Consensus document ANMCO/FADOI/SIAARTI/SIC/SIMG/SIMI/SIMEU: The clinical-diagnostic and therapeutic pathway of patients with acute heart failure in the Emergency Department

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ABSTRACT

Acute heart failure (HF) involves hospitals throughout the world and, as well as other acute cardiac pathologies such as coronary syndromes, has markedly unfavorable outcomes: the mortality or rehospitalization rate after 3 months is 33%, mortality 1 year after admission varies between 25% and 50%. A critical factor in managing acute HF is the multiplicity of health professionals involved in the diagnostic-therapeutic pathway of this syndrome - general practitioners, emergency doctors, cardiologists, internists, anesthesiologists/resuscitators - and therefore also the need to integrate different knowledge and skills and converge on care goals that can improve clinical outcomes. This consensus document originates from the joint work of the Scientific Societies, representing various professional figures involved in assisting patients with acute HF, and has shared strategies and pathways aimed at guaranteeing both quality care levels and better outcomes. The document details the entire journey of the patient with acute HF from the onset of symptoms at home, diagnosis, home management or sending to the Accident & Emergency/Emergency Admissions Department (A&E/EAD), mode of transport, early therapy, through the instrumental clinical pathways for diagnosis in A&E/EAD and the treatment, risk stratification and discharge of the patient in ordinary hospitalization or at home. It also analyses the possible role of cardiological *fast-track*, Short Intensive Observation and regional welfare taking charge through general medicine and specialist clinics for the care of HF. The growing care burden and the complex problems generated by acute HF cannot find an adequate solution without an integrated multidisciplinary approach that effectively places emergency facilities in the network along with intensive and ordinary hospitalization units and within the context of regional care. Thanks to contributions from the most qualified Scientific Societies, this document pursues this objective by proposing a structured, shared and applicable pathway which can contribute to manage a widespread problem in the country.

Introduction

Rationale and objectives of the document

The rapid onset *ex novo* of a spectrum of signs and symptoms, or the worsening of a pre-existing condition of chronic heart failure (HF) define the acute HF syndrome, a potentially lethal clinical condition, which requires urgent treatment to prevent multiorgan deterioration, secondary to congestion and visceral hypoperfusion.[1,2] The heterogeneity of the clinical phenotypes of acute HF, which includes different pictures such as pulmonary edema, exacerbation of chronic congestive HF, cardiogenic shock, together with the wide spectrum of ventricular dysfunction that can be observed at the same time of diagnosis,[3] contribute to the poor progress made in treating the acute syndrome.

A critical factor in managing acute HF is the multiplicity of health professionals involved in the diagnostic-therapeutic pathway of this syndrome - general practitioners, emergency doctors, cardiologists, internists, anesthesiologists/resuscitators - and therefore also the need to integrate knowledge and different skills and converge on care goals that can improve clinical outcomes.

This inter-organizational consent document promoted by the Heart Failure Department of the National Association of Hospital Cardiologists (ANMCO) arises from the need to channel the skills of the various professionals involved in caring for patients with acute HF in a shared care pathway; from the pre-hospital phase to access and discharge from the Accident & Emergency/Emergency Admissions Department (A&E/EAD) for hospitalization or return home.

The growing care burden and the complex problems generated by acute HF cannot find an adequate solution without an integrated multidisciplinary approach that effectively places emergency facilities in the network along with intensive and ordinary hospitalization units and within the context of regional care. The joint work of the Scientific Societies, representing the various professional figures involved in assisting patients with acute HF, therefore appeared a fundamental moment to share strategies and pathways aimed to guarantee both quality care levels and better outcomes, in a potentially similar way throughout the country.

This consensus document aims to analyze the entire pathway of the patient from the onset of acute HF symptoms at home to discharge from A&E/EAD: i) The pre-hospital pathway: diagnosis, home management or referral to A&E/EAD, mode of transport to A&E/EAD, early pre-hospital therapy; ii) Diagnosis in A&E/EAD, clinical instrumental pathways and treatment; iii) Risk stratification and discharge from A&E/EAD; iv) The possible role of the cardiological *fast-track* and the Short Intensive Observation (SIO); v) Home discharge from A&E/EAD: the GP and the specialist clinic for treating heart failure (cardiological/internist/multidisciplinary).

Epidemiology

Acute HF represents a heavy burden for hospitals throughout the world. In the United States and Europe, over 1 million hospitalizations are reported each year for acute HF,[1-4] and the national data related to 2015 document over 220,000 hospitalizations in Italy.[5] In comparison with other acute cardiac pathologies, such as coronary syndromes, the long-term outcomes for patients with acute HF are markedly unfavorable: within 3 months, approximately one third of them are deceased or re-hospitalized, while 1 year after hospitalization, mortality varies between 25% and 50%.[3,6,7]

The A&E/EAD, where the majority of patients with acute HF are admitted, are responsible for diagnosis classification, first clinical stabilization and choice of the subsequent care pathway. Although in the majority of cases A&E/EAD represents the first point of access to hospital care for patients with acute HF, the literature data on clinical features and treatments adopted come mainly from registers, especially the cardiological ones,[3,8] for patients who are already hospitalized, or from administrative databases, lacking clinical correlation and with a fragmented picture of the syndrome complexity. Few studies have specifically analyzed non-hospitalized patients who are discharged directly from A&E/EAD.[9-14]

Acute HF is a syndrome of the elderly with an average age in the eighth decade of life, a gender distribution that follows the demographics of old age and a high prevalence of recurrent forms of chronic exacerbated HF. In the absence of consolidated recommendations, the choice of pathway for the patient with acute HF to follow downstream of A&E/EAD is, to date, based mainly on the clinical presentation and internal organization of the hospital; the great variability in hospitalization rates is therefore not surprising. While in the US about 80% of patients coming to A&E/EAD are admitted,[4] as well as seen in the Italian SAFE study (77.2%),[14] in other countries up to a third of patients are discharged directly from A&E/EAD.[10-13]

In Italy, the data analyzed for patients admitted to the EAD, compared to cardiology registers,[14-17] show a higher age and a greater frequency of medical comorbidities, due to the high proportion of patients (65-75%), that are hospitalized in internal medicine departments, rather than in cardiology (Table 1).

Table 1. Italian observational studies on patients with acute heart failure.

	SAFE[14] (n=2683)	AHF Survey[15] (n=2897)	IN-HF Outcome[16] (n=1855)	CONFINE[17] (n=1411)
Context	A&E/EAD	Cardiology	Cardiology	Medicine
Age (years)	84±12	73±11	72±12	78.7±9.6
Sex: female (%)	55.8	39.5	39.8	51.6
De novo heart failure (%)	55	44	43	37
Hypertension (%)	na	65.6	57.8	62.8
CRF (%)	26.6	24.7	32.5	44.2
COPD (%)	29.8	29.7	30.1	26.7
Diabetes (%)	31.1	38.4	40.4	32.5
Anemia (%)	nd	49	38.7	40.5
Ischemic etiology (%)	23.8	46	42.3	44.5
Atrial fibrillation (%)	47.1	21	37.7	42.7
Ejection fraction (%)	35.8% (<40%)	66% (40%)	38±14	43.1±12.3
Systolic blood pressure (mmHg)	138±40	141±37	134±33	141±27
Blood sodium <136 mEq/L (%)	–	45	19	28
Blood creatinine (mg/dL)	50±22*	1.7±1	1.2 (1.0-1.6)	1.5±0.9
In-hospital mortality (%)	2.5 (in EAD)	7.3	6.4	4.4
Duration of stay (days)	–	9 [6-13]	10	14.1±10
Infusion therapy (%)				
Diuretics	69.2	95.3	99.4	–
Nitrates	19.7	49.5	29.9	–
Inotropes	NA	24.6	19.4	–

COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; NA, not available; A&E/EAD, Accident & Emergency/Emergency Admissions Department. *Glomerular filtration rate in mL/min/1.73 m^2.

Scale of the problem, hospital mortality *vs* non-hospital mortality

Although only a minority (<10%) of patients with acute HF present critical conditions with impaired vital functions,[4-9] there is frequent recourse to hospitalization due to the intrinsic difficulty in confirming the diagnosis and etiological identification, particularly in new-onset HF, and in risk stratification, due to the low probability of resolving short-term symptoms and frequent comorbidities. Moreover, there are few pieces of evidence on the identification of patients at low risk of major events, which can therefore be safely discharged. Analysis of administrative databases shows that in patients with acute HF, direct discharge from A&E/EAD is associated with significant mortality rates (1.3% at 7 days and 4% at 30 days),[10] decidedly higher than the figure of 1% observed in patients with chest pain.

High risk markers are well identified: several studies have highlighted the role of variables such as hypotension, renal dysfunction, hyponatremia, high troponin concentrations and natriuretic peptides, in conditioning an unfavorable prognosis.[18,19]

It is more complex to identify patients who are at low risk of major events in the short term, and therefore eligible for home discharge. The dissemination of tools specifically validated in the context of A&E/EAD for better prognostic stratification could help clinicians in emergency departments to identify patients with acute HF who need to be treated at different care intensity levels in hospital[20,21] (Figure 1).

Pre-hospital management

Onset of symptoms and suspected diagnosis of acute heart failure: pre-hospital diagnosis

In about 50% of patients with acute HF, a long pre-hospital delay has been reported (Table 2) in treating the disease, which can reach up to 7 days.[22] Recognition, interpretation and awareness of the importance of symptoms can influence the delay. Most patients with HF present a gradual worsening of symptoms during the previous days or weeks, and often wait for a long time before seeking medical assistance due to poor awareness.[22-24] Some factors such as character traits, the presence or absence of caregivers and psychological symptoms like depression can prolong pre-hospital care times.[25] Other patients wait longer because they tend to underestimate the symptoms, remembering that they have already gone through similar phases, or only react to very major changes in symptoms, because they have been accustomed to high levels of sufferance.[26] For example, in the multi-

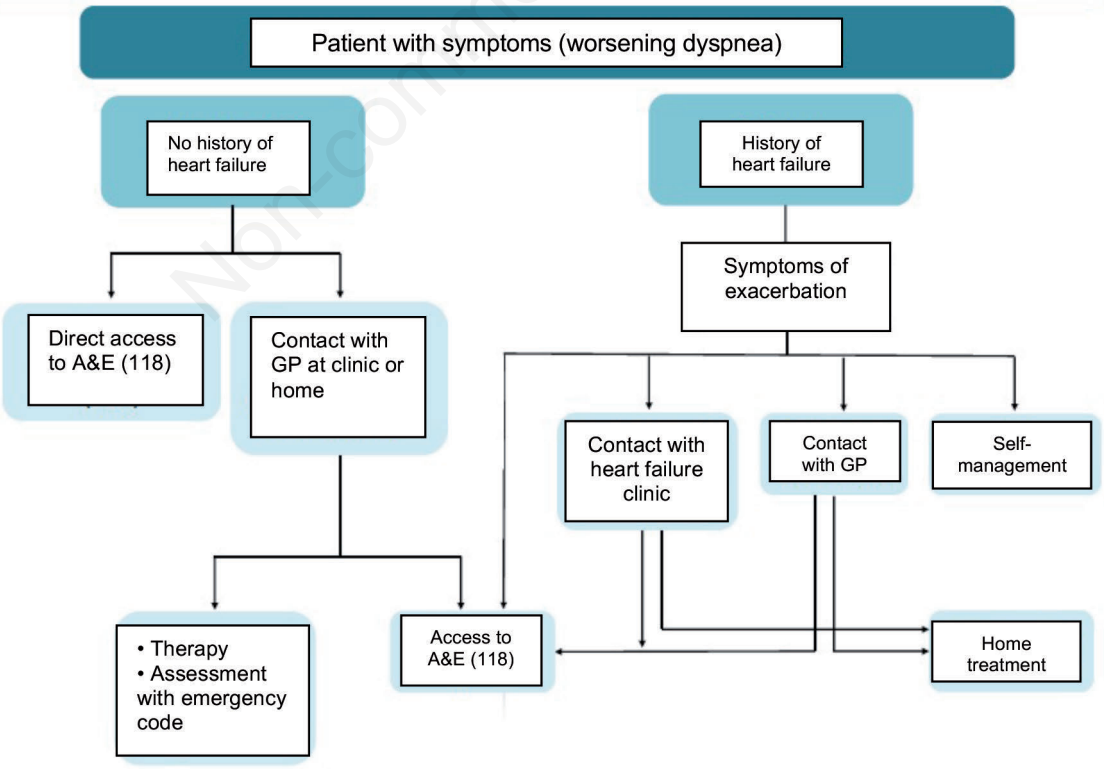

Figure 1. The pathway of the patient with signs and symptoms of heart failure at home. GP, general practitioner; A&E, Accident & Emergency.

method study (individual interviews associated with questionnaires) by Jurgens,[27] over half of the patients studied did not know the cause of their symptoms, and almost a third attributed them to conditions unrelated to heart disease. Furthermore, half of the patients reported that they did not know the symptoms related to HF and did not understand their importance. Nearly 87% of patients felt that their symptoms had a certain degree of severity, but most (80%) preferred to wait before calling for help.

In a relatively recent meta-analysis, Gravely-Witte *et al*.[25] showed that reducing waiting time for effective treatment of HF symptoms could reduce the severity of clinical instability, hospitalization time and mortality. In over 58,000 patients observed in the ADHERE study of 209 American hospitals, the delay between onset of symptoms and treatment, which was also associated with the delay in determining plasma levels of brain natriuretic peptide (BNP), was related to a significant though modest increase in in-hospital mortality, with an adjusted odds ratio (OR) of 1.021 (confidence interval [CI] 95% 1.010-1.033, P<0.0001) for each 4-h delay.[28] A recent paper on the Tokyo emergency network experience, which analyzed the relationship between time of symptom onset for acute HF and arrival to hospital, showed that a shorter time between symptom onset and hospitalization was associated with lower in-hospital mortality (OR 0.71, 95% CI 0.51-0.99; P=0.043).[29] However, other studies have not confirmed these data. Johansson *et al*.[30] analyzed data from 1023 patients hospitalized for acute HF in the COACH study. Patients who arrived to hospital with a delay of less than one day had a shorter hospital stay (10 *vs* 11 days, P=0.033) and a significantly lower BNP value (377 *vs* 492 pg/mL, P<0.05) compared to those who waited several days, but there was no significant difference in terms of mortality and rehospitalization for HF.

In general, both the latest guidelines from the European Society of Cardiology (ESC)[1] and European recommendations for managing patients with acute HF in the pre- and post-hospital phases[31] recommend: i) including patients with chronic HF in disease management programs integrated with tuition in home self-care and knowledge of signs and symptoms; ii) reducing the delay from symptom onset to the beginning of therapy in the case of clinical instability, accelerating the time of access to health facilities but also starting some therapeutic measures outside the hospital (see following paragraphs). However, at the moment the recommendations available are not based on the efficacy documented by clinical studies, but rather on expert opinions.

Diagnosing acute HF at patient's home can be simple, especially in the case of exacerbation of known chronic HF, but often requires health personnel to have experience and knowledge of the patient and the illness. The cardinal point of the diagnosis, even outside the hospital, is recognizing those symptoms that can be strongly indicative of an episode of acute HF (Table 3).

Therapy outside the hospital

Non-hospital treatment of HF has some limiting factors: i) reasonable certainty of the diagnosis in patients with HF *de novo* rather than chronic exacerbations, also considering the importance of the clinical context and risk factors; ii) identification and correction of the triggering factors; iii) the significance of comorbidities with respect to the possibility of stabilizing the clinical picture.

The initial treatments anticipated for the non-hospital phase are to a large extent the same ones that occur in the hospital phase (Table 4): oxygen therapy in patients with significantly reduced oxygen saturation (<90%) and tachypnoea; diuretic therapy in those who are severely congested; vasodilators (sublingual nitroglycerin) in those with high blood pressure, taking into account that diuretic therapy by itself may result in reducing blood pressure, and that aortic murmurs may suggest caution as they are indicative of aortic stenosis. Early use of NIV is in part limited by the availability of adequate technology, as well as

Table 2. When to send patients to Accident & Emergency/Emergency Admissions Department.

Severe exacerbation
• Dyspnea not responsive to diuretic therapy • Acute pulmonary edema • Signs of severe congestion (orthopnea, hepatomegaly, ascites, edema) • Oligoanuria • Severe hypotension (systolic blood pressure <80-90 mmHg)
Causes that cannot be managed at home
• Arrhythmias (tachycardia >120 b/min, arrhythmic pulse, bradycardia <40 b/min) • Myocardial ischemia • Suspected pulmonary embolism • Severe respiratory infections
Inadequate home care

by the presence/absence of evidence of right ventricular dysfunction or valvular diseases - in particular hemodynamically significant aortic stenosis, which may promote or exacerbate hypotension. Other therapies, excluding those for cardiorespiratory and emergency circulatory resuscitation, require a hospital setting to be performed in safety.[31]

Modes of transportation to hospital

Transportation to the hospital should preferably take place in an equipped ambulance.

Among the diagnostic possibilities we should consider simple equipment (oximeter, electrocardiograph), up to more complex instruments with imaging and *point of care* techniques with various biohumoral tests. A position paper by the ESC's Acute Cardiovascular Care Association took into consideration the possible diagnostic and therapeutic equipment that should be present on the ambulance, underlining the fact that they must be adapted to the crew's skills. The patient should be transported safely, after the staff has found a peripheral venous line, applied a monitor-defibrillator and used oxygen in the mask, so as to stabilize the clinical conditions as much as possible. In addition to the measures recommended by manuals for advanced cardiac life support (ACLS), particular attention must be given to ventilation and oxygen therapy. In the event of respiratory distress (arterial oxygen saturation [SaO_2] <90%, respiratory rate >25 breaths/min, orthopnea and increased respiratory work), NIV with continuous positive airway pressure (CPAP) should be favored over oxygen therapy alone.

Regarding patients with significant desaturation, it is important to rule out a picture of chronic respiratory failure due to chronic obstructive pulmonary disease (COPD) where the administration of high-flow oxygen could be fatal.

The patient should be transported in a manner defined by an organizational document, similar to what happens for the STEMI Network. A patient presenting signs of low flow suggesting shock should be transported to dedicated third-level facilities, as recommended by the European and American guidelines.[1,32]

Hospital management

From the onset of symptoms at home, the patient can access A&E/EAD directly by self-presentation or sent by medical personnel (Figure 2). Upon presentation the triage nurse, on the basis of operational

Table 3. Signs and symptoms of acute heart failure.

Symptoms	
More typical	Dyspnea at rest and on exertion, orthopnea, paroxysmal nocturnal dyspnea, asthenia
Less typical	Night cough, dizziness, loss of appetite, dyspepsia, abdominal pain, confusion, loss of consciousness, palpitation
Signs	
More specific	Lung rales, jugular turgor, hepato-jugular reflux, third tone, galloping rhythm, lateralization of the impulse
Less specific	Weight gain or weight decrease, heart murmurs, peripheral edemas, jaundice, reduction of tactile vocal fremitus, respiratory murmur and basal dullness, tachycardia, irregular and hyposphagmatic pulses, tachypnea, hepatomegaly, ascites, skin cold at the extremities, diaphoresis, oliguria

Table 4. Possible therapeutic interventions in the home in relation to clinical scenarios.

Non-hospital scenarios	Therapeutic options	Possible contraindications	Who can do it
SaO_2 <90% in ambient air, tachypneic	O_2 for Venturi, FiO_2 adequate for target (SaO_2≥95%)	Absence of tachypnoea, suspected carbo-narcosis, SaO_2≥95%	Patient, doctor, nurse, 118 [emergency medical service (or equivalent)]
Chest rales, with/without peripheral edema, with/without chest dullness suspected for pleural effusion	Furosemide from 20 to 40 mg IV, repeatable after 5-10 min if congestion persists, tachypnoea, tachycardia and hypertension	Hypotension (systolic blood pressure <90 mmHg), systolic murmur from suspected aortic stenosis	Doctor, 118 (or equivalent)
Systolic blood pressure >160 mmHg and absence of bradycardia (HR >50 b/min)	Furosemide from 20 to 40 mg IV, repeatable after 5-10 min, evaluate sublingual nitroglycerin/ nifedipine	Tachycardia (HR >120 b/min), systolic murmur from suspected aortic stenosis	Doctor, 118 (or equivalent), patient (therapy)

IV, intravenously; HR, heart rate; FiO_2, inspiratory fraction of oxygen; SaO_2, arterial oxygen saturation.

protocols based on rapid data collection, medical history, vital parameters and a brief objective examination, assigns a color code defining the priority of access to medical evaluation and the necessity and timing of re-evaluating the clinical condition. The new ministerial directive, not yet in force, will modify the color code by adding a clinical emergency-urgency criterion.[33]

Triage of the patient with suspected heart failure

Most patients in A&E have a picture characterized by stable hemodynamics with signs and symptoms of congestion. Only a minority of patients present a critical clinical picture, which strongly affects short-term mortality,[7] with impairment of one or more vital functions (Figure 2). Due to the extreme heterogeneity of clinical pictures and presentation modes, in the initial stages critically ill patients are managed by medical personnel with different skills and training (emergency doctor, cardiologist, intensivist). It is crucial to apply a shared diagnosis and treatment pathway in order to accelerate the etiological definition and reduce mortality and hospitalization time,[34,35] thereby improving the prognosis.

Diagnostic-therapeutic pathway of the patient with critical acute heart failure

The medical evaluation - which should take place within 10 minutes - and the warning signs/symptoms, are used to identify highly serious clinical pictures with a risk of unfavorable evolution in the very short term. The elements to be evaluated for clinical decisions include (Figure 2):

1. Main vital parameters: systemic arterial pressure, heart rate, SaO_2, body temperature.
2. Characteristics of the presentation symptom(s), history of chronic HF, triggering factors.[36,37]
3. Physical examination: signs of congestion or hypoperfusion.[38]
4. 12-lead ECG: essential to rule out an acute coro-

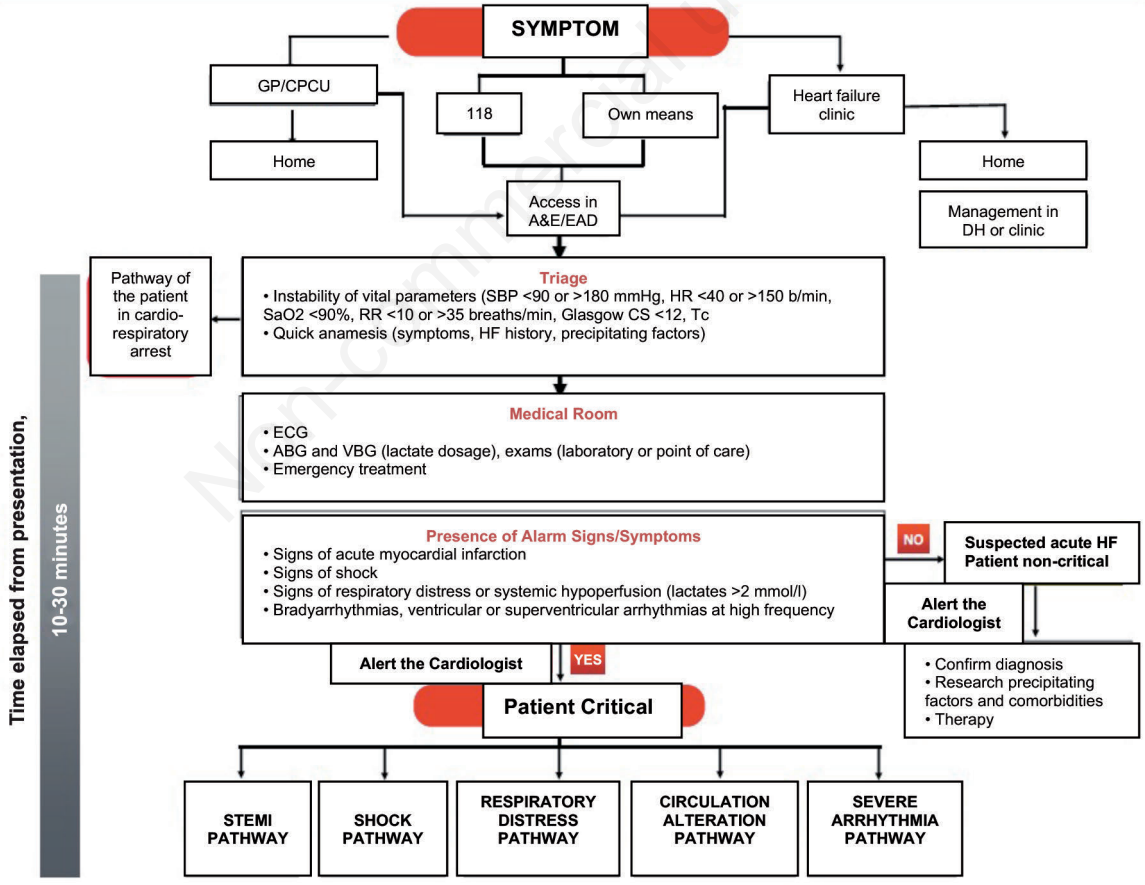

Figure 2. Operational flow chart of the patient accessing Accident & Emergency/Emergency Admission Department (A&E/EAD) from home with suspected symptoms of acute heart failure (HF). CS, coma scale; DH, day-hospital; ECG, electrocardiogram; ABG, arterial blood gas test; VBG, venous blood gas analysis; HR, heart rate; RR, respiratory rate; GP, general practitioner; SBP, systolic blood pressure; SaO_2, arterial oxygen saturation; STEMI, myocardial infarction with ST-segment elevation; CPCU, complex primary care unit.

nary syndrome, but also to highlight the presence of precipitating causes such as atrial fibrillation or a high-frequency ventricular or supraventricular arrhythmia.

5. Arterial blood gas (ABG) analysis on arterial or venous blood: the increase in plasma lactate concentration may be linked to increased production due to reduced oxygen intake or difficult peripheral utilization,[39] reduced elimination (in the case of hepatic or renal insufficiency), or a combination of these.[40] The increase in lactates during shock is a validated diagnostic marker of global tissue hypoxia[35,41] with therapeutic consequences; not only the initial value of lactates, but above all the trend over time is useful in a clinical and prognostic sense.[42-44]
6. Hematochemical tests: these allow diagnostic confirmation of acute coronary syndrome (troponin), acute HF (BNP) or pulmonary embolism (D-dimer),[45] and point to the coexistence of other relevant clinical problems (blood count, creatinine, electrolytes, glycemia, liver function and thyrotropin).

For patients transported by ambulances with medical personnel, the availability of some of the aforementioned information upon arrival in A&E/EAD, facilitates the patient's in-hospital pathway and allows more prompt treatment.

Pathway of the patient in cardiorespiratory arrest

In all unconscious patients presenting a clinical picture of cardiovascular arrest, cardiopulmonary resuscitation must be started/continued and every effort must be made to show the responsible, but potentially reversible, cause of cardiorespiratory arrest (Figure 3).

For such patients the cardiologist must be called immediately, in addition to the emergency medicine doctor and the resuscitator. The first will pay particular attention to the search for electrocardiographic signs of acute myocardial infarction, in order to rapidly start the patient on the STEMI pathway; the second will ensure advanced airway and ventilation management. Together they will evaluate aspects related to advanced care with extracorporeal membrane oxygenation and post-arrest treatment.

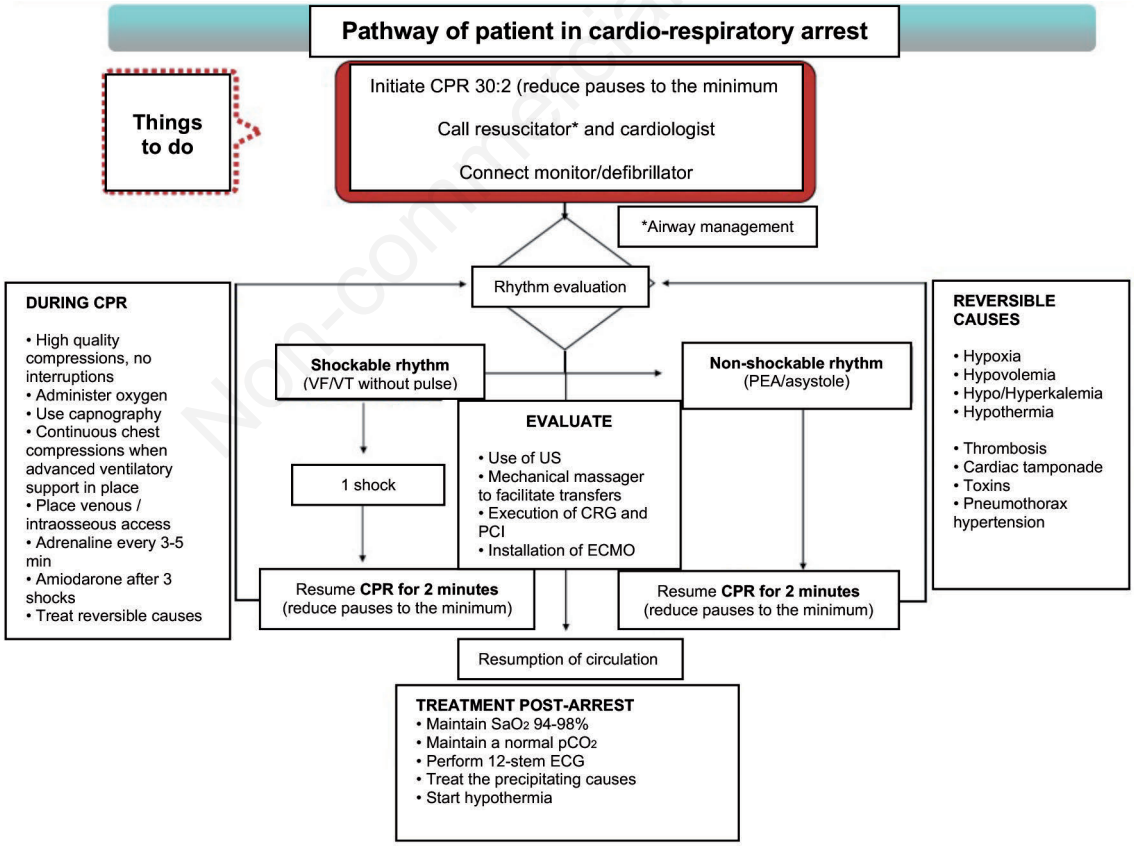

Figure 3. The pathway of the unconscious patient in cardiorespiratory arrest. CRG, coronarography; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; VF, ventricular fibrillation; PCI, percutaneous coronary intervention; pCO_2, partial pressure of carbon dioxide; PEA, pulseless electric activity; CPR, cardiopulmonary resuscitation; SaO_2, arterial oxygen saturation; VT, ventricular tachycardia; US, ultrasound.

Pathway of the patient with acute coronary syndrome

The pathway of the patient with high-risk STEMI or NSTEMI and the signs and symptoms of acute HF must provide for immediate involvement of the specialist cardiologist, to help refine the clinical picture and plan the revascularization strategy, with early deployment of the hemodynamic monitoring room, if available, for emergency coronary angiography.

STEMI pathway

A specific pathway for the patient with STEMI is shown in Figures 4 and 5. The pathway is differentiated based on the availability of a hemodynamic laboratory in the hospital and on the opportunity to perform percutaneous revascularization procedures.[46]

In the presence of respiratory distress or signs of hemodynamic instability, it may be necessary to stabilize the patient in A&E before taking him/her to hemodynamics.

As described in Figure 4, in the absence of hemodynamic and/or respiratory problems, the transfer to the hemodynamic monitoring room must be immediate, to perform primary angioplasty within 60-90 min, pretreating the patient with intravenous (IV) heparin and antiplatelet agents according to the guidelines.[46] While waiting for transport to the hemodynamic monitoring room, the echocardiographic examination allows estimation of the left ventricular function before the procedure and assessment of any mechanical complications of the infarct. Pressure values >160 mmHg require starting infusion of vasodilators without delaying the transfer. Patients with STEMI and associated low-flow signs require the administration of vasopressor or/and inotropic agents, often concurrently with transfer to the hemodynamic monitoring room (Figure 5).

Pathway of the patient with respiratory distress

In the patient with respiratory distress, defined as a respiratory rate <10 or >35 breaths/min and/or peripheral oxygen saturation (SpO_2) <90%, the goal of treatment is to restore adequate blood oxygenation, initially administering oxygen to ensure SpO_2 >90% (Figure 6). Where oxygen therapy is insufficient to resolve the picture, NIV devices may be used, including

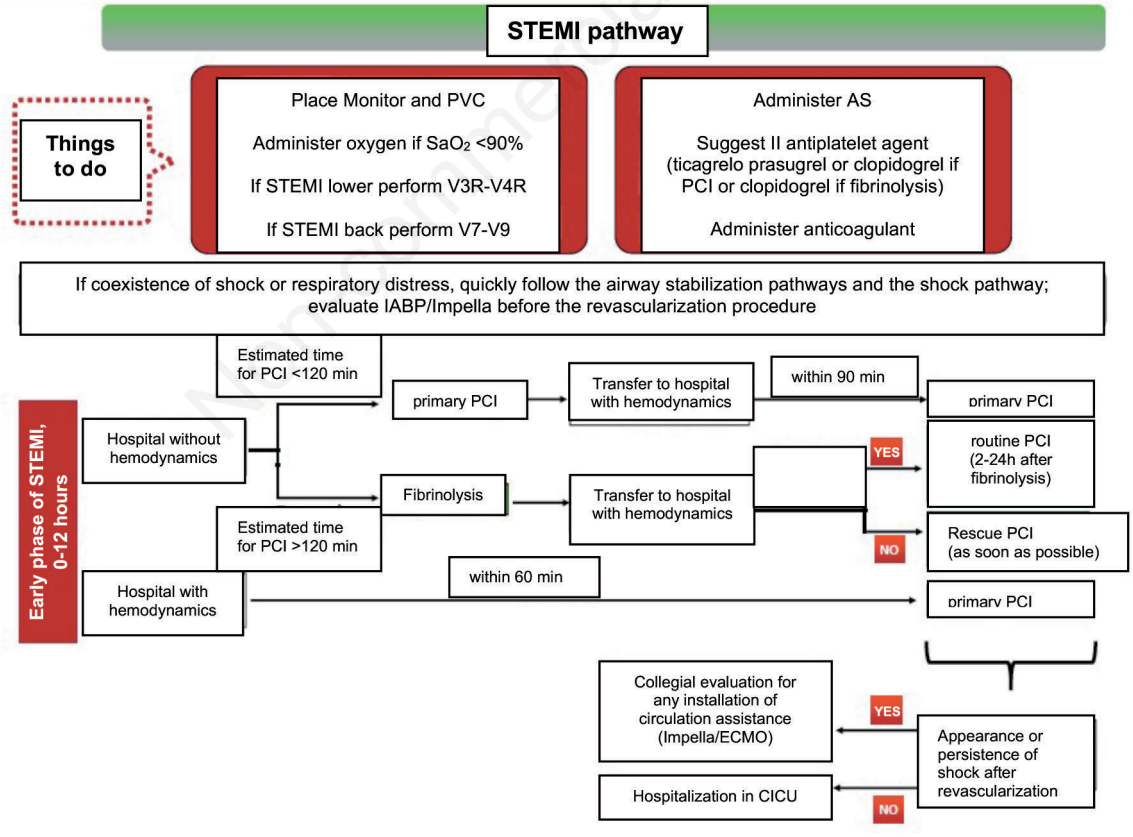

Figure 4. The pathway of the patient with heart failure and acute coronary syndrome, myocardial infarction type with (STEMI) and without high-level ST segment elevation. AS, aspirin; PVC, peripheral venous catheter; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; PCI, percutaneous coronary intervention; CICU, cardiac intensive care unit.

CPAP and pressure support with positive end expiratory pressure (PS-PEEP).

Pathway of the patient with altered circulation and pressure profile

Besides managing respiratory distress, it is essential to control the pressure profile (Figure 7).

Patients who are hypertensive or normotensive at onset are likely to suffer from a maldistribution of fluids, as well as an actual overload. In addition to diuretics, then, the treatment can involve vasodilators, which in Italy are represented only by nitrates (nitroglycerin, isosorbide dinitrate, nitroprusside), as nesiritide is not approved (Table 5).

Pathway of the patient in shock

A patient who is critically ill with clinical and hematochemical signs of peripheral hypoperfusion, except for high-risk electrocardiographic pictures of STEMI or NSTEMI or arrhythmic instability, must be included in the management and treatment pathway dedicated to shock. Figure 8 shows the suggested procedure for patients presenting a picture of shock, defined as SBP <90 mmHg for more than 30 min, associated with signs of pulmonary congestion and at least one sign of organ hypoperfusion. It is important to remember that simple hypotension does not identify a state of shock.

An immediate echocardiographic examination is

Table 5. Method of using nitrates.

Vasodilator	Dose	Side effects	Comments
Nitroglycerin	Starting at 10-20 µg/min Max 200 µg/min	Headache, hypotension	–
Isosorbide dinitrate	Starting at 1 mg/h Max 10 mg/h	Headache, hypotension	Non-linear dose/response
Sodium nitroprusside	Starting at 0.3 µg/kg/min Max 5 µg/kg/min	Marked hypotension, thiocyanate toxicity	Used in CICU not in A&E/EAD

A&E/EAD, Accident & Emergency/Emergency Admission Department; CICU, cardiac intensive care unit.

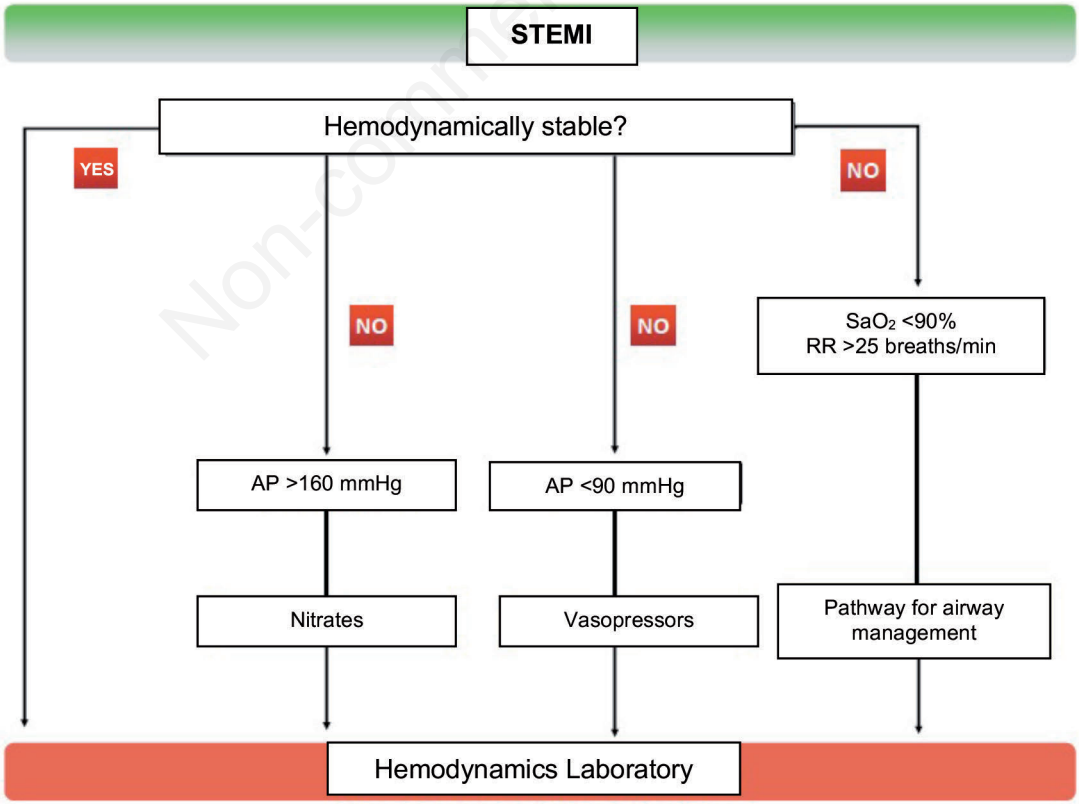

Figure 5. Therapy and transfer of the patient with myocardial infarction with (STEMI) and without elevation of the ST segment at high-risk. RR, respiratory rate; AP, arterial pressure; SaO_2, arterial oxygen saturation.

indicated for all patients who present a picture of cardiogenic shock or hemodynamic instability,[46,47] in order to obtain the important information (Table 6).

Treatment of shock

Cardiogenic shock begins as a purely hemodynamic problem but rapidly evolves into a hemodynamic-meta-

Table 6. Role of echocardiography for the patient in shock.

Evaluation structure	Diagnostic framework	Therapeutic approach
Left ventricle	Sisto-diastolic dysfunction in left ventricle Left ventricle small and hyperkinetic, LVH with obstruction of efflux	Inotropic support Adaptation of blood volume/control of HR
Right ventricle	Dilatation and dysfunction, right ventricle Estimate PAP increase	Research PTE, fibrinolysis Assess inotropic therapy
Lower vena cava (diameter and collapsibility)	Venous congestion Hypovolemia	Diuretics, vasodilators Correction of blood volume
Mitral and aortic valve	MI severe massive Mitral and aortic stenosis Aortic insufficiency	Vasodilator, diuretic Blood volume adjustment, HR and AP control, diuretics
Pericardium	Plugging pericardial effusion	Pericardiocentesis

HR, heart rate; MI, mitral insufficiency; LVH, left ventricular hypertrophy; AP, arterial pressure; PAP, pulmonary arterial pressure; PTE, pulmonary thromboembolism.

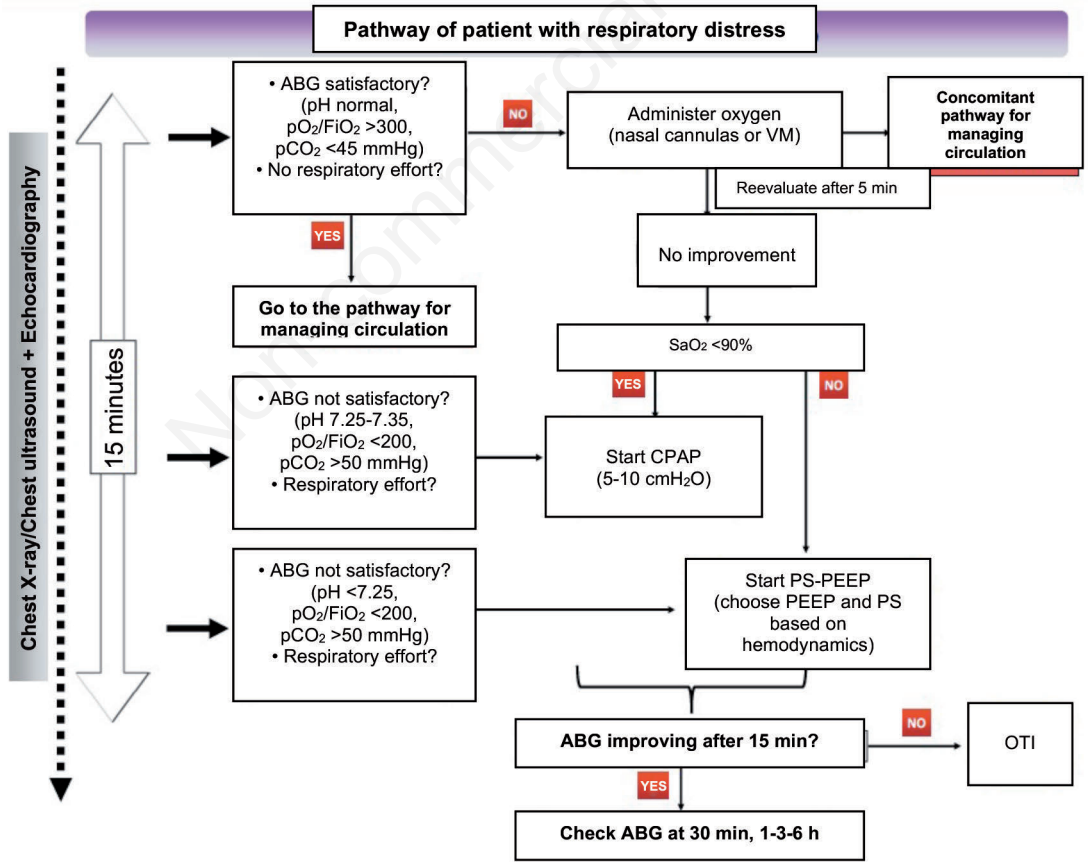

Figure 6. The pathway of the patient with respiratory distress. CPAP, continuous positive airway pressure; ABG, arterial blood gas test; OTI, orotracheal intubation; VM, Venturi mask; pCO_2, partial pressure of carbon dioxide; pO_2/FiO_2, partial pressure of oxygen/inspiratory fraction of oxygen; PS-PEEP, pressure support with positive end-expiratory pressure; SaO_2, arterial oxygen saturation.

bolic syndrome, secondary to multi-organ tissue ischemia, in turn due to the combination of arterial hypoperfusion and venous congestion.[48] In fact, in the patient in cardiogenic shock, one of the main determinants of adverse prognosis is the progression of organ damage (hepatic, renal, cerebral), linked to alterations in microcirculation and activation of the systemic inflammatory response secondary to the reduction of cardiac output and peripheral hypoperfusion.[49]

This chain rapidly evolves, if not corrected, towards irreversible multi-organ failure. The objectives of our intervention can be summarized as follows:

1. Circulation support to maintain systemic perfusion, by increasing mean arterial pressure.
2. Ventricular support to reduce filling pressures and left ventricular overload.
3. Maintenance of coronary artery perfusion, always improving mean arterial pressure and end-diastolic pressures.
4. Systemic decongestion to reduce renal and hepatic ischemia.

In the presence of adequate volume, the cornerstone of pharmacological treatment consists mainly of vasopressors and, only in a second phase, of association with inotropes. Regarding the use of these drugs (Table 7) in the early stages of shock, we will limit ourselves to a few considerations:

- In patients with severe symptoms (SBP <80 mmHg), it is appropriate to start with norepinephrine or adrenaline.
- If signs of shock persist while waiting for a decision to be made on the possible placement of a temporary mechanical support, an inotrope may be associated according to dosages and methods reported in Table 7.
- In patients who are unresponsive to the association of vasopressors and inotropes, or in those with mechanical infarct complications (*e.g.* severe ischemic mitral valve failure, post-infarct interventricular defect), early recourse to mechanical circulation support should be considered.
- In the STEMI shock, inotropic drugs increase the mean arterial flow and mean pressure, but also myocardial oxygen consumption, afterload and therefore left ventricular overload, ultimately reducing coronary perfusion and aggravating ischemia. According to some authors, the early use of mechanical support for circulation (through aortic

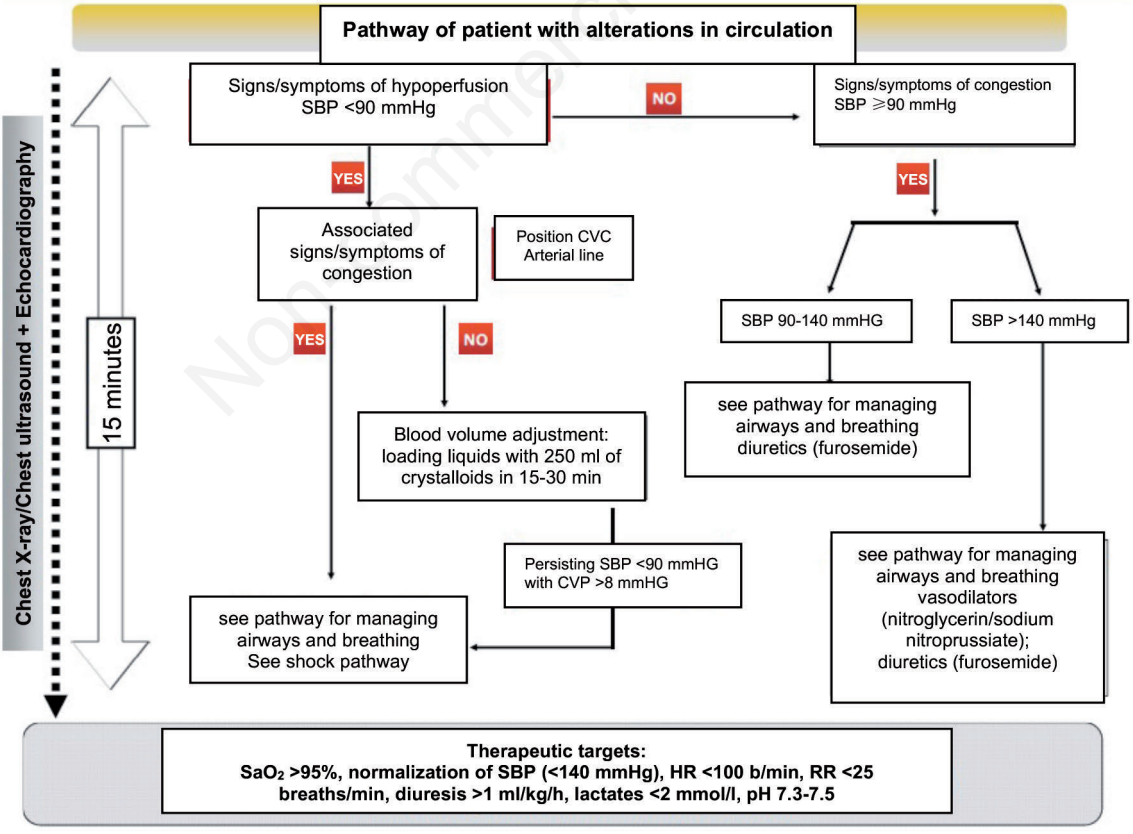

Figure 7. The pathway of the patient with alterations in circulation and pressure profile. CVC, central venous catheter; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; CVP, central venous pressure; SaO_2, arterial oxygen saturation.

counterpulsation, or Impella in cases of greater left ventricular dysfunction, together with coronary angioplasty in emergency) can avoid the side effects of high doses of vasopressors and inotropes and improve the in-hospital outcome. However, following the results of the IABP-SHOCK[50] studies

Table 7. Inotropic, vasopressor and inodilator therapy: dosage and mechanism of action.

Drug	Therapeutic dosage	Site of action				Hemodnamic effects
		α1	β1	β2	Dopaminergic receptor	
Vasopressor/inotropic						
Dopamine	0.5-3 μg/kg/min	–	+	–	+++	↑CO
	3-10 μg/kg/min	+	+++	+	++	↑↑CO, ↑SVR
	10-20 μg/kg/min	+++	++	–	++	↑↑SVR, ↑CO
Noradrenaline	0.05-0.4 μg/kg/min	++++	++	+	–	↑↑SVR, ↑CO
Adrenaline	0.05-0.5 μg/kg/min	++++	++++	+++	–	↑↑CO, ↑↑SVR
Vasopressin	0.02-0.04 U/min	Stimulates V1 receptors in smooth muscle				↑↑SVR, ↔PVR
Inodilator						
Dobutamine	2-20 μg/kg/min (IC)	+	++++	++	–	↑↑CO, ↓SVR, ↓PVR
Isoproterenol	2-20 μg/min	–	++++	+++	–	↑↑CO, ↓SVR, ↓PVR
Milrinone	0.125-0.75 μg/kg/min	Phosphodiesterase 3 inhibitor				↑CO, ↓SVR, ↓PVR
Enoximone	2-10 μg/kg/min	Phosphodiesterase 3 inhibitor				↑CO, ↓SVR, ↓PVR
Levosimendan	0.05-0.2 μg/kg/min	Phosphodiesterase 3 inhibitor, sensitizing calcium				↑CO, ↓SVR, ↓PVR

CO, cardiac output; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

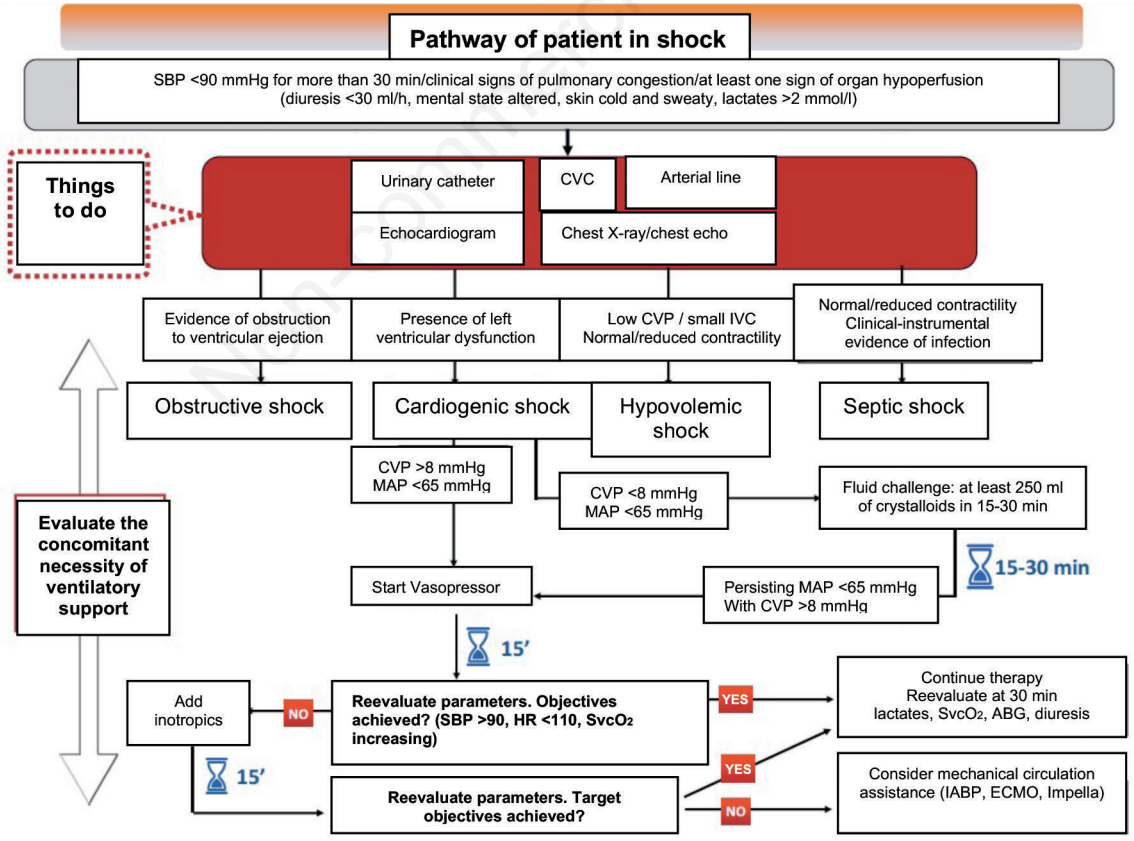

Figure 8. The pathway of the patient with shock. CVC, central venous catheter; ECMO, extracorporeal membrane oxygenation; HR, heart rate; IABP, intra-aortic balloon pump; MAP, mean arterial pressure; SBP, systolic blood pressure; CVP, central venous pressure; $SvcO_2$, central venous oxygen saturation; IVC, inferior vena cava.

and data from a recent meta-analysis,[51] the guidelines do not recommend extensive use of the aortic counterpulsator.[1]

The Network for cardiogenic shock

The literature documents a lower in-hospital mortality rate for patients with cardiogenic shock admitted to high-volume centres.[52] It is therefore desirable to set up a dedicated Network,[53] with a model that has been proved to be effective for STEMI, where the referring center in question has the role of a Hub with peripheral Spoke centers belonging to it.

Pathway of the patient with severe arrhythmias

Arrhythmias of any origin are a frequent cause of HF instability[54] in patients with pre-existing structural cardiopathy (*e.g.* left ventricular dysfunction, valvulopathies), and for this reason they should always be identified, clinically defined and possibly treated.

At the first medical contact with a patient presenting to hospital with acute HF, it is important to accurately define the clinical weight of the arrhythmia against the event and exclude from treatment those situations where changes in heart rate and/or rhythm are secondary to the general situation and not the cause of it (*e.g.* sinus tachycardia during acute respiratory failure, or atrial fibrillation with high average ventricular frequency in a patient with pre-existing atrial fibrillation). The first question to ask, therefore, is whether the arrhythmia is the main cause of the symptoms reported by the patient. The next step is to identify whether the altered heart rate causes hypoperfusion by recognizing critical elements: i) hypotension (arterial pressure <90 mmHg) and signs of shock; ii) syncope; iii) acute changes in mental status; iv) association of typical chest pain. At the same time, it is fundamental to:

- Obtain anamnestic information (*e.g.* nature of symptoms, previous history of HF, known level of ventricular function and presence of valvulopathies) and home blood pressure values.
- Perform a 12-lead ECG and compare it, where possible, with a basic ECG performed under conditions of hemodynamic compensation.
- Obtain venous access and take a sample (also *via* venous ABG) to assess the presence of ionic imbalance, which must be treated as soon as possible.
- Because patients with acute HF may frequently present with comorbidities that may act as triggers for arrhythmia,[3,6,13,14,55] it is important to evaluate, as soon as possible, specific conditions such as the presence of hyperthyroidism, anemia, respiratory tract infections, renal failure, acute exacerbation of chronic bronchopathies, and acute coronary syndrome.

This information is essential for all types of arrhythmia that the patient with HF may present. According to the European guidelines,[1] we can define arrhythmias in the course of HF as: i) bradyarrhythmias: heart rate <40 b/min; ii) tachycardias: heart rate >120 b/min.

Bradyarrhythmias (heart rate <40 b/min)

The algorithm for managing bradyarrhythmias is summarized in Figure 9.

Tachyarrhythmias (heart rate >120 b/min)

Supraventricular tachyarrhythmias

The more frequent supraventricular tachyarrhythmias (Figure 10) are atrial fibrillation, atrial flutter and reentrant supraventricular tachycardia.

Atrial flutter responds poorly to the control of frequency. For this reason, it is always better to start the procedure of electrical or pharmacological cardioversion if the onset of the arrhythmia is <48 h, or otherwise after performing the transesophageal echocardiogram, similar to what was said regarding atrial fibrillation. If it is not possible to proceed with cardioversion or transesophageal echocardiography, the next step can be a temporary check of the frequency of atrial flutter with IV verapamil. For negative verapamil inotropism this therapy can be used for a maximum of 24-48 h but in general the favorable hemodynamic effect of reducing the ventricular response of the flutter outweighs the unfavorable effect of the drug negative inotropism. Administration of digitalis IV in repeated boluses is less effective. In any case, it is then necessary to proceed as soon as possible by stopping the arrhythmia, if not hemodynamically tolerated. Paroxysmal supraventricular tachycardia is decidedly rarer than the previous ones in this context. The treatment algorithm, in addition to performing the carotid sinus massage, includes administering adenosine, or verapamil in bolus or amiodarone IV.

Ventricular tachyarrhythmias

In the case of ventricular tachyarrhythmias (Figure 11) in association with signs and symptoms of HF, we are faced in most cases with an extremely critical situation. We distinguish between ventricular fibrillation and ventricular tachycardia. The first corresponds to cardiac arrest, so it follows the specific ACLS99 protocol focused on emergency defibrillation and cardiopulmonary resuscitation.[56] The second one can be with or without hemodynamic compromise, up to ventricular tachycardia without pulse (this also follows ACLS protocol for cardiac arrest).

The treatment of SV and ventricular arrhythmias is summarized in Table 8.

Risk stratification and transfer of the critical patient from Accident & Emergency/Emergency Admissions Department

Patients suffering from acute HF who present with critical conditions must be managed in an environment

Table 8. Pharmacological treatment of arrhythmias during acute heart failure.

Bradyarrhythmias	
Bradyarrhythmia	- Atropine IV (first dose 0.5 mg; repeatable every 3-5 min; max 3 mg) - Dopamine IV: 2-10 µg/kg/min - Adrenaline IV: 2-10 µg/min
Supraventricular tachyarrhythmias	
Atrial fibrillation	Heart rate control - Digitalis - β-blocker Pharmacological cardioversion: amiodarone - Load 300 mg in 100 ml glucose 5% in 20 min - Following infusion 900 mg in 500 ml glucose 5% in 24 h
Atrial flutter	Frequency control - Verapamil (caution negative inotropism) - Digitalis
PSVT	Unilateral carotid sinus massage - Verapamil 5 mg (caution negative inotropism) - Adenosine 6 mg bolus IV quick, then washing with saline solution; possible second dose 12 mg Frequency control - Digitalis - β-blocker
Ventricular tachyarrhythmias	
Ventricular fibrillation	Defibrillation Cardiopulmonary resuscitation
Ventricular tachycardia (pulse, PA >80 mmHg)	- Hypokalemia correction - Magnesium sulphate - Lidocaine bolus 1 mg/kg repeatable up to 3 mg/kg, or - Amiodarone 300 mg IV in 30 min

IV, intravenously; AP, arterial pressure; PSVT, paroxysmal supraventricular tachycardia.

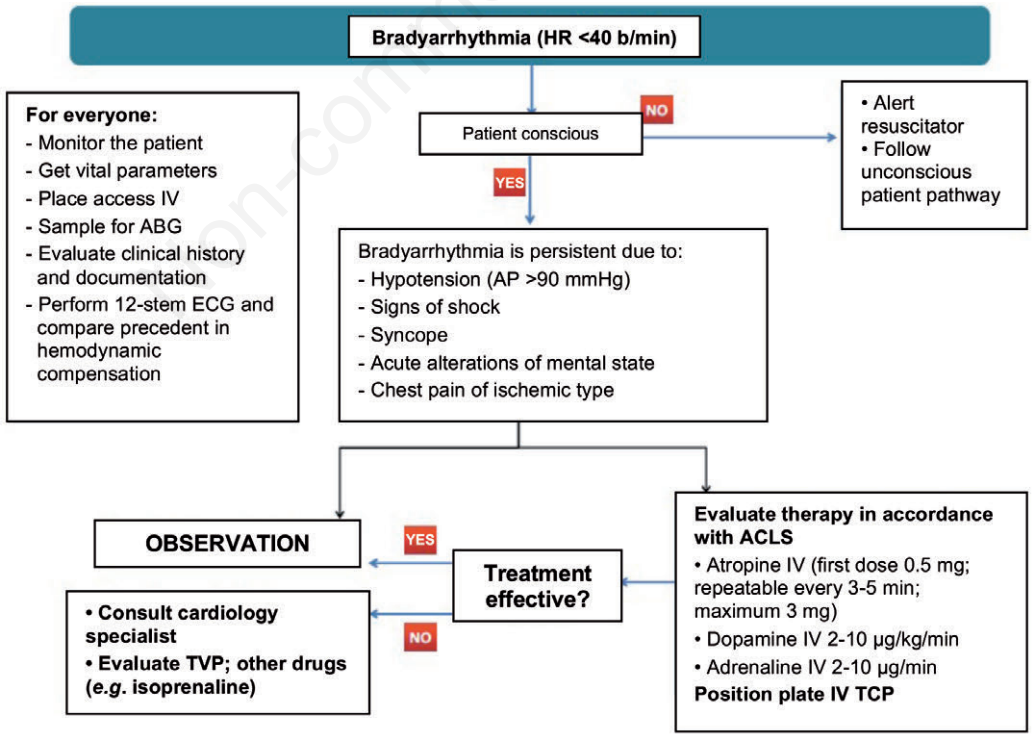

Figure 9. Management algorithm for severe bradyarrhythmias. ACLS, advanced cardiac life support; ECG, electrocardiogram; ABG, arterial blood gas test; IV, intravenously; HR, heart rate; AP, arterial pressure; TCP, transcutaneous pacing; TVP, transvenous pacing.

where advanced monitoring and treatment tools are rapidly available to medical and nursing staff.

In the critical patient with acute HF, the following pathways can be activated:

- Patients with associated acute coronary syndrome (high-risk STEMI or NSTEMI), with a confirmed diagnosis of cardiogenic shock and cardiac arrest due to a cardiac cause, must be inevitably managed from the earliest stages by the cardiologist and intensivist, and their care process must continue in the Coronary Intensive Care Unit.
- In the case of Cardiac Intensive Care Units (CICUs) that are not suitable for managing intubated patients, admission to a general or cardiac surgery intensive care unit may be required.
- It would be desirable for hospital centers to have an organization in the Network for the care of the patient in shock to organize a rapid transfer, if needed, to a third-level center, equipped with a 24h/7d hemodynamic monitoring room and the possibility of installing mechanical circulation support.
- Hospitalization in an intensive environment (CICU/Semi-intensive) is necessary for all patients with acute HF who, after evaluation and initial treatment in A&E/EAD, maintain conditions of instability (SaO_2 <90% despite oxygen supplement, heart rate 40 or 120 b/min, SBP 90 mmHg with signs of peripheral hypoperfusion and evidence of new-onset right ventricular dysfunction), even if there is no validation of these parameters in the literature (Figure 12).

When to evaluate a choice of palliation

The decision to transfer a high-risk patient to intensive care has been one of the most debated topics for decades and among the most difficult for doctors in A&E/EAD. Intensive care offers the possibility of monitoring and vital support which can radically alter the survival chances for patients with acute pathologies like HF, but it represents an extremely expensive, intensive and invasive form of care, which can sometimes be inappropriate, harmful or futile for some types of patients.

The difficulty in predicting whether treatment in the ICU will have significant long-term benefits for a particular patient is the crucial issue in the controversial debate on whether to admit patients to intensive care with limited life expectancy due to their very advanced age, impaired functional status or relevant

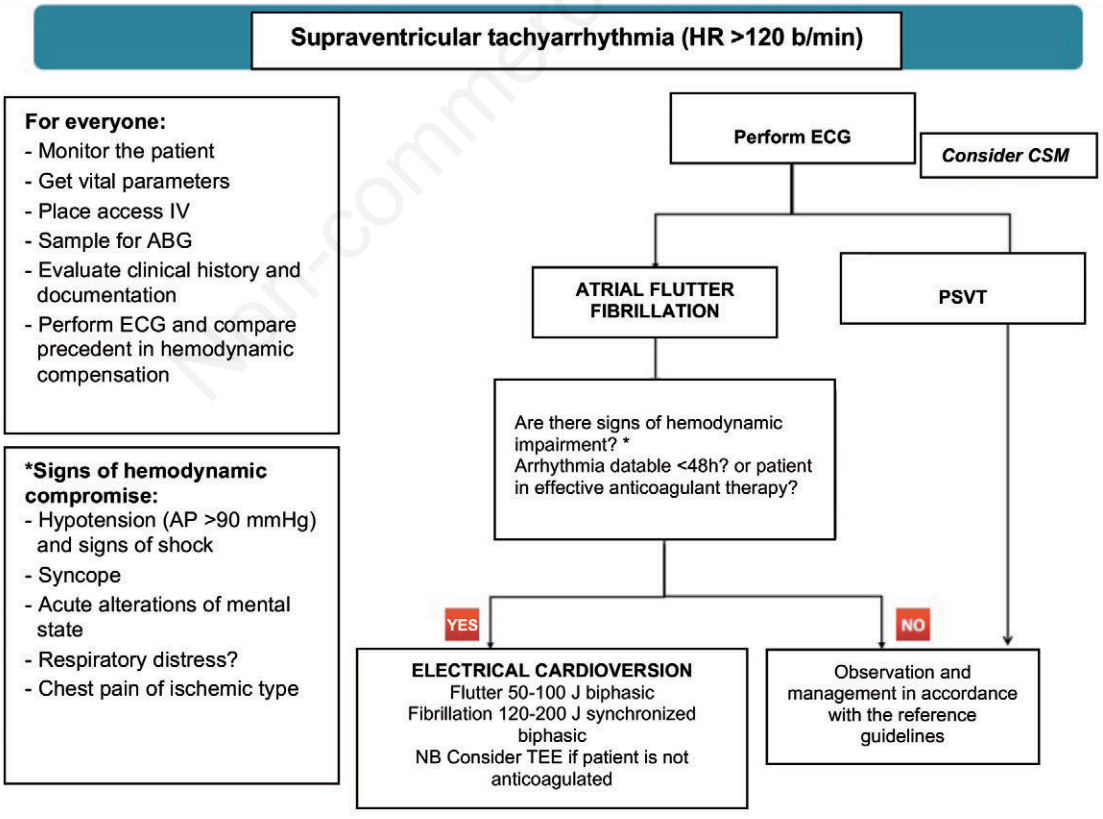

Figure 10. Management algorithm for supraventricular tachyarrhythmias. ECG, electrocardiogram; ABG, arterial blood gas test; TEE, transesophageal echocardiogram; IV, intravenously; HR, heart rate; CSM, carotid sinus massage; AP, arterial pressure; PSVT, paroxysmal supraventricular tachycardia.

chronic conditions. However, the available clinical evidence comes almost exclusively from expert opinions or observational studies. A recent meta-analysis on the impact of the frailty syndrome on the outcomes of intensive care admission for various acute critical diseases, relating to 3030 patients enrolled in 10 studies, documented in fragile patients (30% of the total), compared to non-fragile subjects, a high mortality both in hospital (+71%) and at 6 months (+53%), and a halved probability of being discharged home.[57]

Diagnostic-therapeutic pathway of the patient with non-critical acute heart failure

The diagnostic and therapeutic pathway of the non-critical patient is summarized in Figure 13.

First evaluation and treatment upon entry to Accident & Emergency/Emergency Admissions Department

The steps for correctly diagnosing acute heart failure are summarized in Table 9.

Clinical evaluation

The presentation of acute HF can take place according to two clinical pictures: i) dyspnea as a prevalent symptom and signs of central and/or peripheral congestion; ii) asthenia as a prevalent symptom and signs of low output rate.

Naturally the two pictures can sometimes coexist or present some aspects of both clinical presentations, making the diagnosis and therapeutic choices more complex.

Table 9. The three important steps in correctly diagnosing acute heart failure.

Clinical evaluation	Evaluation of clinical history, symptoms and signs → diagnostic suspicion, context of risk factors and pre-existing cardiopathies, differential or definitive diagnosis of heart failure
Instrumental evaluation	Instrumental signs attributable to acute heart failure → confirmation of diagnosis, differential diagnosis, identification of comorbidity and causative factors
Laboratory assessment	Laboratory indicators → accreditation of differential diagnosis, identification of comorbidity and possible triggers

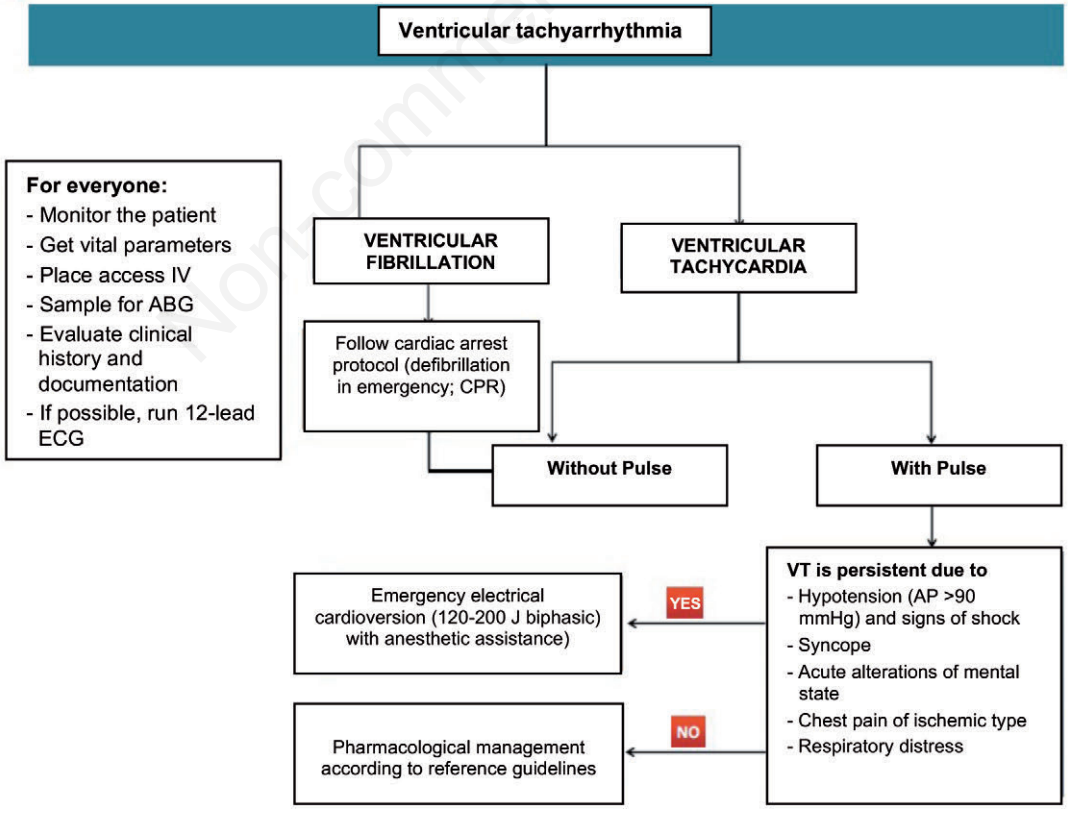

Figure 11. Management algorithm for ventricular tachyarrhythmias. ECG, electrocardiogram; ABG, arterial blood gas test; IV, intravenously; AP, arterial pressure; CPR, cardiopulmonary resuscitation; VT, ventricular tachycardia.

Instrumental evaluation

The recommended instrumental examinations are an ECG, a chest X-ray, an echocardiogram and, if possible, a thoracic ultrasound. Only in selected cases and in the suspected diagnosis of aortic dissection or pulmonary embolism, a chest angiotomography can be considered.

- *Electrocardiogram:* This is always recommended and rarely appears normal in the presence of acute HF; it is essential for diagnosing possible cardiac causes such as arrhythmias or coronary syndromes.
- *Chest X-ray:* This is a rapid test and is often performed quickly in A&E/EAD, but it must be remembered that it identifies the signs of pulmonary venous congestion and interstitial and alveolar edema in 80% of cases, so in patients with paroxysmal or worsening dyspnea, the lack of X-ray signs cannot rule out the diagnosis. In any case, chest X-ray is useful for identifying associated clinical pictures or triggering factors, such as lung parenchyma and pneumothorax, infections, and provide rough indications of cardiac volume, useful in *de novo* patients.
- *Chest ultrasound:* This is very useful in identifying the signs of pulmonary congestion, and there is an increasing number of training initiatives to teach this method to various specialist doctors. In fact, as explained above, about 20% of patients may have acute HF but a chest X-ray with no pathognomonic signs. The typical sign of pulmonary congestion on chest ultrasounds is the presence of hyperechoic white lines, the deep B lines, which originate from the pleural line and move in concert

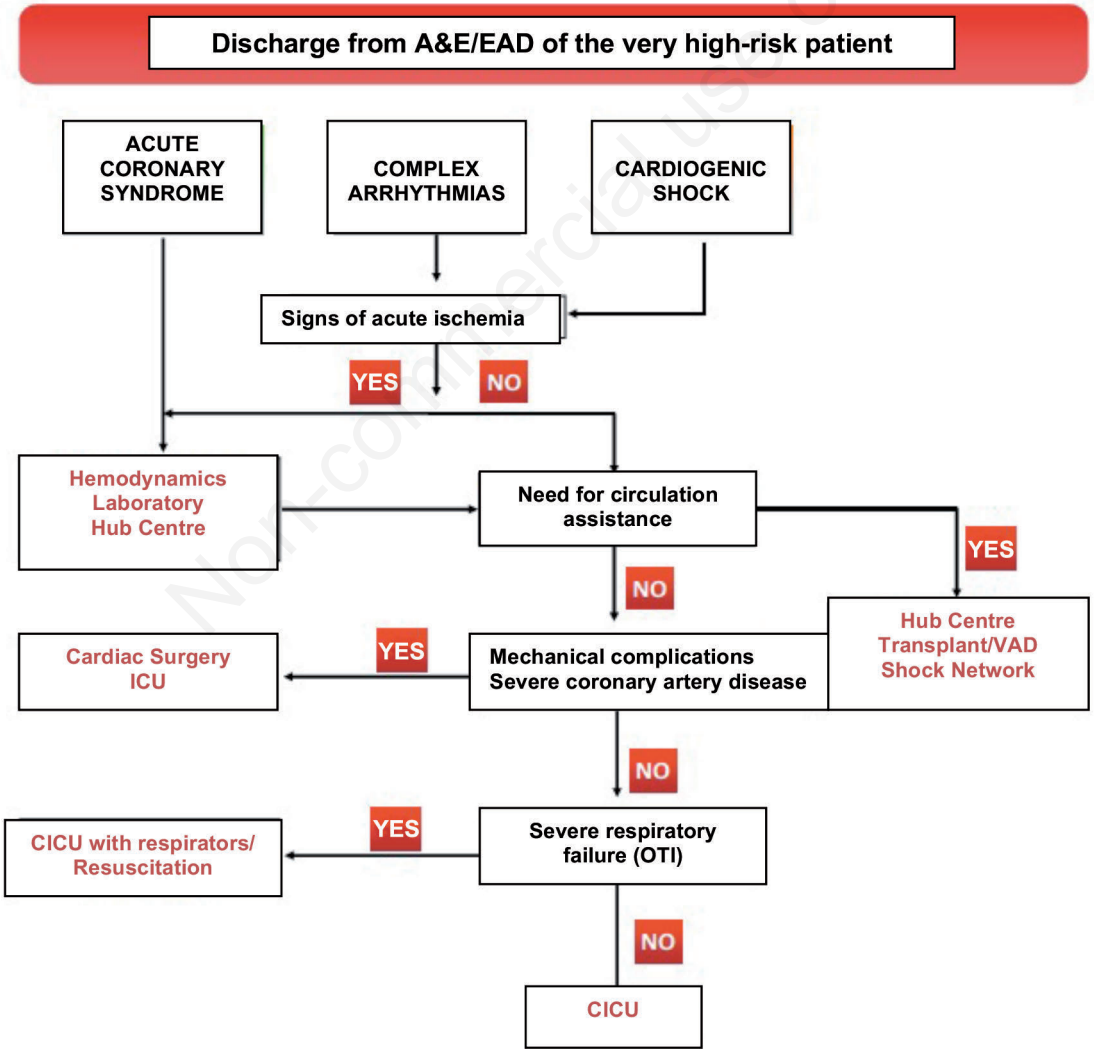

Figure 12. Organizational hypothesis of the in-hospital transfer of the patient with critical acute heart failure. OTI, orotracheal intubation; A&E/EAD, Accident & Emergency/Emergency Admissions Department; ICU, intensive care unit; CICU, cardiac intensive care unit; VAD, ventricular assist device.

with breaths; furthermore, pulmonary ultrasound can identify pleural strata.

- *Echocardiogram:* This is always recommended when acute HF is suspected in A&E/EAD, and now it is also performed frequently by emergency doctors as well as cardiologists. It should be used as soon as possible in the presence of hemodynamic instability or in the patient with acute HF *de novo*, and it is therefore desirable that all A&E/EAD facilities are able to perform an echocardiogram (referred to as *eco-fast*) dedicated to finding cardiovascular emergencies in the first hours after the patient's arrival in A&E/EAD. In any case, an echocardiogram must be scheduled for patients presenting with exacerbation of chronic HF.
- *Chest angiotomography:* Angiotomography of the chest in a patient with acute HF is considered a first-level investigation, especially when pulmonary embolism or aortic dissection are suspected.

Laboratory evaluation

- *Natriuretic peptides:* BNP natriuretic peptides or N-terminal fragment of proBNP (NT-proBNP) have a high negative predictive power (BNP thresholds <100 pg/mL, NT-proBNP 300-400 pg/mL) for acute HF and should always be measured, especially in *de novo* patients and/or with nuanced symptoms. In patients with acute HF and a history of chronic HF, high levels of natriuretic peptides, especially when compared to a value obtained in clinically stable conditions, can identify hemodynamic destabilization and help prognostic stratification.[45]

Measuring high sensitivity troponin (hsTn) can provide two distinct pieces of information:

1. to contribute to the differential diagnosis of acute coronary syndrome, which can be associated or may be the cause of hemodynamic instability; the hsTn must always be measured when a previous or ongoing ischemic event is suspected (symptoms, electrocardiographic alterations +/- anomalies of segmental kinetics in the echocardiogram);
2. to represent an index of acute myocardial damage (myocarditis, myopericarditis) or progressive myocardial damage not directly linked to clear signs of ischemia or inflammation of the myocardium; in this second case, it can represent an important prognostic index (*e.g.* cardio toxicity from chemotherapeutic drugs, action of inflammatory agents, cytokines, but also isolated cell damage in progress).[45] Furthermore, hsTn during acute dyspnea, without significant signs of pulmonary congestion and/or acute ischemia, contributes to differential diagnosis and prognostic stratification in the case of pulmonary embolism.[58]

Precipitating factors and comorbidities that complicate the diagnosis

The possible precipitating factors that complicate the diagnosis are summarized in Table 10.

Table 10. Possible precipitating factors in a clinical picture of acute heart failure.

• Acute coronary syndrome
• Uncontrolled hypertension, hypertensive crisis (SBP ≥240 mmHg and/or PAD ≥140 mmHg)
• Tachyarrhythmias (atrial fibrillation, ventricular tachyarrhythmias) and bradyarrhythmias
• Exacerbated chronic obstructive pulmonary disease
• Inadequate food intake (excessive or lacking)
• Acute inflammatory states with increased metabolic needs (pneumonia, infective endocarditis, sepsis)
• Acute cardiac mechanical complications from: post-infarct heart rupture, interventricular defect, acute mitral insufficiency, thoracic trauma, aortic dissection complicated by severe aortic insufficiency and/or cardiac ischemia, acute dysfunction of valvular prostheses
• Endocrinopathies and hormonal dysfunction (thyroid dysfunction, diabetic ketoacidosis, adrenocortical diseases, pregnancy, peripartum gestosis)
• Chemotoxic drugs, corticosteroids, NSAIDs, sodioritative drugs (including insulin), negative inotropics (β-block excess, anti-arrhythmic drugs)
• Pulmonary embolism
• Acute cerebrovascular diseases
• Increased reflex adrenergic state (pain, stress-anxiety, hypoxia, hypotension, *etc*.)
• Intermediate and major surgeries, perisurgical states complicated by infections, anemia, volume overload, unbalanced nutritional and hydro-electrolytic intake
• Intoxication from alcohol and drugs

Comorbidities

Patients with HF frequently have comorbidities that may be associated with left ventricular dysfunction.[3,6,13,14,55] Elderly patients, with significant underlying fragility, may not fully show the symptoms and signs of HF, thus making the differential diagnostic framework more complex.

Patients with non-critical HF may be largely divided into two groups (Figure 13): i) HF with prevailing cardiac pathology; ii) HF with prevalent comorbidity.

Recognizing comorbidities and above all evaluating their role in the onset of the symptoms that brought the patient to A&E/EAD is often not a simple process, and requires experience and competence both from an internist and cardiologic point of view. Figure 14 shows the comorbidities present in patients hospitalized for acute HF or worsening of a known chronic HF picture in observational research conducted on patients admitted to an internist context.[17] As can be seen, kidney failure, anemia, decompensated diabetes and COPD are often present, as well as cancer and other chronic inflammatory diseases. Fragility and neurological pathologies such as dementia or Alzheimer's disease are also present with a high prevalence, and as many as 22% of patients have a cognitive impairment which must be taken into account in the hierarchy of care provided.

In patients with HF with predominant cardiac pathology, even if of advanced age, therapeutic services, even complex and expensive ones, are often appropriate since, if treated according to the guidelines, their survival and quality of life can improve. This is true both for pharmaceutical expenditure and for the use of devices or cardiac surgery.

In the patient with cardiac HF with prevalent comorbidity, survival and quality of life could be compromised independently of any aggressive cardiological therapy, and therefore greater reflection on treatments is needed. Evaluating the patient in terms of survival, not so much based on the severity of heart failure, but on the comorbidities and functional status, becomes essential. In fact, it is possible to select patients with a relatively good prognosis who will benefit from a therapeutic approach that is both pharmacological and interventional, even aggressive; patients with multiple comorbidities, high degree of dependence, and cognitive impairment, for whom the short-term prognosis is in any case poor, should therefore be directed to drug therapy and, in the most advanced cases, palliative treatment. This is also contemplated in the recent ESC guidelines.[1]

One of the most important issues is identifying these patients and making a correct prognostic stratification. In this regard, scores can be used to stratify

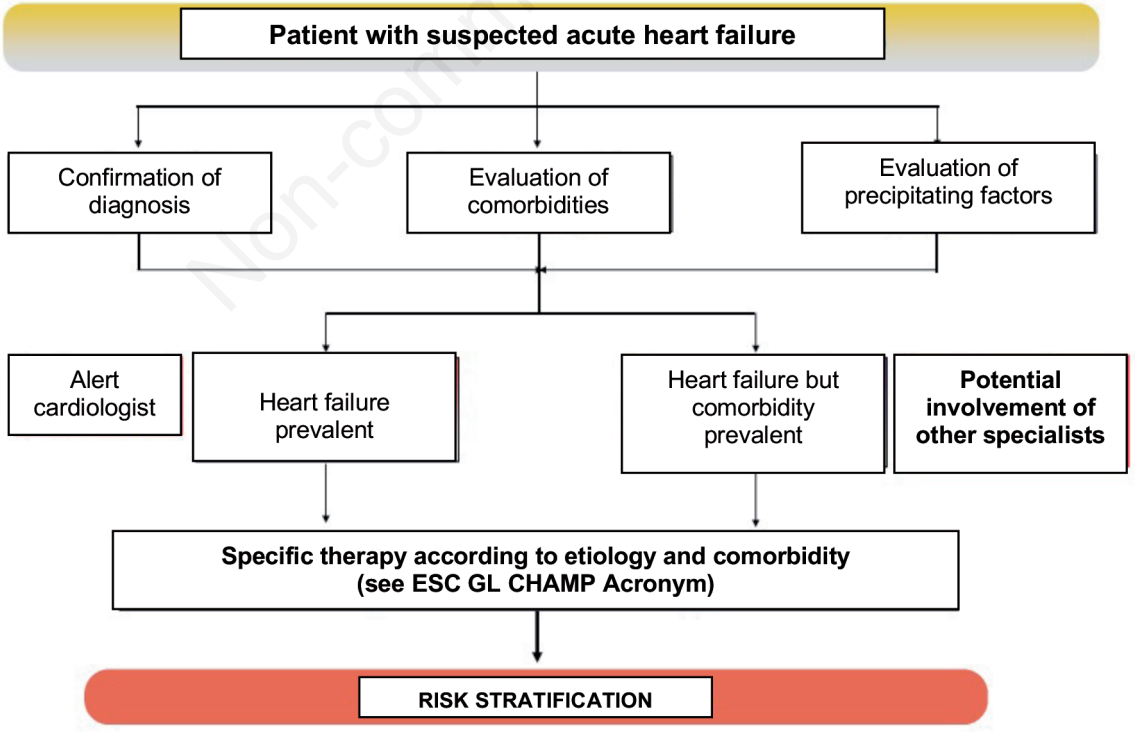

Figure 13. The diagnostic-therapeutic pathway of the non-critical patient. CHAMP, acute Coronary syndrome; Hypertension emergency; Arrhythmia; acute Mechanical cause; Pulmonary embolism; ESC, European Society of Cardiology; GL, guidelines.

the prognosis in complex patients. One of these is the MPI (Multidimensional Prognostic Index),[59] which takes into account *a series of variables that belong to 8 domains:* ADL (Activities of Daily Living), IADL (Instrumental Activities of Daily Living), SPMSQ (Short Portable Mental Status Questionnaire), MNA (Mini Nutritional Assessment), Exton-Smith Scale, CIRS (Comorbidity Index Rating Scale), drugs taken, and housing status. This score can provide a good prognostic stratification, but is fairly complex and time-consuming. FADOI (Federation of Associations of Internist Hospital Managers) is working on a new score[60] that takes into account two variables: dependence (COMPLIMED score 1, CS1) and comorbidities (COMPLIMED score 2, CS2). CS1 is mainly based on the Barthel index and the Exton-Smith Scale, while CS2 is based on the Charlson score calculation. The sum of the CS1 and CS2 scores can predict mortality at 3 months, 6 months and 1 year. The COMPLIMED score, if compared with the MPI score by means of ROC curves, shows a higher specificity and sensitivity. Furthermore, this score is simple and fast and could be used to evaluate the patient with acute heart failure in A&E/EAD, opening up different therapeutic strategies and type of hospitalization. The other fundamental point of the patient who presents at A&E/EAD with dyspnea and therefore with suspected acute HF is the differential diagnosis with other pathologies such as the exacerbation of COPD, pulmonary embolism or neoplastic pictures. In this case it is important to rule out cardiac involvement in the first instance. In these cases, it is correct to address the diagnostic suspicion with an accurate methodology, as reported above, which involves clinical, instrumental investigations and blood chemistry tests.

Acute coronary syndrome, myocardial infarction type, without ST segment elevation with signs of left ventricular dysfunction in the context of the non-critical patient

Acute *de novo* HF, particularly in a context of known cardiovascular risk factors, must always make doctors think of coronary artery disease in the first instance. Most of these patients have a multivessel coronary artery disease and/or a common trunk, which is more common in NSTEMI-type acute coronary syndrome.

During acute coronary syndrome, the increase in left ventricular end-diastolic pressure, a trigger of acute HF, is one of the main causes of increased oxygen consumption, along with reflex tachycardia. At the same time the decrease in oxygen supply, resulting from acute ischemia, can increase the left filling pres-

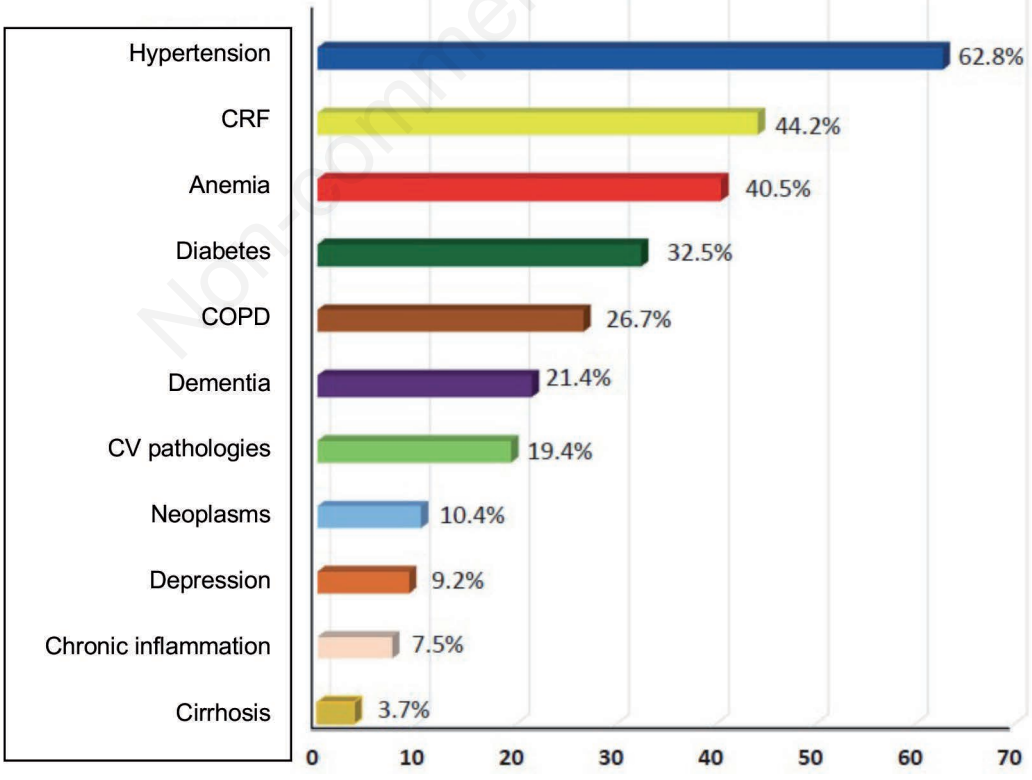

Figure 14. Comorbidity of patients admitted to Internal Medicine with heart failure. CONFINE study data, average age 79 years. COPD, chronic obstructive pulmonary disease; CV, cardiovascular; CRF, chronic renal failure. Modified from Biagi *et al.*[17]

sures and cause ventricular dysfunction. The ESC guidelines on coronary syndromes without elevation of the ST[61] segment recommend performing coronary angiography in emergency (within 2 hours) in the presence of acute HF.

Potential of a cardiological fast-track

For some patients who present at A&E/EAD with a picture of acute HF, and in any case in compliance with the organizational arrangements envisaged in the different A&E/EAD departments, a protocol could be established that involves the specialist cardiologist very early with respect to the emergency doctor or the one on duty in A&E/EAD.

Risk stratification of the patient with non-critical acute heart failure

Evaluating a patient with acute HF who presents in A&E/EAD has the first objective of excluding evolutionary situations such as incipient cardiogenic shock (SBP <90 mmHg with initial signs of organ hypoperfusion), worsening respiratory distress, the presence of an acute ischemic type STEMI, the accentuation of signs of severe congestion, *etc*.

Furthermore, accurate and repeated stratification of the risk is necessary in order to identify the most appropriate care setting.

Serial assessments may make possible to observe the response to therapy undertaken or to understand clinical conditions that are not initially obvious.

Four scores were tested and validated in the A&E/EAD patient population.[62-65] The EHMRG (Emergency Heart Failure Mortality Risk Grade, http://ehmrg.ices.on.ca)[62] assessed mortality both in-hospital and at 30 days, managing to discern between two extreme groups, one with very low risk (0.3%) and one at high risk (8.5%). The MEESSI-AHF (Multiple Estimation of Risk Based on the Emergency Department Spanish Score) has been tested and validated in patients attending A&E/EAD, making possible to identify a very low-risk group and a very high-risk one with mortality at 30 days.[65]

Therapy in A&E/EAD for patients with non-critical acute heart failure

The ESC guidelines[1] propose a simple acronym: CHAMP (acute Coronary Syndrome; Hypertension emergency; Arrhythmia; acute Mechanical cause; Pulmonary embolism) aimed at facilitating early diagnosis and rapid therapy targeting the underlying cause. Following this acronym, Table 11 shows the main pharmacological and non-pharmacological interventions proposed in relation to the words that comprise it.

How to deal with home therapy: In the case of a new episode of acute HF, in a patient with known cardiopathy, all efforts must be made to continue the oral therapy recommended by clinical trials and guidelines for HF (Table 12), while in the case of acute HF *de novo*, the goal must be to start the aforementioned therapies as soon as acceptable hemodynamic stability is achieved.

Table 11. CHAMP acronym from the 2016 European guidelines.[1]

CHAMP	Diagnostic tricks	Therapy
C. coronary syndrome	STEMI/NSTEMI ECG alterations; positivity of cytochrome/ troponin indices	Treatment in accordance with guidelines for acute coronary syndromes Immediate (<2 h from admission to hospital) invasive strategy for NSTEMI patients with acute HF in analogy to the patient with STEMI, independently of ECG or biomarker modifications
H. Hypertensive crisis	In most cases, the clinical picture is represented by edema acute pulmonary	The association of vasodilators and diuretics IV (*e.g.* nitroglycerin 10-200 µg/min; furosemide IV bolus + infusion), represents the principal main, to start as soon as possible
A. Arrythmias	12-lead ECG and ECG monitoring during the observation period	Medical therapy (*e.g.* atropine, adrenaline, isoprenaline, antiarrhythmics), electric cardioversion, temporary pacing (external or internal)
M. Mechanical cause	Fast echocardiogram to detect heart rupture, interventricular septal defects, acute mitral insufficiency, trauma	Usually surgical therapy
P. Pulmonary embolism	D-dimer, troponin, BNP; echocardiogram for the study of RV	Variable in relation to the clinical picture: thrombolysis in high-risk patients, anticoagulant in others

BNP, brain natriuretic peptide; ECG, electrocardiogram; IV, intravenously; NSTEMI, myocardial infarction without ST elevation; HF, heart failure; STEMI, myocardial infarction with ST-segment elevation; RV, right ventricle.

Treatment of comorbidities

Comorbidities are normally managed in agreement with other specialists. These must be identified and recognized promptly, because in the presence of HF the specific management of the pathology can be mutually different. Comorbidities can, in fact, interfere with the diagnostic process (*e.g.* COPD), aggravate symptoms and worsen the quality of life, contribute to hospitalizations and mortality, and make difficult to use therapies for HF (*e.g.* inhibitors of angiotensin-converting enzyme/angiotensin receptor antagonists contraindicated for severe renal failure; beta-blockers relatively contraindicated for asthma).[66]

Evidence-based treatment for HF is also limited in the presence of comorbidity, as these patients were mostly excluded from clinical trials. Medications used for comorbidities may worsen or cause HF (*e.g.* non-steroidal or chemotherapeutic anti-inflammatory drugs).[67] Finally, there are interactions between drugs for comorbidity and those for HF (*e.g.* beta-blockers for HF with reduced ejection fraction and beta-agonists for COPD and asthma).[67]

Pathway of patients with acute heart failure at the end of clinical assessment in A&E/EAD (IM) and admission of patients. When in Medicine/Cardiology/Emergency Medicine/Short Intensive Observation

For patients with HF at the end of the classification assessment phase in A&E/EAD, risk stratification plays a fundamental role in deciding the pathway inside and outside the hospital, which will be different depending on the clinical characteristics and the risk of re-hospitalization and mortality.

A recent consensus document produced by the ESC Heart Failure Association, the European Society of Emergency Medicine and the Society of Academic Emergency Medicine on pre-hospital and hospital management of acute HF can be helpful.[68] The document outlines the need for close interaction between the different facilities within the hospital network, and proposes a general algorithm to be applied when evaluating patients suffering from acute HF (Figure 15).

The pathway of patients with acute HF admitted to A&E/EAD is identified based on risk. Table 13 summarizes the cardiovascular and other criteria on which the risk should be based.

Discharge from A&E/EAD should be made only for patients with:[31]

- significant response to initial treatment with evidence of the following indicators: i) subjective improvement of symptoms; ii) resting heart rate <100 b/min; iii) absence of orthostatic hypotension; iv) adequate diuresis; v) SaO_2 >90%; v) absence of significant worsening of renal function (reduction of glomerular filtrate <25% or increase in creatinine 0.3 mg/dL).
- identification of what triggered the acute episode.
- presence of HF Clinics with dedicated intervention programs for HF patients and the possibility of short-term follow-up.

Importance of the SIO: Some studies[30,69,70] report a significant increase in the risk of re-hospitalization and new emergency access for patients with HF who are discharged directly from A&E/EAD. In this perspective, SIO departments have been set up in many regions to allow the patient to stay for 24-48 hours, offering a window of opportunity to implement the treatment by monitoring vital parameters, diuresis and weight, to complete basic diagnostic tests such as echocardiography and biomarkers, and assess the response to therapy in a sufficient time interval and to resolve symptoms in many cases. The SIO, which in the last decade has involved less than 5% of pa-

Table 12. How to use ongoing drug therapy in the case of acute heart failure.

	Blood pressure (mmHg)		Heart rate (b/min)			Potassium (mg/dL)		Renal function	
	Normal/high	85-100	<85	60-≥50	50	≤3.5	5.5	Cr 2.5 GFR >30	Cr 2.5 GFR <30
ACEi/sartans	Review/increase	Reduce/stop	Stop	Maintain	Maintain	Review/increase	Stop	Review	Stop
Beta-blockers	Maintain	Reduce/stop	Stop	Reduce	Stop	Maintain	Maintain	Maintain	Maintain
MRA	Maintain	Maintain	Stop	Maintain	Maintain	Review/increase	Stop	Reduce	Stop
Diuretics	Increase	Reduce	Stop	Maintain	Maintain	Review/maintain	Review/increase	Maintain	Review
Vasodilators (e.g. nitrates)	Increase	Reduce/stop	Stop	Maintain	Maintain	Maintain	Maintain	Maintain	Maintain
Drugs for control of HR (CCA, amiodarone, ivabradine)	Reevaluate	Reduce/stop	Stop	Reduce/stop	Stop	Reevaluate/stop	Maintain	Maintain	Maintain

ACEi, angiotensin converting enzyme inhibitors; CCA, calcium channel antagonists; Cr, blood creatinine (mg/dL); HR, heart rate; GFR, glomerular filtration rate (mL/min/1.73 m^2); MRA, antialdosteronics. Modified from Mebazaa *et al.*[42]

Table 13. Cardiovascular and non-cardiovascular criteria for risk assessment.

High risk	Intermediate risk	Low risk	
Cardiovascular factors	- Persistence of dyspnea (RR >25 breaths/min) despite initial treatment and need for NIV - Lung congestion which does not respond to diuretic therapy - HF *de novo* - Acute coronary syndrome - High risk score	- Improvement of dyspnea after initial treatment with persistence of signs of congestion - SBP >100 mmHg and HR in range 50-120/min - Moderate risk score	- Resolution of dyspnea and signs of congestion - Low risk score
Non-cardio-vascular factors	- Respiratory failure from lung diseases or severe inflammatory picture inflammatory picture - Exacerbated chronic renal failure or acute renal failure with need for intensive diuretic treatment and/or renal replacement therapy - Episode of cerebral ischemia - Diabetes mellitus in HF - Severe anemia - Thyrotoxicosis associated with electrical instability	- Exacerbation of COPD not associated with respiratory failure and/or severe - Exacerbated chronic renal failure without need for intensive diuretic treatment and/or renal replacement therapy - Hb values > 8 g/dL	- Absence of severe precipitating comorbidity

COPD, chronic obstructive pulmonary disease; RR, respiratory rate; Hb, hemoglobin; NIV, non-invasive ventilation; SBP, systolic blood pressure; HF, heart failure.

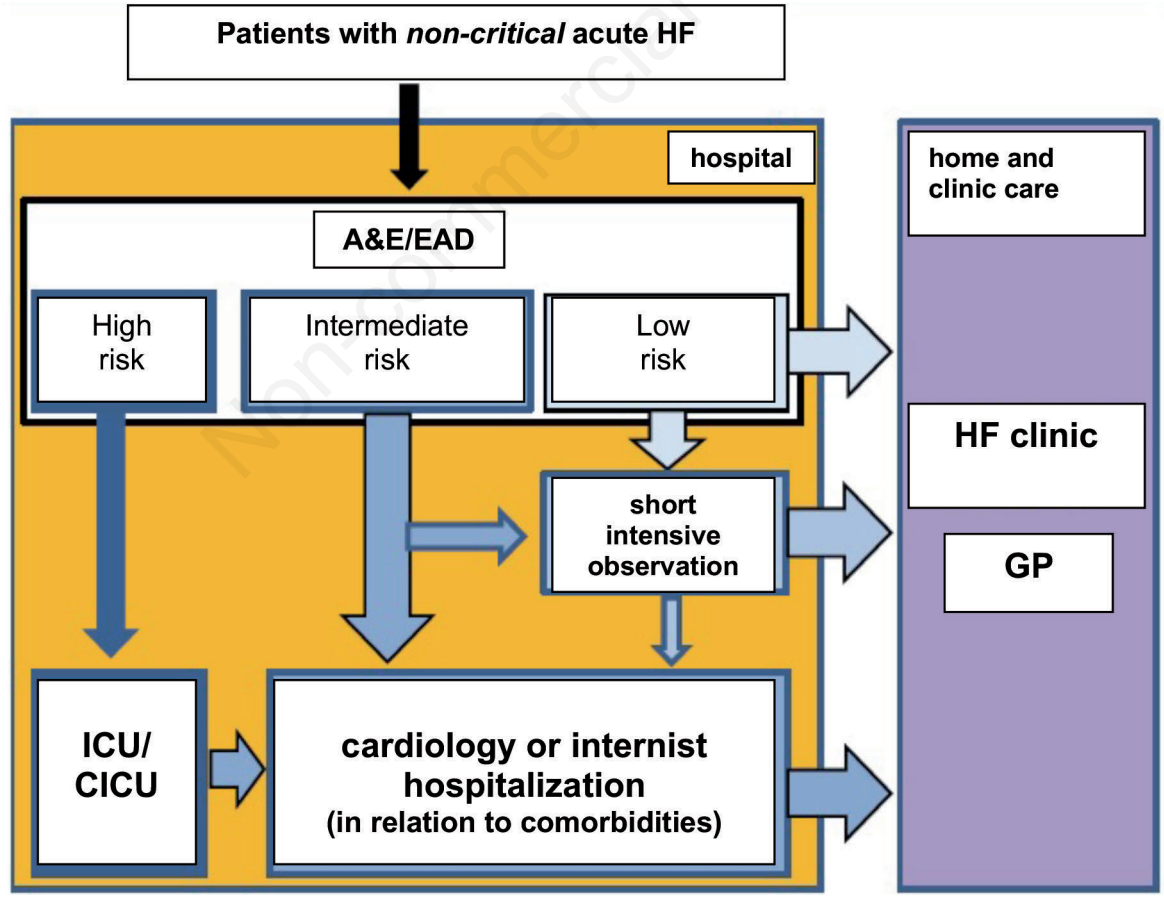

Figure 15. The pathway of patients with non-critical acute heart failure (HF) admitted to Accident & Emergency/Emergency Admissions Department (A&E/EAD), identified based on the risk profile. ICU, intensive care unit; GP, general practitioner; CICU, cardiac intensive care unit.

tients coming to the EAD with symptoms of acute HF, could avoid hospitalization in almost half of the cases.

The pathway outside the hospital after discharge from A&E/EAD

Discharge after admission for acute HF represents not only the end of a particularly critical episode in the patient's history, but above all the beginning of an equally delicate phase, defined as a *transition*, between the hospital and the territory.[71] The patient's care after discharge must be directed above all at preventing re-hospitalization, which is particularly frequent in the first 30 days after discharge, limiting mortality in the short-medium-long term, and improving the quality of life.

Role of the general practitioner

For accessibility and overall knowledge of clinical history and its social and family context, primary care represents the ideal place for treatment and follow-up for patients with HF as part of continuing care in coordination with hospital HF Clinics.

In 2016, the Italian Health Search network[72] reported data on 13,670 patients with HF from a total population of over 1 million attending to by 800 GPs offices, which confirms the epidemiology deducible from studies focused on access to A&E/EAD: HF is present in about 5% of patients aged between 75 and 84, and in almost 12% of those over 85, with a median of 4 comorbidities per patient.

Preventing avoidable re-hospitalizations by integrating assistance between the hospital and the territory represents a valuable goal for improving the quality of care.

Patients discharged after an episode of acute HF present a high rate of re-hospitalization in the short (30 days) and often very short (7 days) term. The Italian data in the National Outcome Plan of AGENAS (National Agency for Regional Health Services) show a national rate of around 14% in 2016 for the indicator *30 days readmission*, with moderate interregional variability.[73]

Two Italian studies, conducted on administrative databases in Bologna's Local Health Authority, analyzed the role of general medicine and cardiology in the outcomes of patients admitted for acute HF.[74,75] While no association has been proven between the patient load or organizational modes of general medicine and rehospitalization in general, the GP's adoption of an integrated care pathway for heart failure, centered on adherence to guidelines, nurses involvement in patient education and preferential access to specialist diagnostics, was associated with a lower rate of re-admissions for HF in the short, medium and long term.[74] In the same context, discharge from a cardiology department or cardiological follow-up was associated with greater adherence, after correction for age and comorbidity, to beta-blocker therapy (+46%) and renin-angiotensin system inhibitors (+53%), which in turn correlated with a lower mortality rate.[75]

In determining early and frequent return to the hospital more components are intertwined, linked both to individual clinical and socio-welfare characteristics, and to system organizational factors underlying a lack of transition between hospital and territory, which must be properly identified and addressed to improve outcomes (Table 14).

The first critical factor at the individual patient level is documenting for the GP the achievement of adequate clinical stabilization, a fundamental condition for discharge from the hospital. Appropriate decongestion markers should therefore be reported at discharge, such as control of symptoms with oral therapy, achievement of the *dry* weight, hemoconcentration secondary to restoration of euvolemia, concentration of natriuretic peptides in absolute value.[76] Natriuretic peptide levels, that are associated in the literature with a lower risk of death and re-hospitalization (BNP <250 pg/mL and NT-proBNP 3000 pg/mL), can represent a useful threshold indicator for deciding how frequently to schedule monitoring of the individual patient between the hospital and region.[77]

The second important aspect is profiling the patient in terms of need of care. It is therefore desirable for practitioners to systematically report functional status, using standardized scales where possible (Barthel index or IADL and BADL), cognitive deficits and parameters related to socio-economic situation (housing, possibility of transport to access check-ups, presence of caregivers) for their HF patients, so as to facilitate interactions during hospitalization and planning for interventions at discharge.

The GP's main tasks for following up the patient with acute HF after discharge are summarized in Table 15.

Role of the dedicated heart failure clinic

In a recent joint ANMCO (National Association of Hospital Cardiologists)/SIC (Italian Society of Cardiology) document published in 2016, the role of the HF clinic was redefined in great detail.[78]

The HF Clinic, integrated in the patient's care management with the GP, can be very effective in preventing re-hospitalizations by performing actions essential for the patient's clinical stabilization,[78] especially in patients with a more severe disease (Table 16).

The document, dealing with the network and organization of clinics for treating HF,[78] explains in detail how to provide care in relation to the

epidemiological reality of the HF population and the hospital facilities. It also suggests the specific organizational profiles to be created for the various HF Clinics, in order to respond to patient needs at different stages of the disease. They must therefore be identified for specific geographical area:

1. The *regional HF Clinics/Centers*, aimed at the large number of people with heart failure, with a defined diagnostic-therapeutic procedure and with disease stability. They are interfaced with primary care to support management of stable patients, periodic re-evaluation to check new diagnostic needs or therapeutic options arising during the natural course of the disease, and prompt management of incipient instabilities.
2. The *hospital HF Clinics/Centers* taking care of patients with new-onset disease who need a diagnostic definition and therapeutic approach or at an early post-discharge stage after admission for acute HF, interfacing with the medical departments, to verify the stabilization and conclusion of the diagnostic-therapeutic process through their own facilities or departmental links.
3. *Advanced HF Clinics/Centers* taking care of the minority of patients in an advanced stage of the disease which, due to the instability of their clinical condition and their eligibility for high-cost treatment options, require super-specialist skills and equipment.

National/regional centers that are specifically regulated must also be included, sharing skills, protocols and pathways to carry out assessments and procedures prior to candidacy for heart replacement or implantation of circulatory support devices.

Table 14. Planning interventions to be implemented for integrated care continuity after discharge based on the different parties involved.

Patient-caregiver	
Cognitive deficits	Provide screening Interface with the caregiver Ensure home support
Depression	Provide screening Evaluate specific drug therapy
Inadequate literacy	Provide screening Multi-professional educational reinforcement
Inadequate home help	Activate social services Schedule telephone contacts and plan home care
Functional state	Fragility screening Nutritional planning, physiotherapy
Socio-economic situation	Verification of the possibility of access to medicines, home care, transport
Chronicity	Classification noted at the multi-professional level to increase the type and frequency of checks
GP	
Towards the patient	Educational reinforcement, verification of understanding and adherence
Towards the hospital doctor	Inform about previous medical history, functional status, social welfare problems
Medical therapy review	Verify the reconciliation between pre- and post-discharge therapy Update the list of outpatient medicines
Follow-up checks in progress	Make sure to receive results that have not yet been communicated
Follow-up visits	Regularly offer appointments to discharged patients within 7 days
Hospital doctor	
Towards the patient	Indications on contacts in case of post-discharge queries
Towards the GP	Clear information on hospital course and post-discharge plan
Quality of hospital care	Verification of clinical stability during discharge
Instructions written on discharge	Clear and understandable with checklist to limit possibility of error
Verbal instructions on discharge	Verify patient understanding and concordance of sources
Pharmacological reconciliation	Verify correct reconciliation between admission and discharge therapy
Pending results	Update and communication of pending results to the GP
Home care	Activate social services and verify that patients are informed of contacts to use

GP, general practitioner.

Table 15. Tasks of the general practitioner towards the patient with heart failure.

Patient discharged from A&E/EAD
• Acquisition of information provided on discharge • Reassessment of the prescribed discharge therapy and concomitant therapies • Educational intervention for the patient, caregiver and family
Patient in follow-up
• Periodic reinforcement of the educational intervention • Monitoring and prevention of exacerbations • Monitoring of underlying heart failure therapy with constant attention to comorbidities • Integration with other professional figures (regional cardiologist, Heart Failure Clinic, primary care nurse) • Management of complex and/or fragile patients • Participation in palliative care management

A&E/EAD, Accident & Emergency/Emergency Admissions Department.

Table 16. The most important tasks of the Heart Failure Clinic.

Action	Instrument	Intervention
Identify early signs and symptoms of hemodynamic instability	Remote monitoring or self-assessment of the patient	Modification of therapy Urgent visit HF Clinic/DH
Taking over after discharge together with the GP	Visit within 10-30 days	Letter of discharge shared
Educational action on the patient and caregivers	Interviews with the nursing staff, illustrative material	Regular telephone calls Evaluation sheets Questionnaires
Check on comorbidity and precipitating factors in the multi-specialist context and in agreement with the GP	Preparation of a detailed schema that defines the comorbidity and the precipitating factors	Coordinate specialist visits, prepare an agreed program with the GP

DH, day-hospital; GP, general practitioner; HF, heart failure.

Conclusions

Acute HF represents a typical multidisciplinary challenge to tackle as a team, with solid cardiological expertise. Its etiological and pathophysiological heterogeneity has long hindered the development of new treatments, with unsatisfactory prognostic perspectives in the face of a burden on healthcare resources that is difficult to sustain, due to the progressive increase in the average age of patients.

Only by identifying and implementing shared management protocols, which involve many specialists both in the hospitalization and post-hospital phases, and without neglecting the fundamental importance of the GP in the subsequent management, will make possible to create a system adapted to patients' needs. This system will entail rapid clinical assessment and diagnosis, treatment that begins promptly, and choices that combine clinical appropriateness and sustainability.

The referral to specialized facilities, differentiated by intensity of care and complexity of protocols, constitutes a fundamental element of organizational appropriateness. The Evaluation of organ damage and treatment of factors that may precipitate the acute syndrome, as well as that of comorbidities, represent an essential step.

It is fundamental to define the heart failure's etiology and make the effort to start optimizing therapy before discharge, creating bridges of continuity with the organization that will then take care of patients, avoiding their dispersion, funneling them to dedicated specialist clinics and referring them to pathways also shared with GPs. This document, thanks to contributions from the most qualified Scientific Societies, pursues the aim of proposing for each patient a structured, shared and applicable path, which returns from the pre-hospital phase, after discharge, to the territory.

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