State-of-the-art Treatment of Hypertension

Dietrich Strödter
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UNI-MED Verlag AG, one of the leading medical publishing companies in Germany, presents its highly successful series of scientific textbooks, covering all medical subjects. The authors are specialists in their fields and present the topics precisely, comprehensively, and with the facility of quick reference in mind. The books will be most useful for all doctors who wish to keep up to date with the latest developments in medicine.

Preface and acknowledgements

Hypertension is common and dangerous. One in four to five adults has the disease. Since hypertension causes few or no symptoms at first, only half the hypertensives know they are affected. Only every fourth hypertensive is treated for this condition, but only half of them adequately, i.e., reaching the target blood pressure.

According to the current Global Burden of Disease Study (Lancet 2012), high blood pressure causes the highest health risk! So far the bad news.

In contrast, the good news: Hypertension is not only easy to treat, but good management of blood pressure also reduces cardiovascular morbidity and mortality, thereby improving prognosis.

For clinically successful antihypertensive treatment, not only the lowering of the blood pressure is crucial, but also the selection of antihypertensive drugs used. I.e., based on the same blood pressure reduction, some antihypertensive agents or certain antihypertensive combinations reduce the incidence of serious cardiovascular events more than other antihypertensive agents. These organ-repairing and organ-protective effects – beyond blood pressure reduction –, should be utilised in regard to the patients' comorbidities. Since most hypertensives require a multiple drug combination to achieve blood pressure control, complementary mechanisms of action of the combined drugs are preferred. In such cases, the use of fixed-dose combinations is sensible! The choice of antihypertensive agents is also determined by their tolerance, which in turn affects treatment adherence, the major problem in patients with hypertension. In addition, the blood pressure reduction must be effective over 24 hours, which can be monitored using ambulatory 24-hour blood pressure monitoring (ABPM).

In addition to diagnosis and aetiology, this book also takes into account the pathophysiology of high blood pressure. This includes not only the pathogenesis of end-organ damage, but also coronary, renal and cerebral perfusion. The focus of this book is on antihypertensive therapy in therapeutically significant comorbidities such as diabetes mellitus, metabolic syndrome, nephropathy, coronary heart disease, heart failure and stroke, all under the slogan: What is evidence-based? Also, the current data for renal sympathetic denervation is presented.

Designed as a workbook "from practice, to practice" the extensive data is clearly structured, concise and comprehensively illustrated – all ingredients for a quick reference for the health professional standing before a treatment decision. The international guidelines conclude each chapter.

Our thanks for their support in this work go to UNI-MED publishers.

Lahnau und Jakarta, August 2013

Dietrich Strödter
Frans Santosa

Forewords

I highly anticipate the publication of "State-of-the-art Treatment of Hypertension" by Dr. med. Frans Santosa, SpJP, in collaboration with his mentor Prof. Dr. med. Dietrich Strödter from Germany. This book is truly an international scientific collaboration between Germany and Indonesia.

Dr. med. Frans Santosa, SpJP, has repeatedly published educational books to further the knowledge of colleagues of the profession, especially primary care physicians. Care of patients with hypertension should begin at the primary care level to prevent long-term organ damage.

As a radiologist, it is always with a heavy heart that I diagnose strokes, both haemorragic and ischaemic. The questions as to why they keep happening, why hypertension is not detected early and whether it was treated optimally beg to be asked.

I hope this book will provide instrumental for colleagues throughout the profession, especially in Indonesia, as it covers evidence-based, up-to-date knowledge on the pathophysiology and therapy of hypertension.

Jakarta, August 2013

Dr. Prijo Sidipratomo, SpRad
IDI Committee
Director of the Ethics Medical Board

Cardiovascular diseases are the top cause of mortality in the world for four decades running, not just in the developed countries, but also in developing nations.

Hypertension is one of the triggers of cardiovascular diseases, in addition to other contributors such as diabetes, hyperlipidaemia, smoking, etc., which further accelerate progression to fatal organ damage. Hypertension during pregnancy deserves special attention, as is poses additional risk to the foetus.

This book is based on the current evidence base in hypertension and gives modern pointers to the management of hypertension. I proudly support the publication of this book by Dr. med. Frans Santosa, SpJP, in collaboration with his mentor Prof. Dr. med. Dietrich Strödter from Germany, and hopes it proves useful to all physicians, both general practitioners and specialists, wherever they are, to guide the management and treatment of their patients.

Finally, I hope this book will complete medical libraries of all medical faculties in Indonesia.

Jakarta, August 2013

Prof. Dr. Dr. Farid Anfasa Moeloek, SpOG
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1. Definition and risk of hypertension

1.1. Definition of hypertension

Blood pressure values ≥140/90 mmHg are considered as hypertension. These threshold values have been established on the basis of epidemiological and clinical studies since the risk of cardiovascular complications and mortality markedly increases from these values, and even more so as blood pressure values increase still further.

In view of the variability of blood pressure with fluctuations of up to 60/30 mmHg (situational hypertension, white coat hypertension) at different blood pressure measurements, however, several measurements are needed for a diagnosis. This means that the less the measured blood pressure exceeds the threshold value, the more measurements need to be done. In order to clarify the actual blood pressure relationships, 24-hour blood pressure measurement is a significant help (☞ Chapter 2.9).

A distinction is made between:

- systolic/diastolic hypertension
- isolated systolic hypertension
- isolated diastolic hypertension

Usually, there is systolic/diastolic hypertension, i.e. both blood pressure values are increased.

- Systolic pressure = maximum blood pressure generated during the ejection phase by the left ventricle
- Diastolic blood pressure = blood pressure at the end of the relaxation phase of the left ventricle

The blood pressure is the driving force for blood flow. The parameter that best describes this driving force is not, however, the systolic blood pressure that is elevated in the periphery with major fluctuations, but the mean arterial pressure, which is practically the same in the entire arterial system.

Blood pressure also shows major fluctuations not just during the day but also from one day, month, and time of year to another. The diagnosis of hypertension should therefore always be based on several blood pressure measurements. The lower the blood pressure at the first measurement, the more measurements are therefore needed to confirm the diagnosis.

In their 2007 guidelines, the ESH and ESC recommend that the diagnosis of hypertension be based on at least 2 measurements at 2-3 visits. However, in severe hypertension, one measurement may already be enough to make the diagnosis (1).

1.2. Pathophysiology of hypertension

In terms of pathophysiology, hypertension is the result of

- an increased cardiac output (CO),
- elevated peripheral resistance (TPR)
- or both factors.

Hypertension usually begins initially as hypertension due to increased CO, which then transitions into hypertension due to elevated TPR, which may be associated with normalisation of CO and ultimately even a reduction in CO.

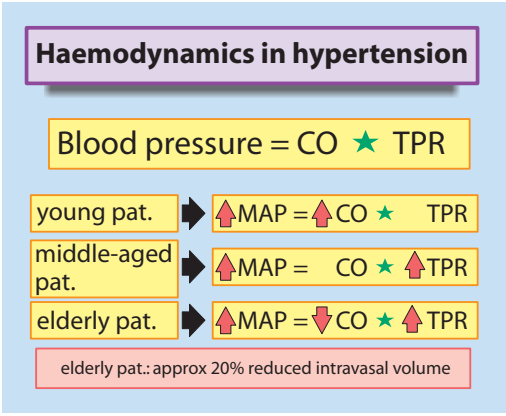


Figure 1.1: Haemodynamics in hypertension depending on age.

1.3. Severity of hypertension

In 2007, the ESH/ESC (1) incorporated the definition of grades of severity of hypertension and normotension based on the classification of the 6th Joint National Conference (JNC) (2) and the WHO/ISH (3). However, in these definitions

- the designation of hypertension as mild, moderate and severe was not used but instead the more neutral terms grade 1, 2 and 3 were used,

in order to avoid confusion with regard to the cardiovascular risk. The term mild hypertension suggests in fact a low cardiovascular risk, which can, however, be equivalent to the risk of severe hypertension if other risk factors are present.

The target blood pressure in patients with a high risk was set at <130/<80 mmHg in these guidelines. However, evidence for these low target levels has come from prospective studies only to an incomplete extent or not at all but these values were accepted only on the basis of retrospective analyses.

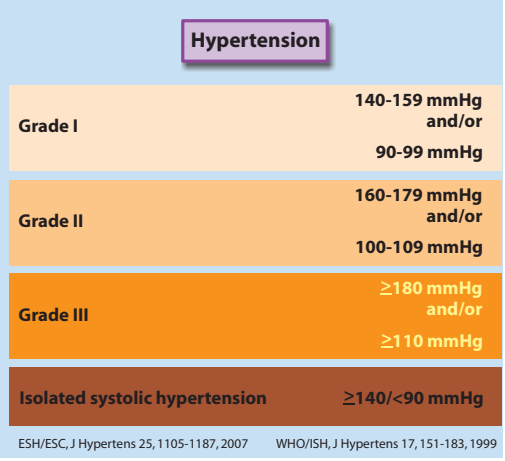


Figure 1.2: Classification of the severity of hypertension according to the 2007 ESH/ESC guidelines. If the SBP and DBP are in different categories, the higher blood pressure determines the degree of severity that the patient should be classified as having.

A distinction is also made between benign and malignant hypertension according to the clinical course. The term malignant hypertension describes a syndrome with a massive rise in blood pressure (usually >140 mmHg diastolic) and evidence of considerable damage to retinal vessels such as haemorrhage, exudates and papilloedema. However, there is no uniform definition with the result that severe progressive forms of hypertension are also occasionally referred to by this name. On the other hand, there is also an overlap between resistant (☞ Chapters 17.8 and 19) and malignant hypertension. The most dangerous situation in this context is hypertensive encephalopathy. If untreated, the mortality with this form is 50% in 1 year (1).

The term labile hypertension describes the situation where alongside hypertensive blood pressure readings normal blood pressure levels are also measured. This term has now become redundant since the advent of 24-hour blood pressure recording.

1.4. Normotension vs. hypotension

Normal blood pressures are considered to be <140/<90 mmHg. But again, according to the ESH/ESC, a distinction is made between

- the optimal (<120/<80 mmHg),
- normal (120-129/80-84 mmHg)
- and high-normal range (130-139/85-89 mmHg).

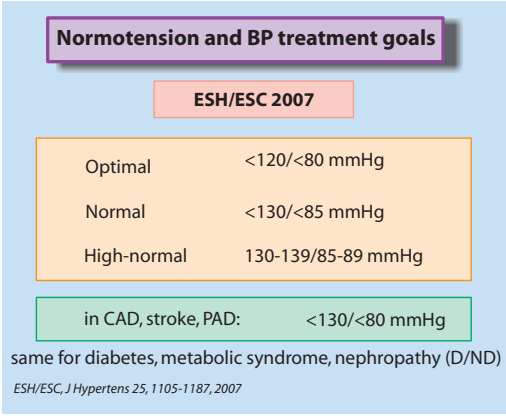


Figure 1.3: Normal blood pressure and blood pressure treatment goals today (ESH/ESC 2007).

The cardiovascular risk varies even in the normotensive blood pressure range.

A lower limit for optimal blood pressure values has not been defined.

Chronic arterial hypotension is also unclearly defined. Systolic blood pressure values <100 mmHg are generally referred to as hypotension. But this only becomes clinically relevant if symptoms of decreased cerebral perfusion appear.

1.5. Prehypertension

The US Joint National Committee Guidelines (JNC 7) have introduced the term prehypertension (= blood pressure 120-139/80-89 mmHg), which thus covers the normal and high-normal range (4). The reason for this is the observation in the Framingham study that these patients develop hypertension more frequently than individuals with blood pressure values <120/80 mmHg (5, 6).

Prehypertension =
blood pressure 120-139/80-89 mmHg

In 2007, the ESC/ESH did not go along with this new terminology, which has its opponents even in the USA.

The reasons for this are:

- Individuals with high-normal blood pressure more frequently develop hypertension than individuals with normal blood pressure (7). It is therefore not reasonable to include both groups in the one group.
- In view of the ominous diagnosis hypertension, the diagnosis of prehypertension could lead to unnecessary anxiety and excessive medical consultations and investigations
- Even more important: This category encompasses a non-homogeneous population with extremes consisting of individuals who do not require any treatment (elderly individuals with blood pressure of 120/80 mmHg), but on other hand also individuals with a high or a very high risk profile (e.g. after a stroke or those with diabetes mellitus) in whom antihypertensive therapy would be entirely reasonable.

But this also makes it clear that the border between hypertension and normotension is flexible depending on the risk profile.

1.6. Risk in hypertension

The cardiovascular risk in hypertension is therefore not just related to how high the blood pressure is but to the overall risk which is determined by

- other risk factors
- target-organ damage
- or associated diseases.

Among the concomitant conditions, the metabolic syndrome was added for the first time in 2007.

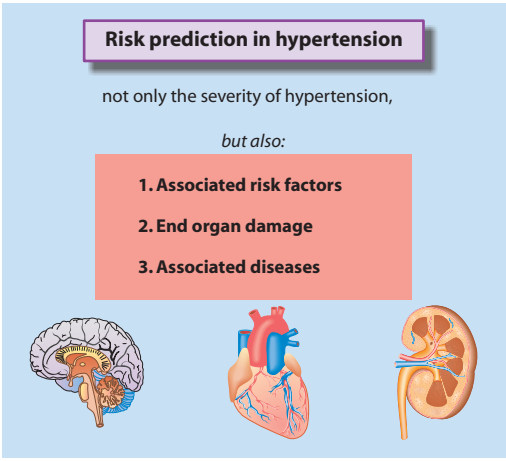


Figure 1.4: Predictors of risk in hypertension.

Hypertension is a risk factor for many cardiovascular complications such as

- (direct consequence) haemorrhagic stroke, left ventricular hypertrophy (LVH), atrial fibrillation, heart failure, nephrosclerosis, aortic dissection or
- (indirect consequence) atherosclerosis of the vessels such as coronary artery disease (CAD), peripheral arterial disease (PAD), ischaemic stroke.

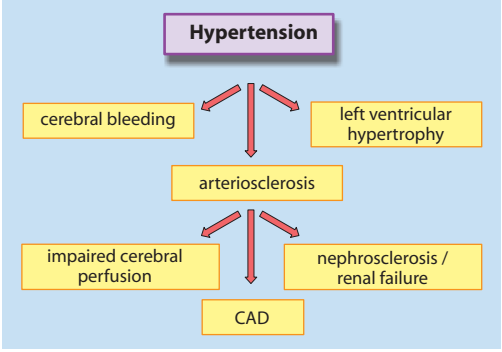


Figure 1.5: Hypertension: direct and indirect consequences.

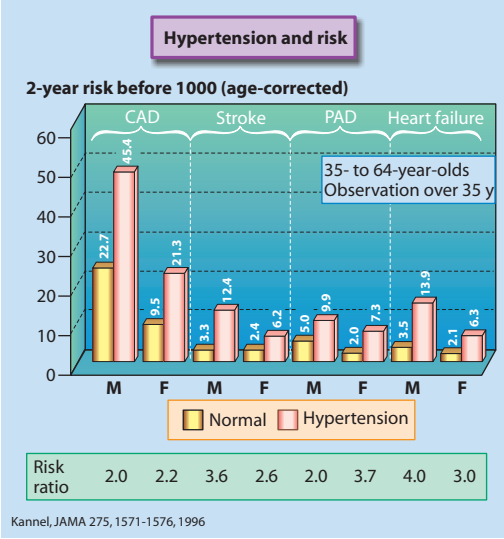


Figure 1.6: Hypertension as a risk factor for complications. M = males, F = females.

1.6.1. Risk stratification

Risk stratification is therefore based on various parameters, starting from the blood pressure value, through the number of risk factors, to established cardiovascular or renal disease. Among risk factors, ≥3 correspond to diabetes mellitus, metabolic syndrome or proven target-organ damage (1).

This highlights that knowledge of the blood pressure level alone is not sufficient for risk stratification or for deciding on whether treatment is indicated, expedient concomitant therapy or antihypertensives to be chosen.

Prior to treatment, an extensive investigation programme is therefore needed (except in a hypertensive crisis).

Although the cardiovascular risk in hypertension grade I is low if there are no other risk factors, diabetics with this grade, for example, already belong to the high-risk population. They have the same risk as hypertensive individuals with blood pressure values ≥180/110 mmHg. Diabetics with diabetic nephropathy have a very high cardiovascular risk, i.e. an even higher risk.

Definition of risk (3):

- Low risk: <15% cardiovascular events in 10 years
- Moderate risk: 15-20% cardiovascular events in 10 years
- High risk: 20-30% cardiovascular events in 10 years
- Very high risk: >30% cardiovascular events in 10 years

Risk in hypertension

Other RFs	140-159/ 85-89	160-179/ 100-109	≥180/ ≥110 mmHg
none	low	moderate	high
1 to 2 RFs	moderate	moderate	very high
≥3 RF, MS diabetes, end-org. dam.	high	high	very high
clinical end organ damage	very high	very high	very high

ESH/ESC, J Hypertens 25, 1105-1187, 2007

Figure 1.7: Risk stratification in hypertension depending on risk factors, target-organ damage and clinical sequelae.

1.6.2. Risk factors, target-organ damage and associated disorders

Only knowledge about and consideration of all these factors leads to a successful prevention approach.

The risk factors, target-organ damage and associated disorders that underlie risk stratification are summarised in Figure 2.7. Thus, importance is attached to the recognition of subclinical hypertension-induced target-organ damage.

But the subclinical forms of target-organ damage also include

- an ankle/brachial blood pressure index <9 (ABI),
- an estimated GFR <60 ml/min/1.73 m² (Cockroft Gault formula)
- or creatinine clearance <60 ml/min (MDRD formula).

The test for microalbuminuria (30-300 mg/24 h) has been included in the basic diagnostic work-up.

Proteinuria in the context of an associated disorder is defined as >300 mg/24 h (1).

However, determination of the pulse wave velocity (>12 m/sec) and intima-media thickness (>0.9 mm) have also been included.

LVH

- is assumed if the relative wall thickness (=2 × wall thickness/LVEDD) ≥0.42
- or if there is an LV mass index (LVMI) ≥125 g/m² in males, ≥110 g/m² in females
- or a Sokolow-Lyon index >3.8 mm or a Cornell QRS product >2440 mm × msec = >240 mV × msec (Cornell index = R in aVL plus S in V_3).

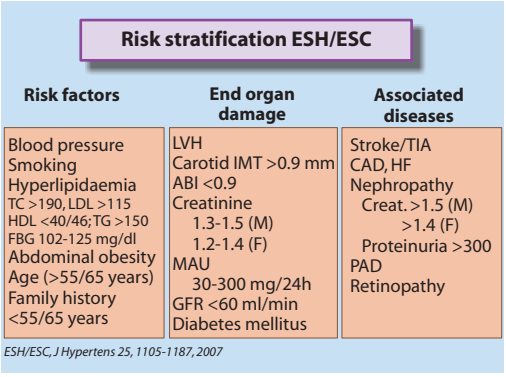


Figure 1.8: Risk factors, target-organ damage and associated disorders that are taken into consideration. For the ages shown in this figure, the 1st value in each case relates to males, and the 2nd value to females.

All factors that influence the prognosis in hypertension have been confirmed by the 2012 ESC guidelines. Impaired fasting glucose (IFG) is stated as being fasting plasma glucose of 100-125 mg/dl (which converts to: 5.5-6.9 mmol/l) (10).

Impaired fasting glucose is considered as a risk factor.

Diabetes mellitus (fasting plasma glucose ≥7 mmol/l or ≥126 mg/dl) on repeated measurements or a plasma glucose value ≥11 mmol/l or ≥198 mg/dl after an oral glucose tolerance test, but also the metabolic syndrome (newly added in 2007) are equivalent to ≥3 risk factors according to their importance.

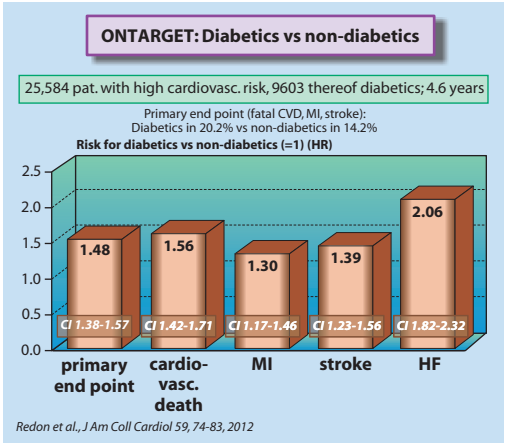
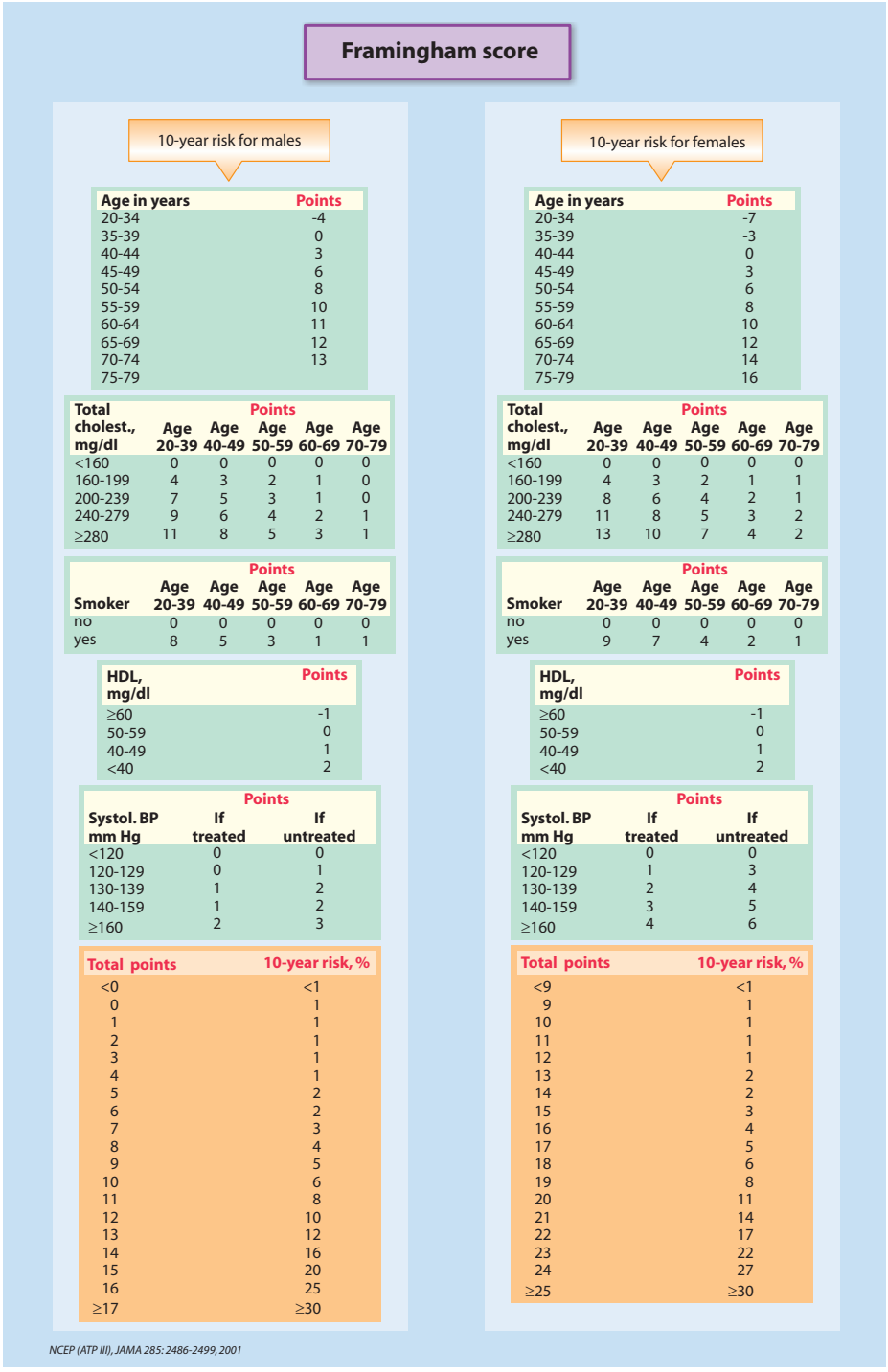


Figure 1.9: Risk of diabetics vs. non-diabetics with underlying vascular disease and comparable blood pressure values, results of a post-hoc analysis of the ONTARGET study (HF=heart failure) (8).

1.6.3. Risk scores

The risk (which is very much dependent on ethnicity, thus risk decreases in Europe, for example, from the north to the south) can be read from risk scores depending on systolic blood pressure and further risk factors, of which 3 scores are shown:

- The Framingham score (9)
- The ESC risk score (10)
- The Procam score for German males and females (11)



Framingham score

10-year risk for males

Age in years	Points
20-34	-4
35-39	0
40-44	3
45-49	6
50-54	8
55-59	10
60-64	11
65-69	12
70-74	13
75-79	

Total cholest., mg/dl	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

	Points				
Smoker	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
no	0	0	0	0	0
yes	8	5	3	1	1

HDL, mg/dl	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systol. BP mm Hg	Points	
	If treated	If untreated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Total points	10-year risk, %
<0	<1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥17	≥30

10-year risk for females

Age in years	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total cholest., mg/dl	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

	Points				
Smoker	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
no	0	0	0	0	0
yes	9	7	4	2	1

HDL, mg/dl	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systol. BP mm Hg	Points	
	If treated	If untreated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Total points	10-year risk, %
<9	<1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥30

NCEP (ATP III), JAMA 285: 2486-2499, 2001

Figure 1.10: The Framingham risk score.

Risk factors	Test results	Points

LDL cholesterol (mg/dl)

≤100	= 0 points	151 - 155	= 11 points		
101 - 105	= 1 point	156 - 160	= 12 points		
106 - 110	= 2 points	161 - 165	= 13 points		
111 - 115	= 3 points	166 - 170	= 14 points		
116 - 120	= 4 points	171 - 175	= 15 points		
121 - 125	= 5 points	176 - 180	= 16 points		
126 - 130	= 6 points	181 - 185	= 17 points		
131 - 135	= 7 points	186 - 190	= 18 points		
136 - 140	= 8 points	191 - 195	= 19 points		
141 - 145	= 9 points	196 - 200	= 20 points	mg/dl	
146 - 150	= 10 points	>200	= 21 points		

Systolic blood pressure (mmHg)

<110	= 0 points	150 - 159	= 5 points		
110 - 119	= 1 point	160 - 169	= 6 points		
106 - 129	= 2 points	170 - 179	= 7 points		
111 - 139	= 3 points	≥180	= 8 points	mmHg	
140 - 149	= 4 points				

Fasting blood glucose ≥120 mg/dl or diagnosis of diabetes mellitus

0 points	no ☐		
9 points	yes (males) ☐		
11 points	yes (females) ☐		

HDL cholesterol (mg/dl)

≤35	= 11 points	46 - 47	= 5 points		
36 - 37	= 10 points	48 - 49	= 4 points		
38 - 39	= 9 points	50 - 51	= 3 points		
40 - 41	= 8 points	52 - 53	= 2 points		
42 - 43	= 7 points	54 - 55	= 1 point		
44 - 45	= 6 points	>55	= 0 points	mg/dl	

Triglycerides (mg/dl)

<100	0 points	150 - 199	= 3 points		
100 - 149	2 points	≥200	= 4 points	mg/dl	

Current cigarette consumption

0 points	no ☐		
12 points	yes ☐		

Positive family history:
MI in one parent or sibling before the age of 60 years.

0 points	no ☐		
5 points	yes ☐		

Total points:	
see 2nd step: 10-year risk for myocardial incarktion	%

Figure 1.11a: The PROCAM score (Weibull model) for estimation of the risk of acute coronary events, now for males and females. First step for risk stratification; determination of the points depending on the severity of the relevant risk factors.

green = low risk (<10%)	yellow = intermediate risk (10-20%)	red = high risk (>20%)

Males — Total points			Age (years)	Females — Total points		
≤70			20-26	≤72		
≤69	≥70		27	≤72		
≤67	≥68		28	≤72		
≤64	≥65		29	≤72		
≤62	≥63		30	≤72		
≤60	61-69	≥70	31	≤72		
≤58	59-67	≥68	32	≤72		
≤56	57-65	≥66	33	≤72		
≤54	55-63	≥64	34	≤72		
≤52	53-62	≥63	35	≤72		
≤61	52-60	≥61	36	≤72		
≤49	50-58	≥59	37	≤70	≥71	
≤48	49-57	≥58	38	≤68	≥69	
≤46	47-55	≥56	39	≤66	≥67	
≤45	46-54	≥55	40	≤64	≥65	
≤43	44-53	≥54	41	≤62	≥63	
≤42	43-51	≥52	42	≤60	61-69	≥70
≤41	42-50	≥51	43	≤58	59-67	≥68
≤39	40-49	≥50	44	≤55	57-65	≥66
≤38	39-48	≥49	45	≤55	56-64	≥65
≤37	38-46	≥47	46	≤53	54-62	≥63
≤36	37-45	≥46	47	≤51	52-60	≥61
≤35	36-44	≥45	48	≤50	51-59	≥60
≤34	35-43	≥44	49	≤48	49-57	≥58
≤33	34-42	≥43	50	≤47	48-55	≥57
≤32	33-41	≥42	51	≤45	46-54	≥55
≤31	32-40	≥41	52	≤44	45-53	≥54
≤30	31-39	≥40	53	≤42	43-51	≥52
≤29	30-38	≥39	54	≤41	42-50	≥51
≤28	29-37	≥38	55	≤40	41-49	≥50
≤27	28-37	≥38	56	≤39	40-47	≥48
≤26	27-36	≥37	57	≤37	38-46	≥47
≤26	27-35	≥36	58	≤36	37-45	≥46
≤25	26-34	≥35	59	≤35	36-44	≥45
≤24	25-33	≥34	60	≤34	35-42	≥43
≤23	24-33	≥34	61	≤32	33-41	≥42
≤22	23-32	≥33	62	≤31	32-40	≥41
≤22	23-31	≥32	63	≤30	31-33	≥40
≤21	22-30	≥31	64	≤29	30-38	≥39
≤20	21-30	≥31	65	≤28	29-37	≥38
≤20	21-29	≥30	66	≤27	28-35	≥37
≤19	20-28	≥29	67	≤26	27-35	≥36
≤18	19-28	≥29	68	≤25	26-34	≥35
≤17	18-27	≥28	69	≤24	25-33	≥34
≤17	18-26	≥27	70	≤23	24-32	≥33
≤16	17-26	≥27	71	≤22	23-31	≥32
≤16	17-25	≥26	72	≤21	22-30	≥31
≤15	16-24	≥25	43	≤20	21-29	≥30
≤14	15-24	≥25	74	≤19	20-28	≥29
≤14	15-23	≥24	75	≤19	20-27	≥28

Figure 1.11b: The coronary risk depending on the risk factor score (☞ Figure 1.12), age and sex. Second step for risk stratification: starting from the patient's age in the sex-related table, determine the degree of risk.

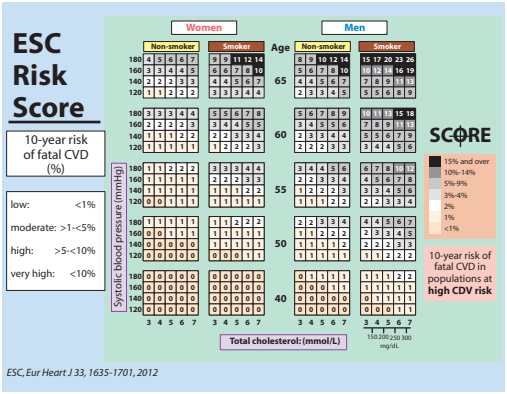


Figure 1.12a: The ESC risk score for males and females with a low risk (Western Europe). For East Europeans with their higher risk, there is a separate score.

The ESC risk score relates to the risk of fatal cardiovascular disease and is thus 3 times smaller than scores that cover fatal and non-fatal cardiovascular events. Only in the elderly does this factor of 3 become somewhat lower as more cardiovascular events are fatal in this age group (10).

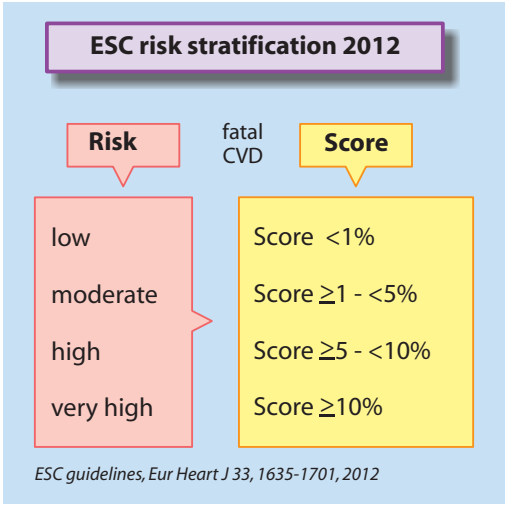


Figure 1.12b: Definitions of severity in the ESC risk stratification.

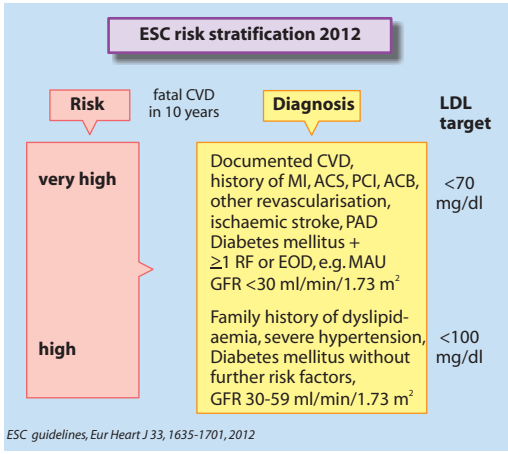


Figure 1.12c: Diseases with high and very high risk in the ESC score risk stratification.

1.6.4. Hypertensive individuals with high and very high risk

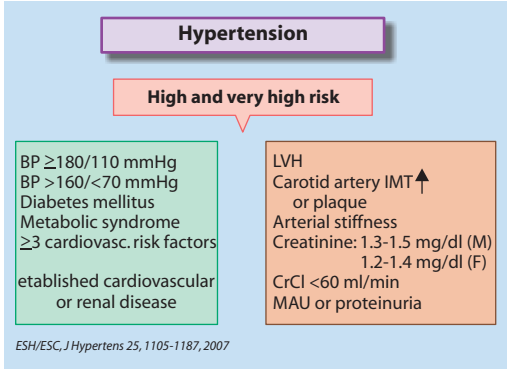


Figure 1.13: Hypertensive individuals with high and very high risk according to the 2007 ESH/ESC (1).

The ESH/ESC define the established cardiovascular disorders as:

- cerebrovascular: ischaemic stroke, cerebral haemorrhage, TIA
- cardiac: myocardial infarction, angina, coronary revascularisation, heart failure
- renal: diabetic nephropathy, renal failure (creatinine >1.5 mg/dl (M), >1.4 mg/dl (F), proteinuria (>300 mg/24 h)
- arterial: PAD
- retinal: advanced retinopathy with haemorrhage or exudates, papilloedema

Approximately 14% of all deaths worldwide are due to elevated blood pressure, according to estimates. The treatment of hypertension is therefore of fundamental importance (12).

1.7. Risk in normotension

There are differences in prognosis even in the normotensive range of the current definition.

In the high-normal range, the cardiovascular risk is much higher than in the normal or optimal blood pressure range. In this context, males always have a higher risk than females, for the same blood pressure values (7). Females evidently tolerate hypertension better than males. At the same hypertensive blood pressure values, they also always have a lower morbidity and mortality rate according to another study (13).

The same phenomenon also applies in relation to cholesterol levels. Male sex is a risk factor which cannot be influenced (14)!

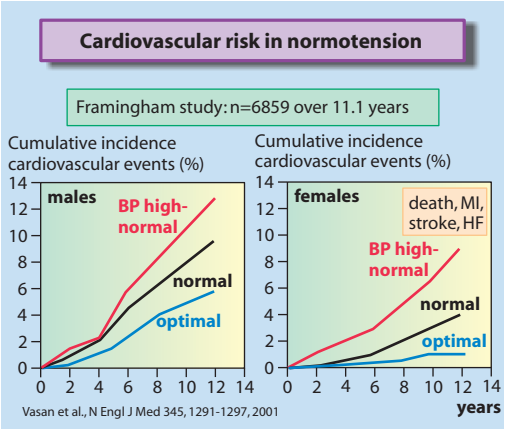


Figure 1.14: Prognosis in optimal, normal and high-normal blood pressure values. MI = myocardial infarction, HF= Heart failure.

Thus, antihypertensive therapy is indicated even in patients with high and very high risk and blood pressure values in the upper range of normal (according to the 2007 ESH/ESC guidelines), with the target blood pressure <130/80 mmHg.

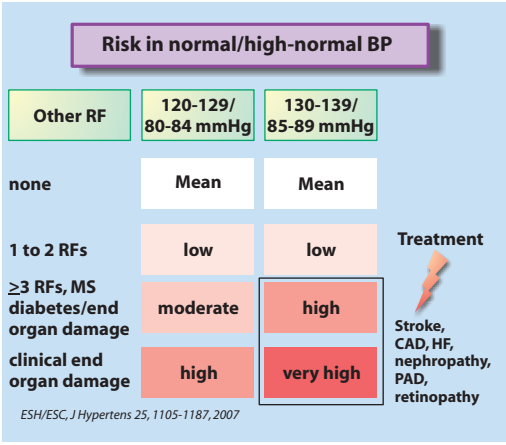


Figure 1.15: Risk in normal and high-normal blood pressure depending on risk factors and associated disorders.

The lowest risk in relation to mortality from CAD and stroke is, according to a meta-analysis of 61 studies (n=958,074, 40- to 89-year-olds), at blood pressure values ≤115/75 mmHg, independently of the respective decade of age. The analysis also shows the higher risk of age that is independent of blood pressure and cannot be influenced. Young hypertensives have the same risk as normotensives who are 2 decades older. Or, to put it another way: for the same baseline blood pressure values, elderly individuals have a much higher risk. This applies both to systolic and diastolic blood pressure. The study shows, however, that even elderly patients benefit from blood pressure lowering (15).

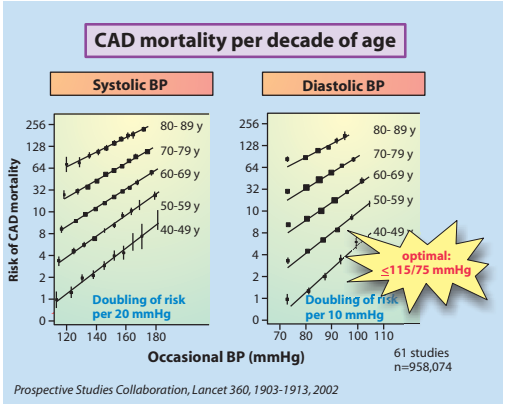


Figure 1.16: CAD mortality depending on the systolic and diastolic blood pressure (the same relationship is found for stroke-related mortality).

1.8. Isolated systolic hypertension (ISH)

During systole, the aorta acts as a blood reservoir in accordance with its windkessel function. About 40% of the stroke volume is initially stored here in order to then continue to flow during diastole. If the elastic vessels close to the heart were completely rigid, the blood pressure during systolic would risk to very high values, but in diastole they would fall to hydrostatic pressure. The reason for this is the abolished windkessel function, as a result of which no portion of the stroke volume could be made available centrally for diastole.

- Isolated systolic hypertension (≥140/<90 mm Hg, formerly ≥160/<90 mmHg) is therefore burned out systolic/diastolic hypertension (Bulpitt) and is accompanied by the highest risk.

It is the result of generalised atherosclerosis with a reduction in the compliance of the aorta and afferent vessels. The increased pulse wave reflection (elevated systolic blood pressure) and abolished windkessel function (lowered diastolic pressure) are responsible for the large blood pressure amplitude. Isolated systolic hypertension is the typical form of hypertension in the elderly, but also occurs disproportionately often in diabetics (16).

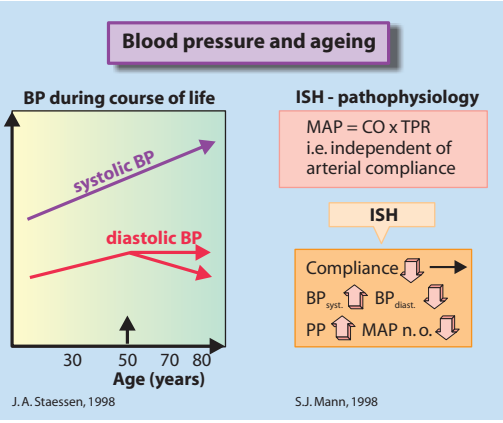


Figure 1.17: Blood pressure over the course of life. ISH = isolated systolic hypertension.

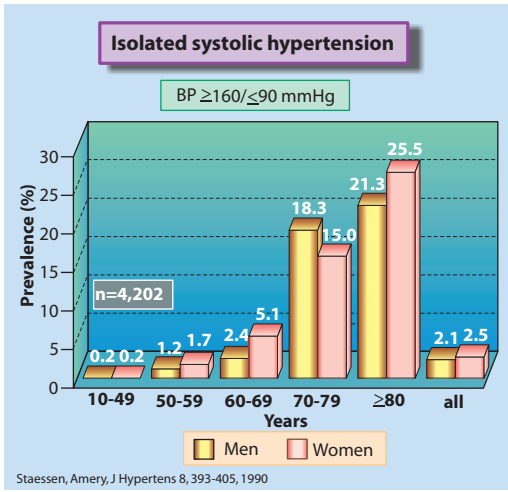


Figure 1.18: The prevalence of isolated systolic hypertension.

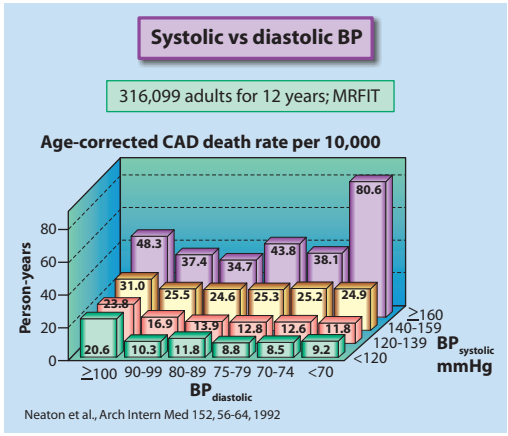


Figure 1.19: The prognosis in isolated systolic hypertension. Results of the MRFIT study in relation to CAD-related death depending on the systolic vs. diastolic blood pressure. The result is comparable as regards stroke.

What happens first, stiffening of the vessels or hypertension? According to the results of the Framingham Offspring Cohort Study (n=1759, 2 examinations 7 years apart, measurement of blood pressure, pulse wave velocity and augmentation index), the increased stiffness is the precursor to, and not the result of, high blood pressure. Whereas the tonometric parameters in the first period showed increased stiffness, there was a significant association with the incidence of hypertensive blood pressure values in the second period. Con-