An Unusual Presentation of Hypertension in Pregnancy

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UKCOM Class of 2024

BEST CHILDREN'S HOSPITALS U.S.News CARDIOLOGY & HEART SURGERY 2022-23

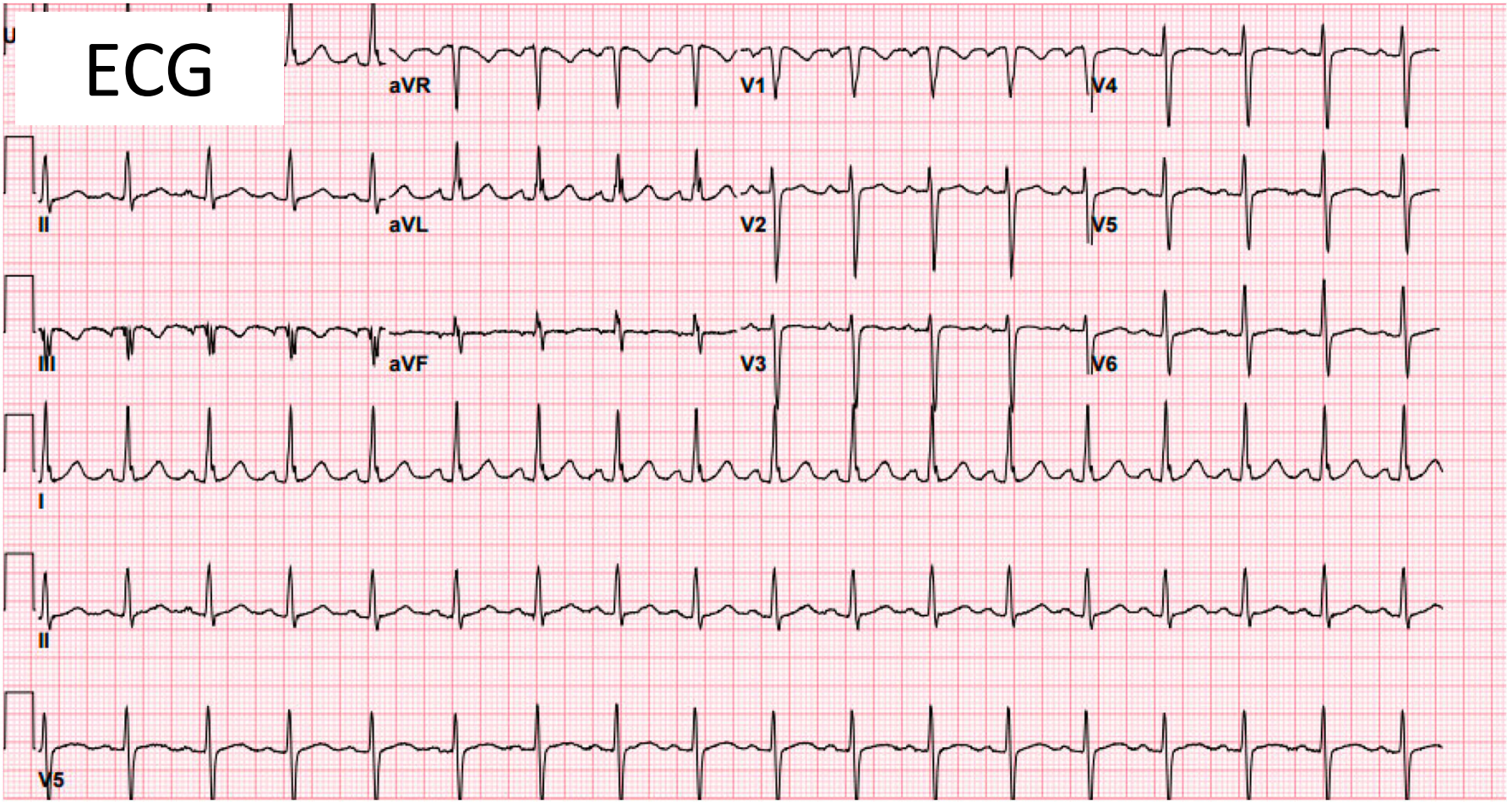
Disclosures

I have no disclosures.

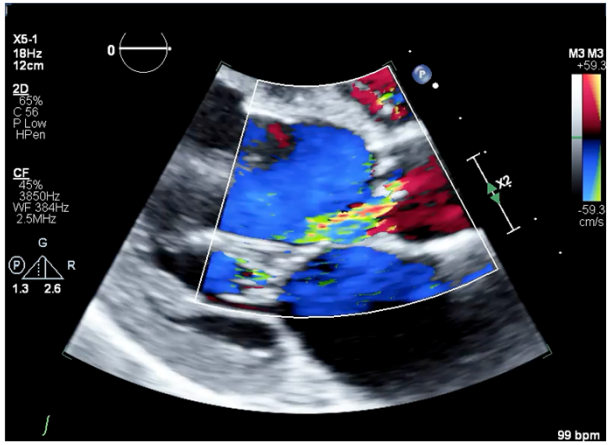
Clinical Presentation

- 16-year-old G1P0 with a history of chronic HTN and gestational diabetes presents at 32 weeks with vaginal bleeding and for blood pressure of 171/96
- Brother on ECMO as an infant for pulmonary hypertension and a cousin's child who passed away from sudden infant death syndrome (SIDS)
- Meds:
  - Labetalol 400 mg TID & Aspirin 81 mg QD
- Blood pressure right arm 138/71 mmHg; left arm 128/67 mmHg; left leg 84/63 mmHg
- Auscultation:
  - 1/6 systolic ejection murmur with ejection click at right upper sternal border
  - 2/4 early diastolic murmur at left lower sternal border

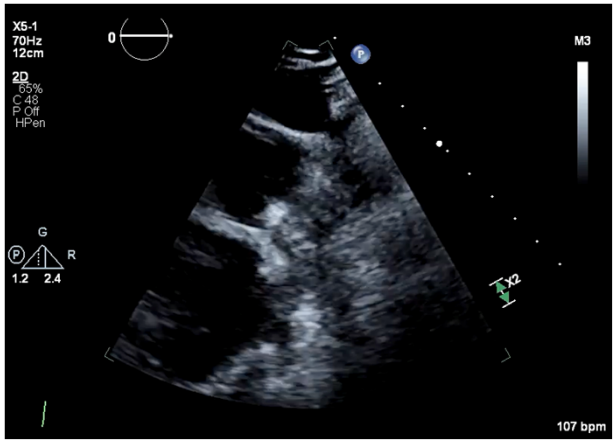
ECG



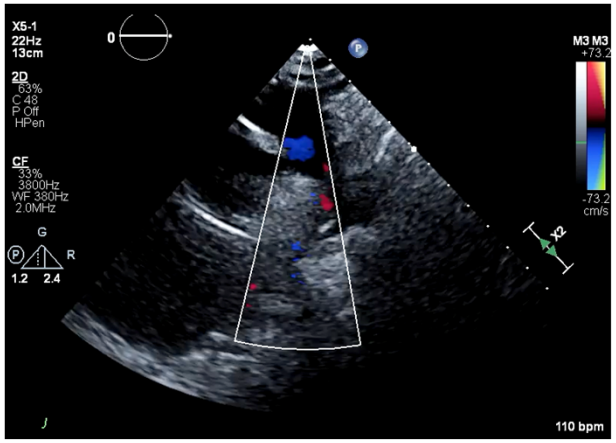
Echocardiography Findings



Parasternal long axis view showing left ventricular hypertrophy & aortic insufficiency



Suprasternal long axis view showing aortic arch with severe luminal narrowing at level of isthmus suggestive of coarctation



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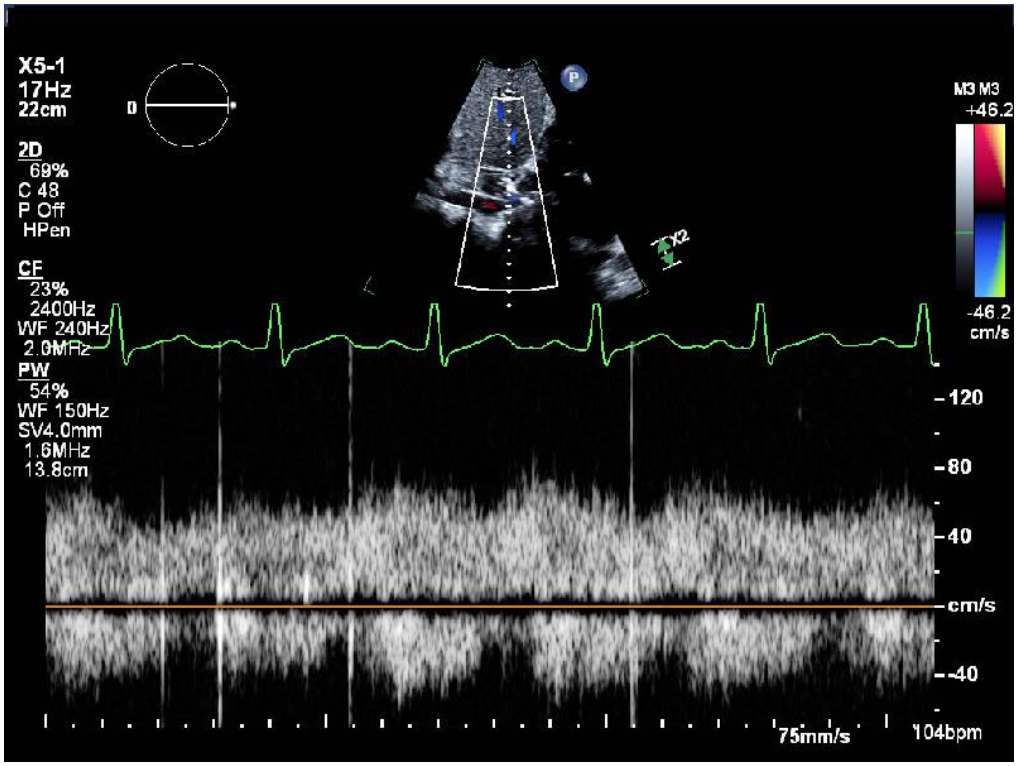
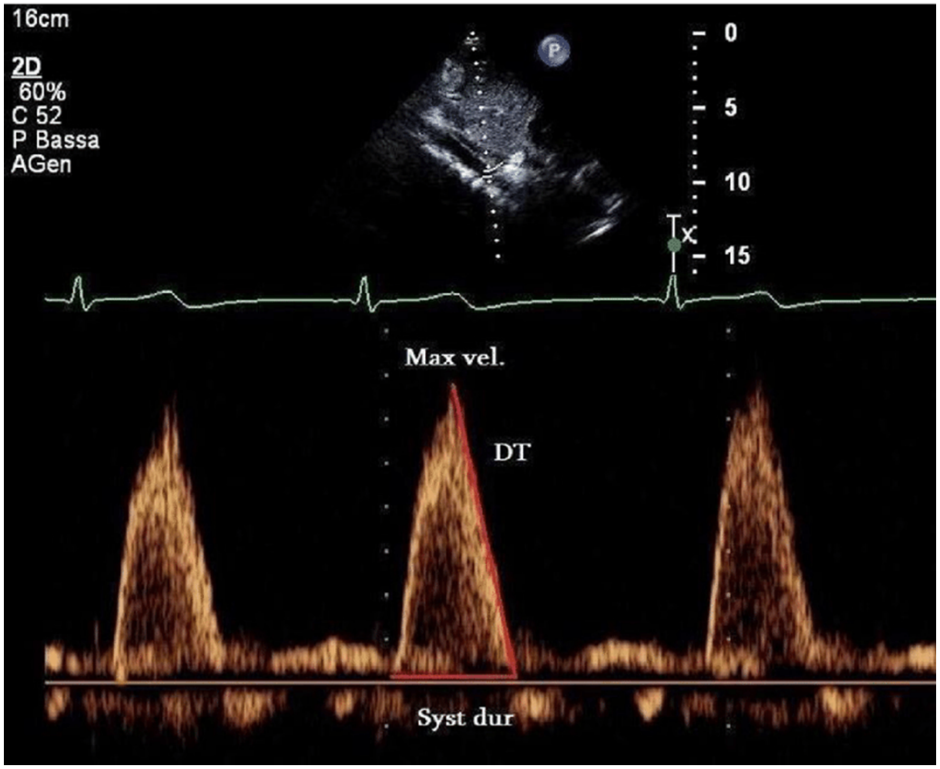


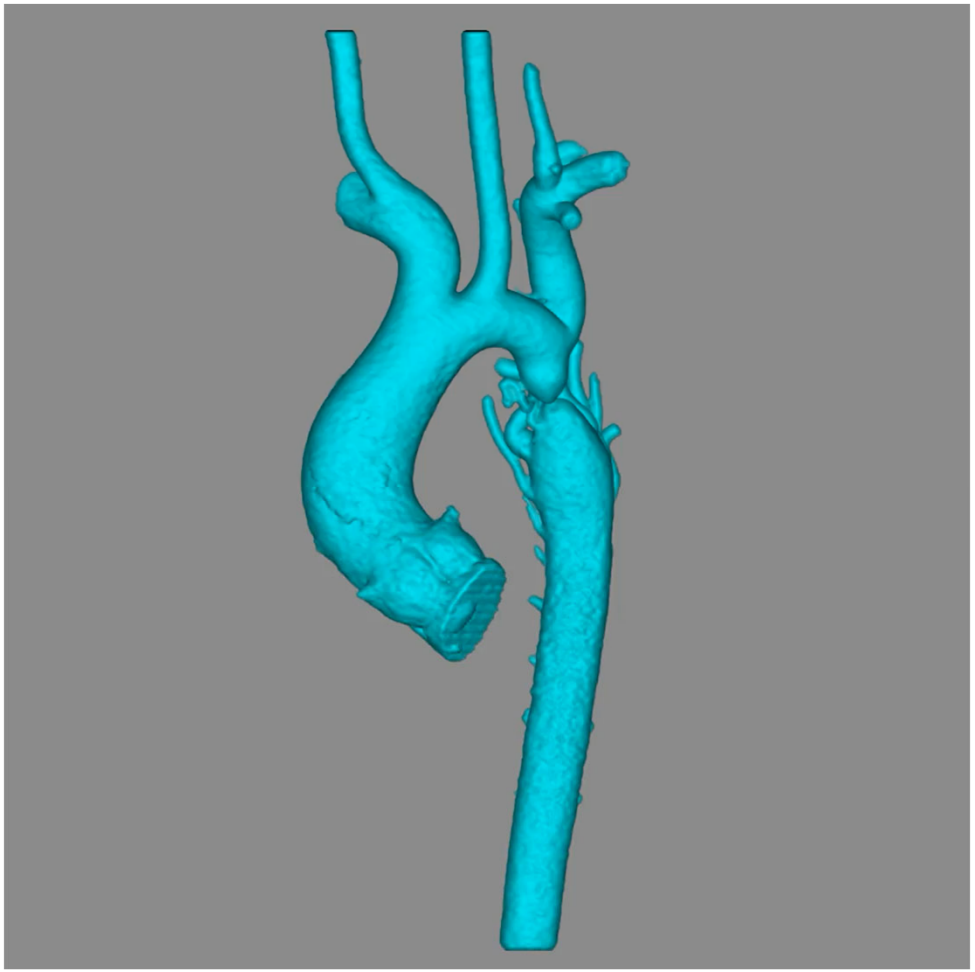
Doppler profile of abdominal aorta showing a blunted appearance with forward flow in diastole



Doppler profile of abdominal aorta in a healthy patient

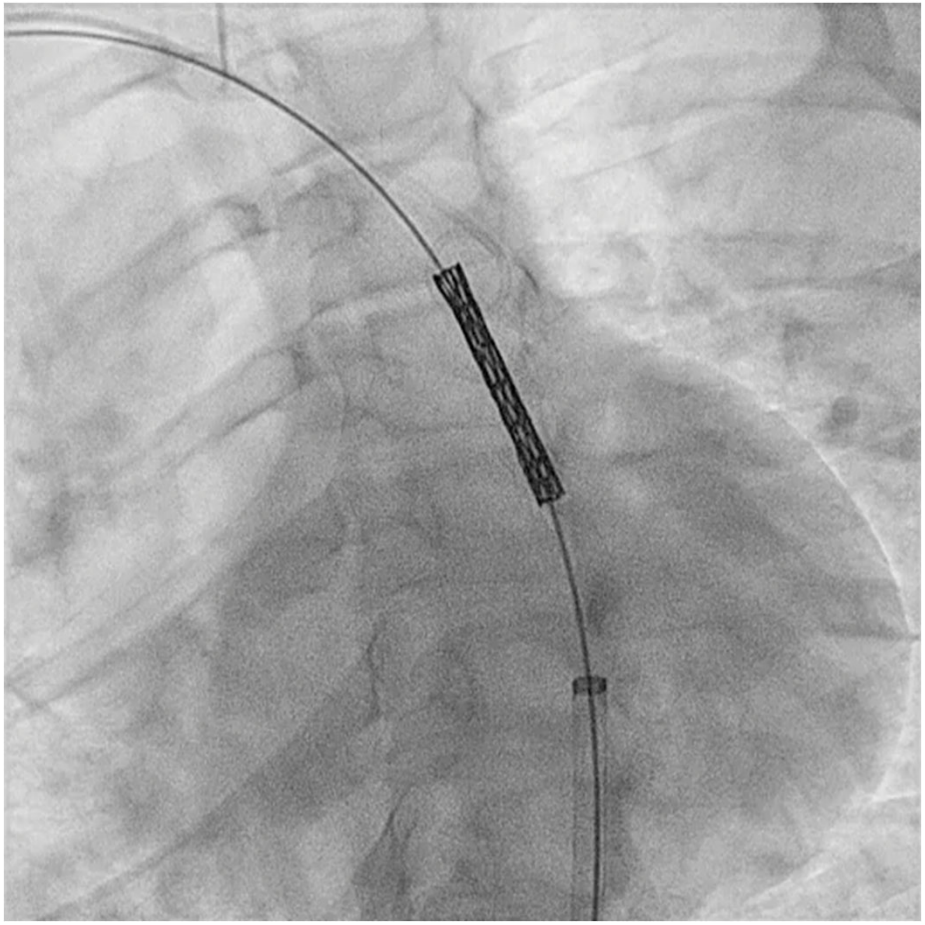
CT Angio 3D Volume Rendered Reconstruction

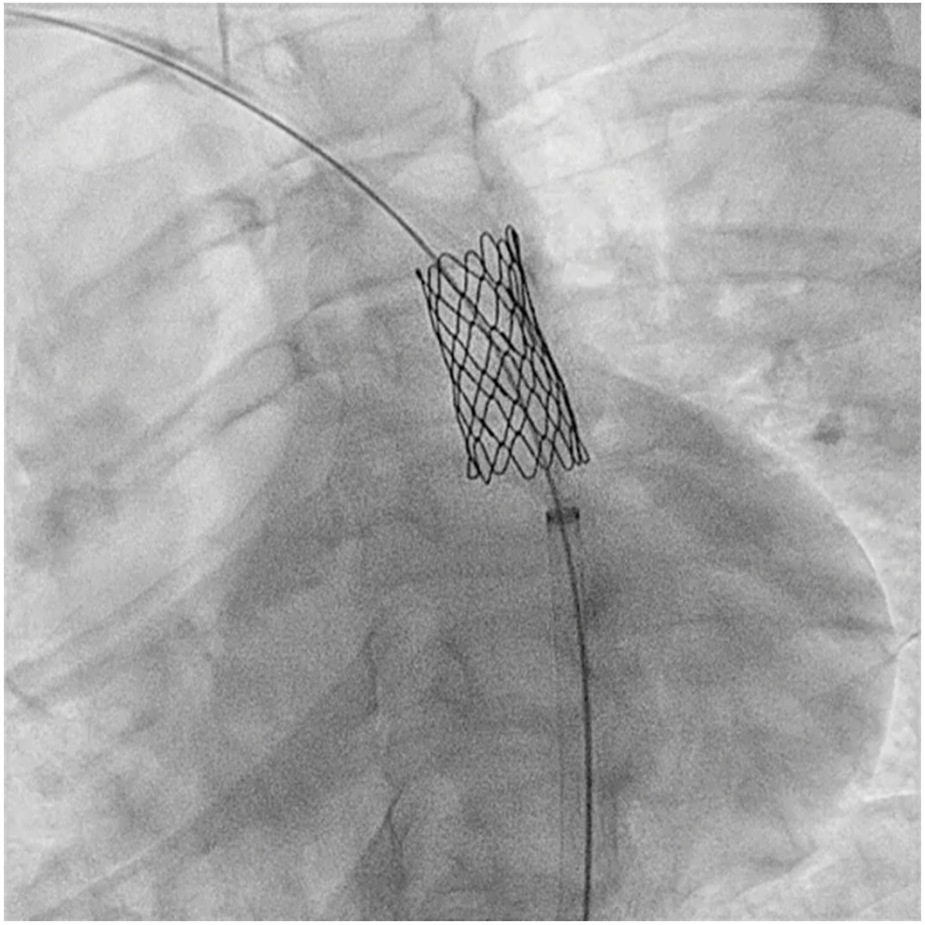
- Near interruption versus severe coarctation
- Dilated right and left subclavian artery
- Extensive collateral supply

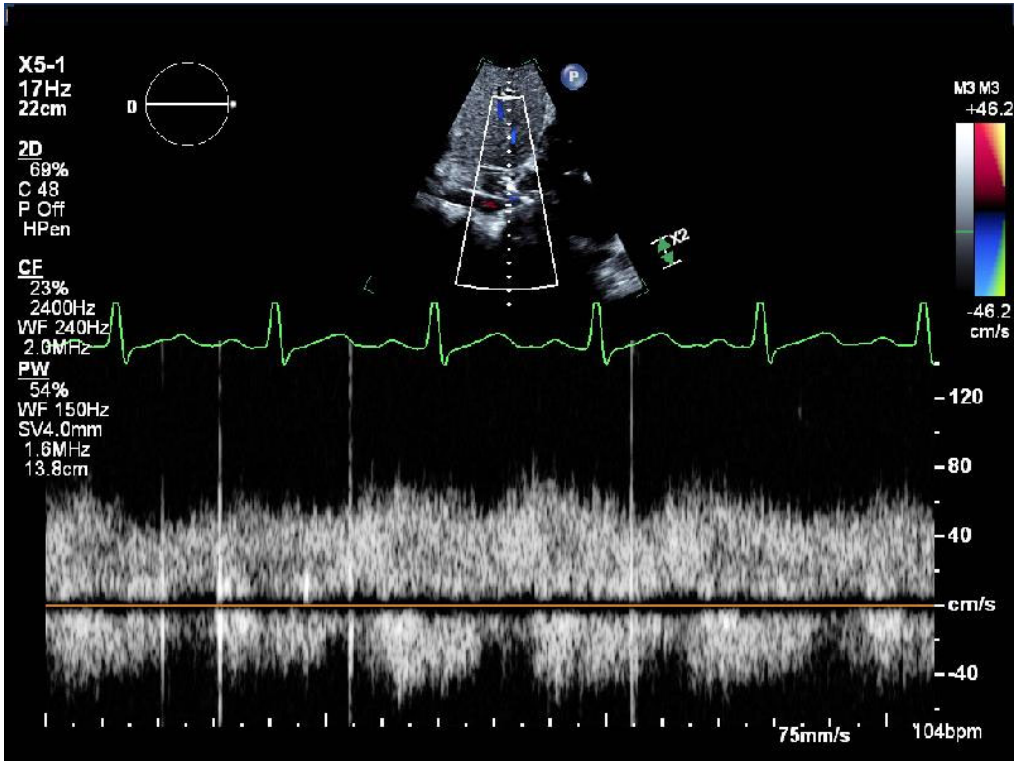


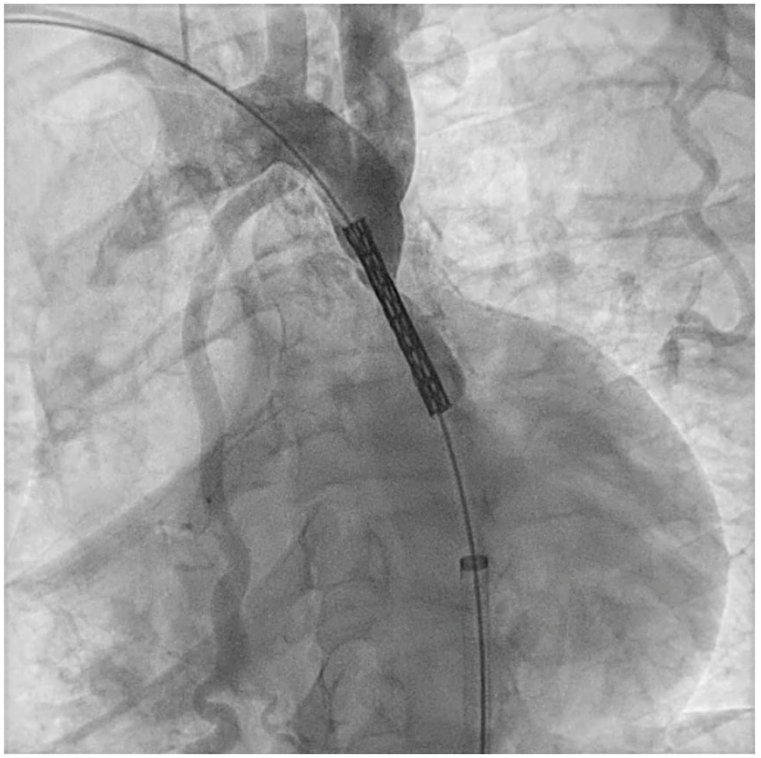
Hospital Course & Delivery

- Hypertension managed with Nifedipine and Labetalol
- Fetal echo performed to screen fetus for any congenital heart disease (CHD)
- Delivery uncomplicated
  - Forceps assisted vaginal delivery with A-line monitoring
  - APGARs 3/5/8
- 6 months after delivery patient underwent coarctation stent placement in the cath lab
  - 14 mm x 3.4cm pre-mounted covered CP stent
  - 58 mmHg → 3 mmHg gradient
- Labetalol 200 mg BID at follow up









Pulse wave doppler profile shows the same flow velocity of continuous flow with lack of prominent systolic flow. This represents pure collateral flow supplying the descending aorta.

Differential Diagnoses for HTN in Pregnancy

- Chronic hypertension
- Gestational hypertension
- Pre-eclampsia
  - Superimposed on chronic hypertension
  - With severe features
- Eclampsia
- Structural causes:
  - Renal artery stenosis, FMD
  - Coarctation of aorta
- Other:
- Multifactorial: Atherosclerotic disease, genetic predisposition, lifestyle
- Primary aldosteronism
- Hyperparathyroidism
- Hyper-/Hypothyroidism
- Pheochromocytoma

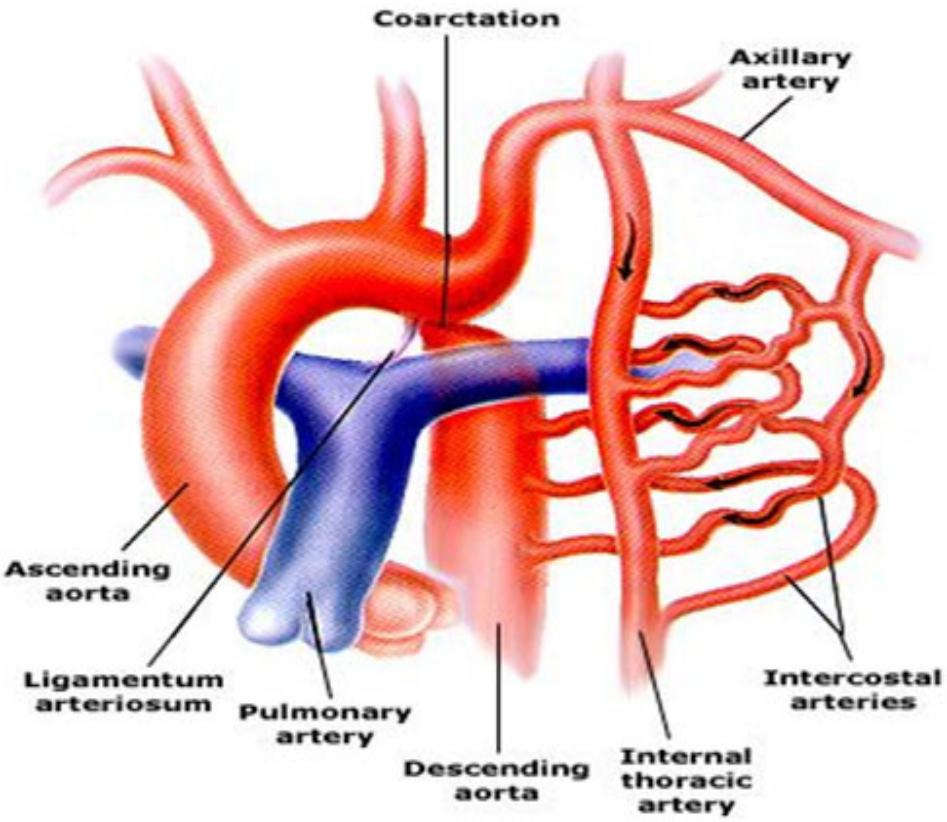
Epidemiology

- 7% patients with CHD
- Coarctation has the highest risk of vascular complications in CHD
  - 3.2% with stroke/transient ischemic attack
  - 5.1% with myocardial infarction

Verheugt et al (2008)
Int J Cardiol 131: 25-32

Clinical Features

- Upper extremity hypertension is most common presenting symptom
  - LV dysfunction
  - Cerebral artery aneurysm (10%)
- Presentation in adulthood is less severe as the obstruction may be bypassed by collateral formation



Collateral Vessels

- Collateral flow is present before vessels can be visualized on cross-sectional imaging

- The pressure gradient measured on doppler echocardiography may not reflect the severity of coarctation due to:
  - Aorta compliance
  - Length of obstruction
  - Extent of collateral circulation

- Cardiac MRI can be used for flow mapping and quantitative estimation of collateral flow

Fratz et al (2013) JCMR 15(1):51

HealthCare
KENTUCKY CHILDREN'S HOSPITAL

		Therapeutic
I	B-NR	6. Surgical repair or catheter-based stenting is recommended for adults with hypertension and significant native or recurrent coarctation of the aorta (S4.2.6-1, S4.2.6-2, S4.2.6-8–S4.2.6-12).
I	C-EO	7. GDMT is recommended for treatment of hypertension in patients with coarctation of the aorta (S4.2.6-13).
IIb	B-NR	8. Balloon angioplasty for adults with native and recurrent coarctation of the aorta may be considered if stent placement is not feasible and surgical intervention is not an option (S4.2.6-14).

Stout et al (2018) J ACC 73:12

Future Vascular Risk Throughout Life

- Systemic hypertension
- Aortic wall stiffness
- Endothelial dysfunction

Tanous et al (2009) Curr Opin Cardiol 24: 509-15

CV Risk

- Abnormal vascular characteristics exist that predispose to increased CV risk even in normotensive patients
  - 46 subjects

Swan et al (2008) Int J Cardiol 139:283-8

CV Risk

- teristics
  oatients
  ased CV

Table 1
Coarctation subjects vs. controls — baseline data (mean (SD)).

	Coarctation	Control	*p*
Numbers	46	20	
Male:female	24M:22F	11M;9F	
Age (years)	31.0 (9.5)	33.2 (6.8)	0.36
Family history of hypertension	14/46 (30.4%)	7/20 (35%)	0.36
Family history of ischaemic disease	19/46 (41%)	7/20 (35%)	0.78
Smoker (current)	3/46 (6.5%)	1/20 (5%)	0.58
Weight (kg)	73.7 (19.3)	75.5 (14.1)	0.7
Height (cm)	168.9 (19.7)	174.6 (12.3)	0.24
Body mass index (kg/m^2)	24.3 (4.6)	24.2 (2.9)	0.92
Brachial systolic BP (mmHg)	121 (11.8)	115.5 (12.2)	0.13
Brachial diastolic BP (mmHg)	69.2 (7.9)	71.4 (8.1)	0.34
Brachial mean BP (mmHg)	85.4 (9.0)	85.0 (8.0)	0.87
Arm-leg gradient (mmHg)	−4.1 (16.9)	−19.9 (15.7)	0.002
Total cholesterol (mmol/l)	4.8 (1.0)	4.6 (0.63)	0.57
HDL (mmol/l)	1.48 (.41)	1.37 (0.41)	0.3
Glucose (mmol/l)	5 (0.48)	5.24 (0.87)	0.17

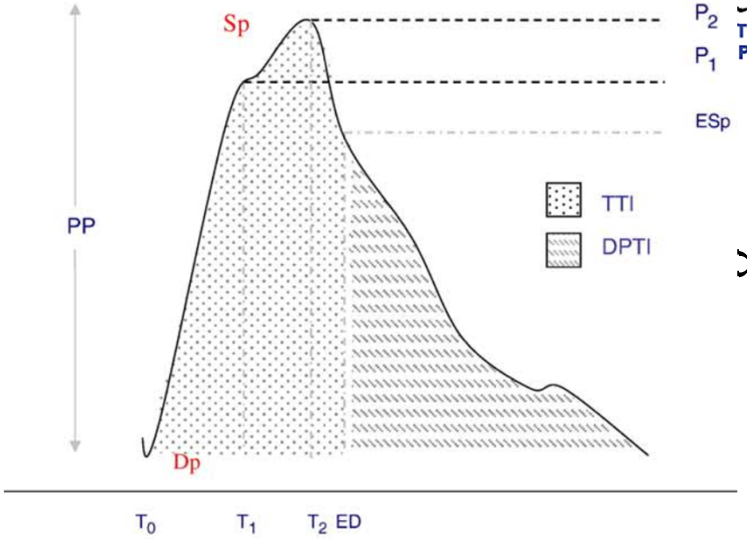


Figure Legend

DPTI	Diastolic pressure-time integral (mmHg.sec/min)
ED	Ejection duration (msec)
ESp	End systolic pressure (mmHg)
P_1	Pressure at time T_1 (mmHg)
P_2	Pressure at time T_2 (mmHg)
PP	Aortic pulse pressure (mmHg)
Sp, Dp	Aortic systolic and diastolic pressure (mmHg)
T_1	Time to 1st aortic peak (msec)
T_2	Time to 2nd aortic peak – inflection point (msec)
TTI	Tension time index (mmHg.sec/min)

Fig. 1. Schematic of aortic arterial pulse.

Swan et al (2008) Int J Cardiol 139:283-8

CV Risk

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Numbers	46
Male:female	24M
Age (years)	31.(
Family history of hypertension	14/4
Family history of ischaemic disease	19/4
Smoker (current)	3/46
Weight (kg)	73.7
Height (cm)	168
Body mass index (kg/m^2)	24.3
Brachial systolic BP (mmHg)	121
Brachial diastolic BP (mmHg)	69.2
Brachial mean BP (mmHg)	85.4
Arm-leg gradient (mmHg)	−4.
Total cholesterol (mmol/l)	4.8
HDL (mmol/l)	1.48
Glucose (mmol/l)	5 (0

Table 2
Coarctation subjects vs. controls — tonometry data (mean (SD)).

	Coarctation	Control	*p* value
Number	46	20	
Heart rate (bpm)	63.8 (10.3)	60.3 (9.0)	0.22
Peripheral pulse pressure (mmHg)	62.5 (11.3)	50.6 (15)	0.0008
Central systolic BP (mmHg)	104.6 (10.1)	101.0 (10.6)	0.24
Central diastolic BP (mmHg)	70.1 (7.9)	72.2 (8.3)	0.36
Central mean BP (mmHg)	84.8 (8.0)	85.4 (8.0)	0.81
Central pulse pressure (mmHg)	34.5 (7.7)	28.7 (4.7)	0.005
Central 1st pressure peak (mmHg)	99.5 (8.8)	98.5 (10.1)	0.56
Central 2nd pressure peak (mmHg)	103.6 (10.6)	101 (10.5)	0.56
Ejection duration (ms)	331 (22.0)	325 (24.3)	0.41
Timing of reflected wave (ms)	149.9 (15.4)	162.6 (17.4)	0.007
Central augmentation index (%)	115.4 (18.8)	111.0 (13.2)	0.35
Tension time index	2050 (335)	1847 (307)	0.03
Diastolic pressure–time integral	3157 (500)	3282 (356)	0.33
Central sub-endocardial viability index (%) DTPI/TTI	159.6 (33.3)	185.7 (31.3)	0.009

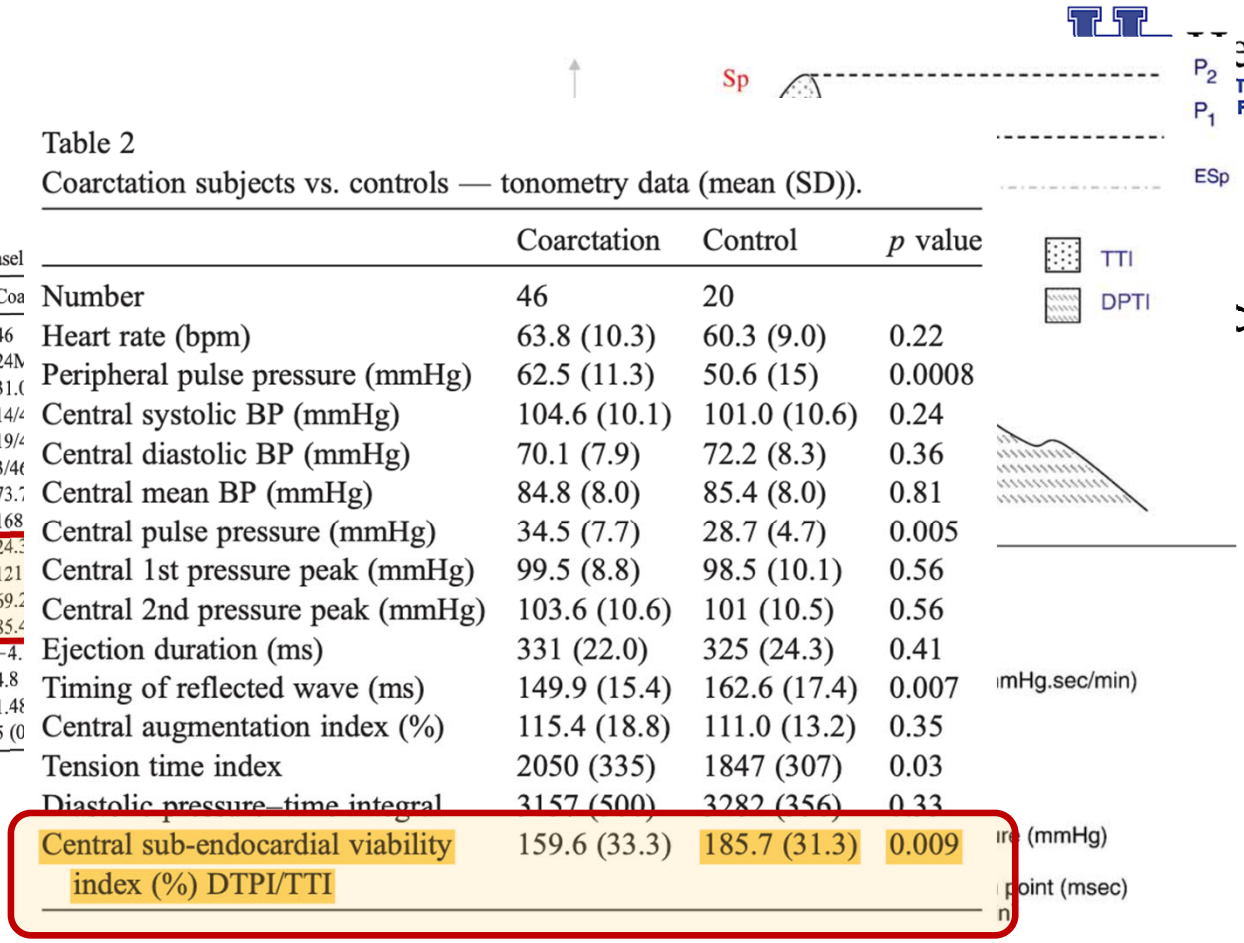

Fig. 1. Schematic of aortic arterial pulse.

Swan et al (2008) Int J Cardiol 139:283-8

Aortic Stiffness

- Aortic stiffness despite BP after stent repair
  - 12 patients
  - Augmentation index

Chen et al (2008) Heart 94:919-924

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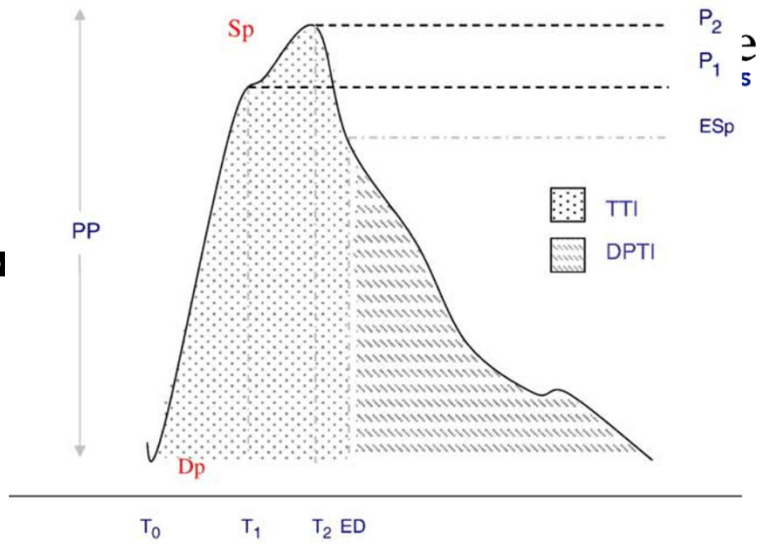

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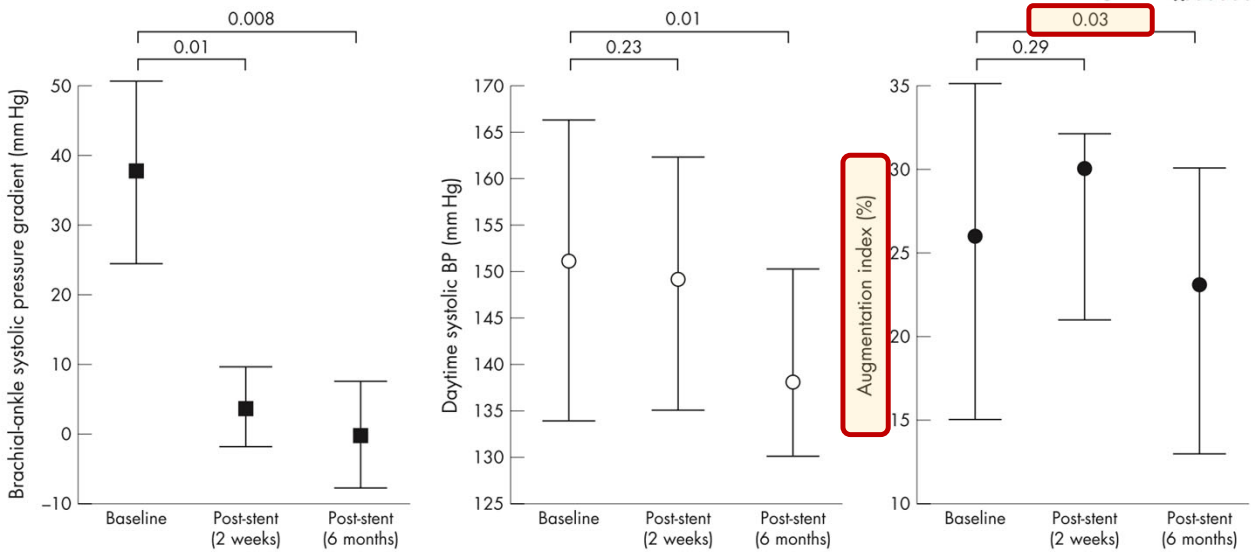

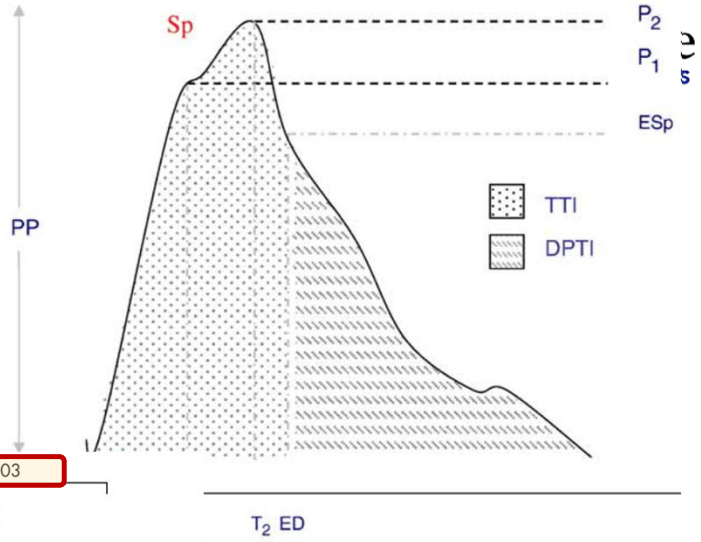

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me index (mmHg.sec/min)

chematic of aortic arterial pulse.

Figure 2 Effect of stenting on ambulatory blood pressure (BP) and central aortic haemodynamics.

n et al (2008) Heart 94:919-924

Endothelial Dysfunction

- Ramipril 5 mg/day improved forearm flow & decreased expression of several endothelial markers despite changes in BP
  - RCT
  - 20 patients
  - RT arm plethysmography/ELISA

Brili et al (2008) J am Coll Cardiol 51: 742-9

Endothelial

- Ramipril 5 mg/d… …d expression of several endotheli…
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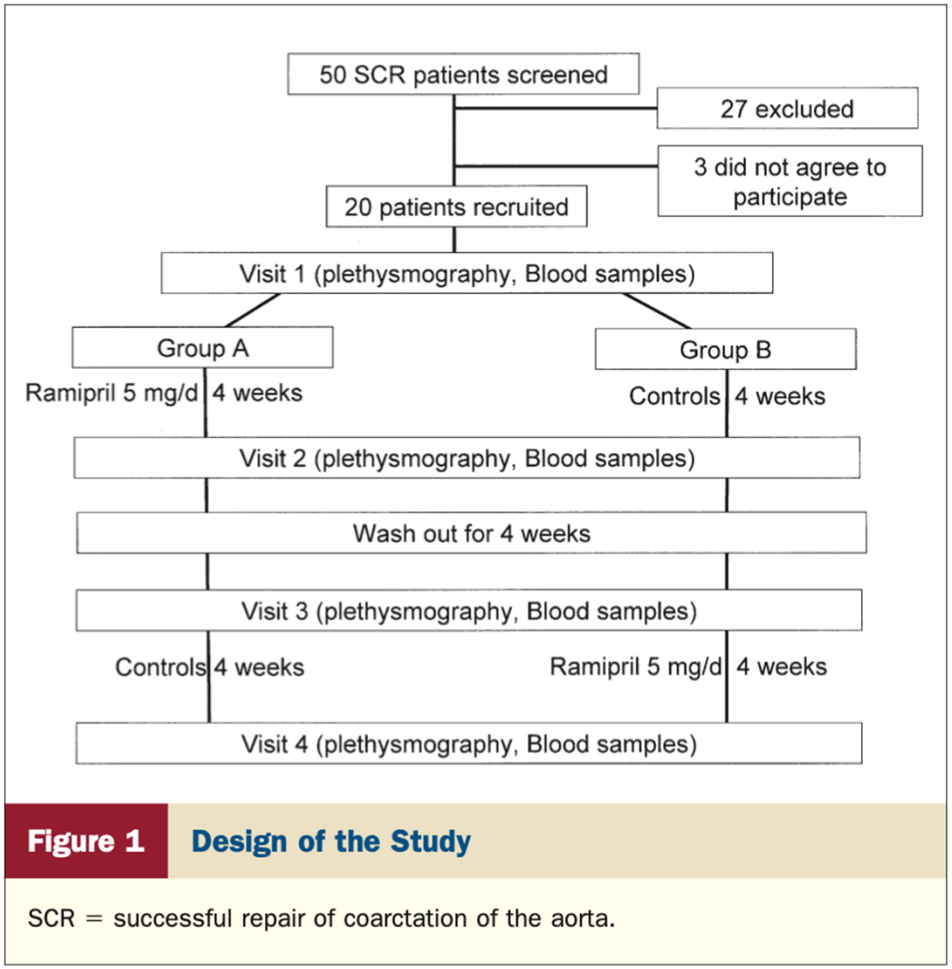

Figure 1 **Design of the Study**

SCR = successful repair of coarctation of the aorta.

Brili et al (2008) J am Coll Cardiol 51: 742-9

Endothelial

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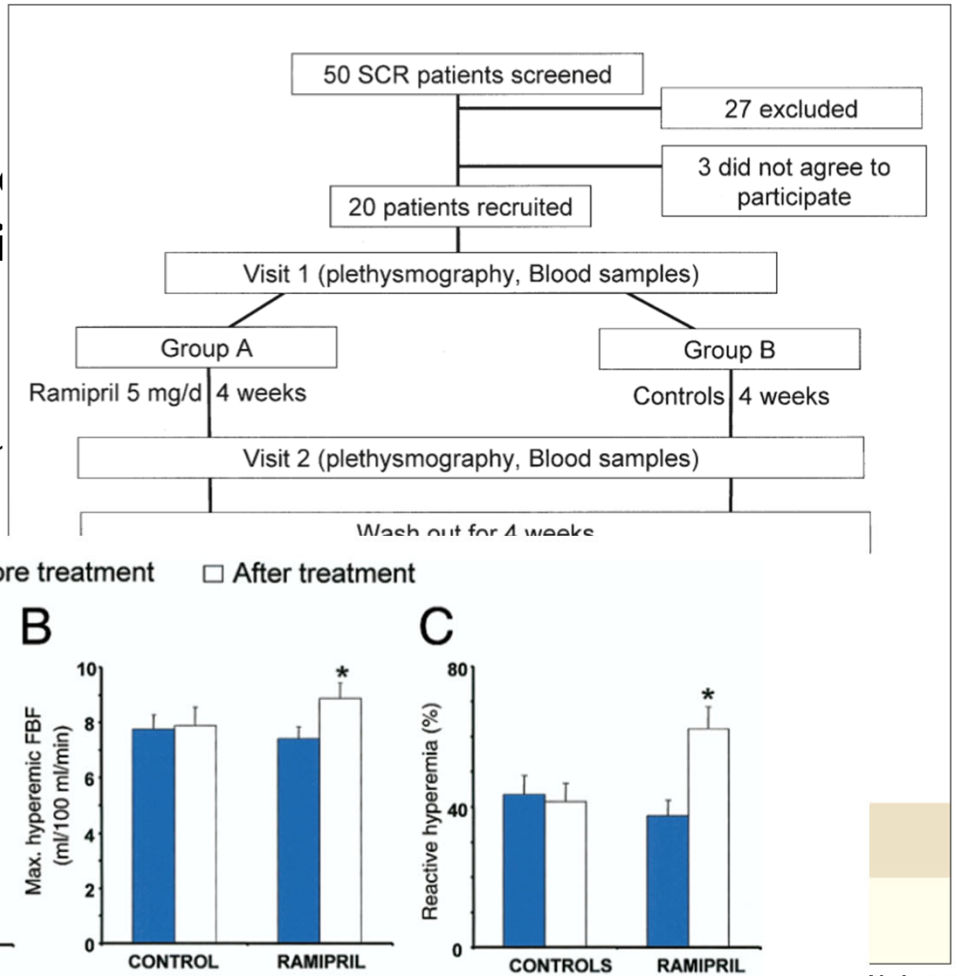

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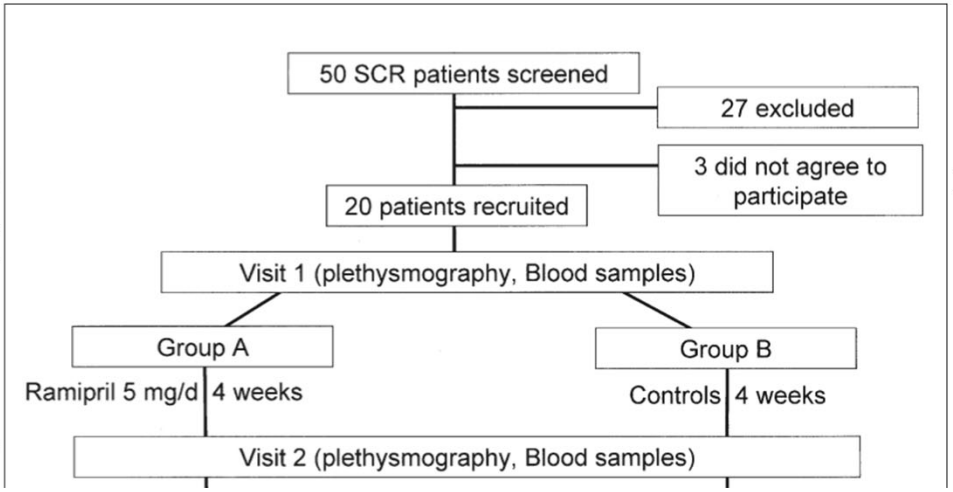

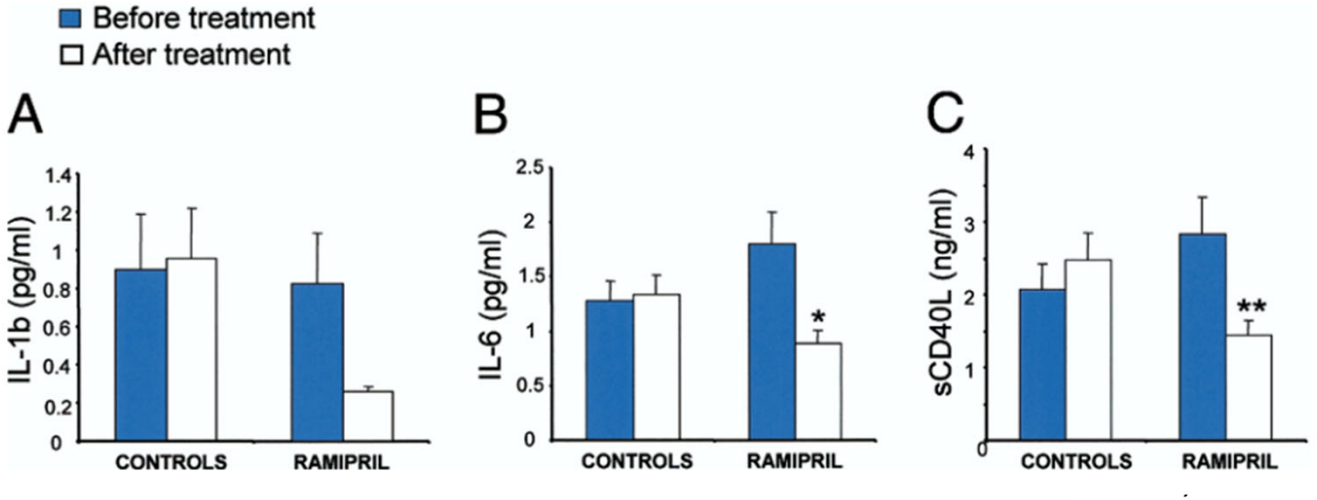

Cardiol 51: 742-9

Conclusion

Coarctation must be considered in the differential in a young patient with severe uncontrolled hypertension

Presentation maybe delayed in adult coarctation due to development of extensive collateral circulation

Majority of adult coarctation can be treated successfully in the cath lab however these patients are at continued risk for long term vascular disease

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Special Thanks

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Preeti Ramachandran, MD
Director of Advanced Pediatric Cardiac Imaging
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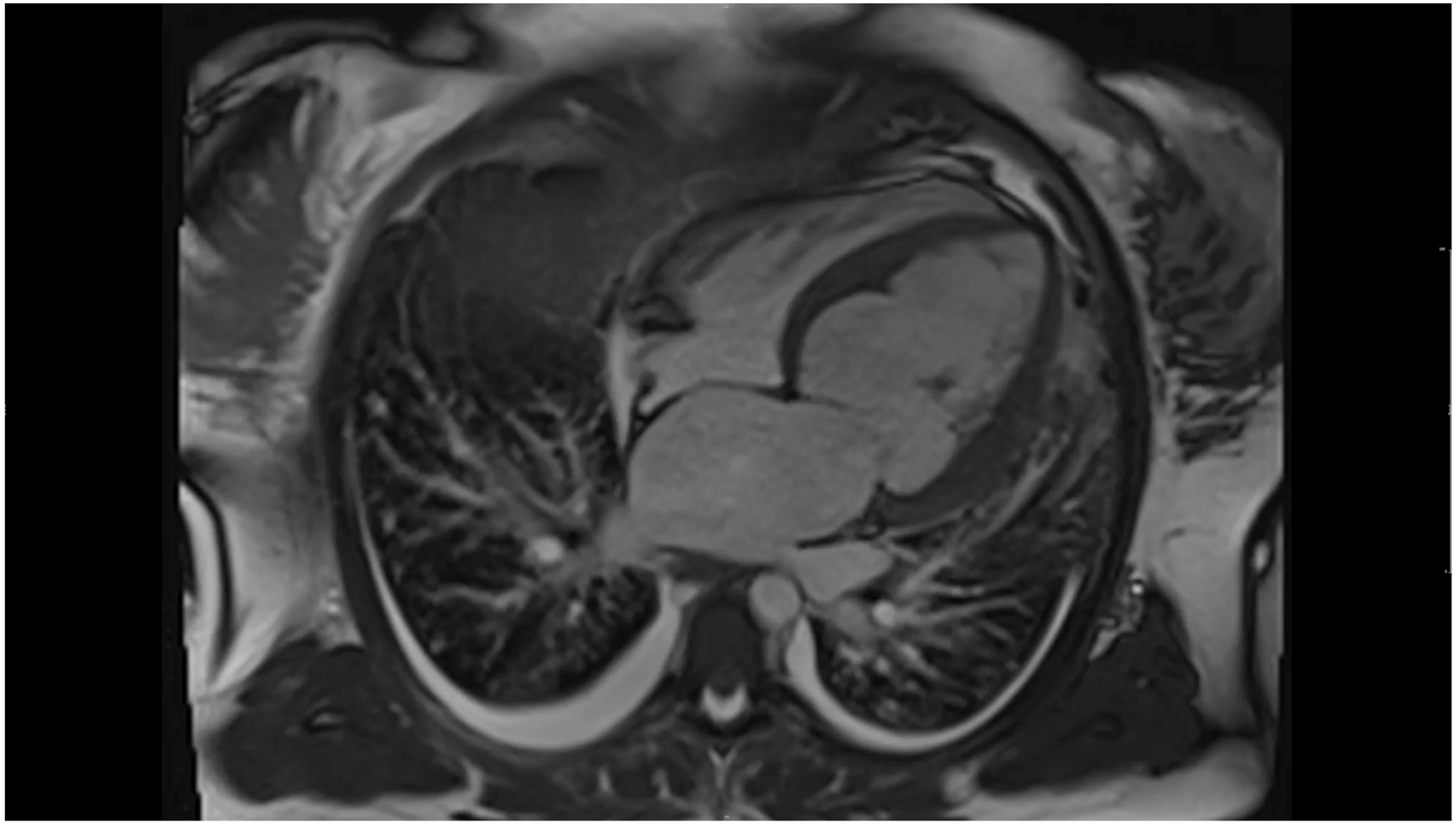


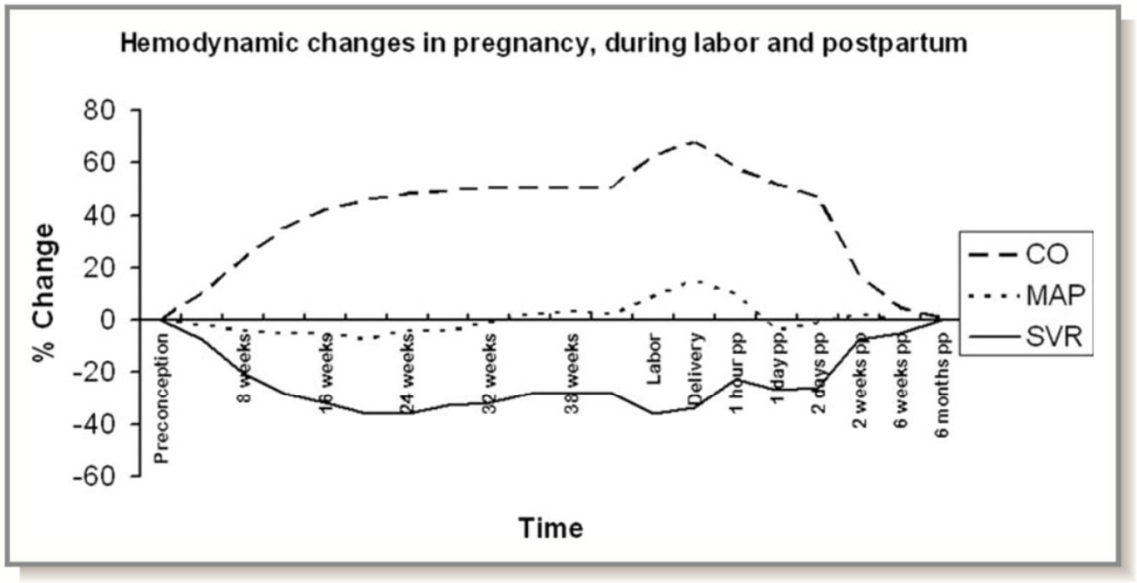


Figure 1. Hemodynamic changes in pregnancy, labor and postpartum. Time on the *x*-axis changes scale. Adapted from Cornetter and Ross-Hesselink,[9] with permission from Springer. CO indicates cardiac output; MAP, mean arterial pressure; PP, postpartum; SVR, systemic vascular resistance.

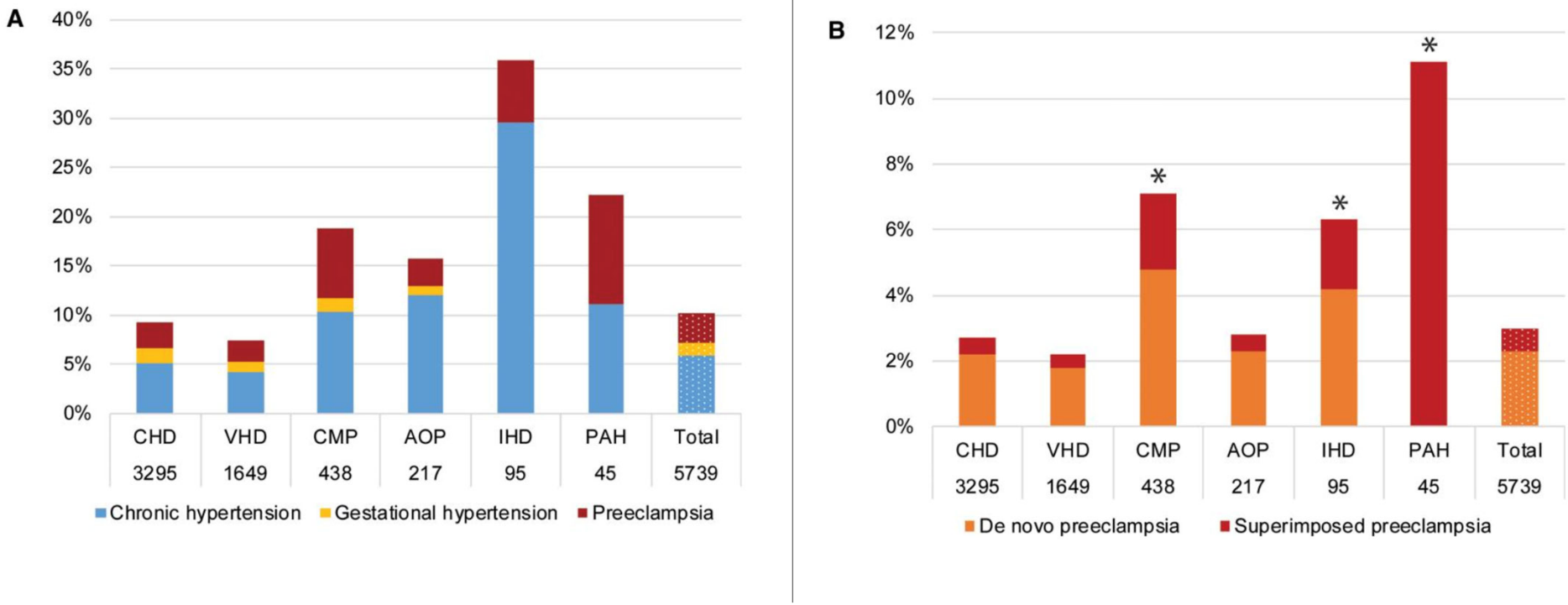


Figure 2 Hypertensive disorders of pregnancy per diagnostic group. * denotes the diagnostics groups with significantly increased risk of pre-eclampsia, with CHD as reference. AOP, aortic pathology; CHD, congenital heart disease; CMP, cardiomyopathy; IHD, ischaemic heart disease; PAH, pulmonary arterial hypertension; VHD, valvular heart disease.

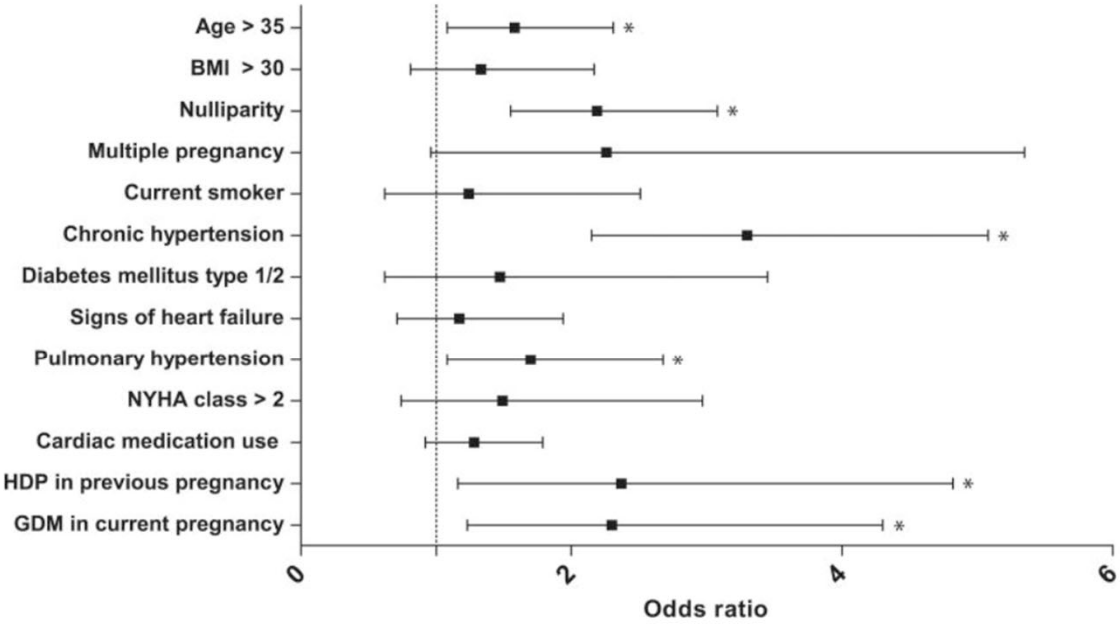
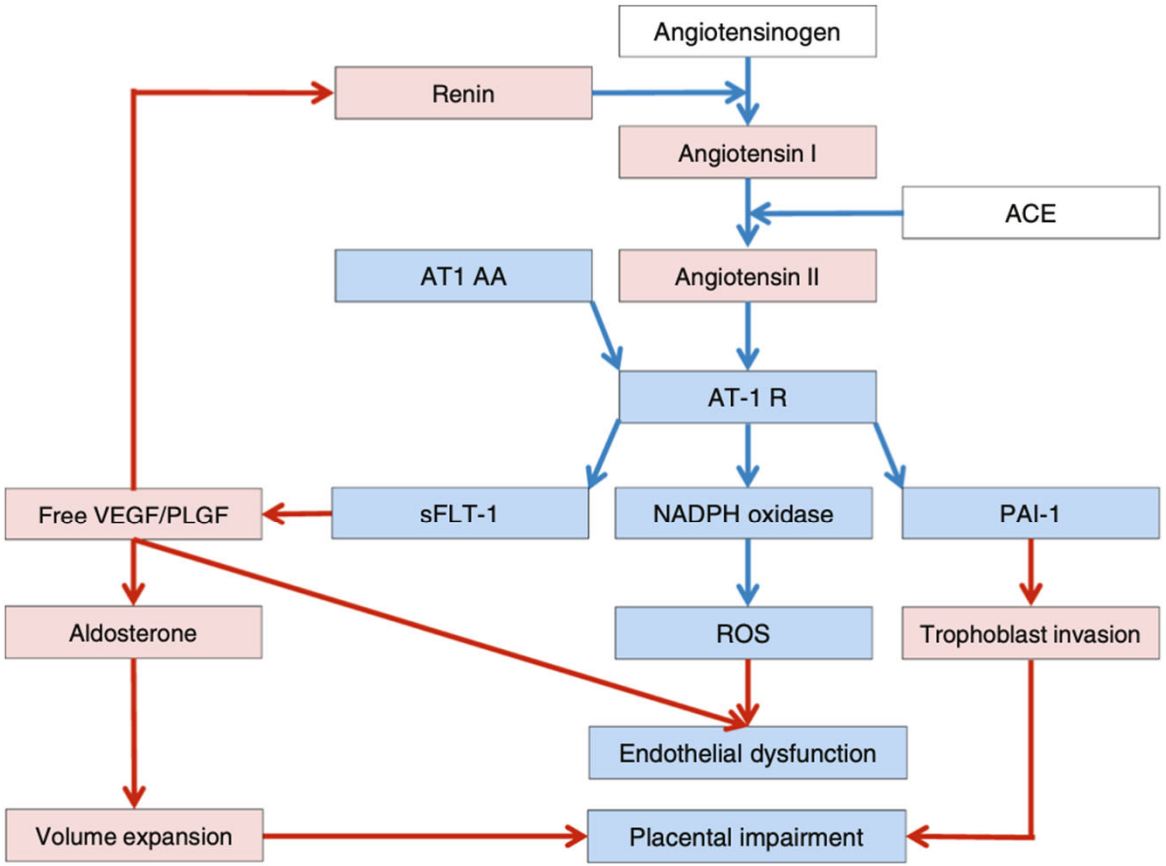


Figure 3 Multivariable regression analysis of predictors of pre-eclampsia in women with structural heart disease. *$P < 0.05$. BMI, body mass index; GDM, gestational diabetes mellitus; HDP, hypertensive disorders of pregnancy; NYHA, New York Heart Association.

FIGURE 1

Interaction between renin-angiotensin-aldosterone system and angiogenic factors in preeclampsia.



Renin cleaves angiotensinogen to produce Ang I, which is further converted to Ang II by ACE. In pregnancies complicated by PE, levels of renin, Ang I and II are reduced. Despite lower levels, women with PE demonstrate increased sensitivity to the vasoconstricting effects of Ang II, partly due to increased peripheral expression of its AT-1 R. Autoantibodies that stimulate the AT-1 receptor (AT 1-AA) have also been reported in women with PE. AT-1 AA activation of AT-1 R up-regulates the production of sFLT-1, PAI-1 and NADPH oxidase. sFLT-1 inhibits VEGF, which further suppresses renin and leads to a reduction in VEGF-mediated production of aldosterone. NADPH oxidase enhances the production of ROS and PAI-1 decreases trophoblastic invasion causing endothelial dysfunction and placental impairment, respectively. In comparison to normal pregnancy, white squares indicate no differences, blue squares indicate increased levels and pink indicate suppressed levels in pregnancies complicated by PE. Adapted from Verdonk et al.[34]

ACE, angiotensin converting enzyme; *Ang*, angiotensin; *AT-1 R*, AT-1 receptor; *PAI-1*, plasminogen activator inhibitor 1; *PE*, preeclampsia; *ROS*, reactive oxygen species; *VEGF*, vascular endothelial growth factor.

Kametas. Screening and diagnosis of superimposed preeclampsia. Am J Obstet Gynecol 2022.