GIMBE®

Gruppo Italiano per la Medicina Basata sulle Evidenze

Evidence-Based Medicine Italian Group

Decisioni Cliniche e Prove di Efficacia

Il Governo Clinico nelle Cure Primarie

Rimini, 3-4 ottobre 2008

Workshop Clinici Interattivi (3)

I percorsi integrati nei pazienti con scompenso cardiaco

Il miraggio diventa realtà?

Marco Grassi
Giancarlo Piovaccari

Premessa

- La storia clinica del paziente si articola dal 1999 ad oggi
- Le decisioni cliniche riportate sono quelle reali
- Nella risposta ai quesiti fare sempre riferimento alle conoscenze oggi disponibili

Scenario Clinico

- La signora Maria è una casalinga di 76 anni, con habitus depressivo, sposata, vive con il marito.

- Non fuma, non beve, moderata attività fisica; nulla di rilevante all'anamnesi familiare e fisiologica

- Da circa 12 anni storia di prurito diffuso che motiva l'assunzione occasionale di antistaminici: qualche anno fa diagnosi di dermatite eczematosa lichenoide diffusa sensibile a conservanti, pesticidi, essenze vegetali

- Riferita allergia/intolleranza a diversi farmaci: mai confermata la reale esistenza (prove allergiche negative)

Scenario Clinico

- Dal 1999, 2-3 episodi/anno di dispnea, sempre interpretati come asma allergico
- Trattati con salbutamolo al bisogno e cicli di beclometasone spray, tali episodi si sono sempre risolti dopo pochi giorni
- Nel dicembre 2001 la dispnea, prevalentemente notturna e associata a tosse secca non risponde più ai farmaci per l'asma
- La signora Maria viene ricoverata d'urgenza

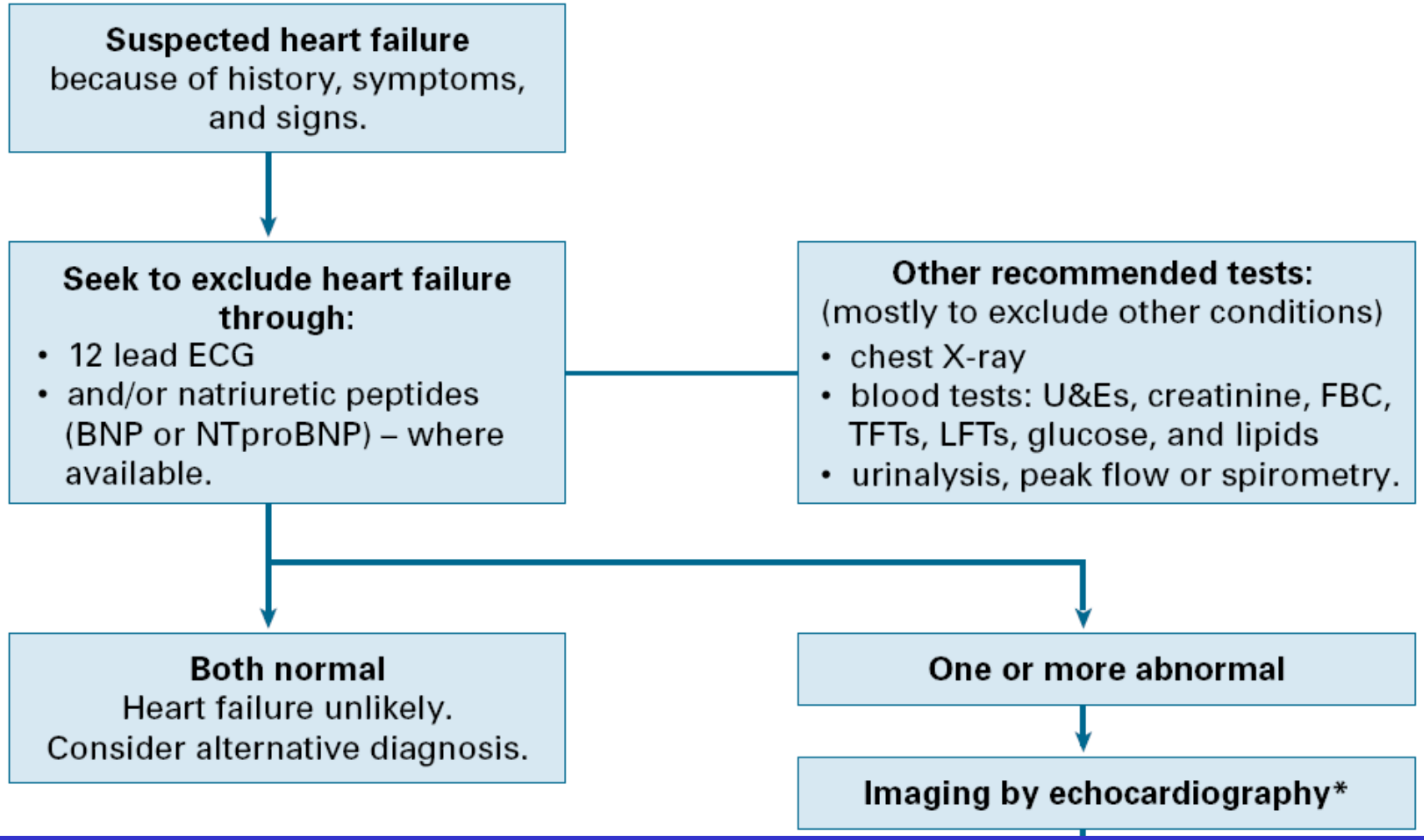
Clinical Question

1. Nei pazienti con sospetto clinico di scompenso cardiaco in medicina generale, il BNP è utile per confermare/escludere la diagnosi?

1. No
2. Sì, sia per escludere, sia per confermare
3. Sì, per escludere
4. Si, per confermare

NHS
National Institute for Health and Clinical Excellence

Algorithm summarising recommendations for the diagnosis of heart failure

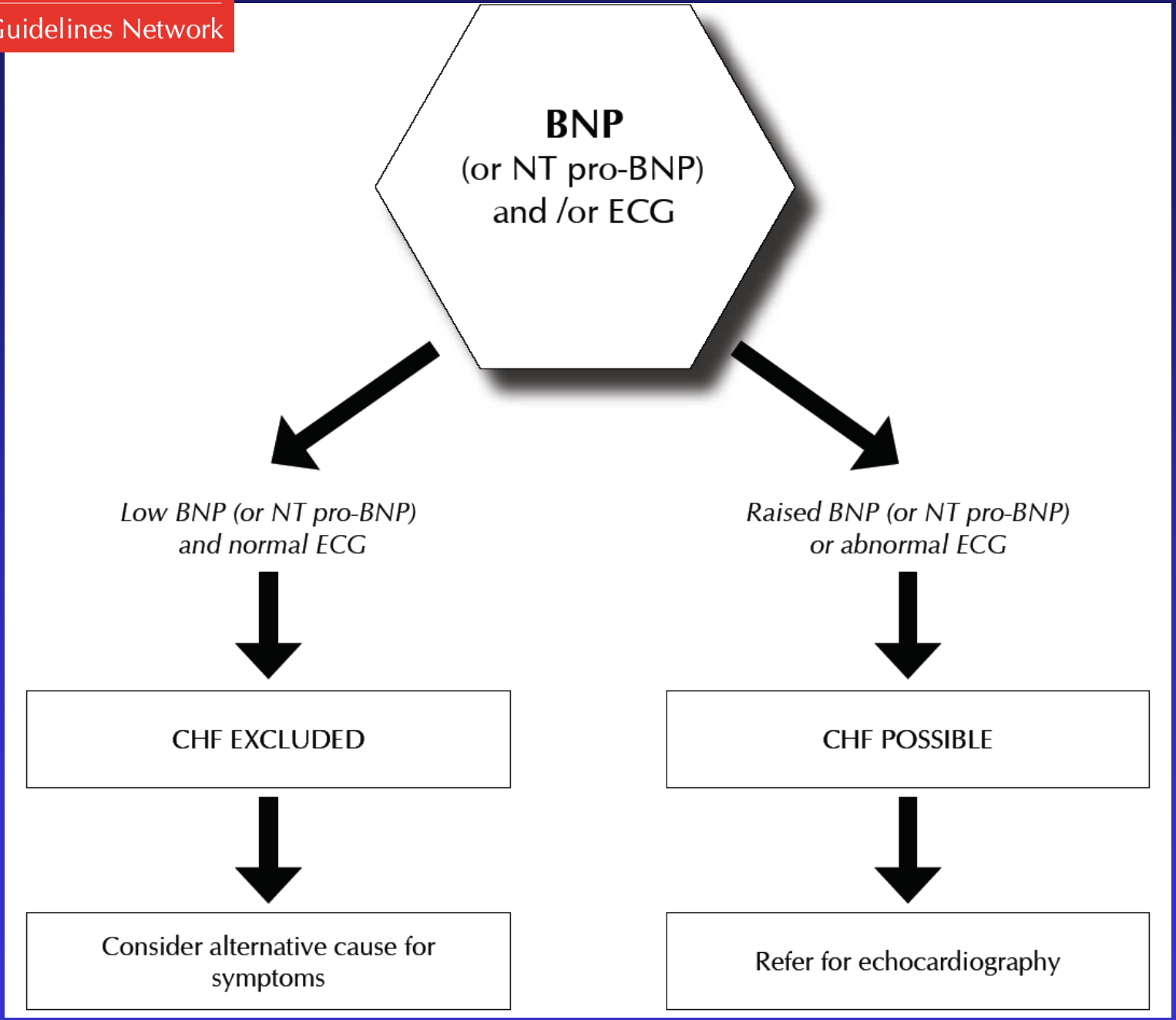


SIGN

Scottish Intercollegiate Guidelines Network

B **Brain natriuretic peptide or NT pro-BNP levels and/or an electrocardiogram should be recorded to indicate the need for echocardiography in patients with suspected heart failure.**

☑ In the assessment of suspected heart failure, brain natriuretic peptide or NT pro-BNP levels should ideally be checked on samples taken prior to commencing therapy.



National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Clinical Utilization of Cardiac Biomarker Testing in Heart Failure

(*Circulation*. 2007;116:e99-e109.)

Class IIa

1. BNP and NT-proBNP testing can be helpful to exclude the diagnosis of heart failure among patients with signs and symptoms suspicious of heart failure in the non-acute setting. (Level of Evidence: C)

Class III

1. *Routine* blood natriuretic peptide (BNP or NT-proBNP) testing is not recommended for screening large asymptomatic patient populations for left ventricular dysfunction. (Level of Evidence: B)

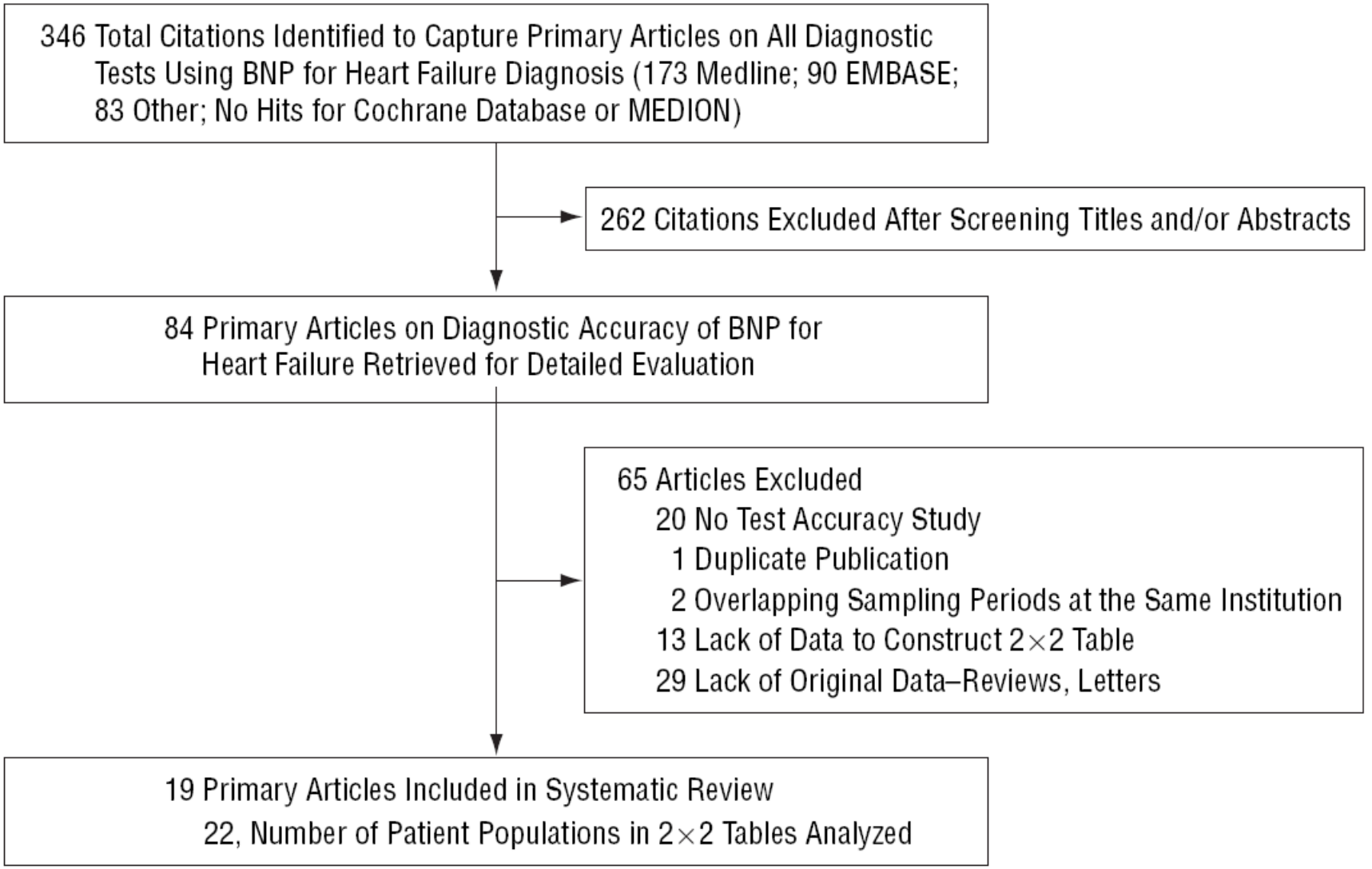
REVIEW ARTICLE

Accuracy of B-Type Natriuretic Peptide Tests to Exclude Congestive Heart Failure

Systematic Review of Test Accuracy Studies

Markus Battaglia, MD, MPH; Daniel Pewsner, MD; Peter Jüni, MD; Matthias Egger, MD, MSc, MFPHM; Heiner C. Bucher, MD, MPH; Lucas M. Bachmann, MD, PhD

Arch Intern Med. 2006;166:1073-1080



Battaglia M, et al. Arch Intern Med, 2006

RESULTS

- 19 studies (9 ELISA, 13 RIA) and 9093 patients were included.
- CHF was verified by diagnostic gold-standard
- The pooled negative likelihood ratio was 0.18 (95% CI, 0.13-0.23).
  - ELISA test 0.12 (95% CI, 0.09-0.16)
  - RIA test 0.23 (95% CI, 0.16-0.32)
- For a pretest probability of 20%, a negative result of the ELISA test would produce a post-test probability of 2.9%; a negative RIA test, a post-test probability of 5.4%.

Battaglia M, et al. Arch Intern Med, 2006

CONCLUSION

- The use of BNP tests to rule out CHF in primary care settings could reduce demand for echocardiography

- The advantages of rapid ELISA tests need to be balanced against their higher cost

Battaglia M, et al. Arch Intern Med, 2006

Scenario Clinico

• Dopo 12 giorni di ricovero, la signora Maria viene dimessa con diagnosi di “scompenso cardiaco acuto in miocardiopatia dilatativa” con la seguente terapia:

- lisinopril 20 mg/die
- furosemide 50 mg/die
- digossina 0,250 mg/die
- potassio canreonato 50 mg/die
- montelukast 10 mg/die
- formoterolo spray 2 puff die
- beclometasone 500 mcg x 2
- salbutamolo al bisogno

Clinical Question

2. Quali farmaci non avresti prescritto alla signora Maria?

1. Avrei prescritto tutti i farmaci
2. FF per asma*
3. FF per asma + lisinopril
4. FF per asma + furosemide
5. FF per asma + digossina
6. FF per asma + potassio canreonato

*montelukast, formoterolo, beclometasone, salbutamolo

SIGN

Scottish Intercollegiate Guidelines Network

A **Digoxin should be considered as an add-on therapy for heart failure patients in sinus rhythm who are still symptomatic after optimum therapy.**

B **Following specialist advice, patients with moderate to severe heart failure due to left ventricular systolic dysfunction should be considered for spironolactone unless contraindicated by the presence of renal impairment or a high potassium concentration.**

There is no evidence that spironolactone is as effective in mild heart failure and no recommendation can be given for this group of patients.

NHS
National Institute for
Health and Clinical Excellence

R31 Digoxin is recommended for:

- worsening or severe heart failure due to LV systolic dysfunction despite ACE inhibitor, beta-blocker and diuretic therapy — A
- patients with atrial fibrillation and any degree of heart failure. — C

R29 Patients with heart failure due to LV systolic dysfunction who remain moderately to severely symptomatic despite optimal therapy (as outlined in the algorithm) should be prescribed spironolactone at a dose of 12.5 to 50 mg once per day – specialist advice should be sought. — A

Scenario Clinico

- La signora Maria viene immediatamente presa in carico dall'ambulatorio scompenso della UO di Cardiologia e seguita regolarmente: prima ogni 2 mesi, poi ogni 6 mesi

- I referti delle visite mi vengono regolarmente portati in visione dalla paziente

Scenario Clinico

2/2002

- classe NYHA II, dispnea per sforzi lievi-moderati
- peso 77 kg, FC 90/min, PA 100/60 mmHg
- EO: soffio mitralico, non stasi toracica, epatomegia, edemi
- ECG: ritmo sinusale, disturbo conduzione IV: BBSn. EASn
- sospesi i farmaci per l'asma

4/2002

- paziente stabile

6/2002

- paziente stabile
- incremento di 2 kg → furosemide 75 mg + 50 mg/die

Scenario Clinico

3/2003

- Notevole riduzione della tolleranza allo sforzo: la dispnea compare per sforzi di minore entità
- Peso 88 kg (+ 11 kg in 8 mesi)
- EO: crepitii alle basi, epatomegalia (4 cm dall'arcata costale), edemi periferici
- ECG: ritmo sinusale con disturbo della conduzione IS BBS
- Ecocardiogramma: trombosi ventricolare sn (FE non riportata)

Clinical Question

3. La stabilizzazione clinica nei primi 6 mesi di follow-up giustifica una minore frequenza di visite specialistiche?

1. No
2. Sì
3. Sì, solo all'interno di un programma di follow-up integrato con la medicina generale

There have been few direct comparisons of the impact of different intensities and frequencies of monitoring of patients with chronic heart failure – although almost all published studies comparing closer, more frequent contact with a healthcare professional who has experience in managing heart failure with 'routine' care report an improvement in quality of life for patients, and a reduction in the need for urgent hospitalisation.[205–208] (I)

R60	All patients with chronic heart failure require monitoring. This monitoring should include: • a clinical assessment of functional capacity, fluid status, cardiac rhythm (minimum of examining the pulse) fluid status, cognitive status and nutritional status • a review of medication, including need for changes and possible side-effects • serum urea, electrolytes and creatinine.*	GPP
R62	The frequency of monitoring should depend on the clinical status and stability of the patient. Monitoring interval should be short (days to two weeks) if the clinical condition or medication has changed, but is required at least six-monthly for stable patients with proven heart failure.	GPP

Clinical Question

4. Il peggioramento dei sintomi in una paziente in trattamento con ACE-inibitore, beta-bloccante, furosemide, spironolattone e digossina, avrebbe giustificato l'aggiunta di un antagonista dei recettori dell'AT II?

1. No
2. Sì, valsartan
3. Sì, candesartan
4. Sì, irbesartan
5. Sì, altro antagonista AT II

ARBs can also be added to ACE inhibitor therapy in patients with chronic heart failure. In the ValHeFT trial, in which 93% of patients were already taking an ACE inhibitor and 35% using a beta blocker, adding the ARB valsartan had no effect on mortality, but it did significantly reduce heart failure hospitalisation and mortality combined (relative risk 0.87, 97.5% CI 0.77 to 0.97; p = 0.009).[67] The CHARM Added trial showed a 15% relative risk reduction (95% CI 4% to 25%, p = 0.01; ARR 4.4%; number needed to treat NNT = 27) for cardiovascular death or hospitalisation for CHF in patients receiving candesartan in addition to an ACE inhibitor.[68] 1+

A **Patients with chronic heart failure due to left ventricular systolic dysfunction alone, or heart failure, left ventricular systolic dysfunction or both following myocardial infarction who are intolerant of angiotensin converting enzyme inhibitors should be considered for an angiotensin receptor blocker.**

B **Patients with heart failure due to left ventricular systolic dysfunction who are still symptomatic despite therapy with an angiotensin converting enzyme inhibitor and a beta blocker may benefit from the addition of candesartan, following specialist advice.**

Scenario Clinico

- La signora Maria viene sottoposta a una rivalutazione clinica e inserita in un programma sperimentale di gestione integrata specialista/MMG
- Il programma prevede una cartella clinica condivisa tra cardiologo e medico di famiglia
- Viene periodicamente effettuato il backup dei dati su floppy disk consegnato alla paziente

Clinical Question

5. Nei pazienti con scompenso cardiaco, la gestione integrata multidisciplinare (MMG, specialista, infermiere) migliora gli esiti?

1. No
2. Sì, gli esiti clinici
3. Sì, gli esiti economici
4. Sì, gli esiti umanistici*
5. Sì, tutti gli esiti

*qualità di vita, soddisfazione del paziente

Multidisciplinary care programmes improve patients' quality of life, satisfaction with care, and the risk of unplanned hospitalisation for heart failure, compared with conventional care.[207,217,218] There is no convincing evidence that such programmes improve survival.[205,217,219] (**Ib**)

Good communication and team working between disciplines, with close contact with patients, was seen by the guideline development group as key for effective heart failure management. (**IV**)

R71	Heart failure care should be delivered by a multidisciplinary team with an integrated approach across the healthcare community.	A

A Comprehensive discharge planning should ensure that links with post-discharge services are in place for all those with symptomatic heart failure. A nurse led, home based element should be included.

A Follow up *(including by telephone)* by trained heart failure nurses should be considered for patients post-discharge or with stable heart failure. Nurses should have the ability to alter diuretic dose and the interval between telephone calls, and recommend emergency medical contact.

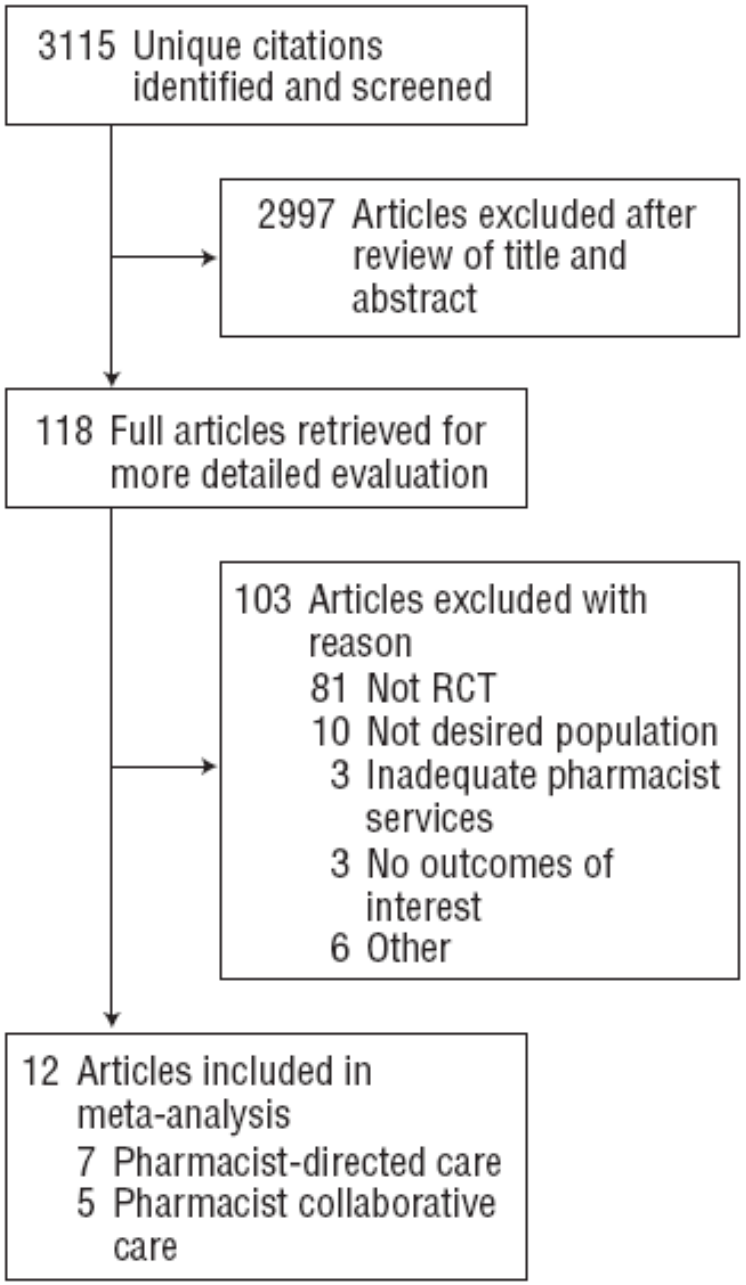
A Patients with heart failure should be offered multidisciplinary follow up, including pharmacy input to address knowledge of drugs and compliance. Follow up should include feedback to clinicians about possibilities for optimising pharmacological interventions.

Pharmacist Care of Patients With Heart Failure

A Systematic Review of Randomized Trials

Sheri L. Koshman, BScPharm, PharmD, ACPR; Theresa L. Charrois, BSc(Pharm), MSc; Scot H. Simpson, BSP, PharmD, MSc; Finlay A. McAlister, MD, MSc, FRCPC; Ross T. Tsuyuki, BSc(Pharm), PharmD, MSc, FCSHP

Arch Intern Med. 2008;168(7):687-694



Koshman SL, et al.
Arch Intern Med, 2008

RESULTS

- 12 RCTs (2060 patients) were identified

- Extent of pharmacist involvement varied among studies

- Pharmacist care was associated with:
  - significant reductions of all-cause and HF hospitalizations
  - nonsignificant reduction in mortality

- Pharmacist collaborative care led to greater reductions in the rate of HF hospitalizations than pharmacist-directed care

Koshman SL, et al. Arch Intern Med, 2008

CONCLUSION

• Pharmacist care in the treatment of patients with HF greatly reduces the risk of all-cause and HF hospitalizations.

• Since hospitalizations associated with HF are a major public health problem, the incorporation of pharmacists into HF care teams should be strongly considered.

Koshman SL, et al. Arch Intern Med, 2008

BMJ Clinical Evidence

Heart failure

Search date January 2007

Robert McKelvie

OPTION MULTIDISCIPLINARY INTERVENTIONS

Mortality

Compared with usual care Multidisciplinary programmes may be more effective at reducing all-cause mortality (low-quality evidence).

Hospitalisation

Compared with usual care Multidisciplinary programmes may be more effective at reducing all-cause hospitalisations, and hospitalisations for heart failure (low-quality evidence).

Scenario Clinico

- Nel maggio 2004 netto peggioramento delle condizioni cliniche e funzionali: classe NYHA III, marcata dilatazione e disfunzione sistolica del VS (FE 15%)

- Ad agosto viene impiantato pacemaker biventricolare + ICD

- La paziente mostra un netto miglioramento:
  - ripristino spontaneo del ritmo sinusale
  - classe NYHA II
  - riduzione di 6 Kg

Clinical Question

6. Nei pazienti con scompenso cardiaco in classe NYHA III-IV, la re-sincronizzazione cardiaca:

1. Riduce la mortalità
2. Migliora sintomi e qualità di vita
3. Riduce l’ospedalizzazione
4. 1 + 2 + 3

CARDIAC RESYNCHRONISATION

A large evidence base has accrued showing the benefits of cardiac resynchronisation therapy (CRT) in addition to optimal medical therapy in terms of improving exercise capacity, reducing NYHA class, improving quality of life and reducing hospitalisations for worsening heart failure.[102,103] Cardiac resynchronisation therapy has been shown to significantly reduce mortality in patients with left ventricular systolic dysfunction (hazard ratio 0.64, 95% CI 0.48 to 0.85; $p < 0.002$).[104] Most of the evidence for CRT applies to patients with CHF who are in sinus rhythm.

1^{++}
1^{+}

A **For patients in sinus rhythm with drug refractory symptoms of heart failure due to left ventricular systolic dysfunction** *(left ventricular ejection fraction ≤35%)* **and who are in NYHA class III or IV and who have a QRS duration of >120 ms, cardiac resynchronisation should be considered.**

Scenario Clinico

Terapia giornaliera prescritta alla dimissione

- carvedilolo 6,25 mg x 2
- canrenoato di potassio 100 mg
- enalapril 10 mg
- allopurinolo 300 mg
- coumadin (INR 2-3)
- furosemide 250 mg h 8 e 50 mg h 16

Scenario Clinico

- Nel corso dell'anno successivo viene attivata l'Assistenza Domiciliare Programmata per l'impossilità della paziente di recarsi a controllo nel mio ambulatorio

- La signora Maria segue scrupolosamente la terapia, i controlli programmati, il controllo del peso (dieta e restrizione idrica)

- Tuttavia, nonostante lo stretto controllo e la buona compliance, si assiste ad un progressivo peggioramento del compenso emodinamico

- Nel gennaio 2005 la signora Maria viene ricoverata

Scenario Clinico

- All'ingresso: dispnea per sforzi minimi, edema interstiziale alla Rx torace, edemi declivi

- L’infusione di dopamina e diuretici e.v. determina un progressivo miglioramento del quadro emodinamico e della dispnea

- Ecocardiografia: disfunzione sistolica importante del ventricolo sinistro (FE 15%), insufficienza mitralica severa, ipertensione polmonare

Scenario Clinico

• Il 9/02/05 veniva posizionato elettrocatetere in seno coronarico: la procedura era priva di complicanze ed il controllo radiologico mostrava il corretto posizionamento.

• Diagnosi di dimissione: “Episodio di scompenso cardiaco congestizio in paziente con cardiomiopatia dilatativa e severa disfunzione sistolica globale del ventricolo sinistro; riposizionamento di elettrocatetere in seno coronarico”

Scenario Clinico

Prescrizioni non farmacologiche

- Riduzione dell'attività fisica e lavorativa
- Limitazione dell’introito di liquidi: 1.000 ml/die
- Controllo giornaliero del peso corporeo
- Regime dietetico ipolipidico e ipoglicidico volto ad ottenere una significativa riduzione del peso corporeo.
- Per difficoltà a mantenere INR adeguati, la signora Maria viene riferita al centro di sorveglianza anticoagulati

Scenario Clinico

Terapia farmacologica

- carvedilolo 12.5 mg x 2
- enalapril 10 mg x 2
- lanoxin 0.125 mg
- furosemide 125 mg
- canrenoato di potassio 50 mg
- coumadin (target INR 2-3)
- allopurinolo 300 mg

Scenario Clinico

- E’ verosimile che l’ultimo episodio di scompenso sia stato conseguente al malfunzionamento del PM: infatti, dopo il suo riposizionamento e la conseguente resincronizazzione la paziente si è mantenuta stabile per oltre un anno in classe NYHA II

- Unico dato di rilevo: non si riesce a ridurre il dosaggio della furosemide (125 mg/die)

Scenario Clinico

- Alla fine del 2006, si rilevano progressivamente:
  - creatininemia 1,7 mg%
  - glicemia 202 mg%
  - trigliceridemia 328 mg%
  - uricemia 11,2 mg%

- La signora Maria viene inviata al centro diabetologico dove, oltre a regime dietetico e periodico follow-up, vengono prescritti:
  - repaglinide 1 mg x 3
  - fenofibrato 200 mg/die

Clinical Question

7. In una paziente con scompenso cardiaco, la repaglinide è il trattamento di prima scelta per il controllo metabolico del diabete?

1. Sì
2. No, metformina
3. No, sulfanilurea
4. No, pioglitazone/rosiglitazone
5. No, insulina
6. No, altro antidiabetico

Benefits and harms of antidiabetic agents in patients with diabetes and heart failure: systematic review

Dean T Eurich, research associate,[1] Finlay A McAlister, associate professor,[2] David F Blackburn, assistant professor,[3] Sumit R Majumdar, associate professor,[2] Ross T Tsuyuki, professor,[4] Janice Varney, librarian,[1] Jeffrey A Johnson, professor[5]

RESULTS

- 3/4 found that **insulin** use was associated with increased risk for all cause mortality
- **Metformin** reduces significantly all cause mortality in two studies compared with other antidiabetic drugs and insulin and is not associated with increased hospital admission
- In 4 studies **thiazolidinediones** were associated with reduced all cause mortality, but they increase the risk of hospital admission for CHF
- 2 studies of **sulfonylureas** had conflicting results, probably because of differences in comparator treatments

Eurich DT, et al. BMJ 2008

CONCLUSION

- Metformin was the only antidiabetic agent not associated with harm in patients with heart failure and diabetes.
- It was associated with reduced all cause mortality in two of the three studies

Eurich DT, et al. BMJ 2008

WHAT IS ALREADY KNOWN ON THIS TOPIC

Diabetes is a common comorbidity in people with heart failure and predicts worse outcomes

The best way to achieve glycaemic control in patients with diabetes and heart failure is unclear

WHAT THIS STUDY ADDS

Current evidence suggests that metformin is the only antidiabetic agent not associated with any measurable harm in patients with diabetes and heart failure

Scenario Clinico

- Ho visto la signora Maria al rientro dalle ferie: la paziente è stabile con una soddisfacente qualità di vita: ha ripreso ad uscire di casa, esegue piccoli lavori di giardinaggio e viene in ambulatorio autonomamente.
- Lo schema terapeutico rimane immodificato