Layered Procedures in Hypertensive Emergencies

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2009-2013 with conclusions Trends in Hypertension

Hypertensive Emergency Case Decision and Classification Therapy and Cardiovascular Complications

Primary Events

Secondary Events

Comparison of Primary and Secondary Events in this Study

Conclusions

Trends in Hypertension

Systolic blood pressure in mmHg (not age-standardized)



In 180 countries

Time period 80 – 09 Values from WHO

Blood Pressure Mean: Men

Average systolic in mmHg (not age-standardized)



Average systolic values from 1980 to 2009 from WHO

Male Blood Pressures

AFG	AGO	ALB	ARE	ARG	ARM	AUS	AUT	AZE	BDI	BEL	BEN	BFA	BGD	BGR	BHR	BHS	BIH
145- 125- 9-225 105-	-			\sim	~							~		~			
BLR	BLZ	BOL	BRA	BRB	BRN	BTN	BWA	CAF	CAN	CHE	CHL	CHN	CIV	CMR	COD	COG	COL
145- 125- 105-	~	\sim	\sim									\smile	\sim	\sim	~	~	\sim
COM	CPV	CRI	CUB	СҮР	CZE	DEU	DJI	DNK	DOM	DZA	ECU	EGY	ERI	ESP	EST	ETH	FIN
145 125 105		\sim	~				~						-			_	
FJI	FRA	FSM	GAB	GBR	GEO	GHA	GIN	GMB	GNB	GNQ	GRC	GRD	GTM	GUY	HND	HRV	НТІ
145- 125- 105-							~	~	~			~	~	-	\sim		~
HUN	IDN	IND	IRL	IRN	IRQ	ISL	ISR	ITA	JAM	JOR	JPN	KAZ	KEN	KGZ	кнм	KOR	к
145 125 105				~	~												
LAO	LBN	LBR	LBY	LCA	LKA	LSO	LTU	LUX	LVA	MAR	MDA	MDG	MDV	MEX	МКД	MLI	MLT
LAO						LSO				MAR	MDA	MDG	MDV		MKD	MLI	MLT
LAO 145- 125- 105- MMR	LBN	LBR	LBY MOZ	LCA	LKA MUS	LSO MWI	LTU MYS		LVA	MAR NGA	MDA	MDG	MDV	MEX	MKD	MLI OMN	MLT
LAO 145- 125- 105- MMR 145- 125- 105-	LBN MNE	LBR MNG	LBY MOZ	LCA MRT	LKA MUS	LSO MWI	LTU MYS		LVA NER	MAR NGA	MDA	MDG NLD	MDV	MEX NPL	MKD NZL	MLI OMN	MLT PAK
LAO 145- 125- 105- MMR 145- 125- 105- PAN	LBN MNE PER	LBR MNG PHL	LBY MOZ PNG	LCA MRT POL	LKA MUS PRK	LSO MWI PRT	LTU MYS PRY	LUX NAM QAT	LVA NER ROU	MAR NGA RUS	MDA NIC RWA	MDG NLD SAU	MDV NOR SDN	MEX NPL SEN	MKD NZL SGP	MLI OMN SLB	MLT PAK SLE
LAO 145- 125- 105- MMR 145- 125- 105- PAN 145- 125- 105- PAN	LBN MNE PER	LBR MNG PHL	LBY MOZ PNG	LCA MRT POL	LKA MUS PRK	LSO MWI PRT	LTU MYS PRY	LUX NAM QAT	LVA NER ROU	MAR NGA RUS	MDA NIC RWA	MDG NLD SAU	MDV NOR SDN	MEX NPL SEN	MKD NZL SGP	MLI OMN SLB	MLT PAK SLE
LAO 145- 125- 105- MMR 145- 125- 105- PAN 145- 125- 105- PAN 145- 125- 105- SLV	LBN MNE PER SOM	LBR MNG PHL SRB	LBY MOZ PNG STP	LCA MRT POL SUR	LKA MUS PRK SVK	LSO MWI PRT SVN	LTU MYS PRY SWE	LUX NAM QAT SWZ	LVA NER ROU SYC	MAR NGA RUS SYR	MDA NIC RWA TCD	MDG NLD SAU TGO	MDV NOR SDN THA	MEX NPL SEN TJK	MKD NZL SGP TKM	MLI OMN SLB TLS	MLT PAK SLE TON
LAO 145- 125- 105- MMR 145- 125- 105- PAN 145- 125- 105- SLV 145- 125- 105- SLV	LBN MNE PER SOM	LBR MNG PHL SRB	LBY MOZ PNG STP	LCA MRT POL SUR	LKA MUS PRK SVK	LSO MWI PRT SVN	LTU MYS PRY SWE	LUX NAM QAT SWZ	LVA NER ROU SYC	MAR NGA RUS SYR	MDA NIC RWA TCD	MDG NLD SAU TGO	MDV NOR SDN THA	MEX NPL SEN TJK	MKD NZL SGP TKM	MLI OMN SLB TLS	MLT PAK SLE TON
LAO 145- 125- 105- MMR 145- 125- 105- PAN 145- 125- 105- SLV 145- 125- 105- SLV 145- 125- 105- TTO	LBN MNE PER SOM	LBR MNG PHL SRB	LBY MOZ PNG STP TZA	LCA MRT POL SUR UGA	LKA MUS PRK SVK	LSO MWI PRT SVN	LTU MYS PRY SWE USA	LUX NAM QAT SWZ UZB	LVA NER ROU SYC	MAR NGA RUS SYR VEN	MDA NIC RWA TCD	MDG NLD SAU TGO VUT	MDV NOR SDN THA WSM	MEX NPL SEN TJK YEM	MKD NZL SGP TKM ZAF	MLI OMN SLB TLS ZMB	MLT PAK SLE TON ZWE

Blood Pressure Mean: Women

Average systolic in mmHg (not age-standardized)



Average systolic values from 1980 to 2009 from WHO

Female Blood Pressures

AFG	AGO	ALB	ARE	ARG	ARM	AUS	AUT	AZE	BDI	BEL	BEN	BFA	BGD	BGR	BHR	BHS	BIH
130- 110-		~		-				~									-
BLR	BLZ	BOL	BRA	BRB	BRN	BTN	BWA	CAF	CAN	CHE	CHL	CHN	сі	CMR	COD	COG	COL
130- 110				\sim								~					\sim
СОМ	CPV	CRI	CUB	СҮР	CZE	DEU	DJI	DNK	DOM	DZA	ECU	EGY	ERI	ESP	EST	ETH	FIN
130- 110-			~										_				
FJI	FRA	FSM	GAB	GBR	GE0	GHA	GIN	GMB	GNB	GNQ	GRC	GRD	GTM	GUY	HND	HRV	нті
130- 110-																	
HUN			IRL		IRQ	ISL	ISR		JAM	JOR	JPN	KAZ	KEN	KGZ	КНМ	KOR	к₩Т
130- 110 -									~							~	
LAO	LBN	LBR	LBY	LCA	LKA	LSO	LTU	LUX	LVA	MAR	MDA	MDG	MDV	MEX	MKD	MLI	MLT
LA0		LBR				LSO				MAR	MDA	MDG	MDV		MKD	MLI	MLT
LAO 130- 110- MMR		LBR MNG	LBY MOZ	LCA	LKA MUS	LSO MWI	LTU MYS			MAR	MDA	MDG		MEX	MKD	MLI	MLT
LAO 130- 110- MMR 130- 110-	LBN MNE	LBR MNG	LBY MOZ	LCA MRT	LKA MUS	LSO MWI	LTU MYS	NAM	LVA NER	MAR NGA	MDA NIC	MDG NLD		MEX NPL	MKD NZL	MLI OMN	MLT PAK
LAO 130- 110- MMR 130- 110- PAN	LBN MNE PER	LBR MNG PHL	LBY MOZ PNG	LCA MRT POL	LKA MUS PRK	LSO MWI PRT	LTU MYS PRY	LUX NAM	LVA NER ROU	MAR NGA RUS	MDA NIC RWA	MDG NLD SAU	MDV NOR SDN	MEX NPL SEN	MKD NZL SGP	MLI OMN SLB	MLT PAK
LAO 130- 110- MMR 130- 110- PAN 130- 130- 110-	LBN MNE PER	LBR MNG PHL	LBY MOZ PNG	LCA MRT POL	LKA MUS PRK	LSO MWI PRT	LTU MYS PRY		LVA NER ROU	MAR NGA RUS	MDA NIC RWA	MDG NLD SAU	MDV NOR SDN	MEX NPL SEN	MKD NZL SGP	MLI OMN SLB	MLT PAK SLE
LAO 130- 110- MMR 130- 110- PAN 130- 110- SLV	LBN MNE PER SOM	LBR MNG PHL SRB	LBY MOZ PNG STP	LCA MRT POL SUR	LKA MUS PRK SVK	LSO MWI PRT SVN	LTU MYS PRY SWE	LUX NAM QAT SWZ	LVA NER ROU SYC	MAR NGA RUS SYR	MDA NIC RWA TCD	MDG NLD SAU TGO	MDV NOR SDN THA	MEX NPL SEN TJK	MKD NZL SGP TKM	MLI OMN SLB TLS	MLT PAK SLE TON
LAO 130- 110- MMR 130- 110- PAN 130- SLV 130- 130- 110- SLV	LBN MNE PER SOM	LBR MNG PHL SRB	LBY MOZ PNG STP	LCA MRT POL SUR	LKA MUS PRK SVK	LSO MWI PRT SVN	LTU MYS PRY SWE	LUX NAM QAT SWZ	LVA NER ROU SYC	MAR NGA RUS SYR	MDA NIC RWA TCD	MDG NLD SAU TGO	MDV NOR SDN THA	MEX NPL SEN TJK	MKD NZL SGP TKM	MLI OMN SLB TLS	MLT PAK SLE TON
LAO 130- 110- MMR 130- 110- PAN 130- 110- SLV 130- 110- SLV 130- 110- TTO	LBN MNE PER SOM	LBR MNG PHL SRB	LBY MOZ PNG STP TZA	LCA MRT POL SUR UGA	LKA MUS PRK SVK UKR	LSO MWI PRT SVN URY	LTU MYS PRY SWE USA	LUX NAM QAT SWZ UZB	LVA NER ROU SYC	MAR NGA RUS SYR VEN	MDA NIC RWA TCD VNM	MDG NLD SAU TGO VUT	MDV NOR SDN THA WSM	MEX NPL SEN TJK YEM	MKD NZL SGP TKM ZAF	MLI OMN SLB TLS ZMB	MLT PAK SLE TON

Simple Trends in Blood Pressure



Simple Trends in Blood Pressure

- if the development is towards higher values of blood pressure (or negligible in male), female trends are ever so often more rapid
- if the development is towards lower values of blood pressure, it is usually more rapid in the female sex

female trends are highly significant

 \Rightarrow countries with largest *gender gaps* are...

Top 2%	Burkina Faso Mali Niger Nigeria	towards higher values
Тор 2%	Czech Republic Spain Estonia Malta	towards lower values

Physiology: Male and Female with 3 Parameters



Trends in Hypertension: 2016

Non-linear predictions; Average systolic blood pressure



Predictions based on 1980 – 2009 Raw Values from WHO

Trends in Hypertension

Hypertensive Emergency Case Decision and Classification Therapy and Cardiovascular Complications

Primary Events

Secondary Events

Comparison of Primary and Secondary Events in this Study

Conclusions

Hypertensive Emergencies

- available patient cohort study from May 2008 in Kanton Basel (BS, BL) and Luzern
- inclusion criteria: blood pressure >180 mmHg/>110 mmHg, age > 20 y
- discriminant analysis, logistic regression, categorical regression, multi layer perceptrons
- primary care questionnaire

... in addition to Age and Gender, data on Blood pressure, Drugs, Emergency therapy, Follow-up therapy, Cardiovascular risk factors were requested to be answered. Further questions referred to Accompanying conditions and the History of cardiovascular complications, Cardiovascular complications within 3 months

• 1 year follow-up

... Cardiovascular events, Follow-up therapy changes and data on newly described Cardiovascular risk factors were requested to be answered

Hypertension Prevalence in the Elderly



Age group (approx.) 65-74

Wolf-Maier et al. (2003); Kearney et al. (2005); Pitsavos et al. (2006) ; eurostat.ec.europa.eu (2008); National Health and Nutrition Survey of Japan (2006) and WHO

Test: Hypertensive Emergencies and Case Decision

Modelling of the "clinical decision" path



Hypertensive Emergencies: Symptoms

abdominal painabdominal painataxiaaltered mental statuschest painAngstconfusionatactic gaitdizziness/vertigocold intolerancedropsdizziness/vertigodropsdizziness/vertigodyspnoeadyspnoeaheadacheepiphoraincontinencegait disturbanceslimb weaknessflushnauseagait disturbancespallorheadachepalpitationslimb painpruritusnauseaspeech disturbancespalpitationsvisual disturbancespruritusvomitusrestlessnessshoulder painsweatingvisual disturbancespruritussub and the painsweatingpalpitationstitusnauseatitussub andsweatingpalpitationstitusrestlessnessshoulder painsweatingtitussweatingtitus<

* Does not lead to Emergency or Urgency classification

Differential Diagnosis

	Medical conditions
cardiac	acute pulmonary edema with systolic/diastolic dysfunction
	malignant hypertension, stroke, aortic dissection
neurologic	intracranial / subarachnoid hemorrhage, cerebral embolism / stroke, hypertensive encephalopathy
traumatic	head trauma
renal	chronic pyelonephritis, renal parenchymal diseases (glomerulonephritis), renovascular disease
drugs	monoamine oxidase inhibitor interactions, cocaine overdose
endocrine	pheochromocytoma (excess catecholamines), aldosteronism, renin-secreting tumors, glucocorticoid excess
metabolic	hypercalcemia
pregnant	preeclampsia, eclampsia
psychogenic	hyperventilation, Angst, sympathetic hyper-tonus, panic attack

"Available Patient Cohort" Study

time course 18.4 months



Cardiovascular Differential Diagnosis: Reevaluation

8 Cases were selected



Hospitalization of Patients

Emergency hospitalization

patient	class	diagnosis
1	Emergency	acute myocardial infarction
2	Emergency	acute coronary syndrome
3	Emergency	suspected cerebrovascular insult
4	Emergency	suspected cerebrovascular insult
5	Emergency	suspected cerebrovascular insult
6	Emergency	hypertensive encephalopathy
7	Emergency	hypertensive encephalopathy
8	Emergency	hyponatremia, hypertensive encephalopathy
9	Urgency	mesenteric ischemia, bowel obstruction, hyperthyroidism
10	Urgency	suspected cerebrovascular insult

Summary of Patient Data

m f

164 patients					
sex	f 103 m 61				
age Average	70,4 years (21-96)	ſ			
		100-			
Asymptomatic (n)	99	80-			38
Urgency (n)	50				
Emergency (n)	15	-09 ber			
		unu		57	
systolic hypertension (n)	153	40-			61
diastolic hypertension (n)	40	20-		53	
sytol./diastol. hypertension (n)	29		6		
		ــــ	Emergency	Urgency	Asymptomat
systolic blood pressure Median	195 mmHg (145-255)			Classificatio	n
diastolic blood pressure Median	100 mmHg (60-130)				
hypertension	78,7%				
first observed hypertensive emergency	62.2%				

Therapy by Emergency Classes



Time-Series



Cardiovascular Risk Factors



Sex-Specific Distribution



Factors

Sex

Cardiovascular Risk Factors After 1 Year

comparison study start - 1 year



Accompanying Medical Conditions



Patients and Frequency

correlative evidence shows...

- first hypertensive emergencies occur often with new patients
- White Coat hypertensive patients show fewer symptoms upon examination
- symptoms correlate with stress, NSAR medication and infects

Neural Network

NEURAL COMPUTATION

(modified from Baxt 1990)

The network identified 92% of the patients with acute myocardial infarction, 96% of the patients without infarction. When all patients with the ECG evidence of infarction were removed from the cohort, the network correctly identified 80%

Neural Network

Key Question

"Does the evaluation contain *previously inapparent information* that can be used to improve on the diagnostic accuracy of predicting..." Baxt, 1990

- hypertension
- gender
- lack of exercise / obesity

Retained Parameters in Logistic Regression



Dynamic Scaling of Emergency Classes



Separation of U and A requires use of Symptom variable?

Dynamic Scaling of Emergency Classes



"Structural Equation" model without parameters

Classification in Hypertensive Emergencies

Model unifying 7 different "output functions" counting 2400



Optimized Top 500 Models of 2400

Hidden Layer AF

Hyperbolic tangent	321
Sigmoid	182

Ouput Layer AF

Hyperbolic tangent	83
Identity	93
Sigmoid	37
Softmax	290

AUCs ≥ 0.986



Output layer activation function: Softmax

Optimized Top 500 Models of 2400

Model unifying 7 different "output functions" - Top 500


Classification in Discriminant Analysis



Classification in Discriminant Analysis



Hypertensive Emergency: Goodness of Classification

New data on hypertension			
	Method	% Classification Overall Error	
1	Neural network	1,0 (+/- 0,6%) - 5,0 (+/- 2,4%)	
2	Discriminant analysis	10,0	
3	CatReg	16,0	
4*	Logistic regression	≤ 29 ,9	

*Symptoms were not introduced

The logistic regression was included with absolute values of blood pressure as a covariate – these results suggested that these could be used and led to 0% classification error at, however, low statistical significance. Yet, this furthermore indicates that future emergency schemes or health advice can be generated and replaced with medical data and binary decisions (>180 mmHg systolic / >110 mmHg diastolic) on blood pressure, if required, without the predicted loss of accuracy.

Treatment



Patient Recall?



Scale: Nominal.

Drug History and Emergency Therapy

p <0.05

Cardiovascular treatment track

- •ACE inhibitors in drug history lead to a significantly higher prescription rate of sedatives
- previous treatment with ARB results in frequent emergency treatment with ARB
- ARBs in drug history lead to infrequent therapy with ACE inhibitors in hypertensive emergencies
- patients receiving ARB in emergency treatment regularly receive ARB in follow-up treatment

Adverse Effects in Therapies

Causative drugs	Etiologies of hypertension	Strategies to treat hypertension
NSAIDs	Water/Na retention and vasodilator suppression through the inhibition of renal prostaglandin production, attenuation of the antihypertensive effects of ACE inhibitors/ARBs/β-blockers/ diuretics	Dose reduction/discontinuation of NSAIDs, dose elevation of an antihypertensive drug that has been administered, Ca channel blockers
Glycyrrhiza (licorice), therapeutic drugs containing glycyrrhizin, drugs for digestive disorders, <i>kampo</i> drugs, supplements, cosmetics	Water/Na retention and K reduction through the enhancement of intrinsic steroid actions related to the prolongation of the half-life of cortisol associated with the inhibition of 11β-hydroxy- lated steroid dehydrogenase	Dose reduction/discontinuation of <i>kampo</i> drugs, aldosterone antagonist
Glucocorticoids	Increases in renin-substrate and erythropoietin productions and the inhibition of NO production may be involved in the mechanism, but it remains to be clarified.	Dose-reduction/discontinuation of glucocorticoids, Ca channel blockers, ACE inhibitors, ARBs, β-blockers, diuretics
Cyclosporine, tacrolimus	Nephrotoxicity, activation of the sympathetic nervous system, inhibition of calcineurin, vascular endothelial cell dysfunction	Ca channel blockers, combination therapy with Ca channel blockers and ACE inhibitors, diuretics

Drugs causing drug-induced hypertension and hypertension treatment

Therapy: According to Guideline

Combination Therapy

Blood pressure reduction	Sub-group	Significance p<0.05
6 h systolic	alltogether	yes
1 h systolic	E	yes

Mono-Therapy

Blood pressure reduction	Sub-group	Significance p<0.05
all systolic	alltogether or E, U, A	none
all diastolic	alltogether or E, U, A	none

Mann-Whitney U Test

Time-Series



Time-Series: Emergency

Acutely treated patients



Time-Series: Urgency

Acutely treated patients



Time-Series: Asymptomatic

Acutely treated patients



Time-Series: Emergency

Acutely treated patients



Time-Series: Urgency

Acutely treated patients



Time-Series: Asymptomatic

Acutely treated patients



Average of Blood Pressures: Treated Versus Non-Treated

All emergency classes

Time	Treatment	None
Initial	200 / 102	194 / 98
1 h	186 / 97	186 / 92
6 h	160 / 87	163 / 80

in mmHg

Textbook Guideline

blood pressure* reduction achieved by 20-30% in 1-2 hours

- the acutely treated study population was not over-treated, one emergency and three urgency, and no other cases were likely loosing systolic blood pressure too fast (not all 6 hour blood pressure values were obtained)
- at least 16 cases showed systolic blood pressure values of more than 160 mmHg at 6 hours

* Dieterle T, Zeller A, Martina B, Battegay E. Der hypertensive Notfall. Praxis. 2001

Average of Blood Pressures: Treated Versus Non-Treated

All emergency classes

	Treatment			
		Initial 0 h	1 h	6 h
Systolic	% above 160	99,0	95,2	55,2
Diastolic	% below 100	40,4	55,4	75,9

in mmHg

	No Treatment			
		Initial 0 h	1 h	6 h
Systolic	% above 160	96,7	92,7	44,4
Diastolic	% below 100	43,3	63,4	88,9

in mmHg

Cardiovascular Complications



Arrhythmias were not considered as primary events in the following canonical correlation. They were only included with secondary events if they led to or were followed by death. **Trends in Hypertension**

Hypertensive Emergency Case Decision and Classification Therapy and Cardiovascular Complications

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Recurrent Hypertensive Crises - Model and Correlation



Perceptrons: Primary Events and Predictors



Perceptrons: Primary Events and Predictors

Classification

Тор 1%		2400 models		
1° Event	94.9% +/-2.5%	1° Event	40.4% +/-26.7%	
Total	98.6% +/-2.5%	Total	91.2% +/-2.7%	
(+/- SD)				

Other 2 selected models

1° Event	100.0% +/-0.0%
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Total 98.4% +/-0.8%

(+/- SD)

Obesity Paradox

Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories

Conclusions and Relevance Relative to normal weight, both obesity (all grades) and grades 2 and 3 obesity were associated with significantly higher all-cause mortality. Grade 1 obesity overall was not associated with higher mortality, and overweight was associated with significantly lower all-cause mortality. The use of predefined standard BMI groupings can facilitate between-study comparisons.

Flegal, K. M., Kit, B. K., Orpana, H., & Graubard, B. I. (2013). Association of allcause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA*, *309*(1), 71–82.

Perceptrons: Primary Events and Predictors



Error Bars: 95% CI

Models of Primary Events: Discriminant Analysis

Agep=0.011Multiple (recurrent) hypertensive crisesp=0.004

in stepwise algorithm

(no prior probabilty) set classified 78.2%

Perceptrons: Primary Events and Predictors



Primary Events: Goodness of Classification

Classification			
	Method Average	Overall %	Primary Events %
1	neural network	91,2 - 98,4	40,4 - 100,0
2	discriminant analysis	64,1 - 84,8	9,1 - 63,3
3	logistic regression	88,0 - 89,1	9,1 - 27,3

n=92

Trends in Hypertension

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Diastolic Blood Pressure - Model and Correlation



Cerebral blood flow (% control)

New Tentative Guideline for Secondary Prevention

Non-Linear Blood Pressure Model with CatReg

Parameter	Importance	P of β (regression)
Age	0.122	0.254
Sex	0.237	0.148
Systolic	0.291	0.034
Diastolic	0.349	0.005

Day 6

 $R^2 = 0.51$

Tentative New Guideline for Secondary Prevention

Blood Pressure of day 6



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Secondary Versus Primary in 2198 neural Networks: Classification of 100% versus <90%



Secondary Versus Primary Event in Categorical Regression



Stratification


Stratification: Risk Ratios

- in patients with hypertensive emergencies *history of cardiovascular events* is associated with *hyperlipidemia* with a RR 3.3 (Cl 1.2-8.9); p=0.017 (Fisher Exact)
- a *history of cardiovascular events* is associated with *antihypertensive pretreatment* with a RR 4.4 (CI 1.2-15.8); p=0.024 (Fisher Exact)
- *secondary cardiovascular events* are associated with *smoking* with a RR 3.2 (CI 0.8-12.6); p=0.1 (Fisher Exact)

this is relative to healthy cohort patients

Stratified Population: Further Predictions

GLM





Model prob. p = 0.005; df 21

Sympathetic Drive

sub-category	
pulmonary	reflexes stemming from cardiopulmonary volume-sensitive receptors
vascular	arterial chemoreceptors altered in obesity or overweight- dependent OSAS
metabolic	leptin, insulin
renal on neuronal	angiotensin II
neuronal on renal	subfornical organ and median preoptic nucleus in part via hypothalamus
nutritional/ behavioral	low sodium intake, alcohol excess

Grassi (2009) Assessment of sympathetic cardiovascular drive in human hypertension. Hypertension Llewellyn et al. (2011) MnPO and SFO drive renal sympathetic nerve activity via a glutamatergic mechanism within the paraventricular nucleus.* Am J Physiol Regul Integr Comp Physiol

Sympathetic Drive



2: Increased secretion of renin, which results in higher angiotensin II levels

* Neuronal on renal signalling

Cardiovascular Progression Model from Strata

3200 models / selection of 1 best predictor



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White Coat Hypertension - Model



Health Ranking: The Physiology According to the



Primary Care: Decision Path



The initial decision was obtained without help: equipment was corresponding to technical standards in the ambulatory

Cardiovascular Risk Factors: Not Known?

- primary cardiovascular outcome (primary event) in this study cohort does not positively correlate with the number of risk factors
- secondary cardiovascular outcome and risk factor association is shown for renal insufficiency and smoking
- neural networks can produce predictions for primary events based on known cardiovascular risk factors
- causal relationships in these neural networks may end upside down
 reasons are discovered in the obesity and low alcohol consumption

(Hyperplane Extraction Procedures may be found in e.g. Saad and Wunsch II, Neural Networks 20 (2007), 78)

Study: Results

- primary cardiovascular events after multiple hypertensive emergencies are elevated to a rate (per year) of **56%**
- multiple hypertensive crises are overwhelmingly important in the neural network prediction
- in models with stratification, white coat hypertension has protective influence relative to hypertension
- in non-linear models, secondary or higher ranked events might be prevented by slightly elevated diastolic blood pressure of 90 mmHg and higher after hypertensive emergencies during 6 days, and systolic values from 130 – 165 mmHg

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