Καρδιακή ανεπάρκεια σε ασθενή με χρόνια νεφρική ανεπάρκεια τελικού σταδίου

Βασιλική Μπιστόλα

Καρδιολόγος

Β' Πανεπιστημιακή Καρδιολογική Κλινική

ΠΓΝ Αττικό

National and Kapodistrian UNIVERSITY OF ATHENS

ATTIKON

Conflict of interest

- None related to this presentation.

Mrs M.T., 20 years old

- Referred to the outpatient HF clinic by the Renal Department on 3/2016 due to dyspnea on exertion and fatigue
- Currently under kidney pre-transplant evaluation due to rapidly progressive sclerotic glomerulonephritis

Medical history

1/2014 Acute pulmonary-renal syndrome (lung hemorrhage and glomerulonephritis) due to microscopic polyangiitis (kidney biopsy)

- **Treated with Cyclophosphamide (total dose 3.5gr; 1-4/2014), Corticosteroids, Immuno-absorption**
- Normal cardiac function

1/2015 Progressively worsening renal function- Hemodialysis commenced via AV fistula

3/2016 Evaluation for kidney transplantation

CV Risk factors: Arterial hypertension (secondary due to chronic renal failure)

Microscopic polyangitis

- Small vessel vasculitis
- Kidney (80%), weight loss (70%), skin lesions (60%), neuropathy (60%), fever (55%), lung hemorrhage (12%)
- Heart involvement has been described less frequently
- In a small case series (85 patients): Heart failure 10-15%, pericarditis (10%), subclinical myocardial infarctions (less common).

Guillevin L, Arthritis Rheum 1999.

- MPA with lung and kidney involvement appears to be associated with P-ANCA, whereas heart involvement more frequent in ANCA-negative patients.

Clinical evaluation

- Dyspnea on exertion and fatigue, NYHA III
- Height 157cm, weight 48kg, BSA 1.46m^2
- BP 160/100mmHg, HR 85bpm, $SatO_2$ 96% (FiO_2 21%)
- No rales/peripheral edema
- S3 gallop, no audible murmurs

Laboratory & Medications

Full blood count

Ht 33%

Hb 10.9 g/dL

PLT 233 K/μl

WBC 8690/μl

- Neutrophils 63%
- Lymphocytes 32%
- Monocytes 4%
- Eosinophils 1%

Immunology

CRP 2.7 mg/dl

p-ANCA negative

c-ANCA negative

Biochemistry

Creatinine 5.33mg/dL

BUN 49mg/dL

AST 13 U/L

ALT 16 U/L

TBIL 0.43 mg/dL

Na 140 mmol/l

K 4.1 mmol/l

Ca 9.5 mg/dl

NT-proBNP 18200 pg/mL

hsTroponin 59 pg/ml

TSH 1.15 μIU/ml

B12 602 pg/ml

Ferritin 389ng/ml

Tsat 40%

Glucose 76 mg/dl

HbA1c 5.6%

Mg 1.9 mg/dl

Total cholesterol 180mg/dl

HDL 56 mg/dl

LDL 97 mg/dl

Triglycerides 135 mg/dl

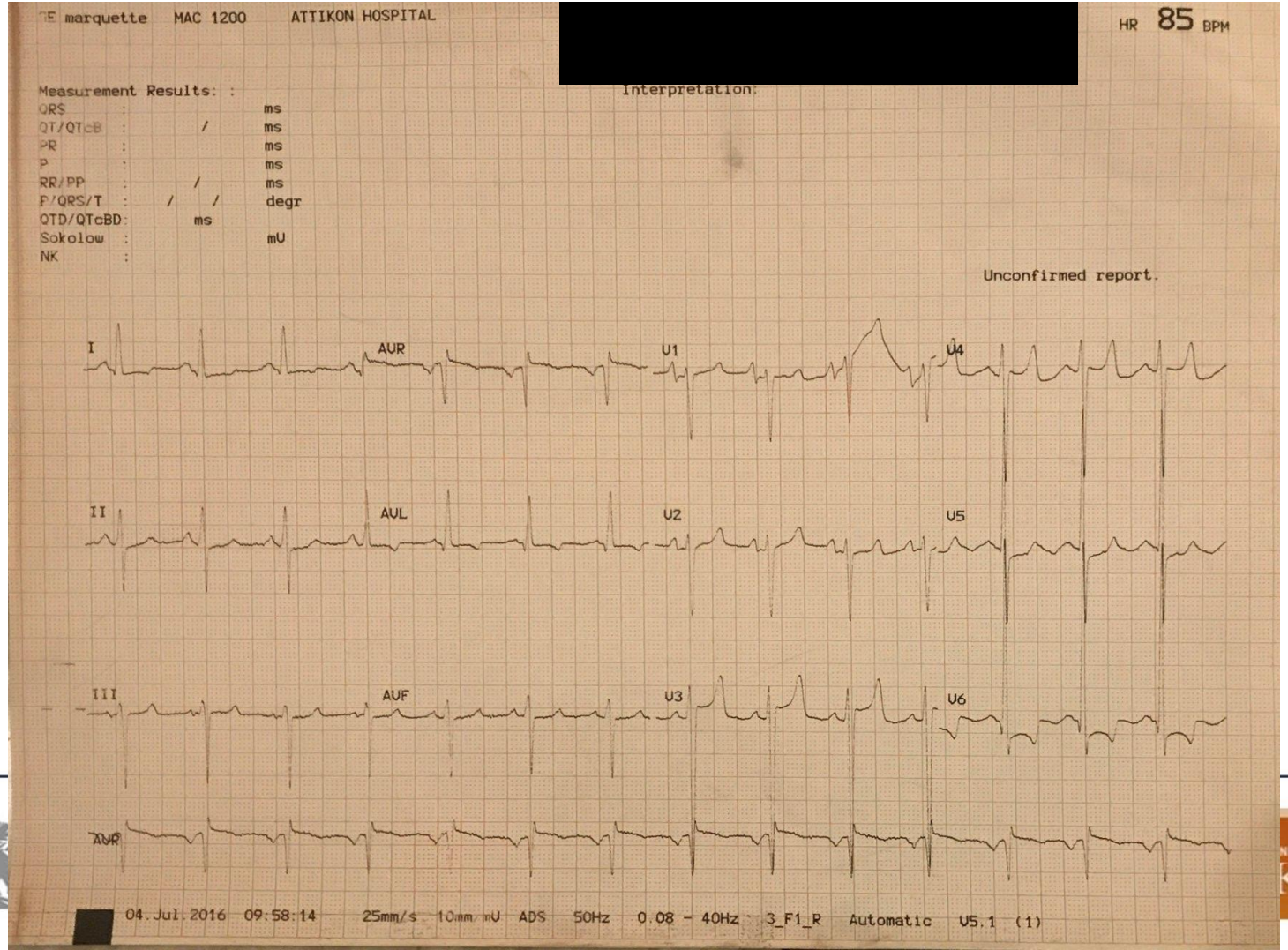
Medications

Carvedilol 12.5mg BID

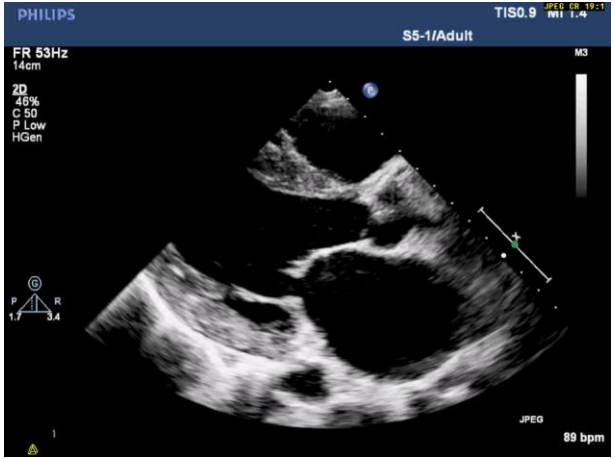
Amlodipine 10mg OD

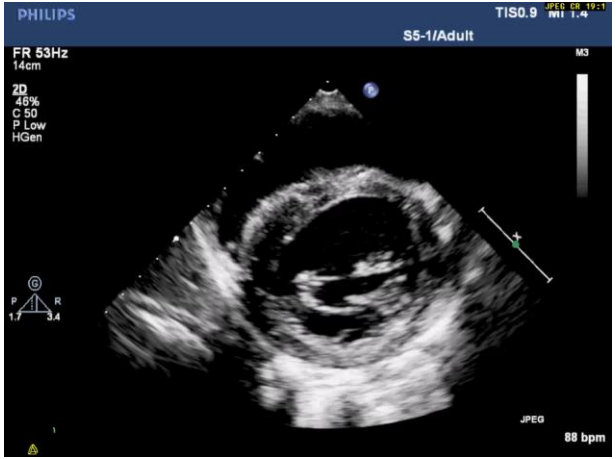
Methylprednisolone 6mg OD

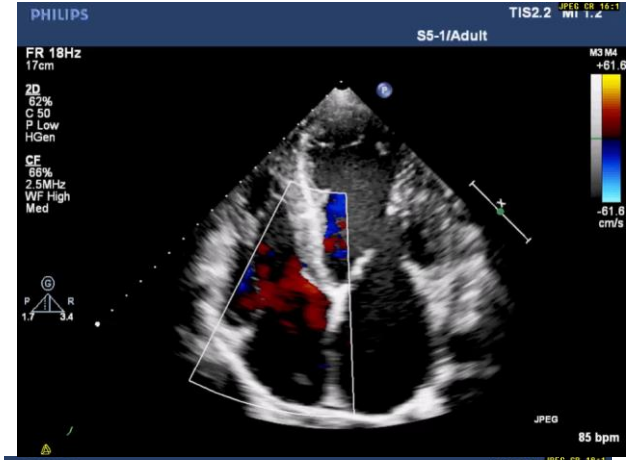
Erythropoeitin 30mcg per 2 weeks


ATTIKON HOSPITAL
HR 85 BPM
Measurement Results: :
QRS :
QT/QTcB :
PR :
P :
RR/PP :
P/QRS/T :
QTD/QTcBD:
Sokolow :
NK :
Interpretation:
Unconfirmed report.
I
AUR
U1
U4
II
AUL
U2
U5
III
AUF
U3
U6
AVR
04.Jul.2016 09:58:14 25mm/s 10mm/mV ADS 50Hz 0.08 - 40Hz 3_F1_R Automatic V5.1 (1)

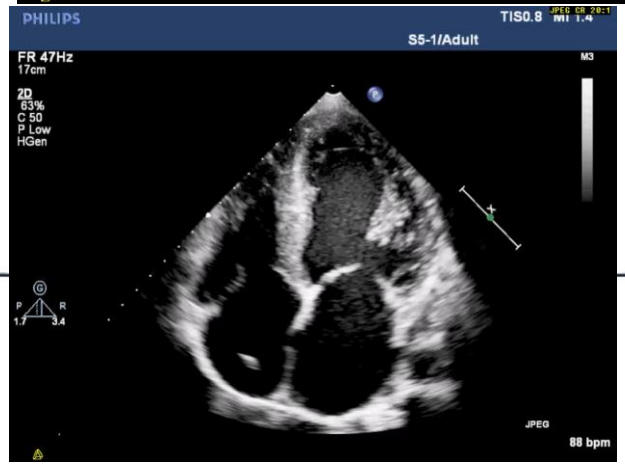
Echocardiogram

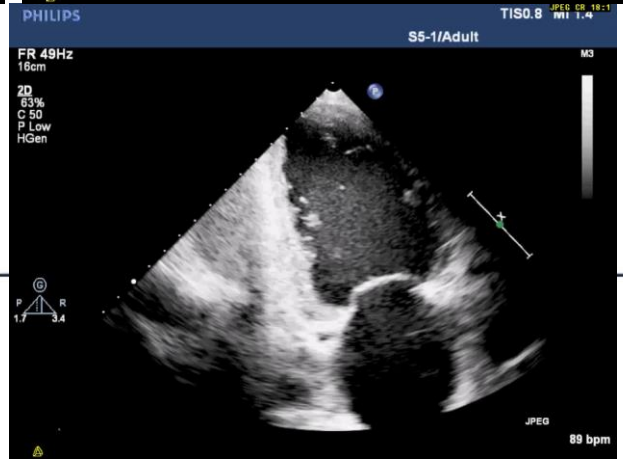






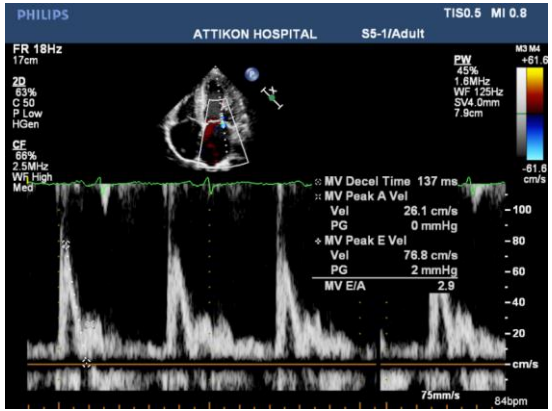
LV hypertrophied, dilated with global severe hypokinesia
LVEDD 54/LVESD 46mm, LVEF 30%
IVS 13/PW 13 mm
RV mildly dilated

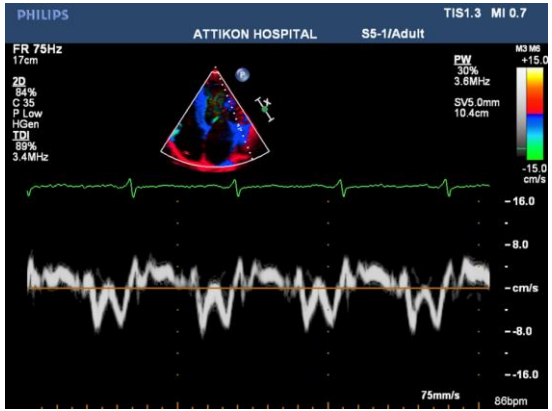


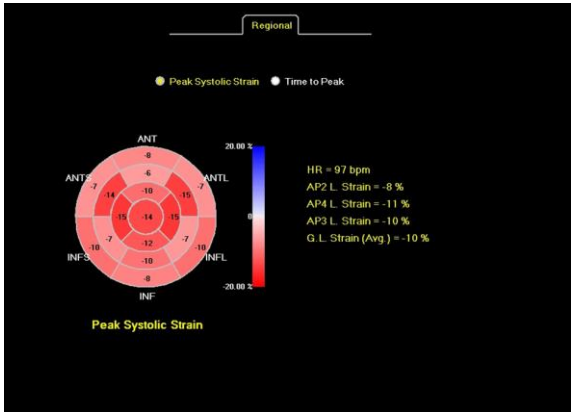


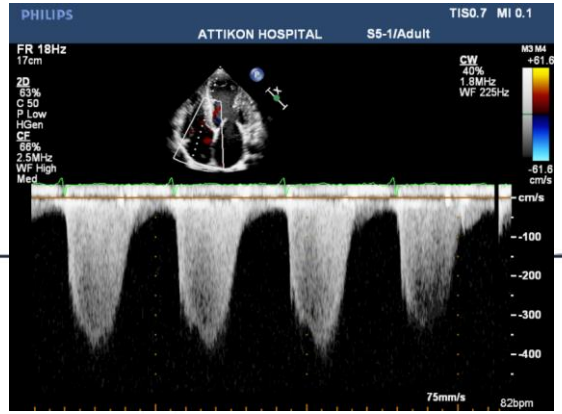
National and Kapodistrian
UNIVERSITY OF ATHENS

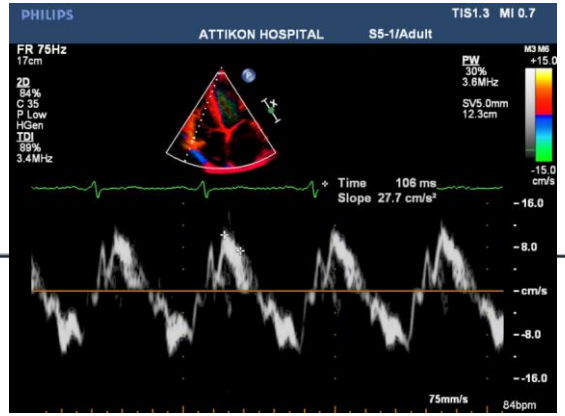
Echocardiogram











- LV: Grade III diastolic dysfunction
- TDI RV: mildly reduced systolic function
- Moderate TR, PASP 70mmHg

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ATTIKON

Ερώτηση 1

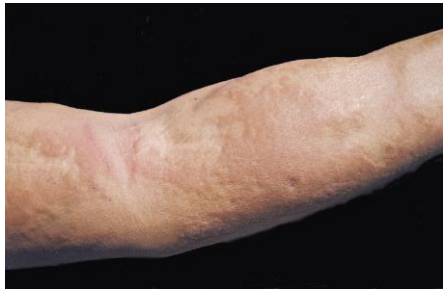
Ερώτηση 1: Ποια από τις παρακάτω διαγνωστικές εξετάσεις ΔΕΝ θα πραγματοποιούσατε στην ασθενή;

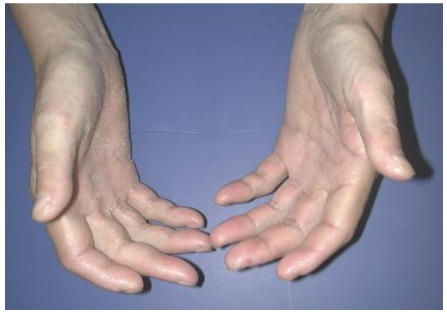
1. Στεφανιογραφία
2. Μαγνητική καρδιάς
3. Ενδομυοκαρδιακή βιοψία
4. Δεξιός καθετηριασμός

Ερώτηση 1: Ποια από τις παρακάτω διαγνωστικές εξετάσεις ΔΕΝ θα πραγματοποιούσατε στην ασθενή;

1. Στεφανιογραφία
2. **Μαγνητική καρδιάς**
3. Ενδομυοκαρδιακή βιοψία
4. Δεξιός καθετηριασμός

Nephrogenic systemic fibrosis





- NSF is an adverse reaction to non-ionic gadolinium contrast agents, which occurs in patients with impaired renal function.
- It involves skin & subcutaneous tissues (thickening & pruritus), but also other organs (lung, heart, joints).
- Prevalence: **30% in dialysis patients**
- **Mortality: 48% at 2 years**
- **No effective treatment**
- Prevention (ESUR Guidelines v10.0):
  - Contrast agents type I (non-ionic) are contraindicated in CKD4, CKD5, and patients on dialysis and AKI (class I, LOE B)
  - Contrast agents type II, III should be used with CAUTION in CKD4, CKD5, patients on dialysis and AKI (class IIb, LOE C)

Coronary arteriography

No hemodynamically significant coronary lesions

Right heart catheterization

RA	**12** mmHg
RV	**58/10** mmHg
PA	**58/24/35** mmHg
PCW	**24** mmHg
AO	**145/95** mmHg
CO	**5** L/min
CI	**3.4** L/min/m2
SVR	**1600** dynes/s*cm^5
SVRI	**2353** dynes*m^2/s*cm^5
PVR	**176** dynes/s*cm^5
PVRI	**259** dynes*m^2/s*cm^5

Endomyocardial biopsy

Histology

Endocardium normal without fibrosis.

Normal interstitial cell content without relevant lymphocytes/histiocytes. Minimal peri-vascular & interstitial fibrosis.

Cardiomyocytes hypertrophied and lengthened, regularly oriented, no areas of acute inflammation/necrosis.

Vascular capillaries without signs of inflammatory infiltration.

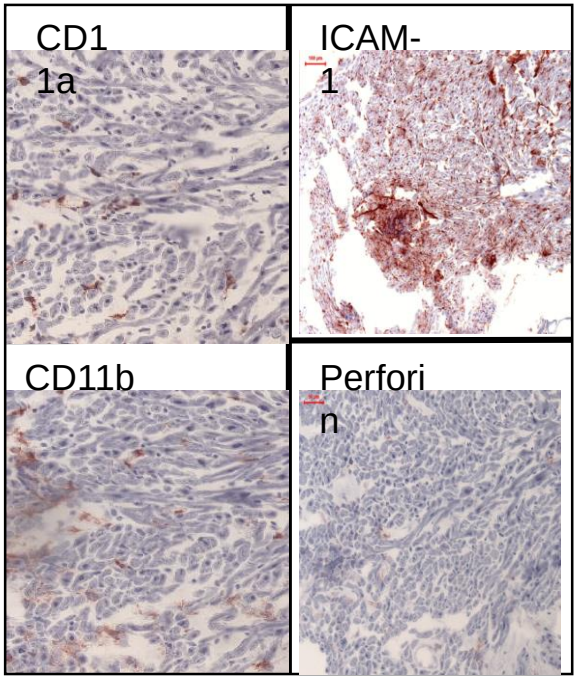
Immunohistology

CD+ lymphocytes (CD11a)/macrophages (CD11b/MAC3) below threshold.

No cytotoxic T lymphocytes (perforin negative). Mildly enhanced ICAM-1 staining.

Molecular analysis

nPCR/QPCR for enterovirus, adenovirus, human herpes virus, erythrovirus, ebstein-barr virus **negative**



National and Kapodistrian
UNIVERSITY OF ATHENS

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ
ATTIKON

Ερώτηση 2

Ερώτηση 2: ποια η διάγνωση και τι θεραπεία προτείνετε;

1. Μυοκαρδίτιδα. Απαιτείται εντατικοποίηση της φαρμακευτικής θεραπείας ΚΑ, χορήγηση ανοσοσφαιρίνης & ΕΦ κορτικοειδών.
2. Υπερφόρτιση όγκου. Απαιτείται εντατικοποίηση των συνεδριών αιμοκάθαρσης, και οποιεσδήποτε θεραπείες για βελτίωση των συνθηκών φόρτισης της αριστερής κοιλίας.
3. Μυοκαρδιοπάθεια συνεπεία προσβολής από την αγγειίτιδα. Απαιτείται εντατικοποίηση ανοσοθεραπείας.
4. Καρδιοτοξικότητα λόγω κυκλοφοσφαμίδης. Απαιτείται εντατικοποίηση της φαρμακευτικής θεραπείας ΚΑ & εκτίμηση για διπλή μεταμόσχευση καρδιάς- νεφρού.

Ερώτηση 2: ποια η διάγνωση και τι θεραπεία προτείνετε;

1. Μυοκαρδίτιδα. Απαιτείται εντατικοποίηση της φαρμακευτικής θεραπείας ΚΑ, χορήγηση ανοσοσφαιρίνης & ΕΦ κορτικοειδών.
2. **Υπερφόρτιση όγκου. Απαιτείται εντατικοποίηση των συνεδριών αιμοκάθαρσης, και οποιεσδήποτε θεραπείες για βελτίωση των συνθηκών φόρτισης της αριστερής κοιλίας.**
3. Μυοκαρδιοπάθεια συνεπεία προσβολής από την αγγειίτιδα. Απαιτείται εντατικοποίηση ανοσοθεραπείας.
4. Καρδιοτοξικότητα λόγω κυκλοφοσφαμίδης. Απαιτείται εντατικοποίηση της φαρμακευτικής θεραπείας ΚΑ & εκτίμηση για διπλή μεταμόσχευση καρδιάς- νεφρού.

Excluded diagnoses

1. Vasculitis-related cardiomyopathy
   - EMB **negative** for inflammatory infiltration/wall destruction of blood vessels.
   - **Negative CRP & ANCA autoantibodies** suggestive of no relapse.
2. Myocarditis
   - EMB histology/immunohistology **negative** for inflammatory cell infiltration.
   - **PCR for viruses negative**
3. Cyclophosphamide cardiotoxicity
   - Cyclophosphamide cardiotoxicity is dose related, toxic dose >100mg/kg body weight
   - **Total dose received per kg was 73mg/kg**

Volume overload HF and the role of arterio-venous fistula

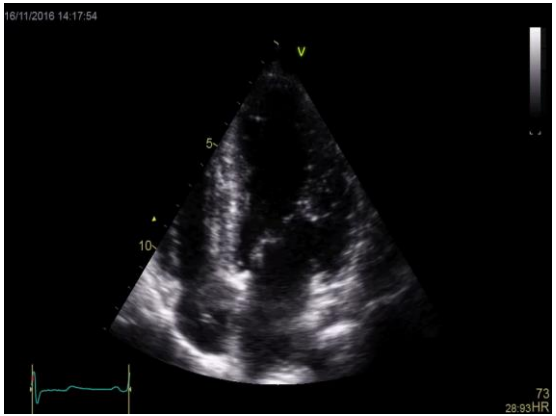
Supportive findings

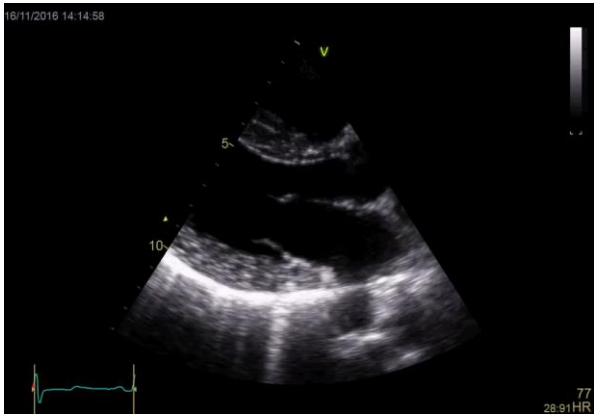
1. **Right heart catheterization:**
   CI 3,4lt/min/m_2
   SVR and PVR in normal range
2. **ECG:** LVH + diastolic strain
3. **High-flow fistula**
   Q_{AVF}=2.4L/min (>2L/min)
   Q_{AVF}/CO=0.48 (>0.3)
   Right upper arm AVF

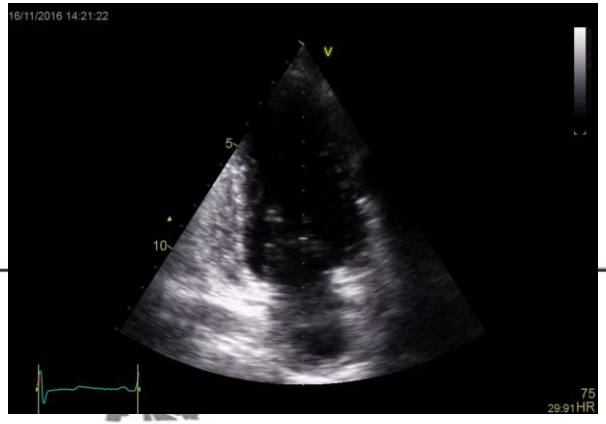
Management

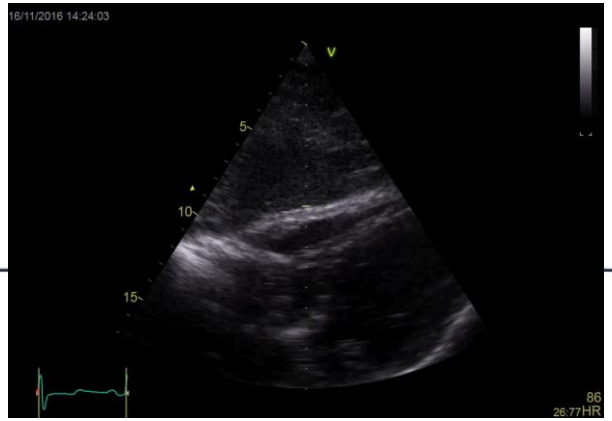
1. Intensify hemodialysis (reduce patient's dry weight)
2. Intensification of HF therapies: commencement of ACEi (Enalapril 2.5mg BID)
3. Arteriovenous fistula closure

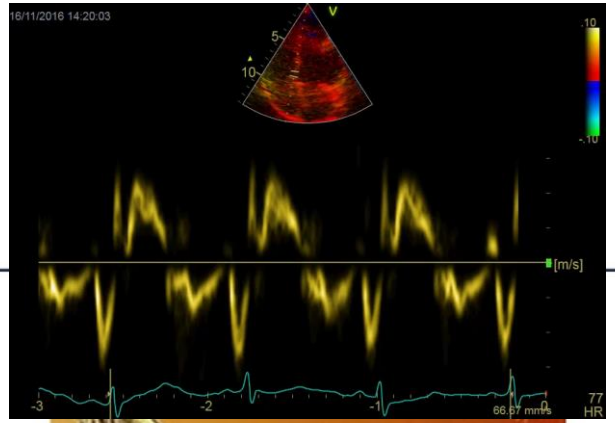
Follow up echocardiogram 2 months after therapy



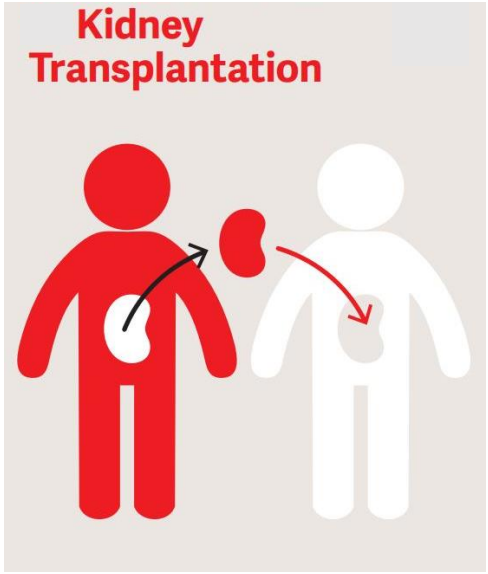


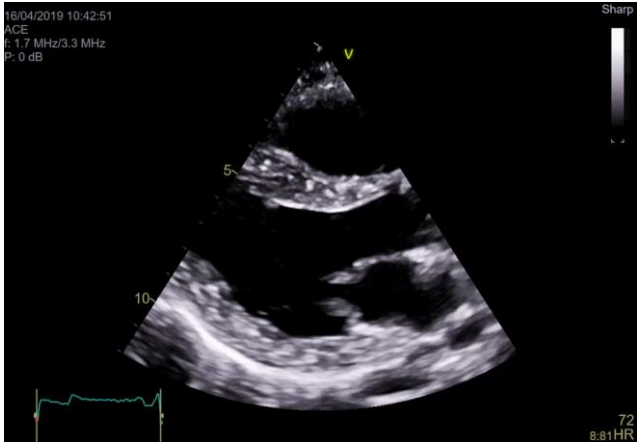


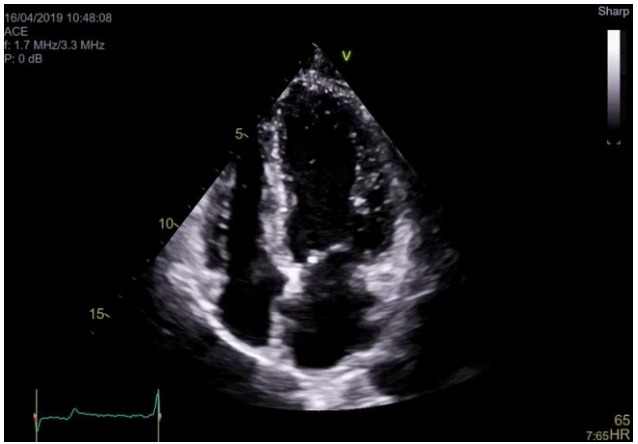




Evolution





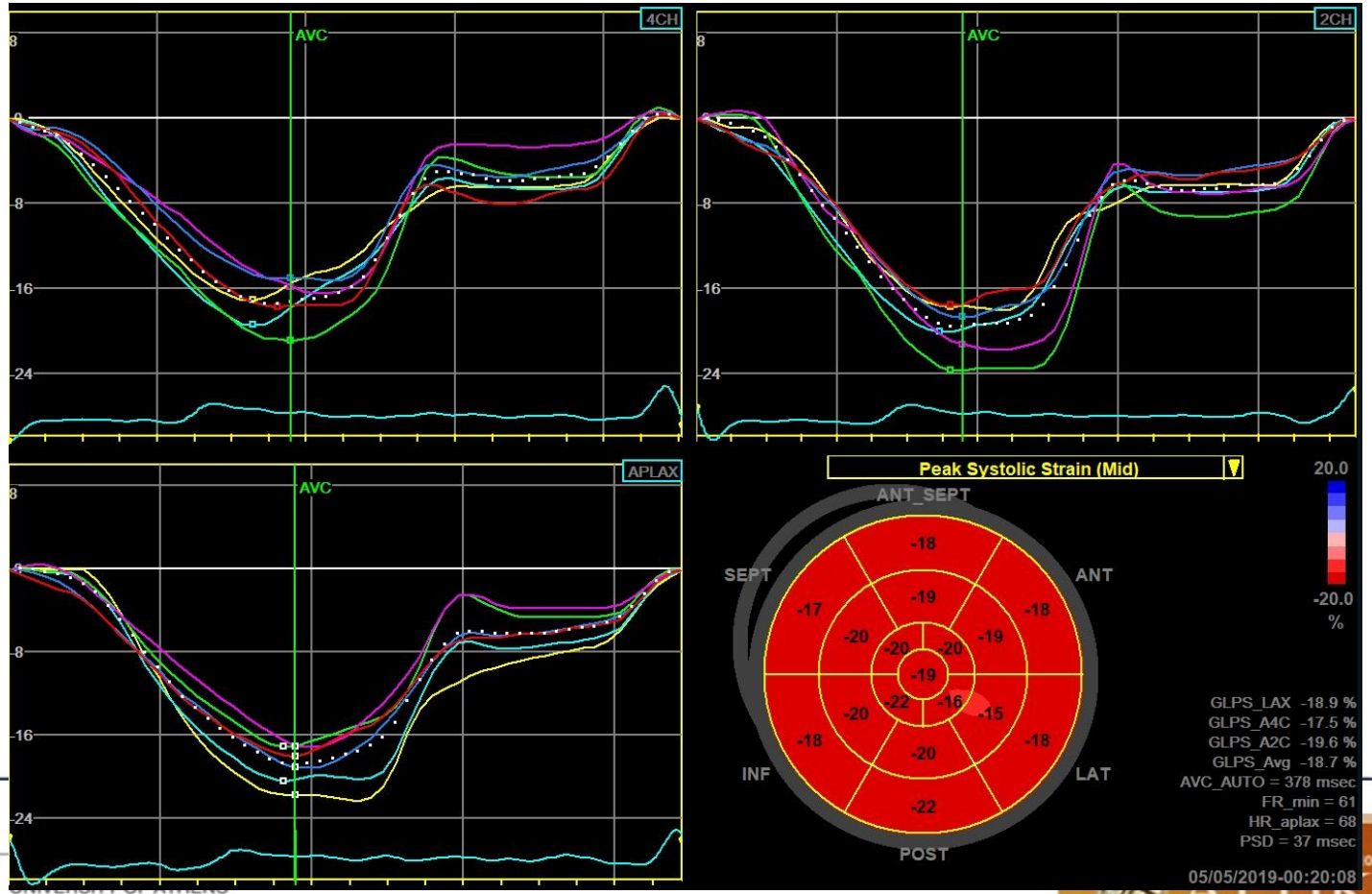


- Uncomplicated course after kidney transplantation
- Normalized cardiac function

2017 → **2019**

National and Kapodistrian
UNIVERSITY OF ATHENS

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ
ATTIKON


4CH
AVC
2CH
AVC
APLAX
AVC
Peak Systolic Strain (Mid)
ANT_SEPT
SEPT
ANT
INF
LAT
POST
-18
-19
-17
-18
-20
-20
-19
-20
-22
-16
-15
-18
-18
-20
-22
20.0
-20.0
%
GLPS_LAX -18.9 %
GLPS_A4C -17.5 %
GLPS_A2C -19.6 %
GLPS_Avg -18.7 %
AVC_AUTO = 378 msec
FR_min = 61
HR_aplax = 68
PSD = 37 msec
05/05/2019-00:20:08

Take home message

- HF is multifactorial in patients with end-stage renal disease
- High output HF is a common cause of HF in end-stage renal failure
- Reversible causes of HF should always be excluded and treated appropriately to improve patients' outcome.

DISEASED MYOCARDIUM		
Ischaemic heart disease	Myocardial scar	
	Myocardial stunning/hibernation	
	Epicardial coronary artery disease	
	Abnormal coronary microcirculation	
	Endothelial dysfunction	
Toxic damage	Recreational substance abuse	Alcohol, cocaine, amphetamine, anabolic steroids.
	Heavy metals	Copper, iron, lead, cobalt.
	Medications	Cytostatic drugs (e.g. anthracyclines), immunomodulating drugs (e.g. interferons monoclonal antibodies such as trastuzumab, cetuximab), antidepressant drugs, antiarrhythmics, non-steroidal anti-Inflammatory drugs, anaesthetics.
	Radiation	
Immune-mediated and inflammatory damage	Related to infection	Bacteria, spirochaetes, fungi, protozoa, parasites (Chagas disease), rickettsiae, viruses (HIV/AIDS).
	Not related to infection	Lymphocytic/giant cell myocarditis, autoimmune diseases (e.g. Graves' disease, rheumatoid arthritis, connective tissue disorders, mainly systemic lupus erythematosus), hypersensitivity and eosinophilic myocarditis (Churg–Strauss).
Infiltration	Related to malignancy	Direct infiltrations and metastases.
	Not related to malignancy	Amyloidosis, sarcoidosis, haemochromatosis (iron), glycogen storage diseases (e.g. Pompe disease), lysosomal storage diseases (e.g. Fabry disease).
Metabolic derangements	Hormonal	Thyroid diseases, parathyroid diseases, acromegaly, GH deficiency, hypercortisolaemia, Conn's disease, Addison disease, diabetes, metabolic syndrome, phaeochromocytoma, pathologies related to pregnancy and peripartum.
	Nutritional	Deficiencies in thiamine, L-carnitine, selenium, iron, phosphates, calcium, complex malnutrition (e.g. malignancy, AIDS, anorexia nervosa), obesity.
Genetic abnormalities	Diverse forms	HCM, DCM, LV non-compaction, ARVC, restrictive cardiomyopathy (for details see respective expert documents), muscular dystrophies and laminopathies.
ABNORMAL LOADING CONDITIONS		
Hypertension		
Valve and myocardium structural defects	Acquired	Mitral, aortic, tricuspid and pulmonary valve diseases.
	Congenital	Atrial and ventricular septum defects and others (for details see a respective expert document).
Pericardial and endomyocardial pathologies	Pericardial	Constrictive pericarditis Pericardial effusion
	Endomyocardial	HES, EMF, endocardial fibroelastosis.
High output states		Severe anaemia, sepsis, thyrotoxicosis, Paget's disease, arteriovenous fistula, pregnancy.
Volume overload		Renal failure, iatrogenic fluid overload.
ARRHYTHMIAS		
Tachyarrhythmias		Atrial, ventricular arrhythmias.
Bradyarrhythmias		Sinus node dysfunctions, conduction disorders.

National and Kapodistrian UNIVERSITY OF ATHENS

ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ATTIKON