Le novità nella terapia dell'ipertensione arteriosa sistemica

Milano 9-10 aprile 2015

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Ospedale Valduce – Como

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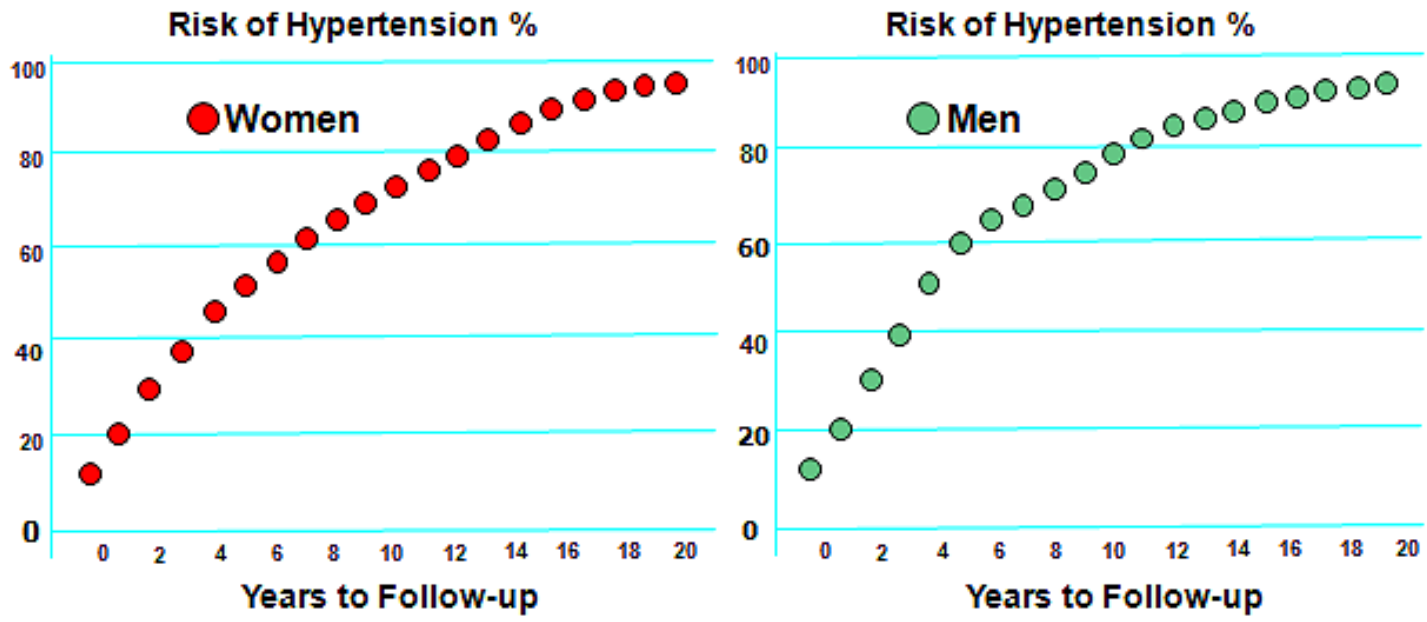
CONFLITTI DI INTERESSI : NESSUNO

La prevalenza

Overall the prevalence of hypertension appears to be around 30–45% of the general population, with a steep increase with ageing.

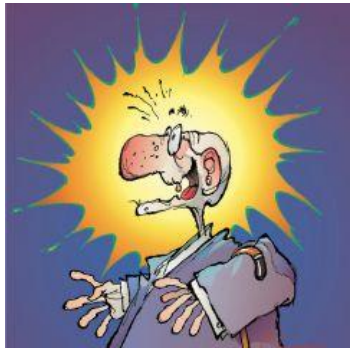


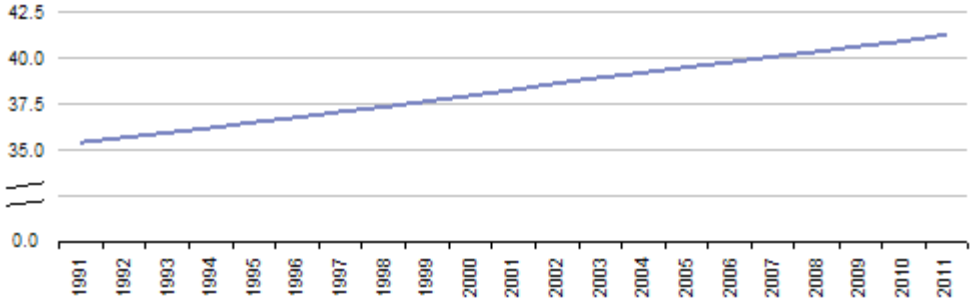
JAMA 2002: Framingham data.

CHEP

Hypertension CANADA

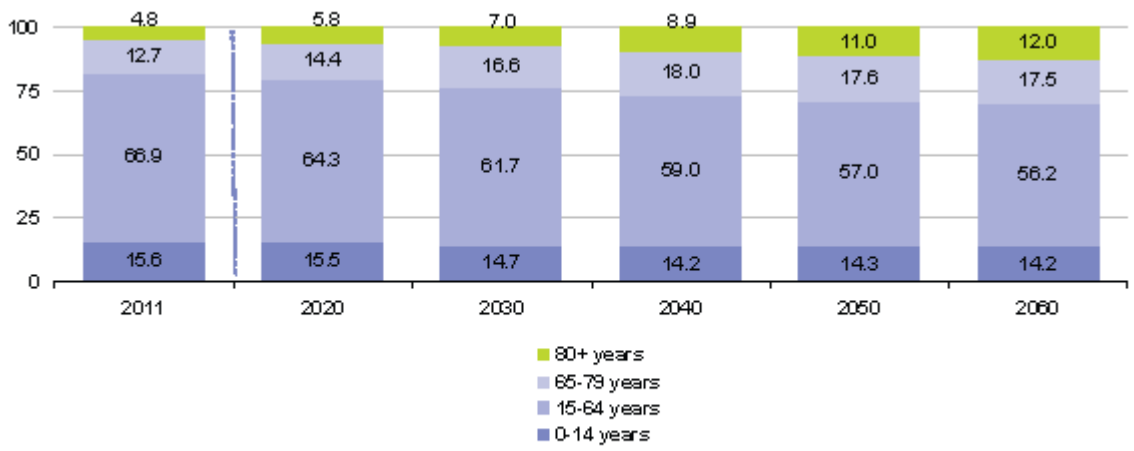
Demografia





(1) Excluding French overseas departments before 1998; 2009-2011, provisional.
Source: Eurostat (online data code: demo_pjanind)

Median age of population, EU-27, 1991-2011 (years)



(1) 2011, provisional; 2020-2060 data are projections (EUROPOP2010 convergence scenario).
Source: Eurostat (online data codes: demo_pjanind and proj_10c2150p)

Population structure by major age groups, EU-27, 2011-2060 (% of total population)

La diagnosi

Table 3 Definitions and classification of office blood pressure levels (mmHg)[a]

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

[a]The blood pressure (BP) category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.

Table 6 Definitions of hypertension by office and out-of-office blood pressure levels

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Office BP	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake)	≥135	and/or	≥85
Nighttime (or asleep)	≥120	and/or	≥70
24-h	≥130	and/or	≥80
Home BP	≥135	and/or	≥85

BP = blood pressure.

European Heart Journal (2013) 34, 2159–2219
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

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Table 5 Office blood pressure measurement

When measuring BP in the office, care should be taken:
• To allow the patients to sit for 3–5 minutes before beginning BP measurements.
• To take at least two BP measurements, in the sitting position, spaced 1–2 min apart, and additional measurements if the first two are quite different. Consider the average BP if deemed appropriate.
• To take repeated measurements of BP to improve accuracy in patients with arrhythmias, such as atrial fibrillation.
• To use a standard bladder (12–13 cm wide and 35 cm long), but have a larger and a smaller bladder available for large (arm circumference >32 cm) and thin arms, respectively.
• To have the cuff at the heart level, whatever the position of the patient.
• When adopting the auscultatory method, use phase I and V (disappearance) Korotkoff sounds to identify systolic and diastolic BP, respectively.
• To measure BP in both arms at first visit to detect possible differences. In this instance, take the arm with the higher value as the reference.
• To measure at the first visit, BP 1 and 3 min after assumption of the standing position in elderly subjects, diabetic patients, and in other conditions in which orthostatic hypotension may be frequent or suspected.
• To measure, in case of conventional BP measurement, heart rate by pulse palpation (at least 30 s) after the second measurement in the sitting position.

BP = blood pressure.

La diagnosi

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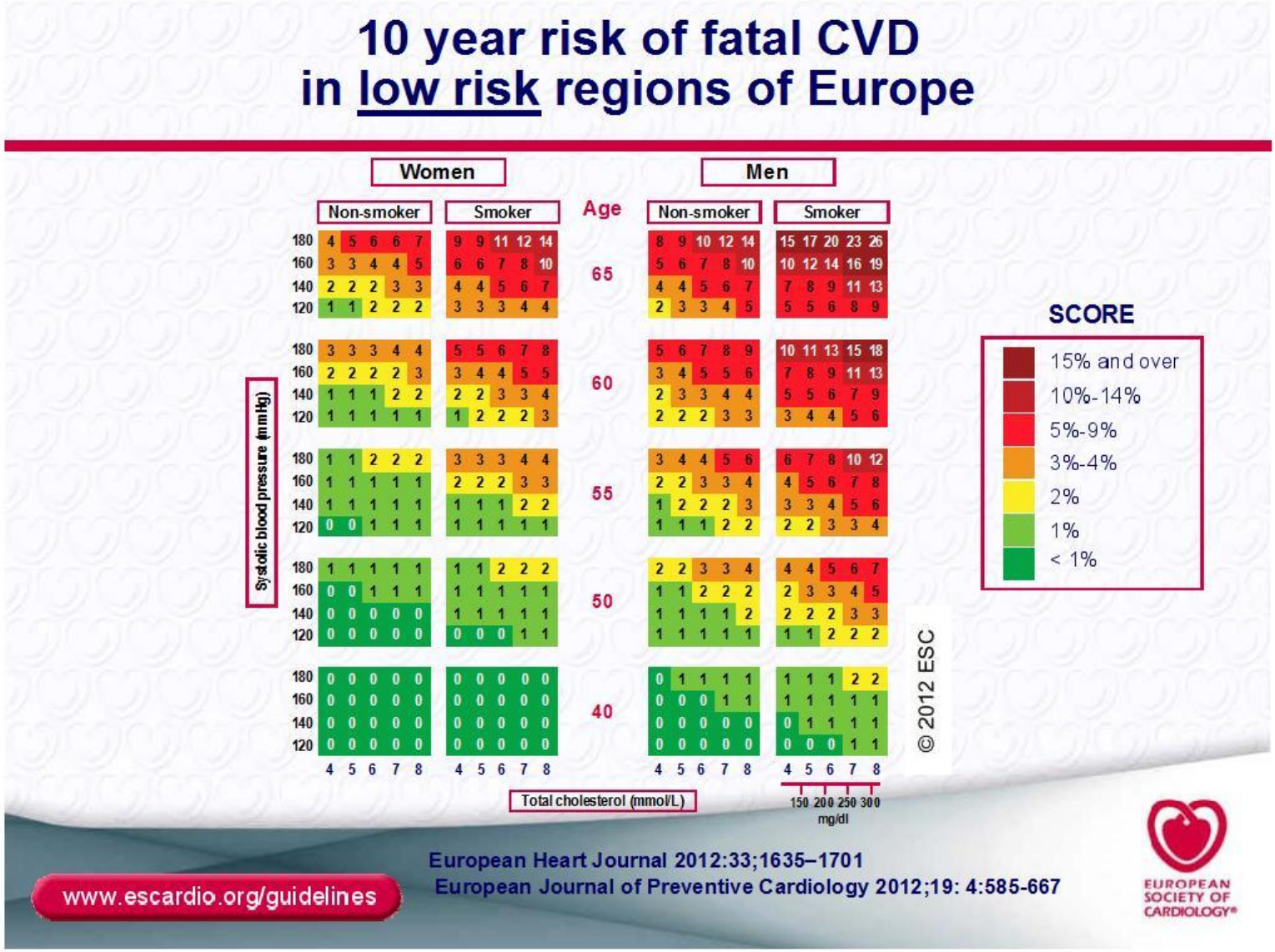
Stratificazione del rischio

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to Moderate risk	Moderate to high risk	High Risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Figure 1 Stratification of total CV risk in categories of low, moderate, high and very high risk according to SBP and DBP and prevalence of RFs, asymptomatic OD, diabetes, CKD stage or symptomatic CVD. Subjects with a high normal office but a raised out-of-office BP (masked hypertension) have a CV risk in the hypertension range. Subjects with a high office BP but normal out-of-office BP (white-coat hypertension), particularly if there is no diabetes, OD, CVD or CKD, have lower risk than sustained hypertension for the same office BP.



Prediction is very difficult, especially if it is about the future

Nils Bohr (1885-1962)

Strategy of prevention: lessons from cardiovascular disease

GEOFFREY ROSE

BRITISH MEDICAL JOURNAL VOLUME 282 6 JUNE 1981

MEDICAL PRACTICE

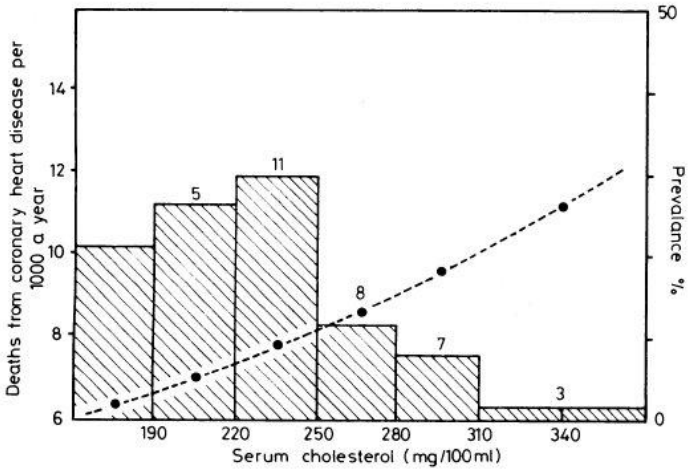


FIG 3—Prevalence distribution of serum cholesterol concentration related to coronary heart disease mortality (- - - -) in men aged 55-64. Number above each bar represents estimate of attributable deaths per 1000 population per 10 years. (Based on Framingham Study.[4])

Conversion: SI to traditional units—Cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.

TABLE II—*Relative and absolute benefits from the treatment of hypertension, according to age and the presence of cardiovascular-renal abnormality*[3]

Age (yr)	Cardiovascular renal abnormality	Treatment effectiveness (%)	Lives saved per 100 treated
50	–	59	6
	+	62	14
50	–	50	15
	+	60	29

cases of coronary heart disease there is no contact with physicians at all, the first recognised occurrence being sudden death. It follows inexorably that prevention is essential. With coronary heart disease, the recent experience of Australia and the United States shows also that prevention is possible, at least in part.

The preventive strategy that concentrates on high-risk individuals may be appropriate for those individuals, as well as being a wise and efficient use of limited medical resources; but its ability to reduce the burden of disease in the whole community tends to be disappointingly small. Potentially far more effective, and ultimately the only acceptable answer, is the mass strategy, whose aim is to shift the whole population's distribution of the risk variable. Here, however, our first concern must be that such mass advice is safe.

Il paradosso di ROSE
Strategie di popolazione e strategie individuali, con target obiettivi e metodi ≠

Stratificazione del rischio

Table 4 Factors—other than office BP—influencing prognosis; used for stratification of total CV risk in *Figure 1*

Risk factors
Male sex
Age (men ≥55 years; women ≥65 years)
Smoking
Dyslipidaemia
Total cholesterol >4.9 mmol/L (190 mg/dL), and/or
Low-density lipoprotein cholesterol >3.0 mmol/L (115 mg/dL), and/or
High-density lipoprotein cholesterol: men <1.0 mmol/L (40 mg/dL), women <1.2 mmol/L (46 mg/dL), and/or
Triglycerides >1.7 mmol/L (150 mg/dL)
Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dL)
Abnormal glucose tolerance test
Obesity [BMI ≥30 kg/m^2 (height^2)]
Abdominal obesity (waist circumference: men ≥102 cm; women ≥88 cm) (in Caucasians)
Family history of premature CVD (men aged <55 years; women aged <65 years)
Asymptomatic organ damage
Pulse pressure (in the elderly) ≥60 mmHg
Electrocardiographic LVH (Sokolow–Lyon index >3.5 mV; RaVL >1.1 mV; Cornell voltage duration product >244 mV*ms), or
Echocardiographic LVH [LVM index: men >115 g/m^2; women >95 g/m^2 (BSA)][a]
Carotid wall thickening (IMT >0.9 mm) or plaque
Carotid–femoral PWV >10 m/s
Ankle-brachial index <0.9
CKD with eGFR 30–60 mL/min/1.73 m^2 (BSA)
Microalbuminuria (30–300 mg/24 h), or albumin–creatinine ratio (30–300 mg/g; 3.4–34 mg/mmol) (preferentially on morning spot urine)
Diabetes mellitus
Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) on two repeated measurements, and/or
HbA_{1c} >7% (53 mmol/mol), and/or
Post-load plasma glucose >11.0 mmol/L (198 mg/dL)
Established CV or renal disease
Cerebrovascular disease: ischaemic stroke; cerebral haemorrhage; transient ischaemic attack
CHD: myocardial infarction; angina; myocardial revascularization with PCI or CABG
Heart failure, including heart failure with preserved EF
Symptomatic lower extremities peripheral artery disease
CKD with eGFR <30 mL/min/1.73m^2 (BSA); proteinuria (>300 mg/24 h).
Advanced retinopathy: haemorrhages or exudates, papilloedema

BMI = body mass index; BP = blood pressure; BSA = body surface area; CABG = coronary artery bypass graft; CHD = coronary heart disease; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; EF = ejection fraction; eGFR = estimated glomerular filtration rate; HbA_{1c} = glycated haemoglobin; IMT = intima-media thickness; LVH = left ventricular hypertrophy; LVM = left ventricular mass; PCI = percutaneous coronary intervention; PWV = pulse wave velocity.

[a]Risk maximal for concentric LVH: increased LVM index with a wall thickness/radius ratio of >0.42.

Stratificazione del rischio

Total cardiovascular risk assessment

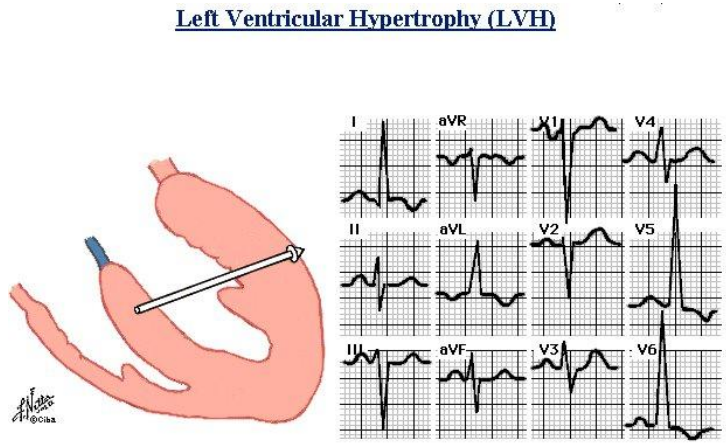
Recommendations	Class [a]	Level [b]	Ref. [c]
In asymptomatic subjects with hypertension but free of CVD, CKD, and diabetes, total CV risk stratification using the SCORE model is recommended as a minimal requirement.	I	B	43
As there is evidence that OD predicts CV death independently of SCORE, a search for OD should be considered, particularly in individuals at moderate risk.	IIa	B	51, 53
It is recommended that decisions on treatment strategies depend on the initial level of total CV risk.	I	B	41, 42, 50

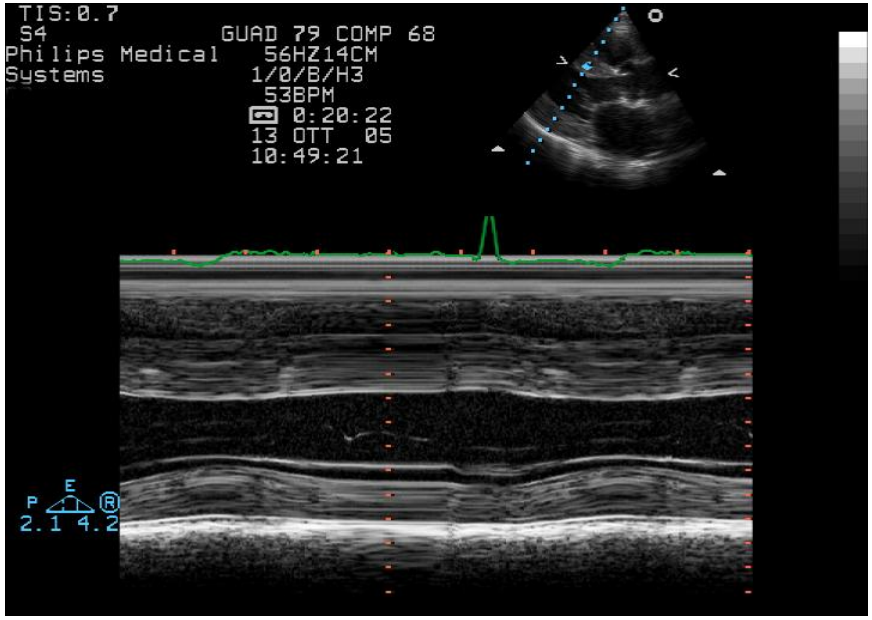
CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; OD = organ damage; SCORE = Systematic COronary Risk Evaluation

[a]Class of recommendation.

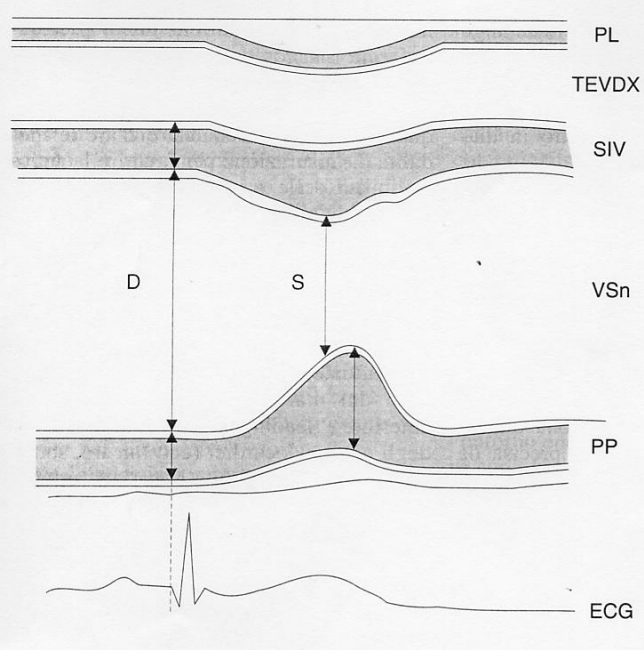
[b]Level of evidence.

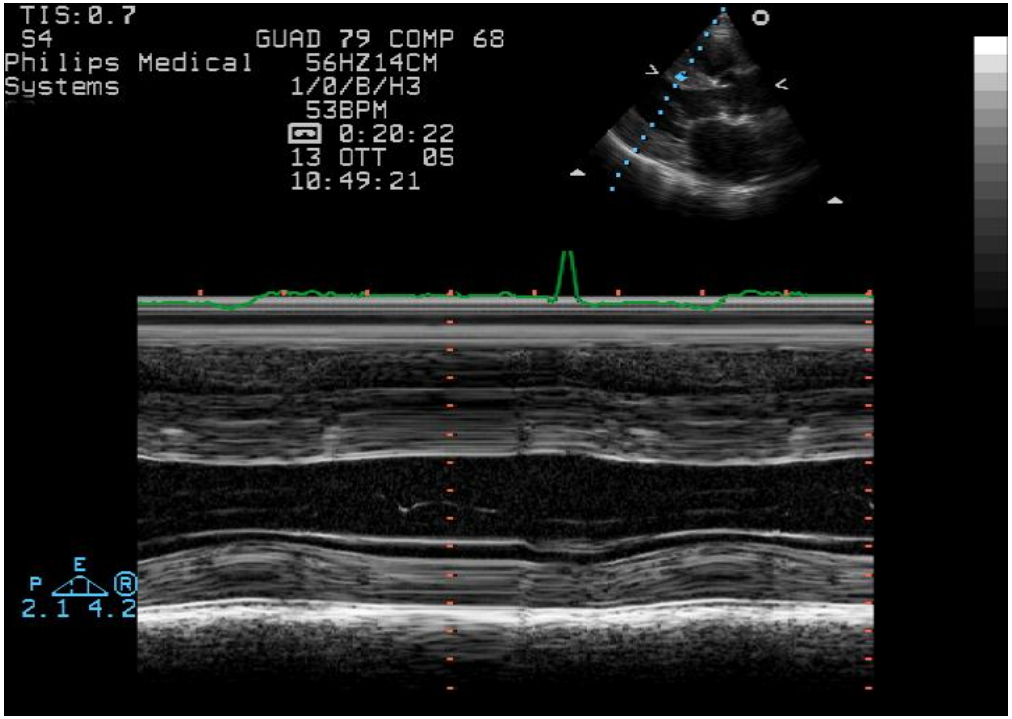
[c]Reference(s) supporting recommendation(s).





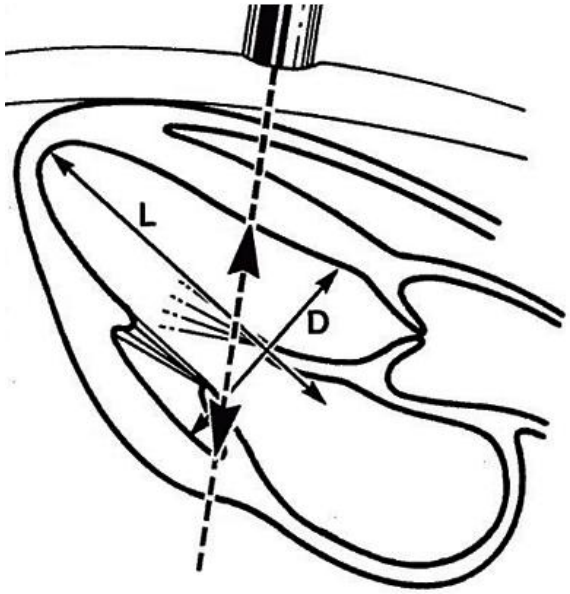
Ecocardiografia nell'ipertensione arteriosa

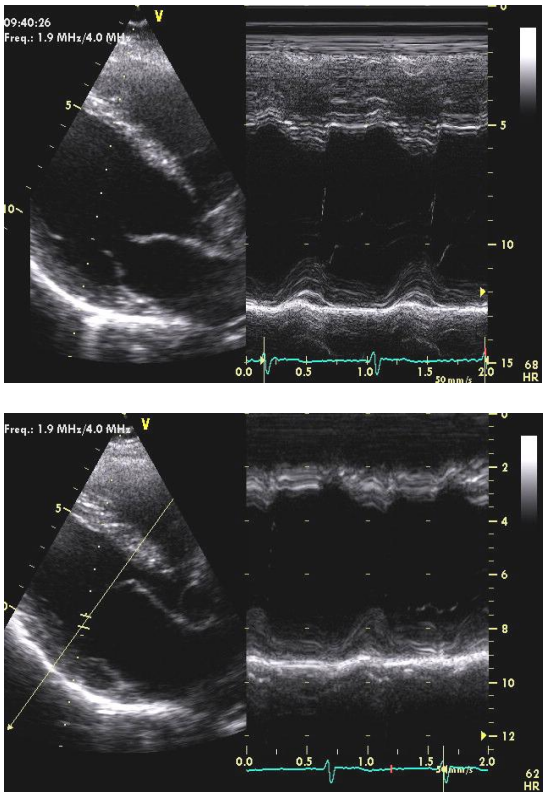




$$MVS = 0.8 \times 1.04 \times [\,(DTD + PP + SIV)^3 - DTD^3\,] + 0.6\ gr$$

Ecocardiografia nell'ipertensione arteriosa



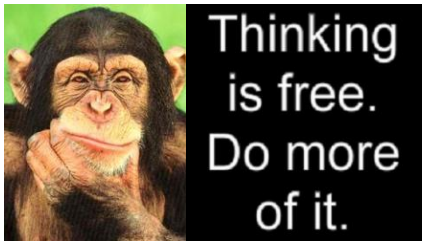


$$MVS = 0.8 \times 1.04 \times [\,(DTD + PP + SIV)^3 - DTD^3\,] + 0.6\ gr$$

Ecocardiografia nell'ipertensione arteriosa

Echocardiographic Measurements

Correct orientation of imaging planes was verified as described previously.[28] Left ventricular internal dimension and wall thicknesses were measured at end-diastole and end-systole by American Society of Echocardiography recommendations[29,30] using a computerized review station; all measurements were verified (and often corrected) or made primarily by experienced investigators.



ORIGINAL CONTRIBUTION

Prognostic Significance of Left Ventricular Mass Change During Treatment of Hypertension

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Kristian Wachtell, MD, PhD
Eva Gerdts, MD, PhD
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Jens Rokkedal, MD
Katherine Harris, DrPH
Peter Aurup, MD
Björn Dahlöf, MD, PhD

Context Increased baseline left ventricular (LV) mass predicts cardiovascular (CV) complications of hypertension, but the relation between lower LV mass and outcome during treatment for hypertension is uncertain.

Objective To determine whether reduction of LV mass during antihypertensive treatment modifies risk of major CV events independent of blood pressure change.

Design, Setting, and Participants Prospective cohort substudy of the Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) randomized clinical trial, conducted from 1995 to 2001. A total of 941 prospectively identified patients aged 55 to 80 years with essential hypertension and electrocardiographic LV hypertrophy had LV mass measured by echocardiography at enrollment in the LIFE trial and thereafter were followed up annually for a mean (SD) of 4.8 (1.0) years for CV events.

Main Outcome Measures Composite end point of CV death, fatal or nonfatal myocardial infarction, and fatal or nonfatal stroke.

Results The composite end point occurred in 104 patients (11%). The multivariable Cox regression model showed a strong association between lower in-treatment LV mass index and reduced rate of the composite CV end point (hazard ratio [HR], 0.78 per 1-SD (25.3) decrease in LV mass index; 95% confidence interval [CI], 0.65-0.94; $P=.009$) over and above that predicted by reduction in blood pressure. There were parallel associations between lower in-treatment LV mass index and lower CV mortality (HR, 0.62; 95% CI, 0.47-0.82; $P=.001$), stroke (HR, 0.76; 95% CI, 0.60-0.96; $P=.02$), myocardial infarction (HR, 0.85; 95% CI, 0.62-1.17, $P=.33$), and all-cause mortality (HR, 0.72; 95% CI, 0.59-0.88, $P=.002$), independent of systolic blood pressure and assigned treatment. Results were confirmed in analyses adjusting for additional CV risk factors, electrocardiographic changes, or when only considering events after the first year of study treatment.

Conclusion In patients with essential hypertension and baseline electrocardiographic LV hypertrophy, lower LV mass during antihypertensive treatment is associated with lower rates of clinical end points, additional to effects of blood pressure lowering and treatment modality.

JAMA. 2004;292:2350-2356 www.jama.com

DESPITE SUBSTANTIAL BENefits from lowering blood pressure (BP), conventional treatment does not normalize the risk of major cardiovascular (CV) events in patients with hypertension.[1-5] Progress has been made in predicting risk of hypertension by evaluating preclinical CV disease.[6] Left ventricular hypertrophy (LVH), ie, pathologically increased left ventricular mass, independently predicts adverse outcomes in diverse populations,[7-12] including patients with hypertension.[7,11] These findings suggest that the level of left ventricular mass and mass reduction during treatment of hypertension may provide independent information about disease progression or control. This hypothesis has been supported by data from some,[13,14] but not other,[15,16] electrocardiographic studies. Echocardio-

See also pp 2343 and 2396 and Patient Page.

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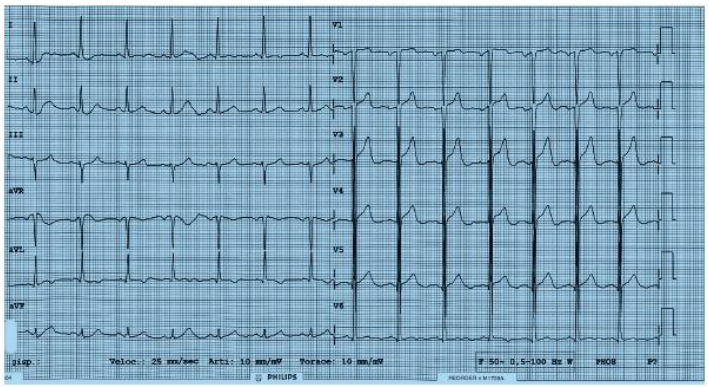
Ecocardiografia nell'ipertensione arteriosa

- Echocardiography is useful for:
  - Assessment of left ventricular dysfunction and the presence of left ventricular hypertrophy
- Echocardiography is not useful for routine evaluation of hypertensive patients



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An echocardiogram should be considered to refine CV risk, and confirm ECG diagnosis of LVH, left atrial dilatation or suspected concomitant heart disease, when these are suspected.	IIa	B

Stratificazione del rischio

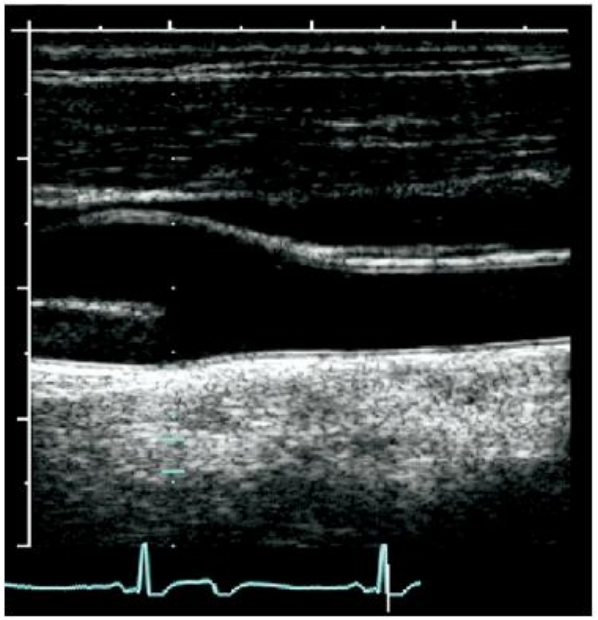
ASE CONSENSUS STATEMENT

Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force

Endorsed by the Society for Vascular Medicine

James H. Stein, MD, FASE, Claudia E. Korcarz, DVM, RDCS, FASE, R. Todd Hurst, MD, Eva Lonn MD, MSc, FASE, Christopher B. Kendall, BS, RDCS, Emile R. Mohler, MD, Samer S. Najjar, MD, Christopher M. Rembold, MD, and Wendy S. Post, MD, MS, *Madison, Wisconsin; Scottsdale, Arizona; Hamilton, Ontario, Canada; Philadelphia, Pennsylvania; Baltimore, Maryland; and Charlottesville, Virginia*

Measuring CIMT and identifying carotid plaque by ultrasound are most useful for refining CVD risk assessment in patients at intermediate CVD risk (FRS 6%-20% without established CHD, peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm).



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Arteries		
Ultrasound scanning of carotid arteries should be considered to detect vascular hypertrophy or asymptomatic atherosclerosis, particularly in the elderly.	IIa	B
Carotid–femoral PWV should be considered to detect large artery stiffening.	IIa	B
Ankle–brachial index should be considered to detect PAD.	IIa	B

Ricerca di un'origine secondaria

Table 13 Clinical indications and diagnostics of secondary hypertension

	Clinical indications			Diagnostics	
Common causes	**Clinical history**	**Physical examination**	**Laboratory investigations**	**First-line test(s)**	**Additional/ confirmatory test(s)**
Renal parenchymal disease	History of urinary tract infection or obstruction, haematuria, analgesic abuse; family history of polycystic kidney disease.	Abdominal masses (in case of polycystic kidney disease).	Presence of protein, erythrocytes, or leucocytes in the urine, decreased GFR.	Renal ultrasound	Detailed work-up for kidney disease.
Renal artery stenosis	Fibromuscular dysplasia: early onset hypertension (especially in women). Atherosclerotic stenosis: hypertension of abrupt onset, worsening or increasingly difficult to treat; flash pulmonary oedema.	Abdominal bruit	Difference of >1.5 cm in length between the two kidneys (renal ultrasound), rapid deterioration in renal function (spontaneous or in response to RAA blockers).	Renal Duplex Doppler ultrasonography	Magnetic resonance angiography, spiral computed tomography, intra-arterial digital subtraction angiography.
Primary aldosteronism	Muscle weakness; family history of early onset hypertension and cerebrovascular events at age <40 years.	Arrhythmias (in case of severe hypokalaemia).	Hypokalaemia (spontaneous or diuretic-induced); incidental discovery of adrenal masses.	Aldosterone–renin ratio under standardized conditions (correction of hypokalaemia and withdrawal of drugs affecting RAA system).	Confirmatory tests (oral sodium loading, saline infusion, fludrocortisone suppression, or captopril test); adrenal CT scan; adrenal vein sampling.
Uncommon causes					
Pheochromocytoma	Paroxysmal hypertension or a crisis superimposed to sustained hypertension; headache, sweating, palpitations and pallor; positive family history of pheochromocytoma.	Skin stigmata of neurofibromatosis (café-au-lait spots, neurofibromas).	Incidental discovery of adrenal (or in some cases, extra-adrenal) masses.	Measurement of urinary fractionated metanephrines or plasma-free metanephrines.	CT or MRI of the abdomen and pelvis; 123 I-labelled meta-iodobenzyl-guanidine scanning; genetic screening for pathogenic mutations.
Cushing's syndrome	Rapid weight gain, polyuria, polydipsia, psychological disturbances.	Typical body habitus (central obesity, moon-face, buffalo hump, red striae, hirsutism).	Hyperglycaemia	24-h urinary cortisol excretion	Dexamethasone-suppression tests

CT = computed tomography; GFR = glomerular filtration rate; MRI = magnetic resonance imaging; RAA = renin–angiotensin–aldosterone.

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Le malattie rare talora sono tali perché non riconosciute

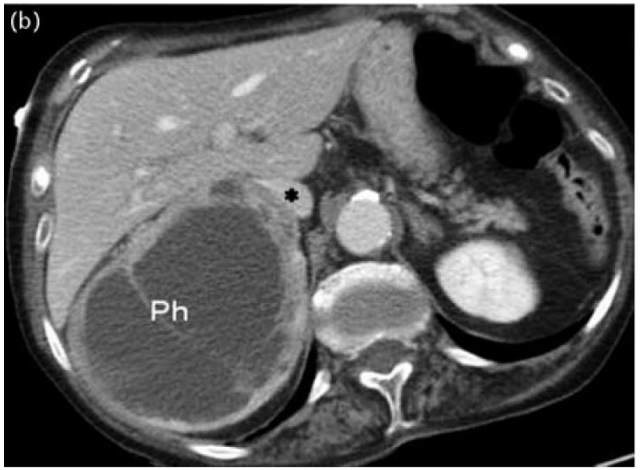
Images in cardiovascular medicine

FIC Federazione Italiana di Cardiologia
Italian Federation of Cardiology

Giant cystic pheochromocytoma

Mauro Santarone[a], Claudia Borghi[b], Emilio Miglierina[a], Sergio Senatore[c] and Giovanni Corrado[a]

Journal of Cardiovascular Medicine 2008, 9:971–972



Le novità nella terapia dell'ipertensione arteriosa sistemica

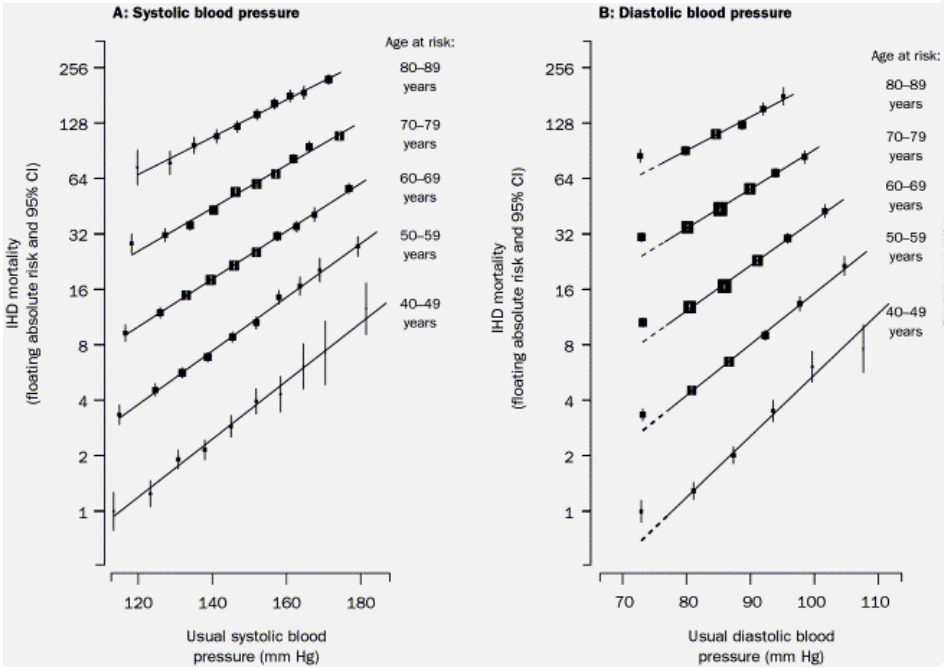
Milano 9-10 aprile 2015

Giovanni Corrado, FESC

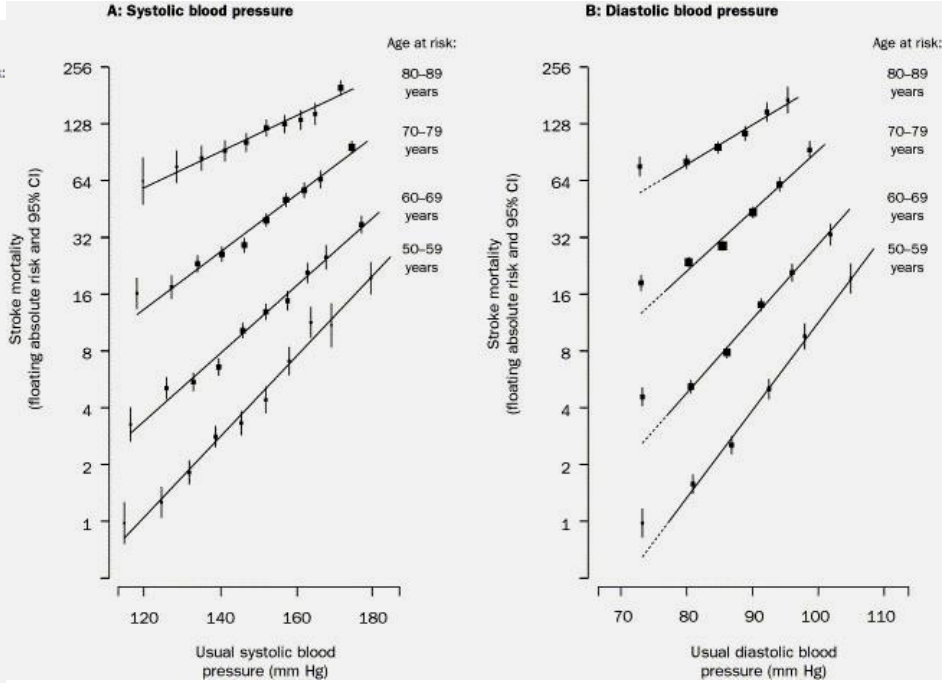
PERCHE' UNA TERAPIA

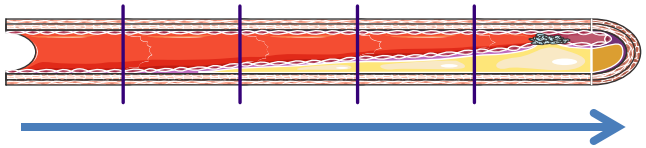
Mortalità cardiovascolare in rapporto alle varie fasce d'età

Ischaemic heart disease



Stroke

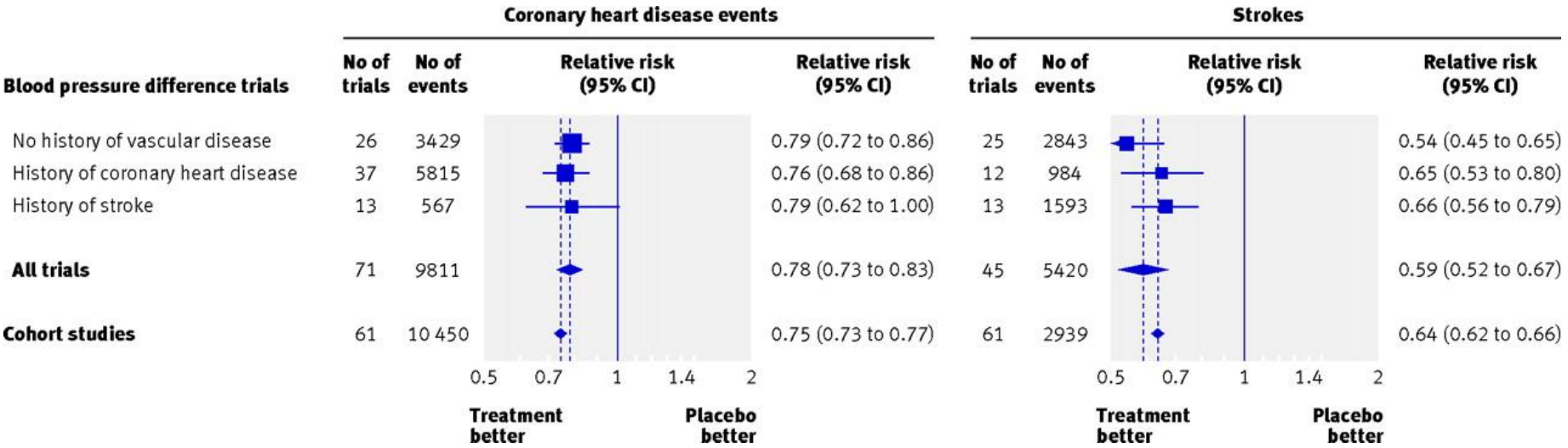


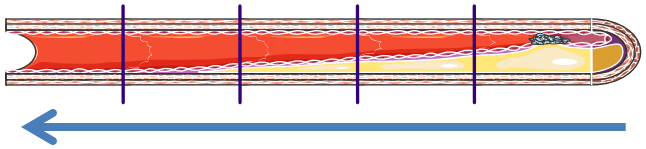


Prospective Studies Collaboration, Lancet 2002

Too much load is bad for the heart

Stime del rischio relativo di eventi cardiovascolari e ictus associato ad una riduzione della pressione sistolica di 10 mm Hg o diastolica di 5 mm Hg in trials e studi di coorte epidemiologici





BMJ RESEARCH

Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies

M R Law, professor of epidemiology | K Morris, professor of medical statistics N J Wald, professor of environmental and preventive medicine

Quando iniziare la terapia

Recommendations on the initiation of antihypertensive treatment are as follows:

- High or very high risk: prompt initiation of antihypertensive drugs, together with lifestyle measures.
- Low or moderate risk: antihypertensive drugs should be considered if BP remains >140/90 mmHg after, respectively, several months or weeks of appropriate lifestyle measures, or in case of persistent elevated out-of-office BP after appropriate lifestyle measures.
- In elderly hypertensive patients antihypertensive drug treatment is recommended when systolic BP is ≥160 mmHg; drug treatment may also be considered in the elderly (at least when younger than 80 years and depending on the patient's risk category (see table above)) when systolic BP is in the 140-159 mmHg range, provided that antihypertensive treatment is well tolerated.
- High normal BP and younger patients with isolated systolic hypertension: drug treatment is not recommended.

European Society of Hypertension

EUROPEAN SOCIETY OF CARDIOLOGY

Hypertension

GUIDELINES FOR THE MANAGEMENT OF ARTERIAL HYPERTENSION

Quando iniziare la terapia

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Figure 2 Initiation of lifestyle changes and antihypertensive drug treatment. Targets of treatment are also indicated. Colours are as in *Figure 1*. Consult Section 6.6 for evidence that, in patients with diabetes, the optimal DBP target is between 80 and 85 mmHg. In the high normal BP range, drug treatment should be considered in the presence of a raised out-of-office BP (masked hypertension). Consult section 4.2.4 for lack of evidence in favour of drug treatment in young individuals with isolated systolic hypertension.

ESH AND ESC GUIDELINES

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Gli obiettivi della terapia

Blood pressure goals in hypertensive patients

Recommendations	Class [a]	Level [b]
A SBP goal <140 mmHg:		
a) is recommended in patients at low–moderate CV risk;	I	B
b) is recommended in patients with diabetes;	I	A
c) should be considered in patients with previous stroke or TIA;	IIa	B
d) should be considered in patients with CHD;	IIa	B
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A

CHD = coronary heart disease; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

European Heart Journal (2013) 34, 2159–2219
doi:10.1093/eurheartj/eht151

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Gli obiettivi della terapia

Which is the target blood pressure during antihypertensive treatment?

Target BP is <140/90 mmHg with few exceptions.

Target BP is <140/85 mmHg in diabetes.

In elderly patients the target systolic BP is 140-150 mmHg, but <140 mmHg may be considered in fit elderly. In individuals older than 80 years it is recommended to reduce systolic BP to 140-150 mmHg if they are in good physical and mental condition.

European Society of Hypertension

EUROPEAN SOCIETY OF CARDIOLOGY

Hypertension

GUIDELINES FOR THE MANAGEMENT OF ARTERIAL HYPERTENSION

Gli obiettivi della terapia

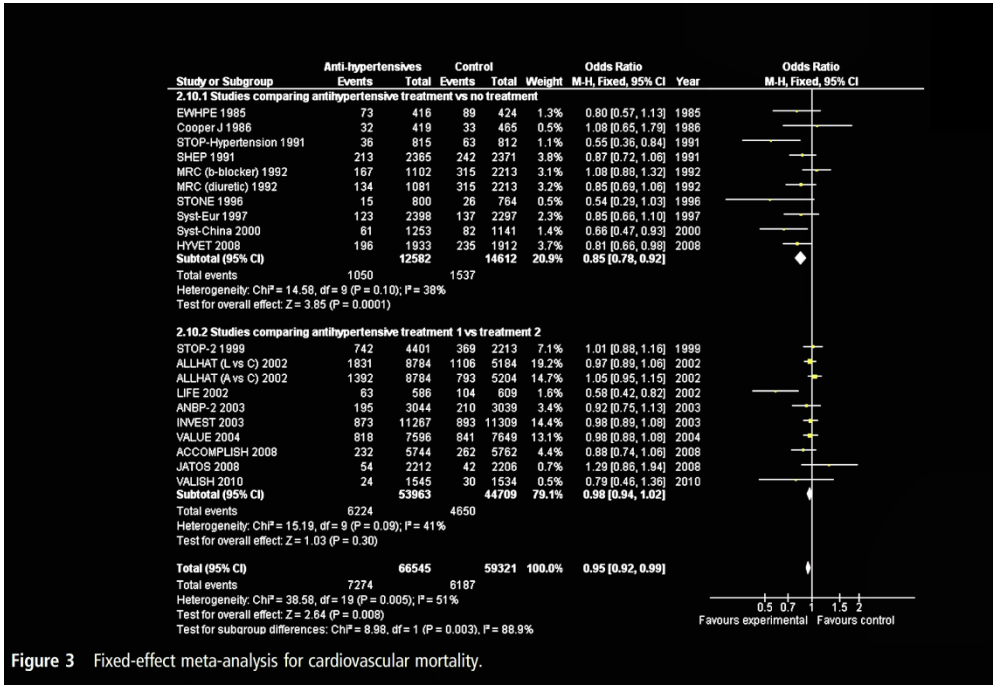

Figure 3 Fixed-effect meta-analysis for cardiovascular mortality.

Conclusion Reducing BP to a level of 150/80 mmHg is associated with large benefit in stroke, cardiovascular and all-cause mortality as well as heart failure risk in elderly individuals. Different antihypertensive regimens with equal BP reduction have similar effects on cardiovascular outcomes. SBP rather than DBP reduction is significantly related to lower cardiovascular risk in this population.

Effects of antihypertensive treatment in patients over 65 years of age: a meta-analysis of randomised controlled studies

Alexandros Briasoulis,[1] Vikram Agarwal,[2] Dimitris Tousoulis,[3] Christodoulos Stefanadis[3]

Heart

Briasoulis A, *et al*. *Heart* 2014;**100**:317–323. doi:10.1136/heartjnl-2013-304111

Original Investigation

Effects of Low Blood Pressure in Cognitively Impaired Elderly Patients Treated With Antihypertensive Drugs

Enrico Mossello, MD, PhD; Mariachiara Pieraccioli, MD; Nicola Nesti, MD; Matteo Bulgaresi, MD; Chiara Lorenzi, MD; Veronica Caleri, MD, PhD; Elisabetta Tonon, MD, PhD; M. Chiara Cavallini, MD, PhD; Caterina Baroncini, MD; Mauro Di Bari, MD, PhD; Samuele Baldasseroni, MD, PhD; Claudia Cantini, MD, PhD; Carlo A. Biagini, MD; Niccolò Marchionni, MD; Andrea Ungar, MD, PhD

IMPORTANCE The prognostic role of high blood pressure and the aggressiveness of blood pressure lowering in dementia are not well characterized.

OBJECTIVE To assess whether office blood pressure, ambulatory blood pressure monitoring, or the use of antihypertensive drugs (AHDs) predict the progression of cognitive decline in patients with overt dementia and mild cognitive impairment (MCI).

DESIGN, SETTING, AND PARTICIPANTS Cohort study between June 1, 2009, and December 31, 2012, with a median 9-month follow-up of patients with dementia and MCI in 2 outpatient memory clinics.

MAIN OUTCOMES AND MEASURES Cognitive decline, defined as a Mini-Mental State Examination (MMSE) score change between baseline and follow-up.

RESULTS We analyzed 172 patients, with a mean (SD) age of 79 (5) years and a mean (SD) MMSE score of 22.1 (4.4). Among them, 68.0% had dementia, 32.0% had MCI, and 69.8% were being treated with AHDs. Patients in the lowest tertile of daytime systolic blood pressure (SBP) (≤128 mm Hg) showed a greater MMSE score change (mean [SD], −2.8 [3.8]) compared with patients in the intermediate tertile (129-144 mm Hg) (mean [SD], −0.7 [2.5]; $P = .002$) and patients in the highest tertile (≥145 mm Hg) (mean [SD], −0.7 [3.7]; $P = .003$). The association was significant in the dementia and MCI subgroups only among patients treated with AHDs. In a multivariable model that included age, baseline MMSE score, and vascular comorbidity score, the interaction term between low daytime SBP tertile and AHD treatment was independently associated with a greater cognitive decline in both subgroups. The association between office SBP and MMSE score change was weaker. Other ambulatory blood pressure monitoring variables were not associated with MMSE score change.

CONCLUSIONS AND RELEVANCE Low daytime SBP was independently associated with a greater progression of cognitive decline in older patients with dementia and MCI among those treated with AHDs. Excessive SBP lowering may be harmful for older patients with cognitive impairment. Ambulatory blood pressure monitoring can be useful to help avoid high blood pressure overtreatment in this population.

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Invited Commentary

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Corresponding Author: Enrico Mossello, MD, PhD, Division of Geriatric Cardiology and Medicine, Department of Medicine and Geriatrics, Azienda Ospedaliero Universitaria Careggi and University of Florence, Viale G. Pieraccini 6, 50141 Florence, Italy (enrico.mossello@unifi.it).

PRIMUM NON NOCERE

Conclusions

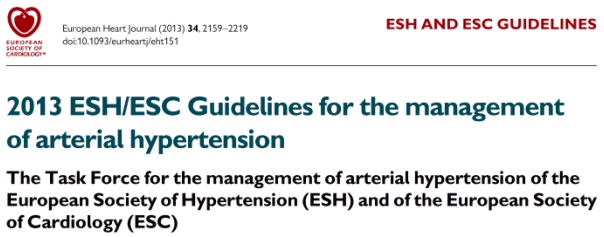
The present study adds information about older outpatients with MCI and dementia, suggesting that strict control of SBP may negatively affect cognition, with daytime SPBs of 130 to 145 mm Hg being the most appropriate therapeutic targets. Longitudinal ABPM studies of larger samples with longer follow-up periods are needed to fully evaluate the long-term prognostic effects of blood pressure in older adults with cognitive impairment. Randomized clinical trials would be able to assess the risks and benefits of antihypertensive treatment with different targets in this population.

IL GIOVANE SOSTITUTO

RITORNO AL FUTURO

Terapia farmacologica

- In the 2003 and 2007 versions, the ESH/ESC Guidelines reviewed the large number of randomized trials of antihypertensive therapy and concluded that **the main benefits of antihypertensive treatment are due to lowering of BP per se and are largely independent of the drugs employed.**
- the current Guidelines reconfirm that diuretics (including thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE-I and angiotensin receptor blockers are all suitable for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations.



Terapia farmacologica

Table 14 **Compelling and possible contra-indications to the use of antihypertensive drugs**

Drug	Compelling	Possible
Diuretics (thiazides)	Gout	Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia
Beta-blockers	Asthma A–V block (grade 2 or 3)	Metabolic syndrome Glucose intolerance Athletes and physically active patients Chronic obstructive pulmonary disease (except for vasodilator beta-blockers)
Calcium antagonists (dihydropyridines)		Tachyarrhythmia Heart failure
Calcium antagonists (verapamil, diltiazem)	A–V block (grade 2 or 3, trifascicular block) Severe LV dysfunction Heart failure	
ACE inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Angiotensin receptor blockers	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Mineralocorticoid receptor antagonists	Acute or severe renal failure (eGFR <30 mL/min) Hyperkalaemia	

A-V = atrio-ventricular; eGFR = estimated glomerular filtration rate; LV = left ventricular.

Terapia farmacologica

Table 15 **Drugs to be preferred in specific conditions**

Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist
Other	
ISH (elderly)	Diuretic, calcium antagonist
Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
Diabetes mellitus	ACE inhibitor, ARB
Pregnancy	Methyldopa, BB, calcium antagonist
Blacks	Diuretic, calcium antagonist

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BB = beta-blocker; BP = blood pressure; CV = cardiovascular; ESRD = end-stage renal disease; ISH = isolated systolic hypertension; LVH = left ventricular hypertrophy.

Monoterapia vs associazione

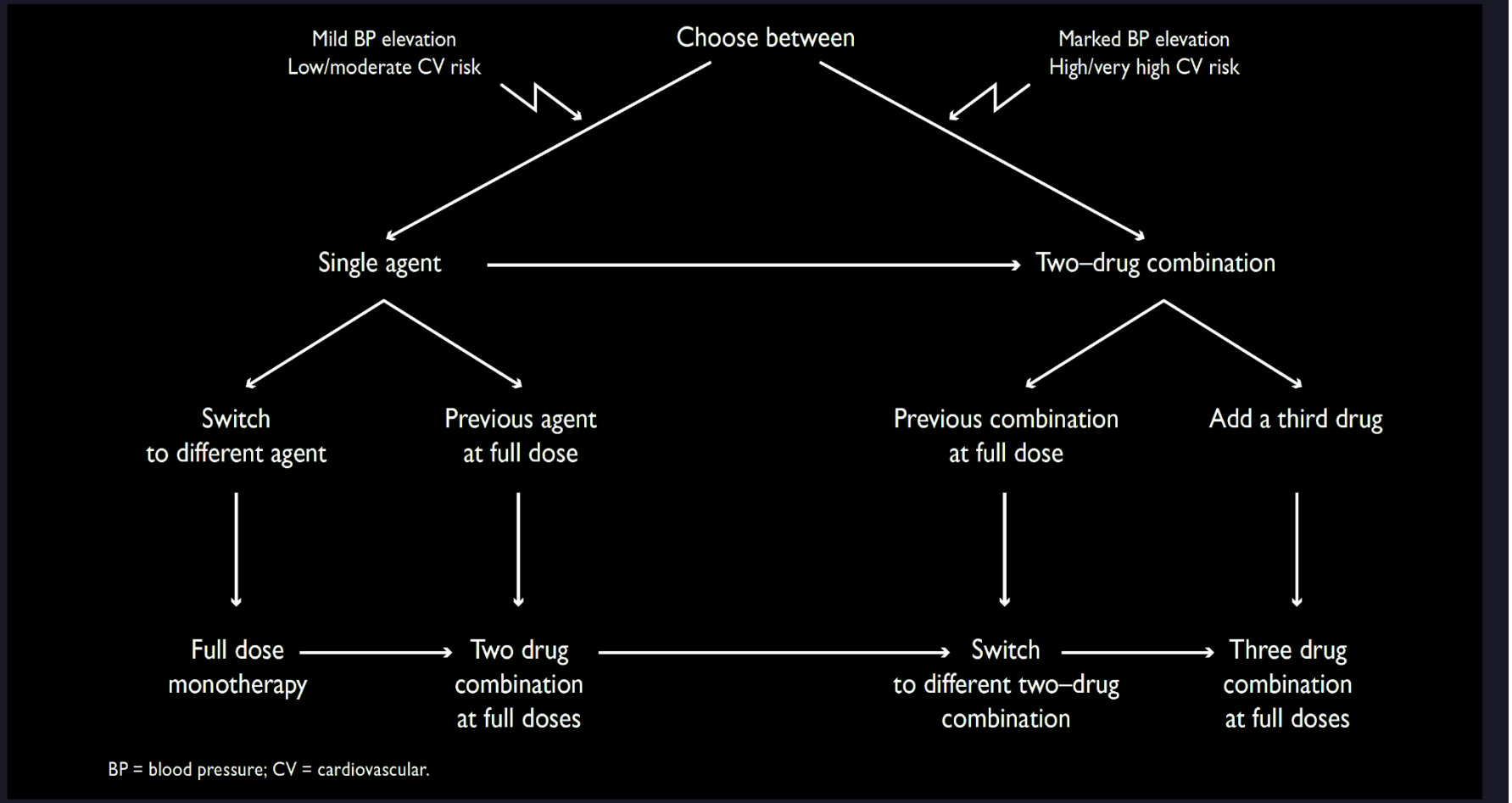


Figure 3 Monotherapy vs. drug combination strategies to achieve target BP. Moving from a less intensive to a more intensive therapeutic strategy should be done whenever BP target is not achieved.

Terapia di associazione

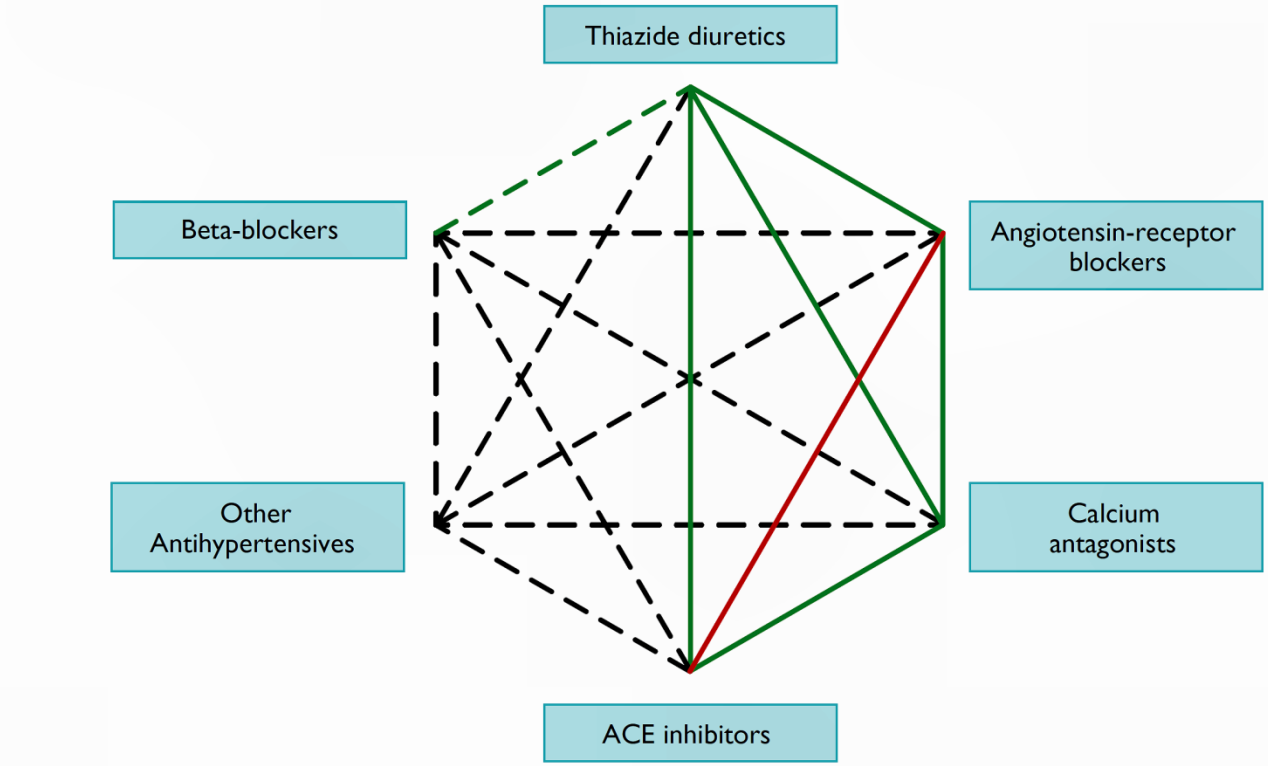


Figure 4 Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed line: useful combination (with some limitations); black dashed lines: possible but less well-tested combinations; red continuous line: not recommended combination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

Strategie terapeutiche e scelta dei farmaci

Treatment strategies and choice of drugs

Recommendations	Class [a]	Level [b]
Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with each other.	I	A
Some agents should be considered as the preferential choice in specific conditions because used in trials in those conditions or because of greater effectiveness in specific types of OD.	IIa	C
Initiation of antihypertensive therapy with a two-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	IIb	C
The combination of two antagonists of the RAS is not recommended and should be discouraged.	III	A
Other drug combinations should be considered and probably are beneficial in proportion to the extent of BP reduction. However, combinations that have been successfully used in trials may be preferable.	IIa	C
Combinations of two antihypertensive drugs at fixed doses in a single tablet may be recommended and favoured, because reducing the number of daily pills improves adherence, which is low in patients with hypertension.	IIb	B

ACE = angiotensin-converting enzyme;
BP = blood pressure;
CV =cardiovascular;
OD = organ damage;
RAS = renin-angiotensin system.

European Heart Journal (2013) 34, 2159–2219
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

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Aderenza

- **Among those with a diagnosis of hypertension, the WHO has stated that low adherence to treatment is a key factor impeding good control and has called for research into adherence promoting interventions.**
- **Estimates of the rate of poor adherence or non-adherence to treatment range from 30-50%. The causes of poor adherence are complex and include complicated drug regimens, the costs of drugs, older age, poor social support, cognitive problems, and depression.**

Drugs don't work in patients who don't take them
Orsterberg L and Blaschke T, *N Engl J Med* 2005;353:487-97


BMJ

BMJ 2012;344:e3953 doi: 10.1136/bmj.e3953 (Published 9 July 2012) Page 1 of 16

RESEARCH

Lay perspectives on hypertension and drug adherence: systematic review of qualitative research

OPEN ACCESS

Iain J Marshall *clinical academic fellow*[1], Charles D A Wolfe *professor of public health medicine*[1,2], Christopher McKevitt *reader in social science and health*[1]

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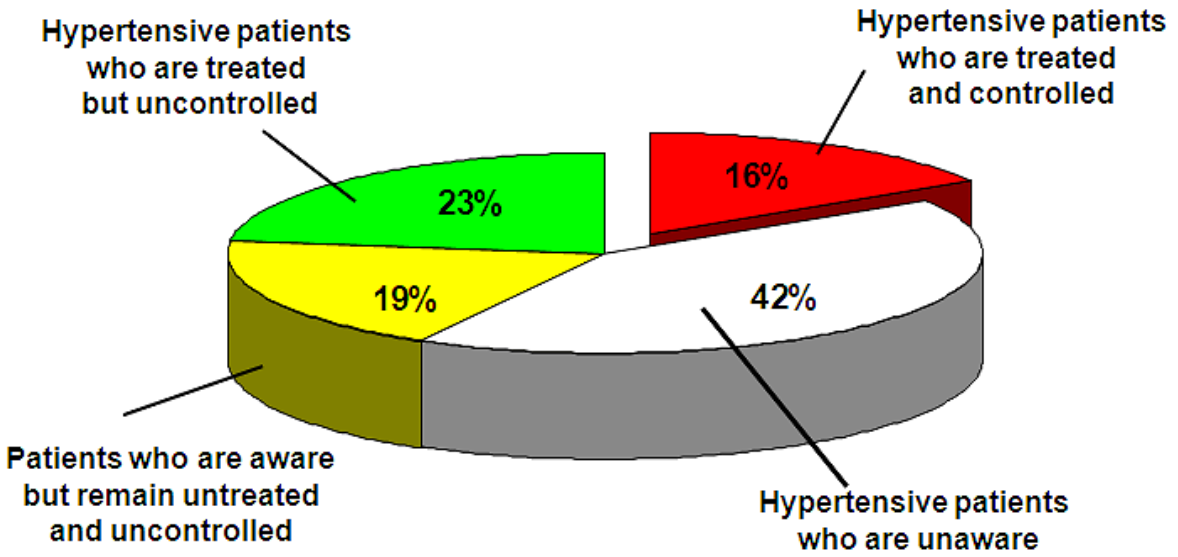
La sfida

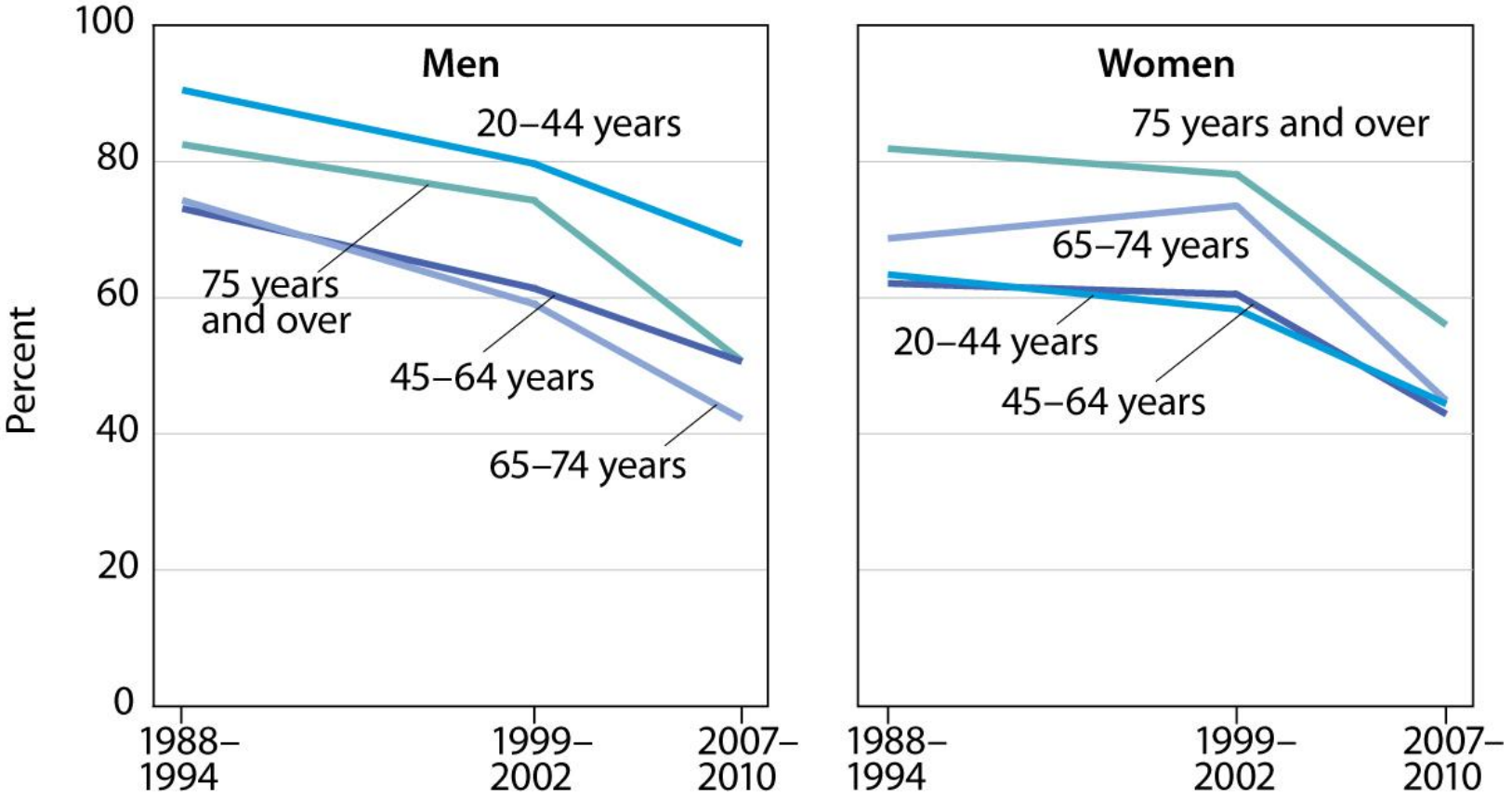
Introduction IV
The Challenge

22% of Canadian adults 18 to 70 years of age have hypertension



Source : Joffres et al. (1997) Am. J. Hypertension 10: 1097-1102

Uncontrolled high blood pressure for adults with hypertension



NOTE: Uncontrolled high blood pressure is a measured systolic blood pressure of at least 140 mm Hg or a measured diastolic blood pressure of at least 90 mm Hg among those with measured high blood pressure or who reported taking antihypertensive medication.
SOURCE: CDC/NCHS, *Health, United States, 2012*, Figure 9. Data from the National Health and Nutrition Examination Survey.

La sfida: prevenzione primaria

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Hypertension

Trends in Prevalence, Awareness, Management, and Control of Hypertension Among United States Adults, 1999 to 2010

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Birmingham, Alabama; Salt Lake City, Utah; and Lexington, Kentucky

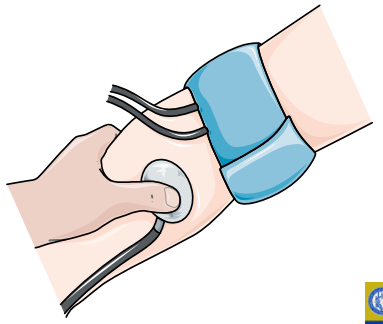
Objectives The purpose of this study was to quantify the trends in blood pressure (BP), and the prevalence, awareness, management, and control of hypertension in U.S. adults (≥20 years of age) from 1999 to 2010, and to assess the efficacy of current clinical measures in diagnosing and adequately treating hypertensive patients.

Background Hypertension is a major independent risk factor for cardiovascular disease and stroke. Recent data indicate a decreasing trend in hypertension prevalence, along with improvements in hypertension awareness, management, and control.

Methods The study used regression models to assess the trends in hypertension prevalence, awareness, management, and control from 1999 to 2010 among 28,995 male and female adults with BP measurements from a nationally representative sample of the noninstitutionalized U.S. population (National Health and Nutrition Examination Survey [NHANES] 1999 to 2010), with special attention given to 5,764 participants in NHANES 2009 to 2010.

Results In 2009 to 2010, the prevalence of hypertension was 30.5% among men and 28.5% among women. The hypertension awareness rate was 69.7% (95% confidence interval [CI]: 62.0% to 77.4%) among men and 80.7% (95% CI: 74.5% to 86.8%) among women. The hypertension control rate was 40.3% (95% CI: 33.7% to 46.9%) for men and 56.3% (95% CI: 49.2% to 63.3%) for women. From 1999 to 2010, the prevalence of hypertension remained stable. Although hypertension awareness, management, and control improved, the overall rates remained poor (74.0% for awareness, 71.6% for management, 46.5% for control, and 64.4% for control in management); worse still, no improvement was shown from 2007 to 2010.

Conclusions From 1999 to 2010, prevalence of hypertension remained stable. Hypertension awareness, management, and control were improved, but remained poor; nevertheless, there has been no improvement since 2007.



Conclusions

In 2009 to 2010, the prevalence of hypertension was 30.5% among men and 28.5% among women. From 1999 to 2010, hypertension prevalence remained constantly high; hypertension awareness, management, and control were significantly improved, but remained poor, and did not improve from 2007 to 2010. Strategies should be taken to improve hypertension prevention in the whole population, to increase hypertension detection, management, and control among men, Mexican Americans, and young people, and to increase control of hypertension among older people and minority groups receiving hypertension treatment.

Le novità nella terapia dell'ipertensione arteriosa sistemica

Milano 9-10 aprile 2015

Giovanni Corrado, FESC

GRAZIE PER L'ATTENZIONE