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REGIONE AUTONOMA FRIULI VENEZIA GIULIA

La selezione del candidato a trapianto di cuore

Percorso
Diagnostico
Terapeutico
Assistenziale

GOVERNO CLINICO

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ASUFC - Udine

Percorso assistenziale del paziente candidato al trapianto di cuore

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ESC
European Society
of Cardiology

European Journal of Heart Failure (2018) 20, 1505–1535
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HFA POSITION STATEMENT

Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology

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Table 1: HFA Criteria for Advanced Chronic HF: Comparison of the 2007 and 2018 Definitions

Criteria in the 2007 HFA position statement[1]	Criteria in the 2018 position statement[2]
Severe symptoms of HF with dyspnoea and/or fatigue at rest or with minimal exertion (NYHA functional class III or IV)	1. Severe and persistent symptoms of heart failure (NYHA class III [advanced] or IV)
Objective evidence of severe cardiac dysfunction, shown by at least one of the following: • low LVEF (<30%); • severe abnormality of cardiac function on Doppler echocardiography with a pseudonormal or restrictive mitral inflow pattern; or • high LV filling pressures (mean PCWP >16 mmHg, and/or mean RAP >12 mmHg by pulmonary artery catheterisation), and/or high BNP or NT-proBNP plasma levels, in the absence of non-cardiac causes.	2. Severe cardiac dysfunction, defined by: • reduced LVEF ≤30% • isolated RV failure (e.g. ARVC) • non-operable severe valve abnormalities • congenital abnormalities persistently high (or increasing) BNP or NT-proBNP values and data showing severe diastolic dysfunction or LV structural abnormalities, according to the ESC definition of HFpEF and HFmrEF
Episodes of fluid retention (pulmonary and/or systemic congestion, or peripheral oedema) and/or of reduced cardiac output at rest (peripheral hypoperfusion) History of ≥1 HF hospitalisation in the past 6 months	3. Episodes of pulmonary or systemic congestion requiring high-dose intravenous diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalisation in the past 12 months
Severe impairment of functional capacity shown by one of the following: • inability to exercise; • 6MWTD < 300 m or less in women and/or patients aged ≥75 years; or • pVO_2 < 12–14 ml/kg/min	4. Severe impairment of exercise capacity with inability to exercise or low 6MWTD (<300 m) or pVO_2 (<12–14 ml/kg/min), estimated to be of cardiac origin
Presence of all features above despite attempts to optimise therapy including diuretics, inhibitors of the renin–angiotensin–aldosterone system, and beta-blockers, unless these are poorly tolerated or contraindicated, and cardiac resynchronisation therapy, when indicated.	In addition to the above, extracardiac organ dysfunction resulting from heart failure (e.g. cardiac cachexia, or liver or kidney dysfunction) or type 2 pulmonary hypertension may be present, but are not required. Criteria 1 and 4 can be met in patients who have cardiac dysfunction (as described in criterion 2), but also have substantial limitation caused by other conditions (e.g. severe pulmonary disease, non-cardiac cirrhosis or, most commonly, renal disease with mixed aetiology). These patients have a limited quality of life and survival because of advanced disease and warrant the same intensity of evaluation as someone in whom the only disease is cardiac; however, the therapeutic options for these patients are usually more limited.

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Criteria for definition of advanced heart failure

ESC

All the following criteria must be present despite OMT:

1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].
2. Severe cardiac dysfunction defined by (at least one of the following):
   - LVEF (≤30%)
   - Isolated RV failure (e.g., ARVC)
   - Non-operable severe valve abnormalities or congenital abnormalities
   - Persistently high (or increasing) BNP or NT-proBNP values and severe diastolic dysfunction or LV structural abnormalities (according to the definitions of HFpEF)
3. Episodes of pulmonary or systemic congestion requiring high-dose i.v. diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalization in the last 12 months.
4. Severe impairment of exercise capacity with inability to exercise or low 6MWT (<300 m) or pVO2 <12 mL/kg/min or <50% predicted value, estimated to be of cardiac origin.

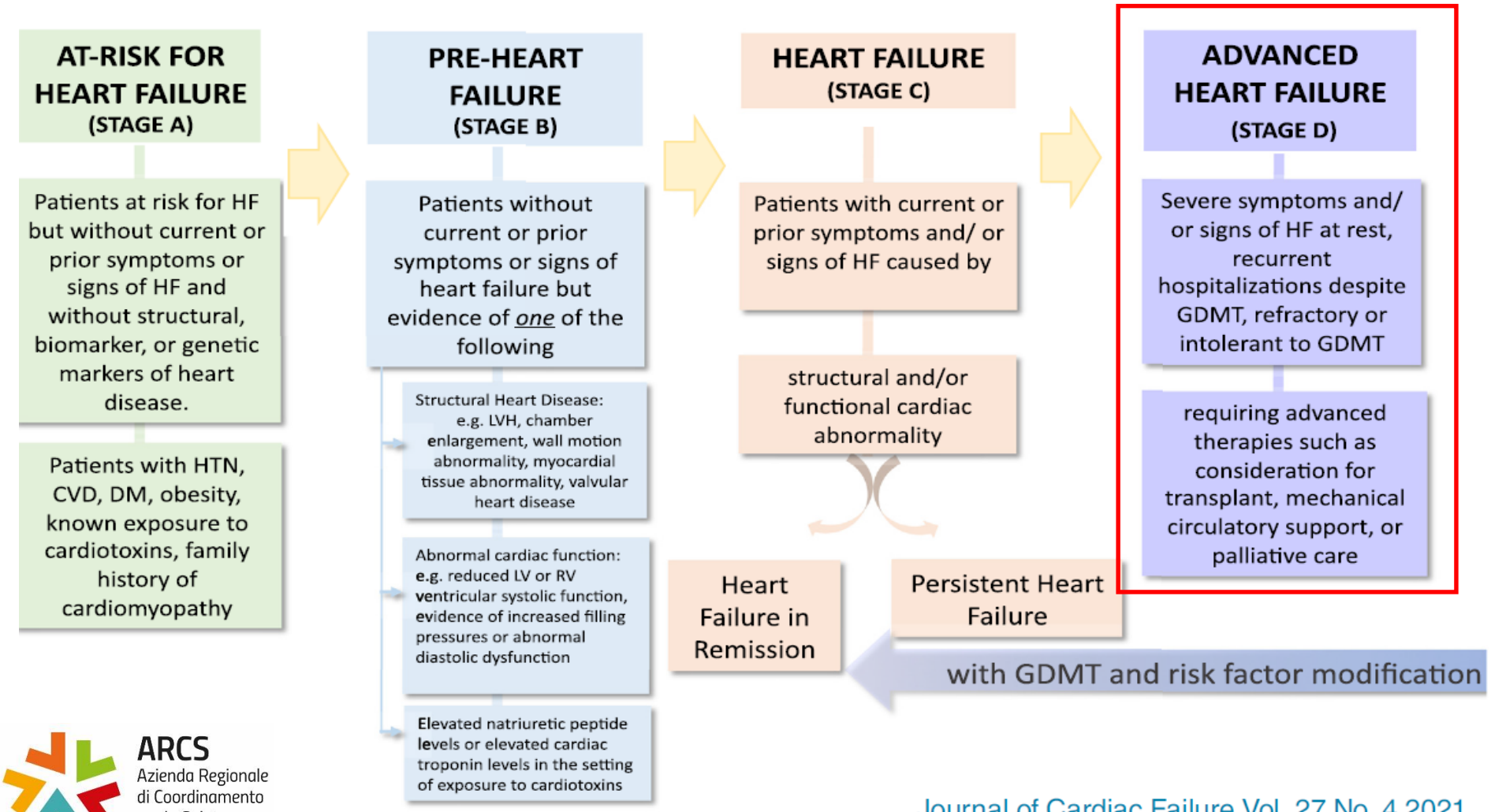
6MWT= 6-minute walk test; ARVC = arrhythmogenic right ventricular cardiomyopathy; BNP = B-type natriuretic peptide; HFpEF = heart failure with preserved éjection fraction; i.v. = intravenous; LV = left ventricular; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA =New York Heart Association; pVO2 = peak oxygen consumption; RV = right ventricular.

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)

Universal Definition and Classification of Heart Failure

A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure

Endorsed by Canadian Heart Failure Society, Heart Failure Association of India, the Cardiac Society of Australia and New Zealand, and the Chinese Heart Failure Association



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INTERMACS

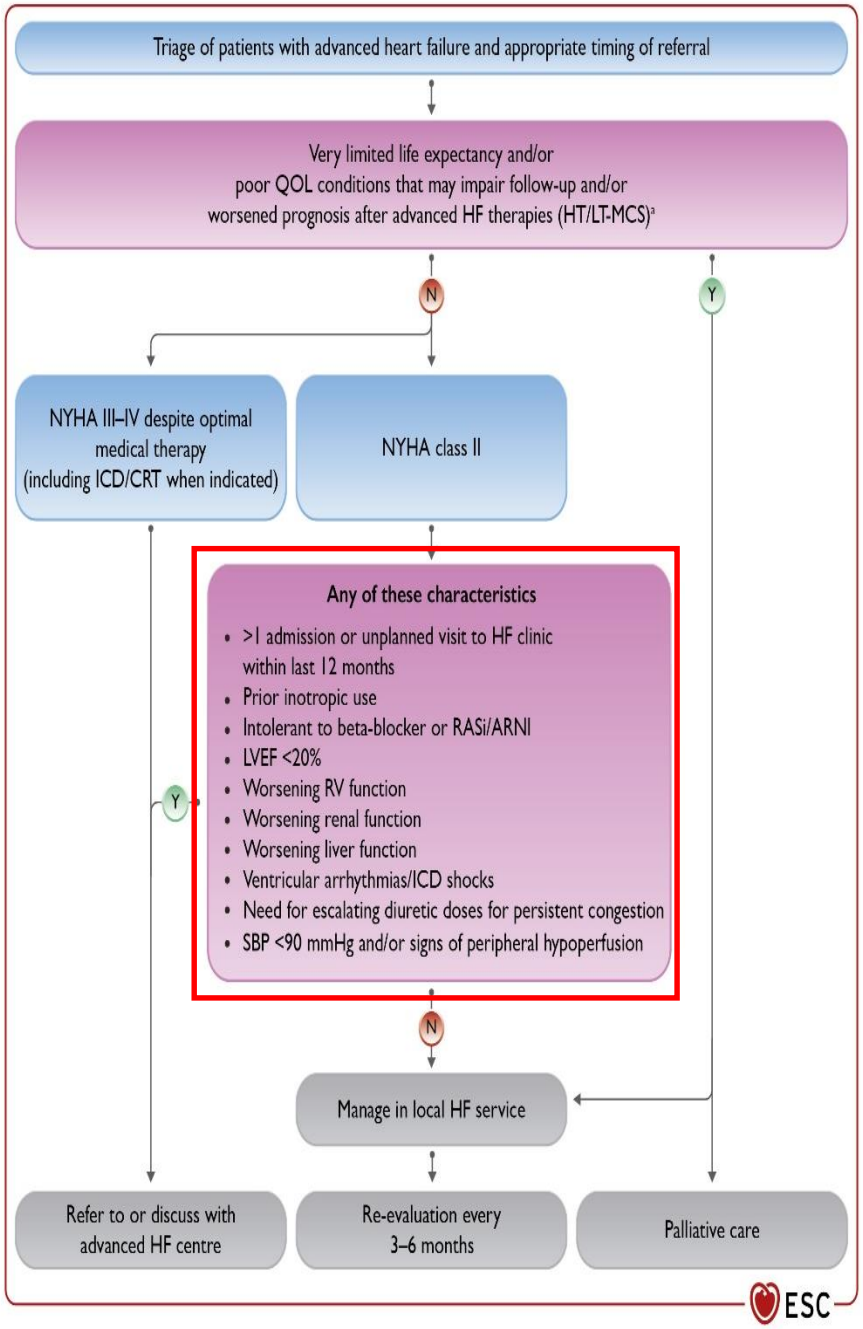
(Interagency Registry for Mechanically Assisted Circulatory Support)

Proposta di classificare i differenti gradi di severità dello S.C.avanzato

Table 8. INTERMACS Clinical Profiles

Level	Description	Hemodynamic Status	Time Frame for Intervention
1	Critical cardiogenic shock, "crash and burn"	Persistent hypotension despite rapidly escalating inotropic support and eventually IABP, and critical organ hypoperfusion	Within hours
2	Progressive decline on inotropic support, "sliding on inotropes"	Intravenous inotropic support with acceptable values of blood pressure and continuing deterioration in nutrition, renal function, or fluid retention	Within days
3	Stable but inotrope dependent, "dependent stability"	Stability reached with mild to moderate doses of inotropes but demonstrating failure to wean from them because of hypotension, worsening symptoms, or progressive renal dysfunction	Elective over weeks to months
4	Resting symptoms, "frequent flyer"	Possible weaning of inotropes but experiencing recurrent relapses, usually fluid retention	Elective over weeks to months
5	Exertion intolerant, housebound	Severe limited tolerance for activity, comfortable at rest with some volume overload and often with some renal dysfunction	Variable urgency, dependent on nutrition and organ function
6	Exertion limited, "walking wounded"	Less severe limited tolerance for activity and lack of volume overload, fatigue easily	Variable urgency, dependent on nutrition and organ function
7	Advanced NYHA III "symptoms, placeholder"	Patient without current or recent unstable fluid balance, NYHA class II or III	Not currently indicated

INTERMACS indicates Interagency Registry for Mechanically Assisted Circulatory Support; IABP, intra-aortic balloon pump; and NYHA, New York Heart Association. Adapted from Alba et al.[76]



Triage of patients with advanced heart failure and appropriate timing of referral

ARNI = angiotensin receptor-neprilysin inhibitor; CRT = cardiac resynchronization therapy; HF=heart failure; HT = heart transplantation; ICD=implantable cardioverter-defibrillator; LT-MCS = long-term mechanical circulatory support; LVEF=left ventricular ejection fraction; NYHA = New York Heart Association; RASi = renin-angiotensin system inhibitor; RV = right ventricular; SBP = systolic blood pressure; QOL = quality of life.

[a]Limited life expectancy may be due by major comorbidities such as cancer, dementia, end-stage organ dysfunction; other conditions that may impair follow-up or worsen post-treatment prognosis include frailty, irreversible cognitive dysfunction, psychiatric disorder, or psychosocial issues.

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Table 11 'I Need Help'—Markers of advanced heart failure

I	**I**notropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
N	**N**YHA class/ natriuretic peptide	Persisting NYHA class III or IV and/or persistently high BNP or NT-proBNP
E	**E**nd-organ dysfunction	Worsening renal or liver dysfunction in the setting of heart failure
E	**E**jection fraction	Very low ejection fraction <20%
D	**D**efibrillator shocks	Recurrent appropriate defibrillator shocks
H	**H**ospitalizations	More than 1 hospitalization with heart failure in the last 12 months
E	**E**dema/escalating diuretics	Persisting fluid overload and/or increasing diuretic requirement
L	**L**ow blood pressure	Consistently low BP with systolic <90 to 100 mmHg
P	**P**rognostic medication	Inability to up-titrate (or need to decrease/cease) ACEI, beta-blockers, ARNIs, or MRAs

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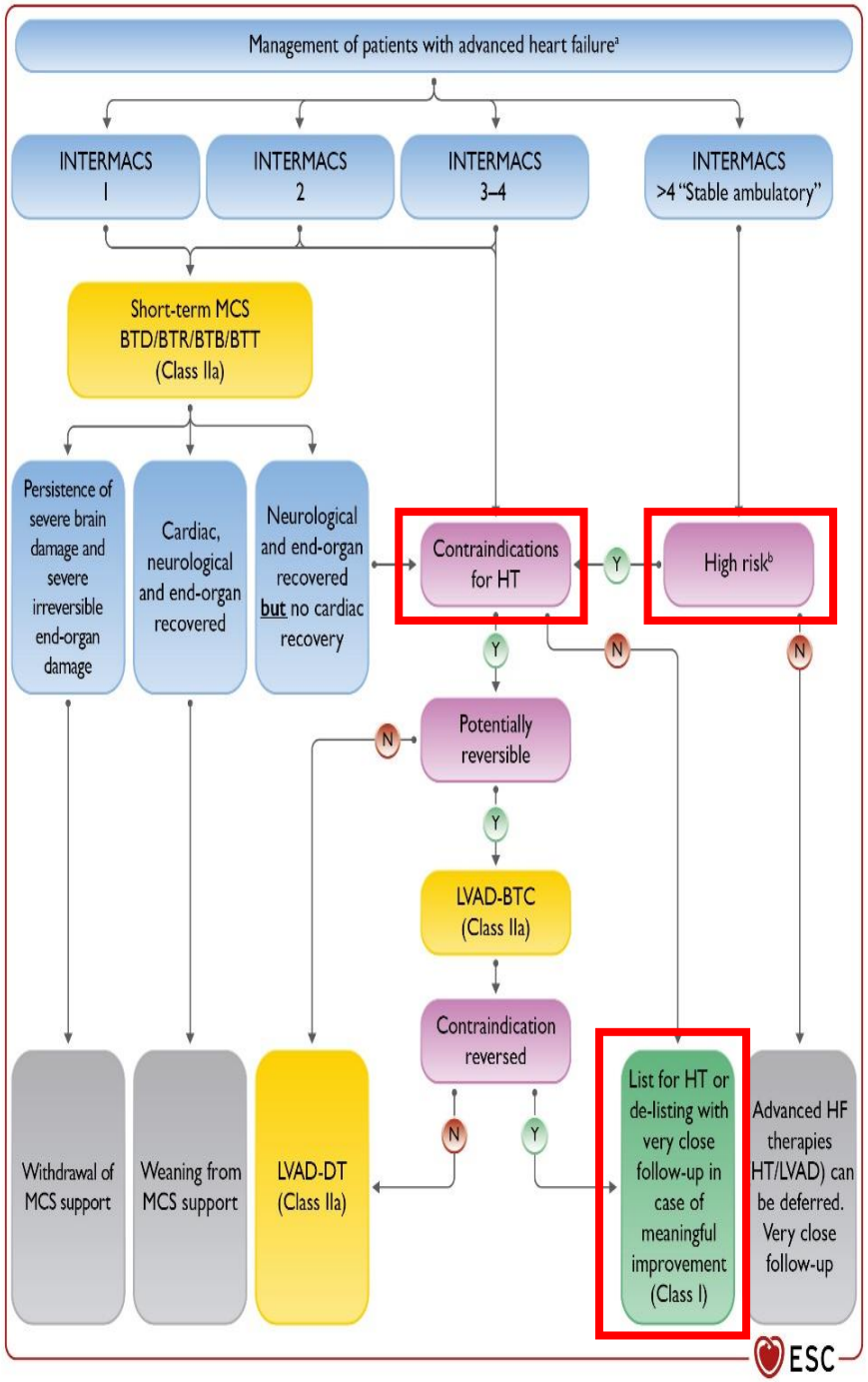
Table 6 Suggested clinical, laboratory, and echocardiographic criteria to trigger referral*

Clinical	Laboratory	Imaging	Risk score data
• >1 HF hospitalization in last year • NYHA class III–IV • Intolerant of optimal dose of any GDMT HF drug • Increasing diuretic requirement • SBP ≤90 mmHg • Inability to perform CPET • 6MWT • CRT non-responder clinically • Cachexia, unintentional weight loss	• eGFR <45 mL/min • SCr ≥160 mmol/L • K >5.2 or <3.5 mmol/L • Hyponatraemia • Hb ≤120 g/L • NT-proBNP ≥1000 pg/mL • Abnormal liver function test • Low albumin	• LVEF ≤30% • Large area of akinesis/dyskinesis or aneurysm • Moderate†-severe mitral regurgitation • RV dysfunction • PA pressure ≥50 mmHg • Moderate-severe tricuspid regurgitation • Difficult to grade aortic stenosis • IVC dilated or without respiratory variation	• MAGGIC predicted survival ≤80% at 1 year • SHFM predicted survival ≤80% at 1 year



Algorithm for the treatment of patients with advanced heart failure

BTB = bridge to bridge; BTC=bridge to candidacy; BTD = bridge to decision; BTR = bridge to recovery; BTT = bridge to transplantation; CA = cardiac amyloidosis; DT = destination therapy; ESC = European Society of Cardiology; HCM = hypertrophic cardiomyopathy; HF = heart failure; HFA = Heart Failure Association; HT = heart transplantation; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; LVAD-BTC = left ventricular assist device bridge to candidacy; LVAD-DT = left ventricular assist device destination therapy; MCS = mechanical circulatory support.

[a]This algorithm can be applied to all patients with advanced HF defined according to the ESC/HFA criteria, with exception of HCM, CA, arrhythmic storm, adult congenital heart disease, refractory angina.

[b]Recurrent hospitalization, progressive end-organ failure, refractory congestion, inability to perform cardiopulmonary exercise test or peak oxygen consumption <12 mL/min/kg or <50% of expected value.

Colour code for classes of recommendation: Green for Class of recommendation I and Yellow for Class of recommendation IIa (see Table 1 for further details on classes of recommendation

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Recommendations for the treatment of patients with advanced heart failure

Heart transplantation is recommended for patients with advanced HF, refractory to medical/device therapy and who do not have absolute contraindications.	I	C

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IL PERCORSO ASSISTENZIALE DEL PAZIENTE CANDIDATO AL TRAPIANTO DI CUORE

FASI DEL PERCORSO	ATTIVITÀ
Pre-trapianto	Inquadramento diagnostico del problema clinico
	Selezione del paziente candidato al trapianto
	Reclutamento
Trapianto	Intervento chirurgico
Post-trapianto	Gestione clinico-assistenziale del paziente (follow-up)

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Inquadramento Diagnostico del Problema Clinico

- I pazienti con cardiopatia avanzata tale da compromettere in maniera significativa la loro aspettativa e qualità di vita e non suscettibile di miglioramenti terapeutici, possono essere considerati candidati al trapianto di cuore.

- I criteri per l'indicazione al trapianto sono quelli condivisi tra i diversi Centri di Trapianto di cuore, adottati dal Centro Nazionale Trapianti sulla base delle Linee Guida internazionali pubblicate da The International Society for Heart and Lung Transplantation.

- I pazienti candidabili al trapianto di cuore che possono essere iscritti in lista d'attesa di trapianto sono quelli assistiti dal Servizio Sanitario Nazionale e segnalati dal Cardiologo di riferimento tramite contatto diretto o invio di documentazione sanitaria al CTC.

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The Journal of
Heart and Lung
Transplantation
http://www.jhltonline.org

ISHLT GUIDELINE

The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update

Mandeep R. Mehra, MD (Chair), Charles E. Canter, MD,
Margaret M. Hannan, MD, Marc J. Semigran, MD, Patricia A. Uber, PharmD,
David A. Baran, MD, Lara Danziger-Isakov, MD, MPH, James K. Kirklin, MD,
Richard Kirk, MD, Sudhir S. Kushwaha, MD, Lars H. Lund, MD, PhD,
Luciano Potena, MD, PhD, Heather J. Ross, MD, David O. Taylor, MD,
Erik A.M. Verschuuren, MD, PhD, Andreas Zuckermann, MD
and on behalf of the International Society for Heart Lung Transplantation (ISHLT)
Infectious Diseases, Pediatric and Heart Failure and Transplantation Councils

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INDICAZIONI

Paziente con insufficienza cardiaca avanzata refrattaria alla terapia medica orale:

- con caratteristiche di progressione nel tempo nonostante conduzione corretta delle cure
- non migliorabile con la terapia medica, con procedure interventistiche, o con terapia CCH
- IC avanzata determinata da disfunzione ventricolare destra pura
- Aritmie minacciose non domabili con terapia medica o procedure interventistiche

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CARDIOPATIE CANDIDABILI

Cardiopatie che possono essere considerate per trapianto cardiaco dopo adeguata valutazione clinico-strumentale:

- Cardiomiopatia dilatativa (ischemica, idiopatica, valvolare, …)
- Cardiomiopatie restrittive, tra cui l'amiloidosi
- Cardiomiopatie ipertrofiche
- Displasie aritmogene
- Cardiopatie congenite

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CONTROINDICAZIONI ASSOLUTE

- Attuale abuso di alcool/droghe
- Ipertensione arteriosa polmonare irreversibile
- Psicopatie importanti
- Neoplasie attive o pregresse a prognosi infausta
- Patologie multiorgano o sistemiche
- Ulcera peptica attiva sanguinante

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CONTROINDICAZIONI RELATIVE

- Età > 70 anni
- Severa insufficienza renale (salvo trapianto combinato)
- Severa insufficienza epatica (salvo trapianto combinato)
- Vasculopatia polidistrettuale
- Severa obesità / Cachessia
- Severa osteoporosi
- Recente tromboembolia polmonare
- Pregressa Cardiochirurgia multipla
- BPCO severa
- Diabete insulino-dipendente con danno d'organo
- Ridotta compliance individuale e/o familiare
- Iperimmunizzazione
- Sieropositività per HIV

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PUNTI CHIAVE

- **TEST CARDIOPOLMONARE** per valutazione riserva funzionale
- **CATETERISMO CARDIACO DESTRO**
- **SCORE DI RISCHIO**

CRITERI DI INCLUSIONE

- CATETERISMO CARDIACO DESTRO per valutazione delle pressioni polmonari

- Valutazione **COMORBIDITÀ**
  - *Età*
  - *Obesità*
  - *Insufficienza renale*
  - *Diabete mellito*
  - *Arteriopatia periferica*
  - *Malattie cerebrovascolari*
  - *Malattie neoplastiche e malattie infettive*
  - *Compliance alla terapia ed alle norme comportamentali*

CRITERI DI ESCLUSIONE

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TEST CARDIOPOLMONARE

- In pazienti *intolleranti* ai β-bloccanti dovrebbe essere usato un valore soglia di picco di consumo di ossigeno

< 14 mL/Kg/min — I B

- In pazienti *in terapia* con β-bloccanti dovrebbe essere usato un valore soglia di picco di consumo di ossigeno

< 12 mL/Kg/min (la presenza di CRT non modifica i cut off) — I B

- In pazienti **< 50 anni** e di sesso **femminile** è ragionevole considerare l'utilizzo di standards alternativi in combinazione con il picco di O2 per l'inserimento in lista TCO, inclusa una **% predetta di picco di consumo di ossigeno < 50%** — IIa C
- Se il test da sforzo cardiopolmonare è submassimale (RER < 1,05) potrebbe essere considerato usare gli **equivalenti ventilatori per l'anidride carbonica (> 35)** per l'inserimento in lista — IIb C
- Nei pazienti obesi (**BMI > 30**) potrebbe essere considerata la correzione del picco di O2 per la massa magra → un **picco corretto per la massa magra** < **19 mL/Kg/min** può servire come soglia ottimale per guidare la prognosi — IIb C
- Non si dovrebbe basare l'immissione in lista dei pazienti unicamente sulla misura del picco di consumo di O2 — III C

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RUOLO DEL CATETERISMO DESTRO

- Il cateterismo destro dovrebbe essere eseguito in tutti i candidati ***adulti*** in previsione dell'inserimento in lista TCO e ***periodicamente*** fino al trapianto cardiaco. **I C**
- Il cateterismo destro dovrebbe essere eseguito ad **intervalli di 3-6 mesi nei pazienti in lista TCO** (***necessaria individualizzazione***), specialmente in presenza di *ipertensione polmonare reversibile* o *peggioramento dei sintomi* da scompenso cardiaco **I C**
- Un **test di reversibilità con vasodilatatori** dovrebbe essere somministrato se: **I C**
  - *PAPs 50 mmHg;*
  - *Gradiente transpolmonare > 15 mmHg;*
  - *Resistenze vascolari polmonari (PVR) > 3 unità Wood con PAS sistemica > 85 mmHg*
- Se il **test con vasodilatatori è negativo**, si dovrebbe ospedalizzare il paziente per eseguire un **monitoraggio emodinamico continuo** (le PVR diminuiranno in 24-48 ore dopo somministrazione di terapia diuretica, inotropi ed agenti vasoattivi -NO2 inalatorio-) **I C**

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IPERTENSIONE POLMONARE

- Se la terapia medica non riesce ad ottenere dei parametri emodinamici accettabili e se il ventricolo sinistro non riesce ad essere «scaricato» con dispositivi meccanici (IABP e/o LVAD), è ragionevole concludere che l'ipertensione polmonare sia **irreversibile**.

IIb C

- ***Dopo l'utilizzo di un LVAD dovrebbe essere eseguita una rivalutazione dei parametri emodinamici dopo 3-6 mesi per accertare l'eventuale reversibilità dell'ipertensione polmonare***

IIa C

SCORE DI SOPRAVVIVENZA NELLO SCOMPENSO CARDIACO

- Gli score prognostici dello scompenso cardiaco dovrebbero essere ***valutati <u>insieme</u> al test da sforzo cardiopolmonare*** per determinare la prognosi del paziente «ambulatoriale» e guidarne l'inserimento in lista TCO

IIb C

  - **<u>Seattle Heart Failure Model</u> (SHFM) < 80%**
  - **<u>Heart Failure Survival Score</u> (HFSS) in classe a medio/alto rischio**

Dovrebbero essere considerati come cut-off ragionevoli per l'immissione in lista

- ***N.B.: la valutazione dei pazienti basata esclusivamente sugli score prognostici di sopravvivenza nello scompenso cardiaco non dovrebbe essere eseguita***

III C

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LA NECESSITÀ DELLA STRATIFICAZIONE

Despite many prognostic parameters (*Supplementary Table 13*), predicting outcomes remains difficult and patients are often referred to advanced HF centres too late. Identifying warning signs in patients with non-advanced symptoms may allow early referral so that MCS and heart transplantation may be offered before the development of end-organ failure (*Figure 5*; *Supplementary Table 14*).[376,386] An organizational model between centres with different levels of care complexity, based on a 'Hub and Spoke' network is the key to good patient management.[376]

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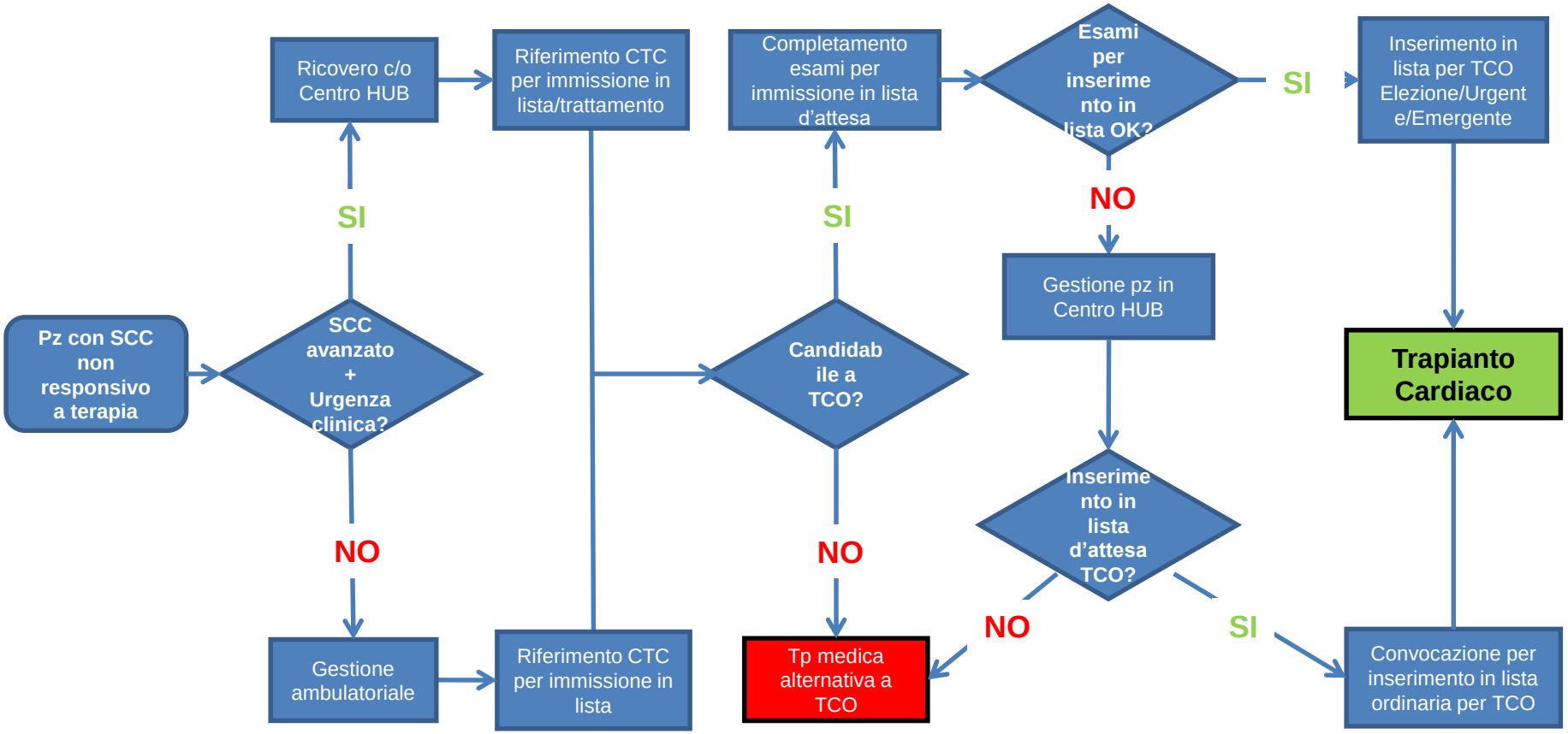

GRAZIE PER L'ATTENZIONE!

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