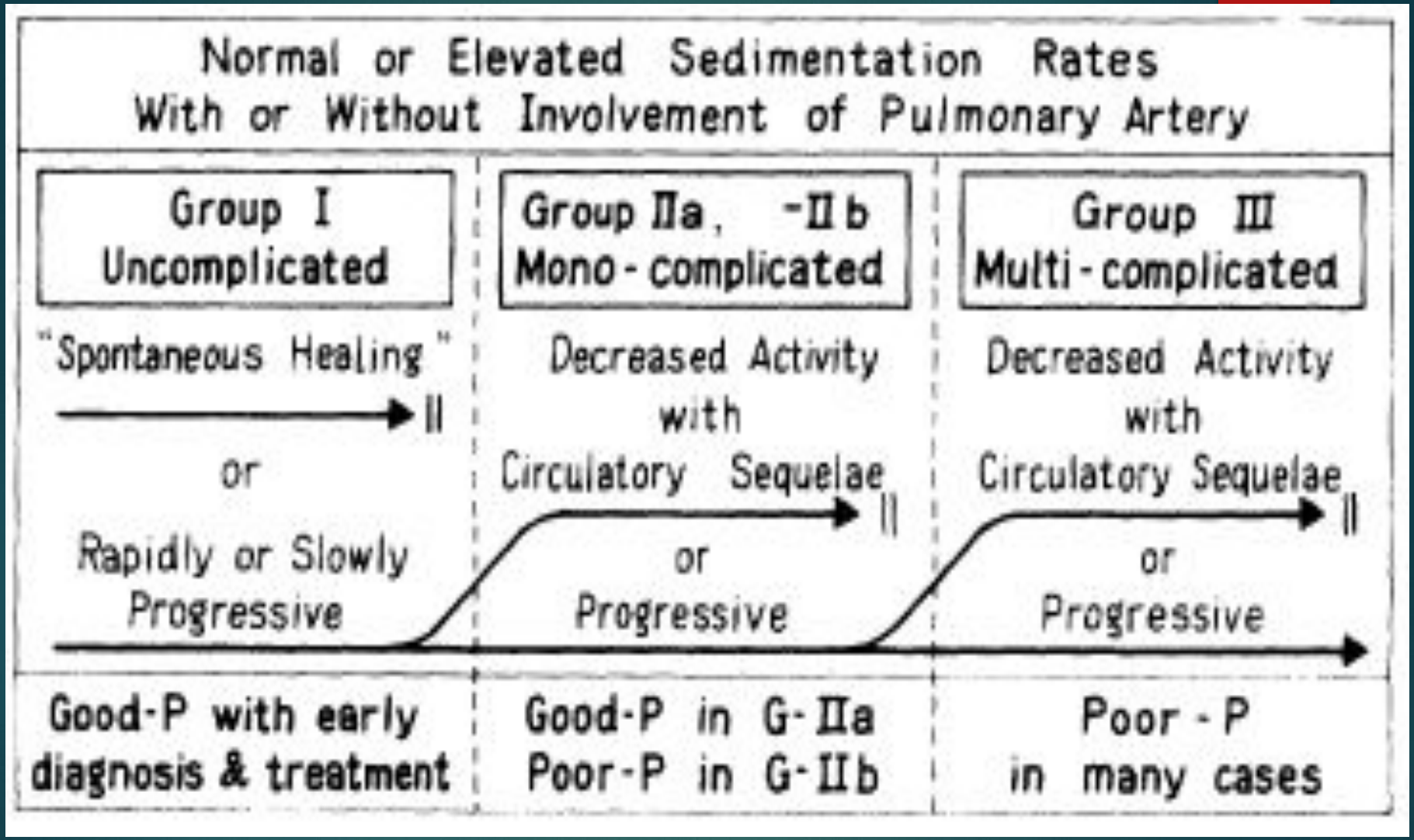
Fujio NUMANO and Yasushi KOBAYASHI
Internal Medicine Vol. 38, No. 3 (March 1999)

Ishikawa clinical classification of Takayasu arteritis 1978

Group	Clinical features
Group I	Uncomplicated disease, with or without pulmonary artery involvement
Group IIA	Mild/moderate single complication together with uncomplicated disease
Group IIB	Severe single complication together with uncomplicated disease
Group III	Two or more complications together with uncomplicated disease

4 Complications

Retinopathy, **Secondary HTN**, **AR**, & **Aneurysm**


Normal or Elevated Sedimentation Rates
With or Without Involvement of Pulmonary Artery
Group I
Uncomplicated
Group IIa, -IIb
Mono-complicated
Group III
Multi-complicated
"Spontaneous Healing"
or
Rapidly or Slowly
Progressive
Decreased Activity
with
Circulatory Sequelae
or
Progressive
Decreased Activity
with
Circulatory Sequelae
or
Progressive
Good-P with early
diagnosis & treatment
Good-P in G-IIa
Poor-P in G-IIb
Poor-P
in many cases

Cumulative survival

- 5years -91% (event free survival -74.9%)
- 10 years -84% (event free survival -64%)

Single mild complication or no complication

- 5 year event free survival 97%

Single severe or multiple complications

- 5 year event free survival 59.7%

No deaths in groups I and IIA

19.6% mortality in groups IIB and III (CVA,CCF)

Subramanyan R, Joy J, Balakrishnan KG, et al.SCT. Natur
history of aortoarteritis (Takayasu's arteritis). *Circulation* 1989; 80: 429-37.

American College of Rheumatology criteria for clinical diagnosis of Takayasu's arteritis.

Table 3. American College of Rheumatology criteria for clinical diagnosis of Takayasu's arteritis.

Criterion	Definition
1. Age at disease onset < 40 years	Development of symptoms or findings related to Takayasu arteritis at age < 40 years
2. Claudication of extremities	Development and worsening of fatigue and discomfort in muscles of one or more extremity while in use, especially the upper extremities
3. Decreased brachial artery pulse	Decreased pulsation of 1 or both brachial arteries
4. Blood pressure difference > 10 mmHg	Difference of > 10 mmHg in systolic blood pressure between arms
5. Bruit over subclavian arteries or aorta	Bruit audible on auscultation over one or both subclavian arteries or abdominal aorta
6. Arteriogram abnormality	Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper and lower extremities, not caused by atherosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental

A diagnosis of Takayasu's arteritis requires that at least three of the six criteria are met.

Sharma modified criteria for clinical diagnosis of Takayasu's arteritis.

Major criteria
1. Left midsubclavian artery lesion: stenosis or occlusion 1 cm proximal to the left vertebral artery orifice up to 3 cm distal
2. Right midsubclavian artery lesion: stenosis or occlusion from the right vertebral artery orifice to 3 cm beyond
3. Characteristic signs and symptoms (> 1-month duration)
A. Limb claudication
B. Pulselessness or blood pressure differential > 10 mmHg in arms
C. Exercise ischaemia
D. Neck pain
E. Fever
F. Amaurosis fugax
G. Syncope
H. Dyspnoea
I. Palpitations
J. Blurred vision

Sharma modified criteria for clinical diagnosis of Takayasu's arteritis.

Minor criteria
1. High ESR: Westergren ESR > 20 mm/h
2. Carotodynia
3. Hypertension: brachial blood pressure > 140/90 mmHg o popliteal blood pressure > 160/90 mmHg
4. Aortic regurgitation or annuloaortic ectasia: determined by auscultation, arteriography or echocardiography
5. Pulmonary artery lesion: lobar or segmental artery occlusion, or stenosis or aneurysm of pulmonary trunk
6. Left middle common carotid artery lesion: stenosis or occlusion of middle 5 cm portion starting 2 cm from its orifice
7. Distal innominate artery lesion: stenosis or occlusion in the distal third
8. Descending thoracic aorta lesion: narrowing, aneurysm, or luminal irregularity
9. Abdominal aortic lesion: narrowing, aneurysm, or luminal irregularity
10. Coronary artery lesion: documented by arteriography in patients < 30 years of age and without risk factors for atherosclerosis

Two major, or one major and two minor, or four minor criteria indicate a high probability of Takayasu's arteritis. ESR, erythrocyte sedimentation rate.

Sharma BK, Jain S, Suri S, Numano F. Diagnostic criteria fo
Takayasu arteritis. *Int J Cardiol 1996; 54 : S141-S147*

Angiographic classification of Takayasu's arteritis.

Type	Vessel involvement
Type	Vessel involvement
Type I	Branches from the aortic arch
Type IIa	Ascending aorta, aortic arch and its branches
Type IIb	Ascending aorta, aortic arch and its branches, thoracic descending aorta
Type III	Thoracic descending aorta, abdominal aorta and/or renal arteries
Type IV	Abdominal aorta and/or renal arteries
Type V	Combined features of types IIb and IV

According to this classification system, involvement of the coronary or pulmonary arteries should be designed as C(+) or P(+), respectively.

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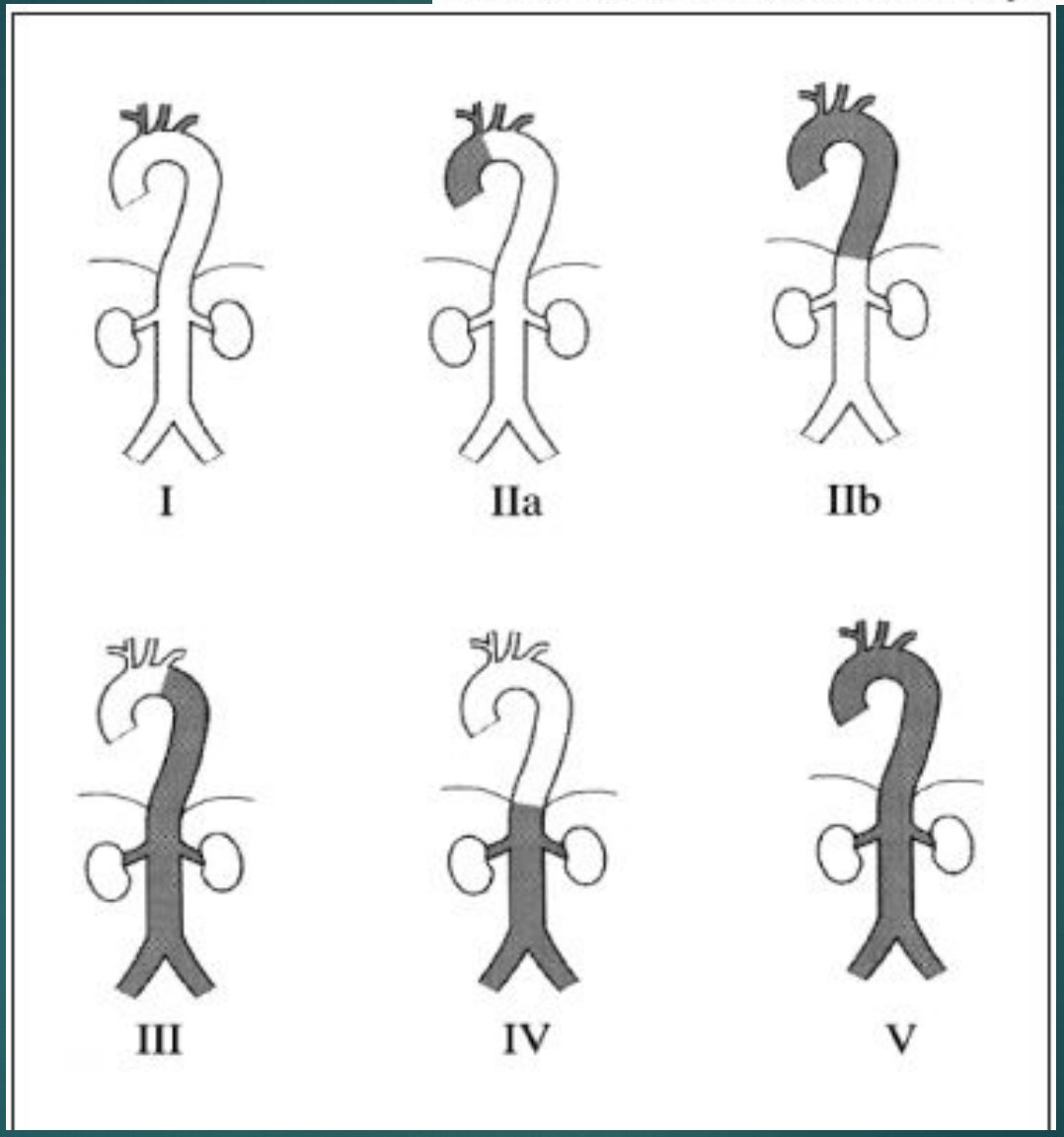
New classification of angiogram

International Conference on Takayasu Arteritis, 1994



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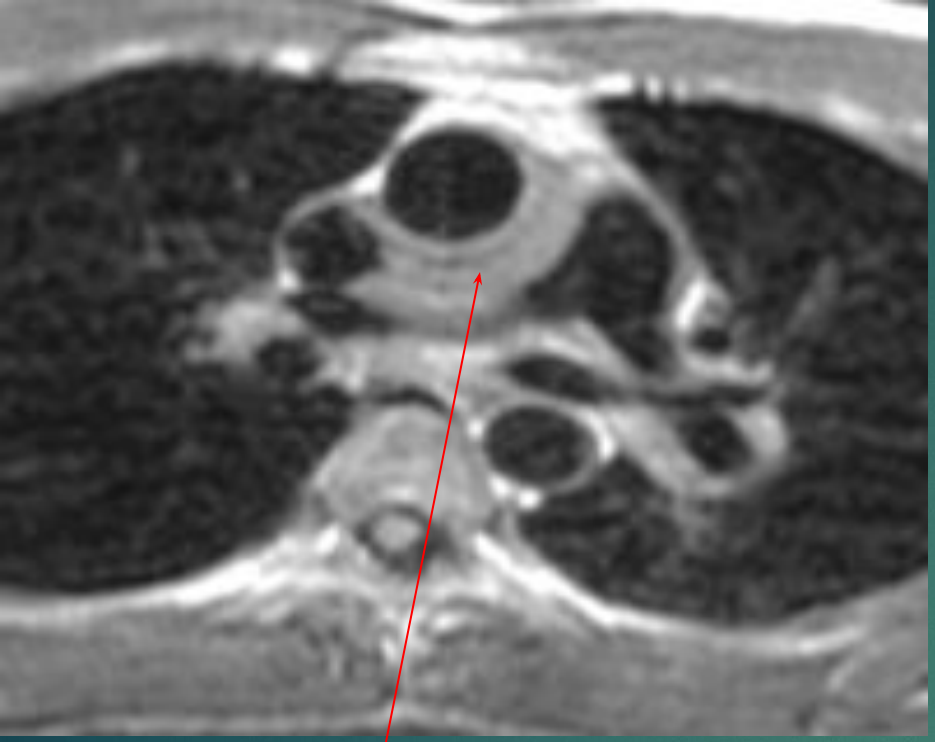
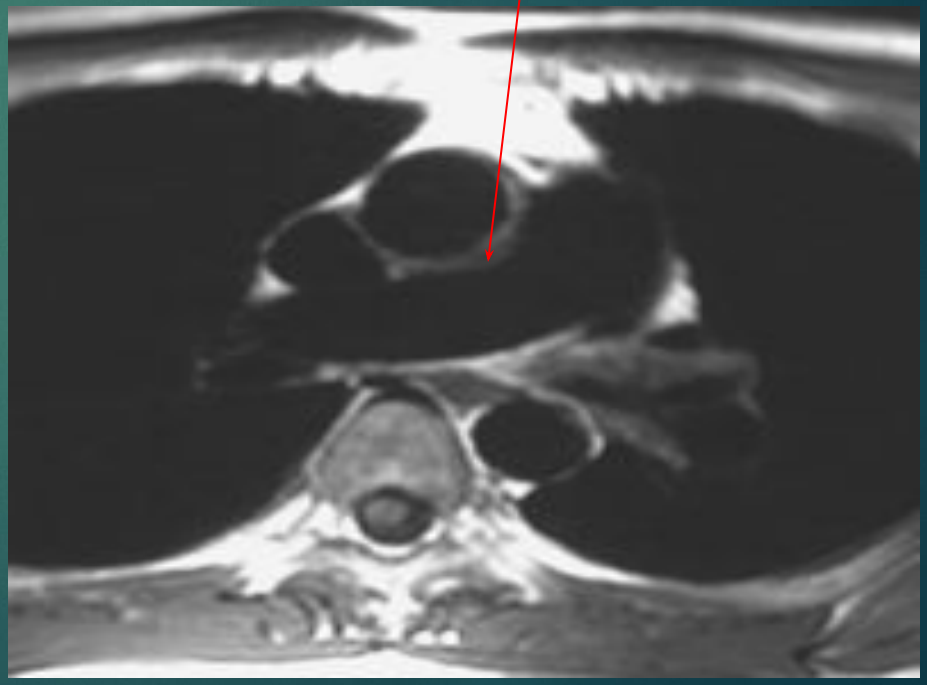


a/c phase-Axial T1-weighted image wall thickening of As aorta and PA

Axial T1-weighted image- improvement of wall thickening of As Ao and PA after steroid therapy



Findings of TA on MRI

- mural thrombi
- signal alterations within and surrounding inflamed vessels
- vascular dilation
- thickened aortic valvular cusps
- multifocal stenoses
- concentric thickening of the aortic wall

- Disadvantages

  difficulty in visualizing small branch vessels and poor visualization of vascular calcification

  may falsely accentuate the degree of vascular stenoses (renal & subclavian)

[18F]fluorodeoxyglucose PET for diagnosing Takayasu's arteritis

- common [18F]FDG uptake pattern TA

  early phase - linear and continuous

  late phase-patchy rather than continuous ,linear

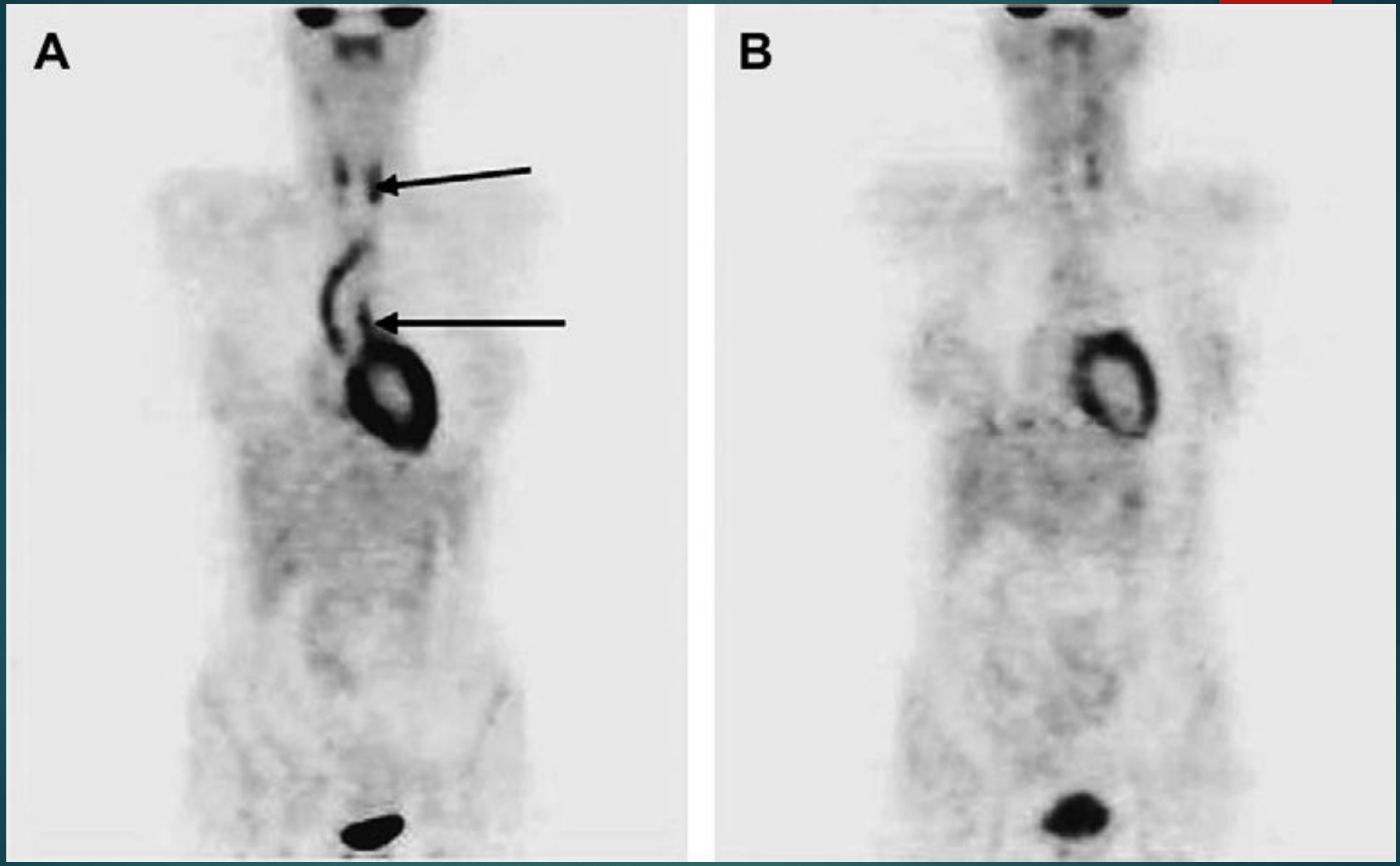
- shown to identify more affected vascular regions than morphologic imaging with MRI
- does not provide any information about changes in the wall structure or luminal blood flow

- sensitivities of 83% and specificity 100%

  (Meller Jet al. Value of F-18 FDG hybrid camera PET and MRI in earlyTakayasu aortitis. Eur Radiol 2003)

- Sensitivity of 92%, specificity of 100% and a diagnostic accuracy of 94%

  (Webb M et al. The role of 18F-FDG PET in characterising disease activity in Takayasu arteritis. Eur J Nucl Med Imaging 2004



remission after treatment

Treatment of TA

Control of vasculitis

Steroids

↓ If uncontrolled

- immunosuppressants : Cyclosporine,Cyclophosphamide, Mtx,Mycophenolate mofetil

Symptomatic occlusion

angioplasty/surgery

thrombosis

Anti-platelet therapy（low-dose Aspirin）

Medical treatment

0.7-1 mg/kg/day –prednisolone for 1-3 months

common tapering regimen once remission
↓ pred by 5 mg/week → 20 mg/day.

Thereafter, ↓by 2.5 mg/week → 10 mg/day

↓1 mg/day each week, as long as disease does not become more active

Pulse iv corticosteroids - CNS symptoms- no data to support

- Steroids → 50% response
- Methotrexate →further 50% respond
- 25% with active disease will not respond to current treatments
- resistant to steroids/ recurrent disease once corticosteroids are tapered

  cyclophosphamide (1-2 mg/kg/day),

  azathioprine (1-2mg/kg/day), or

  methotrexate (0.3 mg/kg/week)

  Mycophenolate mofetil/ anti TNF a agents-
  infliximab

- Critical issue is in trying to determine whether or not disease is active

- During Rx- regular clinical examination and ESR+ C-RP initially - every few days

- CT or MR angio - 3 to 12 months - (active phase of Rx), and annually thereafter

- Criteria for active disease

1.	Systemic features (fever, musculoskeletal symptoms, etc.)
2.	Elevated erythrocyte sedimentation rate
3.	Features of vascular ischaemia or inflammation (claudication, vascular pain as carotodynia, diminished or absent pulse, vascular bruit), asymmetric blood pressure in either upper or lower limbs or both
4.	Typical angiographic features

New onset or worsening of two or more features indicates "active disease".

- chronic phase- persistent inflammation

  steroids should be continued –

  <1.0 mg/dL of s.C-RP and 20 mm/h of ESR

Surgical treatment

- HTN with critical RAS
- Extremity claudication limiting daily activities
- Cerebrovascular ischaemia or critical stenoses of ≥3 cerebral vessels
- Moderate AR
- Cardiac ischaemia with confirmed coronary involvement
- Aneurysms

Recommended at quiescent state-avoids compli

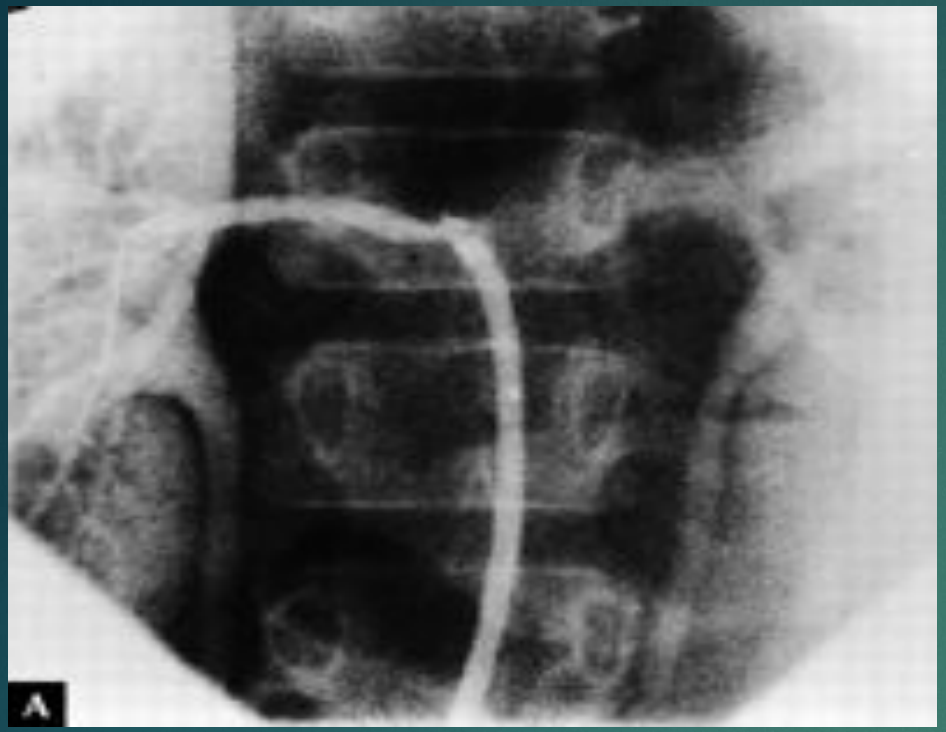
(restenosis, anastamotic failure, thrombosis, haemorrhage, & infection)

Surgical techniques

- Carry high morbidity & mortality
- Steno /aneurysm -anastomotic points
- Progressive nature of TA
- Diffuse nature of TA

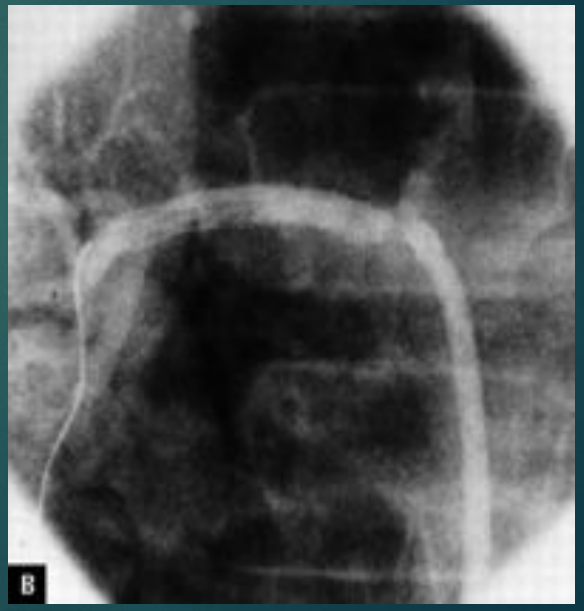
Renal artery involvement

- Best treated by PTA
- Stent placement following PTA
  - Ostial lesions
  - Long segment lesions
  - Incomplete relief of stenoses
  - Dissection



ostial stenosis of the right renal artery

after deployment of a stent



- Renal PTA - 33 stenoses (20 pts)
- Indi-sev HTN,angio 70% stenosis with pr grad 20mm, nl-ESR
- Tech success -28 lesions (85%) clin success-14(82%)
- Failures - Coexistent abd Ao disease & tight, prox RAS
- Tech diffi - tough, noncompliant stenoses, difficult to cross & resisted repeated, prolonged balloon inflations - backache & ↓SBP during balloon inflation
- Follow-up –mean (8/12) -restenosis in 6 (21%)

- Renal PTA in TA -tech difficulties; Short-term results - good, Complication rate-acceptable

Sharma s et al, AIIMS
Am J Roentgenol. 1992 Feb;158(2):417-22

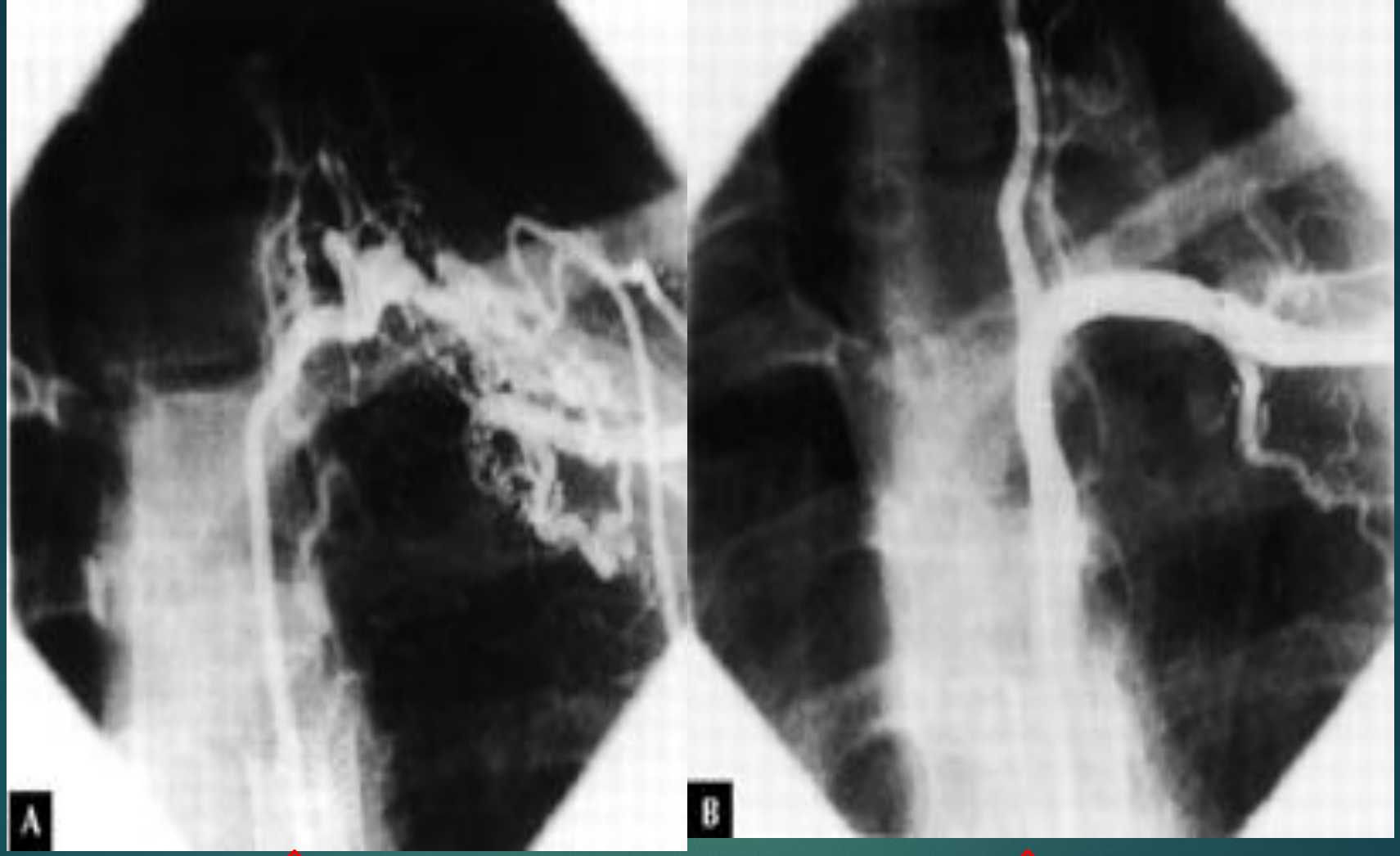
Aortoarteritic lesions

Balloon dilation

- safe & reasonably effective
- Can be performed repeatedly without any added risks

Balloon dilation diff from atherosclerotic lesions

- Minimal intimal involvement –permits easy wiring and balloon crossing
- Resistance to dilation – high fibrotic element in the stenotic lesion
- restenosis> frequent in TA - diffuse and long stenotic lesions



Left subclavian angiograms- 95% stenosis with extensive collaterals

Post angioplasty and stenting.

Joseph s et al, SCT
J Vasc Interv Radiol 1994;5:573–580

- PTA- Scl A in TA
- 24 pts →26 Scl A
  VB insufficiency, UL claudication, or both
- Aortography → (focal-14 ,< 3 cm,extensive-12)
- Initial tech & clinical success – 81% (17 /19 steno,4/7occlu)
- Follow-up → mean26 months → ISR -6 (all ext)
- Cumu patency –S/L-100/50%
- Long-term results -excellent in focal lesions ,less durable extensive disease

Tyagi s et al, GB Pant
Cardiovasc Intervent Radiol. 1998 May219-24

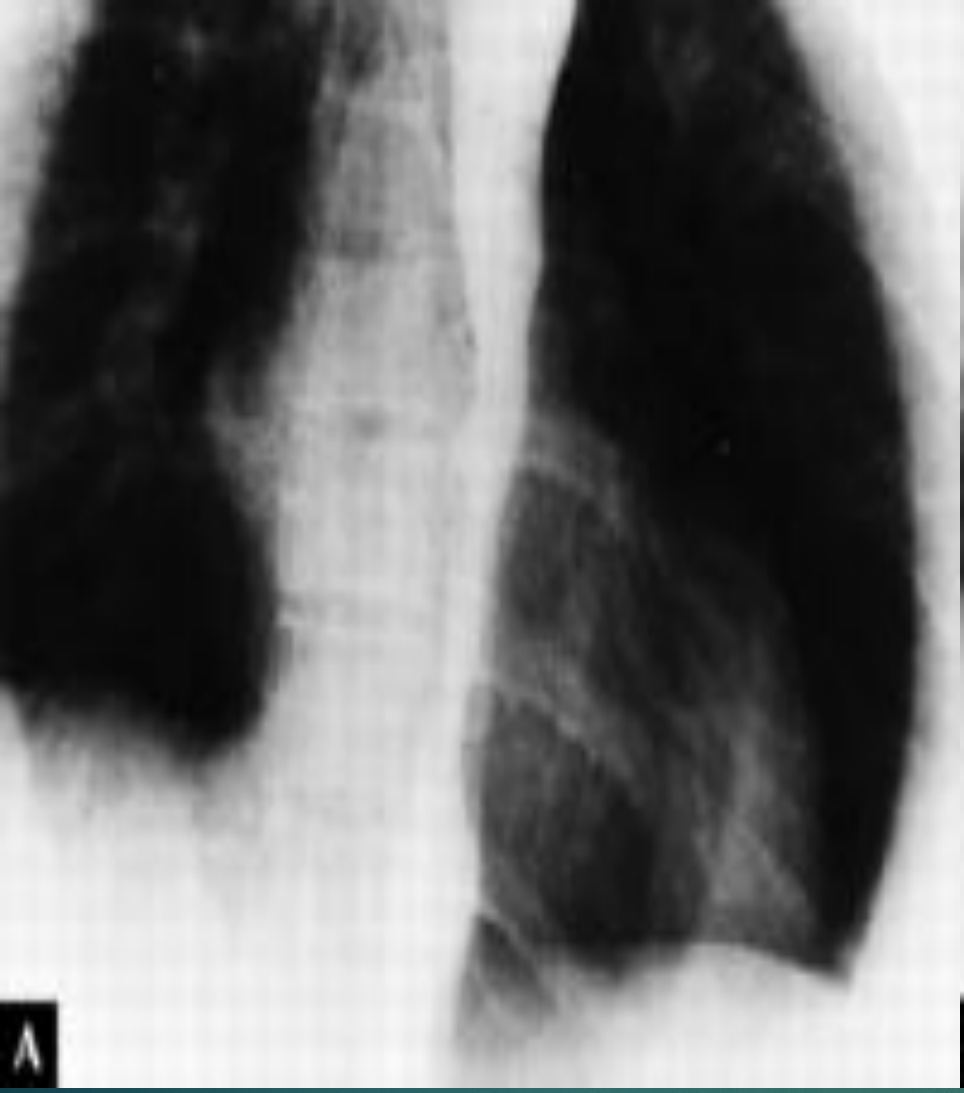
- To compare PTA- Scl A in TA & athero
- 61 Scl A PTA (TA = 32 & athero = 23)
- PTA succ in 52 stenotis,3 occl
- TA -Higher balloon inflation P
- TA -more residual stenosis
- TA –restenosis more
- restnosis could be effectively redilated
- TA -Subclavian PTA - Safe, can be performed as effectively as in athero, good long-term results

Aortoplasty and Stenting

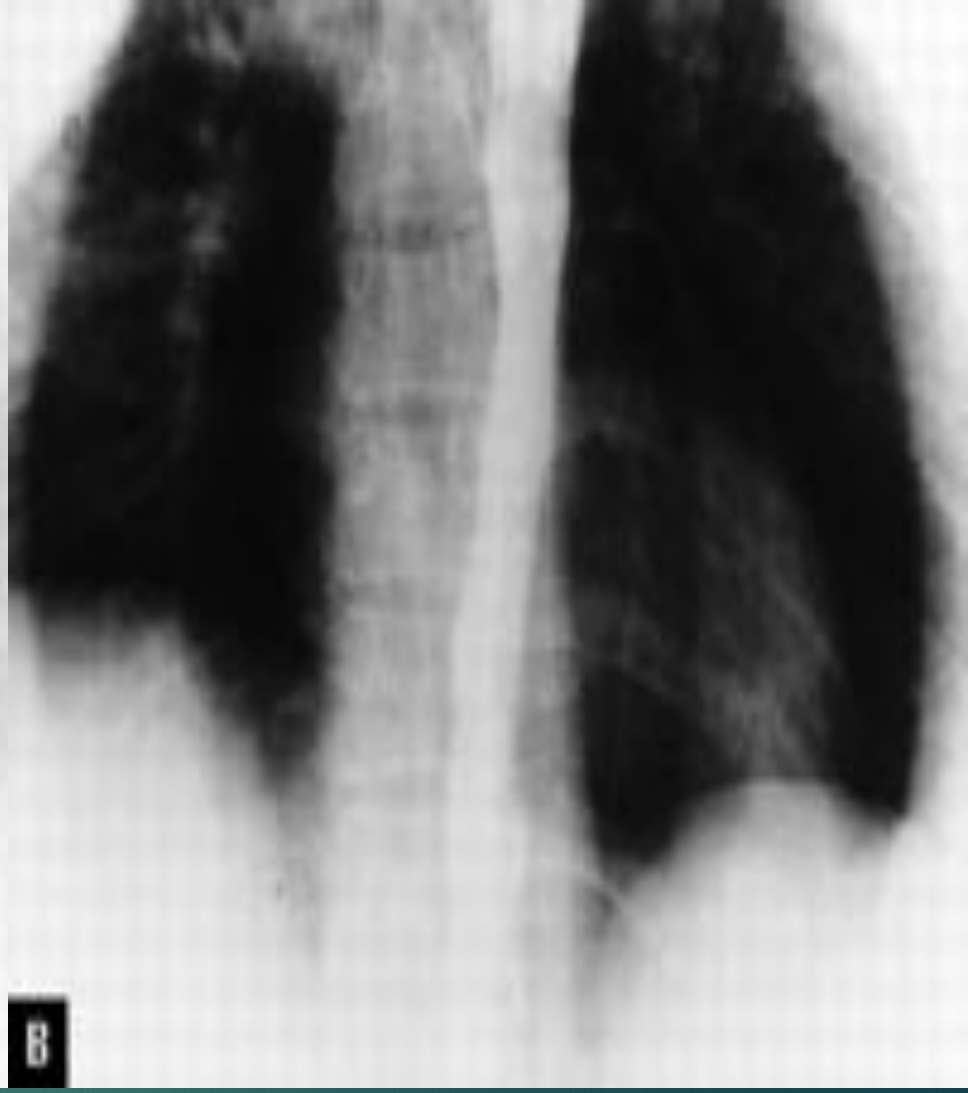
- PTA -desc thoracic and/or abd Ao (TA) stenosis
- 16 pts (12+4)- HTN/severe b/l- LL claudication
- Aortography – stenosis→ DTA-5, abd Ao-10, Both -1
- Initial tech & clinical success -100%
- patency rate of 67% in a 52-month follow-up
- Follow-up (mean 21months)- Restenosis -3
- PTA has a definite role in TA management
- residual gradient < 20 mm -criterion for successful aortoplasty
- long-segment disease, dissection or persistence of a grad > 20 mm Hg after PTBA- aortic stenting

Rao AS et al, SCT

Radiology. 1993



long-segment diffuse stenotic involvement of the DTA



after deployment of stents.

Treatment for cor A occulusion in TA

Surgery (CABG)- often not indicated

- IMA can't be used often
  - occlu of Innomi A / Scl A
  - calcification of aorta

High incidence of restenosis:36%

Angioplasty(PTCA)

- alternative to surgery

Very high incidence of restenosis:78%

DES-effectiveness ?

Percutaneous Management of Aneurysmal Lesions

- Aneurysmal dilatation- isolation or together with stenotic lesions
- fusiform or saccular
- one of the major complications related to the prognosis in TA
- Incidence of aneurysm rupture -low
- Management - mainly surgical.
- Covered stent-grafts may be useful