Autopsy investigations on the operated heart & vessels

End stage heart disease: pathology of cardiac assist and replacement

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succession of pioneering and avant-garde therapies

heart transplantation

mechanical circulatory support (MCS)

MCSs are relatively new and call for a knowledge of bioengineering alongside the more traditional clinical and surgical studies
- Heart failure and end-stage heart failure
- End-stage heart disease
- Heart transplantation
- Mechanical circulatory support devices (MCSDs)
- Ventricular assist devices (VADs)
- Complications related to MCSDs
- Autopsy investigation in presence of MCS
- Coordinating autopsy: pathologist and bio-engineer
- Cardiac reverse remodelling and myocardial recovery
Heart failure and End-stage heart failure

Heart Failure (HF) is defined as

“a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress”

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Heart failure

usually indicates

patients with established chronic disease

Acute HF (AHF)

rapid onset or worsening of symptoms and/or signs.

It is a life-threatening condition which may present de novo or more frequently be the result of acute decompensation of chronic HF in the context of pre-existing cardiomyopathy (acute decompensated HF)
Heart failure and End-stage heart failure

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Major public health problem

Prevalence

- approximately 1–2% of the adult population in developed countries
- ≥10% among patients >70

one of the leading causes of hospitalisation and death

Advances in medical and interventional treatments (implantable defibrillators and cardiac resynchronization therapy) have significantly improved the outcome for these patients with the result that an increased number reach

advanced phase of the disease (end-stage, refractory or terminal HF)
End-stage heart failure

- class III–IV of the NYHA functional classification
- stage D of the ACC/AHA classification

Syndrome with persisting signs and symptoms despite optimal medical and device therapy

- cardiac resynchronization therapy (CRT)
- cardiac resynchronization therapy with a defibrillator (CRT-D)

- less than 10% of the total HF population
- high mortality
Examination of native hearts of transplanted patients has offered a valuable opportunity to extend knowledge of the complex pathologic substrates of advanced structural heart disease, (especially for cardiomyopathies) and to describe the varied aspects of myocardial remodelling after interventional procedures (e.g. coronary stents) and traditional surgery (e.g. valvular heart disease, congenital heart defects)

HF aetiology varies in different regions of the world

- ischemic heart disease
- cardiomyopathies

Most frequent causes

Other non-cardiovascular-related conditions can contribute to it
End-stage heart disease
Ischemic heart disease

variable gross appearance
End-stage heart disease
the melting-pot of DCM phenotypes

- genetic forms
- secondary forms
  - infective or immune myocardial disease; toxic CMPs resulting from chemotherapy or radiotherapy

<table>
<thead>
<tr>
<th>Cardio-laminopathy (Leu183Pro mutation in lamin A/C proteins)</th>
<th>Post-lymphocytic myocarditis DCM</th>
<th>Sarcoidosis</th>
<th>Actinic DCM</th>
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</table>
End-stage heart disease
Arrhythmogenic cardiomyopathy

End-stage biventricular arrhythmogenic cardiomyopathy
End-stage heart disease
End-stage/dilated-hypokinetic hypertrophic cardiomyopathy

small vessel disease
### End-stage heart disease

<table>
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<th>Idiopathic restrictive phenotypes</th>
<th>Cardiomyopathies associated to systemic diseases</th>
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<td>3-year-old female native heart Unclassifiable cardiomyopathy with restrictive ventricular filling pattern</td>
<td>Explanted heart of a 40-year-old male affected by Becker disease</td>
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End-stage heart disease

Cardiac amyloidosis
End-stage heart disease
Rarer forms

Heart of a 43-year-old male with nontropical eosinophilic endomyocardial fibrosis (Loeffler disease) in chronic stage

Heart of a 37-year-old female who developed peripartum cardiomyopathy 1 month after the birth
Aetiology of acute heart failure

Most frequent cardiac causes of de novo acute HF:

- acute myocardial dysfunction (ischaemic, inflammatory, toxic)
- acute valve insufficiency
- pericardial tamponade

Decompensation of chronic HF

- with one or more precipitant factors (infection, uncontrolled hypertension, rhythm disturbances, non-adherence to drugs/diet)
- without known precipitant factors
Heart transplantation

- still the gold standard for treating end-stage HF
- the sole therapeutic strategy able to:
  - radically change the natural course of the advanced disease
  - improve quality of life and return to work

  Current survival rates
  1-year survival: 84.5%
  5–year survival: 72.5% (data from ISHLT registry)

Some major challenges

- continuing shortage of donor hearts
- increasing number of transplant candidates
- increasing number of patients refractory to medical and device therapy
- long term complications of immunosuppressive therapy (i.e. antibody-mediated rejection, infection, hypertension, renal failure, malignancy and coronary allograft vasculopathy)
- cases ineligible for transplantation

MCS as a therapeutic option for the failing heart in both short- and mid/long-term
Early days of cardiac surgery

1953

Dr. Gibbon used the heart–lung machine to repair an atrial septal defect in an 18-year-old woman.
1966
the first successful implantation of a DeBakey ventricular assist device in a patient with cardiogenic shock

1967
the first successful use of an intra-aortic balloon pump by Dr. Kantrowitz

1984
the first implantation of a total artificial heart using Jarvik-7 model by Dr. DeVries
Mechanical circulatory support devices
Function and types

MCSDs replace some of the mechanical functions of the failing heart to improve cardiac output and maintain sufficient organ perfusion.

**Classification**

- counter-pulsation pumps (intra-aortic balloon pump-IABP)
- centrifugal pumps
- volume-displacement pumps (first generation ventricular assist devices-VADs)
- axial-flow pumps (second and third generation VADs)
Mechanical circulatory support devices
Strategies of implantation

- a *Bridge to Decision* in patients with acute circulatory collapse at immediate risk of death to sustain life (BTD);
- a *Bridge to Candidacy* to improve end-organ function in order to make an ineligible patient eligible for transplantation (BTC);
- a *Bridge to Transplant* to keep high risk patients alive until a donor organ becomes available (BTT);
- a *Bridge to Recovery* to keep patient alive until cardiac function recovers sufficiently to remove the support (BTR);

*Destination therapy or long-term support*, an alternative to transplantation in end-stage patients ineligible for transplantation (DT)
Mechanical circulatory support devices
Strategies of implantation

Cardiac replacement therapy

Heart transplantation

- long-term assist devices
- total artificial heart: currently approved only for biventricular support as BTT
Short to intermediate-term MCS

- intra-aortic balloon pump (IABP)
- extracorporeal membrane oxygenation (ECMO)

**IABP**

counter-pulsation pump
often the first-line device in treating cardiogenic shock
cylindrical polyethylene balloon
inserted via the femoral artery
and positioned in the proximal descending aorta

**Diastole**
The balloon inflates and increases both systemic and coronary perfusion

**Systole**
The balloon deflates reducing the afterload and draws blood into the aorta
Short to intermediate-term MCS

ECMO
cardio-pulmonary by-pass used for some days to weeks
• bridge to recovery (BTR)
• bridge to decision (BTD) (bridging to long-term devices or to transplant or to DT)

The blood is drained from the venous system

flows through an artificial lung that adds oxygen and warms it to body temperature

is pumped back into the body either to the arterial or to the venous system depending on type of pump
59 year-old man who was implanted with a veno-arterial ECMO as BTT after an extensive antero-septal myocardial infarction due to acute thrombosis of left descending anterior coronary artery on a severe fibro-lipidic atherosclerotic plaque previously treated with angioplasty and stenting.

Twenty days later: heart transplantation

mid-apical aneurysm

ischemic lesion with an extensive haemorrhagic component
Extracorporeal membrane oxygenation as BTT

Histology

- recent coagulative necrosis
- irregularly distributed repair areas in different evolution phases (rich in macrophage inflammation)
Extracorporeal membrane oxygenation as BTT
Histology

Subepicardial tissue

ECMO-related extensive lymphocytic-macrophagic inflammation
57 year-old male with dilated cardiomyopathy
ECMO was positioned because of cardiogenic shock 20 days before transplantation

Extracorporeal membrane oxygenation
+ Venting of left ventricle

Vent catheter in the left ventricle
to completely unload the ventricle
Ventricular assist devices (VADs) are mechanical pumps that supplement or assume the function of the failing ventricles to restore normal circulation. Most frequently VADs are implanted to assist the left ventricle (LVADs) but they can also provide right ventricular (RVADs) or biventricular (BiVAD) support. RVADs are mostly encountered at autopsy or in native hearts, whereas the need for an isolated RVAD is extremely rare.
Ventricular assist devices (VADs)

The technology has advanced

- first-generation pulsatile pumps
- second- and third-generation continuous-flow blood pumps (centrifugal pumps and axial flow pumps)

- impressive survival rate improvement
- most frequently (over 90%) implanted devices

- bridge to recovery (BTR: typically LVAD)
- bridge to transplantation (BTT: LVAD or BiVAD)
- bridge to candidacy (BTC: usually LVAD)
- destination therapy (DT: LVAD)

Gen Thorac Cardiovasc Surg 2013; 61:111-7
Third generation LVADs

Various third generation centrifugal pump models

CorAide LVAS
HeartWare
HeartMate III
Before proceeding to dissection of a native heart with VAD or before autopsy of a VAD patient the pathologist should be familiar with

- the components of the device
- position with regard to the supported ventricle (left, right, or both)
- the main complications associated with VADs
Components of LVADs

- pump
- outflow cannula
- driveline
- controller system with power sources
- inflow cannula
Components of LVADs

- **pump** contains the **inflow cannula**, a tube inserted into the ventricular apex (or into the left atrium), which drains blood from the heart into the pump.

- **outflow cannula** returns blood to the aorta running from the LV apex to the ascending aorta along the extracardiac RV edge.

The **driveline** is an insulated electrical cable which exits the body from the device through an opening in the skin in the upper abdomen (right or left lateral abdominal quadrant).
Components of LVADs

Anastomosis of LVAD in the descending aorta

RVAD
- the inflow cannula is implanted into the right ventricle or right atrium
- the outflow cannula in most cases connects to the pulmonary trunk

Components of LVADs

The driveline is connected to a **digital controller**

- a microprocessor unit that manages the system sending power and operating signals to the blood pump and collecting information (text messages and audible alarms) from the pump
- two power sources for safe operation, usually two batteries (or one battery and an AC or DC adapter)

**Touch screen monitor** with proprietary software

- to display system performance
- to permit adjustment of selected controller parameters
Complications related to LVADs/MCSDs

Principal complications

- bleeding
- thromboembolism
- pump thrombosis
- infections (25-40% of cases)

Less frequent complications

- device structural failure
- right-sided cardiac failure
- air embolism
- progressive multisystem organ failure

Most important factors that disturb coagulation and can cause embolic or haemorrhagic strokes or major thromboembolic events:

- flow stagnation around the VAD cannula or diseased myocardium
- exposure to foreign surfaces (VAD cannulas and pump body)
- changes in coagulation balance
62 year-old male with idiopathic dilated cardiomyopathy who underwent LVAD implantation due to recurrent worsening heart failure. MCS had been held back for a week due to fever and PCR increase.

Hypovolemic cardiogenic shock following massive bleeding into the right pleural cavity and pericardial sac. No obvious source of bleeding at autopsy.
Autopsy investigation in presence of MCSDs

Area around the transcutaneous driveline exit site (including the abdominal wall pocket) should be examined first as it is one of the main entry points for bacterial and fungal infections which may spread along the driveline into the mediastinum.

VAD-specific or -related infections are difficult to treat as they cause the majority of sepsis related deaths.

Ann Cardiothorac Surg 2014; 3: 450-71
Circ Heart Fail 2011; 4: 779-84
Clin Infect Dis 2013; 57: 1438-48
Autopsy investigation in presence of MCSDs

1. *On opening the chest wall*

- dense fibrous adhesions with the mediastinum (particularly tenacious with the passage of time)
- pericardial sac: especially for adhesions between outflow cannula and epicardial surface in order to preserve the VAD components intact
Autopsy investigation in presence of MCSDs

2. After dissection of the pericardial sac

the heart can be removed and separated from all its vascular connections

at least 2 cm above the anastomosis between the outflow graft and the ascending aorta
3. Location of VAD components

- LVAD pump located at the left ventricle apex
- Inflow cannula protruding into the ventricle
- Outflow cannula running along the right ventricle edge (length, signs of tension and kinking)
- Driveline
Autopsy investigation in presence of MCSDs

4. To open the heart

Single transverse section through ventricular walls below the atrio-ventricular valve apparatus and above the apical cannula.

The outflow cannula can also be sectioned

- the base of the heart is opened in the direction of blood flow
- the atrial appendages checked for thrombi
Autopsy investigation in presence of MCSDs

- Exposition of the apical cannula
  - position in relation to the septum and inflow tract
  - distance from the free margin of the anterior mitral valve leaflet

Pump thrombosis
one of the most severe adverse events
Autopsy investigation in presence of MCSDs

The LVAD inflow cannula should be implanted in the LV apex directed towards the mitral valve

- good drainage
- low risk of suction
- optimal washout of the area
- no obstruction by myocardial structures (trabeculae, papillary muscle, left ventricle walls)

- anatomic structures obstruct the lumen of the apical cannula
- possible signs of suction on the endocardial surface in cases of suboptimal positioning
Autopsy investigation in presence of MCSDs

correctly implanted inflow cannulas

**Autoptic cases**
- 63 year-old male
- 50 year-old female

**Native hearts**
- 2 year-old child
- 35 year-old male
Autopsy investigation in presence of MCSDs

61 year-old male
native heart
cannula too close
to the LV inferior wall

1 year-old child
native heart
cannula correctly implanted
but hypertrophy of myocardial walls
has greatly reduced the LV cavity volume
Autopsy investigation in presence of MCSDs

5. Presence of antemortem thrombus within various parts of the VAD system

<table>
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<tr>
<th>Low flow can be caused by:</th>
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<tbody>
<tr>
<td>▪ an inflow opening near lateral or septal wall</td>
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<tr>
<td>▪ altered position of pump causing outflow cannula kinking</td>
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<tr>
<td>▪ angled outflow-graft</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Thrombus can be located in:</th>
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<tbody>
<tr>
<td>▪ the inflow section within or on the luminal surface of the inflow cannula (<strong>pre-pump thrombosis</strong>)</td>
</tr>
<tr>
<td>▪ the pump itself (<strong>pump thrombosis</strong>)</td>
</tr>
<tr>
<td>▪ the outflow graft (<strong>post-pump thrombosis</strong> or graft thrombosis)</td>
</tr>
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</table>
Autopsy case 2

60 year-old male with idiopathic dilated cardiomyopathy implanted with LVAD (Heartware HVAD model) as bridge to transplant.

Two months later

- mediastinal abscess and infection of the driveline by meticillino-resistant Staphylococcus Aureus

Surgery was required and one month later the LVAD alarm system indicated a possible pump thrombosis. Thrombolysis was ineffective and the patient died 1 week later.
Autopsy case 2

The lumen of the inflow cannula was occluded by thrombotic material.
Autopsy case 2

The outflow cannula was thrombosed in the plastic segment

- surrounding fibrous-fatty tissue showed widespread haemorrhagic inflammation
- numerous Gram+ bacterial colonies were present in the plastic tube
6. Long-term complications

Inflow cannula may become covered with fibrous tissue suggestive of re-endothelialization.
Autopsy investigation in presence of MCSDs

6. Long-term complications

Aortic valve

- presence of commissural leaflet fusion frequent with continuous-flow LVAD support depending on pump speed and mechanically induced remodelling of fibrous tissue

Figure 1: Cranial view of aortic valves after cf-LVAD support.
(A) No commissural fusion,
(B) one commissure fused with additionally some fatty streaks,
(C) two commissures fused leading to nodular displacement
(D) all the three commissures fused resulting in a drastic lumen size reduction.

Commissural fusion may lead to valve disruption and insufficiency and cause functional aortic stenosis affecting peripheral blood flow
Autopsy investigation in presence of MCSDs

6. Long-term complications

Mitral valve

- leaflet thickening
- shortening or fusion of the chordae tendineae
Coordinating autopsy: pathologist and bio-engineer

Forensic autopsies

50 year-old female with LVAD

Pump thrombosis

Medico-legal matter

- the alarm system had functioned correctly?
- the bio-engineer analysed all the computerized data from the controller
Cardiac reverse remodeling and myocardial recovery

- myocardial infarction
- inflammatory heart muscle disease
- cardiomyopathy
- conditions (pressure or volume overload)

Cardiac remodeling: changes in heart mass, volume, shape and function due to abnormalities in the biology of cardiac myocyte and extracellular matrix (HF phenotype)

Cardiac reverse remodeling indicates partial reversal of these abnormalities so leading to an improvement in heart geometry, mechanics and function

Douglas L. Mann & Daniel Burkhoff
Is myocardial recovery possible and how do you measure it?
Curr Cardiol Rep 2012; 14:293–298
Reverse remodeling can lead to normalization of molecular, cellular and myocardial changes with two possible clinical outcomes:

1. myocardial recovery, characterized by freedom from future cardiac events;
2. myocardial remission characterized by eventual recurrence of heart failure events

Myocardial Recovery and the Failing Heart
Myth, Magic, or Molecular Target?

Douglas L. Mann, MD,* Philip M. Barger, MD,* Daniel Burkhoff, MD, PhD†
St. Louis, Missouri; and New York, New York

JACC 2012; 60: 2465–72
Cardiac reverse remodelling and myocardial recovery

Cardiac recovery allowing the patient to be weaned off the VAD is much rarer than reverse remodelling.

Recovery

- aetiology of HF
- duration of HF
- patient age
- degree of myocardial fibrosis before VAD implantation

Acute myocarditis shows higher recovery rates than non-ischemic CMPs.

Recovery from ischemic heart disease is rather unusual.
Thank you for the attention