Narrative review

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# An update on hypertensive emergencies and urgencies

Maria Lorenza Muiesan[a], Massimo Salvetti[a], Valentina Amadoro[b], Salvatore di Somma[b], Stefano Perlini[c], Andrea Semplicini[d,e], Claudio Borghi[f], Massimo Volpe[g], Pier Sergio Saba[h], Matteo Cameli[i], Marco Matteo Ciccone[j], Maria Maiello[k], Pietro Amedeo Modesti[l], Salvatore Novo[m], Pasquale Palmiero[k], Pietro Scicchitano[i], Enrico Agabiti Rosei[a], Roberto Pedrinelli[n], on behalf of the Working Group on Hypertension, Prevention, Rehabilitation of the Italian Society of Cardiology, the Societa' Italiana dell'Ipertensione Arteriosa (SIIA)

**Severe acute arterial hypertension is usually defined as 'hypertensive crisis', although 'hypertensive emergencies' or 'hypertensive urgencies', as suggested by the Joint National Committee and the European Society of Hypertension, have completely different diagnostic and therapeutic approaches.**

**The prevalence and demographics of hypertensive emergencies and urgencies have changed over the last four decades, but hypertensive emergencies and urgencies are still associated with significant morbidity and mortality.**

**Different scientific societies have repeatedly produced up-to-date guidelines; however, the treatment of hypertensive emergencies and urgencies is still inappropriate, with potential clinical implications.**

**This review focuses on hypertensive emergencies and urgencies management and treatment, as suggested by recent data.**

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[a]Department of Clinical and Experimental Sciences University of Brescia, 25100 Spedali Civili, Brescia, [b]Department of Medical-Surgery Sciences and Translational Medicine, Emergency Department, University La Sapienza, Sant'Andrea Hospital Rome, Rome, [c]Department of Internal Medicine and Therapeutics, University of Pavia, Lombardy, [d]Department of Internal Medicine 1, USL12 Veneziana, Venice, [e]Department of Medicine, University of Padua, Padova, [f]Department of ScienzeMediche e Chirurgiche, S.Orsola-Malpighi University Hospital, Bologna, [g]Division of Cardiology, Department of Medicina Clinica e Molecolare, University Roma 'Sapienza' – Azienda Ospedaliera Sant'Andrea, and IRCCS Neuromed, Rome, [h]Division of Cardiology, AOU Sassari, Sassari, [i]Department of Cardiovascular Diseases, University of Siena, Tuscany, [j]Cardiovascular Disease Section, Department of Emergency and Organ Tranplantation, University of Bari, Bari, [k]AS Department of Cardiology, Brindisi District, Brindisi, [l]Department of Clinical and Experimental Medicine, University of Florence, Florence, [m]Department of Internal Medicine and Cardiovascular Diseases, University of Palermo, Palermo and [n]Dipartimento di Patologia Chirurgica, Medica, Molecolare e dell'Area Critica, Università di Pisa, Pisa, Italy

Correspondence to Maria Lorenza Muiesan, MD, Department of Clinical and Experimental Sciences University of Brescia, Spedali Civili, Brescia, 25100 Italy
E-mail: marialorenza.muiesan@unibs.it

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## Introduction

Physicians in emergency departments (EDs) frequently triage patients with 'hypertensive crises', that is an acute and severe rise in blood pressure (BP) presenting with highly heterogeneous profiles ranging from absence of symptoms to life-threatening target organ damage.[1–3] The approach in the acute hypertensive setting has not been well established,[4] in contrast with the evidence-based recommendations guiding the appropriate management of chronically elevated BP.[1,5] In addition, a large number of patients in EDs are affected by chronic hypertension, and do require referral to outpatient care rather than acute interventions.[6,7] Most importantly, few randomized clinical trials have addressed the short-term and long-term effects of acute BP lowering on cardiac and cerebrovascular morbidity and mortality.[1,8–10]

## Definition and cause

A hypertensive emergency is defined as an acute increase in BP associated with severe, potentially life-threatening target organ damage; in this condition, hospitalization, preferably in an ICU, is required for prompt BP control (minutes or a few hours) by intravenous administration of antihypertensive drugs (Table 1). The most common presentations of hypertensive emergencies in the ED are cerebral infarction, pulmonary oedema, hypertensive encephalopathy and congestive heart failure, and also include aortic dissection, intracranial haemorrhage, sympathetic crises (cocaine toxicity/pheochromocytoma), eclampsia, myocardial infarction and malignant hypertension. The aim of treatment is to avoid an acute worsening of organ damage and further long-term complications.[8,11–14]

Hypertensive urgency, on the contrary, is characterized by an acute increase in BP in the absence of symptoms suggesting acute organ damage. Hospitalization is not necessary and this condition may be managed effectively with close outpatient follow-up. The decrease in BP may be obtained in hours or even days by oral antihypertensive


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**Table 1 Differences between hypertensive emergencies and urgencies**

| Variable | Emergencies | Urgencies |
|---|---|---|
| Symptoms | Yes | No or minimal |
| Acute BP increase | Yes | Yes |
| Acute target organ damage | Yes | No |
| BP reduction rate | Minutes to hours | Hours to days |
| Evaluation for secondary hypertension | Yes | Yes |

BP, blood pressure.

treatment. Hypertensive urgencies and emergencies are not completely distinct entities, as unrecognized or untreated urgencies may evolve into emergencies (Table 1).

The levels of BP for the definition of hypertensive emergencies and urgencies are not clearly established, and the same degree of BP increase in one patient may translate into severe symptoms indicating target organ injury or may not confer any symptoms at all in another patient. In the Studying the Treatment of Acute hyperTension (STAT) registry, inclusion criteria for hypertensive emergency or urgency were SBP more than 180 mmHg and/or DBP more than 110 mmHg, although patients with subarachnoid haemorrhage (SAH) were included if they had a BP measurement more than 140 mmHg systolic and/or more than 90 mmHg diastolic.[5] There is a general consensus indicating that an SBP of more than 180 mmHg and or a DBP more than 120 mmHg may deserve intervention[1,4] (Fig. 1).

Hypertensive urgencies may be difficult to differentiate from 'uncontrolled hypertension', characterized by the presence of chronically elevated BP values, despite (often inappropriate) antihypertensive treatment, in the absence of target organ damage. In other circumstances, an abrupt BP increase may represent the consequence of acute anxiety, panic attacks, painful syndromes, venous epistaxis or alcohol withdrawal; the treatment of these conditions (pseudo hypertensive crisis) is associated with a concomitant reduction of BP.

The factors leading to the severe and rapid elevation of BP in patients with hypertensive emergencies have been investigated but remain poorly understood.[14] An acute increase in humoral vasoconstrictors and systemic peripheral resistance cause an increase in mechanical stress on the vascular wall, endothelial damage and vascular permeability, activation of platelets and coagulation cascade, associated with fibrin deposition, induction of oxidative stress and inflammatory cytokines.[15] Vasoconstriction and thrombosis, as a result of vascular damage lead to hypoperfusion, end-organ ischemia and autoregulatory dysfunction.

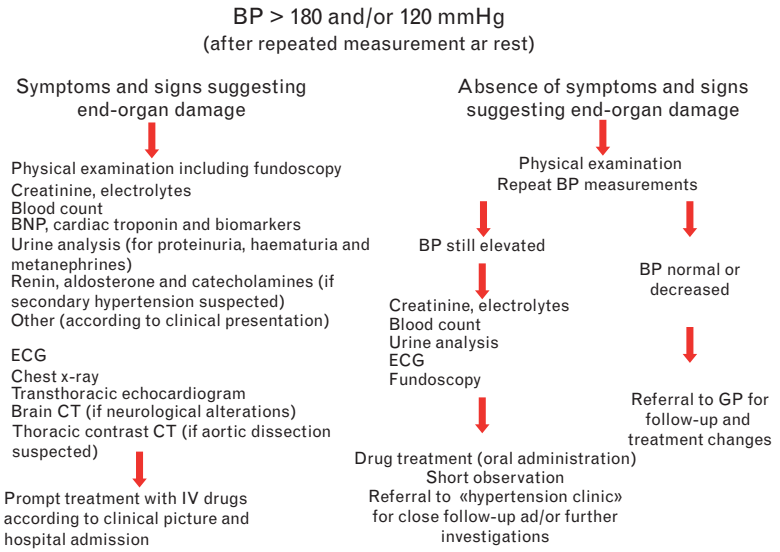
Elevated markers of inflammation, coagulation, platelet activation and fibrinolysis have been demonstrated in patients with hypertensive emergencies.[16] Circulating and endothelial progenitor cells have been measured and found significantly increased in patients with malignant hypertension, as compared with hypertensive patients and normotensive individuals.[17]

## Epidemiology

An Italian study performed in 1992 showed that 'hypertensive crisis' represented 3% of all medical urgencies, with a prevalence of 24 and 76%, respectively, for hypertensive emergencies and urgencies.[18]

Hypertensive emergencies occur in up to 2% of hypertensive patients,[19,20] with a progressive decrease in mortality rate over the past 4 decades.

**Fig. 1**




Evaluation and management of the patients with acute elevation of blood pressure in the emergency department. BNP, Brain-natriuretic peptide; CT, computerized Tomography; GP, general practitioner; IV, intravenous.

The incidence of 'hypertensive crisis' (SBP ≥200 mmHg and/or DBP ≥120 mmHg) was examined in only one prospective longitudinal study; 89 patients with hypertension diagnosis, confirmed by 24 h BP, underwent a follow-up and an acute increase in BP was observed in 13 patients (11 with symptoms) during a mean period of 1.6 years. Risk factors possibly promoting a 'hypertensive crisis' included female sex, higher degrees of obesity, hypertensive or coronary heart disease, higher number of antihypertensive drugs and, most importantly, nonadherence to medication.[21]

A higher incidence of cardiovascular events was also observed in patients with hypertensive urgencies, as compared with hypertensive patients with similar BP values.[22]

In the West Birmingham Malignant Phase Hypertension Study, 203 (55%) and 39 (11%) patients were dead or had started dialysis, respectively, after a median follow-up of 7 years.[19,23] Lane *et al.*[19] followed about 500 patients with hypertensive emergencies, including malignant hypertension (i.e. DBP >130 mmHg in association with bilateral retinopathy, i.e. haemorrhages and/or cotton wool spots or exudates, with or without papilloedema), for a median follow-up of up to 104 months, and the 5-year survival rate was significantly improved, from 37% (in those diagnosed before 1977) to 91% (in patients observed later, between 1997 and 2006).[19]

More recent data have examined the prevalence of hospitalization for a hypertensive emergency from 2000 to 2007 in the United States, and showed a high and increasing incidence (from 50 000 to 60 000 per year) with a progressive decline in mortality (from 3 to 2.5%) since 2005–2007. Increasing age, male sex and a higher Charlson comorbidity index were among the stronger predictors of mortality for these patients; fatal events were lower among these patients after the publication of the JCVII guidelines, which recommended BP control and focused on the diagnostic approach and treatment of specific hypertensive emergencies.[24]

In the Studying the Treatment of Acute hypertension (STAT) registry, including 25 institutions in the United States, 1588 patients treated with intravenous therapy for severe acute hypertension were enrolled between January 2007 and April 2008, with a 6.9% hospital mortality and 37% 90-day readmission rate.[5] A retrospective analysis of the STAT registry has shown that approximately 29% of patients readmitted to the hospital after a first hypertensive emergency were rehospitalized for hypertension. Lack of compliance to the hypertensive treatment, substance abuse and dialysis use for chronic kidney disease were the main characteristics associated with a readmission for hypertension.[25]

## Initial recognition of acute hypertension

A complete history including any previous diagnosis of hypertension/cardiovascular disorders/endocrine disorders and surgeries should be performed. Alcohol consumption, some food ingestion or the use of drugs (such as corticosteroids and mineralocorticoids, oestrogens, NSAID, cyclosporine, carbamazepine, metoclopramide and angiogenesis inhibitors) should be investigated. If the patient is hypertensive, disease duration, previous BP control, current antihypertensive medications with dosing and compliance should be recorded; it should be kept in mind that the rate of increase in BP may be even more important than the absolute level of BP at presentation.

Illicit drug use has been also reported to be a major risk factor for the development of hypertensive emergencies and approximately 5–10% of ED visits in the U.S. have been attributed to cocaine use.[6] The research for cocaine use by urine analysis is underprescribed because of the considerable increase in the numbers of cocaine-related episodes reported in the last 20 years in Europe.[26,27]

BP measurements should be repeated, following general indications (cuff dimensions, cuff and arm position, and at least three to four consecutive measurements), as BP values tend to decrease in parallel with the number of measurements and with rest. In a group of 549 consecutive patients admitted for a hypertensive urgency, a significant BP reduction was achieved in 31.9% after 30 min of rest alone.[28] This approach may particularly useful in the distinction between hypertensive urgencies or pseudo-urgencies (Fig. 1).

BP should be measured on both arms, and if a large difference between the two arms is detected, BP should also be measured at lower limbs, with the diagnostic hypothesis of aortic dissection. The use of a beat-to-beat device for noninvasive BP measurements has been proposed for a more accurate BP monitoring.[29]

An accurate evaluation of patients' symptoms and signs is mandatory for the distinction between hypertensive emergency and urgency. In the study by Zampaglione *et al.*,[18] the most common presenting symptoms included dyspnoea (22%), chest pain (27%), focal neurologic deficit (21%) and faintness (10%), while in the STAT registry, shortness of breath (29%), chest pain (26%), headache (23%), altered mental status (20%) and focal neurologic deficit (11%) were more frequently reported.[5] Headache, visual abnormalities and reduced level of consciousness are the usual manifestations of hypertensive encephalopathy.

The funduscopic examination may be particularly helpful in identifying exudates, haemorrhages and/or papilledema; the presence of grade 3–4 Keith Wegener retinopathy is associated with the presence of microvascular dysfunction and renal damage. Despite these pieces of evidence, a fundoscopic examination was performed in only 13% of patients enrolled into the STAT registry.[5] New software is currently available for fundus oculi photography, allowing the remote assessment of

retinal fundus images sent to an ophthalmologist, and possibly improving wider use in the ED setting.

Glucose, creatinine, electrolytes and a full blood count should be performed. When a secondary form of hypertension is suspected, a sample for plasma renin activity, aldosterone and catecholamines should be drawn, before giving appropriate therapy. Urinalysis should be performed, searching for proteinuria and haematuria.

Chronic kidney disease is a common comorbidity among patients admitted with acute severe hypertension[30] and acute kidney injury (AKI) is a frequent form of acute target organ dysfunction, particularly in those with baseline chronic kidney disease. The risk of morbidity and mortality increases for any degree of AKI, in particular heart failure and cardiac arrest.

Creatinine level may also identify patients with renal dysfunction in the setting of asymptomatic markedly elevated BP, although it is still unknown whether their prevalence in ED differs from patients presenting at an outpatients hypertension clinic; some recent data suggest that patients presenting with hypertensive emergencies have a higher degree of renal function deterioration, as indicated by the earliest biomarker of kidney injury, neutrophil gelatinase-associated lipocalin (NGAL), and by cystatin C, in comparison with patients with hypertensive urgencies and with controls.[31,32]

Other fundamental diagnostic examinations include a chest radiography in patients with cardiopulmonary symptoms; on the contrary, it has no value in the diagnostic and therapeutic approach in the absence of symptoms. An ECG is always useful for the detection of left ventricular hypertrophy and/or overload and of ischemia; even in asymptomatic patients, new ECG abnormalities may be observed.

An echocardiogram can detect other important information in patients with both hypertensive emergencies and urgencies; in a group of black patients with elevated BP and no symptoms, a high prevalence of left ventricular hypertrophy and cardiac dysfunction was detected.[33] An echocardiogram is particularly indicated in patients with acute heart failure and acute worsening of BP, in order to assess the presence of left ventricular hypertrophy and to evaluate left ventricular systolic and diastolic function by conventional two-dimensional images and advanced Doppler echocardiographic parameters.[34]

Elderly women with diabetes and/or overweight and obesity may quite frequently have a normal ejection fraction and diastolic dysfunction with elevated filling pressures[35]; the acute management of these patients may be different from those patients with predominant systolic dysfunction and those with transient mitral regurgitation.

It has recently been suggested that using speckle-tracking parameters, left ventricular systolic strain and strain rate were depressed during 'hypertensive crisis' and significantly improved after medical treatment, although no significant changes in left ventricular ejection fraction were detected. Left ventricular diastolic function, assessed using conventional and speckle-tracking parameters, was also depressed and significantly improved after treatment.[36] The clinical usefulness of this new methodology needs to be confirmed in future studies.

A head computed tomography (CT) scan is mandatory in a patient with neurologic symptoms. A thoracic contrast CT computerized Tomography scan should be obtained in a patient with suspected aortic dissection, because trans-oesophageal echocardiography should not be performed before reaching adequate BP control.

In asymptomatic patients who present to the ED with markedly elevated BP (including hypertensive urgencies and uncontrolled hypertensive patients), the optimal screening, treatment and follow-up interval, as related to the short-term and long-term clinical outcomes, need to be addressed in the future.[7]

## Initial management

The majority of patients with severe BP increase (SBP >180 mmHg, DBP >110 mmHg) have a hypertensive urgency (no evidence of end-organ damage at initial evaluation in the ED). In these patients, the presence of elevated BP values may reflect inadequate control of chronic hypertension and the best therapeutic approach is the oral administration of antihypertensive drugs aimed to lower BP gradually over 24–48 h. Hospital admission is not indicated, as early clinical surveillance is usually sufficient, and a short-term visit by the general practitioner or a Center for Hypertension 'outpatient clinic' is strongly suggested. The reduction in BP should be gradual, as no benefit, but potential harm, may be associated with a rapid BP decrease, due to a rightward shift in the pressure/flow auto-regulatory curve in critical arterial beds (cerebral, coronary and renal).[37–40]

The use of a combination of antihypertensive drugs may increase the likelihood of effective BP reduction and therefore can be considered for the initial approach. On the contrary, the sublingual administration of nifedipine is not recommended, as it induces an unpredictable, and often too rapid and large, decrease in BP reduction.[41,42]

For hypertensive emergencies (symptomatic patients with target organ damage), admission to an ICU for clinical surveillance and continuous BP monitoring is recommended. No large clinical trials have been conducted to define specific goals of treatment in patients with hypertensive emergency. Prompt intravenous administration of short-acting and titratable drugs is the preferred approach. In the first minutes of treatment and up to 1 or 2 h, the decrease in BP should be around 15–25% of the initial values (or to about 110 mmHg for

diastolic pressure) and a normalization (i.e. <140/90 mmHg) should be gradually achieved in several hours and days.[4]

Several rapid-acting intravenous agents are available for the treatment of hypertensive emergencies and the choice is mainly related to the clinical manifestation of end-organ damage (Table 2).

The effect of these drugs should be carefully monitored in a proper setting, in order to avoid an excessive velocity of BP reduction, leading to ischemic complications such as acute myocardial infarction and stroke, because of altered autoregulation. Unfortunately, an excessive decrease of BP is common among patients admitted to an ED with hypertensive emergency;[43] even in acute stroke patients, in whom the risk of hypoperfusion is well known, the rate of change of BP was frequently greater than recommended, and met American Heart Association recommended treatment criteria in only one-third of patients.[44]

In the Euro-STAT observational study, 791 consecutive patients were enrolled in 11 hospitals in seven European countries, with the aim of evaluating 'real-life' management practices and outcomes in patients who received intravenous antihypertensive therapy to treat an episode of acute hypertension in the ED, ICU or perioperative. The results have shown that intravenous antihypertensive treatment (mainly nitroglycerin, furosemide and urapidil) was associated with hypotension in almost 10% of cases.[45]

The only exception to the approach of a partial and smooth BP reduction is patients with aortic dissection, in whom the goal is to reduce BP to below 120/80 mmHg.[46]

## Choice of treatment

No data are available about the possible drug differences on morbidity and mortality in patients treated for a hypertensive emergency; a systematic Cochrane review published in 2008 examined 15 randomized clinical trials and 869 patients and concluded that there is insufficient evidence from randomized clinical trials to determine which drug is most effective. Despite the lack of evidence, this does translate into the lack of efficacy of antihypertensive treatment in hypertensive emergencies. It is important for the physician to know that treatment is not supported by randomized clinical trial evidence in this clinical setting.[10]

The choice of the best drug(s) with the better benefit–risk ratio depends on the correct recognition of the clinical picture and the consideration of comorbidities (Table 2).

Among the new compounds proposed, some dihydropyridine calcium-channel antagonists are now available for intravenous administration;[47,48] again, it is important to stress that sublingual nifedipine is not recommended.[42,49,50]

Nicardipine has high vascular selectivity, with an onset of action of between 5 and 15 min and a clinical offset of activity (defined as a 10 mmHg increase in SBP or DBP after stopping infusion) within 30 min. Nicardipine's dosage is independent of the patient's weight. The infusion can be started at the initial rate of 5 mg/h, and increased by 2.5 mg/h every 5 min to a maximum of 15 mg/h until the desired BP reduction is achieved. The increase in stroke volume and coronary blood flow render this drug particularly useful in patients with coronary artery disease and systolic heart failure. A systematic review of 10 studies comparing nicardipine and labetalol treatment in hypertensive emergencies has shown comparable efficacy and safety, in spite of more predictable and consistent BP control with nicardipine than with labetalol.[48]

Clevidipine was approved by the United States Federal Food and Drug Administration in 2008 for the reduction of BP when oral therapy is not indicated or feasible. This third-generation calcium antagonist acts by selective inhibition of extracellular calcium influx through the L-type channel, relaxing smooth muscle of small arteries and reducing peripheral vascular resistance. The novelty of clevidipine is the ultra-short half-life of about 1 min and its potent arterial vasodilation. Clevipine does not affect venous capacitance or myocardial contractility[51] and has minimal effects on stroke volume, cardiac output or heart rate.[52,53]

## Acute heart failure

Patients who have systolic and/or diastolic heart dysfunction associated with a history of poorly controlled hypertension can present with an acute increase in BP associated with shortness of breath, leading to acute pulmonary oedema.[4,8,54] In the STAT registry, acute heart failure patients with severe hypertension had similar age and sex when compared with the cohort of patients with hypertension without heart failure, but a higher prevalence of a history of hypertension, renal failure and African American heritage.[5,34]

A chest radiograph may quickly confirm the clinical suspicion of pulmonary oedema raised by the presence of murmurs and/or gallop rhythm and/or pulmonary rales.[54,55] In patients presenting with dyspnoea, it is also crucial to obtain, in addition to an ECG, an urgent echocardiogram to distinguish between diastolic or systolic heart dysfunction and/or mitral or aortic valve regurgitation.[35] Thoracic ultrasound is highly indicated in patients with shortness of breath during a hypertensive emergency and pulmonary congestion is confirmed by the presence of comet tails. Elevations of BP and increased ventricular and vascular wall stress typically trigger an upregulation of brain natriuretic peptide (BNP) gene expression.[56] BNP is a rapid and easy test, used for new onset or decompensated acute heart failure diagnosis in the ED; in addition, BNP measurement represents a

**Table 2 Main hypertensive emergencies and suggested treatment**

| Indication | Drugs | Goal of treatment | BP goal | Adverse effects |
|---|---|---|---|---|
| Acute heart failure systolic dysfunction | Nitroglycerin, sodium nitroprusside, furosemide, nesiritide (for improvement of dyspnoea) | Reduce peripheral resistance and cardiac workload, without affecting cardiac contractility | Reduce ~15% of baseline BP, until resolution of acute pulmonary oedema | Noninvasive ventilation may induce a rapid decrease of BP Avoid SBP reduction <110 mmHg |
| Acute heart failure diastolic dysfunction | Nitroglycerin, furosemide, beta-blockers or non-DHPD CCB | Reduce peripheral resistance and cardiac workload (heart rate) | Reduce ~15% of baseline BP, until resolution of acute pulmonary oedema | Non invasive ventilation may induce a rapid decrease of BP |
| Acute coronary syndrome | Nitroglycerin, sodiumnitroprusside, labetalol, metoprolol, esmolol, nicardipine | Reduce cardiac workload and improve coronary perfusion | Reduce ~25% of baseline BP in 3–4 h | In cocaine-induced acute coronary syndrome avoid beta-blockers and use non-DHPD CCB, benzodiazepine |
| Acute aortic dissection | Labetalol; sodium nitroprusside, nicardipine as well as a betablocker i.v., clevidipine* | Reduce BP and wall shear stress | BP < 120/80 mmHg at least | Avoid i.v. beta-blockers if severe aortic regurgitaion |
| Acute ischemic stroke | Labetalol, esmolol, nicardipine, clevidipine*, nitroglycerin, sodiumnitroprusside (only if DBP >140 mmHg) | Avoid haemorrhagic conversion and enlargement of ischemic penumbra | Reduce ~15% of baseline BP (if >220/115 mmHg) in 2–3 h | Acute but gentle BP reduction indicated only if fibrinolysis is planned (BP <185/110 mmHg) |
| Acute haemorrhagic stroke | Labetalol, esmolol, nicardipine, clevidipine* | Avoid haematoma enlargement and perihaematoma oedema | BP <180/105 mmHg | Avoid sodium nitroprusside (intracranial oedema) |
| Hypertensive encephalopathy | Labetalol, nicardipine, esmolol | Reduce intracranial pressure | Reduce 25% of baseline BP in 2–3 h | |
| Acute renal failure | Nitroprusside, fenoldopam, nicardipine, clevidipine* | Reduce pressure in the kidney | Reduce 25% of baseline BP in 2–3 h | Avoid ACE-inhibitors, angiotensin receptors blockers and diuretics |
| Eclampsia | Hydralazine, labetalol, nicardipine | Reduce intracranial pressure and maintain placental perfusion | DBP <90 mmHg | The definitive treatment is the Caesarian section. |
| Sympathetic crisis | Phentolamine, nitroglycerin, fenoldopam, nicardipne, clevidipine*, labetalol | Reduce vasoconstriction mediated by alfa1 receptors | Symptoms resolution | Use benzodiazepine in cocain or amphetamine induced crisis. Avoid beta-blockers monotherapy (except for labetalol) |
| Pheochromocytoma | Labetalol, phentolamine | Reduce vasoconstriction and heart rate | Symptoms resolution | |

ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; BP, blood pressure; CCB, calcium-channel blocker; DHPD, dihydropiridinic; i.v., intravenous. * not available in Italy.

sensitive tool for confirming the clinical judgement of patients' improved conditions.[57] In hypertensive emergencies, BNP concentration could be significantly higher than in hypertensive urgencies[58] and the increase in BNP blood levels could have a role as a diagnostic tool for a more accurate diagnosis of hypertensive emergencies.[59] NGAL, together with creatinine, can be used to detect AKI.[60] A rapid reduction of BP should be immediately obtained in order to prevent further cardiac damage and patients' death.[35] Nitroglycerin is a venodilator and acts as an arteriolar dilator only in high doses; for this reason, it is a preferred drug for patients with acute heart failure and hypertensive emergencies, reducing BP by decreasing the preload and afterload at higher doses.[51] Intravenous loop diuretics (furosemide, bumetanide and torasemide) should be also administered in all patients.[52,53] Oxygen may be given to treat hypoxemia, which is associated with an increased risk of short-term mortality. Morphine has vasodilator properties and may reduce preload and the sympathetic drive, also because it decreases air anger. Nevertheless, there is no consensus for the need of morphine in all patients with acute heart failure during hypertensive emergencies. Noninvasive ventilation may be used to relieve symptoms in patients with pulmonary oedema and severe respiratory distress or in those patients who fail to improve with pharmacological therapy.[61] The accuracy of BP control is critical in these patients, as declines below 120 mmHg were shown to be associated with increased adverse event rates.[34]

## Acute stroke

Hypertension is common in the first hours after ischemic and haemorrhagic stroke and traditionally indicated as a hypertensive emergency. Hypertensive emergencies mandate quick administration of antihypertensive drugs to save the patient's life. This has encouraged the rapid BP reduction both in haemorrhagic and ischemic stroke irrespective of the fact that until recently, there was no convincing evidence that this is useful to prevent death and disability in both clinical conditions. Two recent studies, the INTERACT2 and the CATIS studies, have shed light on the different impact of antihypertensive treatment in ischemic and haemorrhagic stroke, which therefore need to be considered separately.[62,63]

### Ischemic stroke

Hypertension is a common early finding in patients who have experienced an acute ischemic stroke, which represents 85% of total strokes in western countries.[64] It is observed in both previously normotensive and hypertensive patients, regardless of whether they were receiving antihypertensive therapy prior to the stroke. In many patients, the hypertension that follows an ischemic stroke is transient and often the patients become normotensive within 24–48 h.

The BP rise is due to a number of mechanisms, such as impaired neurogenic cardiovascular control, autonomic dysregulation, baroreflex failure, increased sympathetic drive, reflex response to cerebral ischemia and mental stress.

However, a high baseline BP is not always deleterious and BP reduction with antihypertensive drugs is not always advisable in patients with acute ischemic stroke. This is suggested by two sets of clinical observations. First, patients with lacunar infarctions have higher baseline BPs than patients with atherothrombotic and cardioembolic strokes of the anterior and posterior circulation but a better clinical outcome.[65] Second, the CATIS trial ['China Antihypertensive Trial in Acute Ischemic Stroke' (CATIS)] showed that BP reduction with antihypertensive medications did not reduce the likelihood of death and major disability at 14 days or hospital discharge in patients with acute ischemic stroke compared with the absence of hypertensive medication.[63]

When deciding whether or not to give antihypertensive drugs to reduce the BP after stroke, we should also distinguish the early (the first 24–48 h) from the late phase because of the rapid changes of 'cerebral blood flow autoregulation' that occur after stroke.

In the healthy brain, cerebral blood flow is kept at 50 ml/100 g per min, despite wide fluctuations of the perfusion pressure ranging between 70 and 120 mmHg, through a mechanism known as the 'autoregulation of cerebral perfusion'. Any increase in pressure automatically results in vasoconstriction and any decrease results in vasodilation. These responses lower the risk of cerebral hyperperfusion and hypoperfusion, respectively. After an acute ischemic stroke, the autoregulation of cerebral perfusion is lost in the tissues surrounding the ischemic core, the so-called 'penumbra'. This peri-infarct zone is a moderately ischemic area that suffers from varying degrees of injury. The area can be salvaged if blood flow is rapidly restored because the ionic pumps have not yet failed, even when electrical function is lost. Flow in the range of 10–20 ml/100 g per min is the border between irreversible and reversible damage. In the 'penumbra', injury can be reversed for several hours after the onset of ischemia. Due to the loss of autoregulation, in the 'penumbra' the cerebral perfusion follows the perfusion pressure and a BP fall during this critical time may reduce cerebral perfusion, extend the ischemic area, induce irreversible damage and worsen the disabling consequences of the initial stroke. Therefore, during the first 24–48 h, a high BP appears desirable to reduce the cerebral damage, until the autoregulation is restored and any further neurologic improvement unlikely. In contrast, in the latter phase, a smooth rate of BP reduction is recommended, in order to reduce the risk of cerebral oedema, haemorrhagic transformation, stroke recurrence and cardiovascular complications.

Unfortunately, the impact of BP changes on cerebral perfusion in acute ischemic stroke is difficult to anticipate. Emboli may be dissolved and fragmented by intrinsic thrombolytic mechanisms, migrate to distal branches, and finally disappear within hours or days. High perfusion pressure in this situation may result in luxury perfusion of the previously ischemic area, cerebral oedema and haemorrhagic transformation. Furthermore, even the administration of a thrombolytic agent may be ineffective, leaving uncertainty about whether the artery has been successfully reopened or not. If reopened, there is a risk of luxury perfusion, cerebral oedema and haemorrhagic transformation at high perfusion pressure. On the contrary, the low BP required for a well tolerated intravenous thrombolysis may induce cerebral hypoperfusion and extend the ischemic core, especially if thrombolysis had been ineffective in vessel reopening.

Therefore, the American Stroke Association (ASA) recommend that only BP values repeatedly above 220/120 mmHg should be treated with either labetalol or sodium nitroprusside, intravenously, unless there are other indications for antihypertensive therapy (congestive heart failure, myocardial infarction, aortic dissection).[66] The BP target during the acute phase of an ischemic stroke should not be a normal BP, but rather 180 mmHg systolic–105 mmHg diastolic in previously hypertensive patients and 160–180/90–100 mmHg in previously normotensive patients.[66]

AHA/ASA Recommendations for BP Management in Acute Ischemic Stroke[66] also state that, first, patients eligible for treatment with intravenous thrombolytics or other acute reperfusion intervention and SBP 185 mmHg or DBP 110 mmHg should have BP lowered before the intervention. A persistent SBP of 185 mmHg or a DBP 110 mmHg is a contraindication to intravenous thrombolytic therapy. After reperfusion therapy, keep SBP below 180 mmHg and DBP below 105 mmHg for at least 24 h. Second, patients who have other medical indications for aggressive treatment of BP should be treated. Third, for those not receiving thrombolytic therapy, BP may be lowered if it is markedly elevated (SBP 220 mmHg or DBP 120 mmHg). A reasonable goal would be to lower BP by approximately 15% during the first 24 h after onset of stroke. Fourth, in hypotensive patients, the cause of hypotension should be sought. Hypovolemia and cardiac arrhythmias should be treated, and in exceptional circumstances, vasopressors may be prescribed in an attempt to improve cerebral blood flow.

In patients not on chronic antihypertensive treatment, with a baseline systolic pressure between 180 and 220 mmHg and diastolic pressure below 120 mmHg, antihypertensive therapy should be deferred for the first 48 h after an ischemic stroke, unless thrombolytic therapy is indicated. On the contrary, in patients already on oral antihypertensive therapy prior to the acute event with baseline BP within the above-mentioned range, antihypertensive therapy should be given to avoid rebound hypertension, with the aim of maintaining 180–220 mmHg systolic and less than 120 mmHg diastolic. If systolic pressure is higher than 220 mmHg and diastolic higher than 120 mmHg, intravenous antihypertensive drugs are recommended (i.e. labetalol) to keep BP around 180/100–105 mmHg. It is important to select rapidly reversible agents in case neurologic signs and symptoms worsen with the BP reduction. Later on, BP should be reduced gradually during the first week after ischemic stroke to prevent recurrent stroke and reduce cardiovascular risk.

### Haemorrhagic stroke

Strokes are haemorrhagic in 15% of the patients and patients with intracerebral haemorrhage (ICH) often have elevated BP. Approximately one-third of all patients with ICH presenting within 3 h of symptom onset have a significant expansion of the haematoma over the next 20 h. Initial haematoma volume and haematoma expansion are powerful predictors of mortality after ICH. Some studies have suggested an association between high BP and haematoma expansion.[67] Only recently, it has been demonstrated that intensive lowering of BP improved functional outcomes in patients with intracerebral haemorrhage even if it did not result in a significant reduction in the rate of the primary outcome of death or severe disability.[62]

Accordingly, AHA/ASA Recommendations for BP Management in Acute Cerebral Hemorrhage[68] state that, first, if SBP is higher than 200 mmHg or mean arterial pressure (MAP) is higher than 150 mmHg, consider aggressive reduction of BP. Second, if SBP is higher than 180 mmHg or MAP is higher than 130 mmHg and intracerebral pressure (ICP) may be elevated, consider monitoring ICP and reducing BP to keep cerebral perfusion pressure between 60 and 80 mmHg. Third, if SBP is higher than 180 mmHg or MAP is higher than 130 mmHg and there is no evidence of or suspicion of elevated ICP, consider modest BP reduction (e.g. MAP of 110 mmHg or target BP of 160/90 mmHg).

In patients with SAH, aneurysmal rebleeding is a major cause of morbidity and mortality. Prior studies suggest a relationship between SBP in the range of 160–200 mmHg and aneurysmal rebleeding. Modest elevation of BP (<110 mmHg MAP or <160 mmHg SBP) is likely not associated with aneurysmal rebleeding and modest BP increases do not necessarily need to be treated. Only extreme levels of BP are treated and hypotension is avoided when there is a still unsecured aneurysm. Furthermore, stepwise BP augmentation with careful monitoring of neurologic status has been used to treat delayed cerebral ischemia related to vasospasm.

## Acute aortic dissection

Although relatively uncommon, with an estimated prevalence ranging from 5000 to 10 000 cases in the United

States per year,[69,70] acute aortic dissection represents a major challenge in emergency cardiovascular medicine,[71] with an estimated acute mortality around 40%. Diagnosis is very often delayed or even missed, yielding an additional 1% rate of death per hour. Overall, 1-year mortality is around 90%.[72] A high degree of diagnostic suspicion is very important for the emergency clinician, in order to promptly activate a proper diagnostic workup and the subsequent treatment algorithm, its key decision being related to indication and timing of the surgical option.

In the setting of the ED, the incidence of acute aortic dissection is approximately 1 in 10 000 patients. A 'classical' presentation (i.e. pain of sudden onset or ripping/tearing quality, BP differential and widened mediastinum on chest radiograph) is detectable in only one quarter of cases.[72] Furthermore, signs and symptoms may well be related to any organ system or body part, according to the localization and the progression of the aortic wall dissection and the extension of the false lumen across the ostia of branch arteries, causing acute ischemia of potentially any organ in the body. According to the Stanford classification, Type A dissections involve the ascending aorta, whereas Type B dissections are confined to the descending aorta.[73] Variants of aortic dissection include aortic intramural haemorrhage and penetrating aortic ulcer. Type A dissections are more common, entail a much worse prognosis and may progress proximally causing hemopericardium with cardiac tamponade, acute aortic valve regurgitation as well as acute myocardial infarction. Neurological symptoms may be caused by the involvement of the carotid arteries.

Diagnostic suspicion can be raised by pain at presentation, ischemia-related symptoms and the presence of asymmetric radial, carotid and femoral arteries. When the diagnosis of acute aortic dissection is suspected, prompt imaging evaluation and surgical team consultation might be lifesaving, given the risk of impending free rupture into the chest or abdomen. According to the local availability, aortic imaging via trans-oesophageal echocardiography, CT scan with intravenous contrast or MRI may confirm (or reasonably exclude) the diagnosis.[73] Concomitantly, immediate surgical consultation should be arranged, regardless of anatomic location and cause,[74] although Stanford B dissections may ultimately be managed nonsurgically.[73] Apart from arterial hypertension, several genetic syndromes as well as arterial inflammatory diseases may be associated with a higher risk for acute aortic dissection.[73]

The goal of medical therapy is to control heart rate, BP and pain, in an attempt to minimize further tension and damage to the aortic wall. Treatment with rapid-acting, titratable agents to first lower heart rate (to 60 beats/min) and then SBP to a goal of less than 120 mmHg is mandatory. Ideally, BP should be titrated to as low as end organs allow, with attention to measuring BP in both arms. Obviously, any drug interfering with blood coagulation should be avoided whenever signs or symptoms of myocardial or cerebral ischemia are associated with the suspicion of acute aortic dissection.

## Conclusion

The approach in the acute hypertensive setting is not yet well established. In asymptomatic patients who present to the ED with markedly elevated BP (including hypertensive urgencies and uncontrolled hypertensive patients), the optimal screening, treatment and follow-up interval, as related to the short-term and long-term clinical outcomes, need to be addressed in the future. Treatment aspects of hypertensive emergencies and urgencies vary widely according to a patient's clinical conditions and are largely based on the experience rather than evidence.

Few randomized clinical trials have addressed the short-term and long-term effects of acute BP lowering on cardiac and cerebrovascular morbidity and mortality in the setting of hypertensive emergencies; data are even more scarce in hypertensive urgencies.

Therefore, it would be desirable to collect further, robust data in order to provide evidence-based recommendations on the diagnostic and therapeutic aspects of these conditions.

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