GIMBE®

Gruppo Italiano per la Medicina Basata sulle Evidenze

Evidence-Based Medicine Italian Group

Workshop

Evidence-based Medicine

Le opportunità di un linguaggio comune 3ª ed.

Como, 1-2 aprile 2006

SNAMID

Sezione di Como

Workshop Clinici Interattivi (1)

La gestione integrata del paziente con scompenso cardiaco

Molte evidenze, scarsa integrazione tra i servizi

Danila Briganti
Mauro Santarone

Scenario Clinico (1)

- Il signor Giovanni è un pensionato (grande invalido di guerra) di 81 anni, ex fumatore (oltre 20 sigarette/die dall'età di 20 a 40 anni), vedovo, vive con una nuova compagna in una villetta bifamiliare assieme al figlio e alla nuora entrambi impiegati in banca.

- Conduce una vita attiva e soddisfacente dal punto di vista relazionale.

- E' un buon mangiatore che non disdegna un buon bicchiere di vino rosso ai pasti principali

Scenario Clinico (1)

- Storia di ipertensione arteriosa lieve trattata con ramipril 2,5 mg +idroclorotiazide 12,5 mg e dislipidemia (colesterolo totale 243 mg/dl, HDL 40 mg/dl, trigliceridi 167 mg/dl) accertata da oltre 20 anni e mai trattata farmacologicamente

- Nel 1995 attacco acuto di gotta al piede dx: da allora trattamento con dieta e successivamente allopurinolo (da segnalare due attacchi acuti nel 2002)

Scenario Clinico (2)

• Nel 1998 episodio di broncopolmonite, radiologicamente documentata, trattata a domicilio.

• Il signor Giovanni esegue visita pneumologica e test di funzionalità respiratoria:

- diagnosi di BPCO con deficit ostruttivo
- ipoventilazione per esiti di fibrotorace specifico.
- PO_2 96%, riduzione del FEV1 (64%).

• Il signor Giovanni rispetta scrupolosamente i controlli pressori ambulatoriali (ogni 4 mesi) ed, annualmente, esegue controllo specialistico pneumologico ed esami ematochimici.

Scenario Clinico (3)

• Nel Febbraio 2003, il signor Giovanni viene in ambulatorio riferendo fame d'aria da oltre 2 settimane e lamenta di aver trascorso l'ultima notte in bianco, seduto sul letto.

• Obiettivamente: rumori umidi alle basi polmonari, entrambe ipomobili, assenza di edemi declivi. PA 140/100 mmHg, FC 130/min, aritmica.

• Somministro digossina (0,250 mg e.v.) e furosemide (20 mg, e.v.) e predispongo immediatamente il ricovero ospedaliero.

Scenario Clinico (4)

- Durante il ricovero, si assiste rapidamente, sia ad una risoluzione della dispnea, sia ad una normalizzazione della frequenza cardiaca.

- Nessun sintomo di rilevo da segnalare

Scenario Clinico (5)

Indagini eseguite

• Ecocardiografia: insufficienza mitralica lieve, ventricolo sinistro diffusamente ipocinetico, e dilatazione biatriale (atrio sn 52 mm, atrio dx 48 mm), frazione di eiezione 45%.

• ECG: fibrillazione atriale a 90 b/m con alterazioni della ripolarizzazione frequenza-dipendenti.

• Colesterolo totale 220 mg/dl, HDL 39 mg/dl, trigliceridi 146 mg/dl, LDL 152 mg/dl (formula di Friedewald)

• Uricemia 7.4 mg/dl, bilirubina totale 1.7 mg./dl

CLINICAL QUESTIONS

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A. Ritieni necessario ripristinare il ritmo sinusale nel signor Giovanni?

1. No
2. Sì

Linee Guida Scompenso Cardiaco (2001-2006)

- 2006 Canadian Cardiovascular Society
- 2005 American College of Cardiology/American Heart Association
- 2005 European Society of Cardiology
- 2003 National Institute for Clinical Excellence (NICE) & Royal College of Physicians
- 2001 National Heart Foundation of New Zealand

Johnston BL, Conly BL

Guidelinitis
A new syndrome?

Can J Infect Dis 2000

www.agreecollaboration.org

Full version of

NICE Guideline No. 5

July 2003

CHRONIC HEART FAILURE

National clinical guideline for diagnosis and management in primary and secondary care

Score AGREE totale 90%

clinical evidence

BMJ Publishing Group

Heart failure

Search date February 2004

Robert McKelvie

American Academy of Family Physicians
American College of Physicians

Management of newly detected atrial fibrillation. A clinical practice guideline

Ann Intern Med 2003;139:1009-17

Score AGREE totale 81%

Rate control or rhytm control?

Recommendation 1 (Grade: 2A)

• Rate control with chronic anticoagulation is the recommended strategy for the majority of patients with atrial fibrillation.

• Rhythm control has not been shown to be superior to rate control (with chronic anticoagulation) in reducing morbidity and mortality and may be inferior in some patient subgroups to rate control.

• Rhythm control is appropriate when based on other special considerations, such as patient symptoms, exercise tolerance, and patient preference.

AAP/ACP. December 2003

de Denus S, Sanoski C A, Carlsson J, et al.

Rate vs rhythm control in patients with atrial fibrillation A meta-analysis

Arch Intern Med 2005;165:258-262

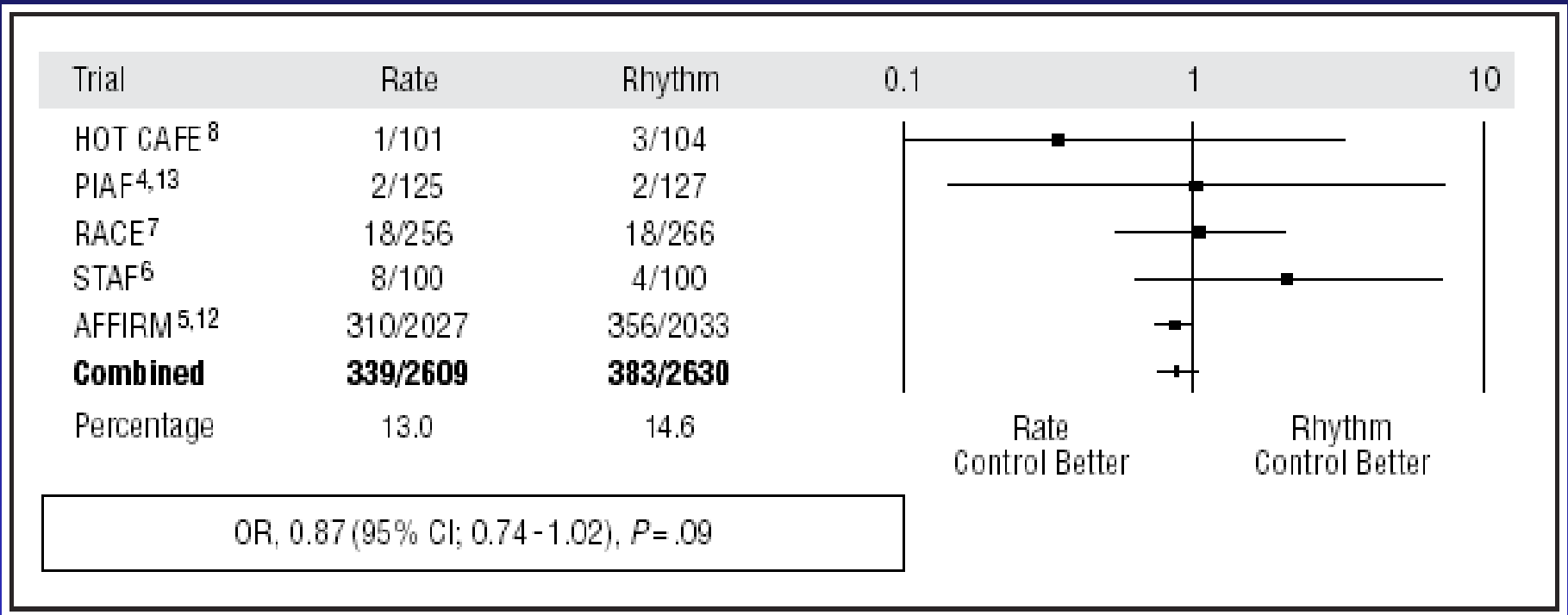

Figure 2. Odds ratios (ORs) for the end point of all-cause mortality for individual trials and the combined analysis. HOT CAFE indicates How to Treat Chronic Atrial Fibrillation; PIAF, Pharmacological Intervention in Atrial Fibrillation; RACE, Rate Control vs Electrical Cardioversion for Persistent Atrial Fibrillation Study; STAF, Strategies of Treatment of Atrial Fibrillation; AFFIRM, Atrial Fibrillation Follow-up Investigation of Rhythm Management; and CI, confidence interval.

de Denus, et al. Arch Intern Med 2005

CLINICAL QUESTIONS

?

B. Quale/i trattamento/i ritieni appropriato/i nel signor Giovanni?

1. Nessuno
2. Statine
3. Dicumarolici
4. Digossina
5. Dicumarolici + Digossina

Chronic Anticoagulation?

Recommendation 2 (Grade: 1A)

• Patients with atrial fibrillation should receive chronic anticoagulation with adjusted-dose warfarin, unless they are at low risk of stroke or have a specific contraindication to the use of warfarin (thrombocytopenia, recent trauma or surgery, alcoholism).

AAP/ACP. December 2003

La stratificazione del rischio

Table 2. **Risk for Stroke Stratified by $CHADS_2$ Score***

$CHADS_2$ Score	Adjusted Stroke Rate (95% CI)	$CHADS_2$ Risk Level
0	1.9 (1.2–3.0)	Low
1	2.8 (2.0–3.8)	Low
2	4.0 (3.1–5.1)	Moderate
3	5.9 (4.6–7.3)	Moderate
4	8.5 (6.3–11.1)	High
5	12.5 (8.2–17.5)	High
6	18.2 (10.5–27.4)	High

AAP/ACP. December 2003

La stratificazione del rischio

The $CHADS_2$ score is calculated by:

- Adding 1 point each for:
  - → Recent congestive heart failure (i.e., active within the past 100 days or documented by echocardiography)
  - → Hypertension (systolic and/or diastolic)
  - → Age at least 75 years
  - - Diabetes mellitus

- Adding 2 points for:
  - - a history of stroke or transient ischemic attack

AAP/ACP. December 2003

Table 2. Risk for Stroke Stratified by $CHADS_2$ Score*

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AAP/ACP. December 2003

Digitalis?

Recommendation 3 (Grade: 1B)

• For patients with atrial fibrillation, the following drugs are recommended for their demonstrated efficacy in rate control during exercise and while at rest: atenolol, metoprolol, diltiazem and verapamil (drugs listed alphabetically by class).

• Digoxin is only effective for rate control at rest and therefore should only be used as a second-line agent for rate control in atrial fibrillation.

AAP/ACP. December 2003

Digitalis?

Digoxin

1.2.2.11 Digoxin is recommended for:

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

NICE. July, 2003

clinical evidence

BMJ Publishing Group

Beneficial

- **Digoxin (improves morbidity in people already receiving diuretics and angiotensin converting enzyme inhibitors)** One systematic review found that, in people in sinus rhythm with heart failure, digoxin reduced clinical worsening of heart failure compared with placebo. One large RCT in people already receiving diuretics and angiotensin converting enzyme inhibitors found that digoxin reduced the proportion of people admitted to hospital for worsening heart failure at 37 months compared with placebo, but found no significant difference between groups in mortality.

Rathore SS, Curtis, JP, Wang Y, et al.

Association of serum digoxin concentration and outcomes in patients with heart failure

JAMA 2003;289:871-8

Digitalis?

- Post hoc cohort analysis done in men, of a Digoxin Investigation Group trial.

- Serum Digoxin Level (SDL)
  - 0.5-0.8 mg/mL ↓ of mortality
  - 0.9-1.1 ng/mL no effect on mortality
  - ≥ 1.2 ng/mL ↑ of mortality

Rathore SS, et al. JAMA 2003

Horton R

From star signs to trial guidelines

Lancet 2000;355:1033-4

Subgroup analysis

- The most entertaining example of inappropriate subgroup analysis is to be found in a 1988 Lancet paper (ISIS-2)

- Within a complex table reporting subgroup analyses of the odds of vascular death after streptokinase, aspirin, both, or neither for acute myocardial infarction, the first “presentation feature” given is astrological birth sign.

- For people labouring under the star signs Gemini and Libra, aspirin was no better than placebo.

Horton R. Lancet 2000

Statins?

Statins (hydroxymethylglutaryl-coenzyme A reductase inhibitors)

1.2.2.20 Patients with the combination of heart failure and known atherosclerotic vascular disease should receive statins only in accordance with current indications. Specific trials in this area are ongoing.

GPP

NICE. July, 2003

Ramasubbu K, Mann DL

The emerging role of statins in the treatment of heart failure

J Am Coll Cardiol 2006;47:342-4

• Given that our randomized clinical experience with statins in nonischemic cardiomyopathy is limited to several small trials in which < 100 patients have actually been treated, and given that we have no information with respect to the correct dose of statins to use in these patients, it is premature to recommend the use of statins for hearth failure patients.

• There are several ongoing large-scale clinical outcome trials in HF patients:

- CORONA
- GISSI-HF
- UNIVERSE

Ramasubbu K,et al.
J Am Coll Cardiol 2006

Decisioni cliniche (1)

- Non si ritiene necessario ripristinare ritmo sinusale

- Viene instaurata terapia anticoagulante orale con warfarin (target INR 2.0-3.0)

- Non vengono prescritti:
  - digitale
  - statine

Decisioni cliniche (2)

• Dopo 7 giorni di ricovero il paziente viene dimesso - diagnosi di “scompenso cardiaco in fibrillazione atriale parossistica” - con la seguente terapia:

- Ramipril 5 mg + Idroclorotiazide 12,5 mg 1 cpr/die
- Warfarin, come da schema
- Allopurinolo, 300 mg 1 cpr/die

• Informato sulla sorveglianza dell’INR, il signor Giovanni riprende le normali abitudini di vita e si presenta regolarmente ai controlli ambulatoriali (forse con zelo eccessivo, per compensare la relativa incuria precedente).

Scenario Clinico (6)

• Nei primi mesi del 2003 il signor Giovanni sta bene, non lamenta dispnea nemmeno da sforzo, ma riferisce di aver ridotto l'attività fisica a causa di un' incostante fastidiosa astenia.

• Poi, a ciel sereno, si rendono necessari 2 ulteriori ricoveri:
  - a maggio per FA ad alta risposta ventricolare
  - a settembre per edema polmonare acuto.

• Nel corso del secondo ricovero l'ecocardiografia documenta una frazione di eiezione del 30%.

CLINICAL QUESTIONS

?

C. Avresti modificato la posologia di farmaci già assunti dal sig. Giovanni?

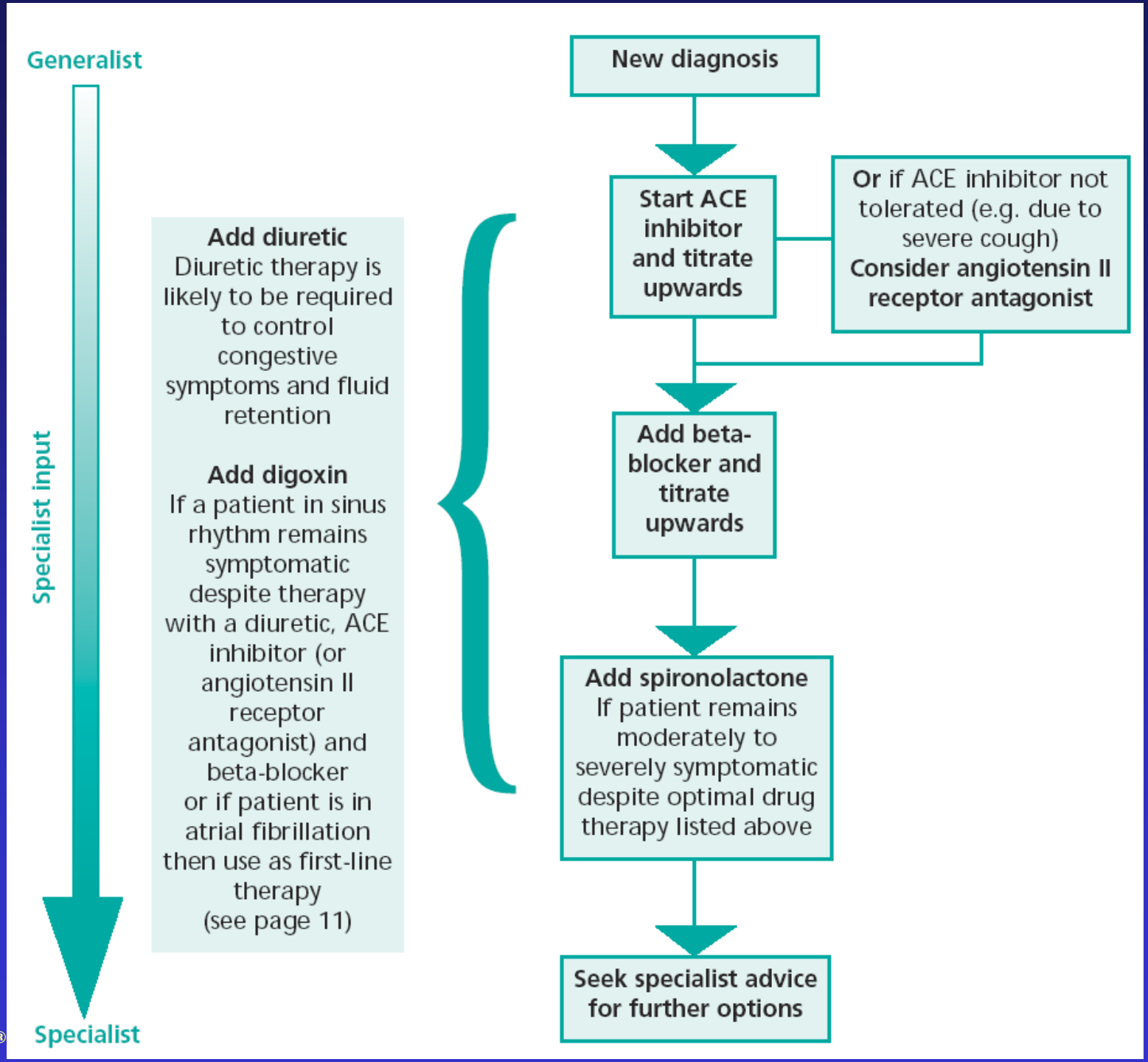
1. No
2. ↑ dose diuretici
3. ↑ dose ACE-inibitore
4. ↑ dose diuretici ed ACE-inibitore

D. Avresti prescritto al sig. Giovanni un beta-bloccante?

1. No
2. Sì

E. Avresti prescritto al sig. Giovanni altri farmaci?

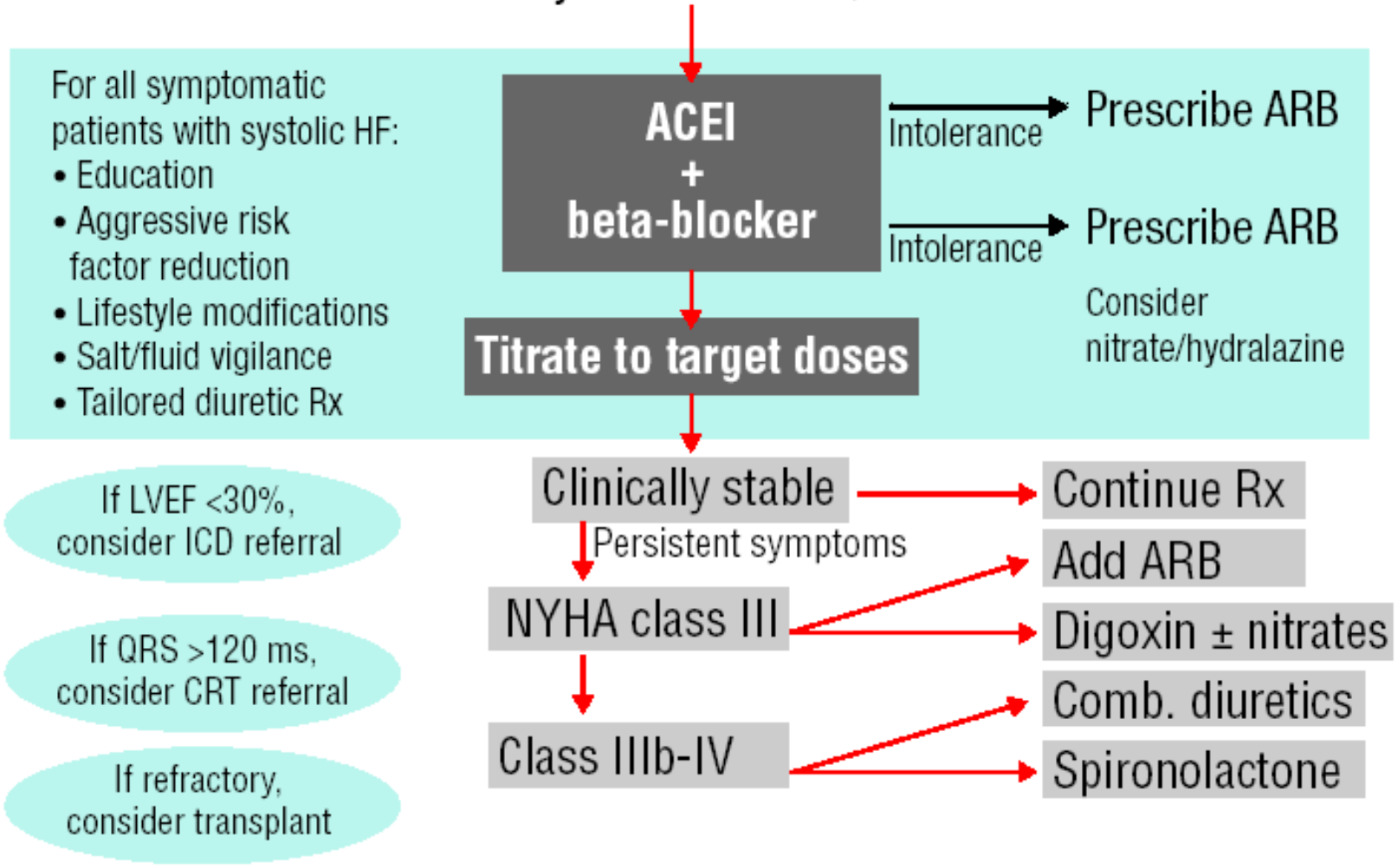
1. No
2. Digossina
3. Spironolattone
4. Entrambi i farmaci



NICE
July, 2003

Treatment of heart failure (HF)

If symptoms severe, refer to specialist: acute to ER, chronic to HF clinic
If HF symptoms but LVEF >40%, treat cause (eg, hypertension, ischemia)
If systolic HF LVEF <40%



Decisioni cliniche (3)

- Viene proposto un follow-up più intensivo, l'attivazione di un'ADI e, in accordo con il cardiologo, una modifica del trattamento farmacologico:

  - furosemide 25 mg 2 cpr/die
  - ramipril 5 mg 1 cpr/die
  - digossina 0.125 mg 1 cpr/die
  - canrenoato di potassio 50 mg 1 cpr/die
  - allopurinolo 300 mg 1 cpr/die
  - warfarin (secondo INR)

Scenario Clinico (7)

• Dopo alcuni mesi di terapia, il sig. Giovanni presenta dispnea, anche in seguito a sforzi lievi ed un controllo ematochimico evidenzia:

- iperglicemia a digiuno (130 mg/dl)
- persistente iperuricemia (7.2 mg/dl)
- sodiemia ai limiti inferiori (136 mEq/l)

• Nel gennaio 2004 vengo chiamata a domicilio per l'aggravamento della dispnea. Obiettivamente: aritmia con frequenza elevata al polso (140/min.) e rantoli bibasilari.

• Cautelativamente, predispongo il ricovero ospedaliero.

CLINICAL QUESTIONS

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F. Nei pazienti con scompenso cardiaco, la gestione multidisciplinare (MMG, specialista, infermiere) ha un impatto favorevole sugli esiti clinici, economici ed umanistici?

1. Sì
2. Sì, ma non è applicabile alla nostra realtà
3. No

1.4.3.1	Heart failure care should be delivered by a multidisciplinary team with an integrated approach across the healthcare community.	A
1.4.2.1	Patients with heart failure should generally be discharged from hospital only when their clinical condition is stable and the management plan is optimised. Timing of discharge should take into account patient and carer wishes, and the level of care and support that can be provided in the community.	GPP
1.4.2.2	The primary care team, patient and carer must be aware of the management plan.	GPP
1.4.2.3	Clear instructions should be given as to how the patient/carer can access advice particularly in the high-risk period immediately following discharge.	GPP

NICE. July, 2003

clinical evidence

BMJ Publishing Group

NON-DRUG TREATMENTS

Likely to be beneficial

Multidisciplinary interventions

- One systematic review has found that multidisciplinary programmes significantly reduce admissions to hospital but did not significantly reduce mortality.
- Telephone contact plus improved coordination of primary care had no significant effect on admission rate.
- Two included RCTs found that that home based support versus usual care significantly reduced cardiovascular events at 3–6 years.
- Subsequent RCTs found that education and nurse led support reduced death and hospital readmission and improved quality of life at 12 weeks to 1 year.

Clinical Evidence. March 2006

McAlister FA, Lawson FM, Teo KK, Armstrong PW.

A systematic review of randomized trials of disease management programs in heart failure

Am J Med 2001;110:378-84

CONCLUSION

- Disease management programs for the care of patients with heart failure that involve specialized follow-up by a multidisciplinary team reduce hospitalizations and appear to be cost saving.
- Data on mortality are inconclusive.
- Further studies are needed to establish the incremental benefits of the different elements of these programs.

McAlister FA, et al. Am J Med 2001

Phillips CO, et al.

Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure A meta-analysis.

JAMA 2004;291:1358-67

- Previous reviews of CHF disease management have emphasized beneficial effects of outpatient care and multidisciplinary teams

- However, the efficacy of programs incorporating discharge planning, transitional care, and postdischarge management for this patient population has not been established

- The aim of this review was to determine the efficacy of interventions that were described as comprehensive discharge planning plus postdischarge support for older inpatients with CHF and to quantify the effect on readmission rate, all-cause mortality, initial length of stay (LOS), quality of life (QOL), and overall medical costs.

Phillips CO, et al JAMA 2004

Components for postdischarge support also varied by study (TABLE 1). Three studies used a single home visit[22-24] during which CHF education and self-care were reviewed and reinforced. Six studies used a home visit and/or frequent telephone contacts[30-36] for this purpose and to facilitate rescheduling of missed appointments. One of 4 studies using increased clinic visits and frequent telephone follow-up[25-29] also used a home visit (1 hour) for intervention patients.[25] Four studies contained components intended to provide continuous multidisciplinary home care.[36-39] Finally, 1 study used a day hospital with an available specialized heart failure unit.[40]

Phillips CO, et al JAMA 2004

DATA SYNTHESIS (1)

• Eighteen studies representing data from 8 countries randomized 3304 older inpatients with CHF to comprehensive discharge planning plus postdischarge support or usual care.

• During a pooled mean observation period of 8 months (range, 3-12 months), fewer intervention patients were readmitted compared with controls (555/1590 vs 741/1714, number needed to treat=12

Phillips CO, et al JAMA 2004

DATA SYNTHESIS (2)

- Analysis of studies reporting secondary outcomes found:
  - a trend toward lower all-cause mortality for patients assigned to an intervention compared with usual care similar initial LOS
  - greater percentage improvement in QOL scores compared with baseline scores
  - similar or lower charges for medical care per patient per month for the initial hospital stay, administering the intervention, outpatient care, and readmission

Phillips CO, et al JAMA 2004

CONCLUSIONS

• Comprehensive discharge planning plus postdischarge support for older patients with CHF significantly reduced readmission rates and may improve health outcomes such as survival and QOL without increasing costs.

• These results have important implications for systems change, health outcomes, and resource utilization for older patients with CHF.

Phillips CO, et al JAMA 2004