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GUIDELINE

Donor heart selection: Evidence-based guidelines for providers

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Abbreviations: ACAOS, anomalous origination of a coronary artery from the opposite sinus; ACC, American College of Cardiologists; BMI, body mass index; BNP, B-type natriuretic peptide; CABG, coronary artery bypass graft; CAD, coronary artery disease; CAV, cardiac allograft vasculopathy; CNS, central nervous system; CO, carbon monoxide; COVID-19, coronavirus disease 2019; CPR, cardiopulmonary resuscitation; CT, computed tomography; ECG, electrocardiogram; ECMO, extracorporeal membrane oxygenation; HIV, human immunodeficiency virus; HLA, human leukocyte antigens; INTERMACS, interagency registry for mechanically assisted circulatory support; ISHLT, International Society for Heart and Lung Transplantation; INH, isonicotinic acid hydrazide; LV, left ventricle; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; MRI, magnetic resonance imaging; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; OPO, organ procurement organization; OPTN, organ procurement and transplantation network; PCI, percutaneous coronary intervention; PGD, primary graft dysfunction; pHM, predicted heart mass; PLSVC, persistent left superior vena cava; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TTE, transthoracic echocardiography; UNOS, united network for organ sharing; VA, veno-arterial; VAD, ventricular assist device; VV, veno-venous; WHO, World Health Organization

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The proposed donor heart selection guidelines provide evidence-based and expert-consensus recommendations for the selection of donor hearts *following brain death.* These recommendations were compiled by an international panel of experts based on an extensive literature review.
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In 1995, Dr J. Copeland noted that "only optimal donors should be accepted for heart transplantation," implying that extended-criteria donor organs may not be viable.[1] Despite this awareness raised from over 25 years ago, this topic has remained much debated. While older donors are more routinely used in Europe, younger donors with short ischemic times are more commonly used in the United States. Mortality rates differ worldwide, and some of these differences are due to donor selection and/or recipient urgency. Seeking a balance between maximizing the number of transplants (by taking greater risk) and minimizing the risk to meet societal needs, while controlling cost, is difficult and frequently related to a lack of reliable data regarding both donors and recipients. The issue is further complicated by the fact that the peri-operative surgical risk is a combination of risk factors that include donor, recipient, and ischemic time. Lastly, meaningful comparisons of transplant outcomes across countries require proper risk-adjustment.

The proposed guidelines provide evidence-based as well as expert-consensus recommendations for the selection of donors *following brain death.* These recommendations were compiled by an international panel of experts based on an extensive literature review. Controversial subjects are dealt with one by one and current state-of-the-art information is provided to help define risk. The strength of each recommendation and the corresponding level of available evidence were classified following the International Society for Heart and Lung Transplantation protocol for developing guideline documents.[2]

Task forces were established with an international panel of experts. The task forces reviewed donor characteristics (Task force 1), international donor practices (Task force 2), donor and recipient matched characteristics (Task force 3), extended donor characteristics (Task force 4), and donor risk scores (Task force 5).

Clinical stability of the donor

Factors considered in the clinical stability of the cardiac donor are hemodynamics, hormonal resuscitation,[3-11] and the restoration of intravascular volume and electrolyte imbalance,[12-22] as well as donor metabolism.

Recommendations for donor hemodynamics:[21,23-31]

Class I

1. Donors receiving low dose norepinephrine (e.g., ≤0.1 μg/kg/min) may be considered suitable for transplantation if (other) inotropes are not required. In general, the higher the dose of norepinephrine in the donor, the poorer the expected outcome after transplant. **Level of Evidence: C.**

Class IIa

1. If inotropes and/or vasopressors are required to maintain adequate circulatory function in the donor, placement of

a Swan-Ganz catheter and goal-directed therapy should be considered to maximize the likelihood of donor heart utilization. **Level of Evidence: C.**
2. Suggested hemodynamic targets for donor hearts include the following:

- Mean arterial pressure >60 mm Hg
- Cardiac index >2.4 liter/min/m^2
- Central venous pressure <12 mm Hg
- Pulmonary capillary wedge pressure <12 mm Hg
- Left ventricular (LV) stroke work index >15 g·min/m^2

Level of Evidence: C.

Recommendations considering donor metabolism:[27,30,32-34]

Class IIa

1. Use of hearts from donors with moderately abnormal serum sodium (outside the 135-145 mEq/liter range) may be considered. **Level of Evidence: C.**
2. Hearts from donors with extreme hypo- or hypernatremia (serum sodium <129 or ≥170 mEq/liter, respectively) should not be used. **Level of Evidence: C.**
3. Donor hyperglycemia should not be a contraindication to use for heart transplantation. **Level of Evidence: C.**

Mechanisms of donor death

The mode of brain death affects clinical outcomes following heart transplantation.[23,35-37] Recommendations are provided for donor death by carbon monoxide (CO) poisoning, explosive brain death, and unexplained causes. Furthermore, the pathophysiology of brain death includes neurohormonal and inflammatory changes that may result in donor organ injury. Beneficial effects of corticosteroid administration to brain-dead donors (hormonal resuscitation therapy) in terms of organ recovery, graft survival, and graft function have been reported, but there are many confounding factors that preclude definitive assessment of the utility of steroid administration during donor management.[3-5]

Recommendations regarding donor death by CO poisoning:[38-48]

Class IIa

1. Donors with CO poisoning should be carefully screened. Risk factors for early heart allograft dysfunction include ischemic electrocardiogram (ECG) changes, troponin I elevations ≥0.7 ng/ml and left ventricular dysfunction. **Level of Evidence: C.**

Class III

1. Donors with CO poisoning and carboxyhemoglobin levels >40%, ischemic ECG changes, elevated levels of cardiac troponin (≥0.7 ng/ml) or ventricular dysfunction should generally be avoided. **Level of Evidence: C.**

Recommendation regarding explosive brain death:[23,35-37,49-53]

Class IIa

1. Donors with explosive brain death may be considered for transplantation. There is evidence suggesting reduced long-term survival of recipients of such donors, possibly due to increased cardiac allograft vasculopathy. **Level of Evidence: C.**

Unexplained cause of donor death

Few reports have been published detailing the outcomes of allografts taken from donors with an unexplained cause of death. When faced with such an offer, centers should consider the more common causes of sudden death in young persons.

Recommendation for the evaluation of unexplained causes of death

Class IIb

1. Donors with unexplained cause of sudden death should be carefully screened with ECG and, when appropriate, coronary angiography for cardiac causes of death including hypertrophic cardiomyopathy, long-QT syndrome, Brugada syndrome, and congenital heart disease includes coronary anomalies. Donors with unexplained sudden death can be considered for transplant if the evaluation is negative. **Level of Evidence: C.**

Donor demographics

Recommendations for donor age:[54-70]

Class I

1. The use of donor hearts <45 years of age is recommended. **Level of Evidence: C.**
2. Donors ≥45 years of age can be used after screening for significant coronary artery disease (e.g., ≤50% narrowing) and if short ischemic times (<4 hours) can be expected. Such screening criteria vary around the world based on risk factors and average population donor characteristics. Considerations should take into account estimated survival benefit, availability of organs, the severity of illness of the recipient, and whether the recipient is on mechanical circulatory support. No established upper age limit currently exists. **Level of Evidence: C.**

Class IIa

1. Donor selection should account for unique recipient characteristics such as older donors to be used in older or highly sensitized recipients (smaller compatible donor pool) who have a negative crossmatch (either prospective or virtual depending on needs of recipient and/or institution) to the prospective older donor. **Level of Evidence: C.**

Donor size

Factors considered in developing guidelines on donor size were sex matching,[71-75] donor weight and height,[64,72,74,76-78] predicted heart mass (pHM),[63,69,79] the role of body mass index,[75,80] oversizing for pulmonary hypertension,[76,81,82] and extreme donor-recipient size mismatch.[63,74,81,83] While there currently is no consensus as to best method of determining size matching, pHM is gaining in popularity.

Recommendations regarding donor size

Class I

1. Allocation of female donors to male recipients may be done safely, especially in recipients without pulmonary hypertension and when adequate donor/recipient weight ratio and/or pHM are ensured. A value of pHM within 20% to 30% of recipient is considered acceptable. **Level of Evidence: C.**

Class IIb

1. Due to the impact on right ventricular dysfunction of the donor allograft, pulmonary hypertension in the intended recipient should be taken into consideration when determining the degree of acceptable size and sex mismatch. **Level of Evidence: C.**

Recommendation on anti-human leukocyte antigens (HLA) compatibility: [68,75,76,84]

Class IIa

1. The presence of preformed human leukocyte antigens (HLA) antibodies should be ascertained and compared against the donor HLA, at least virtually, prior to acceptance for organ transplant. **Level of Evidence: C.**
2. There currently is no agreed-upon standard for which HLA antibodies can be crossed and which should be avoided. Center practice varies based on magnitude, strength of antibodies, whether they are C1q positive (e.g., complement-fixing), and the level of experience with managing sensitization and ability to absorb transplant center risk. **Level of Evidence: C.**

Recommendations on blood group compatibility between donor and recipient: [75,85-87]

(See also Table 1.)

Class I

1. ABO blood group compatibility should be confirmed. **Level of Evidence: C.**
2. Systems of care should be implemented to assure that blood group compatibility is not violated without a specific reason (ABO-incompatible pediatric transplantation). **Level of Evidence: C.**

Recommendations regarding ischemic time:[59,62,68,88-109]

Class I

1. Target total organ ischemic time for cardiac transplantation should be ≤4 hours, to reduce the risk of primary graft dysfunction and early death. **Level of Evidence: C.**

Class IIa

1. A transplant center may allow the total organ ischemic time to exceed 4 hours for donors <45 years of age without compromising early outcomes after heart transplantation. With older donors, it is specifically recommended to avoid long-distance transportation or other factors (e.g., redo sternotomy, ventricular assist device (VAD) explantation, which can cause prolonged operative times) that could result in total donor ischemic times >4 hours. **Level of Evidence: C.**
2. Ex-vivo normothermic heart perfusion platforms can be safely used to decrease ischemic time for distant procurements and potentially to expand the procurement of marginal donors based on metabolic evaluation during ex-vivo perfusion. **Level of Evidence: C**.

Donor comorbidities

Recommendations for left ventricular hypertrophy (LVH)[55,59,81,106,110-115] and hypertension: [54,68,113,116,117]

(See Table 2 for the gradation of left ventricular hypertrophy (LVH).)

Table 1 Compatible Blood Groups

Recipient blood type	Compatible donor
A	A, O
B	B, O
AB	A, B, AB, O
O	O

Table 2 LVH Determined by Measurement of the Interventricular Septum

Level of LVH	Intraventricular septum
Mild	11-13 mm
Moderate	14-16 mm
Severe	≥17 mm

Class I

1. LVH should be assessed by measuring the thickness of the interventricular septum or the posterior wall on echocardiography. **Level of Evidence: C.**

Class IIa

1. Carefully selected donor hearts with LVH >13 mm (measured as outlined above) may be considered, particularly with younger (donors ≤40 years of age) and/or shorter ischemic time (<4 hours). **Level of Evidence: C.**
2. Chronic hypertension (defined by contemporary guidelines) or the use of hearts from donors being treated for hypertension in the absence of LVH do not appear to impact post-transplant outcomes. **Level of Evidence: C.**

Recommendations regarding donors with coronary artery disease (CAD): [55,118-124]

(Table 3 illustrates how recommendations have varied over time and across geographic regions.)

Class IIa

1. Donors with mild luminal irregularities (e.g., ≤50% narrowing) on coronary angiography may be considered for heart transplantation. **Level of Evidence: C.**
2. Coronary angiography should be considered in donors ≥45 years old, depending on geography and other risk factors. See also Table 3. **Level of Evidence: C.**
3. Risk factors suggesting need for coronary angiography include hypertension, diabetes (particularly with longer time of treatment), male sex, obesity, hyperlipidemia, tobacco and/or cocaine/methamphetamine use. **Level of Evidence: C.**
4. Myocardial bridging is rarely a contraindication to transplantation. **Level of Evidence: C**

Class IIb

1. Donors with single-vessel coronary disease amenable to percutaneous or surgical therapy may be considered after balancing the risk of coronary disease progression and the urgency of the recipient. **Level of Evidence: C.**
2. Donors with left main and/or 2 to 3 vessel obstructive (≥50%) coronary disease are best avoided for transplantation in the absence of extenuating circumstances. **Level of Evidence: C.**

Recommendations regarding donors with diabetes: [54,55,58,59,68,69,81,116,117,128-131]

Class IIa

1. Donors with diabetes mellitus and no other risk factors, particularly without coronary artery disease, can be safely used. **Level of Evidence: C.**
2. Coronary angiography should be considered for diabetic donors, and duration of diabetes and donor age should be carefully weighed. **Level of Evidence: C.**

Recommendations regarding donor experiencing cardiopulmonary arrest and the duration of cardiopulmonary resuscitation (CPR): [132-138]

Class IIa

1. Donors with cardiopulmonary resuscitation may be used if heart function is normal (by left ventricular ejection fraction (LVEF) and hemodynamics) at the time of

Table 3 Recommended Age Criteria for the Use of Coronary Angiography in Donor Evaluation Across Time and Geographic Region **(Class IIa/b; Level of Evidence: C)**

Publication	Recommended age for men	Recommended age for women	Region	Year
ACCRecommendations[125]	• Age >45 years • Lower by 5-10 years if risk factors present	• Age >50 years • Lower by 5-10 years if risk factors present	US	1993
Maximizing Use of Organs Recovered From the Cadaver Donor Consensus Conference[27]	• Age >55 years: mandatory • Age >45 years: recommended • Age >35 years if cocaine or 3 risk factors	• Age >55 years: mandatory • Age >50 years: recommended • Age >40 years if cocaine or 3 risk factors	US	2002
United Network for Organ Sharing[126]	• Age >40 years • Younger with risk factors	• Age >45 years • Younger with risk factors	US	2018
European Committee on Organ Transplantation (Council of Europe)[127]	• Age >55 years • Age >45 years if more than 1 risk factor present	• Age >55 years • Age >45 years if more than 1 risk factor present	Europe	2018

procurement, unless the cardiac arrest circumstances raise the suspicion for underlying structural heart disease. **Level of Evidence: C.**
2. The duration of donor cardiopulmonary arrest and of the CPR alone should not be used to exclude donor hearts for transplantation. CPR times >30 minutes in both adult and pediatric donors do not negatively impact post-transplant survival or outcomes if echocardiographic cardiac function and hemodynamics are favorable (e.g., LVEF >50%) after resuscitation. **Level of Evidence: C.**

Donor drug use

Recommendation regarding donor tobacco use: [139-144]

Class IIa

1. Tobacco use of significant pack-years increases the risk of donor coronary artery disease (CAD). Depending on donor age (>45 years), obtaining a donor angiogram may be reasonable. **Level of Evidence: C.**

Recommendation regarding donor alcohol use: [145-153]

Class IIa

1. The hearts of donors with a history of alcohol use may be used for transplantation if cardiac function is preserved on echocardiography. **Level of Evidence: C.**

Recommendations regarding donor use of illicit drugs (cocaine, amphetamine, methamphetamine): [140,154-160]

Class IIa

1. Donors with a history of cocaine use can be considered for heart transplantation if there is no significant LVH (i.e., ≥14 mm; see also the recommendations on donor LVH in this document). **Level of Evidence: C.**
2. Donors with a history of past or active cocaine use should have a coronary angiogram when possible. **Level of Evidence: C.**
3. Donors with toxicology positive for amphetamine or methamphetamine may be utilized for transplant if ventricular function and structure are normal on echocardiogram and imaging. **Level of Evidence: C.**
4. Donors with toxicology positive for multiple substances may be utilized for transplant if ventricular function and structure are normal on echocardiogram and imaging. **Level of Evidence: C.**

Infections in the donor

This section reviews various potential infections in a donor though it is not comprehensive of all possibilities. Infectious disease thoracic transplant physician specialists should be consulted for unique donor infections as new pathogens are always emerging and treatments are constantly evolving.

Recommendation regarding bacterial infections in the donor: [63,161-165]

Class IIa

1. Transplantation of hearts from bacteremic donors is feasible, provided that the recipient, after being informed of the associated risks, is treated with targeted antimicrobials for an appropriate duration post-transplant. **Level of Evidence: C.**

Recommendations regarding fungal infections: [166-173]

(See Table 4.)

Recommendations regarding bloodborne viral infections in the donor

(Recommendations concerning donors with hepatitis B,[127,174-188] hepatitis C,[189-198] and human immunodeficiency virus (HIV)[199-207] are summarized in Table 5.)

Table 4 Fungal Infections

Pathogen	Recommendation	Strength/level of evidence
Aspergillus, active	If disseminated, do not utilize	III /C
Aspergillus, active (lung only)	If lung only, consider taking heart with post-transplant prophylaxis	IIb /C
Aspergillus, history of disease	If findings, send workup to rule out active disease, possible post-transplant prophylaxis	IIa /C
Coccidiomycosis, active disease	Do not utilize	III /C
Coccidiomycosis, history of disease	If findings, send workup to rule out active disease, possible post-transplant prophylaxis	IIa /C
Cryptococcus, untreated	Do not utilize	III /C
Cryptococcus, actively treated	Consider risks/benefits	IIa /C
Histoplasmosis, active disease	Do not utilize	III /C
Histoplasmosis, history of disease	If findings, send workup to rule out active disease	IIa /C

Table 5 Bloodborne Infections

Pathogen	Recommendation	Strength/level of evidence
Hepatitis B Ag+	Should be limited to carefully selected, consented recipients.	IIa /C
Hepatitis B **c**Ab+	With appropriate post-transplant monitoring and prophylaxis, HBcAb + donor organs may be used for transplantation.	IIa /C
Hepatitis C (anti-HCV+, HCV-RNA-)	Generally safe for transplantation but requires post-transplant HCV-RNA monitoring.	IIa /C
Hepatitis C (anti-HCV+, HCV RNA+)	Should be limited to consented recipients with appropriate post-transplant treatment and monitoring.	IIa /C
HIV	Transplantation of HIV seropositive hearts into HIV seropositive recipients is reasonable with full informed consent and involvement of local infectious disease experts in advance.	IIa /C

Table 6 Recommendation Regarding Donors with Tuberculosis

Pathogen	Recommendation	Strength/level of evidence
Mycobacterium tuberculosis, active disease	Consider taking organ, consult infectious disease specialist for follow up and isonicotinic acid hydrazide (INH) for 6 months	IIb /C
Mycobacterium tuberculosis, history of disease	Accept organ, consult infectious disease specialist for follow up and consider INH 3-6 months	IIa /C

Recommendation regarding donors with tuberculosis:[208]

(See Table 6.)

Recommendation regarding donors with increased infection risk:[127,193,209-226]

(See also Table 7.)

Table 7 Behavioral, Social, Medical, and Other Factors that Increase Risk for Recent Hepatitis B, Hepatitis C, or HIV Infection in Organ Donors Per US Guidelines[217]

Risk criteria (in the preceding 30 days):

- Sex[a] with a person known or suspected to have HIV, HBV, HCV infection
- Man who has had sex with another man
- Sex in exchange for money or drugs
- Sex with a person who had sex in exchange for money or drugs
- Drug injection for non-medical reasons
- Sex with a person who injected drugs for non-medical reasons
- Incarceration (confinement in jail, prison, or a juvenile correctional facility) for ≥72 consecutive hours
- Child breastfed by a mother with HIV infection
- Child born to a mother with HIV, HBV, or HCV infection
- People in whom medical and social histories cannot be obtained or is unknown

[a]The term sex refers to vaginal, anal or oral sexual contact.

Class I

1. Carefully selected donors at increased risk for unrecognized/recent hepatitis B, hepatitis C, and HIV may be selected for transplantation with surveillance post-transplant for disease transmission. **Level of Evidence: B.**

Recommendations regarding emerging viral pathogens:[227-243]

(See Table 8.)

Recommendations regarding parasitic infections in the donor:[180,244-252]

(See Table 9.)

Recommendations regarding central nervous system infections in the donor: [253,254]

(See Table 10.)

Malignancies in the donor

Recommendations regarding malignancy in donors:[255-261]

(See also Table 11.)

Class IIa

1. Donors with non-melanoma skin cancers and low-grade primary central nervous system tumors should be

Table 8 Emerging Viruses

Virus	Recommendation	Strength /level of evidence
SARS-CoV-2, active confirmed	Should be limited to informed recipients. Ideally should be offered to immunized recipients or with perioperative prophylaxis.[a]	IIb /C
SARS-CoV-2, recovered	Can be utilized for informed recipients. Ideally should be offered to immunized recipients or with perioperative therapies.[a]	IIb /C
West Nile virus, IgM+, NAT+, active confirmed	Do not utilize.	III /C
West Nile virus, IgG+, history of disease	Consider utilization	IIa/C
Zika virus, IgM+, active confirmed	Do not utilize.	III /C
Zika virus, IgG+, history of disease	Consider utilization	IIb/C

[a]As COVID-19 therapies are rapidly evolving, so is the utilization of these donors.

Table 9 Parasitic Infections

Infection	Recommendation	Strength /level of evidence
Trypanosoma cruzii (Chagas disease) confirmed	Do not utilize.	III /C
Strongyloides stercoralis	May be used with prophylaxis and surveillance post-transplant.	IIa /C

Table 10 CNS Infections

Infection	Recommendation	Strength /level of evidence
Viral meningoencephalitis	Do not utilize.	III /C
Fungal meningoencephalitis	Do not utilize.	III /C
Amebic meningoencephalitis	Do not utilize.	III /C
Bacterial meningitis	Donors with treated bacterial meningitis are suitable for heart transplantation.	IIa /C

considered favorably as potential donors because the risk of cancer transmission is low. **Level of Evidence: C.**

2. The tumor type, histology, disease stage, disease-free interval, and the recipient's risk of dying on the waiting list should be considered when making decisions regarding the suitability of organs for transplantation. **Level of Evidence: C.**

Class IIb

1. Donors with a history of melanoma, choriocarcinoma, breast or colon adenocarcinoma, lymphoma, or leukemia are considered at high risk for transmission. **Level of Evidence: C.**
2. There should be high level of suspicion for a metastatic tumor in potential donors with a past history of malignancy who experience a nontraumatic cerebral hemorrhage. In such cases, a thorough thoracic and abdominal exploration is recommended before recovering organs for transplantation, with possible biopsy and pathologic evaluation. **Level of Evidence: C.**

Diagnostic studies

Cardiac biomarkers

The measurement of biomarkers is an established method of predicting risk for many cardiovascular conditions, including myocardial injury and heart failure, and has drawn considerable interest in the assessment of organ donors. B-type Natriuretic Peptide (BNP), NT-proBNP, and troponin are elevated after brain death, particularly subarachnoid hemorrhage, likely due to increased sympathetic activity and release of catecholamines with associated elevated wall stress and myocardial injury.[263,264]

Recommendations regarding troponin: [265-268]

Class IIb

1. Coronary angiography should be considered for potential donors with significantly increased troponin concentrations (with quantitative limits being institution-

Table 11 Risks and Recommendations Regarding Malignancy (By Risk and Tumor Type) for the Utilization of Donor Hearts[262]

Risk category	Tumor characteristics	Recommended clinical use	Strength/level of evidence
No significant risk	Benign tumors in which malignancy is excluded	Standard donor	IIa /C
Minimal risk (<0.1% transmission)	• Basal cell carcinoma, skin • Squamous cell carcinoma, skin without metastases • Carcinoma *in situ*, skin (non-melanoma) • *In situ* cervical carcinoma • *In situ* vocal cord carcinoma • Superficial (noninvasive) papillary carcinoma of bladder (TONOMO by the TNM staging system) (nonrenal transplant only) • Solitary papillary thyroid carcinoma, ≤0.5 cm • Minimally invasive follicular carcinoma, thyroid, ≤ 1.0 cm • (Resected) solitary renal cell carcinoma, ≤1.0 cm, well differentiated (Fuhrman 1-2)	Clinical judgment with informed consent	IIa /C
Low risk (0.1-1% transmission)	• (Resected) solitary renal cell carcinoma, >1.0 cm ≤2.5 cm, well differentiated (Fuhrman 1-2) • Low grade CNS tumor (WHO grade I or II) • Primary CNS mature teratoma • Solitary papillary thyroid carcinoma, 0.5-2.0 cm • Minimally invasive follicular carcinoma, thyroid, 1.0-2.0 cm • History of treated non-CNS malignancy (≥5 years prior) with >99% probability of cure	Use in recipients at significant risk without transplant. Informed consent required	IIa /C
Intermediate risk (1-10% transmission)	• Breast carcinoma (stage 0, i.e., carcinoma in situ) • Colon carcinoma (stage 0, i.e., carcinoma in situ) • (Resected) solitary renal cell carcinoma T1b (4-7 cm) well differentiated (Fuhrman 1-2) stage I • History of treated non-CNS malignancy (≥5 years prior) with probability of cure between 90% and 99%	Use of these donors is generally not recommended. Lifesaving transplant may be acceptable in circumstances where recipient expected survival without transplantation is short (e.g., a few days or less). Informed consent required.	IIb /C
High Risk (>10% transmission)	• Malignant melanoma • Breast carcinoma >stage 0 (active) • Colon carcinoma >stage 0 (active) • Choriocarcinoma • CNS tumor (any) with ventriculoperitoneal or ventriculoatrial shunt, surgery (other than uncomplicated biopsy), irradiation or extra-CNS metastasis • CNS Tumor WHO grade III or IV • Leukemia or lymphoma • History of melanoma, leukemia or lymphoma, small cell lung/neuroendocrine carcinoma • Any other history of treated non-CNS malignancy either (a) insufficient follow-up to predict behavior, (b) considered incurable or (c) with probability of cure <90% • Metastatic carcinoma • Sarcoma • Lung cancer (stages I-IV) • Renal cell carcinoma >7cm or stage II-IV • Small cell/neuroendocrine carcinoma, any site of origin • Active cancer not listed elsewhere	Use of these donors is discouraged except in rare and extreme circumstances. Informed consent required and consult with oncology may be desired.	III /C

dependent) depending on clinical context of donor cause of death and risk factors for CAD. **Level of Evidence: C.**
2. Troponin levels may be elevated (with quantitative limits being institution-dependent) following brain death but are not independent reasons to decline a donor. Correlation with echocardiography and clinical scenario is necessary. **Level of Evidence: C.**

Recommendation regarding B-type natriuretic peptide (BNP) and NT-proBNP: [269,270]

Class IIa

1. BNP levels may be elevated following brain death but are not independent reasons to decline a donor. Correlation with echocardiography and clinical scenario is necessary. **Level of Evidence: C.**

Recommendation for cardiac imaging:[271-281]

Class I

1. Echocardiography should be conducted and imaging available for review as part of donor evaluation. **Level of Evidence: C.**
2. Serial echocardiography in donors with initial LV dysfunction after brain death may be useful to identify donors with reversible LV dysfunction. **Level of Evidence: C.**
3. Computed tomography (CT) angiography for coronary artery disease is a reasonable alternative to traditional angiography in some centers. **Level of Evidence: C.**

Recommendation for pharmacological stress echocardiography: [272,277,280]

Class IIa

1. Pharmacologic stress echo may be used in the assessment of dysfunctional donor hearts to distinguish between CAD or subclinical cardiomyopathy and reversible left ventricular dysfunction. **Level of Evidence: C.**

Recommendation for strain rate imaging: [282-288]

Class IIa

1. Myocardial strain echo may assist to distinguishing between ischemic and stunned myocardium. **Level of Evidence: C.**

Recommendation for contrast-enhanced 3D echocardiography: [276,278,279,281]

Class IIa

1. Use of echo contrast agents should be considered to improve myocardial visualization when images are suboptimal. **Level of Evidence: C.**

Recommendation for cardiac magnetic resonance imaging (MRI):[289-291]

Class IIb

1. Cardiac MRI is a useful option for visualization of structure and function of donor hearts, but availability and ease of performance limit its use. **Level of Evidence: C.**

Coronary angiography

While there are no evidence-based findings with respect to coronary angiography, it is reasonable to consider performing this test in donors who are considered to have high risk for coronary artery disease.

Recommendation for coronary angiography

Class IIb

1. A coronary angiogram should be obtained in donors at high risk of CAD, such as age >45 years and those with diabetes or tobacco use or illicit drug use (e.g., cocaine, amphetamine, methamphetamine). **Level of Evidence: C.**

The rational use of donor hearts meeting extended criteria

Utilization of extended-criteria donor hearts has the aim to expand use while mitigating recipient risk. Considerable debate exists on how to define "extended criteria" with the greatest emphasis on traditional risk factors such as increased donor age, left ventricular dysfunction, left ventricular hypertrophy, and prolonged ischemic time.[263,292,293] These risk factors, as well as others (diabetes, hypertension, death due to stroke), have been evaluated in single-center studies and in analyses of large databases such as the UNOS registry.[59,294] However, careful evaluation of the data would suggest that a closer look is warranted.

Recommendation for the utilization of extended-criteria donor hearts: [59,127,294-296]

Class IIa

1. For recipients who are challenging to match (e.g., highly sensitized patients, patients on temporary circulatory support, VAD complications) consideration of an extended-criteria donor may be lifesaving. Acceptance of such donors should be considered in the context of concurrent risk factors. **Level of Evidence: C.**

Recommendation regarding the use of donor hearts with low ejection fraction:
[62,67,74,75,106,113,117,120,271,273,274,294,297-316]

(See also Table 12).

Table 12 Recommendations for the Use of Donor Hearts with Ventricular Abnormalities

Donor concern	Recommended intervention	Outcomes	Strength/level of evidence
LVEF <45%	Dobutamine stress echocardiography, repeat transthoracic echocardiography (TTE)	Ventricular wall augmentation predicts improvement in LVEF	IIa /C
LVH >1.4 cm	None	Poor outcomes if concurrent donor age >55 years and ischemic time ≥4 hours [106]	IIa /B
Donor/recipient size mismatch	Calculate predicted heart mass (pHM)	Lower survival with pHM difference >10%-15% [74]	IIa /B
Donor CAD	Percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG)	Slightly lower survival in 1 vessel disease, worse survival in multivessel disease [120]	IIa/C

Class IIa

1. Hearts with an initially low LVEF, especially from young brain-dead donors, should be aggressively pursued. It is reasonable to repeat echocardiographic assessments to determine improvement of such donors. **Level of Evidence: C.**
2. It is reasonable to consider a heart with reduced but improved LVEF in the setting of a young donor especially for recipients with an urgent clinical need (e.g., INTERMACS Class 1 or 2), balancing risks and benefits. **Level of Evidence: C.**

Recommendation regarding the use of donor hearts with valvular abnormalities [27,311,317-328]

Class III

1. In the case of some donor valvular defects (e.g., mild-to-moderate mitral or tricuspid insufficiency), a pre-transplant surgical repair strategy may be considered appropriate for very severely ill patients at extremely high risk of death. This strategy can be considered especially for recipients who are challenging to match (e.g., highly sensitized patients, patients on short-term mechanical support or with VAD complications). **Level of Evidence: C**.

Recommendation regarding donors with prior transplant:[329]

Class IIa

1. Donors with prior non-cardiac solid organ transplants may be utilized for heart transplantation. **Level of Evidence: C.**

Prior chest surgery in the donor

Few, if any, published reports exist on outcomes of cardiac transplantation using donors with prior chest surgery (e.g., thoracotomy). In such instances, radiographic evaluation via chest computed topography scan would be necessary to determine proximity of mediastinal structures to the sternum and technical planning for chest reentry.

Recommendation regarding donors with prior chest surgery

Class IIa

1. Donors with prior thoracic surgery may be utilized for heart transplantation with careful screening and preoperative review. **Level of Evidence: C.**

Recommendations regarding donors on extracorporeal membrane oxygenation (ECMO):[330,331]

Class IIa

1. Donors with veno-venous extracorporeal membrane oxygenation (ECMO) support may be utilized for heart transplantation. **Level of Evidence: C.**

Class IIb

1. Donors with veno-arterial ECMO support due to hemodynamic instability associated with brain death may be utilized for heart transplantation if the organ can be weaned off support. **Level of Evidence: C.**

Recommendation regarding domino transplantation:[332-334]

Class IIa

1. Domino heart transplantation, in which the explanted heart from an en-bloc heart-lung recipient is utilized as a donor organ for a second heart recipient, can be considered with careful consideration of the recipient condition and informed consent from the recipient. **Level of Evidence: C.**

Recommendations regarding donors with persistent left superior vena cava (PLSVC): [335-348]

Class IIa

1. Hearts with persistent left superior vena cava (PLSVC) can be used successfully. **Level of Evidence: C.**
2. In case the right superior vena cava is absent or narrow, the donor heart can be utilized in a bi-atrial transplant technique. **Level of Evidence: C.**
3. The left superior vein should in any case be ligated at the entrance to the coronary sinus/ left atrium. In the case of PLSVC drainage into the coronary sinus a close examination of the coronary sinus roof (and closure) from the left atrial side is necessary to avoid right-to-left cardiac shunt after transplantation. **Level of Evidence: C.**

Recommendations regarding coronary artery anomalies in the donor: [349-358]

Class IIa

1. Unexplained ischemia or regional wall motion abnormalities after transplantation should be promptly evaluated by angiography to determine if anomalous origination of a coronary artery from the opposite sinus (ACAOS) was present in the donor. **Level of Evidence: C.**

Class III

1. Donor hearts with ACAOS should not be utilized. **Level of Evidence: C.**

Recommendations regarding donors with patent foramen ovale: [327,359-363]

Class I

1. Screening for inter-atrial shunts should be performed routinely by visual examination, palpation of the donor heart, and routine probe examination of the atrial septum. **Level of Evidence: C.**
2. All atrial septal defects should be securely closed at the time of procurement. **Level of Evidence: C.**

Donor characteristics and risk scores

Multiple risk scores have been developed in an attempt to address donor risk,[55] recipient risk, and the combination of recipient and donor risks[55,92,364] with the potential of using these risks to drive allocation.[365] Validation of these risk scores has been established via associations with mortality outcomes.[55,366-369]

Table 13 summarizes all published risk scores (as identified in a recent meta-analysis[370]) that aim to inform allocation and donor selection. These scores incorporate donor characteristics into the prediction of post-transplant

Table 13 Summary of Published Risk Prediction Scores that Incorporate Donor Characteristics

	Donor variables included												
Source	Age	Ischemic time	Sex or sex-mismatch	Size or size-mismatch	Diabetes mellitus	Hepatitis C infection	Inopressor dose	Cause of death	Blood group (ABO)	# other donor factors	# recipient factors	C-statistic in external validation
Anyanwu 1999[374]	x	x	x	x	x		x			1	7	-
Hong 2011[92]	x	x	x		x	x				9	12	0.56-0.58
Weiss 2012[59]	x	x								2	0	0.54-0.55
Smits 2012[55]	x						x	x		8	0	-
Nilsson 2015[375]	x	x	x	x				x	x	4	32	0.59-0.63
Johnston 2016[376]	x	x	x							1	8	0.60-0.64
Trivedi 2016[377]	x	x	x		x					0	9	-
Joyce 2018[378]	x	x	x							0	8	-
Yoon 2018[379]	x	x	x	x	x	x			x	1	21	-
Jasseron 2019[81]	x		x							0	7	-

Level of evidence: C (For all risk score models).
An "x" indicates the inclusion of a given donor risk factor in the corresponding risk score. "Size" refers to donor height and/or weight either in absolute terms or relative to that of the recipient. The listed donor factors consist of all that were included in more than one risk score. For scores that have been validated in a distinct (non-derivation) cohort, the range of reported c-statistics across published validation studies is listed.

mortality, either in isolation or in conjunction with recipient factors. While the majority of these risk scores include donor age, ischemic time, and sex (and/or sex-mismatch), the selection of donor characteristics is otherwise highly variable. External validation (when performed) indicates that these scores have limited predictive ability. Accordingly, they should not be considered definitive or substitute for clinical judgement, but may compliment a more holistic assessment of potential donors.

In general, the different allocation systems in place throughout the world may influence the decision of how much donor risk to take in individual cases.[371-373]

International donor heart selection practices

A shortage of donor organs exists throughout the world. Factors accounting for this shortage vary among countries and include lack of awareness about organ donation, lack of organ donor registries,[380] evolving donor allocation policies, as well as logistical, legal, religious, and political barriers. Donor and recipient demographics also vary by geographical region and change over time. In an analysis of global organ donation rates, the highest donor rates were in countries with an organized health care donation system. This was more important than socio-economic factors or the human development index.[381] In countries with well-established transplant programs and national donor registries, a variety of strategies have been employed in an attempt to increase the supply of donor organs, mostly centered on variations of either opt-in or opt-out consenting guidelines for the potential donor and their family and the associated legislation. In general, a country's selection criteria and utilization rates are impacted by unique social and environmental factors such as aging of the population, fatality causes and rates, cultural and religious beliefs regarding the donation process or geographic constraints.

Recommendations regarding international donor heart selection practices: [117,302,315,380-414]

Class I

1. Education strategies including donor awareness campaigns, e-campaigns, the capability to register for organ donation on mobile phones and social media can improve organ donation and should include OPOs. **Level of Evidence: C.**
2. National organized processes for organ allocation are most effective. **Level of Evidence: C.**

Class IIb

1. Neither "opt-in" (where there is a requirement to sign up to register to be an organ donor) nor "opt-out" (where organ donation will occur by default unless a specific request is made prior to death for organs not to be taken; also known as "presumed consent") has demonstrated superiority in donor organ utilization. **Level of Evidence: C.**
2. The decision to change donation consent from opt-in to opt-out likely has to be part of a broader nationwide strategy to increase organ donation rates which includes promotional campaigns, organizational changes, infrastructural support. **Level of Evidence: C.**
3. Prioritizing transplant candidates for those individuals who have agreed to be potential organ donors is another strategy proposed to promote organ donation ("reciprocal altruism"). **Level of Evidence: C.**
4. Data sharing among countries is encouraged in order to enhance the knowledge in the field of donor heart selection. Those analyses may provide data to identify opportunities for broadening of donor pools while maintaining optimal long-term outcomes. **Level of Evidence: C.**

Class III

1. Financial incentives to donors and their families, such as payment for cells, tissues, and organs, are discouraged because they likely take unfair advantage of the poorest and most vulnerable groups, undermine altruistic donations, and lead to profiteering and human trafficking. **Level of Evidence: C.**

Limitations

This document includes recommendations for the selection of donors following brain death. The utilization of donor hearts following circulatory death has been restricted, until recently, to relatively small areas of the world. While its application is currently becoming more wide-spread, there is not enough consensuses yet to form recommendations.

The recommendations herein are based on professional opinion and, if available, on published data, mostly consisting of retrospective single-institution studies. The recommendations must be taken in the context of regional donor availability which varies worldwide. For example, the age of the available donor pool differs widely among countries. Centers, physicians, and surgeons, must select the best donor for the recipient, based on the urgency of the candidate list for transplant, the severity of the candidate's illness, risk of dying on the waitlist, all within the context of available donors and the degree of regulatory oversight (or lack thereof) that can hinder or augment donor acceptance rates. This also means that not all recommendations listed herein are equally relevant for all parts of the world based on practices and on donor and recipient demographics. Furthermore, if the risk factors present in a given donor are outside the geographically accepted "normal," then additional informed consent from recipient may be required.

Conclusion

This document establishes a foundation of knowledge about donor risk factors, which physicians, surgeons, transplant clinicians, and transplant centers may use as a guide when evaluating a donor heart. All donor heart selection must be evaluated in the context of the heart transplant candidate and what risk is acceptable to that individual.

Disclosure statement

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