BIELLA CUORE
12-13 SETTEMBRE 2025

«Ipertensione Arteriosa resistente: Indicazione a Denervazione»

Mimmo Tavella MD

R.O.F. GITIAR

Gruppo **I**nterdisciplinare per lo studio e il **T**rattamento
dell'**I**pertensione **A**rteriosa **R**esistente

U.O.C Cardiologia
AOUI Verona

AZIENDA OSPEDALIERA
UNIVERSITARIA INTEGRATA
VERONA

CardioVr.it

Ipertensione arteriosa resistente

1. BP >140/90 mmHg (130/80 mmHg nei pazienti con diabete o insufficienza renale cronica) in paziente che assume 3 o più farmaci antipertensivi diversi, a dosi ottimali, di cui uno sia un diuretico.

2. Buon controllo pressorio, ma è necessaria una terapia composta da 4 o più farmaci antipertensivi diversi

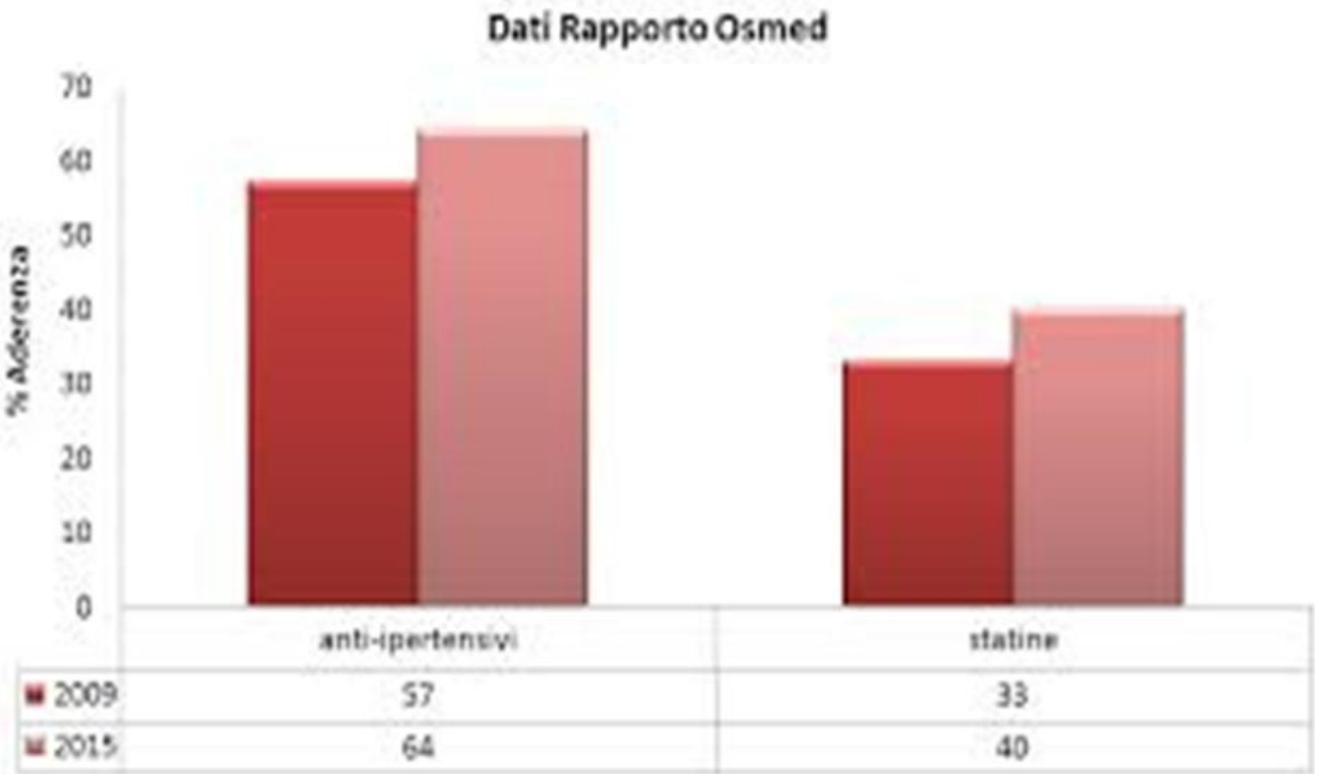
- Mancato raggiungimento del target pressorio nonostante l'utilizzo di almeno tre farmaci antipertensivi, dei quali un diuretico, correttamente titolati.

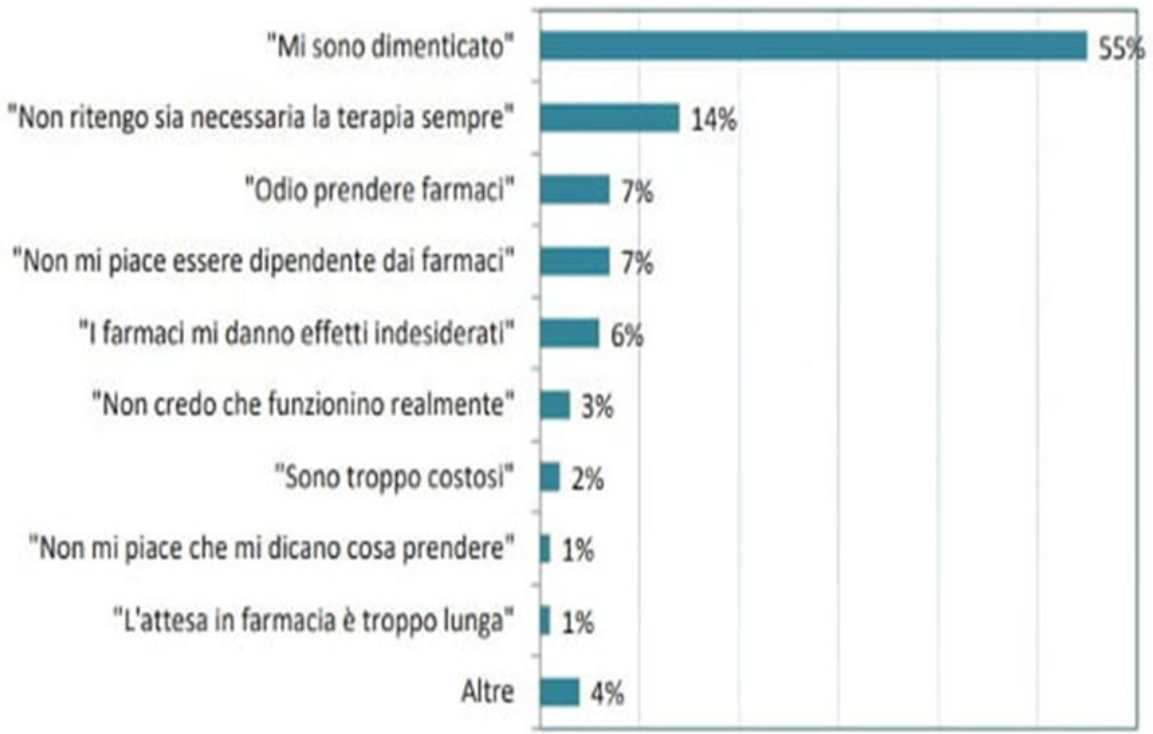
- Prevalenza del 10,3% (95% CI 7.6% to 13.2%), aumenta nei pazienti con insufficienza renale e negli anziani.

- Fattore di rischio cardiovascolare indipendente (> rischio di morte CV, IRC e danno d'organo).

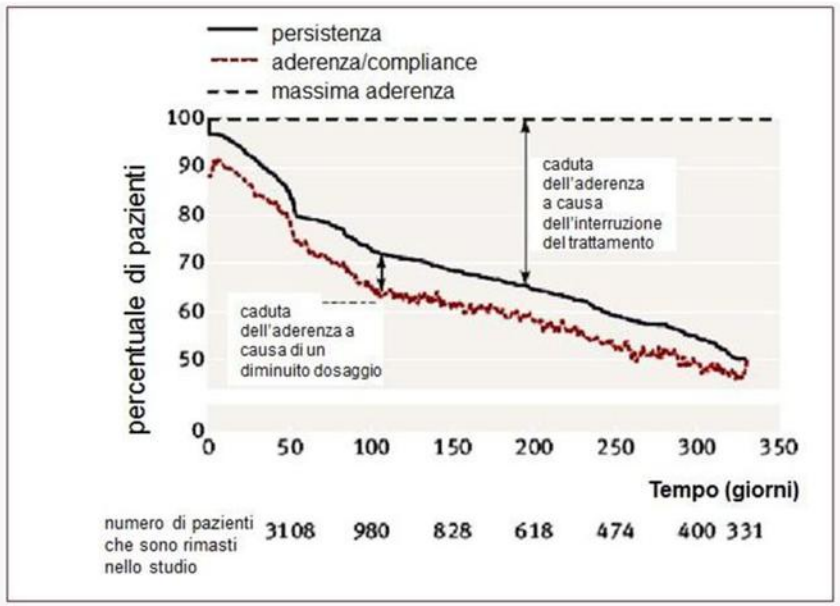
- Global prevalence of resistant hypertension: a meta-analysis of data from 3.2 million patients. Jean Joel Bigna et al.; BMJ 2018
- Incidence and prognosis of resistant hypertension in hypertensive patients; Michael Ho et al.; Circulation 2012


..SENTINELLA A RAPPORTEN!.. NOVITÀ DELLA NOTTEN?..
..FIN'ORA NULLA DA SEGUALAREN...
..MA DA KUALKE MINUTEN SCORGO UNO STRANO UND IN-QUIETANTEN BAGLIORE ALL'ORIZZONTEN...
ECCO!.. IL BAGLIORE SI FA PIU' VIVO ED AUMENTA DI INTENSITÀ IN MODO SOSPETTEN...
..PERBACCO!. ADESSO SI STA TINGENDO DI ROSA...
..SERGENTE, SPIEGHI A KUESTO IMBECILLEN IL SEMPLICE CONCETTO DI ALBA...
3950


Dati Rapporto Osmed
% Aderenza
70
60
50
40
30
20
10
0
anti-ipertensivi
statine
2009
57
33
2015
64
40


"Mi sono dimenticato" 55%
"Non ritengo sia necessaria la terapia sempre" 14%
"Odio prendere farmaci" 7%
"Non mi piace essere dipendente dai farmaci" 7%
"I farmaci mi danno effetti indesiderati" 6%
"Non credo che funzionino realmente" 3%
"Sono troppo costosi" 2%
"Non mi piace che mi dicano cosa prendere" 1%
"L'attesa in farmacia è troppo lunga" 1%
Altre 4%

Andamento temporale di aderenza, compliance e persistenza



A distanza di un anno meno della metà dei pazienti continua la terapia e meno della metà ha una buona aderenza

BMJ 2008;336;1114-1117; 14 May 2008;

SIMPeSV
Società Italiana di Medicina di Prevenzione e degli Stili di Vita

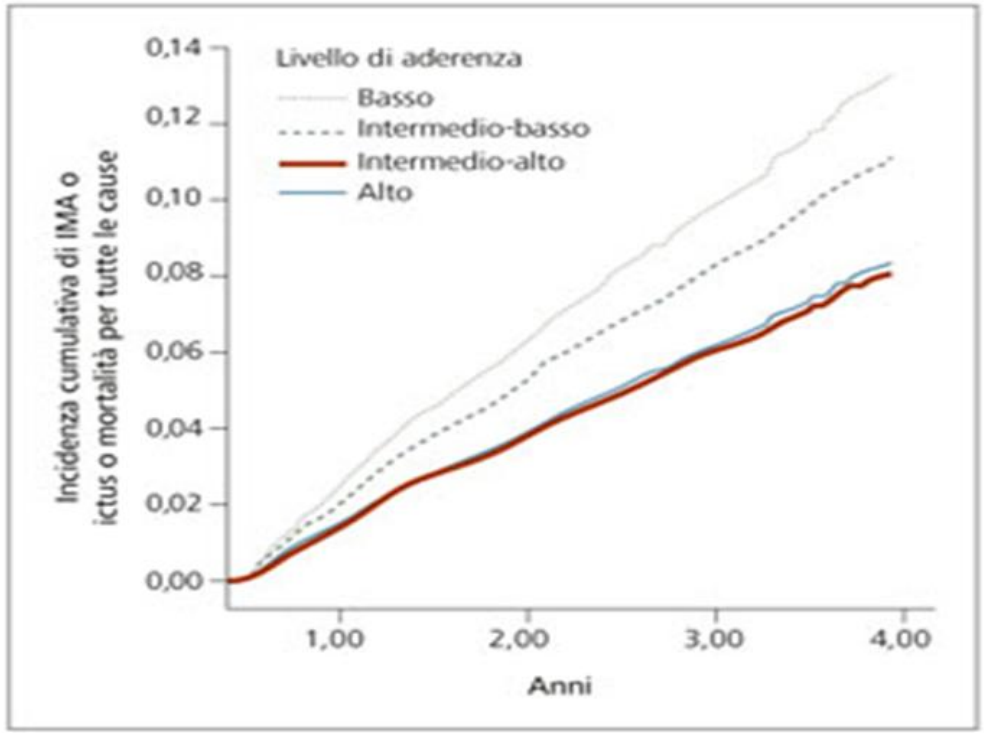
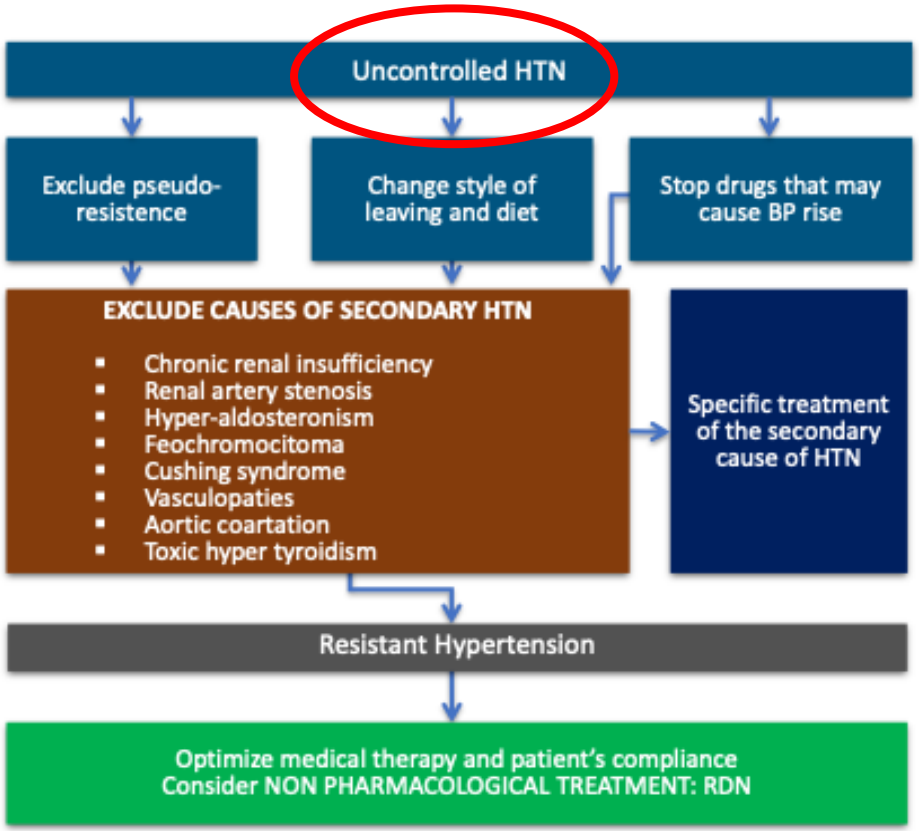


Figura 2. La mortalità e gli eventi cardiovascolari maggiori aumentano nei pazienti con scarsa aderenza alla terapia.
IMA, infarto miocardico acuto.
Adattata da Degli Esposti et al.[15].

Step 1: Identification of patients with true Resistant HTN



Mahfoud F et al. *Dtsch Arztebl Int*. 2011;136:248.

Contemporary Reviews in Cardiovascular Medicine

Epidemiology of Uncontrolled Hypertension in the United States

Thomas J. Wang, MD; Ramachandran S. Vasan, MD

1656 *Circulation* **September 13, 2005**

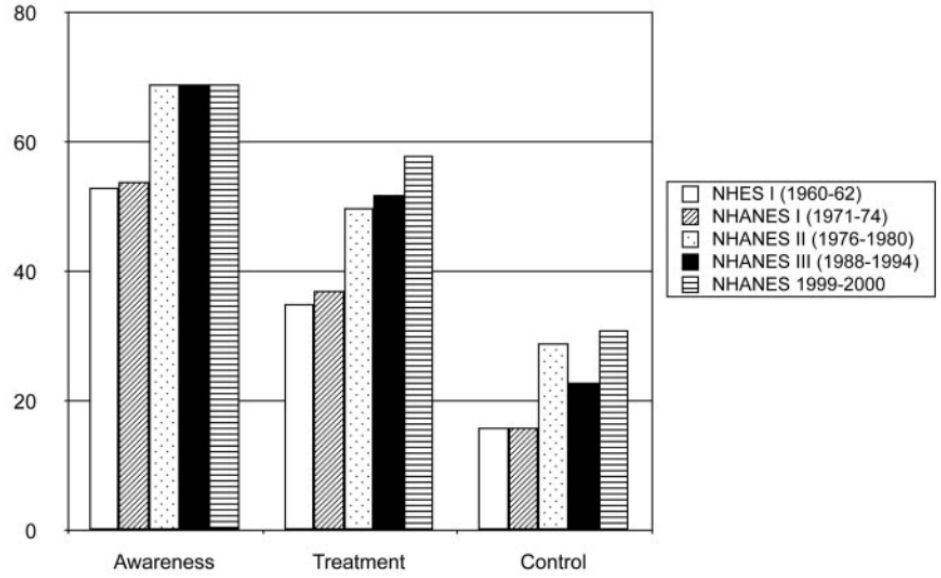
Pz età > 55 anni obeso in terapia

Pz con precedenti CCV (F

Il valore pressorio non è relativo al carico di terapia del pz

Pz iperteso in terapia ad elevato profilo dismetabolico

Pz con scompenso cardiaco recidivante



2024 ESC Guidelines for the management of elevated blood pressure and hypertension

Developed by the task force on the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) and *endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO)*

Authors/Task Force Members: John William McEvoy *†, (Chairperson) (Ireland), Cian P. McCarthy ‡, (Task Force Co-ordinator) (United States of America), Rosa Maria Bruno ‡, (Task Force Co-ordinator) (France), Sofie Brouwers (Belgium), Michelle D. Canavan (Ireland), Claudio Ceconi (Italy), Ruxandra Maria Christodorescu (Romania), Stella S. Daskalopoulou (Canada), Charles J. Ferro [1] (United Kingdom), Eva Gerdts (Norway), Henner Hanssen (Switzerland), Julie Harris (United Kingdom), Lucas Lauder (Switzerland/Germany), Richard J. McManus (United Kingdom), Gerard J. Molloy (Ireland), Kazem Rahimi (United Kingdom), Vera Regitz-Zagrosek (Germany), Gian Paolo Rossi [2] (Italy), Else Charlotte Sandset [3] (Norway), Bart Scheenaerts (Belgium), Jan A. Staessen (Belgium), Izabella Uchmanowicz (Poland), Maurizio Volterrani (Italy), Rhian M. Touyz *†, (Chairperson) (Canada), and ESC Scientific Document Group

Recommendation Table 12 — Recommendations for resistant hypertension work-up (see Evidence Table 18)

Recommendation	Class[a]	Level[b]
Patients with resistant hypertension should be considered for referral to clinical centres with expertise in hypertension management for further testing.[309,312]	IIa	B

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Recommendation Table 20 — Recommendations for device-based treatment of hypertension (see Evidence Table 35)

Recommendations	Class[a]	Level[b]
To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for resistant hypertension patients who have BP that is uncontrolled despite three BP-lowering drug combination (including a thiazide or thiazide-like diuretic), and who express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.	IIb	B
To reduce BP, and if performed at a medium-to-high volume centre, catheter-based renal denervation may be considered for patients with both increased CVD risk and uncontrolled hypertension on fewer than three drugs, if they express a preference to undergo renal denervation after a shared risk-benefit discussion and multidisciplinary assessment.[564,566–568,586–590]	IIb	A
Due to a lack of adequately powered outcomes trials demonstrating its safety and CVD benefits, renal denervation is not recommended as a first-line BP-lowering intervention for hypertension.	III	C
Renal denervation is not recommended for treating hypertension in patients with moderate-to-severely impaired renal function (eGFR <40 mL/min/1.73 m^2) or secondary causes of hypertension, until further evidence becomes available.	III	C

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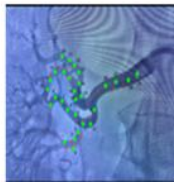
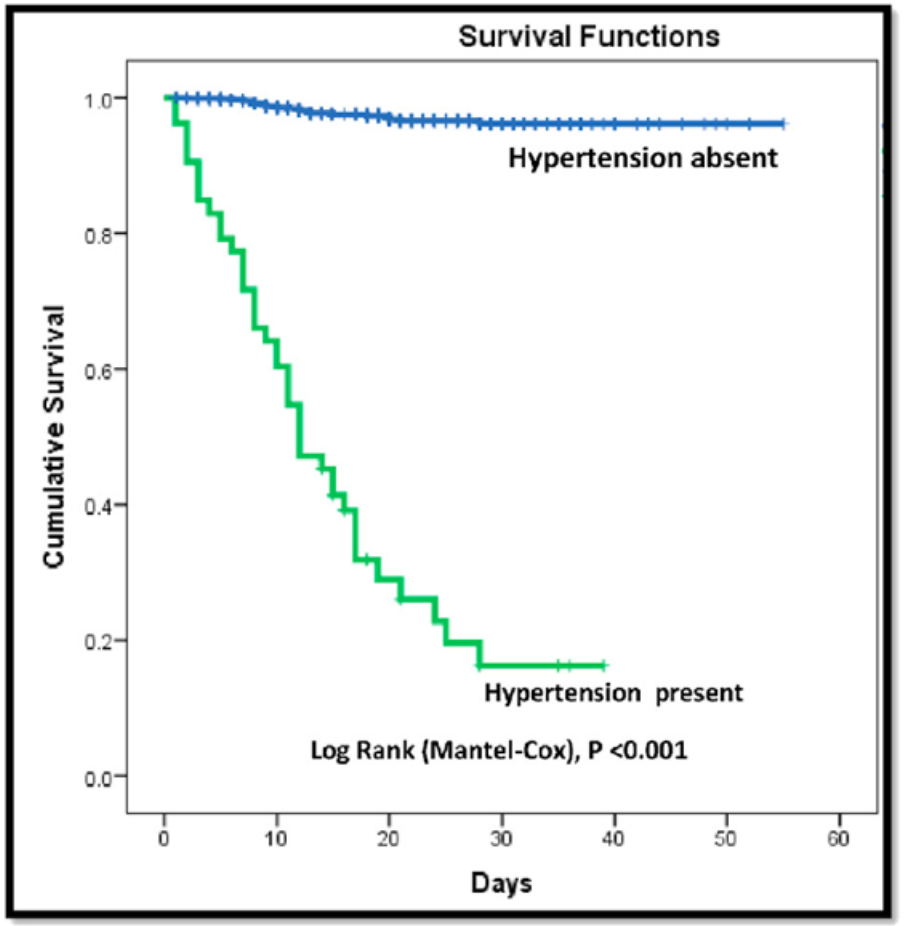
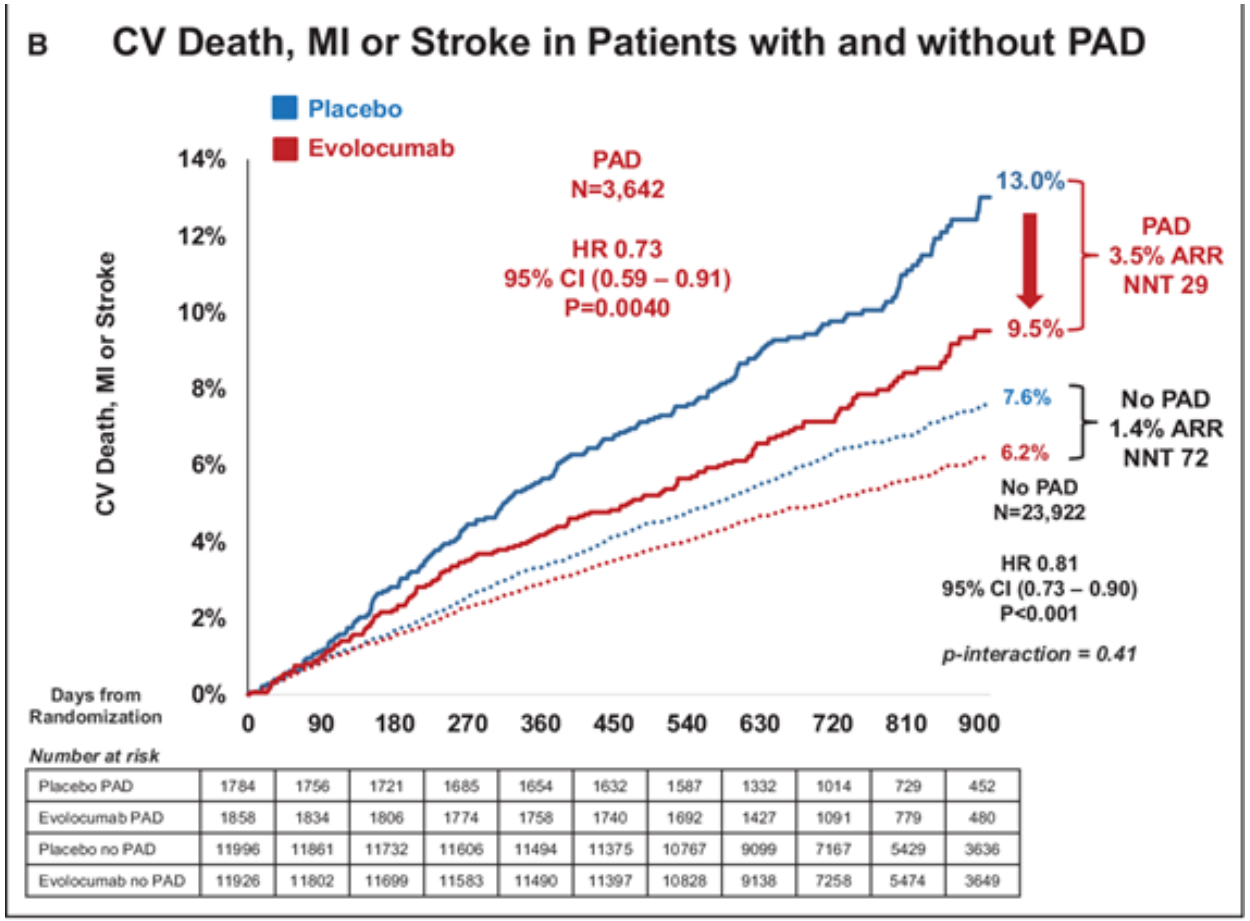
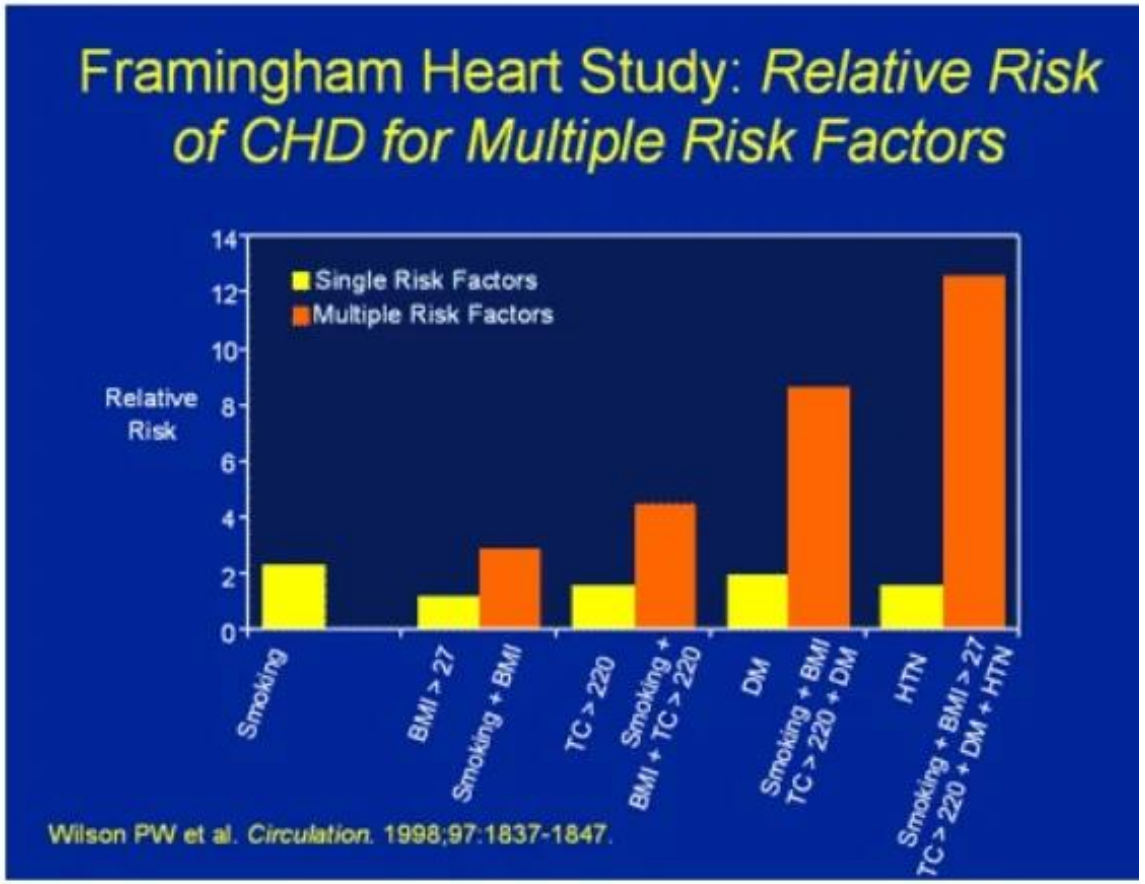
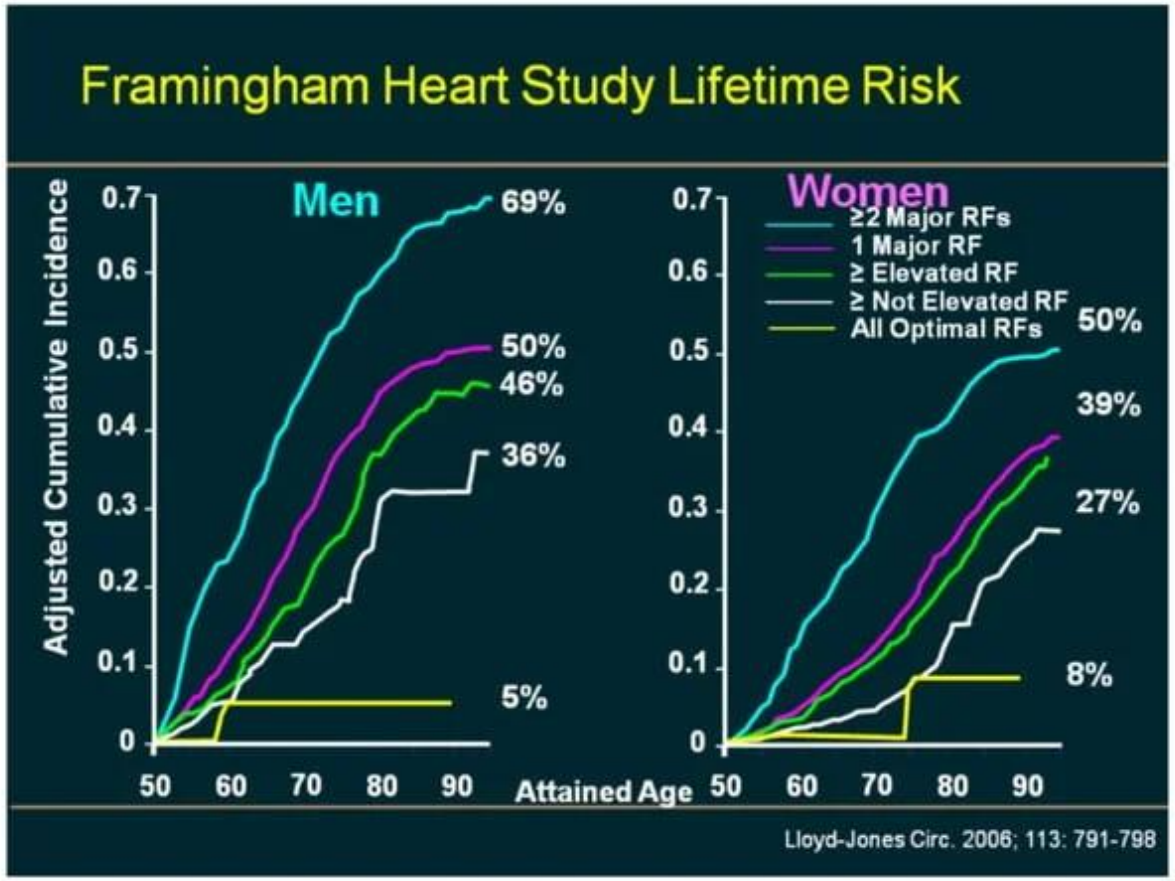






Placebo PAD	1784	1756	1721	1685	1654	1632	1587	1332	1014	729	452
Evolocumab PAD	1858	1834	1806	1774	1758	1740	1692	1427	1091	779	480
Placebo no PAD	11996	11861	11732	11606	11494	11375	10767	9099	7167	5429	3636
Evolocumab no PAD	11926	11802	11699	11583	11490	11397	10828	9138	7258	5474	3649


Framingham Heart Study: Relative Risk of CHD for Multiple Risk Factors
Relative Risk
Single Risk Factors
Multiple Risk Factors
Smoking
BMI > 27
Smoking + BMI
TC > 220
Smoking + BMI + TC > 220
DM
Smoking + BMI TC > 220 + DM
HTN
Smoking + BMI > 27 TC > 220 + DM + HTN
Wilson PW et al. Circulation. 1998;97:1837-1847.

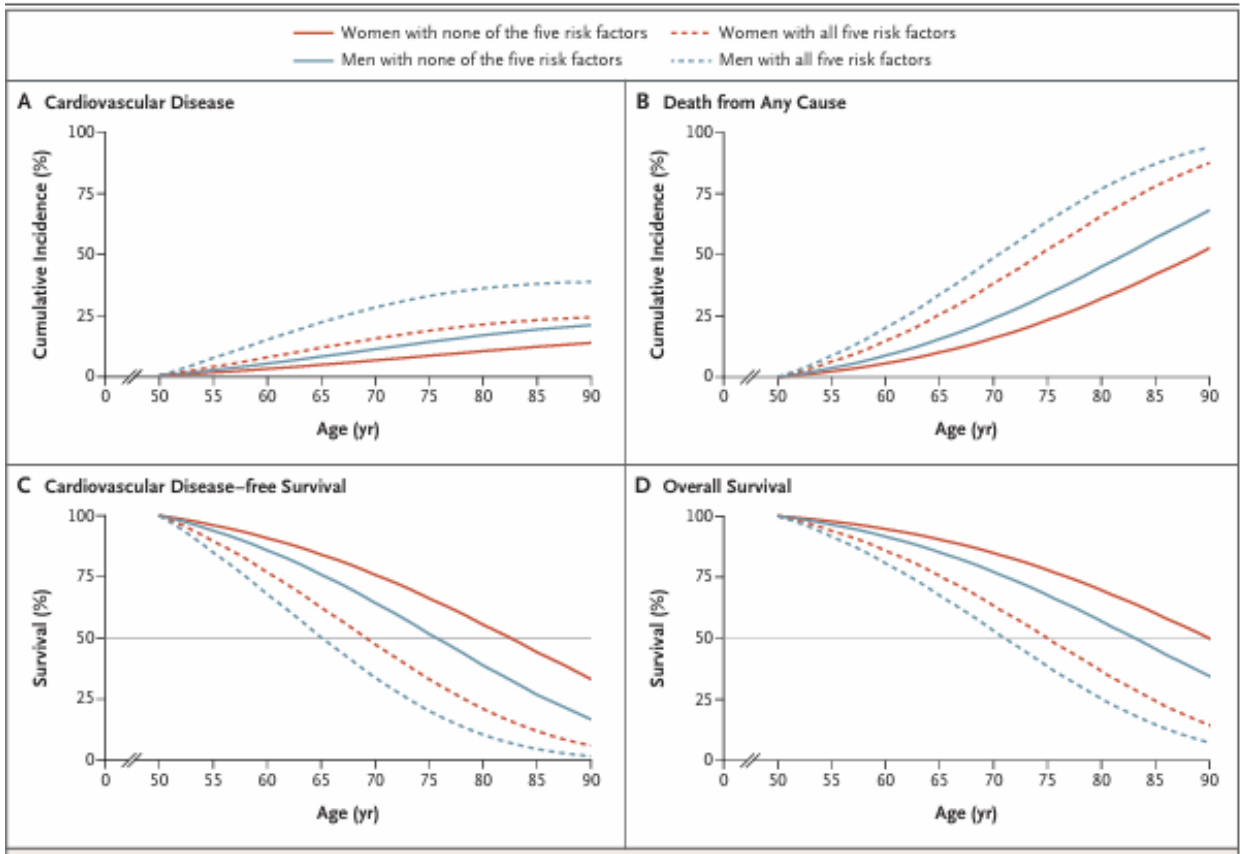

Framingham Heart Study Lifetime Risk
Adjusted Cumulative Incidence
Men
69%
50%
46%
36%
5%
Women
≥2 Major RFs
1 Major RF
≥ Elevated RF
≥ Not Elevated RF
All Optimal RFs
50%
39%
27%
8%
Attained Age
Lloyd-Jones Circ. 2006; 113: 791-798

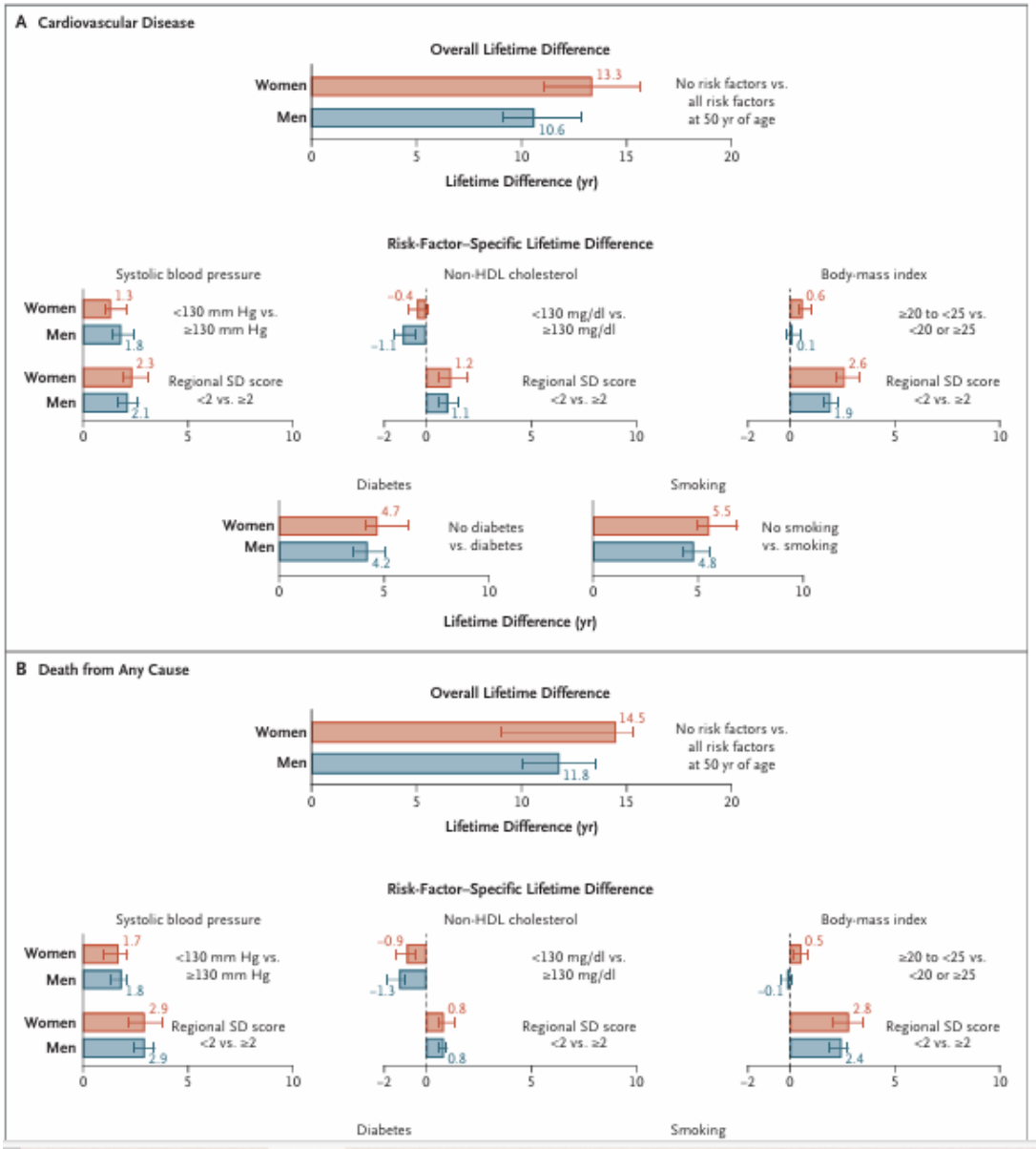
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Global Effect of Cardiovascular Risk Factors on Lifetime Estimates

The Global Cardiovascular Risk Consortium



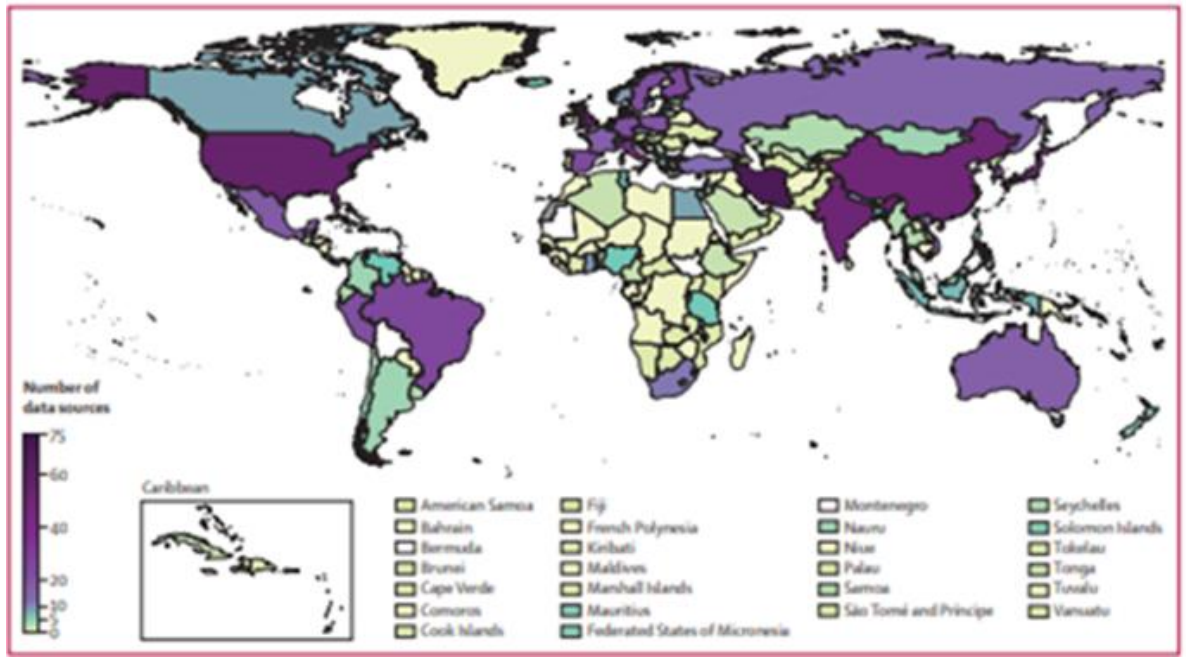


Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants

NCD Risk Factor Collaboration (NCD-RisC)*

thelancet.com Vol 398 September 11, 2021

104 milioni pz



Journal of Human Hypertension (2015), 1–6
© 2015 Macmillan Publishers Limited All rights reserved 0950-9240/15
www.nature.com/jhh

ORIGINAL ARTICLE

Blood pressure levels and control in Italy: comprehensive analysis of clinical data from 2000–2005 and 2005–2011 hypertension surveys

G Tocci[1,2], A Ferrucci[1], R Pontremoli[3], C Ferri[4], EA Rosei[5], A Morganti[6], B Trimarco[7], G Mancia[8], C Borghi[9] and M Volpe[1,2]

This analysis is aimed to determine blood pressure (BP) levels and BP control rates in a large population of hypertensive patients in Italy. Data were taken from two large and inclusive cross-sectional surveys, which covered two distinct and subsequent time periods (2000–2005 and 2005–2011, respectively). Observational clinical studies and surveys, which reported average systolic/diastolic clinic BP levels, proportions of treated/untreated and controlled/uncontrolled patients, and prevalence of cardiovascular risk factors in hypertensive patients followed in either outpatient clinics, hypertension centres or general practice, were considered for the analyses. The overall sample included 211 591 hypertensive patients (119 997 (56.7%) women, age 57.0 ± 10.0 years, body mass index 26.9 ± 4.0 kg m^{-2}, BP levels 146.9 ± 16.7/88.7 ± 9.6 mm Hg). BP levels were 148.2 ± 15.4/87.5 ± 9.3 mm Hg in patients followed by general practitioners (n = 168 313, 79.5%), 148.1 ± 17.3/90.1 ± 9.7 mm Hg in those followed by hypertension centres (n = 28 180, 13.3%), and 142.4 ± 17.6/86.6 ± 9.8 mm Hg in those followed by outpatient clinics and hospital divisions (n = 15 098, 7.1%). Among treated hypertensive patients (n = 128 079; 60.5%), 43 008 (33.6%) were reported to have controlled BP levels. Over one decade of observation, we reported that ~60% of hypertensive patients were treated and among these only 33% achieved effective BP control. These findings highlight the need for more effective interventions to improve management of hypertension in Italy.

Journal of Human Hypertension advance online publication, 12 February 2015; doi:10.1038/jhh.2015.4

Modello Verona

Ambulatorio
Ipertensione Arteriosa

Ambulatori Specialistici
di riferimento

GITIAR
Gruppo
Interdisciplinare per
la diagnosi e il
Trattamento
dell'Ipertensione
Arteriosa Resistente

Cardiologo clinico
Interventista
Specialista Ipertensione
Internista
Nefrologo
Geriatria
Endocrinologo – Spec Fibrosi Cistica

RDN

ESCLUSIONE

FOLLOW-UP
Visita – laboratorio - ABPM
1 mese
3 mesi
6 mesi
12 mesi

@ Buon controllo in TX
@ IP SECONDARIA
@ ALTRE CAUSE

@ ATS RENALE

PTA RENALE

+ ECOD Art Renali 6-12 mesi
+ MicroALB

Ambulatorio
Ipertensione Arteriosa

Ambulatori Specialistici
di riferimento

@ Valutazione/Modifiche Stile di Vita
@ Valutazione RCV Globale/ Funzione Renale
@ Inizio terapia o ottimizzazione terapia in atto
@ Educazione alla misurazione domiciliare della PA
@ Monitoraggio PA – OFFICE/ABPM a 3 mesi
@ Verifica aderenza alla terapia
@ ECODOPPLER Art Renali
@ Esclusione laboratoristica Causa Secondaria

Se ATS nota o clinicamente dubbia

@ANGIO-RM Addome/Art Renali

Modello Verona

Ambulatorio
Ipertensione Arteriosa

Ambulatori Specialistici
di riferimento

GITIAR
Gruppo
Interdisciplinare per
la diagnosi e il
Trattamento
dell'Ipertensione
Arteriosa Resistente

Cardiologo clinico
Interventista
Specialista Ipertensione
Internista
Nefrologo
Geriatria
Endocrinologo – Spec Fibrosi Cistica

RDN

ESCLUSIONE

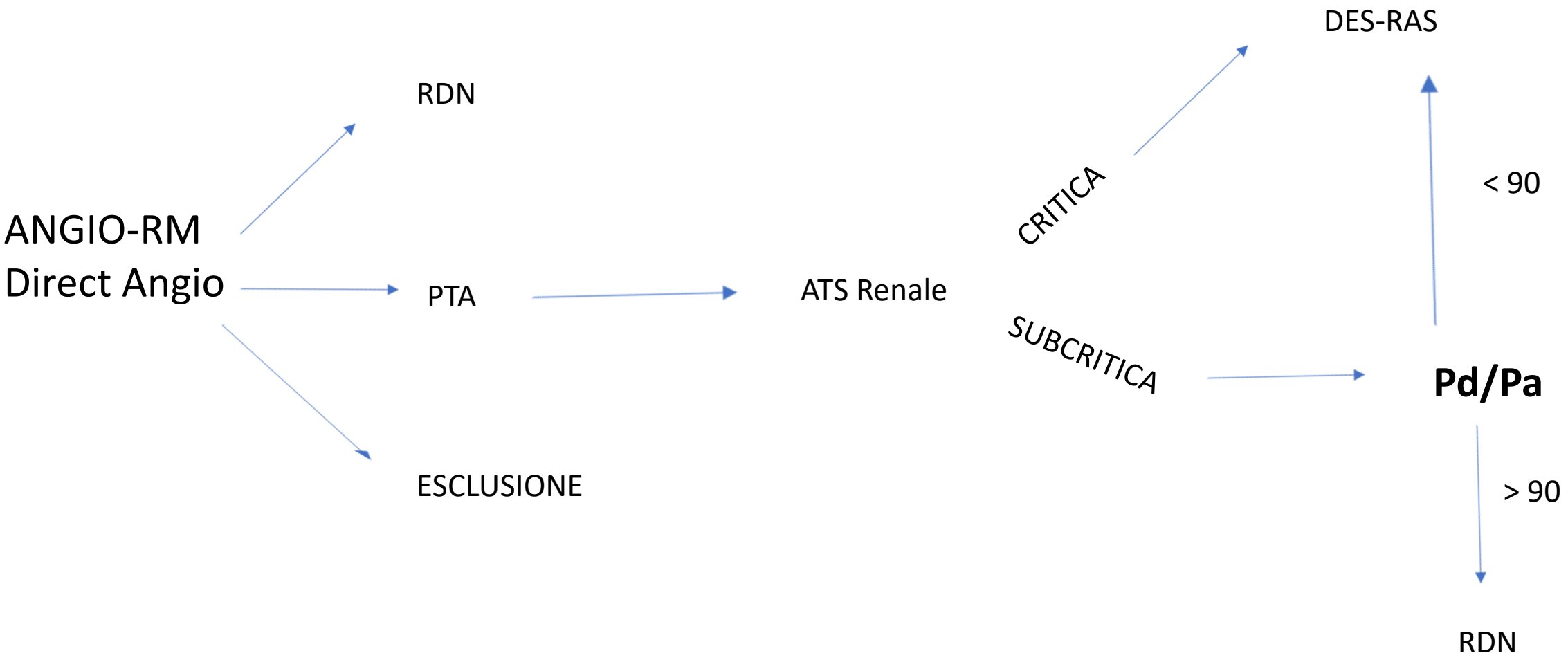
FOLLOW-UP
Visita – laboratorio - ABPM
1 mese
3 mesi
6 mesi
12 mesi

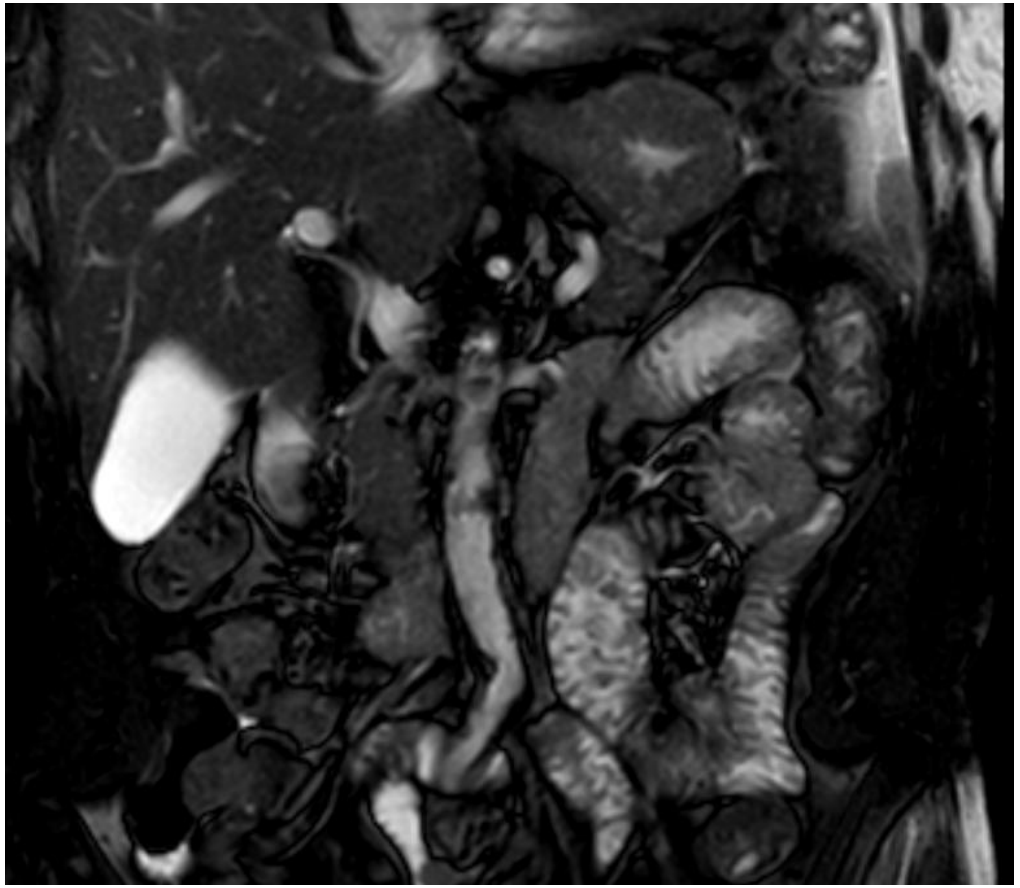
@ Buon controllo in TX
@ IP SECONDARIA
@ ALTRE CAUSE

@ ATS RENALE

PTA RENALE

+ ECOD Art Renali 6-12 mesi
+ MicroALB


ANGIO-RM
Direct Angio
RDN
PTA
ESCLUSIONE
ATS Renale
CRITICA
SUBCRITICA
DES-RAS
< 90
Pd/Pa
> 90
RDN



Congratulations and thank you to our top 10 legacy GSR enrolling centers!

	Site Name	Country	Legacy GSR
1	Universitätsklinikum des Saarlandes	Germany	151
2	Saint Vincent's Hospital, Melbourne	Australia	89
3	The Alfred Hospital	Australia	76
4	Universitätsklinikum Halle (Saale)	Germany	75
5	Institute of Cardiology, Siberian Branch, Russian Academy of	Russia	73
6	Universitätsklinikum Freiburg	Germany	69
7	Universitätsklinikum Erlangen	Germany	65
8	Azienda Ospedaliera Universitaria Integrata Verona	Italy	61
9	Universitäts-Herzzentrum Freiburg - Bad Krozingen GmbH	Germany	59
10	Deutsches Herzzentrum Berlin	Germany	53

Additionally, a big thank you and congratulation to the GSR DEFINE enrolling centers for kicking off the expansion!

	Site Name	Country	GSR DEFINE only
1	Azienda Ospedaliera Universitaria Integrata Verona	Italy	16
2	Chest Disease Hospital	Kuwait	15
3	Universitätsklinikum des Saarlandes	Germany	12
4	University Hospital Galway	Ireland	12
5	Institut Jantung Negara National Heart Institute	Malaysia	10
6	Hospital Clinico San Carlos	Spain	9
7	Cardiocentro	Switzerland	8
8	Hospital Germans Trias i Pujol	Spain	7
9	Clemens Hospital	Germany	7
10	Azienda Ospedaliera di Cosenza	Italy	7

Medtronic Engineering the extraordinary

GSR/GREAT DEFINE *Newsletter*

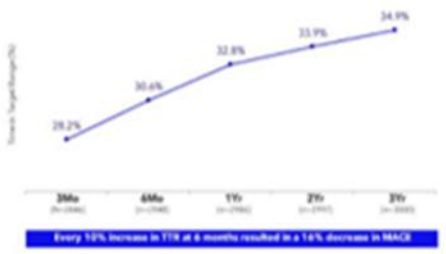
Issue 33 • September 2022

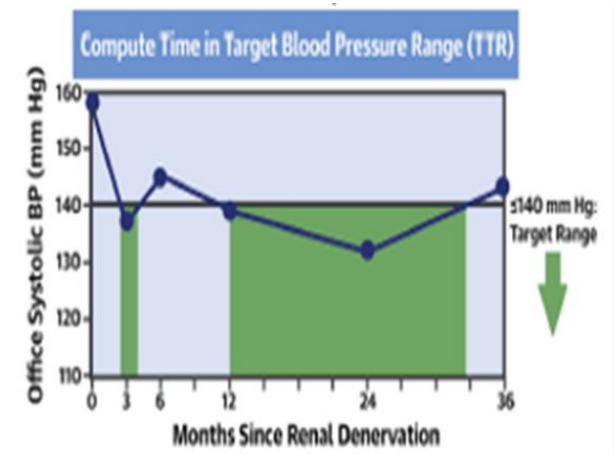
New data at EuroPCR 2022: Increased time in BP target range following RDN leads to MACE reductions in GSR

During a LBCT session at EuroPCR, Professor Felix Mahfoud presented new data from the Global SYMPLICITY Registry showing significant, sustained office and 24hr SBP reductions over 3 years in a real-world setting. Additionally, improved blood pressure control following the Symplicity blood pressure procedure with significantly higher time in target range (TTR) was associated with fewer cardiovascular events including stroke, MI, and CV death through 3 yrs in GSR-DEFINE. For more information, see the attached slides.

Significant, sustained office and 24hr SBP reductions over 3 years in real -world setting
GSR DEFINE

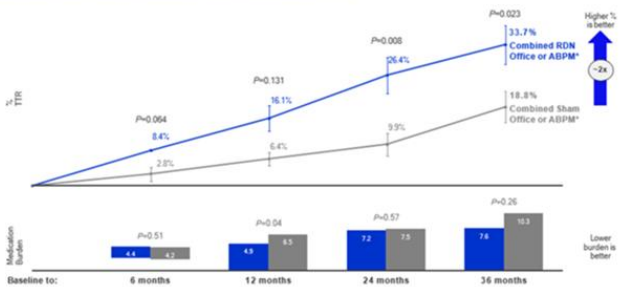
Time in Target Range increased to nearly 35% over 3 years in a real -world setting
GSR DEFINE

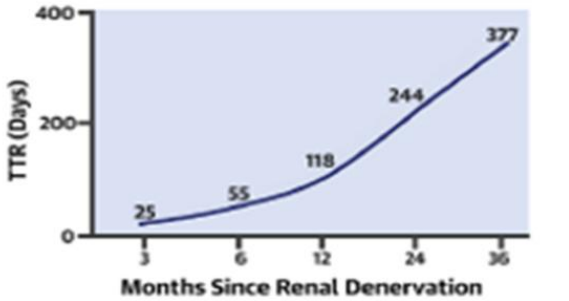




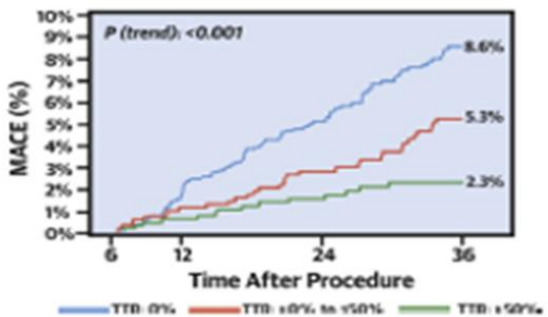
Nearly 2x greater time spent at target in RDN patients vs. sham through 3 years

With numerically lower medication burden –SPYRAL HTN-ON MED Pilot

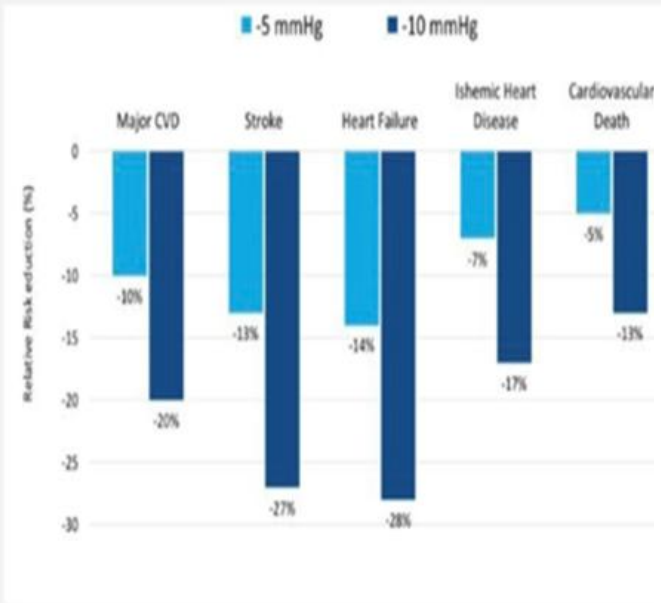




Time in Therapeutic Range Increased Over Time and Was Associated With Reduced Cardiovascular Risk



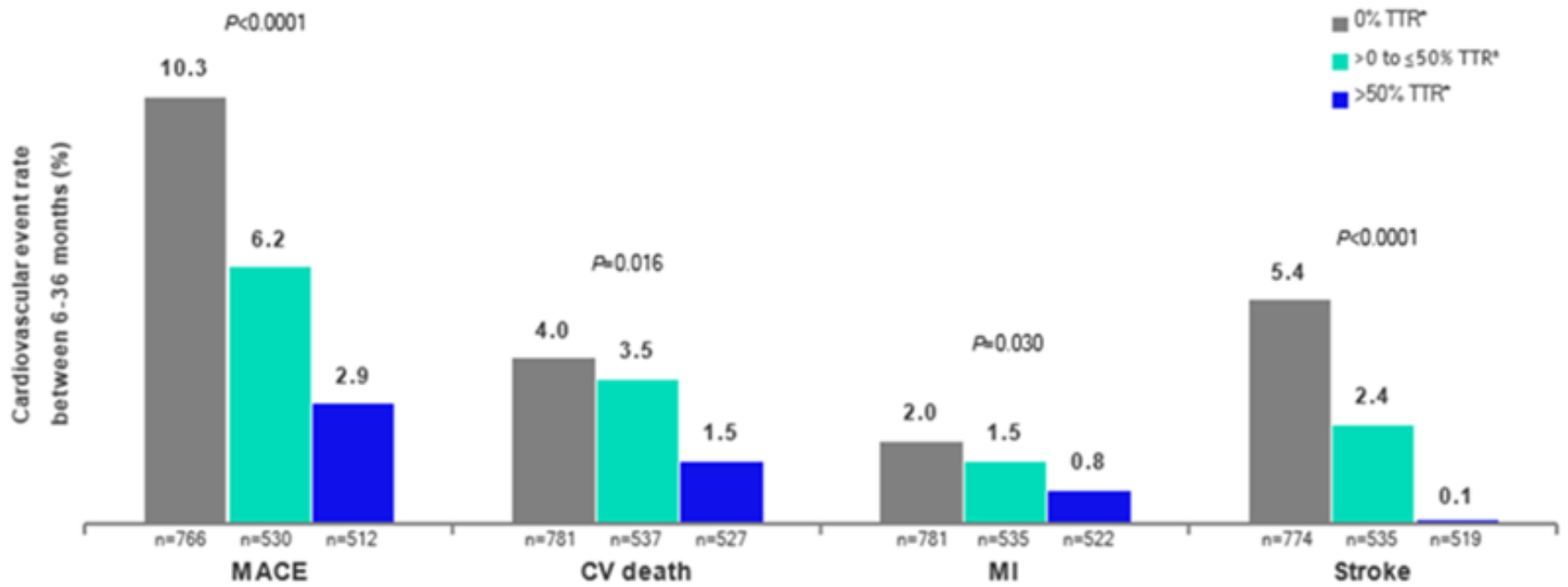
A 5 MMHG[1] OR 10 MMHG[2] DROP IN SYSTOLIC BLOOD PRESSURE IS ASSOCIATED WITH MEANINGFUL RISK REDUCTION IN CARDIOVASCULAR EVENTS



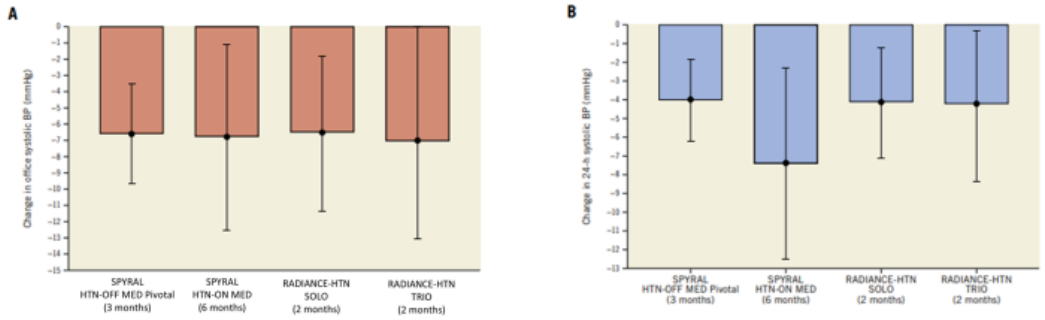
10% TTR/6 mesi > - 16% MACE

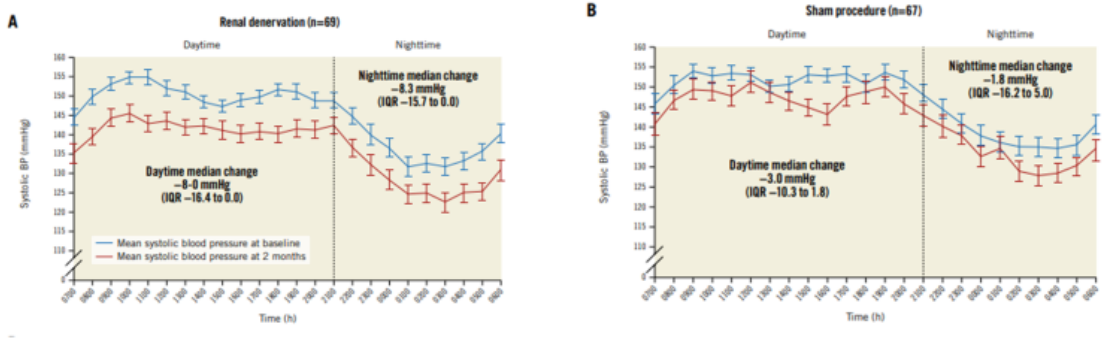
Higher TTR associated with significant CV event reductions from 6 to 36 months

GSR DEFINE



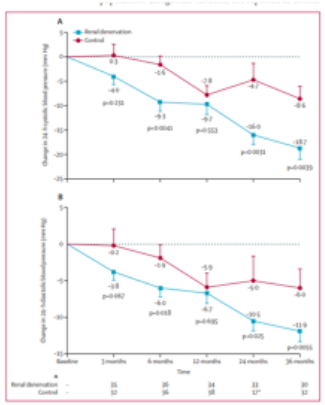
RDN RESULTS





ALWAYS ON EFFECT

E. Barbato et Al: "Renal denervation in the management of hypertension in adults."
A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)
EuroIntervention 2023;18-online publish-ahead-of-print February 2023

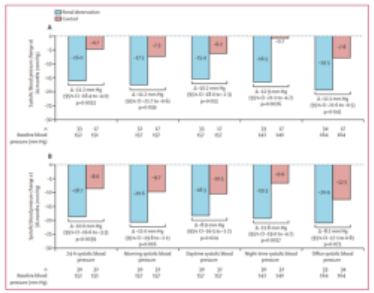


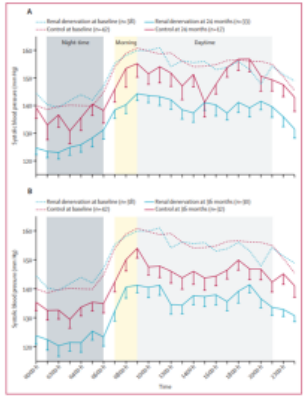
Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): a randomised, sham-controlled trial

Felix Mahfoud, David E Kandzari, Kazuomi Kario, Raymond P Townsend, Michael H Weber, Roland E Schmieder, Konstantinos Tsioufis, Stuart Pocock, Kyriakos Dimitriadis, James W Choi, Cara East, Richard B D'Souza, Andrew S P Sharp, Sebastien Ewen, Antony Walton, Ingrid Hopper, Sandeep Brar, Pamela Mckenna, Martin Fahy, Michael Bohm

thelancet.com Published online April 4, 2022 https://doi.org/10.1016/S0140-6736(22)00455-X

Interpretation Radiofrequency renal denervation compared with sham control produced a clinically meaningful and lasting blood pressure reduction up to 36 months of follow-up, independent of concomitant antihypertensive medications and without major safety events. Renal denervation could provide an adjunctive treatment modality in the management of patients with hypertension.





E. Barbato et Al: "Renal denervation in the management of hypertension in adults."
A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)
EuroIntervention 2023;18-online publish-ahead-of-print February 2023

Hypertension

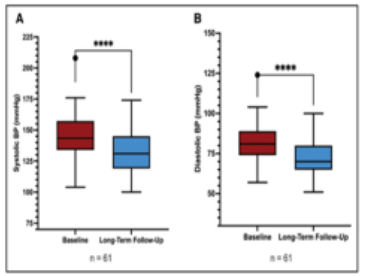
ORIGINAL ARTICLE

Catheter-Based Renal Denervation: 9-Year Follow-Up Data on Safety and Blood Pressure Reduction in Patients With Resistant Hypertension

Gianni Sesa-Ashton, Janis M. Nolde, Ida Muente, Renathy Carnagarin, Rebecca Lee, Vaughan Macefield, Tye Dawood, Yusuke Sata, Elisabeth A. Lambert, Gavin W. Lambert, Antony Walton, Marcio G. Kiuchi, Murray D. Esler, Markus P. Schlaich

CONCLUSIONS RDN results in a significant and robust reduction in both office and ambulatory systolic and diastolic BP at 4-year FU after catheter-based RDN on less medication and without evidence of adverse consequences on renal function.

(Hypertension. 2022;80:00-00. DOI: 10.1161/HYPERTENSIONAHA.122.20053.)



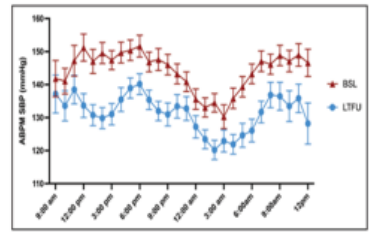
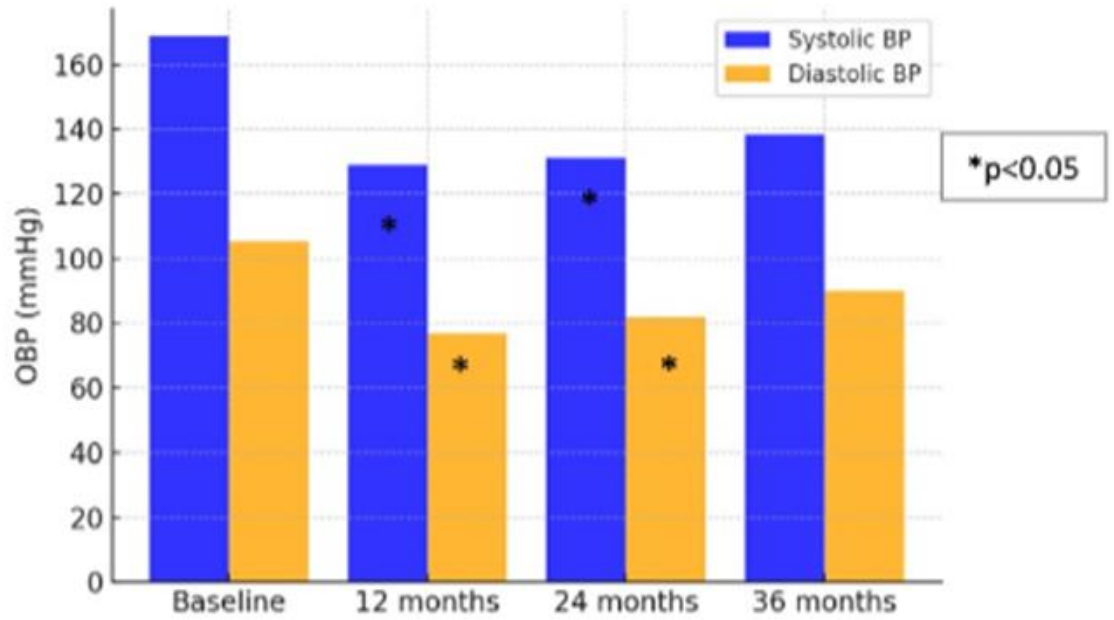
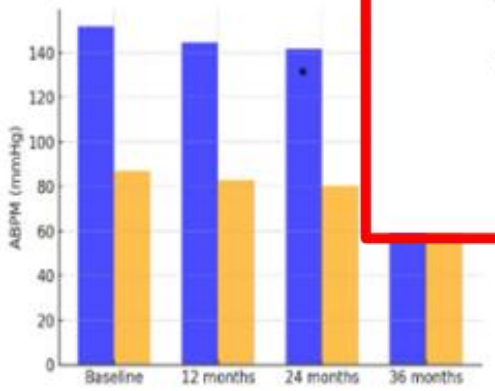


Figure 2. ABPM results in all pat

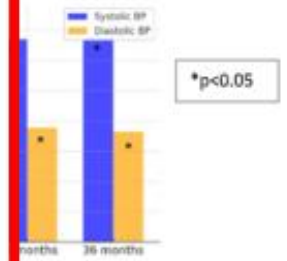
e) OBP results in patients with kidney failure undergoing dialysis.



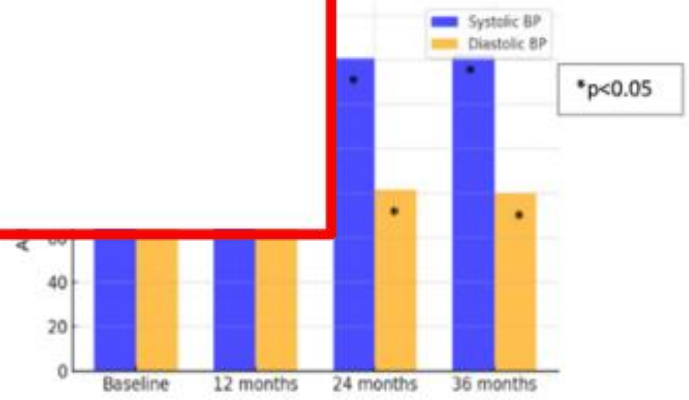
a) ABPM results in patien



tients with eGFR 60-89 mL/min/1.73 m²



tients with eGFR<40 mL/min/1.73 m²



EuroIntervention accepted

Spontaneous, independent, single-center RDN registry of a resistant hypertension multidisciplinary team

S. Fezzi, G. Castaldi, M. Widmann, F. Marin, V. Galli, A. Ruzzarin, G. Pesarini, R. Scarsini, M. Pighi, D. Tavella, F. Ribichini
Integrated University Hospital of Verona, Verona, Italy

Uncontrolled resistant hypertension (URH) is related with poor prognosis and high risk of MACCEs

Renal sympathetic denervation (RDN) has proved efficacy in different hypertensive population in SPYRAL (RF) and RADIANCE (US) studies. However CKD IIIB-V stages (i.e. GFR<45 ml/min) have been systematically excluded from RCTs

	Overall	eGFR<45	eGFR≥45	p-value
	N=72 (100%)	N= 27 (37.5%)	N= 45 (62.5%)	
Age (years)	69.4 ± 11.1	68.8 ± 17.0	69.8 ± 14.0	p= 0.789
Male gender	52 (72.2%)	22 (81.5%)	30 (66.7%)	p=0.174
BMI (kg/m2)	30.0 ± 5.5	29.6±6.0	30.2±5.2	p= 0.682
Smoking	35 (48.6%)	13 (37.8%)	22 (51.6%)	p= 0.284
eGFR (ml/min)	57.2 ± 30.3	26.7±12.9	77.2±20.8	p<0.001
CKD	43 (59.7%)	27 (100%)	16 (35.6%)	p<0.001
Stage V CKD	7 (9.7%)	7 (25.9%)	-	-
Diabetes, Type 2	31 (43.1%)	14 (51.9%)	17 (37.8%)	p= 0.437
IHD	38, 52.8%	15, 48.1%	25, 55.6%	p= 0.362
PAD	24 (33.3%)	12, 44.4%	12, 26.7%	p= 0.307
CAD	18, 25%	5, 18.5%	13, 28.9%	p=0.386
COPD	12, 16.7%	5 (18.5%)	7 (15.6%)	p=0.822
OSAS	7 (9.7%)	3 (11.1 %)	4 (8.9%)	p=0.810
Antihypertensive medications	5.3 ± 1.1	5.5 ± 0.9	5.1 ± 1.2	p= 0.305

Table 1. Patients characteristics

Aims and Methods

To evaluate the efficacy and safety of RF-RDN in a daily practice real-world population of patients with URH, on top of medical therapy

EFFICACY:
Interindividual change of **OBP and ABPM** from baseline to 3-month, 6-month and 12-month follow-up

SAFETY:
Absence of any device-related major complication (BARC), end-stage renal disease, stroke, acute myocardial infarction and any cause of death within 1 month of the procedure; interindividual change of eGFR from baseline to 12-month follow-up

EXCLUSION CRITERIA
- secondary forms of hypertension
- significant valvular heart disease
- recent acute cardiovascular events
- hemodynamically significant renal artery stenosis

MULTIDISCIPLINAR DISCUSSION
Interventional cardiologist, clinical cardiologist, nephrologist, hypertension specialist

RULED OUT
- Non-adherence to medical therapy (direct questioning)
- White coat hypertension (home blood pressure diary, and/or ABPM).

72 patients with uncontrolled-resistant hypertension underwent RDN between 2013-2023

Figure 1. Study flow-chart

Results

- Baseline OBP 158.8/86.6±23.4/15.3 mmHg, ABPM 151.4/87.6±18.8/14.2 mmHg
- Tetrapolar radio-frequency catheter (91.7%), 37.3±14.3 number of ablations per-procedure, 72.1±38.1 ml amount of contrast medium
- Follow-up data available for 58/72 patients (9/72 lost, 5/72 still on-going)

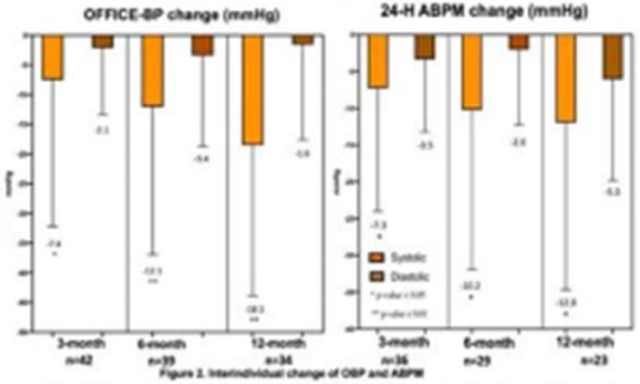


Figure 2. Interindividual change of OBP and ABPM

- BP reduction among patients with eGFR < 45 ml/min was similar to that obtained in patients with higher eGFR
- No major complications were observed and renal function was stable up to 12 months, even in patients with lowest eGFR at baseline

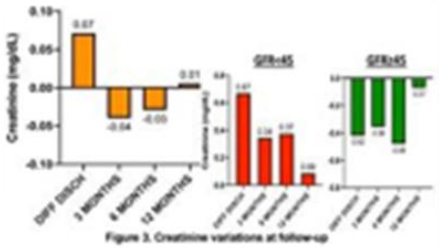


Figure 3. Creatinine variations at follow-up

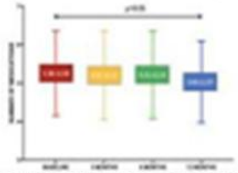
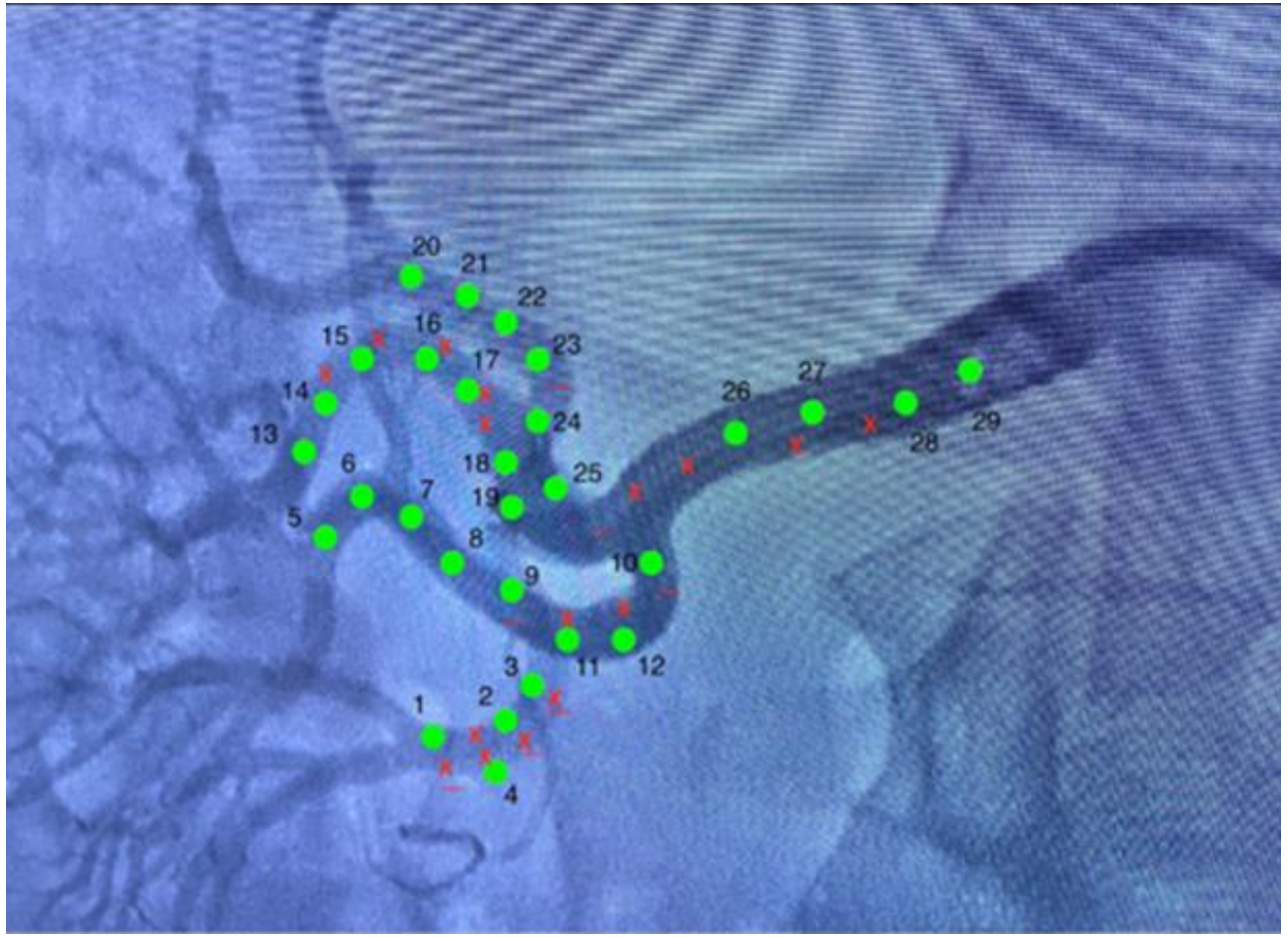


Figure 4. Number of anti-hypertensive medications

Conclusions

- In a "real-life population" with URH RDN showed to be a safe and feasible strategy when applied on top of OMT
- RDN confirmed safety and efficacy in patients with CKD
- RDN resulted in a significant reduction in systolic BP for up to 12 months after the procedure and a trend towards a reduction in diastolic BP
- Central role of the multidisciplinary team discussion for the tailored management of URH patients
- Two patients with ESRD underwent successful kidney transplantation after improving BP control post-RDN, with good BP control after transplantation


FOV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THM

Il termine di Ipertensione Resistente è oramai obsoleto e fuorviante

Il controllo del valore pressorio è necessariamente da relativizzare alle patologie del pz anche anamnestiche

La procedura di RDN non è da «consigliare» solo ed esclusivamente per la cosmesi del valore pressorio che non ci piace..
O perché non sappiamo cosa altro fare..

L'efficacia e la sicurezza della procedura sono sempre più confermate anche oltre le LG

Grazie per l'attenzione....

domenico.tavella@aovr.veneto.it denervazionerenale@cardiovr.it