Red Whale

The GP Update Handbook

2018

Abbreviations used in the GP Update Handbook

We try to avoid using abbreviations except where they are universally recognised (MI, COPD). The only exceptions to this are the abbreviations of some of the journals we use:

AFP	Australian Family Physician
AMH	Australian Medicines Handbook
Ann. Int. Med.	Annals of Internal Medicine
Arch. Int. Med.	Archives of Internal Medicine
BJGP	British Journal of General Practice
BMJ	British Medical Journal
DTB	Drugs and Therapeutics Bulletin
JAMA	Journal of the American Medical Association
MeReC	National Prescribing Centre Bulletins *(not exactly an abbreviation!)*
NEJM	New England Journal of Medicine
NICE	National Institute for Health and Clinical Excellence
RACGP	Royal Australian College of General Practice
SIGN	Scottish Intercollegiate Guidelines Network

Statistical abbreviations are listed in the statistics chapter.

A note on Cochrane references

Cochrane reviews are referenced as: Cochrane 2005;CD002946. Go to www.cochrane.org (NOT cochrane.co.uk!) and type the 'article number' without the date (e.g. CD002946) into the search engine.

At the end of each section in the Handbook you will find a summary box, which include the key take home messages, some ideas to help you apply your learning and some useful websites.


This icon occurs where we list **Take home messages**


This icon occurs where we list possible ideas for **CPD actions**

This icon occurs where we list **Useful websites**


This icon shows where you can add your own **Notes**

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature, and this should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular you should check drug doses, side-effects and interactions with the manufacturer and with the relevant National Formulary for Australia. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages.

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Welcome to the GP Update Handbook

Following on from successful courses in 2016 and 2017, Primary Care International is delighted to offer this series of one-day GP Update courses in Australia once again in 2018. Primary Care International is a sister organisation of Red Whale|GP Update who have a proven track record in delivering high quality education for primary care clinicians in the UK, with around half of all British GPs attending our courses every year.

In 2014, Red Whale|GP Update set up a social enterprise, Primary Care International, to extend its reach outside of the UK. Revenue from GP Update courses delivered in settings such as Australia will be used to support PCI's operational costs as it develops projects in low and middle-income countries. PCI partners with organisations such as WHO and Médecins Sans Frontières among others, to deliver health worker training on Non-Communicable Diseases in refugee camps and other humanitarian settings, and partners with local health organisations in developing contexts to test new approaches to primary care through a Healthcare Innovation Programme.

For this series of courses, we have once again been working with local partners to adapt our resources to the Australian context. We are well aware that in the current climate, new evidence is constantly emerging resulting in frequent guideline changes: as a result, it can be difficult for even the most dedicated of GPs to keep up. However, help is at hand as we have done the legwork for you by trawling through the journals to bring you up to speed on the latest issues, literature, research and guidelines in Australian General Practice. Everything that you will learn on our fun and entertaining courses (plus more!), is covered in this handbook so that you can reinforce your learning and reference the relevant information when you need it. We hope that this will prove to be a valuable resource in helping you to deliver the best care for your patients.

We are again pleased to be able to add topics from the Royal Australian College of General Practitioner (RACGP) Handbook of Non-Drug Interventions (HANDI) to the GP Update course. HANDI has been led by Professor Paul Glasziou and the RACGP HANDI Project team over a number of years. Non-drug interventions include physiotherapy, exercise, devices and use of apps. HANDI aims to make effective non-drug treatments more visible and easier to use, making 'prescribing' a non-drug therapy almost as easy as writing a prescription. Every intervention is supported by evidence. We are grateful to Professor Glasziou, the Project team and the RACGP for allowing us to use this material. The resource is also available online at: www.racgp.org.au/your-practice/guidelines/handi.

This course is delivered in partnership with HealthCert, Australia's leading provider of certified and accredited education for medical professionals. HealthCert is an authorised provider of accredited activities under the RACGP QI&CPD Program.

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CATEGORY 2

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Chronic heart failure

Heart failure affects about half a million Australians and costs our economy $1 billion annually (MJA 2013; 199:334; Lancet 2009;373:941). GPs play a key role in diagnosing and managing this condition.

Heart failure: prevention and hypertension

Hypertension is a contributory cause of CHF in approximately two-thirds of cases. So can hypertension control reduce the development of heart failure and if so are any drugs better at doing this than others?

This meta-analysis of almost a quarter of a million patients with hypertension (in 26 trials), looked at exactly this question (Arch Intern Med 2010, doi:10.1001/archinternmed.2010.427).

- Diuretics were the most effective drug at reducing the risk of developing heart failure (odds ratio 0.59, CI 0.47–0.73). Interesting given that they have been relegated to third line in the new NICE hypertension guidelines!
- ACE inhibitors/ARBs were the next most effective (OR 0.71 and 0.76, respectively).
- Calcium channel blockers, beta-blockers and alpha-blockers were the least effective at preventing the onset of CHF.

Terminology

There are two types of heart failure (Editorial 2009;338:b52):

Left ventricular systolic dysfunction (LVSD): the breathless patient with a large flabby heart that contracts poorly (as the editorial so beautifully put it!).

Heart failure with preserved ejection fraction (HFPEF): previously called diastolic failure. The breathless patient with normal LV ejection fraction but with left ventricular hypertrophy and left atrial enlargement on echo and raised atrial pressure (the latter diagnosed on echo or by raised natriuretic peptide) (European Society of Cardiology diagnostic criteria).

Why might the differences arise?

The editorial suggests that most LVSD is caused by infarction, whereas heart failure with preserved ejection fraction is mainly caused by diabetes and hypertension.

Infarction triggers significant remodelling, whereas hypertension and diabetes promote only slow and gradual remodelling. Although the latter process may eventually end in a picture of LVSD, in the interim you may see a picture of heart failure with preserved ejection fraction.

Importantly:

- **More people worldwide are admitted to hospital with heart failure with preserved ejection fraction than are admitted with systolic heart failure.**
- **Mortality is similar for both types of failure.**
- **Recognition of preserved ejection fraction heart failure is poor.**
- **There have been few trials of therapy in those with heart failure with preserved ejection fraction (most require LVSD as a condition of entry).**

Guidelines for the prevention, detection and management of chronic heart failure

In October 2011 the Heart Foundation updated its guidance on the prevention, diagnosis and management of heart failure. The key messages from this guideline include:

- **All patients suspected of having CHF should have an ECG, chest X-ray, echocardiogram, FBE and UEC** even if physical examination is normal.
- **Ideally GPs should obtain a specialist opinion for all people with CHF** as research indicates specialist involvement is associated with improved outcomes and fewer hospitalisations (although this could be quite a challenge in practice, especially for those living in rural settings!).
- **ACE inhibitors and beta blockers are first line therapy.**

Self-weighing

Patients are recommended to weigh themselves every morning (after waking and voiding, but before dressing and eating).

- **Any weight gain of more than 2kg over 2 days should be reported to the GP, specialist or heart failure nurse (time to increase the diuretics for a few days).**

I've found this really useful in some of my patients with moderate–severe heart failure as a way of catching deteriorations early and preventing admissions. I don't use it in mild disease, as these people rarely end up in hospital.

Does it matter which beta-blocker?

Cardio-selective beta-blockers (e.g. bisoprolol and carvediol) are now widely used for heart failure. But are they any better than older beta-blockers such as atenolol and metoprolol? The latest data suggests not!

This meta-analysis of 23 000 patients with heart failure concluded that (BMJ 2013;346:f55):

- **No one beta-blocker was better than another. This is a class effect.**
- Reminded us of the benefits of beta-blockers over placebo in reducing all-cause mortality in heart failure (NNT 15 to prevent one death, although no time frame is given, I think the time frame is 12m given the other data).

The editorial concluded that 'some beta-blocker is better than no beta-blocker' (BMJ 2013;346:f480).

Diagnosis of chronic heart failure

Diagnosis of chronic heart failure

If CHF is suspected from the history and examination then investigate. All patients should have an ECG, chest X-ray, echocardiogram, FBE and UEC. Measurement of serum natriuretic peptide (BNP or N-terminal proBNP; a hormone secreted by the left ventricle in response to stress) may be useful in people with new symptoms, where the diagnosis is unclear following initial assessment and there is a delay in obtaining an echocardiogram.

- If levels of natriuretic peptide are NORMAL then heart failure is unlikely: consider other diagnoses.
- If levels are ABOVE NORMAL, further assessment and echo is required. The UK NICE guidelines remind us that there are a number of conditions that can cause 'false positives' (raised natriuretic peptide but no failure). These are as follows:
  - LVH
  - Ischaemia
  - Tachycardia
  - Right ventricular overload
  - Hypoxaemia (including PE)
  - COPD
  - Diabetes
  - Cirrhosis
  - eGFR <60
  - Age >70y
  - Sepsis

Natriuretic peptide may be lowered (causing false negatives) by:

- Obesity
- Drugs (diuretics, ACE inhibitors/ARBs, beta-blockers, aldosterone inhibitors).

A BMJ clinical review reminds us that in the presence of a normal BNP and ECG heart failure is HIGHLY UNLIKELY (BMJ 2013;346:f2442).

After echo, failure will be classified as either:

Systolic dysfunction (typically an LV ejection fraction <40%); LVSD

OR

Heart failure with preserved ejection fraction (HFPEF) /diastolic dysfunction, i.e. symptoms of CHF with an LV ejection fraction >45%.

Management of chronic heart failure

- **Throughout take a multidisciplinary approach with education, lifestyle changes and rehabilitation.** Stop smoking, annual flu jabs and pneumococcal immunisation (note: the number of injections required depends on age at diagnosis; refer to the Australian Immunisation Handbook). Regular physical activity is associated with improved clinical outcomes and quality of life. Ideally this should occur in a structured or rehabilitation program.
- **Diuretics** used for symptom control (congestion and fluid retention). Titrate up and down as necessary.
- The Heart Foundation guidelines are somewhat unclear as to whether aspirin should be prescribed to reduce the risk of further cardiovascular disease. However, NICE guidelines provide some clarity: **Aspirin** should be offered if failure AND atherosclerotic arterial disease (e.g. CHD, TIA) *(so, those with non-atherosclerotic valve disease but with failure do not need aspirin).*
- **Drug therapy depends on whether it is failure with LVSD or with preserved ejection fraction.**

For those with failure with LVSD:

- **Offer both ACE inhibitors AND beta-blockers (those licensed for heart failure) as 1st line therapy.**

- **For ACE inhibitors:** Australian Medicines Handbook (AMH) recommends to start low and titrate upwards at 2–4w intervals, measuring U&Es and eGFR prior to initiation and 1–2w after every dose increase. Use ARBs if ACE inhibitors not tolerated.
- **For beta-blockers:** AMH and Therapeutic Guidelines recommend the use of bisoprolol, carvedilol, controlled release metoprolol succinate or nebivolol (stable heart failure, aged >70y).

  AMH suggests:

  'Start low and go slow': check pulse, BP and clinical status after each titration.

  For those on a beta-blocker for another indication (e.g. atenolol for hypertension), swap them to a beta-blocker recommended for heart failure. These beta-blockers can and should be used in those with COPD (without reversibility), diabetes, interstitial pulmonary disease, peripheral vascular disease and erectile dysfunction.

  The DTB reviewed the evidence for cardioselective beta-blockers in COPD. Although most heart failure trials exclude people with COPD, what evidence there is from retrospective observational studies (often in people with COPD with acute coronary syndrome or undergoing major vascular surgery) shows that cardioselective beta-blockers lower mortality in those with COPD & CVD. **The DTB therefore says that patients with COPD and CVD should not be denied the potential CV benefits of cardioselective beta-blockers** (DTB 2011;49(1):2).

If symptoms persist despite above, seek specialist advice. The following can be considered as add-on therapy:

Aldosterone antagonist licensed for heart failure (AMH and Therapeutic Guidelines indicate spironolactone and eplerenone are suitable)

- Aldosterone antagonists are particularly used if NYHA ≥2 with persistent oedema despite the use of ACE inhibitors and diuretics.
- Monitor U&Es. Seek specialist advice if hyperkalaemia develops or renal function deteriorates.

Adding ARB licensed in heart failure (Therapeutic Guidelines indicate candesartan and valsartan are suitable)

- Use if unable to tolerate ACEI. Heart Foundation states that ARBs can also be considered for patients who remain symptomatic despite the use of ACEI. Generally, the combination of an ACEI and an ARB is not recommended so I would seek specialist advice regarding this (see section below on "What about combining an ACE with an ARB?")
- Monitor U&Es and eGFR.

Hydralazine and nitrate in combination may be used by specialist if:

- Severe symptoms (NYHA Class 4) not responding to first line therapy
- African or Caribbean in origin
- Intolerant of ACE and ARBs

- **If symptoms persist consider cardiac resynchronisation (+/– implanted defibrillator) or digoxin.**

For failure with preserved ejection fraction:

- Manage co-morbidities (hypertension, IHD, diabetes, etc.)
- Refer for specialist assessment.
- Drug therapy. There is a much smaller evidence base for drug therapy in heart failure with preserved ejection fraction (discussed later). Diuretics should be used if fluid overload. Conventional therapies for LVSD are often used in this group although the evidence suggests that some of these drugs, including ACE/ARBs may not be beneficial. Other drug therapy is based on specialist recommendation; however, we note that many (e.g. those with hypertension/diabetes) will already be on ACE inhibitors/beta-blockers.

Long-term monitoring of those with heart failure

Australian guidelines don't state how often people with CHF should be monitored, however, NICE guidelines suggest 6 monthly if stable and more frequently if clinical deterioration or titrating therapy.

Routine review should include:

- **Clinical assessment:**
  - Functional capacity
  - Cardiac rhythm
  - Cognitive status
  - Nutritional status
  - U&Es and eGFR.

Serum natriuretic peptide not recommended routinely as part of review process, but may be indicated for those in whom uptitration is difficult or those admitted to hospital.

- **Look for and manage anxiety and depression.**

End of life care

Ensure patients given the opportunity to talk about the issues of sudden death and living with uncertainty at all stages of the illness. Identify any palliative care needs.

New York Heart Association classification of heart failure

New York Heart Association (NYHA) classification of heart failure	
Grade 1	No limitation. Ordinary physical exercise causes no problems.
Grade 2	Slight limitation of physical activity: comfortable at rest. Ordinary activity causes fatigue, dyspnoea or palpitations.
Grade 3	Marked limitation of physical activity: comfortable at rest but less than ordinary physical activity causes symptoms.
Grade 4	Symptomatic at rest. Unable to carry out any physical activity without discomfort.

What drugs for failure with preserved ejection fraction?

This editorial reviews the few trials that have included patients with preserved ejection fraction failure (for references for each of these studies please go to the editorial) (BMJ 2009;338:b52).

ACE inhibitors or angiotensin receptor blockers (ARBs)

- The CHARM study (candesartan) showed that an ARB reduced admissions with heart failure but not mortality.
- A larger RCT (4000+ patients) showed that an ARB (irbesartan) did not improve cardiovascular or all-cause mortality in these individuals.
- The editorial highlights that the lack of benefit from ACE and ARB is surprising given what we know about how they work and their benefits in LVSD.

Diuretics

- A smaller RCT showed diuretics improved symptoms and quality of life but that adding in an ACE or ARB gave no additional benefit.

Spironolactone

- A large RCT of almost 3500 patients with HFPEF showed that spironolactone (versus placebo) had no impact on cardiovascular mortality, but did reduce hospitalisation for failure. No serious harms were reported from using spironolactone in these patients (NEJM 2014;370:1383).

Drugs in CHF: what are the optimum doses? Does it matter?

The National Heart Failure Audit in the UK showed that many people with CHF are on sub-optimal doses of their medications. However, the Heart Foundation guidance does not specify optimum or target doses, although it does imply we should 'titrate up' the dose of both ACE inhibitors/ARBs and beta-blockers.

Therapeutic Guidelines define 'target' doses as shown below:

Drug	Starting dose	Target maintenance dose
ACE inhibitors		
Captopril	6.25mg twice daily	25–75mg twice daily
Enalapril	2.5mg daily	10–20mg twice daily
Fosinopril	5mg daily	20–40mg daily
Lisinopril	2.5mg daily	20–40mg daily
Perindopril arginine	2.5mg daily	5–10mg daily
Perindopril erbumine	2mg daily	4–8mg daily
Quinapril	2.5mg daily	20–40mg daily
Ramipril	1.25mg daily	5–10mg daily
Trandolapril	0.5mg daily	2–4mg daily

Drug	Starting dose	Target maintenance dose
Angiotensin 2 receptor blockers		
Candesartan	4mg daily	8–32mg daily
Eprosartan	400mg daily	600–800mg daily
Irbesartan	75mg daily	150–300mg daily
Losartan	25mg daily	50–100mg daily
Olmesartan	10mg daily	20–40mg daily
Telmisartan	40mg daily	60–80mg daily
Valsartan	20mg twice daily	40–160mg twice daily
Beta-blockers		
Bisprolol	1.25mg daily	10mg daily
Carvedilol	3.125mg twice daily	25mg twice daily
Metoprolol succinate controlled release	23.75mg daily	Increase to highest tolerated dose, up to maximum of 190mg daily
Nebivolol	1.25mg daily	10mg daily

Does dose matter?

A meta-analysis looked at those on beta-blockers for heart failure to see whether dose or resting heart rate was more important in terms of reducing mortality. Almost 20000 patients (in 23 trials) were included (Ann Int Med 2009;150:784).

- **For every 5bpm reduction in resting heart rate with beta-blockers there was an 18% reduction in risk of death (CI 6–29%).**
- **There was no correlation between dose and death, i.e. those on high doses were no less likely to die than those on low doses.**

Now there are limitations to a study such as this – calculations are based on aggregate data, not individuals, so you cannot say that lowering the pulse of the person in front of you by 5bpm will reduce their risk of death by about 20%, **but the study does suggest that reduction in resting pulse is more important than the actual dose.**

Dose of ACE in CHF

A trial of losartan suggests dose might be important. Over 3500 patients with heart failure were randomised to losartan 150mg or 50mg daily. Follow-up was for a median of 4.7y. All were intolerant of ACE inhibitors (Lancet 2009;374:1840).

The study showed that higher doses of losartan were associated with:

- No change in mortality rates (hazard ratio 0.94, CI 0.84–1.04).
- Reduced risk of admission for heart failure (hazard ratio 0.87, CI 0.76–0.98).

BUT there were more adverse events in the higher dose group (renal impairment, hypotension and hyperkalaemia), although this did not lead to significantly different discontinuation rates.

Beware the composite endpoint!

This paper also used a composite endpoint of death or admission with heart failure – which was (just!) statistically significant, but you can't really compare dying with admission to hospital, can you? And in fact the benefit was entirely due to reduction in admissions, not deaths – but beware – the makers of losartan could quite accurately say that 'losartan reduces deaths and admissions from heart failure…'.

And more recently a cohort study in Canada compared those with heart failure on high to moderate dose ACE/ARBs with those on low dose (Arch Intern Med 2012;172:1263). They found that higher doses resulted in lower mortality (HR 0.88, CI 0.79–0.98 for ACE and similar for ARBs).

What does this mean in practice?

I try to titrate patients up to target doses, provided they can tolerate the drug.

What about combining an ACE with an ARB?

There are some theoretical benefits to combining an ACE and ARB in heart failure (and other conditions), and this is increasingly seen in clinical practice. But does this translate into clinical benefit? No! In fact it may result in harm!

This meta-analysis combined 33 RCT (almost 70000 patients) and looked at safety (adverse incidents over 4w) and efficacy (over 12m). Some trials were for heart failure and others were for other cardiovascular disease (including hypertension) (BMJ 2013;346:f360).

Compared with monotherapy (either an ACE or an ARB), dual therapy (both an ACE and an ARB) was associated with:

- No difference in all-cause mortality.
- No difference in cardiovascular mortality.
- A significant reduction in admissions to hospital with heart failure, mainly in the heart failure cohort (18% relative reduction).
- A significant increase in hyperkalaemia (55% increased risk) and hypotension (66% increased risk) and over 1 in 4 stopped therapy because of adverse events.
- **The authors concluded that the harms of dual therapy outweigh the risks, particularly in those without heart failure, who get harms with no real benefit.**

Aspirin and warfarin in heart failure

Heart failure is associated with a hypercoagulable state, and therefore it has been suggested that oral anticoagulation/antiplatelets might reduce CV-related morbidity and mortality.

This trial (NEJM 2012;366:1859) was an RCT of just that. It recruited 2300 patients with heart failure (LVSD) and randomised them to aspirin (325mg) or warfarin (target INR 2–3.5) and followed them over 6 years – so a big long-term study. All were in sinus rhythm, so this was not treating unidentified AF!

- There was no significant benefit between aspirin or warfarin over the trial, except that warfarin was associated with a slightly lower stroke rate, offset by a higher risk of major haemorrhage.
- **The editorial concludes that the benefits of warfarin in those with heart failure (in sinus rhythm) are too low to justify routine use because of the increased bleeding risk.**

Drug dilemma: spironolactone with ACE inhibitors/ARBs

As a result of 3 fatalities due to hyperkalaemia with concomitant spironolactone and ACE inhibitor/ARB use, the MHRA has issued the following advice (MHRA Drug Safety Update February 2016):

- Concomitant use of spironolactone with ACE inhibitors/ARBs is not recommended, especially if marked renal impairment.
- If co-administered use the lowest possible dose.
- Regularly monitor serum potassium and renal function (they don't specify what 'regularly' means!). Stop treatment if hyperkalaemia occurs.

The AMH states that a potassium level of >5mmol/L is a contraindication to commencing spironolactone. They also suggest checking renal function and potassium at baseline, within 1w, monthly for the first 3m after starting or changing dosage, every 3m for a year and then every 4–6m or when clinically indicated. Dose reduction is also recommended for creatinine clearance 30–50ml/min.

Sacubitril–valsartan (Entresto): a new drug

Sacubitril–valsartan is available in Australia but is not currently on the PBS. It is indicated for heart failure (NYHA class II–IV) with reduced ejection fraction (but not heart failure with preserved ejection fraction).

It must not be used alongside an ACE inhibitor or another ARB (high risk of angioedema).

Pharmacology

- This is a new class of drug called ARNI (angiotensin receptor–neprilysin inhibitor).
- 26mg of valsartan in this combination is equivalent to 40mg in other products.
- Sacubitril is a neprilysin inhibitor.

- Neprilysin inhibition increases the concentration of natriuretic peptides which:
  - Improves vasodilatation
  - Reduces sympathetic drive
  - Inhibits the renin–angiotensin system
  - Has anti-hypertrophy effects.

What is the evidence?

The evidence for sacubitril–valsartan comes from the Paradigm HF trial (NEJM 2014;371:993). Over 8000 patients with stable heart failure were randomised to receive either sacubitril–valsartan or enalapril (10mg twice daily – the 'target' dose for enalapril as defined by the European Society of Cardiology but half the maximum dose licensed for heart failure).

- The trial was terminated early (after 27m) because of a reduction in death in the sacubitril arm (NNT 32 over 27m).
- There was a reduction in hospitalisations.
- There was more hypotension in the sacubitril–valsartan group, but this rarely resulted in stopping the drug. There were no significant differences in other side-effects.

A subsequent paper suggested that, extrapolating the data from the 27m trial, the average increase in life expectancy most patients would get would be 1–2y. This was fairly constant at most ages from 45 to 75y (NEJM 2015;373:2289).

The DTB reviewed the evidence for sacubitril–valsartan and concluded (DTB 2016;54(6):66):

- The results of the trial are encouraging and there may be benefits from sacubitril–valsartan (compared with ACE/ARB alone) in some with heart failure with reduced ejection fraction.
- However, caution is needed because the primary composite endpoint (CV mortality, admission with heart failure) did not reach statistical significance in those:
  - Aged over 74y
  - Of 'western European' or 'Asia–Pacific' origin
  - With more severe heart failure (NYHA class 3 or 4).
- **The lack of evidence in those aged 75y and over is particularly concerning.**

What about ivabradine?

Ivabradine is an inhibitor of the sinoatrial node and therefore slows heart rate. Beta-blockers also slow heart rate, but have a detrimental effect on myocardial contractility, so using ivabradine could provide some of the benefits of beta-blockers without the downsides. Ivabradine is currently being reviewed by the European Medicines Agency because of a trial that showed a slight increased risk of death in those with symptomatic angina. The trial was not for people with heart failure, and the doses used were above the usual recommended dose (DTB 2014;52(7):74).

Heart Foundation on ivabradine for heart failure, 2011

- Consider for patients with impaired systolic function + recent hospital admission + sinus rhythm with HR ≥70bpm despite attempts at maximum beta blockade.
- However, current PBS criteria differs from this requiring all of the following criteria to be met for ivabradine to be considered:
  - Symptomatic with NYHA Class 2 or 3
  - In sinus rhythm
  - Pulse ≥77bpm
  - Given alongside standard therapy (ACE inhibitors, beta-blocker, aldosterone antagonist) (although can also be used if beta-blockers are contraindicated)
  - LVEF 35% or less.

What is the evidence?

In LVSD, studies have shown that a heart rate above 70bpm is associated with an increased risk of death and admission with failure.

The SHIFT trial took over 6000 patients with LVSD and a pulse of 70 or more and randomised them to ivabradine or placebo (Lancet 2010;376:875).

- Ivabradine reduced admissions for failure by 5% and this was statistically significant (HR 0.74, CI 0.66–0.83).
- Ivabradine reduced deaths due to heart failure by 2%, from 5% to 3% (HR also 0.74, CI 0.58–0.94).
- Symptomatic bradycardia was more common in the ivabradine group (5% vs. 1% and this difference is statistically significant).

In the BEAUTIFUL trial (RCT of 10000 people comparing ivabradine vs. placebo), there was no difference in outcomes between the ivabradine group and the placebo group overall after 19m. There were no harms either (Lancet 2008;372:807).

The DTB reviewed the evidence and suggested that there was a limited role for ivabradine, and that it should be initiated in the specialist setting only, i.e. not by GPs! (DTB 2012;10:117).

- **Ivabradine may become increasingly common in the management of heart failure, but should currently be at the recommendation of specialists, not something we start in primary care.**

CABG in heart failure

In CHF, would re-perfusion help improve cardiac function? An RCT of over 1200 patients with severe heart failure showed that outcomes were the same whether they were randomised to medical therapy alone or medical therapy with CABG (NEJM 2011;364:1607). This was also true when they stratified patients to identify those with the most viable myocardium (most likely to benefit from re-perfusion) (NEJM 2011;364:1617)

Cardiac resynchronisation in heart failure

Basically this involves pacing both ventricles – so leads pace the right atrium and ventricle AND the left ventricle. (A normal pacemaker is either single chamber (pacing just the right ventricle) or dual chamber (pacing the right atrium and ventricle).) Pacing both ventricles improves coordination of atria and both ventricles, to get more efficient cardiac function. Various trials have shown it reduces hospitalisation, mortality and is cost-effective too. Patients of all ages benefit, so this can be considered even in those who are quite elderly (BMJ 2009;338:b1265).

Evidence is now emerging that suggests only those with left bundle branch block are likely to get benefit and that there are benefits (reduced mortality) even in those with mild heart failure (NEJM 2014;370:1694).

Clearly we won't be making this decision, but we probably will see increasing numbers of our patients with heart failure being fitted with a pacemaker for this reason.

Heart failure and gout

Loop diuretics can precipitate gout. There is no evidence around management. SIGN suggests treating acute attacks of gout in those with heart failure with colchicine and adding a prophylactic once stable.

Exercise in heart failure

Is exercise safe in heart failure? This RCT of over 2000 people with severe heart failure (NYHA stages 3 & 4) were randomised to 36 supervised aerobic sessions followed by training at home or usual care (JAMA 2009;301:1439 & 1451).

- **Exercise did not improve mortality or admissions to hospital but it was not harmful and seems to improve harder to measure things such as well-being.**

A small trial of 100 patients with CHF, showed that 12 weeks of Tai Chi significantly improved quality of life, mood and confidence compared to no intervention. There were no changes in physical ability or walking distance (Arch Int Med 2011;171:750).

So maybe exercise improves the things that matter most to patients, such as mood, quality of life, well being, etc.

Pulmonary artery pressure as a guide to dose adjustment

Don't worry, we are not suggesting you start doing cardiac catheterisations in your surgery! In this trial 5000 people with heart failure had a pulmonary artery sensor fitted in hospital that was able to transmit daily pulmonary artery pressures via telemonitoring to the hospital. In half, their heart failure drugs were adjusted according to their pulmonary artery pressure. In the other half, the drugs were adjusted according to usual care.

- There was a significant reduction in all-cause admission to hospital (NNT = 4).

- There was no mortality benefit (Lancet 2016;387:453).

Clearly this is not a widely available procedure at present, but watch this space!

Palliative care in heart failure

This BMJ article didn't give a step-by-step guide to palliation in heart failure, but it did discuss some of the issues that make recognising and planning for the end difficult (BMJ 2016;352:i1010).

- At the end stage of heart failure, the disease often affects quality of life more than other diseases, so good palliative care is essential.
- Complicating this, co-morbidity is very common, polypharmacy is the norm and patients are often frail.
- Palliative care in heart failure needs to address all these issues
- One of the challenges is the uncertain trajectory of the disease. Whereas people with cancer tend to slowly deteriorate, those with heart failure tend to have periods of stability with sudden exacerbations and during these exacerbations it is difficult to predict whether this dip is recoverable or a terminal event. This is challenging for patients, carers and professionals!
- One study showed that patients tend to overestimate their life expectancy by over 40%, suggesting they may not be ready to discuss end of life issues when perhaps those conversations are needed.
- Good communication with other professionals involved is important: if primary care is having end of life discussions, and the cardiologists are offering some kind of pump assist device or implanted defibrillator, the patient may well be confused, although doing both may be entirely reasonable!
- A phrase I often use to communicate the uncertainties is "let's hope for the best, but plan for the worst".

This article raised a number of questions about how we provide care for people with heart failure:

- Have you given your heart failure patients the opportunity to ask/talk about their prognosis?
- Have you talked about symptom control, symptom by symptom?
- Have you talked about non-drug options too – we know about opioids and benzodiazepines for breathlessness, but what about a fan to blow air across the face?
- Have you given them the opportunity to talk about end of life issues (advance directives, DNAR, preferred place of death)?
- Have you looked for and treated depression and anxiety?

Liraglutide for heart failure?

A small study looked at the use of liraglutide in people admitted with heart failure (without diabetes). They found it wasn't beneficial. The trial was done because a previous small trial had suggested it might be (JAMA 2016;316:500).

Driving and heart failure – Austroads 2016

- **Private drivers (ordinary drivers) have no restrictions on their licence if they have heart failure *unless* they have symptoms on moderate exertion.** A conditional licence may be granted for these people if there is satisfactory response to treatment and there are minimal symptoms relevant to driving, e.g. breathlessness, palpitations, chest pain.
- **Commercial drivers cannot have an unconditional licence if they have heart failure.** A conditional licence may be issued following review by a specialist if there is satisfactory response to treatment and all of the following criteria are met:
    - exercise tolerance is ≥90% of that predicted by the Bruce Protocol
    - LV ejection fraction is ≥0.4
    - the underlying cause of the heart failure is considered
    - there are minimal symptoms relevant to driving, e.g. breathlessness, palpitations, chest pain.

Chronic heart failure

- The Heart Foundation guidance advocates measuring natriuretic peptide if you suspect heart failure, and there is a delay in accessing an echocardiogram.
- Be aware of the causes of false positives and negatives with the natriuretic peptide test.
- After echo, the diagnosis of heart failure will be whether failure with LVSD or failure with preserved ejection fraction.
- Failure with LVSD is treated with dual therapy first line (beta-blockers and ACE inhibitors).
- In heart failure with preserved ejection fraction the central tenant of management is to control any underlying pathology (hypertension and diabetes). There is less evidence for drug therapy in HFPEF, although the drugs used in LVSD are widely used.
- All should use diuretics for symptomatic relief.
- Aspirin is warranted if evidence of arteriosclerotic disease.
- Cardiac resynchronisation with biventricular pacing can help in some with CHF.

Austroads guidelines: www.onlinepublications.austroads.com.au/items/AP-G56-16

Heart Foundation guidelines: https://heartfoundation.org.au/images/uploads/publications/Chronic_Heart_Failure_Guidelines_2011.pdf

My notes