MHIF FEATURED STUDY:
MINT

DESCRIPTION:
MINT is a multicenter randomized clinical trial comparing red blood cell transfusion strategies for patients who have had a myocardial infarction and are anemic (positive troponins and a hemoglobin of less than 10 g/dL).

The trial will enroll 3500 hospitalized patients diagnosed with myocardial infarction who are anemic (have blood counts less than 10 g/dL) to receive either a liberal or a restrictive transfusion strategy. Patients will be followed for 6 months to assess how well they are recovering from their heart attack.

CRITERIA LIST/QUALIFICATIONS:
Inclusion
Positive Troponin and a hemoglobin of less than 10 g/dL

Evidence suggests it is safe to wait to give a blood transfusion; however, for those who have suffered a heart attack, there is a lack of high quality evidence to guide transfusions. The study’s results will influence transfusion practice worldwide.

CONDITION: Myocardial Ischemia and Transfusion
PI: Jay Traverse, MD
RESEARCH CONTACT: Rose Peterson
SPONSOR: NIH Trial

Please Refer Patients!
Case Carousel

Amit Sharma
Cardiology Fellow (PGY-6)
Monday October 8th, 2018

DISCLOSURES

- I have no disclosures relevant to the topics discussed in this presentation
OBJECTIVES

- Understand the clinical, echocardiographic, and hemodynamic features of constrictive pericarditis
- Discuss the diagnosis and clinical management of left ventricular tract obstruction
- Know when to order a stress echocardiogram and how to risk stratify patients non-invasively

OBJECTIVE #1

Understand the clinical, echocardiographic, and hemodynamic features of constrictive pericarditis
CONSTRUCTIVE PERICARDITIS

- Most common causes in the United States and developed world are thoracic radiation, prior cardiac surgery, sequelae of inflammatory/infectious process, connective tissue disorder, ESRD, neoplasia, and less commonly tuberculosis
- Most common cause worldwide is tuberculosis
- Hallmark is encasement of the heart and limitation in cardiac filling secondary to a rigid and restrictive pericardium
- Consider this diagnosis in the setting of heart failure symptoms, especially right sided, in the presence of a normal ejection fraction

CASE: CP

- 52 year old male originally from Liberia who arrived in the United States in April 2018
- Past medical history significant for gout
- No pertinent past surgical history or medications
- Presented to the hospital on April 29th, 2018 with progressive dyspnea, lower extremity edema, volume overload, and weight gain
Vital signs on admission notable for respiratory rate of 22, heart rate of 110, and oxygen saturation of 95%.

Chest X-Ray showed a large right-sided pleural effusion.

Labs on admission:
- Total bilirubin: 0.4
- Alkaline phosphatase: 203
- INR: 1.4
- NT-pro-BNP: 605
- Sodium: 134
- Potassium: 3.1
- WBC: 12.7
- LD/troponin negative
- Quantiferon gold positive and AFB negative
- Blood cultures, HIV, and hepatitis work-up negative

Underwent a therapeutic and diagnostic thoracentesis.

Pleural fluid LD: 104 (systemic: 287) and protein: 3.1 (systemic: 7) consistent with a transudative process.
CP

- TTE ordered on April 30th, 2018
Normal LVEF of 55%, PA pressure of 18 mm Hg + RA pressure, RV enlargement with decreased function, paradoxical septal motion, large predominantly anterior pericardial effusion, 50% respiratory alteration in mitral E-wave velocity, and mildly elevated right atrial pressure based on IVC dimensions and collapsibility. Final impression was of possible effusive-constrictive pericarditis with question of early tamponade physiology.

Given the echocardiographic findings, the patient underwent a bilateral heart catheterization and diagnostic/therapeutic pericardiocentesis. RHC showed a mean RA 28 mmHg, RV 50/21 mmHg, PA 47/31 mmHg with mean 34 mm Hg, PCWP 27-28 mmHg, and cardiac output 4.4 L/min (PA saturation 68%, Index 2.2 L/min/m²). Pericardiocentesis was performed with removal of 200 mL of dark bloody fluid. Repeat RHC performed after pericardiocentesis with no significant change in numbers compared to initial RHC. LVEDP/PCWP/RVEDP/RA remained relatively equalized at ~28 mm Hg. No clear evidence of ventricular interdependence was noted on simultaneous right and left heart catheterization.
Pericardiocentesis labs with lymphocyte predominance, protein 4.6 (65% systemic), LDH 1043, and negative culture/stain/AFB/cytology consistent with an exudative process.

ID was consulted and given concern for effusive-constrictive pericarditis secondary to latent tuberculosis with questionable history of active tuberculosis in Liberia, the patient was started on treatment for latent tuberculosis with a four drug regimen.

Repeat TTE from May 4th, 2018 showed no significant re-accumulation of pericardial fluid.

Discharged home on May 9th, 2018.

Re-admitted on July 6th, 2018 with worsening dyspnea.

A TTE was performed on 7/6/2018.
There is recurrence of a large pericardial effusion with echodense material and fibrin strands suggesting a complex pericardial fluid collection. Additionally, there was thickening of the pericardium around the RV and LV apex. There is impressive interventricular interdependence with respiration and marked respiratory mitral inflow variation consistent with effusive constrictive pericarditis. The medial mitral annular tissue doppler velocity is > lateral, all supporting the above Echocardiographic diagnosis.

In direct comparison to the prior study dated, 5/4/2018, the pericardial effusion is much more organized and echo dense with fibrin strands. The pericardium also appears much more echodense though different echo machine is used now. The interventricular interdependence and evidence for dissociation of intra-thoracic and pericardial pressures are impressive on the current study.
Cardiology was re-consulted and given the re-accumulation of complex pericardial fluid despite treatment for latent tuberculosis, it was recommended the patient be considered for a pericardial window to address his recurrent effusion.

Pericardial window and biopsy performed on 7/11/18 without complications

Pericardial biopsy from benign pericardium with chronic fibrosis with mild lymphoplasmacytic inflammation

Transferred to ICU for worsening respiratory status

Died of bradycardic PEA arrest on 7/15/2018

Autopsy showed extensive PE burden as cause of death along with fibrinous pericarditis

HEMODYNAMICS OF CONSTRICTION

The two hallmark features of constrictive pericarditis are enhanced ventricular interdependence and dissociation of intracardiac and intrathoracic pressures
OBJECTIVE #2

Discuss the diagnosis and clinical management of left ventricular tract obstruction

CASE: LV

- 39 year old male referred to cardiology for an abnormal ECG
- ECG consistent with left ventricular hypertrophy
- Underwent TTE
TTE showed septal hypertrophy with IVS of 2.45 cm, SAM, and posteriorly directed MR. These findings are suggestive of HOCM.
Cardiac MRI performed at OSH and showed a 2.1 cm IVS and delayed enhancement within the inferolateral wall and interventricular septum.

ILR implanted in September 2016 for syncope despite sounding vasovagal. No arrhythmias found to date.

Eventually developed exertional symptoms and a stress TTE was performed which showed resting mean gradient of 6 mm Hg that went up to 77 mm Hg with provocation (exercise and valsalva).

Had been managed on beta blocker and calcium channel blocker therapy but eventually had worsening symptoms and progressive LV outflow tract obstruction and underwent myectomy in 2018 at OSH.
TTE showed normal LVEF, IVS dimension of 1.8 cm (previously 2.45 cm), no SAM, no MR, and no evidence of LVOT obstruction
**LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION**

- Obstruction can be fixed, dynamic, or have a component of both
- By definition, obstruction can be subvalvular, valvular, or supravalvular
  - Valvular = aortic stenosis
  - Supravalvular = usually seen in congenital heart disease (Williams syndrome) and aortic coarctation
  - Subvalvular = subaortic membrane, muscular narrowing, and congenital heart disease (Shone complex)
- Examples of fixed obstruction are subvalvular stenosis due to idiopathic LV outflow tract narrowing, subaortic membrane, congenital heart disease, and supravalvular aortic stenosis
- Examples of dynamic obstruction are those seen in HOCM (may or may not have underlying fixed obstruction at rest), stress cardiomyopathy (commonly seen in elderly patients with sigmoid septum), hyperdynamic LV function in the appropriate setting (see following), and others
- As above, can have underlying fixed obstruction with a dynamic component. An example would be a HOCM patient with resting obstruction worsening with dehydration, Valsalva, or exertion

---

**LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION**

- Clinical suspicion is necessary to diagnose this with a common scenario being hypotension that is “refractory” to or worsened by certain vasopressors and all inotropic agents
- As mentioned, the obstruction is dynamic and worsened by volume depletion, increased contractile state, Valsalva, afterload reduction/vasodilation, hyperdynamic LV function, and conditions leading to distortion of LV geometry (ACS and stress cardiomyopathy, for example)
- Management is ensuring euvolemic state and giving volume, stopping all inotropic agents, beta blockade, and switching to “pure” vasopressors such as Phenylephrine and Vasopressin. Avoid ALL beta agonists.
- Of note, if MR is secondary to SAM, it will be posteriorly directed and treatment is aimed at correcting SAM and LVOT obstruction, not the MV itself
End diastole

Early systole

Late systole

<table>
<thead>
<tr>
<th>Maneuver</th>
<th>Ventricular Volume</th>
<th>Murmur Intensity</th>
<th>LVOT Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand grip</td>
<td>Increase</td>
<td>Decrease</td>
<td>Decrease</td>
</tr>
<tr>
<td>Valsalva</td>
<td>Decrease</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>Amyl nitrite</td>
<td>Decrease</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>Decrease</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Increase</td>
<td>Decrease</td>
<td>Decrease</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>Increase</td>
<td>Decrease</td>
<td>Decrease</td>
</tr>
</tbody>
</table>

LVOT, left ventricular outflow tract.

**Brockenbrough Braunwald Morrow Sign**

HOCM - Post PVC, there is increased ventricular filling but also increased contractility. The latter “offsets” the former leading to increased obstruction and decreased aortic pulse pressure.
CASE: TS

- 72 year old female admitted to the hospital in 2016 following a hit and run car on pedestrian accident
- Significant injuries including multiple long bone and pelvic fractures, rib fractures, flail chest, and intracranial hemorrhage
- In profound shock requiring multiple vasopressors
- Cardiology consulted given refractory shock and abnormal TTE images
CASE: TS

- Initial impression of the TTE was severe RV enlargement and dysfunction, hyperdynamic LV function, LVOT obstruction, and question of severe posteriorly directed MR.
- Due to concern over significant MR and LVOT obstruction in the setting of sub-optimal TTE imaging, a TEE was performed.
TEE showed hyperdynamic LV function, myxomatous MV, SAM with severe posteriorly directed MR, LVOT obstruction by color Doppler, and RV failure secondary to blunt chest trauma. Study was terminated early due to patient instability.

Inotropes were discontinued and vasopressors were changed from Norepinephrine and Dopamine to Vasopressin and Phenylephrine with significant improvement in hemodynamics.

Unfortunately, the patient continued to deteriorate with MOF and care was withdrawn.
Prevalence, associated factors and management implications of left ventricular outflow tract obstruction in takotsubo cardiomyopathy: a two-year, two-center experience

Ole De Backer1,*, Philippe Debonnaire1, Sofie Gevaert1, Luc Missault1, Peter Ghevaert1 and Luc Mayledmans2

Abstract

Background: Some patients with Takotsubo cardiomyopathy (TTC) develop cardiogenic shock due to left ventricular outflow tract (LVOT) obstruction — there is, however, a paucity of data regarding this condition.

Methods: Prevalence, associated factors and management implications of LVOT obstruction in TTC were explored, based on two-year data from two Belgian heart centers.

Results: A total of 32 patients with TTC were identified of 4,372 patients presenting with troponin-positive acute coronary syndrome. In six patients diagnosed with TTC (19%), a significant LVOT obstruction was detected by transthoracic echocardiography. Patients with LVOT obstruction were older and had more often septal bulging, and presented more frequently in cardiogenic shock as compared to those without LVOT obstruction (P < 0.05). Moreover, all patients with LVOT obstruction showed systolic anterior motion (SAM) of the anterior mitral valve leaflet, which was associated with a higher grade of mitral regurgitation (2.2±0.7 vs. 1.0±0.5; P<0.01). Adequate therapeutic management including fluid resuscitation, cessation of inotropic therapy, intravenous lidocaine, and the use of intra-aortic balloon pump resulted in non-inferior survival in TTC patients with LVOT obstruction as compared to those without LVOT obstruction.

Conclusions: TTC is complicated by LVOT obstruction in approximately 20% of cases. Older age, septal bulging, SAM-induced mitral regurgitation and hemodynamic instability are associated with this condition. Timely and accurate diagnosis of LVOT obstruction by echocardiography is key to successful management of these TTC patients with LVOT obstruction and results in a non-inferior outcome as compared to those patients without LVOT obstruction.

Keywords: Takotsubo cardiomyopathy, Apical ballooning, Outflow tract obstruction, Systolic anterior motion, Cardiogenic shock.


Prevalence and characteristics of left ventricular outflow tract obstruction in Tako-Tsubo syndrome

Rami El Mahmoud, MD,1,2 a Nicolas Mansencal, MD, a,4 a Rémy Filliére, MD,1 a Francois Leyrer, MD,1 a Nacéra Abbassi, MD,1 a Pierre Michaud, MD,1 a Olivier Nallet, MD,1 a Franck Déjus, MD,1 a Pascal Lacombe, MD,1 a Simon Cattan, MD,1 a and Olivier Dubourg, MD, FACC, FESC1 b Boulogne and Montfermeur, France

Background and Objective: Tako-Tsubo syndrome is a clinical entity mimicking acute coronary syndrome (ACS). Left ventricular outflow tract (LVOT) obstruction may occur in Tako-Tsubo syndrome. The aim of this study was to determine the prevalence and features of LVOT obstruction in Tako-Tsubo syndrome in a population presenting with ACS.

Methods: This study included consecutive patients admitted to 2 catheterization laboratories for suspected ACS. All patients underwent echocardiography, coronary angiography, and left ventricular angiography if no significant coronary lesions were found.

Results: Among 10,366 patients referred for coronary angiography, the study population consisted of 3,909 patients with suspected ACS. Thirty-two patients (mean age 71 ± 13 years old) presented with Tako-Tsubo syndrome, resulting in a prevalence of 0.8% in our population of ACS and 5% of patients without significant coronary lesions. Eight women (mean age 81 ± 4 years old, P = .01) exhibited LVOT obstruction, a prevalence of 25% among Tako-Tsubo syndrome cases. All patients with intraventricular pressure gradient had systolic anterior motion of the mitral valve and septal bulge. Prevalence of septal bulge was 100% in patients with Tako-Tsubo syndrome and LVOT obstruction versus 29% in patients without LVOT obstruction (P = .002). Mean degree of mitral regurgitation was 2.1 ± 0.7 in cases of LVOT obstruction versus 0.9 ± 0.7 in patients without LVOT (P = .0003) and significantly decreased during follow-up (1 ± 0.8, P = .002). Recovery of left ventricular ejection fraction was similar in patients with and without LVOT obstruction (P = .58).

Conclusions: The present study demonstrates that the prevalence of LVOT obstruction in Tako-Tsubo syndrome is high, with specific characteristics as compared with patients without LVOT obstruction. Echocardiography should be systematically performed for all patients presenting with Tako-Tsubo syndrome for the detection of LVOT obstruction. (Am Heart J 2008;156:543-58)

**OBJECTIVE #3**

Know when to order a stress echocardiogram and how to risk stratify patients non-invasively
STRESS TESTS ARE NOT SIMPLY POSITIVE OR NEGATIVE!!!

ORDERING STRESS TESTS

- When ordering a stress test, there are two things to always consider → modality of stress and imaging
  - Exception to this is cardiac CT where there is no “stress” agent given
- Common options for stress modalities are conventional exercise, Dobutamine, and vasodilators (Adenosine and Regadenoson)
- Options for imaging are basic ECG, echocardiogram, SPECT (Thallium, Tetrofosmin, and Sestamibi), PET (Rubidium)
Step 1

Assess Pretest Probability of obstructive coronary disease

Low

Intermediate

High or known CAD but no concern for ongoing ischemia/negative troponin

Consider Cardiology consultation

Go to step 2

Exercise ECG only

Coronary CT Angiogram

- Normal/interpretable ECG
- No prior CAD or revascularization
- No echo info necessary e.g. EF/PA/valves etc.

- No active arrhythmia
- Able to give beta-blockers for HR control
- Avoid if young/child bearing age/dialysis/renal insufficiency

Step 2

1. Can walk > 4 METS (based on history and test walk)
2. Need to assess functional capacity
3. Absence of LBBB/paced rhythm/atrial fibrillation on resting ECG

Step 3

Exercise Stress Test

Yes

No—go to step 4

Multiple RWMA on previous echo

Exercise echocardiogram

Either exercise echocardiogram or exercise perfusion study (consider repeating previous stress modality if pt has had previous stress test)

Exercise perfusion SPECT Study (i.e. exercise "MIBI")

- Contraindication: recent caffeine/theophylline use within 12 hours
- Avoid in young patients/child bearing age.
**Case: UA**

- 58 year old female with no significant past medical history aside from asthma and hypothyroidism and no traditional risk factors for ASCVD admitted to the hospital with exertional throat discomfort that would resolve with rest while walking her dog.
- Symptoms are new in onset and had been ongoing for the past week.
- Admitted to the hospital for further work-up.
- Lipid panel with LDL of 106 and HDL of 47.
- Hemoglobin A1c unremarkable.
Serial troponin values were undetectable

Given concern over the patient’s history of exertional symptoms, a stress echocardiogram was ordered to evaluate for ischemia.
During stress echocardiogram, the patient exercised for 10.52 minutes and achieved 93% of age predicted maximal heart rate. Peak blood pressure was 164/75 with a double product of 24,764. The total METs were 10.6. Test was terminated due to reproduction of exertional throat tightness and having achieved adequate heart rate goal.

Study interpreted as normal LVEF and no WMA at rest. With exercise, there was a profound decrease in LVEF to 20-25% by Biplane + LV dilatation. There were stress induced WMA in the septum, apex, anterior, lateral, and distal inferior walls. These changes persisted well into recovery.

Given these very high risk stress test findings, the patient underwent coronary angiography on the same day.
Coronary angiogram showed 95% stenosis in the proximal LAD with TIMI 2 flow in the LAD distal to the stenosis. This lesion was treated with a 4 x 20 mm Synergy DES.
The patient was discharged home on DAPT, statin, and beta blocker therapy.
CASE: CP DO I REALLY WANT TO USE THIS CASE?

- 63 year old male with a history of CAD (OM1 PCI in 2010), hyperlipidemia, former tobacco abuse, obesity, hyperlipidemia, and OSA admitted on June 3rd 2018 with chest discomfort
- Admitted for further evaluation and work-up

ECG Image
Serial troponin values were negative
Given the patient’s history, risk factors, and prior CAD, a stress echocardiogram was ordered
During stress echocardiogram, the patient exercised for 6.93 minutes and achieved 90% of age predicted maximal heart rate. Peak blood pressure was 183/72 with a double product of 25,986. The total MET's were 7. Test was terminated due to chest discomfort and having achieved adequate heart rate goal.

Stress echocardiogram interpreted as normal LVEF and no WMA at rest. With exertion, there was development of WMA in the apical anterior and lateral segments.

Given the patient's background medical therapy from prior PCI, decision made to proceed with invasive angiography.
Coronary angiogram showed 90% stenosis in the proximal D1 without other lesions. This lesion was treated with primary PCI.

The patient was discharged home on DAPT, intensified statin therapy, and beta blocker therapy.

**BENEFITS OF STRESS ECHOCARDIOGRAPHY**

- Structural visualization of the LV, RV, and valves allowing for a cardiac assessment outside of simply “ruling out ischemia”
- Can be used not only for ischemia/CAD but also when either exam findings or resting echocardiographic findings are incongruent with patient symptoms
- Other applications are looking for dynamic/ischemic MR, dynamic gradients such as LV outflow tract obstruction, and evaluating valve disease when severity and symptoms are discordant
- No radiation to the patient
- Downside is in patients with sub-optimal imaging and necessity for a well-trained lab and sonographers to rapidly acquire images

Wall motion score index and ejection fraction for risk stratification after acute myocardial infarction.
Møller JE, Hillis GS, Oh JK, Reeder GS, Gersh BJ, Pellikka PA.

BACKGROUND:
The prognostic importance of regional systolic function, as assessed by wall motion score index (WMSI), compared with global function, as assessed by left ventricular ejection fraction (LVEF), has not been assessed in large populations after acute myocardial infarction.

METHODS:
Echocardiograms, including the assessment of WMSI and LVEF, were performed in 767 patients with acute myocardial infarction at a median of 1 day (25th and 75th percentiles 0-2 days) after admission. Patients were followed for a median of 19 months (range 12-28 months). Cox proportional hazards models were constructed for the primary study end point (all-cause mortality) and for a secondary end point (hospitalization for congestive heart failure).

RESULTS:
During follow-up (median 40 months; range 24-50 months), 216 patients died and 54 patients were hospitalized for congestive heart failure. By univariate analysis, both LVEF (P < .0001) and WMSI (P < .0001) were powerful predictors of all-cause mortality. By a forward conditional Cox model, WMSI proved to be an independent predictor of death (hazard ratio 1.15 per 0.2-unit increase, 95% CI 1.10-1.21, P < .0001). When WMSI was included in the model, LVEF did not provide additional prognostic information (P = .77). Wall motion score index also proved to be an independent predictor of hospitalization for congestive heart failure (hazard ratio 1.21 per 0.2-unit increase, 95% CI 1.07-1.37, P = .002), whereas LVEF did not (P = .56).

CONCLUSION:
Both LVEF and WMSI provide powerful prognostic information after acute myocardial infarction; however, the predictive power of WMSI is greater.
Figure 3
Kaplan-Meier survival curves (end point of hard cardiac events) in women according to results of dobutamine stress echocardiography.

*Bia


Figure 7
Cardiac Events Stratified by Percentage of Ischemic Myocardium on Rb-82 PETMPI

**Cerci, M. S. J (2011).** Myocardial perfusion imaging is a strong predictor of death in women. *JACC: Cardiovascular Imaging, 4*(8), 880-888.


REFERENCES


REFERENCES

REFERENCES


