Agenda and Summary

ACvA Heart Failure Clinical Theme Online Workshop 1

Date: Thursday 20th October 2022
Time: 1:30 – 5pm AEDT
Zoom: https://us06web.zoom.us/j/86162733081?pwd=WVYwNWpmcEx0U01YVVRiYlN5YXBkUT09&from=addon

Attendees

Peter Macdonald (Facilitator)	David Playford	Preeti Choudhary
Aaron Sverdlov	Geoff Strange	Scott McKenzie
Andrea Driscoll	Ingrid Hopper	Sean Lal
Andrew Coats	Jamie Vandenberg	Sunita Jha
Andrew Sindone	John Atherton	Sze Yuan Ooi
Caleb Ferguson	Julee McDonagh	Tanya Hall
Chris Hayward	Liza Thomas	Tony Keech
Chris Reid	Nikki Bart	Walter Abhayaratna
David Hare	Louise Hickman	
David Kaye	Sally Inglis	

Apologies: Tom Briffa, Rachael Cordina, John Amerena, Robyn Clark, Ralph Audehm, Kim Delbaere

Agenda

Time	Program	Lead
1.30 – 1:35	Acknowledgement of Country and welcome *We would like to acknowledge the Traditional Owners of the many lands from which we are conducting this meeting and pay our respects to Elders past, present and emerging. We would also like to acknowledge the Traditional Owners' continuous connection to lands, water and community*	Jamie Vandenberg
1:35 – 1:45	Introduction to ACvA Clinical Themes Initiative	Jamie Vandenberg
	Setting the Scene	
1:45 – 1:55	Heart Failure in Australia	Tanya Hall
	Topics for Group Discussion	
1:55 - 2:00	**Topic 1: Systems of Care -** Use of Apps in & out of hospital care *What do we know, what don't we know, and where could we go?*	Sze Yuan Ooi Tony Keech Kim Delbaere Andrea Driscoll
2:00 - 2:15	**Group discussion** *What is the one big thing that would make a difference?*	
2:15 - 2:20	**Topic 2**: **Underlying Mechanisms** – HF-pEF *What do we know, what don't we know, and where could we go?*	David Kaye

2:20 – 2:35	**Group discussion** *What is the one big thing that would make a difference?*	
2:35 – 2:40	**Topic 3: Prevention & Screening** *What do we know, what don't we know, and where could we go?*	Geoff Strange
2:40 – 2:55	**Group discussion** *What is the one big thing that would make a difference?*	Geoff Strange David Playford
2:55 – 3:00	**Topic 4: Emerging causes of HF** *What do we know, what don't we know, and where could we go?*	Nikki Bart Liza Thomas Aaron Sverdlov Preeti Choudhary
3:00 - 3:15	**Group discussion** *What is the one big thing that would make a difference?*	
3:15 – 3:35	*Break*	
3:35 – 3:40	**Topic 5: Frailty/Cachexia** *What do we know, what don't we know, and where could we go?*	Julee McDonagh
3:40 – 3:55	**Group Discussion** *What is the one big thing that would make a difference?*	Julee McDonagh Caleb Ferguson Sunita Jha
3:55 – 4:00	**Topic 6: Management of Acute Heart Failure** *What do we know, what don't we know, and where could we go?*	Scott McKenzie John Atherton
4:00 - 4:15	**Group Discussion** *What is the one big thing that would make a difference?*	
Next Steps and concluding remarks		
4:15 – 5:00	Bringing it altogether - summary from group discussions Next Steps	Peter Macdonald

Heart Failure Workshop 1 Draft Summary
20 October 2022

Heart Failure in Australia

Heart failure causes 61,000 related deaths annually and affects more than half a million Australians with many more potentially diagnosed. It is the number one cause of hopsitalisation among Australians over 65 and results in $3.1 billion in healthcare-related costs and $2 billion in hospital care per year.

Heart failure is becoming increasingly common as more people survive heart attacks, live longer and experience heart issues that lead to this condition. Unfortunately, dangerously low levels of awareness about heart failure are leaving Australians vulnerable and there is an urgent need to improve under-diagnosis and under-treatment of Heart Failure.

Heart Failure Awareness Week was a campaign held this year to raise awareness and educate people about heart failure prevalence and symptoms and encouraging Australians to get their heart checked. The campaign also launched a patient and caregiver charter and designed and distributed GP resources to assist in assessing heart failure diagnosis and treatment in line with the latest international ESC guidelines. Through improved education and shared decision making between healthcare professionals, patients and caregivers, we can disrupt the cycle resulting in thousands of hospitalisations each year, but it will require a commitment from all stakeholders.

Topic Discussions

For each topic there was an expert Chair, who was tasked with setting the scene and leading the discussion. All were asked to consider “what do we know, what don’t we know and where we could go?”. A summary of the discussions from the six topics is provided below.

Systems of Care – Leveraging digital technologies to improve patient care (Sze-Yuan Ooi, Tony Keech, Andrea Driscoll)

Four studies were presented that demonstrated the use of digital technologies in improving patient care.

- BANDAI^{2}D^{2}S in HFrEF – Heart Failure guidelines (Tony Keech)
  - Using digitial technology to optimise uptake of medical therapy and dosing using a web-based app that offers personalised guideline care based on the patient’s phenotype and other co-morbidities with phone and SMS follow-up
  - Large-scale cluster RCT planned
- I-HEART study (Andrea Discoll)
  - Optimising HF treatment for disadvantaged patients and those living in remote, rural and regional (RRR) areas

- Co-design clinical decision support tools (e.g. telehealth, e-prescription) to improve uptake and utilisation of HF treatment and outreach services in RRR Australia

- TeleClinical Care (TCC) - HF study (Sze-Yuan Ooi)
  - Remote monitoring app for cardiovascular patients. Functionalities include:
    - Daily physiological measurements – backend monitoring analytics
    - Automated generation of alerts
    - Automated delivery of messages
    - Virtual exercise program (in collaboration with Kim Delbaere)
    - Cerner eMR integration
  - Pilot study demonstrated improved medication uptake and rehabilitation rates. In process of conducting NSW multisite RCT.
  - Formal implementation will be on Heart Failure patients in NSW
- CardiacAI Data Repository
  - Based on eMR data from cardiovascular, cardiothoracic and stroke patients
  - Comprises of retrospective data from 2017 and nightly prospective eMR data download
  - Data linkage with hospital re-admission data, mortality data
  - Funding received to link with TCC data
  - Funding received to add raw ECG data, imaging data into repository
  - Expanding to other Local Health Districts in NSW
  - Ultimate goal is for researchers to access this repository to build:
    - Clinical operational support tools
    - Clinical quality indicators
    - Clinical decision support tools
    - Pragmatic registry-based research studies including RCTs

<u>Key discussion points</u>

There is opportunity to 'piece together' the different apps and build a national app project with data linkage across different jurisdictions.

- The challenge with large amounts of data/clinical status reports is the clinical implementation
  - Regional, Rural and Remote (RRR) areas are a key site where access to care and capacity are limited e.g. GPs, specialised nurse practioners, nurses stationed at these sites
- An advantage of the digital models e.g. cardiacAI, which has a central admin team is that it 'frees up' the nurse practioners role and enables them to monitor patients and educate patients more efficiently

Underlying mechanisms – HFpEF (David Kaye)

What do we know? What don't we know? And where could we go?

1. Epidemiology – Need for accurate and timely population-level statistics on HF in Australia

- We are lacking up-to-date epidemiological data in Australia to inform treatment planning, particularly for those living in RRR areas where more granular data is required.

- There is opportunity to better define the profile of HFpEF in Australia through biomarker and/or imaging-based approaches
    - Widespread availability of NT-proBNP assays in GP clinics is key to achieving better diagnosis of HFpEF (the assay is currently not reimbursed – application submitted to MSAC)
        - Better education for GPs on the utility and accessibility of NT-proBNP assays
    - There is opportunity to incorporate risk scores, e.g. H2FPEF into GP clinics as a tool for the diagnosis of HFpEF, and link this to hopsitalisation and mortality data

2. Pathophysiology - Is HFpEF preventable? Can we reverse the biology of the ageing heart?

- HFpEF is a disease of ageing plus comorbidities e.g. hypertension, obesity, AF.
- Is HFpEF a disease that could be completely prevented with better and earlier treatment/prevention/control of these comorbidities? Or does it come down to the biology of the ageing heart?
    - What is the biology of the ageing heart?
        - This could focus on biology of fibrosis and the conduction system in a comprehensive way from animal models to clinical and imaging

3. Treatment – leveraging data linkages across the country to look for better treatment and prevention

- Despite recent SGLT2 trials, there are still patients that are difficult to treat.
    - Limitation of clinical trials that often focus on the effects of a single drug and not combination drugs.
- Opportunity to use tools to link PBS, imaging, hospital data and clinical records and investigate drug combinations that could be effective in treating HFpEF and lead to better treatment outcomes

<u>Key discussion points</u>

- We need better characterisation of the HFpEF population in Australia and its distinct pheontypes within the broader definition of 'HFpEF'
    - Better phenotyping of HFpEF patients (clinical, molecular, genetic level) can improve diagnosis and lead to more personalised treatments
    - NT-proBNP assay availabily is critical in RRR areas to achieve this
    - Opportunity to establish a National Heart Failure biobank

Prevention and Screening – NEDA (David Playford, Geoff Strange)

National Echo Database Australia (NEDA) – vendor agnostic database of ECHOs linked with mortality. Currently in the process of acquiring a larger dataset and incorporating AI.

- 45 contributing sites representing every state and territory of Australia
- ~2 million ECHOs broadly representative of the adult population undergoing ECHO –> enriched population of people undergoing ECHO as part of standard care
- Using this data, we have uncovered the treatable burden of disease e.g:

- LV ejection fraction and mortality
- Diastolic function and mortality

- There is a window of opportunity that can be leveraged using big data and AI to treat patients in a lower risk zone (lower cost of care with high impact of care) rather than the current zone of practice (high cost of care, high impact) (Figure 1).

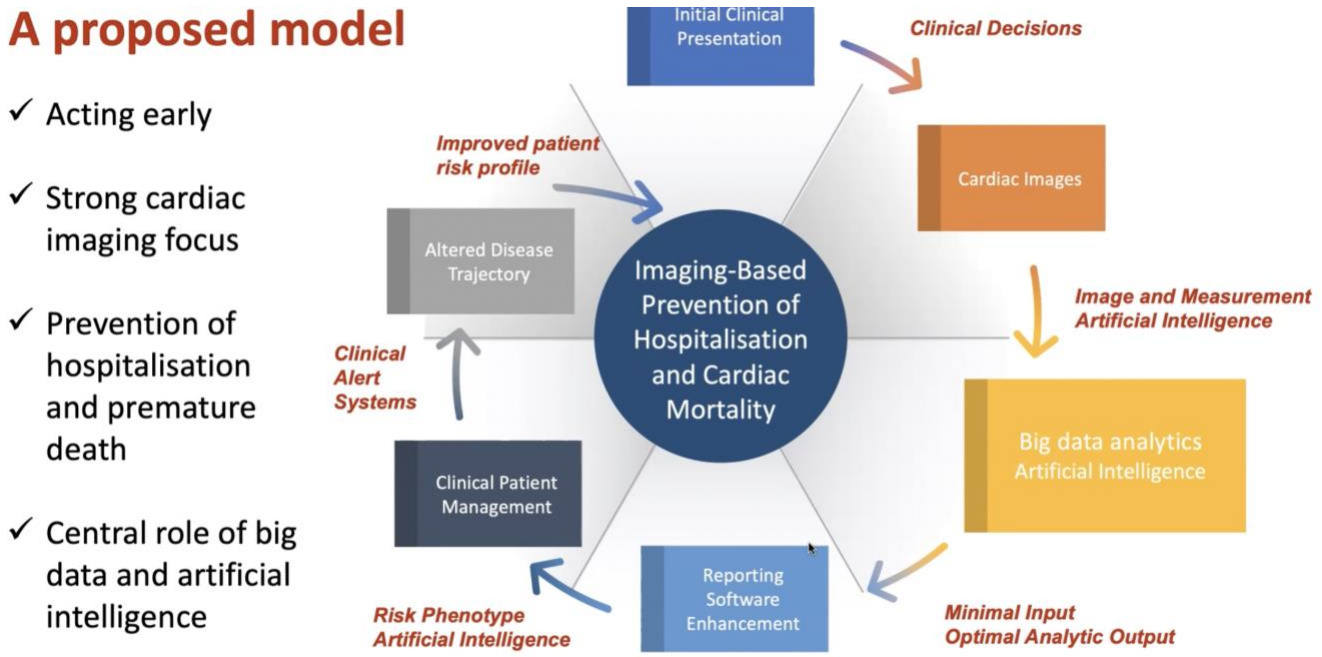


Figure 1. Intervening at the early stages of clinical presention and using cardiac imaging-guided therapeutic strategies to provide feedback on risk stratification models and patient management to alter disease trajectory and improve patient risk profile (through therapeutic/lifestyle changes) rather than waiting for the evolution of disease to drive care, thereby minimising hospitalisation and cardiac mortality.

<u>Key discussion points</u>

- There's been an underlying theme to <u>shift the dial towards earlier detection at the at-risk stage of disease rather than when they've got established heart failure</u>.
  - The NEDA strategy is to give a quantification to the modifiable risks that are often ignored and allow people to understand that they are already early signs of heart failure to change behaviour and limit hopsitlisation and large costs later on
- The next stage would be to implement automated ECHO as a routine screening tool that is more cost effective in high-risk populations and pairing with biomarkers
- Future ECHO systems will be fully automated and have the capability to direct the user to the correct location for image acquisition and analysis and produce personalised risk stratification

Emerging causes of Heart Failure (Aaron Sverdlov, Nikki Bart, Liza Thomas)

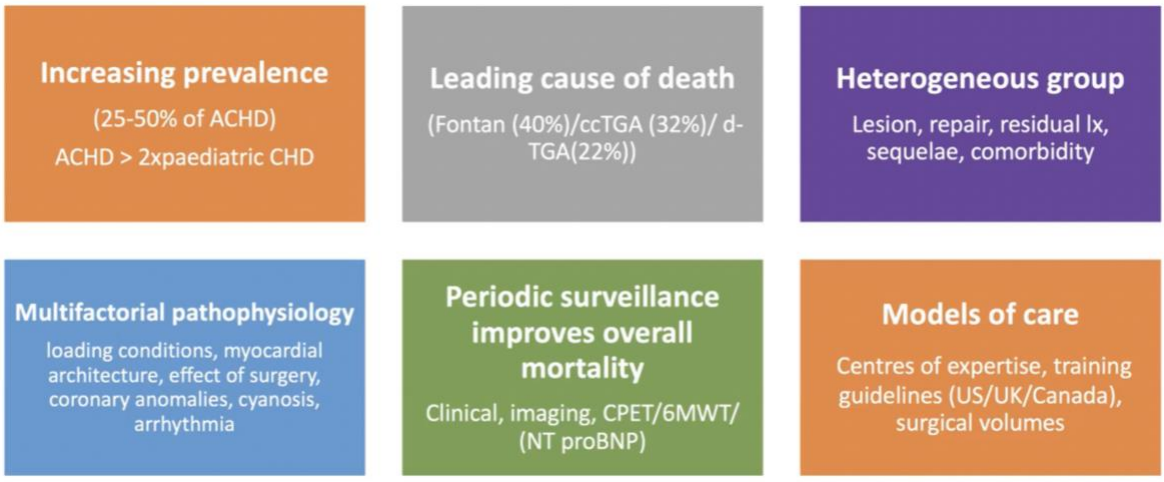
Three emerging areas were presented. They are often under-diagnosed and under-reported and mislabelled as 'rare' diseases, but clinical incidences are rising.

1. Cardio-oncology – focused on the CV health of cancer patients and survivors
   - Advancements in cancer therapy and treatment have resulted in increased survival rates (70%) for all malignant cancers in Australia. This translates to 2 million Australians by 2050. However, CV complications such as ΔLVEF as a result of chemotherapy agents used is not uncommon
   - 2022 ESC guidelines were recently released – 272 recommendations but only 5 Level A recommendations with the majority being Level C.
   - Early detection is key to improved treatment outcomes – biomarkers, imaging, appropriate monitoring

2. Cardiac amyloid
   - Diagnosis of cardiac amyloid have increased as a result of improved detection methods. Recognition that disease prevalence is higher than once thought. However, most therapies are not evidence-based and some can make the disease worse.
   - Early detection with genetic testing, biomarkers and imaging is key

3. Adult congenital heart disease (CHD)

   - What is known?



   - Gaps in adult CHD heart failure
     - No universal risk score to capture deterioration
     - Lack of true denominator – referral, publication bias loss to follow-up between childhood to adulthood, fragmentation of care

- Sparse evidence for GDMT
- Role of biomarkers – biomarkers need further validation
- Distinguishing structural vs myopathic CHD
- Transplantation – selection and timing

Key priority areas

- Early diagnosis – biomarkers, imaging
- Quality use of medicines – informed by guidelines and evidence
- Registry – capture true incidence/prevalence; incorporate biomarkers, imaging data
- Establish minimal standards of care
- Transplantation – selection and timing

Key discussion points

- Early diagnosis is key – genetic testing, establishing registeries, incorporating AI as a prediction tool for early detection (e.g. using ECG and ECHO data)
  - AI could go a long way to 'trigger' the consideration of these alternative diagnoses
- Increasing awareness and education is also important
- What is the role of stress ECHO e.g. exercise in early assessment for these patients?
  - In adult CHD, there is clear evidence that cardiopulmonary exercises is beneficial for earlier detection of heart failure and timing of mechanical intervention. Have not tested on stress ECHO due to lack of availability
- The Congenital Heart Alliance of Australia and New Zealand (CHAANZ) and Heart Research Institute are working on a project with that has brought together nearly 60,000 patients across the country and this may be an ideal population to incorporate ECHO data and utility to monitor progression to heart failure.
- There are many AI programs working on amyloid detection that can be leveraged if there is interest to use AI imaging guided thought processes earlier for disease detection.
- Cardiac sarcoidosis is also another emrging cause that a collaborative approach can be used to gain insights on on prevalence/incidence

Frailty/cachexia (Julee McDonagh, Sunita Jha, Caleb Ferguson)

- Frailty is a complex clinical syndrome of increases vunerability to acute stressors. It's driven by altered stress response systems and age-related molecular changes resulting in 'accelerated aging'. Considered as a pre-disability state that is potentially reversible.
- There are multiple definitions of frailty syndrome. The two broad concepts are:
  - (Fried's) Biologic driven frailty – due age related decline e.g. physical activity, muscle strength, weight loss, energy levels, walking speed
  - Deficit driven frailty – due to accumulating deficits across multiple domains of human function e.g. social vunerability, medical conditions, functional decline, depression, nutrition, cognition

What do we know?

- Frailty is highly prevalent in heart failure patients and is an independent predictor of rehospitalisation and mortality.
- Frailty and Heart Failure are strongly linked and are potentional drivers of each other
- There are over 60 different tools that can be used to assess frailty
    - The frailty phenotype is the most commonly used instrument for the HF population and takes ~10min
    -

What don't we know?

- There's a lack of consensus on what is the best instrument to use, making the comparison of outcomes between studies difficult
- Routine assessment of frailty is yet to be embedded in clinical practice
- Need more frailty-focused studies in heart failure in Australia

Where could we go?

- Routine frailty assessment should be implemented for all HF patients for risk stratification and to guide clinical management
- Further studies regarding strategies to improve and/or reverse frailty in patients with HF is urgently needed

<u>Key discussion points</u>

- ISHLT consensus statement has recently been sent for review - focused on coming to a consensus on the definition of frailty and heart failure and the instrument that would be recommended for implementation to use for heart failure patients. Conclusions:
    - Need to implement an assessment tool – recommended tool based on physical assessment
    - Purpose and timing of when the frailty assessment is conducted e.g. population screening vs comprehensive assessment for transplantation
- Implementation of frailty screening needs to be part of routine practice and using a tool is a good start but also what inteventions (Exercise, rehabilitation, diet) can be done to potentially reverse it
    - Strengthening and resistance training exercises have shown to be beneficial for patients
    - The Standing Tall app (Kim Delbaere) provides a variety of exercises that can be titrated based on the patient's capability and confidence level

Management of acute heart failure (John Atherton, Scott McKenzie)

What we know and don't know

- Current guideline recommendations for the management of acute heart failure in Australia (pharmacological interventions) is based on low or very low quality of evidence

- Acetazolamide in Decompensated heart failure with Volume OverRload (ADVOR) study – evaluated the use of acetazolamide as an adjunctive therapy with loop diuretics for the management of heart failure. Study was positive and achieved the primary endpoint: congestion score ≤1 at Day 3.

  Limitations:
  - Not powered for clinical outcomes
  - PROMs not reported
  - Single country study

What could make a difference?

- Safely achieve decongestion
  - Acetazolamide escalation study in acute HF powered to asses clinical beenfits beyond hospital discharge

Proposal: AARDVARC study

Proposal: Australian Acute heart failure Resistant to loop Diuretics with Volume overload Acetazolamide Rx Comparison (AARDVARC) study

- **Population**
  - AHF with clinical congestion and NTproBNP >300/600 (SR/AF)
  - Received at least 40mg IV furosemide
  - Spot U_{Na} <70 mmol/L
- **Intervention**
  - Add IV acetazolamide 500mg/d until no clinical congestion
- **Comparator**
  - Placebo
- **Outcome**
  - Win ratio (Time to death/ Hosp. days/ KCCQ TSS at 30d)
  - NT-proBNP at 30d

- Start disease modifying therapies
  - Rapid escalation of disease-modifying therapy following actue HFrEF hospitalisation

Proposal: REACH study

Proposal: Rapid **E**scalation following **A**cute heart failure decompensation of **C**ombination **H**FrEF therapy (REACH) study

- **Population**
  - AHF with clinical congestion and NTproBNP >300/600 (SR/AF)
  - LVEF ≤40% (or <50%)
- **Intervention (cluster RCT)**
  - SGLT2I + MRA (Day 1)
  - Add ARNI (if SBP >90 mmHg) or ACEI (Day 2)
  - Add BB (if euvolaemic) (from Day 3)
- **Comparator**
  - Standard care
- **Outcome**
  - ARNI+BB+MRA+SGLT2 prescription rate at 30d
  - Win ratio (Time to death/ Hosp. days/ KCCQ TSS at 90d)
  - NT-proBNP at 90d

Key discussion points

- Two approaches can be taken with the REACH study: develop alogrithms and track one vs another, or provide instructions and let physicians to use their clinical judgement patient profiling and look at an accelerated vs normal treatment pathway
- The REACH study could also be extended to investigate a much faster pathway for the uptitration to optimal dosage of medication post-discharge
- A challenge will be empowering GPs to uptitrate medication on behalf of heart failure clinicians
  - A shared care model has been more successful e.g. with the patient, heart failure cardiologist and nurse practitioner
  - Education and training of GPs required

'Big picture' idea

Develop and establish a national heat failure registry that could allow for deep phenotyping and be incorporated into clinical trials

- Linked to imaging and biomarker platforms
- Need to include high-risk populations (RRR areas, First Nations peoples)
- Could leverage existing infrastructure e.g. CardiacAI, NEDA, QCOR
- Proof of concept could integrate the registry to to the trials proposed by John Atherton
  - the BANDAI^{2}D^2, TCC and I-HEART apps could be incorporated

- emerging causes of HF could be framed as the clinical problem to be addressed where a registry would be helpful

Key Considerations

- Need a clinical problem to be addressed
- National collaboration is key
- Important to not duplicate, and instead to leverage existing platforms e.g. CardiacAI, NEDA and QCOR
- Involving consumers in the co-design will be important

Identified project leads

- Sze-Yuan Ooi
- David Playford
- Tony Keech
- Julee McDonagh
- Ingrid Hopper
- John Atherton

Next steps

- ACvA to arrange a follow-up meeting with project leads in the next two weeks to further develop the 'big picture' idea, including identifying an overaching clinical problem to be addressed.