Società Italiana dell'Ipertensione Arteriosa
Lega Italiana contro l'Ipertensione Arteriosa

EVENTO FORMATIVO INTERREGIONALE SIIA
PIEMONTE | LIGURIA | VALLE D'AOSTA
Torino, 12 ottobre 2024

Ipertensione e patologia aortica

Gian Paolo Fra

Ambulatorio Ipertensione e Malattie Metaboliche
SCDU Medicina Interna 1
AOU "Maggiore della carità" di Novara

UPO
UNIVERSITÀ DEL PIEMONTE ORIENTALE

Dati anamnestici

- Paziente di **21 anni**, nota ipertesa, giungeva in DEA per **cefalea, ipovisus in OS** e **ipovisus a banda orizzontale in OD** e **dolore toracico irradiato al dorso intermittente da 3 giorni**. La **cefalea** viene descritta ad andamento **intermittente compressiva in regione fronto-temporale bilaterale**, senza nausea/vomito ma con **fonofobia**. La pz riferisce che tale cefalea sarebbe presente **"da molti anni"** con frequenza di **2-3 episodi/settimana**, a risoluzione spontanea il giorno successivo e per la quale da alcuni anni non assume alcuna terapia perchè riferisce di non poter assumere FANS in quanto "intollerante"
- **Da un anno** riferita inoltre **dispnea e dolore retrosternale per sforzi lievi**, non riferiti episodi a riposo; non riferiti inoltre episodi di cardiopalmo, lipotimia o sincope.
- **Dall'età di 9 anni**, diagnosi di **ipertensione arteriosa** in altro Paese Europeo. Riferisce **trattamento antipertensivo** con duplice terapia di cui non ricorda il nome, impostata all'estero, e **interrotta circa un paio di anni fa per "episodio di pdc in corso di episodio ipotensivo"**. Riferisce **stabilmente PAS elevata**.
- **Familiarità per malattia vascolare**: **madre** affetta da ipertensione arteriosa e pregresso infarto, **sorelle** con ipertensione arteriosa, due fratelli in abs, **nonna** ipertesa.
- **Tabagismo (30 sigarette/die**), sovrappeso.

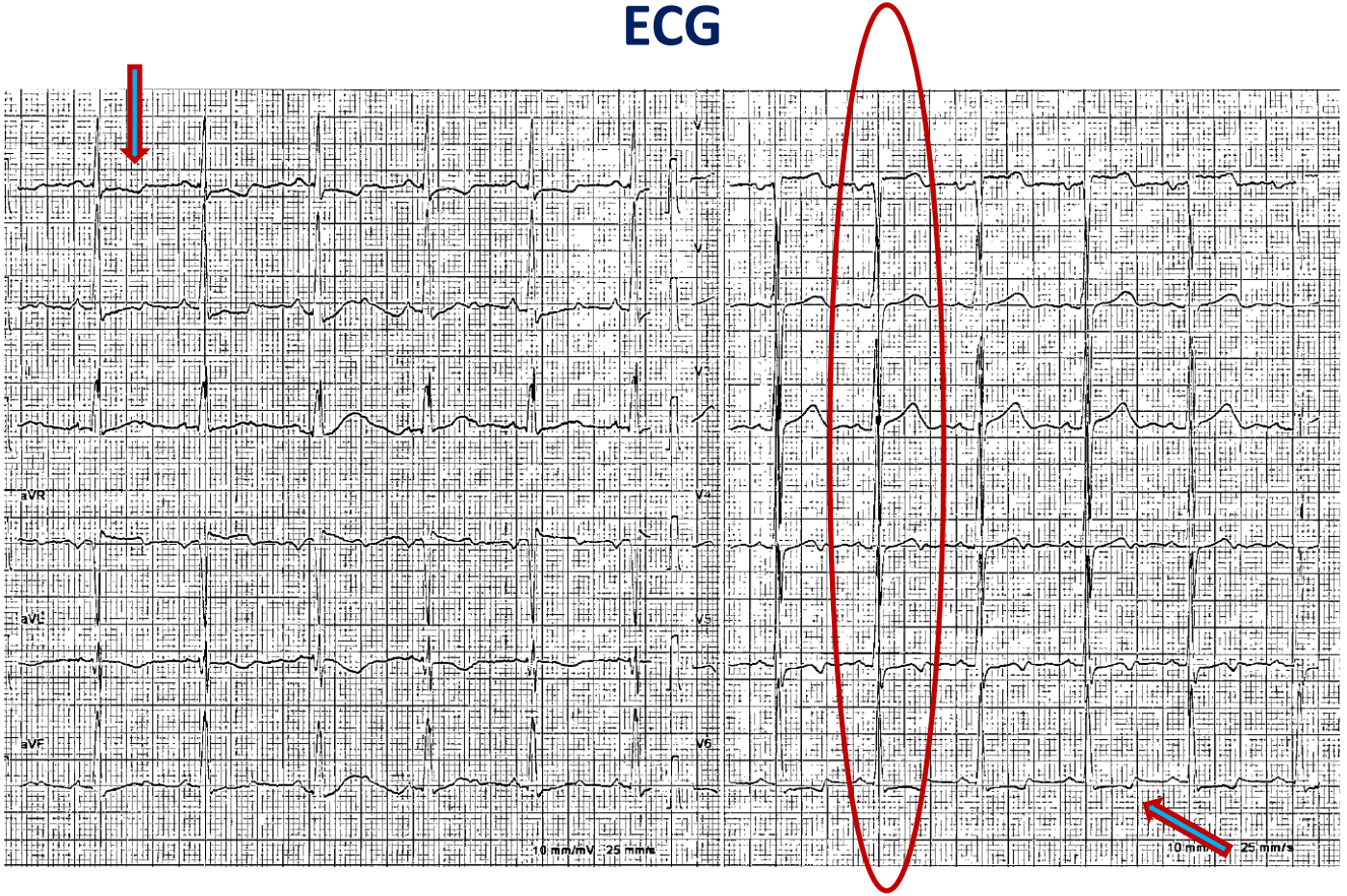
Esame obiettivo

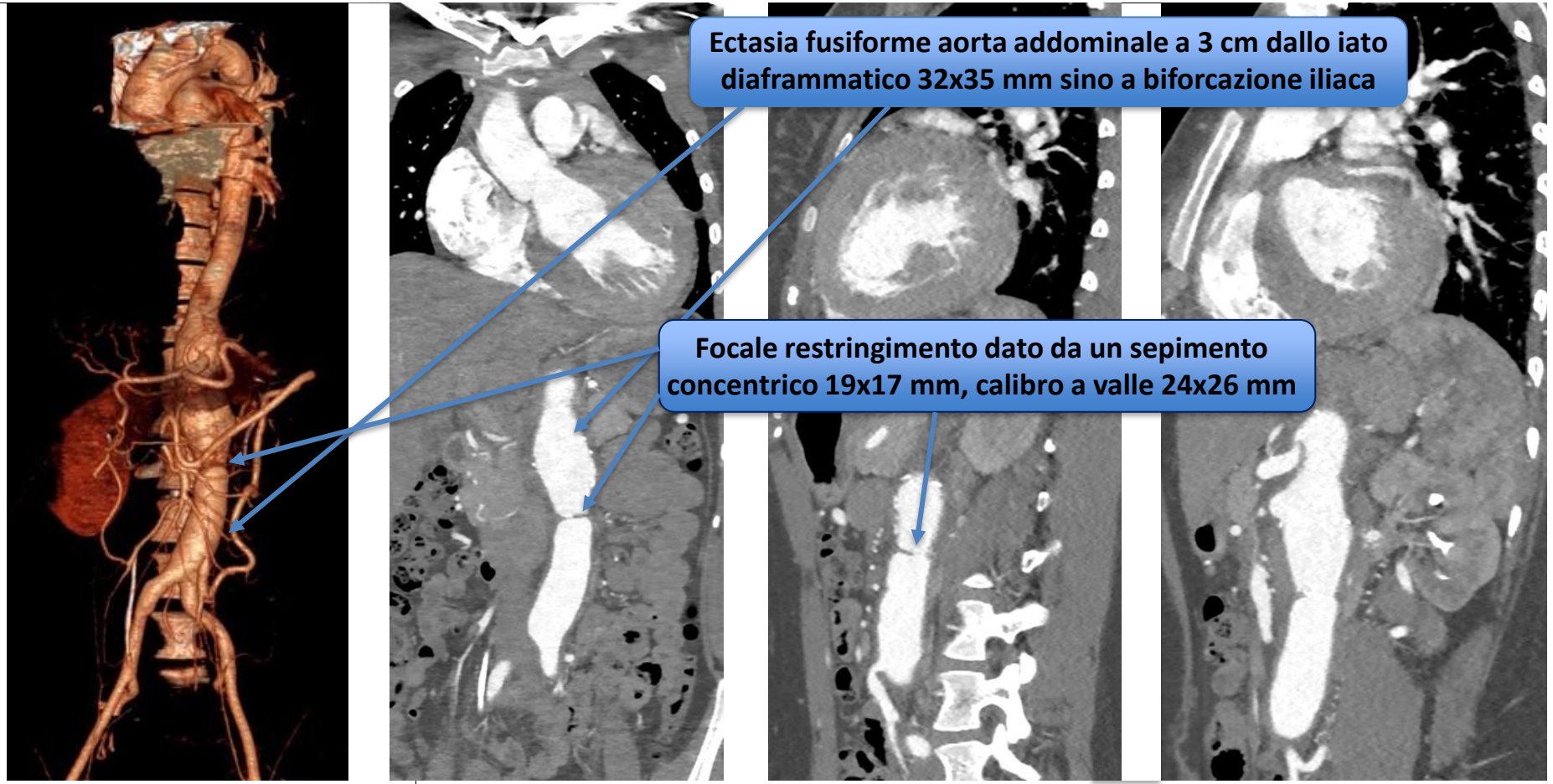
- **PA max: 230/135 mmHg** bilateralmente, FC 100 bpm, Sat.: 98, T. asc.: 36, GCS: 15
- Paziente vigile, collaborante. EON: pupille iso-iso, scarsamente reagenti alla luce. eloquio fluente Ridotta sensibilita' a livello facio-crurale a dx, mingazzini 1 e 2 neg. Non apparenti deficit motori. **Deficit visivo totale a livello dell'occhio sin e parziale a destra con visione orizzontale, deficit visione temporale**.
- Cuore ed apparato vascolare: impurità sistolica in mesocardio. Polsi periferici iso-normosfigmici, simmetrici, non differenza di PA negli arti.
- Addome: trattabile, dolente e dolorabile a livello epigastrico-ipocondrio dx, Fidx. **Soffio addominale udibile a livello mesogastrico maggiormente in sede paraombelicale sinistra rispetto che a destra**
- **ECG:** tachicardia sinusale (100 bpm) con segni di **possibile IVSX e alterazioni della ripolarizzazione diffuse a carattere aspecifico**

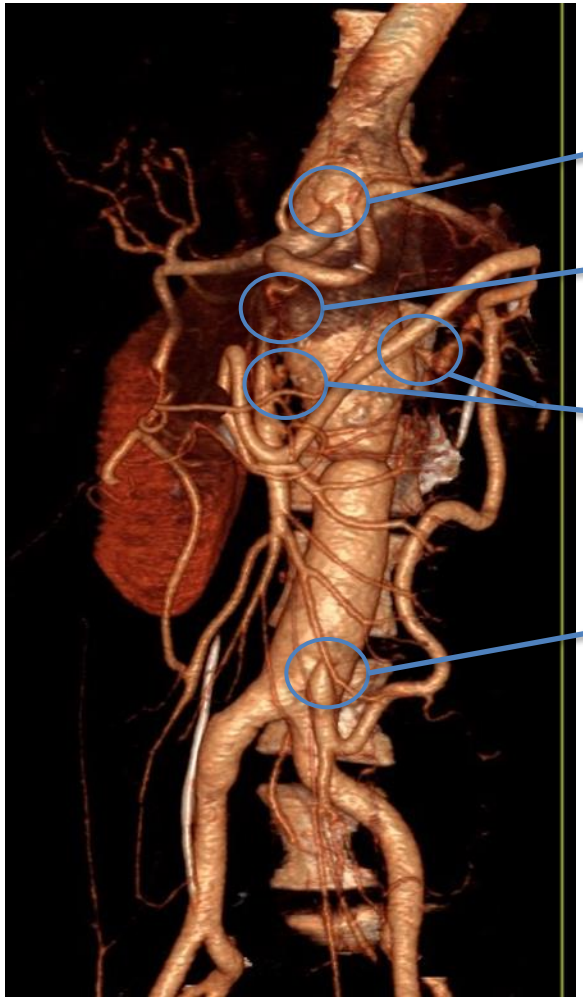
TERAPIA:

- **Labetalolo** 50 mg EV, a seguire labetalolo in infusione continua con buona risposta clinica → 120/88 mmHg sospende labetalolo, avvia terapia per os con **calcio-antagonista.**

ECG




Ectasia fusiforme aorta addominale a 3 cm dallo iato diaframmatico 32x35 mm sino a biforcazione iliaca
Focale restringimento dato da un sepimento concentrico 19x17 mm, calibro a valle 24x26 mm

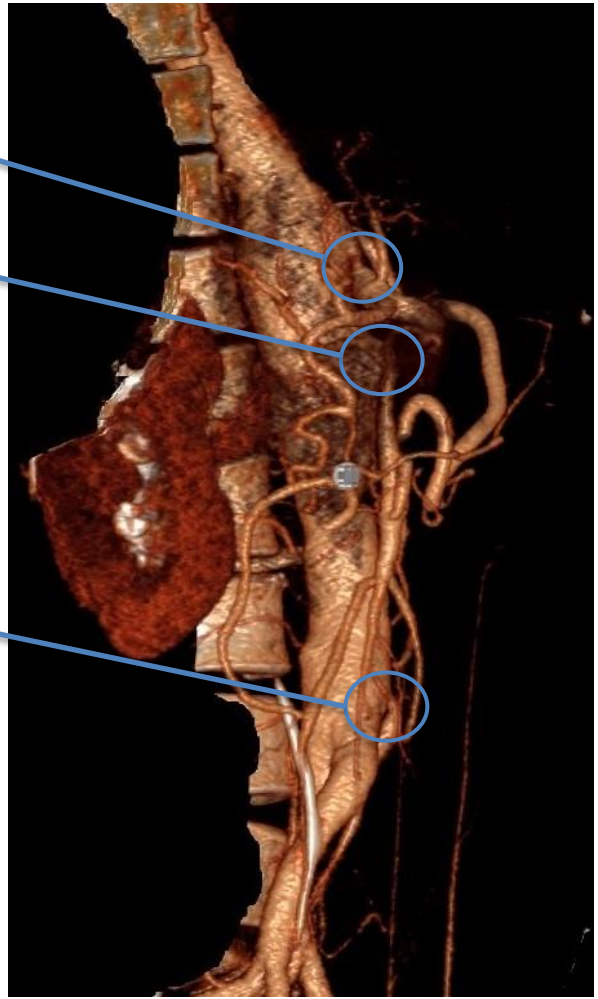


Tripode celiaco

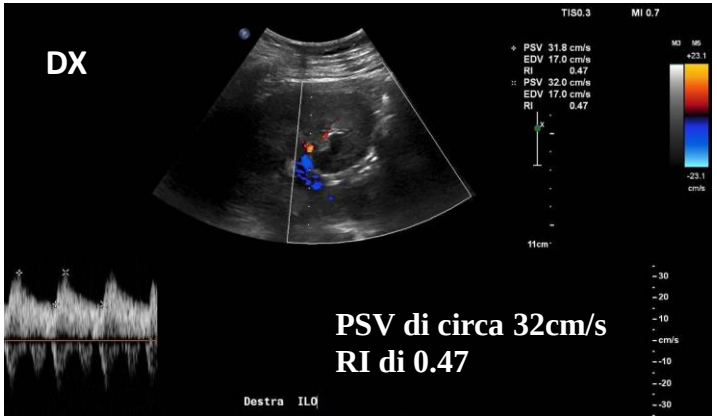
AMS

A Renali Dx e Sx

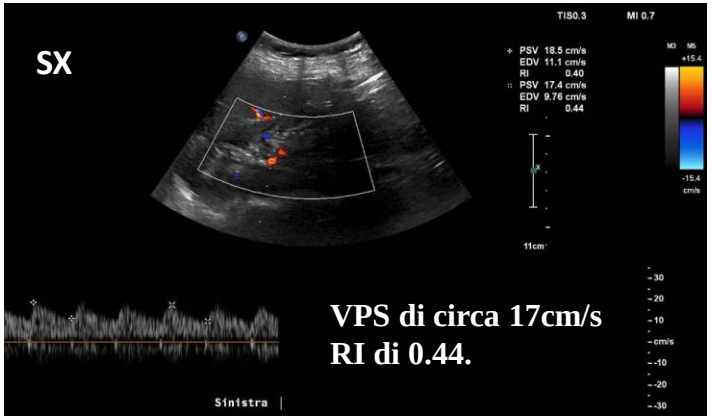
AMI



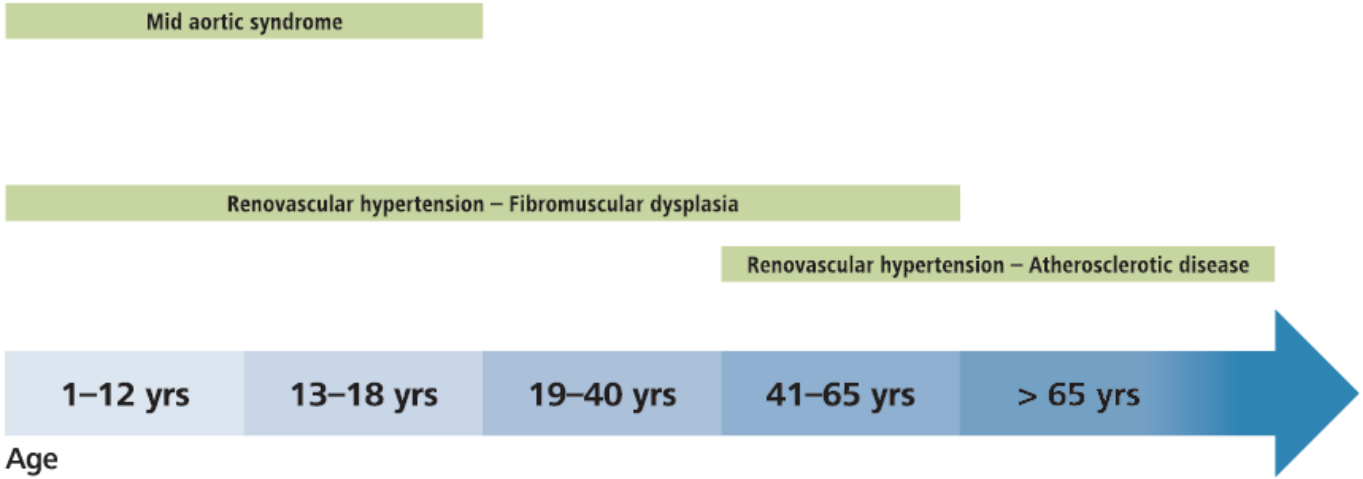
Ecocolordoppler arterie renali



SX: l'arteria renale sinistra non è campionabile all'origine.



Ipertensione Nefrovascolare



Modified from 2023 ESH Guidelines for the management of arterial hypertension

Brit. Heart J., 1963, **25**, 610.

THE MIDDLE AORTIC SYNDROME

BY

P. K. SEN, S. G. KINARE, S. D. ENGINEER, AND G. B. PARULKAR

From the Department of Surgery, Seth G. S. Medical College and K.E.M. Hospital, Bombay 12, India

Received January 12, 1963

Obstructive lesions of the aorta and its branches have been the subject of a great deal of interest and study due to the phenomenal growth of vascular surgery in recent years. With this study has come about a constant reappraisal of our clinical knowledge of these cases. Congenital narrowings of the aorta are nearly all located in the isthmial area, and clinical knowledge of these cases is based upon well-recorded and critically documented writings of many workers. The aortic blocks of acquired origin are, however, still the subject of intensive study and within the past decade clearly defined clinical syndromes have been described, depending on the site of the block. The two best known are the aortic arch syndrome of Takayasu (1908), or Martorell and Fabré Tersol (1944) and the terminal aortic (bifurcation) syndrome of Leriche and Morel (1948) (Fig. 1).

With increasing safety and facility in the use of aortography for the diagnosis of a large number of conditions (apart from those directly vascular), blocks in the middle segment (between the arch and the terminal bifurcation of the aorta) are being diagnosed with greater frequency. The patho-

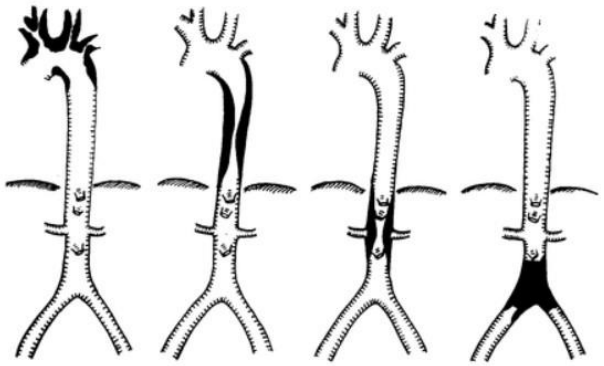
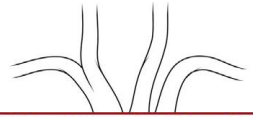


FIG. 1.—Diagrammatic representation of the aortic obliterative syndromes.



0.5-2% delle coartazioni dell'aorta

Fibromuscular Dysplasia

Prevalence:
<1 to 6%[a]

Suggestive symptoms, signs and findings

Early-onset/ severe hypertension
Migraine
Pulsatile tinnitus

1st choice screening test[b]

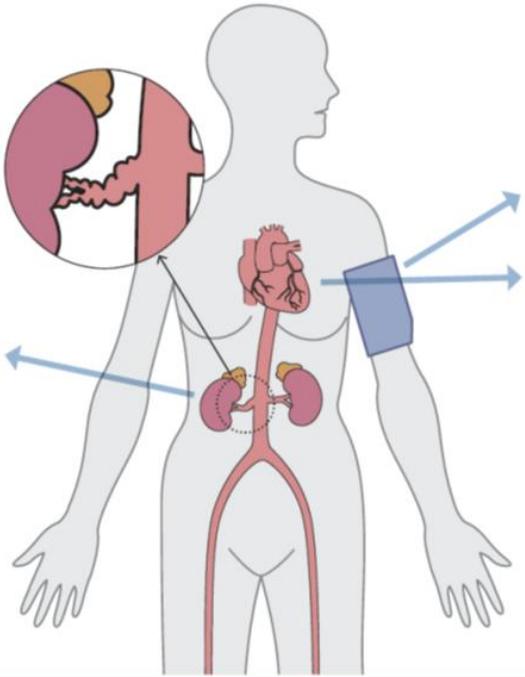
Renal artery duplex ultrasound; otherwise angio-CT or angio-MR

Treatment

Antihypertensive treatment
Angioplasty without stenting[c,d]

Follow-up

- Whole body angio-CT or angio-MR at diagnosis[e]
- Indefinite follow-up



Cardiovascular phenotype

24h ABPM – early onset or resistant hypertension

Frequent in patients with Spontaneous Coronary Artery Dissection (SCAD)

May affect all medium sized arteries (most frequent: renal and cervical arteries)

Often associated with arterial dissections and aneurysms

Cardiovascular phenotype:
From asymptomatic to resistant hypertension, stroke, renal, mesenteric or myocardial infarction

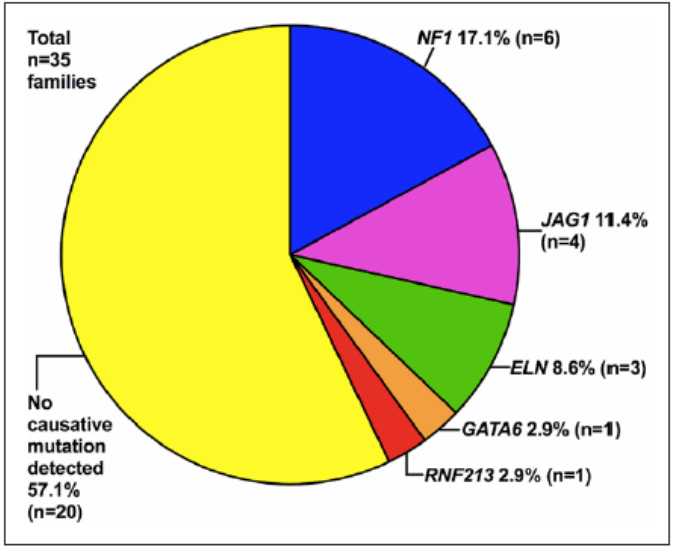
2023 ESH Guidelines for the management of arterial hypertension

Genomics

Whole Exome Sequencing Reveals a Monogenic Cause of Disease in ≈43% of 35 Families With Midaortic Syndrome

Jillian K. Warejko, Markus Schueler, Asaf Vivante, Weizhen Tan, Ankana Daga, Jennifer A. Lawson, Daniela A. Braun, Shirlee Shril, Kassaundra Amann, Michael J.G. Somers, Nancy M. Rodig, Michelle A. Baum, Ghaleb Daouk, Avram Z. Traum, Heung Bae Kim, Khashayar Vakili, Diego Porras, James Lock, Michael J. Rivkin, Gulraiz Chaudry, Leslie B. Smoot, Michael N. Singh, Edward R. Smith, Shrikant M. Mane, Richard P. Lifton, Deborah R. Stein, Michael A. Ferguson, Friedhelm Hildebrandt

Abstract—Midaortic syndrome (MAS) is a rare cause of severe childhood hypertension characterized by narrowing of the abdominal aorta in children and is associated with extensive vascular disease. It may occur as part of a genetic syndrome, such as neurofibromatosis, or as consequence of a pathological inflammatory disease. However, most cases are considered idiopathic. We hypothesized that in a high percentage of these patients, a monogenic cause of disease may be detected by evaluating whole exome sequencing data for mutations in 1 of 38 candidate genes previously described to cause vasculopathy. We studied a cohort of 36 individuals from 35 different families with MAS by exome sequencing. In 15 of 35 families (42.9%), we detected likely causal dominant mutations. In 15 of 35 (42.9%) families with MAS, whole exome sequencing revealed a mutation in one of the genes previously associated with vascular disease (*NF1*, *JAG1*, *ELN*, *GATA6*, and *RNF213*). Ten of the 15 mutations have not previously been reported. This is the first report of *ELN*, *RNF213*, or *GATA6* mutations in individuals with MAS. Mutations were detected in *NF1* (6/15 families), *JAG1* (4/15 families), *ELN* (3/15 families), and one family each for *GATA6* and *RNF213*. Eight individuals had syndromic disease and 7 individuals had isolated MAS. Whole exome sequencing can provide conclusive molecular genetic diagnosis in a high fraction of individuals with syndromic or isolated MAS. Establishing an etiologic diagnosis may reveal genotype/phenotype correlations for MAS in the future and should, therefore, be performed routinely in MAS. **(*Hypertension*. 2018;71:691-699. DOI: 10.1161/HYPERTENSIONAHA.117.10296.)** • Online Data Supplement



Aorta and Major Branches

Eur J Vasc Endovasc Surg (2023) 65, 120–130

EJVES Open Access

SYSTEMATIC REVIEW

Editor's Choice – Therapeutic Options and Outcomes in Midaortic Syndrome: A Systematic Review and Meta-analysis

Kimberley R.G. Cortenbach [a,i], Bahram Yosofi [b,†], Laura Rodwell [c], Jelena Meek [a], Ritesh Patel [d], Siddharth K. Prakash [e], Niels P. Riksen [f], Sjoerd F.M. Jenniskens [g], Mark Dirven [h], Marco C. DeRuiter [i], Roland R.J. van Kimmenade [b,*]

[a] Department of Tumour Immunology, Radboud Institute for Molecular Life Sciences, Radboud University Medical Centre, Nijmegen, the Netherlands
[b] Department of Cardiology, Radboud University Medical Centre, Nijmegen, the Netherlands
[c] Department of Health Evidence, Radboud University Medical Centre, Radboud University, Nijmegen, the Netherlands
[d] Department of Internal Medicine, Division of Cardiology, University of South Florida Morsani College of Medicine, Tampa, FL, USA
[e] Department of Internal Medicine, Division of Cardiology, The John Ritter Research Program in Aortic and Vascular Diseases, Houston, TX, USA
[f] Department of Internal Medicine and Radboud Centre for Infectious Diseases, Radboud University Medical Centre, Nijmegen, the Netherlands
[g] Department of Medical Imaging, Radboud University Medical Centre, Nijmegen, the Netherlands
[h] Division of Vascular and Transplant Surgery, Department of Surgery, Radboud University Medical Centre, Nijmegen, the Netherlands
[i] Department of Anatomy and Embryology, Leiden University Medical Centre, Leiden, the Netherlands

WHAT THIS PAPER ADDS

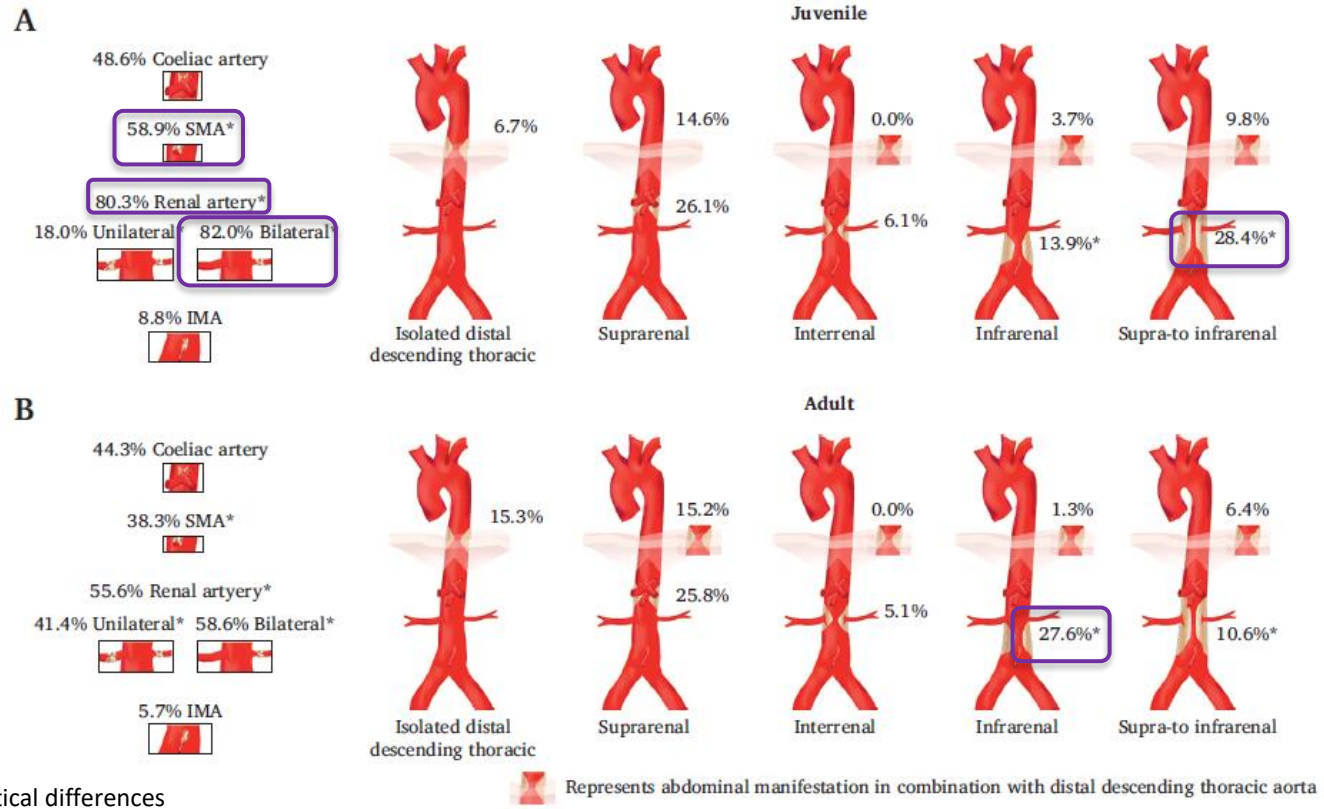
This meta-analysis investigated juvenile and adult patients with midaortic syndrome (MAS), (i.e., narrowing of the descending distal thoracic and or abdominal aorta). This systematic review and meta-analysis investigated the prevalence of hypertension during follow up after medical, endovascular, or surgical therapy. Juvenile patients who underwent endovascular therapy had more complications and hypertension than those who underwent surgery. Adults had more hypertension after surgery compared with endovascular or medical therapy. These results suggest that the optimal treatment for juvenile and adult patients may be different. There should be particular awareness and monitoring of hypertension during follow up after endovascular intervention in children. Clinical studies are required for further guideline recommendations.

Age ≥18 years

Aetiology	Juveniles* (n = 52)	Adults† (n = 59)	p value
Idiopathic	28 (53.9)	19 (32.2)	.034
Congenital	17 (32.7)	10 (17.0)	.076
Neurofibromatosis type 1	8 (15.4)	1 (1.7)	
Williams syndrome	2 (3.9)	1 (1.7)	
Alagille syndrome	1 (1.9)	5 (8.5)	
Mucopolysaccharidosis VII	1 (1.9)	0 (0.0)	
Fibromuscular dysplasia	3 (5.8)	3 (5.1)	
Foetal alcohol syndrome	1 (1.9)	0 (0.0)	
Down syndrome	1 (1.9)	0 (0.0)	
Inflammatory	7 (13.5)	30 (50.9)	<.001
Takayasu's arteritis	6 (11.5)	18 (30.5)	
Systemic lupus erythematosus	0 (0.0)	1 (1.7)	
Non-specific arteritis	1 (1.9)	3 (5.1)	
Atherosclerosis	0 (0.0)	8 (13.6)	

Data are presented as n (%).
* Aetiology reported in 52 from a total of 92 juvenile patients.
† Aetiology reported in 59 from a total of 88 adult patients.

Locations of midaortic syndrome (MAS) and involvement of other vessels in (A) juvenile and (B) adult patients



* Represents statistical differences between juvenile and adulthood MAS.

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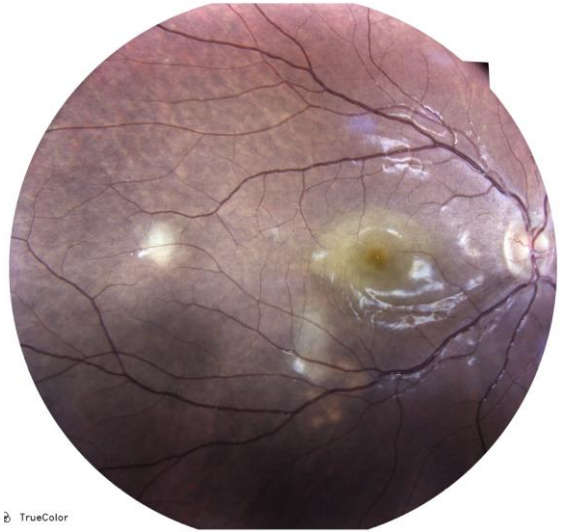
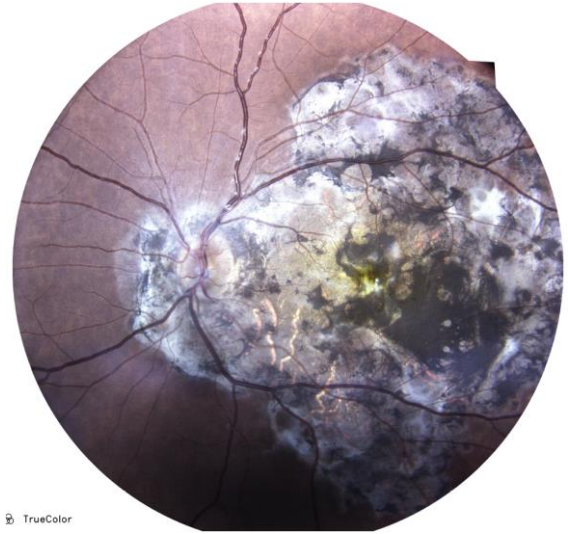
- **Valutazione neurologica:** Non evidenti segni di ipertensione endocranica. Il **quadro clinico non è in prima ipotesi indicativo di una genesi neurologica, utile valutazione oculistica.**

- **Valutazione oculistica – Fundus oculi:**

OD



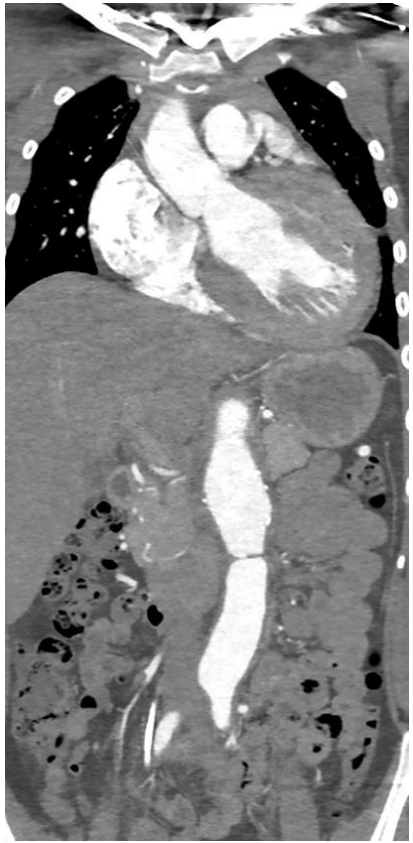


OS

OD atrofia retina esterna, coroidite multifocale; **OS** vasta area di **atrofia al polo posteriore** come da **cicatrice fibroatrofica** con evidenza della sottostante trama coroideale, **coroidite similserpiginosa**.

- **OCT, Fluorangiografia retinica e ICGA: coroidite simil-serpiginosa OS e coroidite multifocale OD**. Quadro suggestivo di **infezione tubercolare o altro quadro infettivo**. Non si esclude possibile **causa immunologica**

Eco-TT:



- Atrio sx di normali dimensioni (vol-i asx 31ml/m2)
- Ventricolo sinistro con **importante ipertrofia concentrica** (Setto 20 mm, PP 21 mm, DTD 40 mm, **RWT 1, Massa/m2 243g**), normali dimensioni endocavitarie, funzione sistolica globale conservata in assenza di difetti di cinetica segmentaria. **FE 54%, ai limiti inferiori di norma (FE 49% all'ecoscopia in DEA)**. Diastole nella norma con fusione E/A.
- Ventricolo destro non dilatato, normocinetico (TAPSE 21 mm), PAP non valutabile per IT non campionabile.
- Bulbo aortico di normali dimensioni (29 mm) con mantenimento della GST e normali dimensioni aorta ascendente (33 mma 50 mmdal piano valvolare)
- **Utile escludere comunque malattie da accumulo con RMN cardiaca** (escludere **Fabry e amiloidosi**, eventuale successivo **test genetico** ambulatoriale)

Esami ematochimici

Creatinina 0.97 mg/dl, eGFR 84 ml/min, Na 139 mEq/L, K 3.6 mEq/L,

Esame urine pH 5.5, PS 1037, **proteine 15 mg/dl**

Microalbuminuria spot ACR 35mg/g

Proteinuria: 105 mg/24h

Renina 65.9 microIU/mL (2.8-40)

Aldosterone 70.9 ng/dL (1.76-23.2)

Troponina T 11 ng/L (0-14), **pro-BNP 1430 pg/ml** (0-125),

glicemia 92 mg/dl, acido urico 5.2 mg/dl, col tot/HDL/TG/LDL 154/49/46/97 mg/dl, coagulazione di norma, funzione epatica di norma, TSH reflex 0.769 mUI/ml,

Autoimmunità

- VES 33 mm/ora, Proteina C reattiva 1.14 mg/dl, Fibrinogeno 486 mg/dl
- ANA, Anticorpi anti-dsDNA, ENA Screening, Anticorpi anti-ANCA: Negativi
- C3 119 mg/dl , C4 26 mg/dl
- **PET 18F-FDG: Negativa**

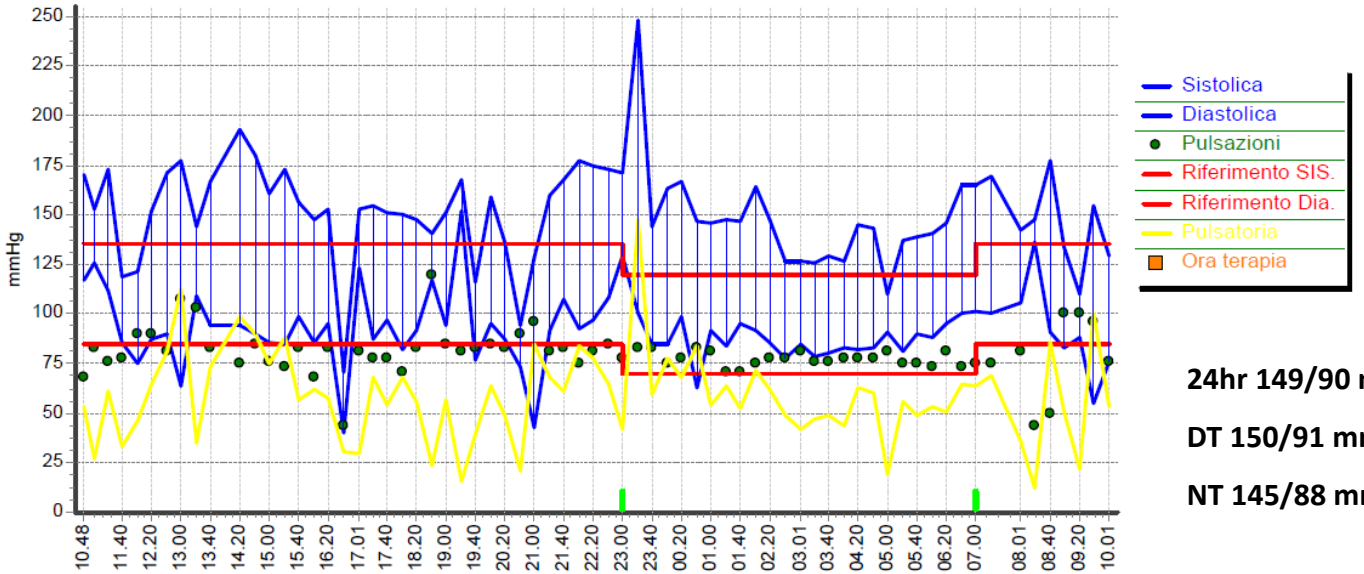
Cause infettive

- Sierologia LUE, Toxoplasma, HBV, HCV, Anticorpi Anti HIV ½: Negativi
- **Diagnostica infezione tubercolari: Quantiferon positivo**

PA 150-160/100-110 mmHg

Nifedipina 20 mg 1 cp h 8 + 2 cp h16 + 1 cp h 22;
Doxazosina 2 mg 1 cp h 8 - 20;
Nebivololo 5 mg 1 cp h 8.

ABMP



24hr 149/90 mmHg **Dip 2.18%**

DT 150/91 mmHg

NT 145/88 mmHg

Terapia consigliata alla dimissione

- Eviti il fumo di sigaretta
- Nidedipina RM 20 mg 1 cp ore 8, 2 cp ore 16 e 2 cp ore 22
- Doxazosina 4 mg 1 cp ore 8 e 1 cp ore 20
- Nebivololo/ Idroclorotiazide 5 mg/ 12.5 mg 1 cp ore 8
- Clopidogrel 75 mg 1 cp ore 8

Controlli post-dimissione

PA domiciliare riferita: 120/85 mmHg. Continua a fumare e non ha intenzione di smettere

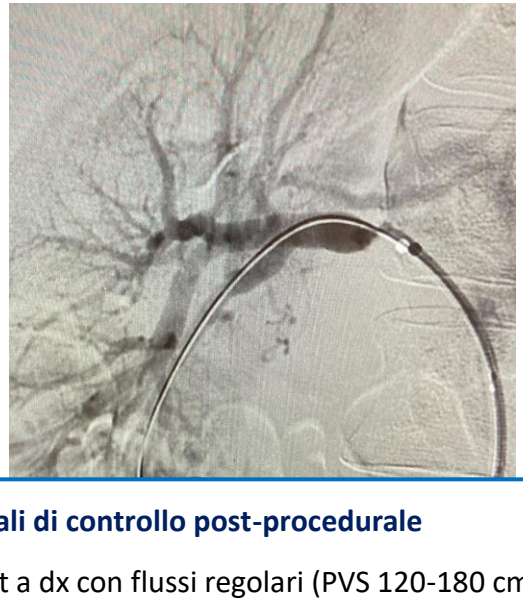
PA office: 140/92 mmHg Fc 70 b/min; Peso 65 Kg (-3).

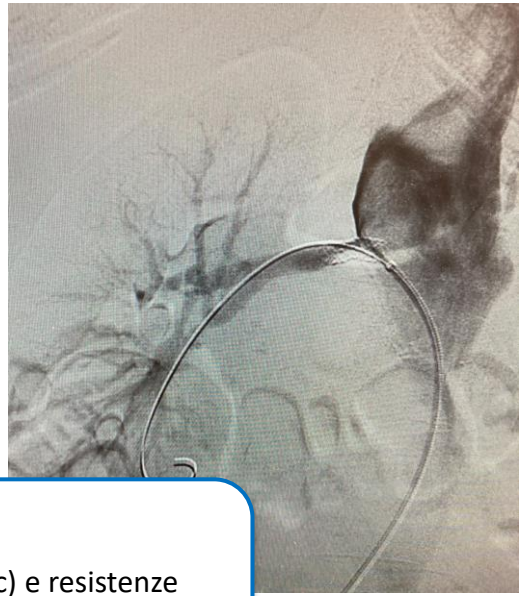
Terapia:

- Nifedipina RM 30 mg 1 cp ore 8 e Nifedipina RM 20 mg 1 cp ore 20
- Doxazosina 4 mg 1 cp x 2 /die
- Nebivololo/HCT 5/12.5 mg 1 co ore 8
- Clopidogrel 75 mg 1 co o a pranzo
- NICOZID 200 mg 1 co + 1/2 co 1 volta al giorno per 6 mesi

Arteriografia renale con PTA + stenting

Plurimi tentativi infruttuosi di PTRA dx senza posizionamento di stent per immediati recoiling per cui posizionato **stent balloon expandable Boston Scientific Express vascular SD 5 x 19 mm** con buon risultato angiografico terminale a dx.
Plurimi tentativi infruttuosi di cateterismo selettivo di arteria renale sinistra.





Ecocolordoppler arterie renali di controllo post-procedurale

Pervietà e buon esito di stent a dx con flussi regolari (PVS 120-180 cm/sec) e resistenze arteriolari intrarenali normali (**IR intraparenchimale renale destro 0.60, AT 60 msec**).

A sinistra confermata stenosi di grado serrato ostiale (**AT 140-160 msec - (IR 0.50**).

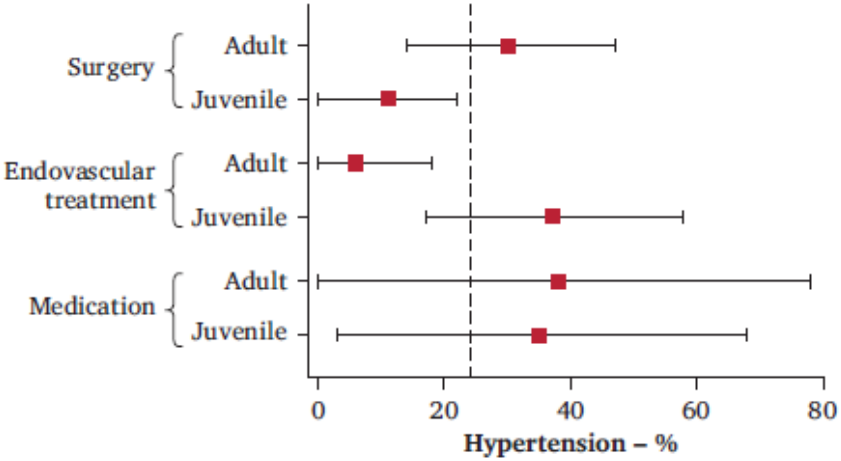
Long term results at the end of follow up in juvenile (A) and in adult patients (B) with MAS per intervention type

A

Long term results	Endovascular (n = 31)	NR – % (endovascular)	Surgery (n = 48)	NR – % (surgery)	p value
Follow up – months	18 (6.0–49.0)	19.4	24 (11.8–87.0)	12.5	.16
Hypertension	8 (38.1)	32.3	4 (10.8)	22.9	.020
Medication	20 (83.3)	22.6	18 (50.0)	25.0	.013
Death	0 (0.0)	19.4	1 (2.3)	10.4	1.0

B

Long term results	Endovascular (n = 24)	NR – % (endovascular)	Surgery (n = 51)	NR – % (surgery)	p value
Follow up – months	12 (6.0–33.0)	12.5	18 (9.8–51.8)	13.7	.098
Hypertension	1 (6.7)	51.6	9 (29.0)	35.4	.13
Medication	12 (70.6)	45.2	20 (64.5)	35.4	.76
Death	0 (0.0)	29.0	1 (2.2)	4.2	1.0



Adjusted predicted probabilities of hypertension at follow up in patients with MAS, by treatment type and age category, and adjusted for gender and aetiology

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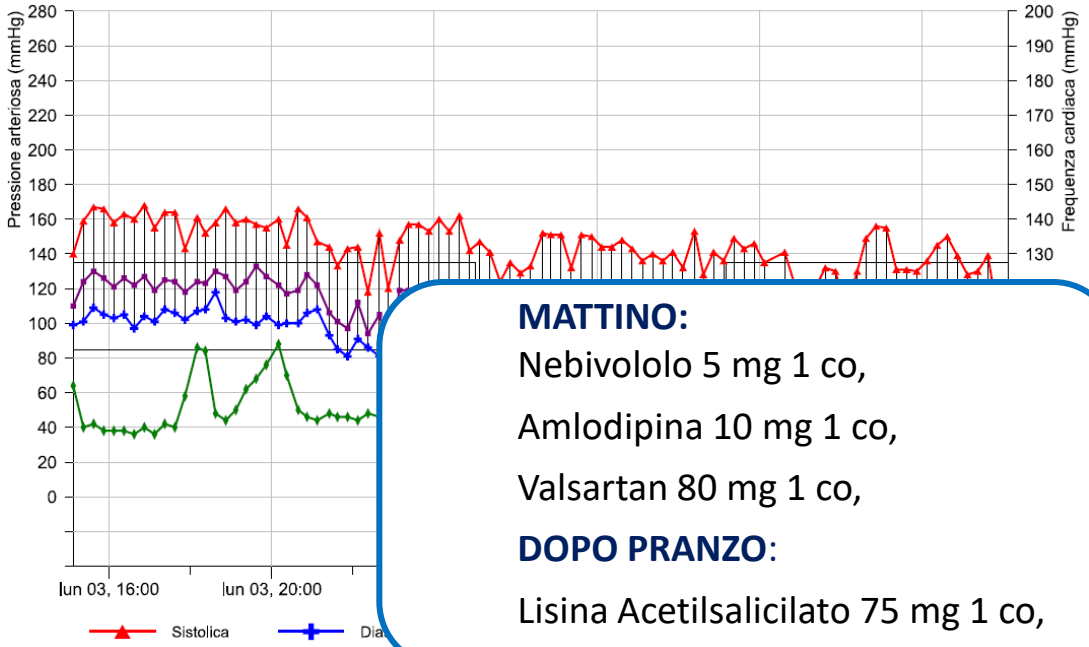
ABMP dopo PTRA + STENTING



MATTINO:

Nebivololo 5 mg 1 co,

Amlodipina 10 mg 1 co,

Valsartan 80 mg 1 co,

DOPO PRANZO:

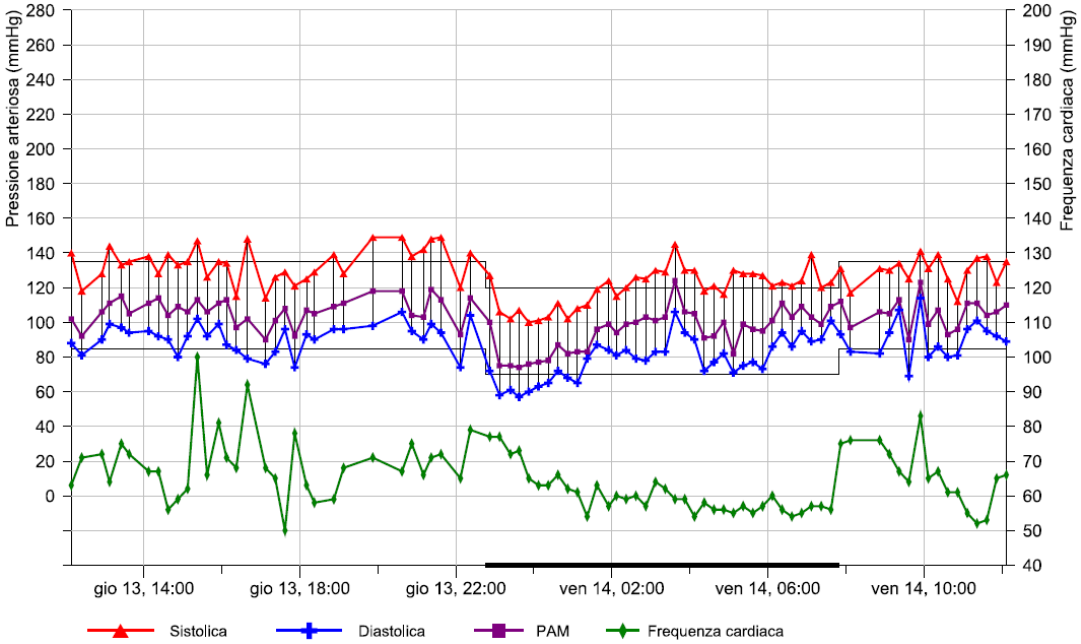
Lisina Acetilsalicilato 75 mg 1 co,

24hr 144/90 mmHg **Dip 3.57%**

DT 146/91 mmHg

NT 140/88 mmHg

ABMP dopo ottimizzazione terapia farmacologica

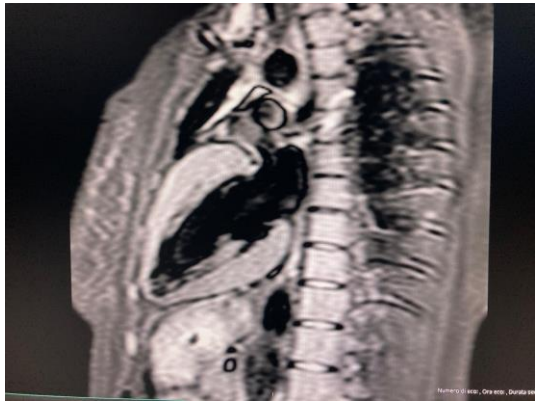
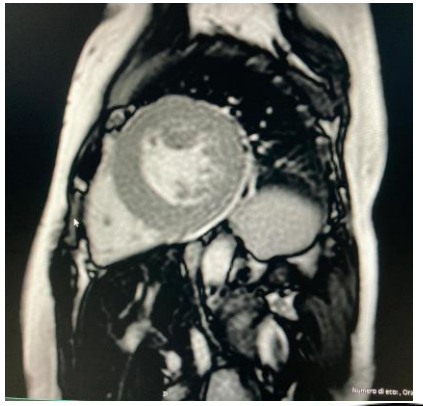
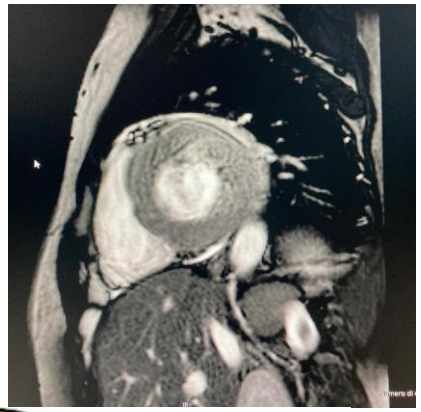
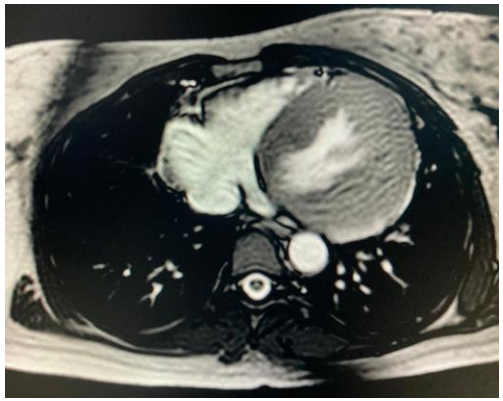


24hr 128/86 mmHg **Dip 9.78%**

DT 133/91 mmHg

NT 120/79 mmHg

RMN cardiaca

- **Ventricolo sinistro** ha pareti … **ervata**. Si associa la presenza di **criteri ancillari miocardici**.
- Ventricolo destro è regolare
- Valori di T1 nativo del tutto l… …lori di ematocrito della paziente (32%), in quanto il … complesso **non si osservano segni RM di edema, danno …**

I reperti descritti **non sono com…** **…ttia di Fabry o Amiloidosi)**, ma nel complesso appaiono di nor… **… miocardica associata a criteri ancillari miocardici** appare più … **…rofico**, mentre meno probabile che il quadro sia correlabile ad …

Diagnosi alla dimissione:

- ✓ **IPERTENSIONE NEFROVASCOLARE IN MID AORTIC SYNDROME CON STENOSI DELLE ARTERIE RENALI BILATERALI SOTTOPOSTA A PTRA + STENTING ARETRIA RENALE DESTRA.**
- ✓ **CARDIOMIOPATIA IPERTROFICA.**
- ✓ **CORIOIDITE TUBERCOLARE.**

Take home message

- MAS rappresenta una rara causa di ipertensione secondaria nefrovascolare, riscontrata prevalentemente in età infantile, ma anche in età adulta
- L'eziologia può essere su base congenita, idiopatica o infiammatoria (come nelle arteriti dei grossi vasi)
- Il trattamento di questa condizione contempla il trattamento farmacologico dell'ipertensione associato all'approccio endovascolare o chirurgico (come l'innesto di bypass aorto-aortico o autotrapianto renale).
- Allo stato attuale non esistono chiare linee guida in merito al trattamento della MAS giovanile ed in età adulta. Secondo dati di una recente metanalisi in età infantile l'approccio chirurgico sembra essere più efficace nel ridurre l'ipertensione arteriosa, mentre nei soggetti adulti pare più efficace l'approccio endovascolare.


Grazie!