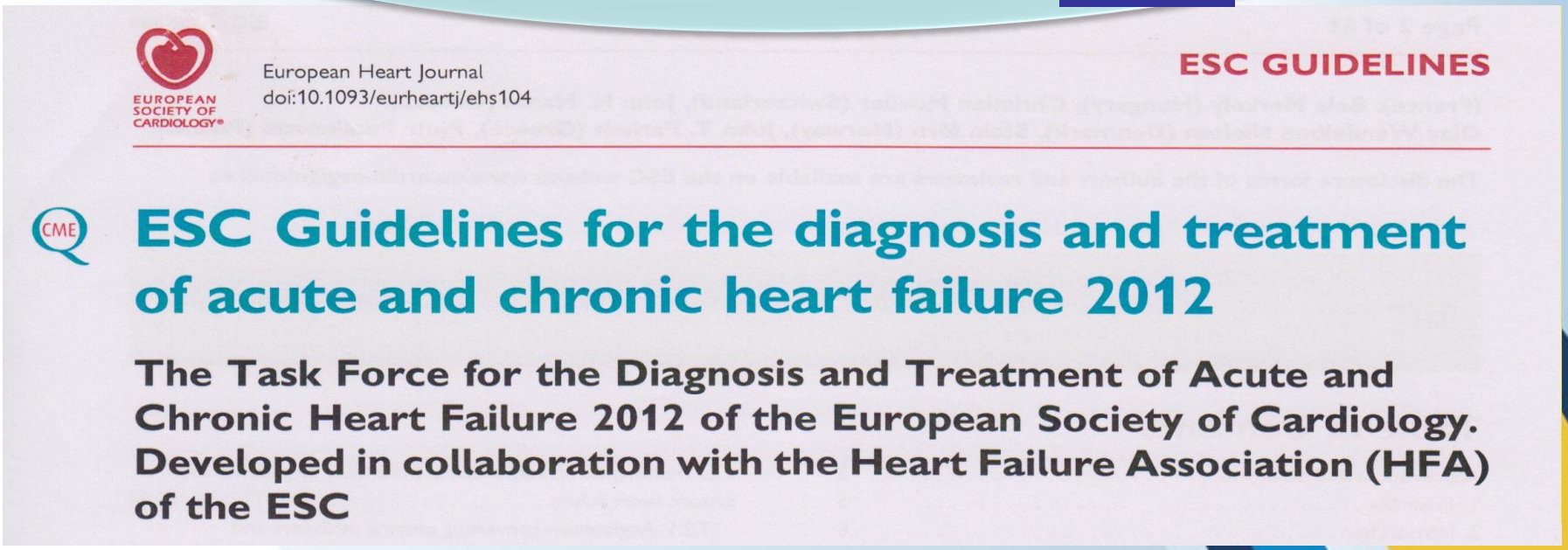
Acute and chronic Heart Failure: the “best” clinical decisions

Impact of the new recommendations on clinical practice

D. Brito



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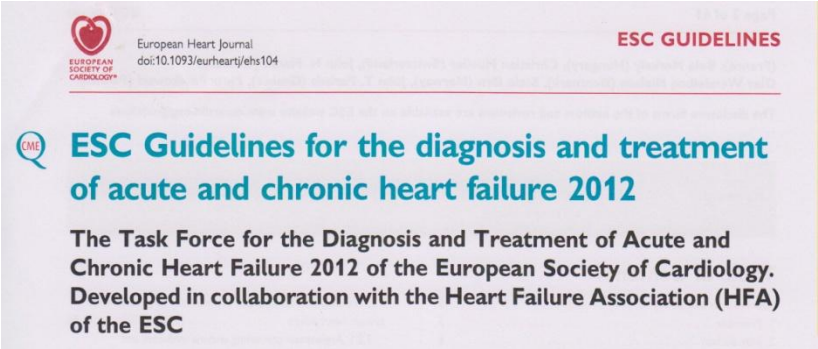
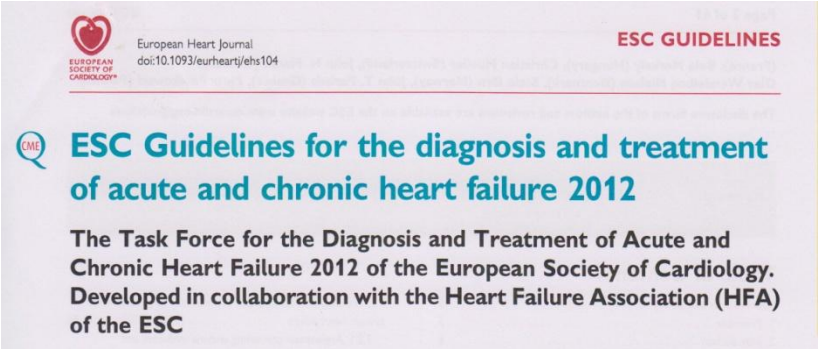


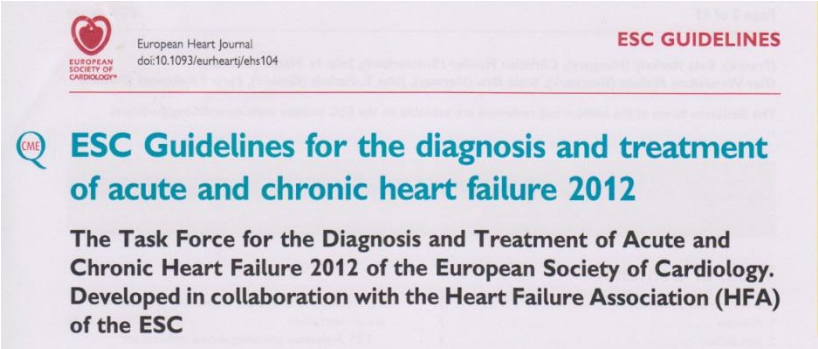
Impact of the new recommendations on clinical practice

- **Most relevant news**
  - ➢ Diagnostic tools for HF
  - ➢ Pharmacological treatment in chronic HF
    - systolic HF (reduced EjF)
    - HF with preserved EjF
  - ➢ Invasive therapy in chronic systolic HF
  - ➢ Treatment of acute HF



Impact of the new recommendations on clinical practice

- **Diagnostic tools for HF - I**
  - MR-proANP (mid-regional Pro-A-Type natriuretic peptide)
    - In the acute setting (acute HF or worsening of symptoms) was shown to be non-inferior to BNP and NT-proBNP
      - Exclusion cut-off point of 120 pmol/L vs 300 pg/ml (NT-proBNP) or 100 pg/ml (BNP) *Maisel A et al.,J Am Coll Cardiol. 2010*
  - TT Echo is still recommended as the first-line imaging investigation in pts with suspected HF … but a new impetus was given to other echo methods and to other different imaging modalities …



Impact of the new recommendations on clinical practice

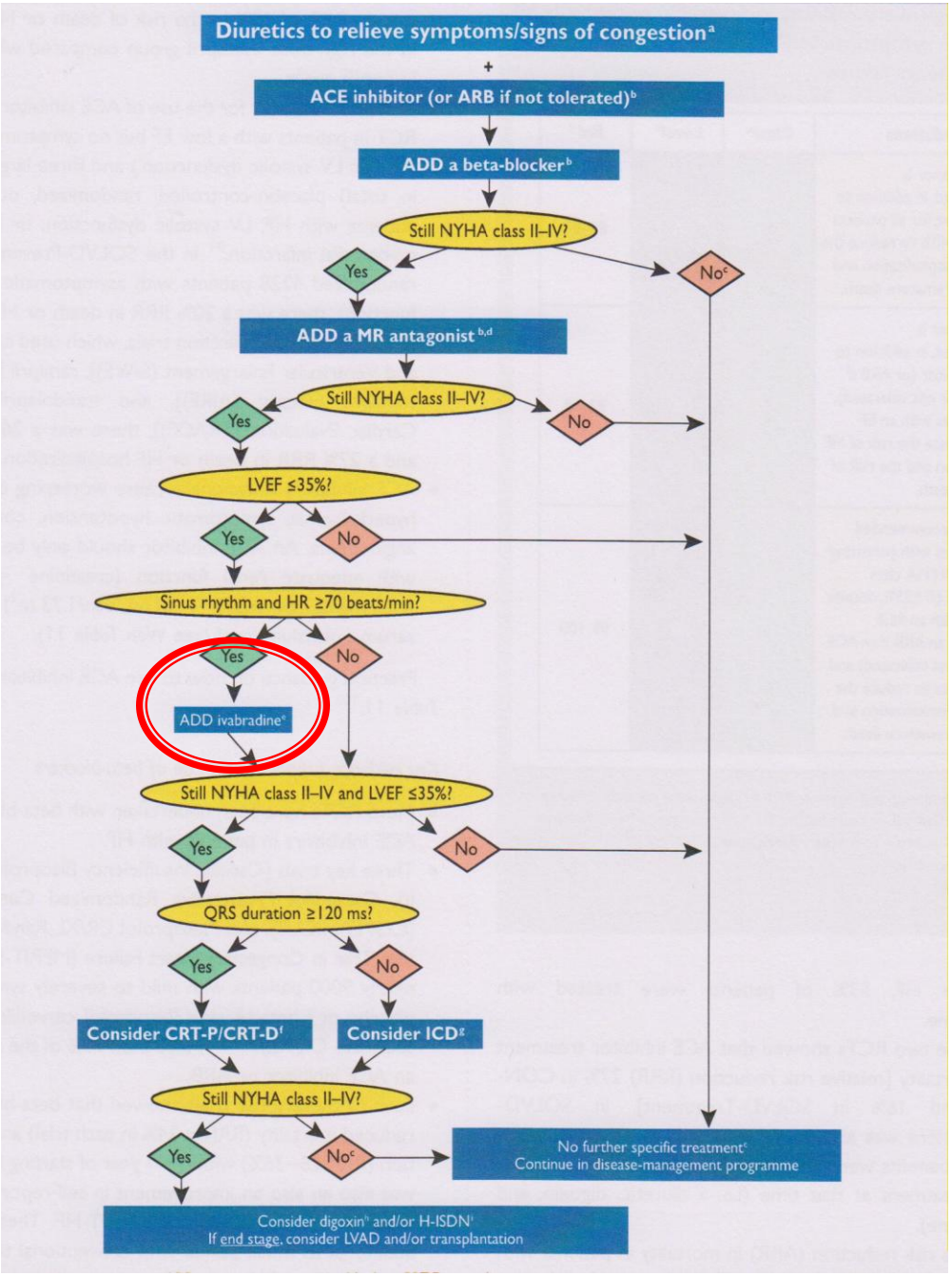
Gap in evidence!
Value in diagnosis of HF-PEjF?

- **Diagnostic tools for HF - II**
  - Diastolic stress testing – emerging procedure …
    - Identification of HF with PEjF in pts with HF, symptoms during physical activity, normal EjF and inclonclusive diastolic function parameters at rest *(Nagueh SF et al, Eu J Echocardiogr 2009)*
  - The relative value and place of CMR, CT angiography and nuclear techiques were commented and discussed. The value of CMR in particular was recognized …
    - High quality images
    - Assessement of congenital heart disease, cardiomyopathies, inflamatory and infiltrative conditions
    - Growing role in the evaluation of ischaemia and viability

- **Pharmacological treatment of chronic systolic HF - I**

  - **Ivabradine** - a drug that inhibits the *I*f (f is for "funny) and reduces cardiac pacemaker activity, slowing the heart rate, and allowing more time for blood to flow into the myocardium.

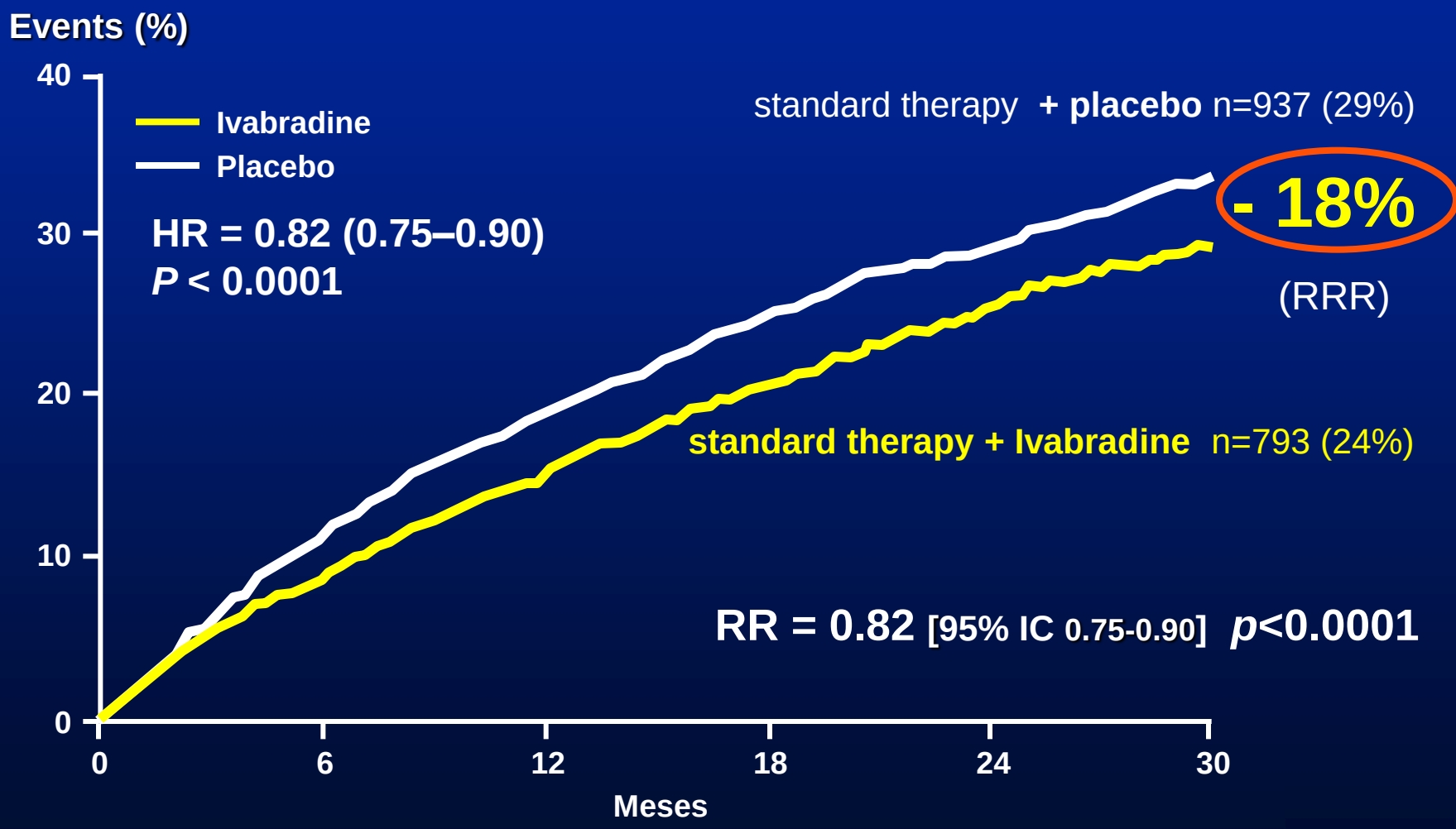
  - Is now recommended in HF pts with reduced EjF (≤ 35%) treated with ACE-I (or ARB) plus a beta-blocker (BB) plus a MR antagonist, if the pt remains symptomatic (class II to IV NYHA) and is in SR with a HR ≥ 70 bpm.



Other treatments with less-certain benefits in patients with symptomatic (NYHA class II–IV) systolic heart failure

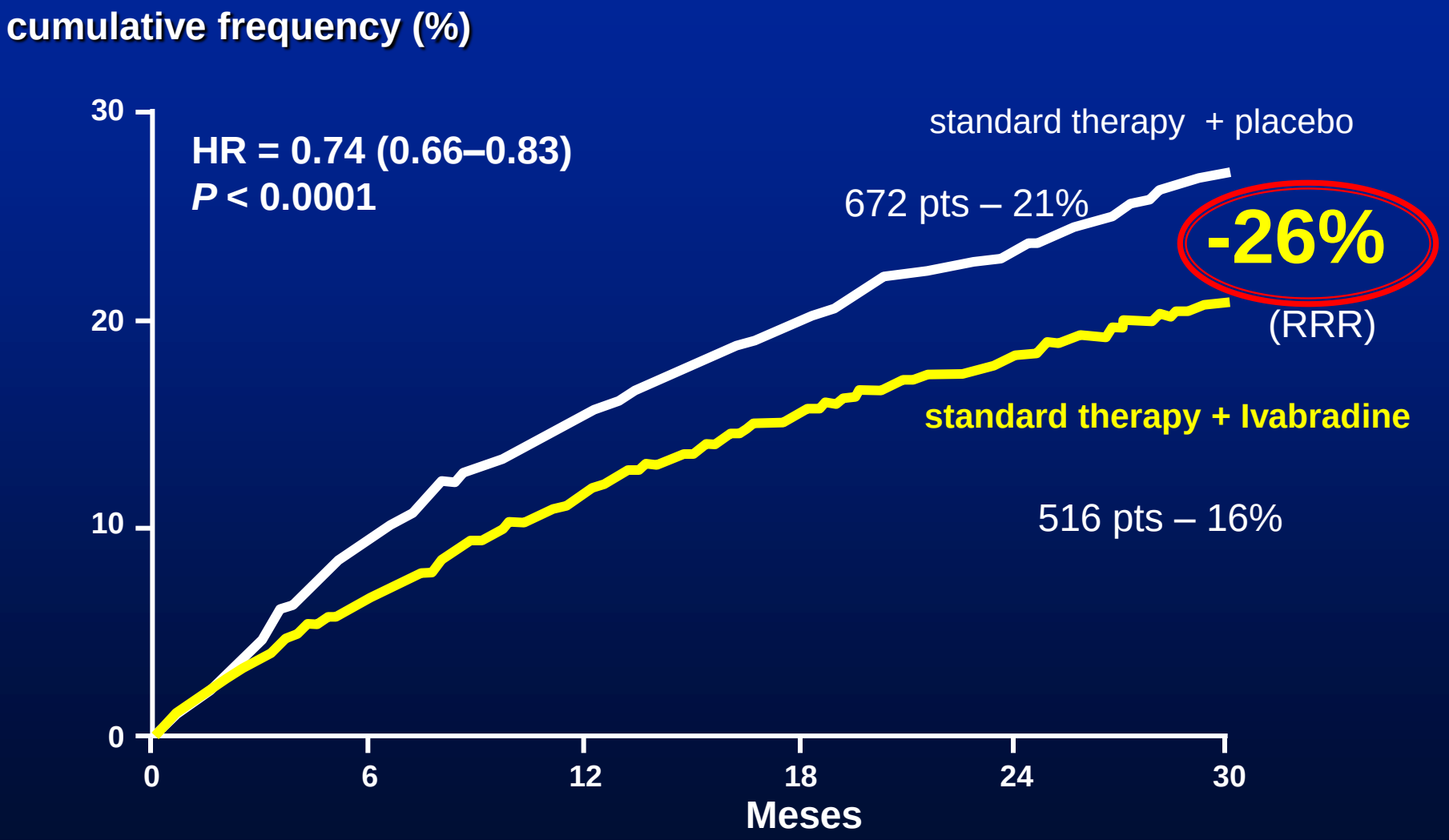
Recommendations	Class[a]	Level[b]	Ref[c]
ARB			
Recommended to reduce the risk of HF hospitalization and the risk of premature death in patients with an EF ≤40% and unable to tolerate an ACE inhibitor because of cough (patients should also receive a beta-blocker and an MRA).	I	A	108, 109
Recommended to reduce the risk of HF hospitalization in patients with an EF ≤40% and persisting symptoms (NYHA class II–IV) despite treatment with an ACE inhibitor and a beta-blocker who are unable to tolerate an MRA.[d]	I	A	110, 111
Ivabradine			
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).[e]	IIa	B	112
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate ≥70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).[e]	IIb	C	–
Digoxin			
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤45% who are unable to tolerate a beta-blocker (ivabradine is an alternative in patients with a heart rate ≥70 b.p.m.). Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).	IIb	B	113
May be considered to reduce the risk of HF hospitalization in patients with an EF ≤45% and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B	113
H-ISDN			
May be considered as an alternative to an ACE inhibitor or ARB, if neither is tolerated, to reduce the risk of HF hospitalization and risk of premature death in patients with an EF ≤45% and dilated LV (or EF ≤35%). Patients should also receive a beta-blocker and an MRA.	IIb	B	114, 115
May be considered to reduce the risk of HF hospitalization and risk of premature death in patients in patients with an EF ≤45% and dilated LV (or EF ≤35%) and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B	116
An *n*-3 PUFA[f] preparation may be considered to reduce the risk of death and the risk of cardiovascular hospitalization in patients treated with an ACE inhibitor (or ARB), beta-blocker, and an MRA (or ARB).	IIb	B	117

Primary composite outcome
Cardiovascular death or HF hospitalization



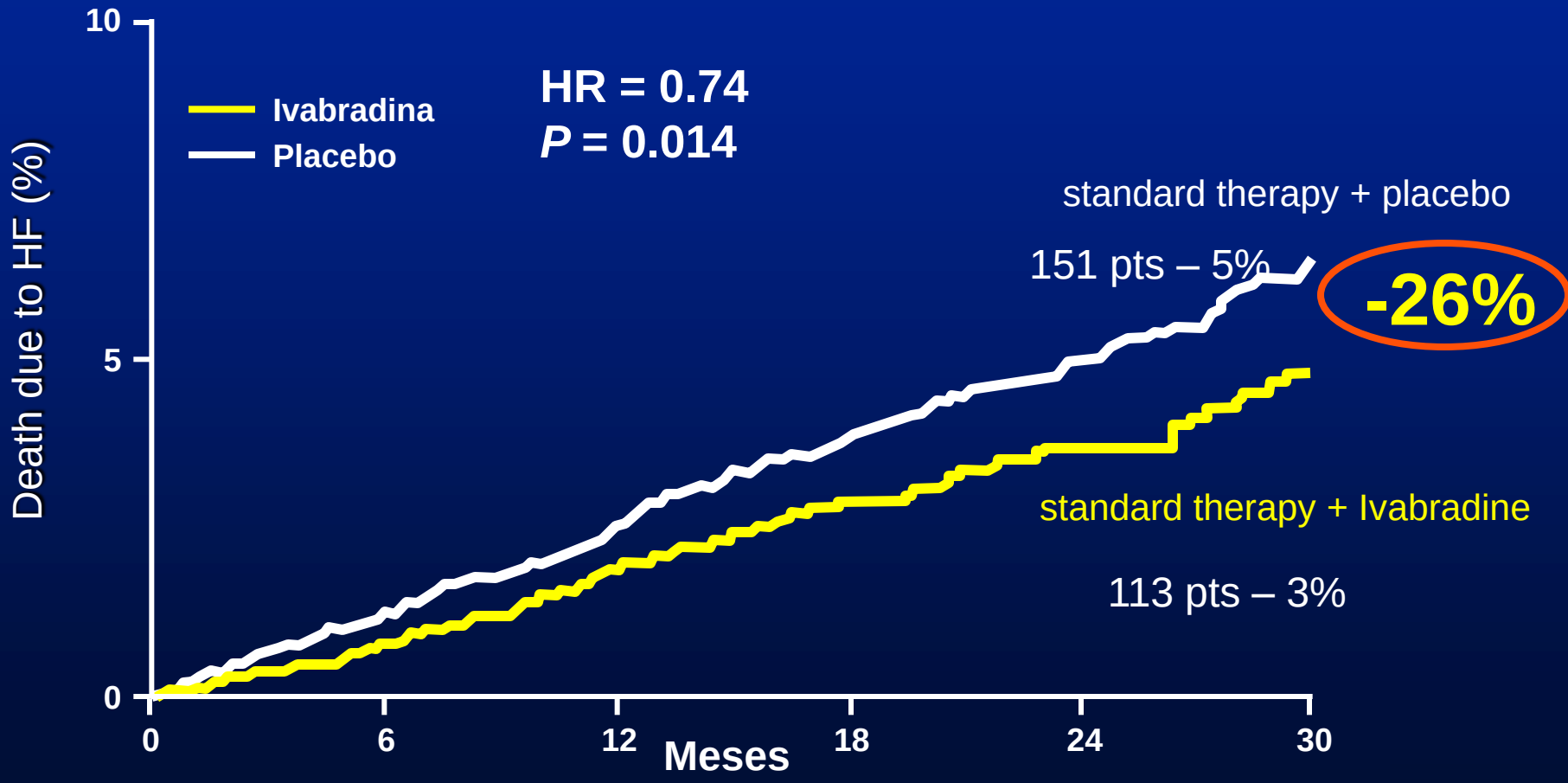
Swedberg K, et al. *Lancet*. 2010;online August 29.

HF hospitalizations



Swedberg K, et al. *Lancet*. 2010;online August 29.

HF mortality



Swedberg K, et al. *Lancet*. 2010;online August 29.

NHS

National Institute for Health and Clinical Excellence

NICE thumbs up for Servier's heart drug Procoralan

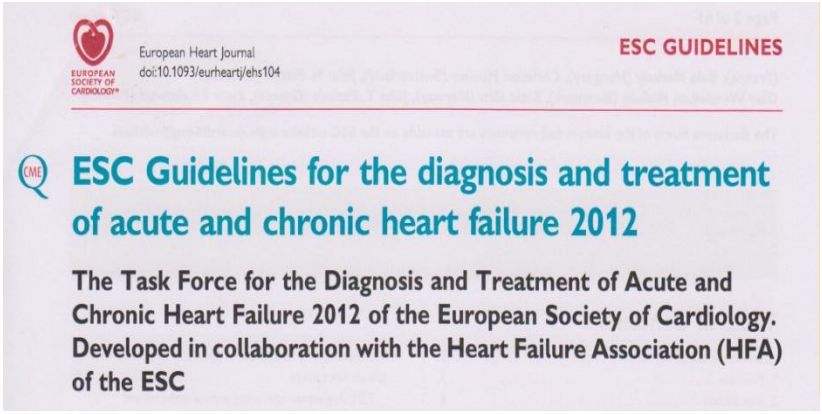
UK NEWS | AUGUST 07, 2012

Servier's *ivabradine* has won the backing of cost regulators for the National Health Service in England and Wales as an option for patients with chronic heart failure (CHF). The National Institute for Health and Clinical Excellence has published draft guidelines this morning (Tuesday) recommending the use of Procoralan (ivabradine) as an option for people with CHF

Cost effective for NHS

Clinical trials of *ivabradine* have demonstrated the drug's ability to reduce mortality and improving quality of life in patients with some types of chronic heart failure. This, coupled with its relatively low cost of £40.17 per 56-tablet pack, led the NICE's Appraisal Committee to agree that the incremental cost for the drug is likely to be around £8,500 per QALY (quality adjusted life year), and that it is therefore **likely to represent value for money as an option to treat CHF.**

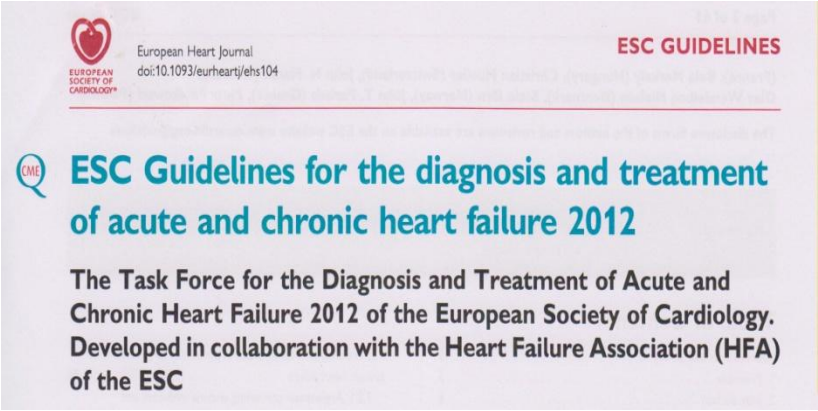
Note: a cost < £20,000 per QALY, is considered by NICE as cost-effective



Impact of the new recommendations on clinical practice

- **Pharmacological treatment of chronic systolic HF - I**
  - **Ivabradine …**

Only 26% of pts were , however, on full-dose BB and so Ivabradine should not be added before BB dosing is optimized



Impact of the new recommendations on clinical practice

- **Pharmacological treatment of chronic systolic HF - II**
  - **Indications for mineralocorticoid receptor antagonists (MRAs) are expended as new evidence with eplerenone sounds relevant (EMPHASIS-HF[1])**
- **The available evidence-data[1-3] favours the consideration that the benefits of MRAs probably extend to all pts with systolic HF**
- **MRAs are recommended in all pts who remain with symptoms on therapy with ACE-i (or ARB) plus BB (plus diuretic if needed)**

[1] Zannad et al. *N Engl J Med* 2011;364: 11-21; [2] Pitt B et al, *N Engl J Med* 1999;341: 709-717;
[3] Pitt B et al. *N Engl J Med* 2003;348: 1309-1321

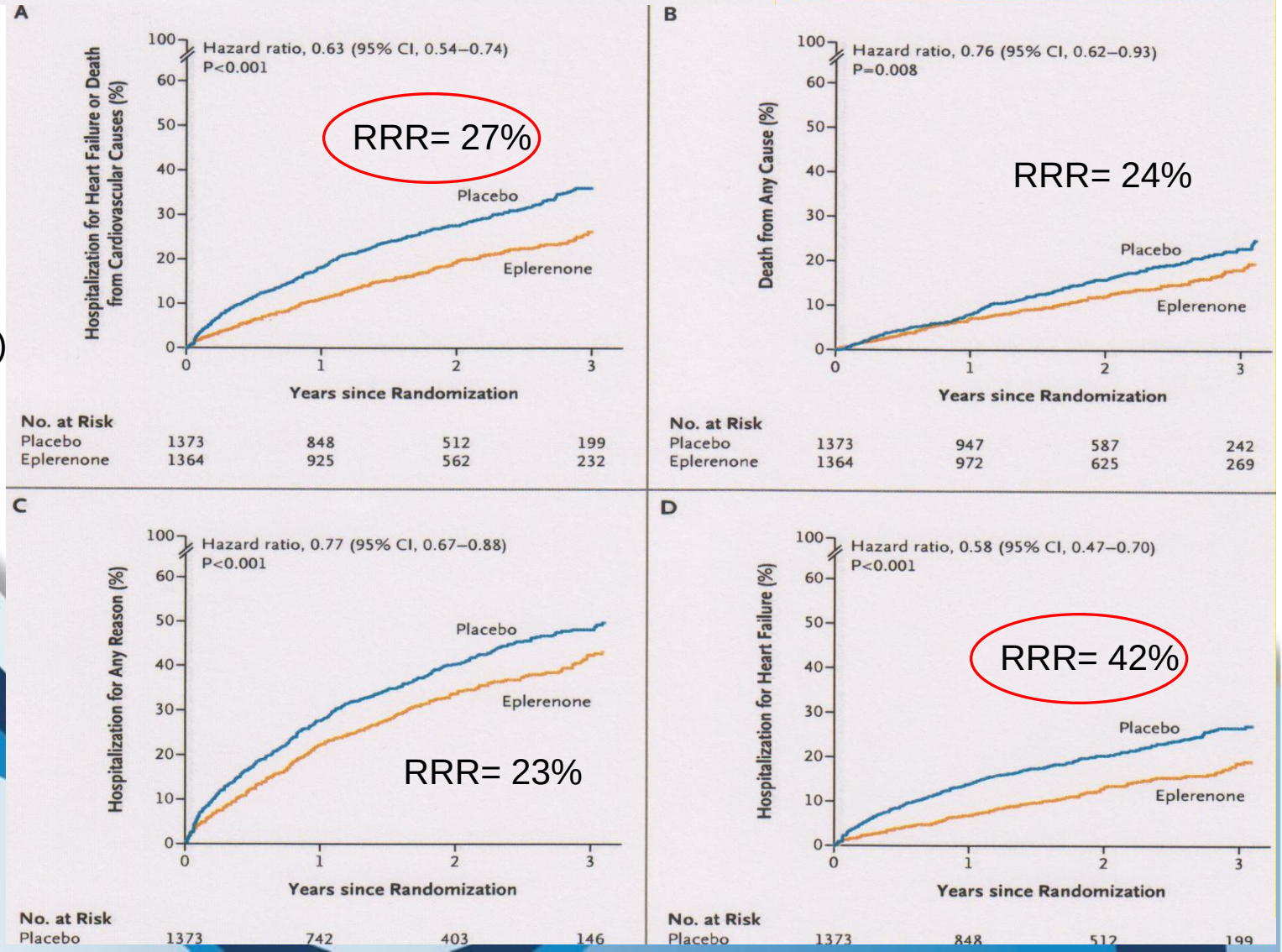
Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms

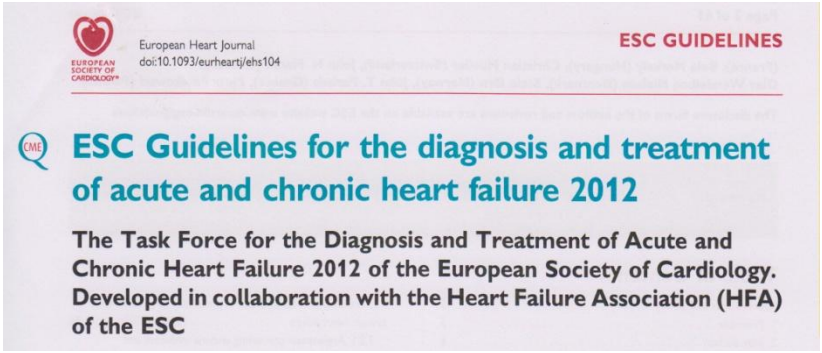
Faiez Zannad, M.D., Ph.D., John J.V. McMurray, M.D., Henry Krum, M.B., Ph.D., Dirk J. van Veldhuisen, M.D., Ph.D., Karl Swedberg, M.D., Ph.D., Harry Shi, M.S., John Vincent, M.B., Ph.D., Stuart J. Pocock, Ph.D., and Bertram Pitt, M.D., for the EMPHASIS-HF Study Group*

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 6, 2011 VOL. 364 NO. 1

N= 2737
NYHA class II
EjF ≤ 35%

Trial stopped prematurely (median Fup 21 m)





Impact of the new recommendations on clinical practice

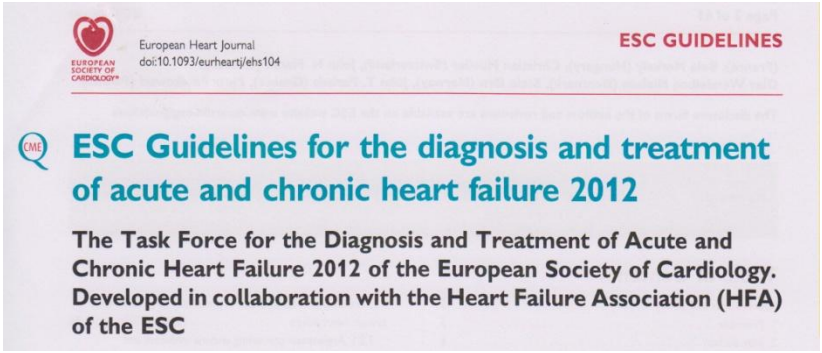
- **Pharmacological treatment of chronic systolic HF - III**
  - **The use of intravenous iron therapy in iron-deficient pts was a discussion point for the Task Force**

    Only a single trial*, with small number of pts, short-term follow-up and "soft" endpoints……. No class and level grading for this therapy in the guidelines

  - **HF with preserved EjF** — **No News!**

    No drugs has received a recommendation (no drug has been shown to date, to improve outcome significantly in this population)

- * Anker SD et al. *N Engl J Med* 2009;361 (25): 2436-48



Impact of the new recommendations on clinical practice

- **Invasive therapy in chronic systolic HF - I**
  - **Cardiac resynchronization therapy (CRT) in chronic systolic HF**
    - **New indication for CRT in pts with mild symptoms**
    - **More "certains" about the effect of CRT**
      - **Pts with LBBB QRS morphology and in SR have the greatest benefit from CRT**
      - **Pts with a non-LBBB QRS morphology and pts in AF have less certain benefit**

Gap in evidence!

Cardiac-Resynchronization Therapy for the Prevention of Heart-Failure Events

Arthur J. Moss, M.D., W. Jackson Hall, Ph.D., David S. Cannom, M.D., Helmut Klein, M.D., Mary W. Brown James P. Daubert, M.D., N.A. Mark Estes III, M.D., Elyse Foster, M.D., Henry Greenberg, M.D., Steven L. Higgins, M.D., Marc A. Pfeffer, M.D., Ph.D., Scott D. Solomon, M.D., David Wilber, M.D., and Wojciech Zareba, M.D., Ph.D., for the MADIT-CRT Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 1, 2009 VOL. 361 NO. 14

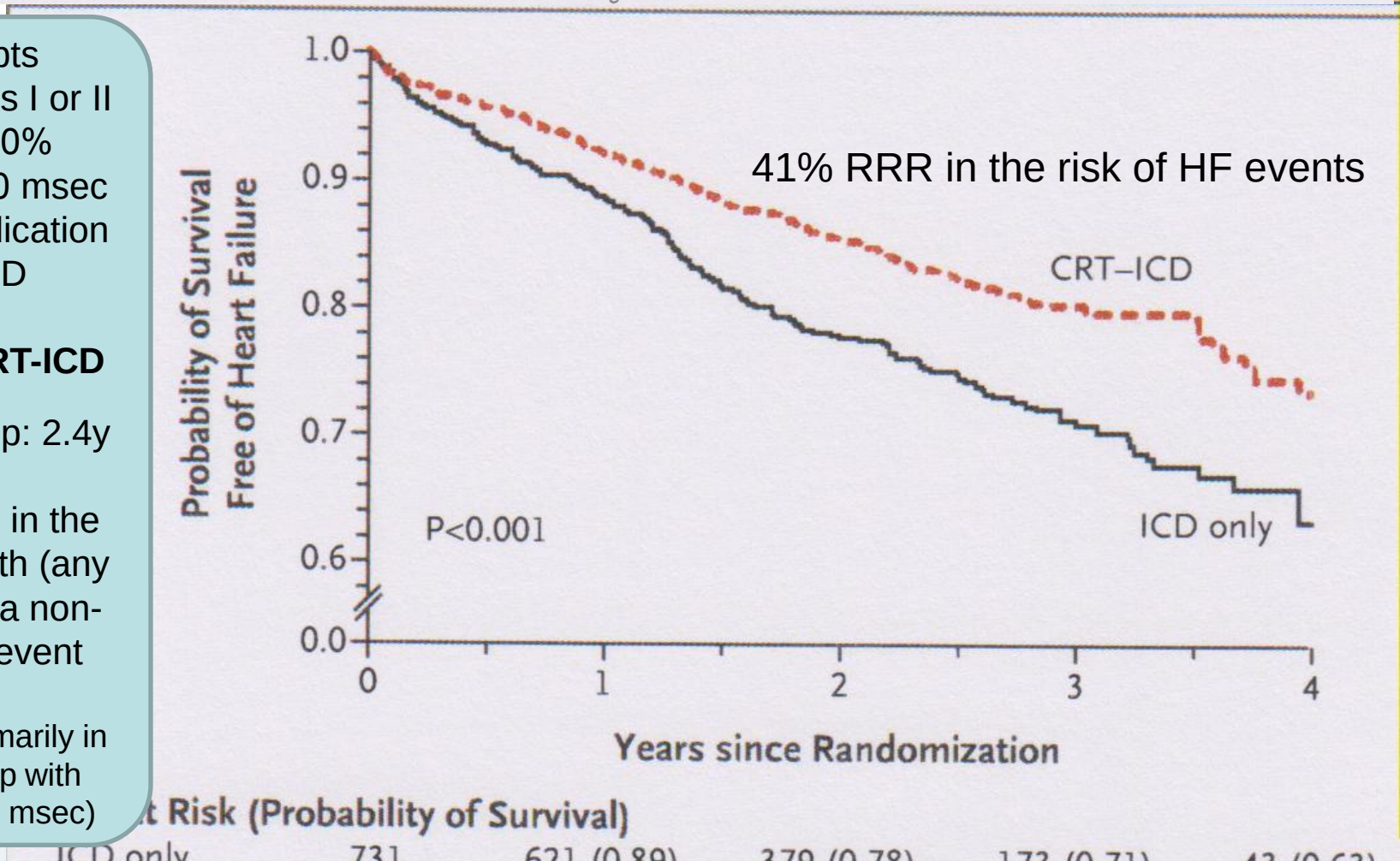
1820 pts
NYHA class I or II
EjF ≤ 30%
QRS ≥ 130 msec
All with indication for ICD

ICD vs CRT-ICD

Median Fup: 2.4y

34% RRR in the risk of death (any cause) or a non-fatal HF event

(evident primarily in a subgroup with QRS ≥ 150 msec)



Cardiac-Resynchronization Therapy for Mild-to-Moderate Heart Failure

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 DECEMBER 16, 2010 VOL. 363 NO. 25

Anthony S.L. Tang, M.D., George A. Wells, Ph.D., Mario Talajic, M.D., Malcolm O. Arnold, M.D., Robert Sheldon, M.D., Stuart Connolly, M.D., Stefan H. Hohnloser, M.D., Graham Nichol, M.D., David H. Birnie, M.D., John L. Sapp, M.D., Raymond Yee, M.D., Jeffrey S. Healey, M.D., and Jean L. Rouleau, M.D., for the Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT) Investigators

1798 pts
NYHA class II or III

EjF ≤ 30%

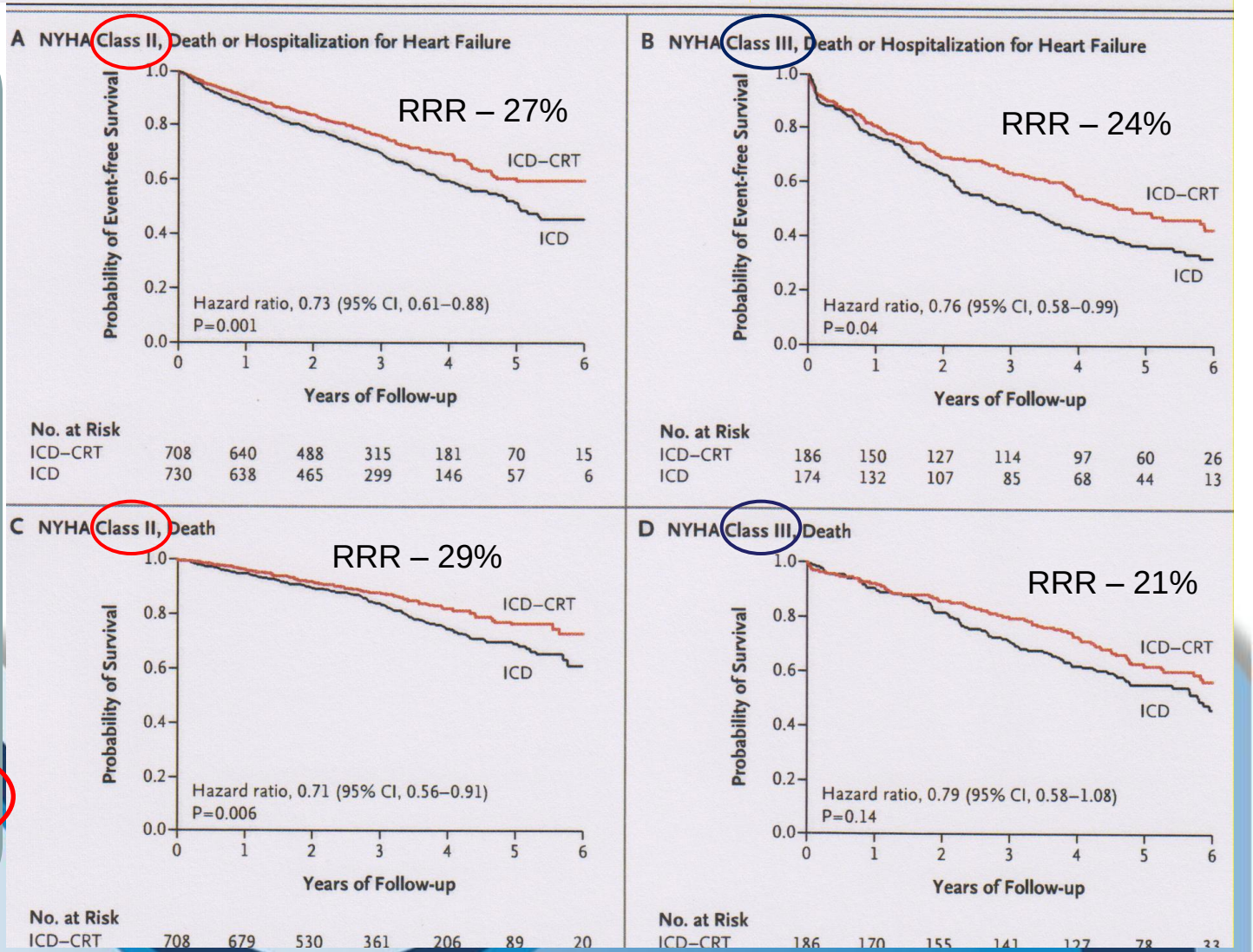
QRS ≥ 120 msec or paced QRS ≥ 200 msec

ICD vs ICD plus CRT

Primary endpoint: death (any cause) or hospitaliz for HF

Median Fup: 40 m

CRT-ICD better than CDI but also more adverse events



Recommendations for the use of CRT where the evidence is strong—patients in sinus rhythm with NYHA functional class III and ambulatory class IV heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy

Recommendations	Class[a]	Level[b]	Ref[c]
LBBB QRS morphology CRT-P/CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥120 ms, LBBB QRS morphology, and an EF ≤35%, who are expected to survive with good functional status for >1 year, to reduce the risk of HF hospitalization and the risk of premature death.	I	A	156, 157
Non-LBBB QRS morphology CRT-P/CRT-D should be considered in patients in sinus rhythm with a QRS duration of ≥150 ms, irrespective of QRS morphology, and an EF ≤35%, who are expected to survive with good functional status for >1 year, to reduce the risk of HF hospitalization and the risk of premature death.	IIa	A	156, 157

CRT-D = cardiac resynchronization therapy defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; EF = ejection fraction; HF = heart failure; LBBB = left bundle branch block; NYHA = New York Heart Association.

[a]Class of recommendation.

[b]Level of evidence.

[c]References.

Recommendations for the use of CRT where the evidence is strong—patients in sinus rhythm with NYHA functional class II heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy

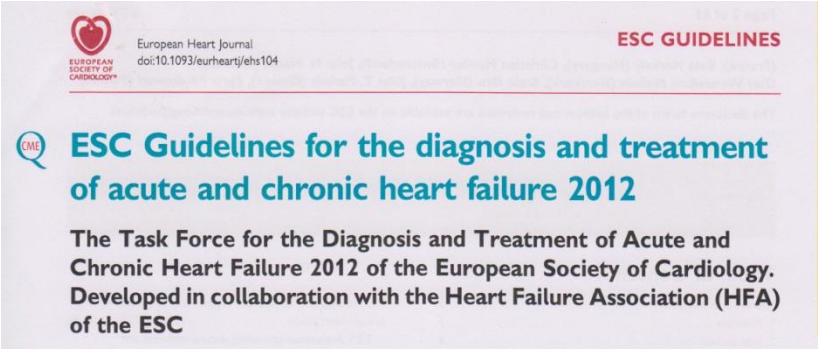
Recommendations	Class[a]	Level[b]	Ref[c]
LBBB QRS morphology CRT, preferably CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥130 ms, LBBB QRS morphology, and an EF ≤30%, who are expected to survive for >1 year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.	I	A	154, 155
Non-LBBB QRS morphology CRT, preferably CRT-D should be considered in patients in sinus rhythm with a QRS duration of ≥150 ms, irrespective of QRS morphology, and an EF ≤30%, who are expected to survive for >1 year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.	IIa	A	154, 155

CRT-D = cardiac resynchronization therapy defibrillator; EF = ejection fraction; HF = heart failure; LBBB = left bundle branch block; NYHA = New York Heart Association.

[a]Class of recommendation.

[b]Level of evidence.

[c]References.



Impact of the new recommendations on clinical practice

- **Invasive therapy in chronic systolic HF – II**
  - Transcatheter aortic valve implantation (TAVI) emerge in the guidelines as an alternative for severe aortic stenosis in patients unsuitable for surgery
    - **PARTNER B Trial** (**TAVI vs MT in inoperable pts with symptomatic AS**) – all cause death < 44%; cardiac death < 37% *(Leon MB et al, NEJM 2010)*
    - **PARTNER A Trial (TAVI vs SAVR in high risk pts with symptomatic AS)** – ≈ all cause death rates and ≈ AVA and mean Ao gradients after 2 years (Smith CR et al, *NEJM* 2011)
  - TAVI is superior to MT and non-inferior compared with SAVR
  - TAVI alleviates symptoms and improves health-related QoL compared with standard MT
  - **Indication: high risk for surgery!**

Low and high-risk pts: what are the limits?

MD CONFERENCE EXPRESS

THE OFFICIAL PEER-REVIEWED HIGHLIGHTS FROM THE

munich ESC CONGRESS 2012

Impact of the new recommendations on clinical practice

TAVI: 10 Years after the First Case

Bernard Prendergast (UK)
B. Lung (F)
M. Thomas (UK)

- **TAVI should be considered for pts with indication for AVR who are high risk for SAVR**
- **Risk assessment is a key issue! How to evaluate the risk?**
  - Risk scores in pts with AS have limitations
  - A better definition of contraindications to SAVR is needed
  - There is a need for better identification of pts who should not have any intervention
  - Clinical judgment through a multidisciplinary approach is essential for optimal patient selection

"Adoption of these new therapies should be based primarily on clinical outcome data rather than on enthusiasm, finances and healthcare systems…"

European Heart Journal
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

- **Invasive therapy in chronic systolic HF – III**
  - New information on coronary revascularization in systolic HF may also change our practice.

STICH trial

- 1212 pts (88% males), Fej ≤ 35%
- 2-vessel (31%) or 3-vessel (60%) CAD
- 68% severe proximal LAD stenosis
- Angina class 0, I, II – 95%
- HF NYHA class I, II, III – 97%

- MT vs CABG + MT
- Median Fup: 56 months

The NEW ENGLAND JOURNAL of MEDICINE

Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction

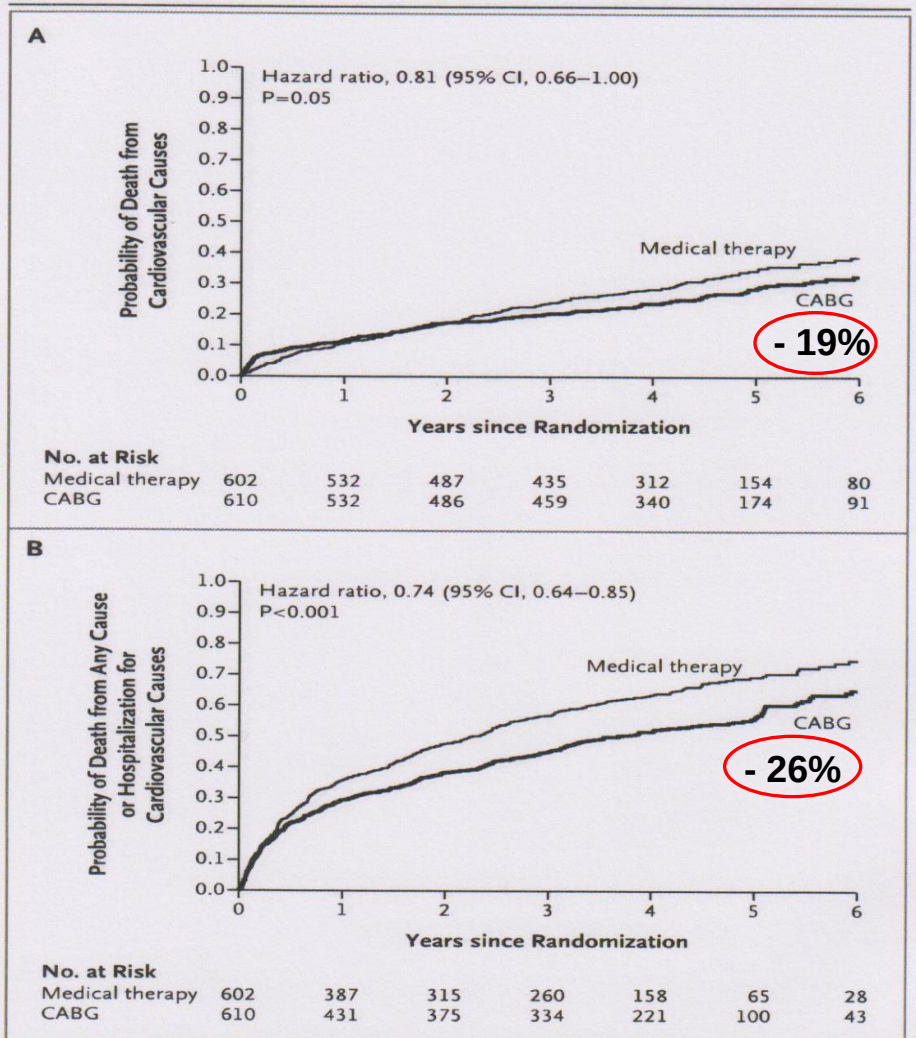


Figure 2. Kaplan–Meier Curves for the Probability of Death from Cardiovascular Causes and of Death from Any Cause or Hospitalization for Cardiovascular Causes.

CABG denotes coronary-artery bypass grafting.

European Heart Journal
doi:10.1093/eurheartj/ehs104

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

- the indication for CABG was extended to "STICH-like" patients.

Recommendations for myocardial revascularization in patients with chronic HF and systolic LV dysfunction

Recommendations	Class[a]	Level[b]	Ref[c]
CABG is recommended for patients with angina and significant left main stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of premature death.	I	C	–
CABG is recommended for patients with angina and two- or three-vessel coronary disease, including a left anterior descending stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of hospitalization for cardiovascular causes and the risk of premature death from cardiovascular causes.	I	B	191
Alternative to CABG: *PCI may be considered as an alternative to CABG in the above categories of patients unsuitable for surgery.*	IIb	C	–
CABG and PCI are NOT recommended in patients without angina AND without viable myocardium.	III	C	–

• Invasive therapy in chronic systolic HF – IV

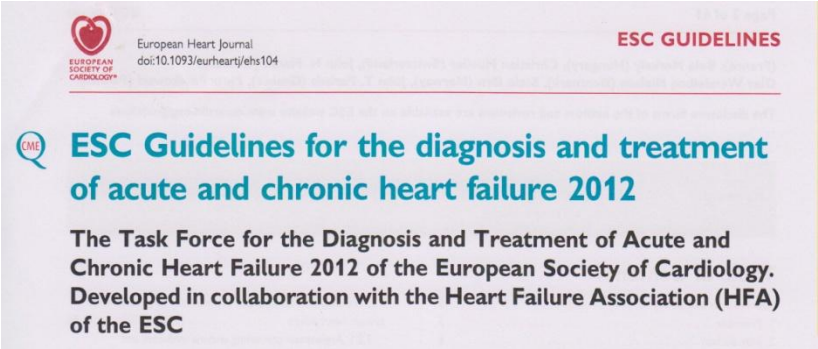
Mechanical circulatory support with LVAD is being increasingly used as a "destination therapy" in pts with end-stage HF not eligible for transplantation (as an alternative to it), to improve symptoms and reduce the risk of HF hospitalization and of premature death.

Table 25 Patients potentially eligible for implantation of a ventricular assist device

Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:
• LVEF <25% and, if measured, peak VO_2 < 12 mL/kg/min
• ≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause
• Dependence on i.v. inotropic therapy
• Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mm Hg and SBP ≤80–90 mmHg or CI ≤2 L/min/m²)
• Deteriorating right ventricular function

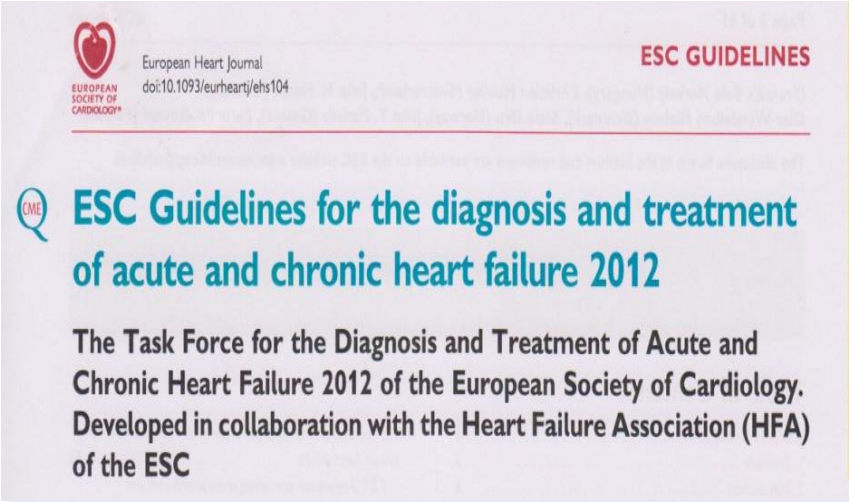
Recommendations for surgical implantation of LVADs in patients with systolic heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
An LVAD or BiVAD is recommended in selected patients[d] with end-stage HF despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation.	I	B	254, 255, 258
An LVAD should be considered in highly selected patients[d] who have end-stage HF despite optimal pharmacological and device therapy and who are not suitable for heart transplantation, but are expected to survive >1 year with good functional status, to improve symptoms, and reduce the risk of HF hospitalization and of premature death.	IIa	B	254



Impact of the new recommendations on clinical practice

- **News in the treatment of acute HF**
  - *Nesiritide* was shown to improve symptoms when added to conventinal treatment (mainly diuretic) and is mentioned as an option (if available) when a intravenous dilator is needed.
  - *Levosimendan* is only mentioned briefly as a potentially inotrope if it is necessary to counteract the effect of a beta-blocker. Its efficacy and safety remains uncertain.
  - *The use of nitrates* to treat acute HF was downgraded from a recommendation class I, level of evidence A (based on acute haemodynamic effects) to a class IIa, level of evidence B (reflecting the higher emphasis placed on symptoms, hospitalization and mortality).



Impact of the new recommendations on clinical practice

- The new ESC Guidelines presented important changes in the management of HF which surely will have a significant impact on clinical practice.
- Nonetheless some practices may continue to be economically unsuitable in some countries.

Congresso

Novas Fronteiras em Cardiologia

Obrigada