Advanced heart failure case - 2016

41yo male referred for advanced HF therapies with multiple co-morbidities

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Cardiac Care Network

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Cardiologist
Toronto General Hospital
2012

38 year old male
April 2012: Initial consult with local cardiologist
Dx. Idiopathic/viral CM 2010 years ago during hospitalization for heart failure (another province)

Medical history: Generally very healthy.
No diabetes, no hypertension, non-smoker, rare alcohol (social in past), depression following father’s death in the last 2 years
2005- ‘asthma’ after investigation for some SOB and cough (Ventolin prn)
History

Father died of MI (age 65), no other cardiac family history,
No history of sudden death or premature death.

Social history
Single, lives alone, mother near by, employed (sedentary),
African American
Very active with sports prior to his diagnosis
2012

Subjective
- Walks several blocks- SOB with hills, unable to play sports
- No orthopnea, PND, swelling,
- No palpitations, syncope, chest discomfort

Medications
Bisoprolol 10 mg daily
Irbesartan 150 mg daily (ACE- cough)
Lasix 20 mg daily
Wellbutrin XL 300 mg daily

On exam
Height 174 cm
Weight 135 Kg
BMI : 45 kg/m²

bp: 128/78 mm Hg
Chest clear
Normal, distant heart sounds
No gallop, 1-2/6 pansys murmurs murmur apex
No elevated JVP
No edema
Abd- unremarkable

ECG: SR 78 bpm
LA enlargement
L posterior fascicular block
Echo-2012

- Dilated LV: diastolic diameter 7.6 cm
- LV Mass index 157 g/m²
- Global HK: EF 25-30%
- Severe restrictive filling LV, marked LA pressure
- Mod enlarged and mod impaired RV systolic function
- Thrombus in apex of LV
- LA severely dilated
- Mild MR, trace TR

Echo 2005

LV diastolic diameter 6.0 cm
LV Mass index 134
EF 43%

Normal RV
RVSP 43 mm Hg
Mild MR, TR
Plan

Thrombosis- apical thrombus
HF clinic- teaching/optimization of medications
ICD referral
Cardiac rehab/CPET
Key events

April 2012
- Initial consult
- NYHA II
- EF <30%

July 2012
- Hospital
- HF
- Soya sauce ‘nobody told me’
- Gout

October 2012
- Hospital
- HF
- ‘nobody told me’
- Gout

January 2013
- Hospital
- HF
- BB intolerance
- Renal injury
- Gout

April 2013
- Hospital
- HF
- Inotropes
- Renal injury
- Gout

July 2013
- Hospital
- HF
- Renal injury
- Gout

October 2013
- Hospital
- VT storm
- Low K+
- Renal injury
- Gout

Cardiac rehab- Social Worker, Registered Dietitian
Medications- BB challenges, ARB dose, MRA added
Referred for transplant assessment
Ongoing challenges

- Self-care- adherence to medications, dietary recommendations, risk factor reduction (rehab, bariatric clinic, OSA)
- Low mood- symptoms of depression
Self care and heart failure

Maintenance
Adherence to medications, dietary recommendations, exercise, risk factor reduction

Symptom Perception
Detection of physical change and interpretation of the meaning: surveillance/monitoring, recognition, interpretation.

Management
The response to symptoms when they occur: independent decisions or provider-directed decisions.

Self management interventions and HF outcomes

• 20 studies, 5624 patients
• Reduced time to combined all-cause death or HF hospitalization (HR 0.80; 95% CI: 0.71-0.89)
• Reduced time to HF hospitalization (HR 0.80; 95% CI: 0.69-0.92)
• Improvement in QOL (HR 0.15; 95% CI: 0.00-0.30)

People with severe depression- increased risk of all-cause mortality

Jenkman et al., Circulation 2016; 133: 1189-1198
Depression and HF outcomes

- Prevalence 10-80%\(^1\)
- Increased risk of all-cause mortality (HR 1.40; 95% CI: 1.22-1.60)\(^1\)
  Higher risk in elderly (age 65) vs younger cohorts\(^2\)
- Associated with worse self-care (r=-0.19 p<0.001)\(^3\)
  Lower self-efficacy\(^4\) and motivation\(^5\)

1. Sokoreli et al., Heart Fail Rev 2016; 21:49-63
2. Gathright et al., J Psychosomatic Research 2017; 94: 82-89
Supporting self-care

Synthesis 33 studies, 3355 participants
• Helping with understanding, improving self-efficacy
• Psychosocial support, improved confidence, hope, lower depression
• Caregiver involvement
• Attention to individual needs and goals
• Rapid feedback or response to worsening symptoms
• Consolidated existing patient-professional relationships
• Technology must be simple, have good tech support, be portable

Clark et al., Heart, 2016
Back to our patient
2014-2016

- No hospital admissions
- Bariatric Clinic- expensive, not working for him
- Sleep study (OSA)- sporadic use of device
- Sporadic appointments in HFC, Cardiac Rehab, Toronto

Fall 2015:
Trip- 2 weeks- HF on return 140 Kg, metolazone, Cr now 255
Medications: Irbesartan 300 mg, Aldactone 25 mg BID, Lasix 120 mg am; 80 mg pm
Multi vitamin, Uloric, Colchicine prn, Metolazone prn

- Jan: Concerns- cardiorenal syndrome, decreasing ARB, MRA, NYHA III
- Feb-March: prolonged ‘vacation’
- April: Returns- within 5 days- Hospitalization: Anasarca- diuresis (LOS 10 days)
- May: Low output/cardiorenal
- End of May-elective admission for inotropes
Case: 41yoM – HF past history

- Non-ischemic cardiomyopathy
- First HF presentation in 2010
- 4-5 HF admissions in the last 2 years
- ICD for primary prophylaxis in 2012
- Previous ventricular tachycardia storm in 2013 profound hypokalemia secondary to metolazone and colchicine
Case: 41yoM – Co-morbidities

- Obesity (135k, BMI 45 kg/m2)
- Chronic kidney disease (baseline creatinine ~200 umol/l and eGFR 40 ml/min)
- Gout
- OSA ᵃ CPAP??
- Non-adherence to diet, medications, and appointments
- Lost to follow up in the past 2 years
Case: 41yo – HF status as an outpatient

- NYHA class 3
- BP 110/80 - HR 88 bpm
- Peripheral edema (moderate-mild)
- Elevated JVP
- CPS
  - Peak oxygen consumption (VO₂) = 7.2 ml/kg/min (20% of predicted). Previous (2014) = 12.2 ml/kg/min (50%)
- BNP 1300, troponins positive
- Creatinine 240 umol/L (eGFR ~30 ml/min)
Case: 41yo - Medications

- No ACEI due to worsening CKD
- Hydralazine 20mg t.i.d.
- Isosorbide dinitrate 20mg t.i.d.
- Spironolactone 12.5 mg o.d.
- Furosemide 120mg b.i.d.
- Intolerance to BB and dig (dizziness and confusion)
Using your intuition:
What is this patient’s 1-year survival?

- 90%
- 70%
- 50%
- <50%
Factors associated with prognosis

Combined evidence

Uncertain future

Clear prognosis and improved outcomes
### Factors associated with prognosis

<table>
<thead>
<tr>
<th>Good prognosis</th>
<th>Poor prognosis</th>
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<tbody>
<tr>
<td>Young age</td>
<td>Intolerance to HF meds</td>
</tr>
<tr>
<td>Non-ischemic CMP</td>
<td>Multiple HF admissions</td>
</tr>
<tr>
<td>Good blood pressure</td>
<td>Impaired kidney function</td>
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<tr>
<td></td>
<td>NYHA class III</td>
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<tr>
<td></td>
<td>Volume overload</td>
</tr>
<tr>
<td></td>
<td>High dose of diuretics</td>
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<td></td>
<td>Decreased VO$_2$</td>
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</tbody>
</table>
The UCLA score

Male Cohort

ACEI tolerance
BNP
NYHA class
Peak VO₂

Event-free survival (%)

Q1
Q2
Q3
Q4

No. at risk

Time (y)

p<0.0001

Chye et al. Circ Heart Fail 2014
Seattle Heart Failure Model

Baseline

Survival
- 1 Year: 77%
- 2 Year: 58%
- 5 Year: 22%

Mortality
- 23%
- 42%
- 78%

Mean life expectancy
- 3.2 years

Clinical
- Age: 42
- Gender: Male
- NYHA Class: 3B
- Weight (kg): 135
- EF: 25
- Syst BP: 110
- Ischemic

Medications
- ACE-I
- Beta-blocker
- ARB
- Statin
- Allopurinol
- Aldosterone blocker

Diuretics
- Furosemide: 240
- Bumetanide: 0
- Torsemide: 0
- Metolazone: 0
- HCTZ: 0
- Chlorothiazide: 0

Diuretics

IV

Lab Data
- Hgb (g/dL): 12
- Lymphocyte %: 24
- Uric Acid (mg/dL): 6.5
- Total Chol (mg/dL): 206
- Sodium: 135

Lab Data

Devices
- None
- BiV Pacer
- ICD
- BiV ICD

Devices

Other
- IABP/Vent/UF
- Pressors/Inotropes

Other

Levy et al. Circulation 2006
Other deleterious predictors

- Non-compliance: 2-fold higher mortality
  Fitzgerald et al. J Card Fail 2011

- Hospitalization in previous year: 2.4-fold increased mortality risk
  Sherwood et al. JACC 2011

- ICD shocks: 1.7 fold increased mortality
  Saxon et al. Circulation 2010

Chances of survival <70% at 1 year
Consideration for heart transplantation

ISHLT 2016 Guideline recommend:

- In patients intolerant of a β-blocker, an oxygen consumption \( (VO_2) \) of < 12 ml/kg/min should be used to guide listing (Class I, Level of Evidence: B).
- An estimated 1-year survival of 75% with a Seattle Heart Failure Model (S) considered as reasonable cut point.

O’Neill et al. Circulation 2005
What is the 1-year survival after transplant?

- 95%
- 85%
- 70%
- <70%
Heart transplant: Best treatment option

Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2014)

1 year = 85%
5 year = 73%

All pair-wise comparisons were significant at p < 0.05.

Median survival (years):
Ventricular assist device: The best alternative

Continuous Flow LVAD/BiVAD Implants: 2008 – 2014, n=12030

1 year = 80%

4 years = 48%

Kirklin et al. JHLT 2015
Impaired quality of life
Increased hospitalization
Poor survival
Heart transplant assessment

1. Is this patient sick enough to need a transplant? ✔ Yes
2. Is this patient a candidate for transplant?
Case: 41yoM – HTx/VAD work up: Issues

- Pulmonary hypertension
  - PA 70/40 mmHg, mean 50 mmHg, TPG 10 mmHg
- Highly sensitized
  - PRA class 1/2 = 79%/27%
- Obesity
  - BMI 44 kg/m²
- CKD
  - Creatinine ~200 umol/L, eGFR ~30 ml/min
  - Absence of proteinuria
- Non-compliance
Is this patient a candidate for transplant or VAD?
Pulmonary hypertension and early post-transplant mortality

3-month post-transplant mortality

<table>
<thead>
<tr>
<th></th>
<th>PVR &gt; 2.5</th>
<th>PVR ≤ 2.5</th>
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</thead>
<tbody>
<tr>
<td>Death due to RV failure</td>
<td>14%</td>
<td>6%</td>
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<tr>
<td>Death due to other causes</td>
<td></td>
<td></td>
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</table>

Post-transplant survival

<table>
<thead>
<tr>
<th>Months</th>
<th>Survival Probability</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>10</td>
<td>0.96</td>
</tr>
<tr>
<td>20</td>
<td>0.93</td>
</tr>
<tr>
<td>30</td>
<td>0.88</td>
</tr>
<tr>
<td>50</td>
<td>0.86</td>
</tr>
<tr>
<td>60</td>
<td>0.77</td>
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Costard-Jackle et al. JACC 1992

Alba et al. JHLT 2009
Pulmonary hypertension

- Pulmonary systolic pressure >50 mmHg
- PVR >3 wood units
- TPG >15 mmHg
- Vasodilator challenge: PVR >2.5 wood units and SBP <85 mmHg

**ISHLT 2016 Guideline recommendation**

Use of *mechanical circulatory support* should be considered for patients with potentially reversible or treatable comorbidities, such as cancer, obesity, renal failure, tobacco use, and *pharmacologically irreversible pulmonary hypertension*, with subsequent re-*evaluation* to establish candidacy (Class IIb, Level of Evidence: C).

Mehra et al. JHLT 2016
Sensitization = high PRA

Post-transplant survival

<table>
<thead>
<tr>
<th>PRA%</th>
<th>30 DAYS</th>
<th>1 YR</th>
<th>3 YRS</th>
<th>5 YRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=25 (7720)*</td>
<td>94.3* (7183)</td>
<td>86.9 (6151)</td>
<td>79.6 (2942)</td>
<td>73.9 (371)</td>
</tr>
<tr>
<td>&gt;25 (440)</td>
<td>88.6 (387)</td>
<td>80.3 (325)</td>
<td>72.2 (146)</td>
<td>65.3 (13)</td>
</tr>
</tbody>
</table>

Time (Years)
P < 0.001

*Number of patients in parentheses  % Survival is shown

Donor specific antibodies (DSA)

- 0% had pre-transplant DSA
- 77% had post-transplant PRA>0%
  - 33% had DSA

HR 4.3 (95%CI 2-10)
Waiting time in VAD patients according to PRA

Alba et al. JHLT 2012
Sensitization = high PRA

- Sensitization is not a contraindication to transplant
- High PRA increases waiting time
- DSA (but not PRA) is associated with high risk of rejection and increased mortality
Obesity is associated with increased post-transplant mortality

- Median follow up = 4 years (IQR 1 - 8 years)
- 12,074 (31%) deaths

<table>
<thead>
<tr>
<th>BMI *</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt;18.5)</td>
<td>1.05</td>
<td>0.96 - 1.14</td>
</tr>
<tr>
<td>Overweight (25-29.99)</td>
<td>1.01</td>
<td>0.97 - 1.05</td>
</tr>
<tr>
<td>Obesity I (30-34.99)</td>
<td>1.12</td>
<td>1.07 - 1.17</td>
</tr>
<tr>
<td>Obesity II (35-39.99)</td>
<td>1.06</td>
<td>0.98 - 1.16</td>
</tr>
<tr>
<td>Obesity III (&gt;40)</td>
<td>1.38</td>
<td>1.12 - 1.68</td>
</tr>
</tbody>
</table>

* Adjusted for recipient and donor age and sex, heart failure etiology, diabetes, hypertension, smoking history, prior cardiac surgery, pulmonary vascular resistance, renal function, transplant year and center volume and use of mechanical circulatory support.

Alba et al. ISHLT 2017
Obesity increases the risk of post-transplant morbidities

Risk at 5 years

- Cancer
- Renal dysfunction
- Diabetes
- Stroke
- Rejection
- CAV

- Underweight
- Normal weight
- Overweight
- Obese
Obesity

- ISHLT guidelines

**2016 Guideline recommendation**

Pre-transplant body mass index (BMI) $> 35$ kg/m$^2$ is associated with a worse outcome after cardiac transplantation. For such obese patients, it is reasonable to **recommend weight loss** to achieve a BMI of $< 35$ kg/m$^2$ before listing for cardiac transplantation (Class IIa, Level of Evidence: C).
**FIGURE 1** Freedom From Death or Delisting While on Left Ventricular Assist Device Support

**Freedom From Death or Delisting with Number of Subjects at Risk**

**Freedom From Death Following Transplantation with Number of Subjects at Risk**

Logrank p = 0.3468

Survival Probability vs. Time for Post-Implant Freedom from Death

- 1: BMI < 18.5
- 2: 18.5 < BMI < 25
- 3: 25 < BMI < 30
- 4: 30 < BMI < 35
- 5: BMI > 35

Survival Probability vs. Time for Post-Transplant Survival (days)

- 1: BMI < 18.5
- 2: 18.5 < BMI < 25
- 3: 25 < BMI < 30
- 4: 30 < BMI < 35
- 5: BMI > 35

Clerkin et al. JACC HF 2016
Renal dysfunction and post-transplant survival

- Retro

Actuarial survival by renal function

Survival by pre-transplant renal function

CrCl ≥ 40 ml/min

CrCl < 40 ml/min

Log Rank P-value = 0.004

Months post-transplant

Odim et al. JHLT 2006
Renal dysfunction (eGFR <30 ml/min)

Patient Survival, Kidney after Heart

Percent Survival

4.5 years

7.5 years

Prior Heart Tx, Waiting for Kidney

Prior Heart Tx, Transplanted with Kidney

p<0.001

Lonze et al. Am J Transplant 2009
2016 Guideline recommendation

Evidence of abnormal renal function should prompt further investigation, including renal ultrasonography, estimation of proteinuria, and evaluation for renal arterial disease, to exclude intrinsic renal disease. It is reasonable to consider the presence of irreversible renal dysfunction (eGFR < 30 ml/min/1.73 m²) as a relative contraindication for heart transplantation alone (Class IIa, Level of Evidence: C).
Non-compliance

- Limited evidence on post-transplant outcomes
- Increased risk of rejection and graft loss

**ISHLT 2016 Guideline recommendation**

Poor compliance with drug regimens is a risk factor for graft rejection and mortality. Patients who have demonstrated an inability to comply with drug therapy on multiple occasions should not receive transplantation (Class III, Level of Evidence: C).
Case: 41yoM – HTx/VAD work up: Issues

- Many relative contraindications for heart transplant:
  - Pulmonary hypertension
  - Obesity: BMI 44 kg/m²
  - Severe renal dysfunction
  - Non-compliance

- Increased waiting time
  - Highly sensitized - PRA class 1/2 = 79%/27%
Is this patient a candidate for transplant?

And VAD?
Case: ICU admission in June 2016

- Cardiogenic shock
- Hemodynamic
  - BP 100/60
- Creatinine 250 umol/L
- BNP 1300
- Positive troponins
- Milrinone, nipride and lasix infusion
INTERMACS Levels: Predicted Survival

Survival with Medical Therapy only

% Survival

Year after Diagnosis

1. 0.00
2. 0.25
3. 0.50
4. 0.75
5. 1.00

0% 6% 25% 50%
Time for a decision: Options

1. Heart transplant (kidney)
2. Ventricular assist device
3. Medical therapy/palliative
Treatment options

Heart transplant:
- Young age
- PAH
- CKD
- Obesity
- Non-compliance

LVAD:
- Young age
- PAH
- High PRA
- CKD
- Non-compliance

Medical therapy:
- Multiple “soft” comorbidities
- Young age
- Low chances of recovery
41yoM – LVAD implant and course

- Jun 2016: HeartMate 3 as bridge to candidacy (PAH and obesity)
- Uncomplicated post-op course
  - Creatinine at discharge 160 umol/L!
  - Great compliance!
  - BMI 38 kg/m² (116 k)
  - Normalization of PAH (PA 28/17, PCWP 19, RA 25)
  - GI bleeding at 3 months of support: OGD, colonoscopy and video capsule negative
  - Listed for transplant 6 months after VAD support
Decision point

- Just after listing (6 months after LVAD support)
- Admitted to ICU with low flow alarms
- CT scan: thrombus in outflow cannula
- Creatinine ~230 (eGFR ~30 ml/min)
What do we do now?!
Heart transplant: 3 weeks after

• Intra-op:
  – Profound coagulopathy and severe bleeding
  – Ischemia time 260 minutes
  – Plasmapheresis: desensitization strategy

• Post-transplant course:
  – AKI requiring permanent dialysis initiating work up for kidney transplant
  – Cross-match after transplant: negative
  – No significant rejection – No DSA
  – BMI 31 kg/m² (95k)
  – Very good compliance 4 months later!
Take-home messages

• Timing of referral for advanced heart failure considerations
  – When you start thinking about it!

• Patients are complex
  – There are many treatment strategies
  – Do not worry about contraindications/comorbidities ☝️ that’s the job of an advanced HF doc!