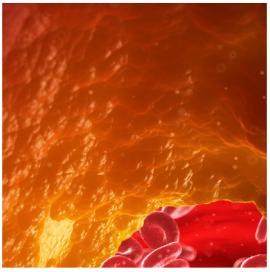
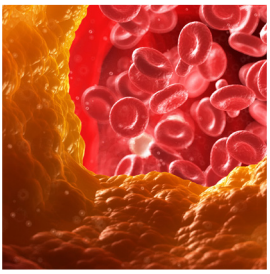
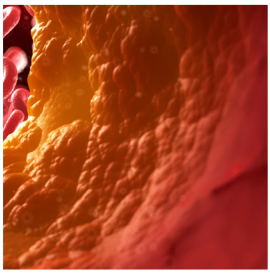
Scientific Highlights of the 2019 EMEA Cardiometabolic Workshop







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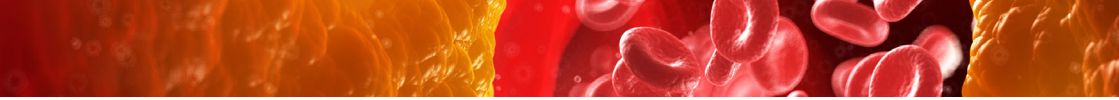

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INTRODUCTION

As a global population, body weight has been gradually increasing year-on-year, until we have reached the point where nearly one in every 3 people are either over-weight or obese. This weight gain is not without consequences, as obesity is a complex and multifactorial disease, and its impact is glaringly apparent in the health of patients in every day clinical practice, an impact that transcends medical specialties. This workshop aims to interweave best practice from the fields of diabetes, hypertension and thyroid disorder, using material directly from published clinical guidelines in each area, to create a full and up-to-date picture of cardiometabolic disease today, its epidemiology, impact, and treatment options.

CHAIR

Ahmed AK Hassoun (United Arab Emirates)

Chairman of Research & Medical Education
Dubai Diabetes Center, DHA
Clinical Professor
Dubai Medical University
Dubai, United Arab Emirates

L1

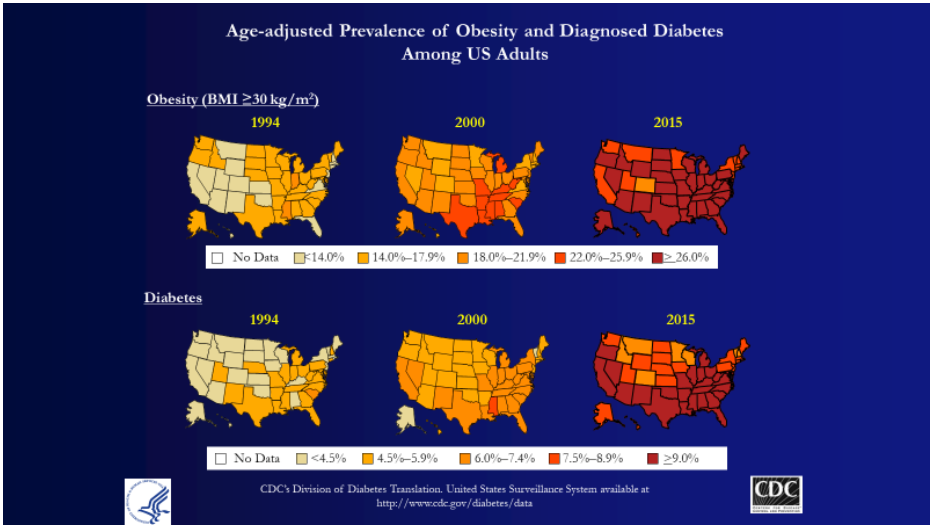
The diabesity pandemic: Why and how to manage prediabetes

Antonio Ceriello

IRCCS Multimedica
Milan, Italy

Professor Ceriello (Milan, Italy and Barcelona, Spain) opened his presentation with a series of images depicting the change in prevalence of both obesity and diagnosed cases of diabetes over time from 1994 until 2015 in the USA. As well as emphasizing the rise in obesity, these images clearly show that the prevalence of diabetes has increased in line with the prevalence of obesity (Figure 1).

Figure 1: Images from 1994, 2000, and 2015 showing the clear increase in both obesity and diagnosed type 2 diabetes mellitus in the US.[1]



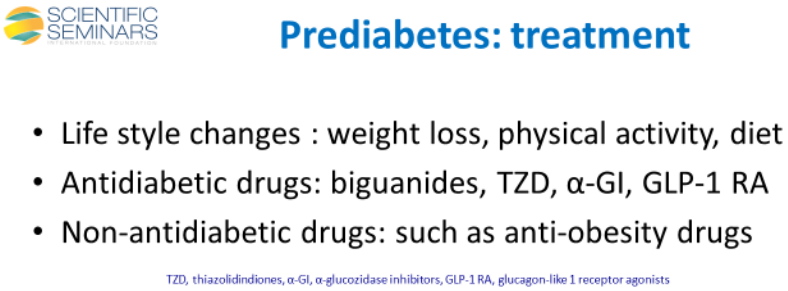
Type 2 diabetes mellitus (T2DM) represents an enormous economic and health burden, and its steep rise in prevalence is apparent globally, including China,

which has seen one of the most dramatic rises in the prevalence of diabetes and diabetic complications anywhere in the world.[2]

As well as the link between obesity and T2DM, there is also a direct and very strong relationship between markers of both obesity and central adiposity with cardiovascular (CV) risk. Pre-diabetes, where blood glucose levels are above normal, but not high enough for a diagnosis of diabetes, still confers increased risk of CV disease and death, and increases the risk of developing T2DM. Pre-diabetes is a reversible cardio-metabolic risk factor, and there are strategies available to prevent progression to overt T2DM, all of which involve weight loss. However, most people with pre-diabetes are unaware that they have it.

A study published in 2016 highlighted the relevance of 1-hour post-load glucose values for estimating risk of developing T2DM and subsequent mortality.[3] This study, which followed >2000 individuals over 33 years found that a 1-h glucose test value >8.6 mmol/l was predictive of mortality even when the 2-h level was <7.8 mmol/l. When the 2-h level is in the impaired glucose tolerance range, the risk of mortality rises significantly, independent of the 1-h value. Thus, individuals at risk for developing diabetes can be identified earlier using the 1-h threshold value of 8.6 mmol/l. Once identified, pre-diabetes can be reversed, reducing morbidity and economic burden, Figure 2.

Figure 2: Treatment options available to reverse pre-diabetes and prevent overt diabetes



The Diabetes Prevention Program[4] investigated >3200 adults of various ethnicities at high risk of developing diabetes and showed that lifestyle intervention and metformin are both able to decrease the risk of T2DM, with lifestyle intervention producing the most effect. However, the implementation of a healthy lifestyle and long-term compliance with the changes may be difficult in real life.

L2

Is type 2 diabetes really reversible?

Mike Lean

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People with T2DM have a reduced life expectancy (by 6 years, despite guidelines and drugs to lower glucose/HbA1c, low-density lipoprotein (LDL) and blood pressure [BP]) and reduced quality of life within that shortened time frame, according to **Professor Lean** (Glasgow, Scotland), Figure 3.

Figure 3: The reality of life for patients with T2DM

As discussed in the previous presentation, and reiterated here - the main driver of T2DM is weight gain. A 15% weight loss results, not only in diabetes remission, but also in normalization of life expectancy.
To explore this concept further, Professor Lean and colleagues undertook the DiRECT study, which enrolled obese patients with T2DM which was controlled

by diet and any combination of glucose-lowering medications, except insulin.[5] Patients were cared for in one of 49 General Practices, 26 of which served as controls, offering patients usual diabetes care to best practice guidelines. The remaining 23 were 'intervention' Practices, where patients were offered a structured weight management program 'Counterweight plus'. At the start of the intervention, patients stopped all hypertensive and anti-diabetic medications, and for 3 to 5 months committed to a low-calorie total diet replacement, using nutritionally complete soups and shakes, which were provided for participants. Target weight loss during this phase was 15 kg for every participant. At the end of this phase, food was gradually re-introduced, with a focus on energy balance, managing food choices and encouraging physical activity. Patients were supported for the remainder of the 2-year study, with emphasis on maintaining the weight loss achieved during the first 3 to 5 months.

The intervention group showed a significant reduction in body weight (mean: -14.5 kg) sustained for 4 months. At 12 months, 68/149 (46%) of intervention participants achieved diabetes remission (HbA1c <6.5%), which fell to 53/149 (36%) at 24 months. This compares with 5 and 6 control group participants at 12 and 24 months respectively achieving diabetes remission. The percentage of patients in diabetic remission was proportional to their weight loss, and was accompanied by a fall in their CV risk, a reduction in reported serious adverse events (diabetes-related CV events and cancers), and an increase in patient-reported quality of life. Remission was also associated with beta-cell remission (capacity normalized slowly over the course of 12 months), supporting a real remission of T2DM.

The annual cost of the intervention study was ~1/3 of the average cost of treating a patient with diabetes for 1 year.

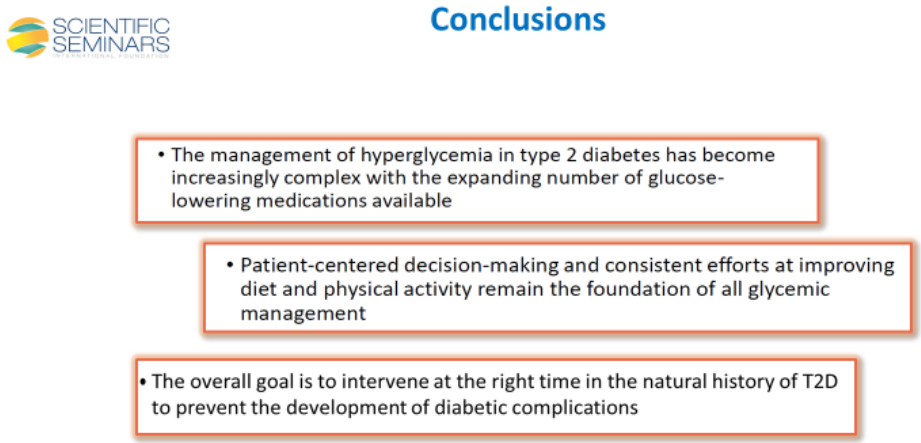
L3

ADA/EASD consensus report for diabetes management: An update

Paolo Pozzilli
University Campus Bio-Medico (UCBM)
Rome, Italy

The new ADA/EASD guidelines[6] put the patient at the center of diabetes treatment, using patient-specific factors, such as disease duration, patient life-expectancy, co-morbidities and patient preference to guide glycemic targets, according to **Professor Pozzilli** (Rome, Italy and London, UK).
Metformin remains the first-line treatment for people with T2DM. In the case of metformin treatment failure, second-line therapy should be chosen on the basis of CV risk. If patients have a positive history of CV disease, a glucagon-like peptide-1 receptor agonist (GLP1 RA) or a sodium-glucose cotransporter-2 inhibitor (SGLT2i) should be used – the SGLT2i option being preferred in patients with a low ejection fraction or chronic kidney disease.

Figure 4: The goals of diabetes management



L4

Hypothyroidism and pregnancy

Bernadette Biondi
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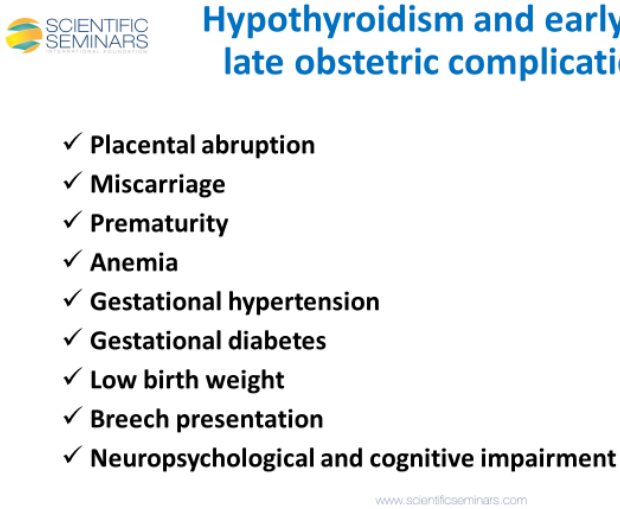
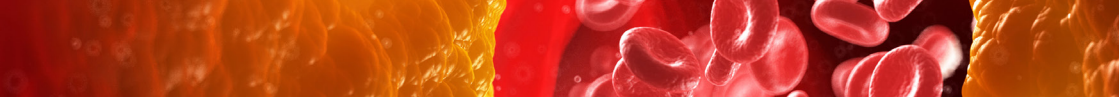
Endocrine Division
University of Naples Federico II
Naples, Italy

The action of human chorionic gonadotropin, estrogens, and placental hormones are responsible for several changes in thyroid pathophysiology during pregnancy, explained **Professor Biondi** (Naples, Italy). These include an increase in thyroid volume, an increase in iodine uptake and an increase in T4 and T3 production.
The American Thyroid Association (ATA) recommends that thyroid-stimulating hormone (TSH) levels should be kept in trimester-specific ranges in pregnant and post-partum patients with thyroid disorders.[7] If population-specific ranges are not available, the ATA recommends an upper reference limit of ~4.0 mU/l. Hypothyroidism in pregnancy can be a serious condition leading to several early and late obstetric complications, Figure 5.

Figure 5: Obstetric complications associated with hypothyroidism during pregnancy





A 2019 Finnish publication[8] has reiterated these findings, but found that consistent LT4 use reduced many of the risks. A systematic data review and meta-analysis[9] looking at pre-term birth incidence in mothers with thyroid function test abnormalities or thyroid autoimmunity found that subclinical hypothyroidism, isolated hypothyroxinemia, and TPO antibody positivity were associated with higher risk of preterm birth. Thus, the ATA guidelines[7] for subclinical hypothyroidism in pregnancy recommend levothyroxine therapy for TPO antibody-positive women with a TSH level above the pregnancy-specific reference range, and for TPO antibody negative women with a TSH >10.0 mU/l. Levothyroxine therapy may also be considered, with weaker evidence, for TPO-antibody-positive women with TSH concentrations >2.5 mU/l and below the upper limit of the pregnancy reference range, and for TPO-antibody negative women with TSH concentrations greater that the pregnancy-specific range and <10.0 mU/l.

In general, TSH should be measured in all pregnant women at high risk for thyroid dysfunction as early as possible in the pregnancy. LT4 is the recommended treatment in pregnant women needing thyroid hormones. T3 and desiccated thyroid should not be used in pregnancy.[7]

L5

Thyroid hormones and cardiovascular disease

Salman Razvi
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International Centre for Life
Newcastle upon Tyne, United Kingdom

Professor Razvi (Newcastle upon Tyne, UK) began his presentation by discussing the observational studies that have established subclinical hypothyroidism as a risk factor for CV disease. These studies have reported higher incidences of myocardial infarction or coronary heart disease in those with subclinical hypothyroidism versus euthyroid individuals. Indeed, coronary heart disease events and mortality both increase proportionally with increasing TSH levels, and especially in those with a TSH concentration ≥10 mIU/l.[10]

Thyroid hormones directly regulate cardiomyocyte activity, which explains the impact of thyroid function on CV homeostasis**.** In cardiac patients, a mildly altered thyroid status is associated with an increased risk of mortality,[11] while treating subclinical hypothyroidism with levothyroxine is associated with fewer ischemic heart disease events in younger individuals, but not in older people.[12] Thus, older individuals with slightly raised TSH levels should be monitored and treatment considered when serum TSH levels rise above 10 mU/l.

L6

Use of beta-blockers in patients with hypertension and diabetes

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Milan, Italy

There is a strong relationship between blood pressure (BP) values and the risk of altered glucose metabolism, explained **Professor Grassi** (Milan, Italy), and the presence of diabetes mellitus in patients with hypertension significantly increases their risk of CV disease. It is increasingly recognized that overactivity of the sympathetic nervous system, reflected by an elevated heart rate, is common in hypertension and contributes to the initiation and evolution of the disease, particularly in patients with diabetes. Patients with hypertension who obtain good control of their heart rate may have additional CV benefits besides those obtained by lowering BP values. Antihypertensive treatment is of fundamental importance for CV protection of patients with diabetes, as demonstrated in several large randomized clinical trials. Positive effects are observed with all major classes of antihypertensive drugs, including beta-blockers, over a range of CV outcomes.

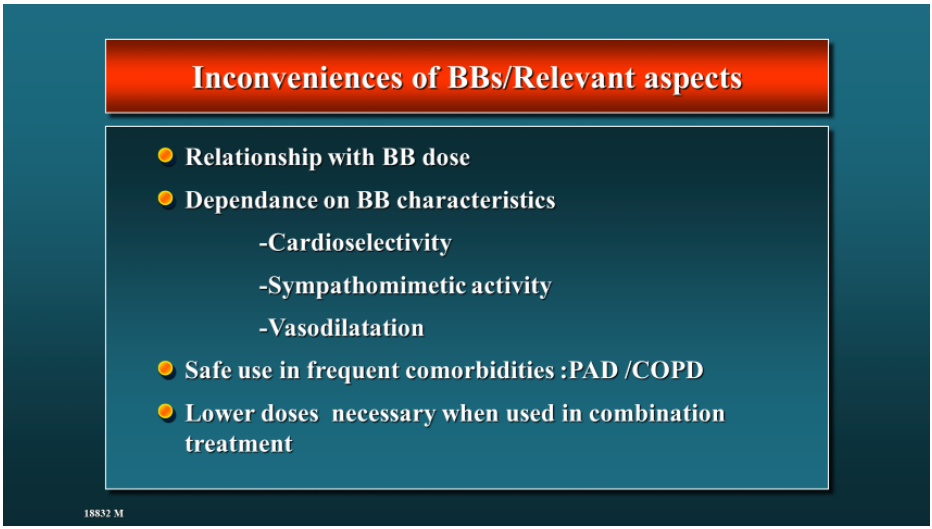
In contrast to some recently published guidelines, in the 2018 European Society of Cardiology (ESC) / European Society of Hypertension (ESH) guidelines[13] beta-blockers are still regarded as a first-line treatment for patients with hypertension due to their ability to reduce BP and, consequently, CV events. They are particularly recommended in specific subgroups of hypertensive patients, including patients with ischemic heart disease, heart failure, atrial fibrillation, elevated heart rate and women with child-bearing potential/planning pregnancy.

The positive impact of beta-blockers on BP and their broad equivalence to other antihypertensive medications on outcome have been confirmed by several randomized clinical trials and large meta-analyses.[14,15]

Although treatment with beta-blockers offers less protection from target organ damage, a less favorable side-effect profile and a higher discontinuation rate compared with other antihypertensive agents, these inconveniences are mainly linked to the dose and characteristics of the beta-blocker used, as are the increased risks of metabolic alterations in those with metabolic syndrome. Key factors that influence the risk of inconveniences associated with beta-blocker treatment in hy-

pertensive patients are the cardioselectivity of the molecule, its sympathomimetic activity and its capacity to induce vasodilation. Also, the ability to use them safely in patients with common co-morbidities, including peripheral arterial disease and chronic obstructive pulmonary disease, should be considered (Figure 6).

Figure 6: Important aspects to consider in the attempt to minimize the risk of inconveniences related to beta-blocker treatment.



The use of combination treatment, which is often needed to obtain adequate BP control in patients with diabetes and is recommended for almost every patient with arterial hypertension by the 2018 ESC/ESH Guidelines[13], enables reduction of the dose of the single agents included in the combination, thus resulting in a reduced risk of side-effects.

L7

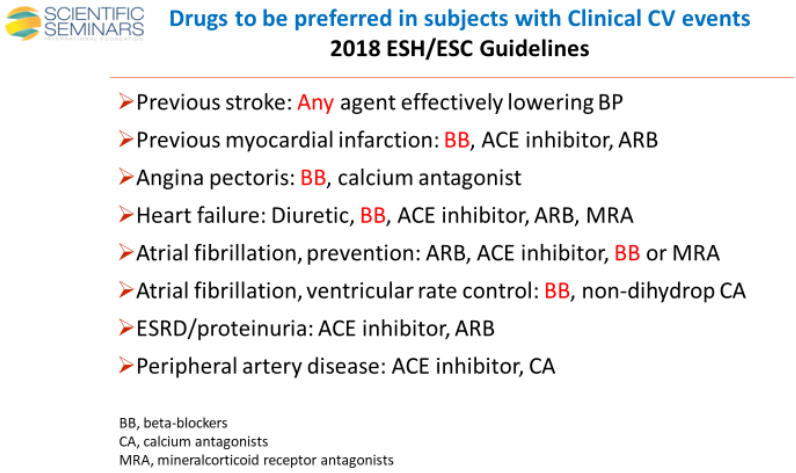
Should increase in heart rate be considered a target in cardiovascular treatment?

Harry AJ Struijker-Boudier

Department of Cardiovascular Research
Maastricht University
Maastricht, Netherlands

Tachycardia is more frequent in patients with hypertension compared with normo-tensive subjects and is a strong predictor for the development of permanent hypertension, said **Professor Struijker-Boudier** (Maastricht, The Netherlands).
The risk of mortality and morbidity increases significantly in patients with hypertension when their heart rate increases to >75-80 bpm.
Beyond its capacity to reflect a sympathetic overdrive and its damaging effects on the CV system, tachycardia might cause mechanical cardiac and vascular damage amplifying the tensile stress in arteries, increasing the pulse wave velocity, the reflected pulse wave and ultimately, aortic pressure. These changes have consequences also on the arterioles, thickening the vessel walls, reducing their lumen, and increasing BP amplification.
Several classes of drugs can be used to reduce the sympathetic overdrive which often underpins an elevated heart rate in hypertension, including centrally-acting antihypertensives, alpha-blockers, non-dihydropyridine calcium-channel blockers, beta-blockers, and ivabradine. Among these, the drug class with the largest amount of data in hypertension are the beta-blockers. Within the class of beta-blockers, there is large heterogeneity among the different molecules regarding the selectivity for B1-adrenergic receptors, half-life, route of clearance and adverse effects on lipid and glucose metabolism. These differences might account for the conflicting results obtained with beta-blocker use in some studies. Advantages of using a B1-selective blocker compared with a non-selective beta-blocker include less bronchoconstriction, less metabolic effects and less circulatory side-effects. Also, beta-blockers with long half-life might confer better BP coverage for the entire 24 hours rather than molecules with a shorter half-life.
Careful selection of the best beta-blocker for an individual patient with hypertension is important as the 2018 ESH/ESC guidelines on arterial hypertension[13] still consider beta-blockers an important antihypertensive drug class which has specific indications in many different subgroups of patients with arterial hypertension, Figure 7.

Figure 7: Guidance from the ESC/ESH for antihypertensive agent choice in particular CV patients



L8

From hypertension to heart failure: Prevention strategies

Erland Erdmann

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University of Köln
Köln, Germany

Hypertension represents the most important risk factor for heart failure (HF), said **Professor Erdmann** (Köln, Germany) at the start of his lecture. The major differences between heart failure with reduced (HFrEF) and preserved (HFpEF) ejection fraction were subsequently discussed as well as the mechanisms that underpin the evolution from hypertension to heart failure, which include cardiac remodeling, with left ventricular hypertrophy (LVH), impaired left ventricular relaxation, left atrial enlargement, and increased risk of arrhythmias, especially atrial fibrillation (Figure 8).

Figure 8: Mechanisms underpinning transition from hypertension to HF

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Hypertension (HTN) is the Major Risk Factor for Heart Failure (HF)

HTN increases the risk for HF:
HF with reduced ejection fraction (HFrEF) and
HF with preserved ejection fraction (HFpEF)

Chronically increased left ventricular (LV) workload in HTN triggers cardiac remodeling, which results in:
LVH, impaired LV relaxation, left atrial enlargement, increased risk of arrhythmias, especially AF.

Moreover, production of reactive oxygen species by coronary microvascular endothelial cells, reduced nitric oxide bioavailability, and decreased protein kinase G activity is known. **This proinflammatory state results in myocyte hypertrophy, titin hypophosphorylation, increased collagen deposition, and decreased left ventricular compliance**.

Beyond its direct cardiac effects, hypertension often coexists with other CV risk factors that are also linked to an increased risk of HF.

The LIFE study[16] has shown that in subjects with established LVH, a heart rate >84 bpm increased the risk of all-cause death by 97% and CV death by 89%

compared with subjects with a heart rate <84 bpm. A similar relationship between elevated heart rate and the risk of CV death was apparent in patients with diabetes.[17] Neurohormonal activation and sympathetic overdrive are present in patients with hypertension, heart failure and coronary artery disease and might account for the strong relationship between these pathological conditions. Indeed, a linear association between elevated heart rate and increased risk of death has also been documented in patients with HFpEF. The pathophysiological chain of events leading to HF from hypertension starts with cardiac injury, proceeds with the activation of counter-regulatory pathways (sympathetic activation), leads to the development of secondary organ dysfunction and ends with the development of final stage HF (NYHA class III and IV).

Meta-analyses of randomized controlled trials have found that a 10 mmHg reduction in systolic blood pressure (SBP) is associated with ~40% reduction of the risk of HF,[18] suggesting that a reduction of blood pressure (BP) is the most effective strategy to reduce the risk of HF, particularly for HFpEF. In the SPRINT trial, the aggressive BP-lowering treatment group experienced a 38% reduction in the risk of HF compared with those allocated to the standard BP-lowering regimen.[19]

Heart failure can be the final common pathway of almost all CV diseases, and prevention of HF largely involves treatment of hypertension and other modifiable risk factors for coronary artery disease.

Recent evidence suggests that diuretics, and more specifically, chlortalidone, might be the most effective agents in preventing HF and should be considered as an important part of therapy in patients with hypertension. However, 2018 ESC/ESH Guidelines[13] on arterial hypertension suggests that antihypertensive treatment should be started with a combination therapy in most patients, given the evidence that the majority of patients with hypertension require more than one drug to obtain good BP control, and that combination therapy is more effective in reaching good BP control within a short time period compared with monotherapy. Combination therapies that might be considered include: diuretic + ACEI; diuretic + beta-blocker; diuretic + ACE-I + beta-blocker, particularly if HF is apparent. Combinations should be prescribed, where possible, as a single pill medicine, as treatment adherence is better when only one tablet is prescribed to hypertensive patients.

In patients with resistant hypertension, renal denervation has been shown to reduce LVH. In patients with diabetes, SGLT2i should be considered in patients at high risk of CV disease and HF, due to their positive effects on BP, body weight, arterial stiffness, and their diuretic-like actions.[20]

CLINICAL CASE 1

Thyroid storm: Treatment and cardiac complications

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Salman Razvi

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Professor Biondi and **Professor Razvi** introduced their clinical case presentation with details of the patient, Figure 9.

Figure 9: Presenting signs and symptoms of the clinical case study

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Clinical case

History

- **A young woman aged 35 years (height 165 cm, weight 65 kg) came to our clinic, ambulatory with dyspnea on exertion, tremor and tachycardia**
- **She was married with 2 children (aged 5 and 10)**
- **She had a family history of autoimmune thyroid disease and systemic autoimmune disease (vitiligo and celiac disease)**
- **She had no history of neck irradiation**
- **She complained about weight loss, weakness, tremor, palpitations, heat intolerance and anxiety**
- **She was a smoker**

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Physical examination revealed an enlarged thyroid gland, systolic hypertension (BP 170/80 mmHg), and an increased heart rate (128 bpm). She had a small goiter. Further investigation of the thyroid by sonography revealed her thyroid gland was enlarged bilaterally, and scintigraphy and a 24-hour radioactive iodine test showed a diffuse increased tracer uptake. Thyroid function tests showed a moderately severe hyperthyroidism, undetectable serum TSH and high levels of thyrotropin receptor antibodies. She also had mild ophthalmopathy.

Therapy was started with methimazole (MMI; 20 mg/day) and propranolol (10 mg 3 times/day), but she developed a minor cutaneous allergic reaction. This was managed using antihistamine alongside the MMI, which improved both the allergy and her hyperthyroidism. Although a definitive treatment with radioiodine or surgery was proposed, the patient refused these options.

After three months of medical treatment, she voluntarily decided to stop MMI and beta-blockers. Two months after MMI withdrawal, she presented at clinic as an outpatient with dyspnea and symptoms of hyperthyroidism. Her thyroid hormone levels had further increased, and she was prescribed propylthiouracil (PTU). However, after 10 days she stopped PTU because of nausea, vomiting and diarrhea. She became breathless at rest, fatigued and had fluid retention with peripheral edema, pleural effusion, hepatic congestion and increased pulmonary arterial pressure. She was then hospitalized due to the onset of atrial fibrillation and the worsening of dyspnea. A Doppler Echocardiograph result was used to diagnose her with 'high-output heart failure', and her Burch and Wartofsky[21] score was 50. Treatment was started with beta-blockers, PTU, digoxin and diuretics, which improved the congestive circulatory symptoms; hydrocortisone, sedation, oxygen and anticoagulation therapy were added and the patient's condition progressively improved. Prior to discharge, the possibility of ischemic heart disease, autoimmne cardiomyopathy or valvular disease were ruled out, and the patient was scheduled for thyroid surgery. In preparation for this, Lugol's solution (10 drops, 3 times daily for 10 days) were administered in the days before surgery.

What was the most likely diagnosis for this patient?

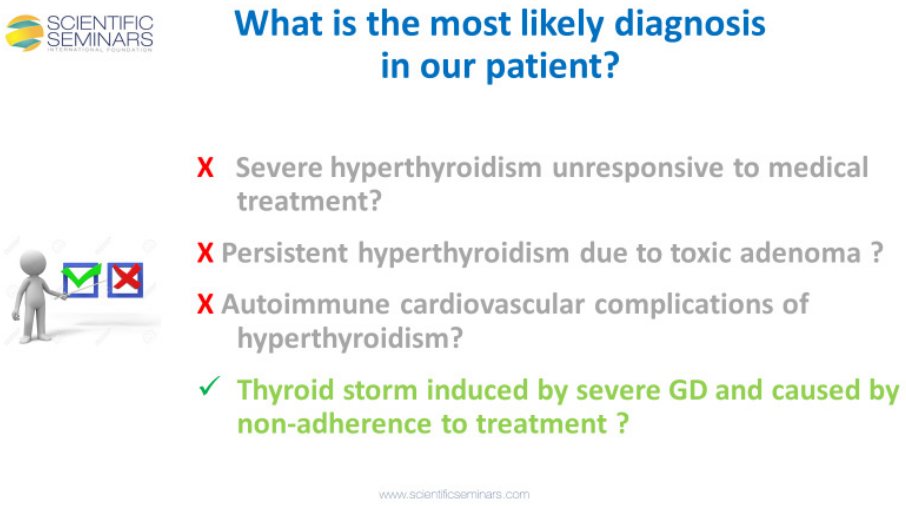
1. Severe hyperthyroidism unresponsive to medical treatment?
2. Persistent hyperthyroidism due to toxic adenoma?
3. Autoimmune cardiovascular complications of hyperthyroidism?
4. Thyroid storm induced by severe Graves' disease and caused by non-adherence to treatment?

Professor Biondi and Professor Razvi presented data from guidelines[22], a review of Graves' Disease[23] and a study of HF and thyroid dysfunction[24] to show that the patient demographically and symptomatically fulfilled the diagnostic criteria for Graves' Disease. Further, her non-compliance with prescribed medication put her at CV risk - seen when hyperthyroidism is untreated (risk of atrial fibrillation,

stroke, HF, coronary heart disease events, CV mortality). In cases of 'high output' heart failure in hyperthyroidism, congestive circulation may occur with increased cardiac output in the absence of underlying heart disease. This is due to the effects of persistent tachycardia, increased cardiac load, reduced systemic vascular resistance, elevated ventricular filling pressure, and increased pulmonary arterial pressure.

For this particular patient, she had autoimmune CV involvement in Graves' Disease (cardiomyopathy, peripartum cardiomyopathy, cardiac valve involvement, pulmonary hypertension), and thyrotoxic crisis (or thyroid storm), a life-threatening exacerbation of the hyperthyroid state characterized by decompensation of one or more organs (Figure 10). Usually it is a complication of Graves' Disease, but can sometimes occur in association with toxic nodular goiter. It accounts for <1–2% of hospital admissions for thyrotoxicosis, and has a high mortality rate (20–30%).

Figure 10: Diagnosis of case study patient



In conclusion, Professor Biondi and Professor Razvi summarized their findings in this patient as thyroid storm complicated by cardiopulmonary failure as the initial presentation of undiagnosed or untreated thyrotoxicosis. They emphasized the importance of quick recognition and treatment of this condition, which is critical for the patient's survival - cardiopulmonary failure is the most common cause of death in thyroid storm.

CLINICAL CASE 2

Hypertensive patient with high heart rate

Harry AJ Struijker-Boudier

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Maastricht University
Maastricht, Netherlands

A 48-year-old male teacher requiring a health check-up is the subject of the case study introduced by **Professor Struijker-Boudier**. The patient had no significant past medical history, was not taking any medication, but smoked 15 cigarettes each day and drank two bottles of beer at the weekend. His physical examination revealed a BMI of 28, BP was 165/94, heart rate was 96 bpm with no cardiac abnormalities. His laboratory readings are presented in Figure 11.

Figure 11: Laboratory readings for the 48-year-old male teacher attending for a health check-up

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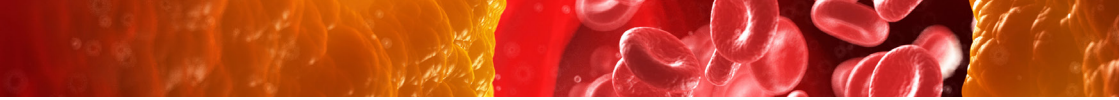
Laboratory investigations

* Fasting blood glucose: 6.0 mmol/l
* HbA1C: 6.0
* Normal free T4, TSH, T3
* LDL cholesterol 3.2 mmol/l
* HDL cholesterol 1.1 mmol/l

What advice should be offered to this patient?

According to the 2018 ESH/ESC guidelines on arterial hypertension[13], he should be counselled on life-style changes, BP-lowering drugs should be prescribed targeting <140/90 and, if tolerated, <130/80 mmHg. Although life-style modifications



(weight reduction, adopting the National Heart, Lung and Blood Institute (NIH, USA) DASH eating plan, reducing dietary sodium, engaging in physical activity and moderating alcohol consumption) can all positively impact BP, this patient seemed likely to be poorly adherent to these lifestyle changes.

In this situation, which anti-hypertensive medication should be prescribed (thiazide diuretic, beta-blocker, calcium-channel blocker, ACE inhibitor, or an angiotensin receptor blocker)?

Referring back to the 2018 ESH/ESC guidelines on arterial hypertension[13], guidelines state that all major classes of antihypertensives are suitable for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combination, and that the specific choice of an antihypertensive (combination) depends on co-morbidities, patient phenotypes and the side-effect profiles of the individual drugs. The majority of hypertensive patients require a combination of two or more antihypertensives to reach target BP (140/90 mmHg).

As this patient also has a raised heart rate – should a beta-blocker be prescribed?

Large clinical trials (Framingham, Syst-EUR, LIFE, VALUE, INVEST) have shown that an increased heart rate is an important risk factor for CV morbidity and mortality, independent of BP level. Pharmacological reduction of heart rate might reduce the risk of CV morbidity and mortality, partly independently of the degree of BP reduction.

During follow-up, the patient managed to stop smoking, but his BMI and cholesterol levels remained the same. Upon examination, his BP was 145/85 mmHg, and his heart rate 74 bpm.

What should the next step be with this patient?

Beta-blocker treatment should be continued, and another anti-hypertensive agent should be added. The drug to be added should be selected based on the synergistic modes of action of the proposed addition and the beta-blocker. Based on this consideration, the selection of a calcium-channel blocker could represent a good therapeutic choice. Indeed, after starting a calcium-channel blocker, the patient achieved good BP control.

In conclusion, Professor Struijker-Boudier explained that the next step should be the use of a combination of 2 or more antihypertensives to reach therapeutic targets. Roughly 75% of hypertensive patients require combination therapy, which reduces the need for relatively high doses of individual antihypertensives and reduces the incidence of unfavorable side-effects. In addition, single pill combination therapy contributes to better patient adherence/compliance.

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