

# MECKI score thresholds for heart transplantation referral of ambulatory heart failure patients

Piergiuseppe Agostoni <sup>1,2,\*</sup>, Arianna Galotta<sup>2</sup>, Elisabetta Salvioni<sup>2</sup>, Massimo Mapelli <sup>1,2</sup>, Michele Emdin<sup>3,4</sup>, Massimo Piepoli<sup>5,6</sup>, Alberto Palazzuoli <sup>7</sup>, Gianfranco Sinagra <sup>8</sup>, Damiano Magri <sup>9</sup>, Stefania Paolillo<sup>10</sup>, Andrea Passantino<sup>11</sup>, Jeness Campodonico<sup>1,2</sup>, Ugo Corrà <sup>12</sup>, Rosa Raimondo<sup>13</sup>, Antonio Cittadini<sup>14,15</sup>, Annamaria Iorio<sup>16</sup>, Andrea Salzano <sup>17</sup>, Roberto Badagliacca<sup>18</sup>, Michele Senni <sup>16</sup>, Pasquale Perrone Filardi<sup>19</sup>, Michele Correale<sup>20</sup>, Enrico Perna<sup>21</sup>, Marco Metra<sup>22</sup>, Carlo Vignati <sup>2</sup>, Mauro Contini <sup>2</sup>, Nikita Baracchini <sup>8</sup>, Gaia Cattadori<sup>23</sup>, Marco Guazzi <sup>24</sup>, Giuseppe Limongelli<sup>25</sup>, Gianfranco Parati <sup>26,27</sup>, Beatrice Pezzuto<sup>2</sup>, Robin Willixhofer<sup>1</sup>, Pietro Palermo<sup>2</sup>, Anna Apostolo <sup>2</sup>, Maria Vittoria Matassini<sup>28</sup>, Francesco Bandera<sup>29,30</sup>, Maurizio Bussotti <sup>31</sup>, Federica Re<sup>32</sup>, Angela B. Scardovi<sup>33</sup>, Susanna Sciommer <sup>19</sup>, Davide Girola<sup>34</sup>, Claudio Passino<sup>3</sup>, Franco La Valle<sup>35</sup>, Fiorella Puttini<sup>2,36</sup>, and Luigi Adamo<sup>37</sup> on behalf of MECKI score research group<sup>†</sup>

<sup>1</sup>Department of Clinical Sciences and Community Health, Cardiovascular Section, University of Milan, Via Parea 4, 20138, Milan, Italy; <sup>2</sup>Centro Cardiologico Monzino, IRCCS, Via Parea 4, 20138, Milan, Italy; <sup>3</sup>Health Science Interdisciplinary Center, Scuola Superiore Sant'Anna, Pisa, Italy; <sup>4</sup>Cardio-Thoracic Department, Fondazione Toscana Gabriele Monasterio, Pisa, Italy; <sup>5</sup>Clinical Cardiology, IRCCS Policlinico San Donato, Milan, Italy; <sup>6</sup>Department of Biomedical Sciences for Health, University of Milan, Milan, Italy; <sup>7</sup>Cardiovascular Diseases Unit, Cardio Thoracic and Vascular Department, S. Maria alle Scotte Hospital, University of Siena, Siena, Italy; <sup>8</sup>Cardiovascular Department, 'Azienda Sanitaria Universitaria Giuliano-Isontina', Trieste, Italy; <sup>9</sup>Department of Clinical and Molecular Medicine, Azienda Ospedaliera Sant'Andrea, 'Sapienza' Università degli Studi di Roma, Roma, Italy; <sup>10</sup>Dipartimento di scienze biomediche avanzate, Federico II University, Naples, Italy; <sup>11</sup>Division of Cardiology, Istituti Clinici Scientifici Maugeri, IRCCS, Institute of Bari, Bari, Italy; <sup>12</sup>Cardiology Department, Istituti Clinici Scientifici Maugeri, IRCCS, Veruno Institute, Veruno, Italy; <sup>13</sup>U.O. Prevenzione e Riabilitazione cardiovascolare, I.R.C.C.S. Ospedale San Raffaele, Milan, Italy; <sup>14</sup>Department of Translational Medical Sciences, Federico II University, Naples 80131, Italy; <sup>15</sup>Interdepartmental Centre for Gender Medicine Research 'GENESIS', Naples, Italy; <sup>16</sup>Cardiovascular Department, Cardiology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy; <sup>17</sup>Cardiac Unit, AORNA Cardarelli, Naples, Italy; <sup>18</sup>Dipartimento di Scienze Cliniche, Internistiche, Anestesiologiche e Cardiovascolari, 'Sapienza', Rome University, Rome, Italy; <sup>19</sup>Department of Advanced Biomedical Sciences, Federico II University of Naples and Mediterranean CardioCentro, Naples, Italy; <sup>20</sup>Department of Cardiology, University of Foggia, Foggia, Italy; <sup>21</sup>Dipartimento Cardio-Toraco-Vascolare, Ospedale Cà Granda- A.O. Niguarda, Milano, Italy; <sup>22</sup>Cardiology Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Brescia, Italy; <sup>23</sup>Unità Operativa Cardiologia Riabilitativa, IRCCS Multimedica, Milano, Italy; <sup>24</sup>Department of Cardiology, San Paolo Hospital, University of Milano School of Medicine, Milano, Italy; <sup>25</sup>Cardiologia SUN, Ospedale Monaldi (Azienda dei Colli), Seconda Università di Napoli, Naples, Italy; <sup>26</sup>Department of Cardiovascular, Neural and Metabolic Sciences, San Luca Hospital, Istituto Auxologico Italiano, IRCCS, Milan, Italy; <sup>27</sup>Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy; <sup>28</sup>Cardiac Intensive Care Unit-Cardiology Division, Cardiovascular Department, Ospedali Riuniti di Ancona, Ancona, Italy; <sup>29</sup>Department of Biomedical Sciences for Health, University of Milano, Milan, Italy; <sup>30</sup>Department of Cardiology, IRCCS Multimedica, Milano, Italy; <sup>31</sup>Cardiac Rehabilitation Unit, Istituti Clinici Scientifici Maugeri, IRCCS, Scientific Institute of Milan, Milan, Italy; <sup>32</sup>Cardiology Division, Cardiac Arrhythmia Center and Cardiomyopathies Unit, San Camillo-Forlanini Hospital, Roma, Italy; <sup>33</sup>Cardiology Division, Santo Spirito Hospital, Roma, Italy; <sup>34</sup>Centro Medico Chiasso Mendrisio, Mendrisio, Switzerland; <sup>35</sup>Osservatorio Ministeriale Medicina di Genere, ISS, Roma, Italy; <sup>36</sup>Department of Cardiology, Tor Vergata Hospital of Rome, University of Rome 'Tor Vergata', Rome, Italy; and <sup>37</sup>Division of Cardiology, Department of Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Received 28 July 2025; revised 28 October 2025; accepted 24 November 2025; online publish-ahead-of-print 8 January 2026

\* Corresponding author. Email: [piergiuseppe.agostoni@ccfm.it](mailto:piergiuseppe.agostoni@ccfm.it)

<sup>†</sup> See Appendix.

© The Author(s) 2026. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [reprints@oup.com](mailto:reprints@oup.com) for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com).

## Abstract

### Introduction

In heart failure (HF) patients, guidelines recommend scores for assessing outcomes and heart transplant (HTX) eligibility. However, scores use remains limited and cut-off values for HTX listing not well established.

Among the available tools, MECKI score is easy to calculate and likely offers the best prognostic accuracy. Compare MECKI score-based survival with that of HTX recipients and identify a MECKI threshold above which survival is inferior to that of HTX recipients at 5-year.

### Methods

Consecutive ambulatory HF patients enrolled in MECKI score programme between January 2010 and January 2022 were evaluated. Primary endpoint was a composite of cardiovascular death, HTX, or left ventricular assist device implantation. Heart transplant survival data were obtained from the International Society of Heart and Lung Transplantation registry updated through 2023. To identify the MECKI score threshold beyond which prognosis is worse than that of HTX recipients, patients were stratified by deciles of MECKI score.

### Results

We analysed 3865 HF patients (mean age  $62.4 \pm 12.6$  years). Peak  $VO_2$  was  $58.2 \pm 18.3\%$  predicted;  $VE/VCO_2$  slope  $33.2 \pm 8.2$ , haemoglobin  $13.5 \pm 1.7$  g/dL,  $Na^+$   $139 \pm 3$  mmol/L, LVEF  $33.7 \pm 10.4\%$ , and eGFR  $73 \pm 26$  mL/min/1.73 m<sup>2</sup>. Periodic breathing occurred in 15.8% of patients. At 5 years, mean survival was 83.7%.

The average 5-year survival of HTX recipients (71.2%) lies between the eighth and ninth MECKI score deciles suggesting a MECKI score value  $\geq 0.1368$  as the proper cut-off for HTX listing.

### Conclusion

MECKI score  $\geq 0.1368$  may warrant HTX listing, while lower scores support clinical deferral.

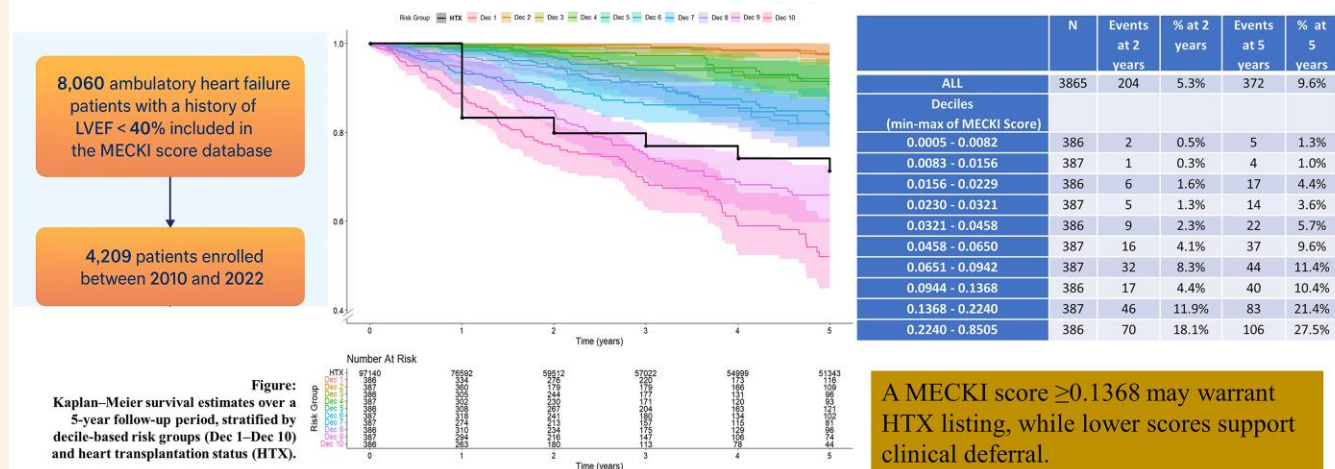
## Graphical Abstract

### MECKI score thresholds for heart transplantation referral of ambulatory heart failure patients

**Background.** In heart failure (HF) patients, guidelines recommend scores for assessing outcomes and heart transplant (HTX) eligibility. However, scores use remains limited and cut-off values for HTX listing not well established.

Among the available tools, MECKI score is easy to calculate and likely offers the best prognostic accuracy.

**Aim.** Compare MECKI score-based survival with that of HTX recipients and identify a MECKI threshold above which survival is inferior to that of HTX recipients at 5-year.



### Keywords

Heart failure • Prognosis • Heart transplantation • Risk score

## Introduction

Several reports and guidelines recommend the use of prognostic scores for assessing outcomes in patients with advanced heart failure (HF) and evaluating their eligibility for heart transplant (HTX) programmes.<sup>1-3</sup> This

stems from the multifaceted nature of HF, which is better captured by composite scores than by individual parameters.<sup>4</sup> However, the systematic use of HF prognostic scores remains limited due to their complexity and the extensive data required for their calculation. Additionally, appropriate cut-off values for HTX listing are not well established.

**Table 1 Patient characteristics in all population and by MECKI score deciles**

	All n = 3685	Dec 1 n = 386	Dec 2 n = 387	Dec 3 n = 386	Dec 4 n = 387	Dec 5 n = 386	Dec 6 n = 387	Dec 7 n = 387	Dec 8 n = 386	Dec 9 n = 387	Dec 10 n = 386	P trend
<b>Age (years)</b>	n = 3865 62 ± 13	58 ± 14	61 ± 13	61 ± 13	62 ± 12	62 ± 12	63 ± 12	64 ± 13	64 ± 13	64 ± 12	65	<.0001
<b>Weight (kg)</b>	n = 3865 78 ± 15	82 ± 16	81 ± 16	82 ± 16	81 ± 16	80 ± 15	78 ± 16	76 ± 15	76 ± 15	75 ± 14	74 ± 13	<.0001
<b>LVEF (%)</b>	n = 3865 34 ± 10	49 ± 10	41 ± 8	38 ± 8	35 ± 7	34 ± 7	32 ± 7	30 ± 7	28 ± 6	26 ± 6	22 ± 6	<.0001
<b>EDV (mL)</b>	n = 3543 181 ± 73	130 ± 51	155 ± 56	162 ± 61	172 ± 62	173 ± 67	183 ± 65	187 ± 69	205 ± 71	212 ± 81	230 ± 84	<.0001
<b>PAPs (mmHg)</b>	n = 3130 36 ± 13	29 ± 9	31 ± 10	32 ± 10	34 ± 10	33 ± 11	35 ± 12	38 ± 13	40 ± 13	42 ± 14	46 ± 13	<.0001
<b>Heart rate (bpm)</b>	n = 3846 70 ± 12	68 ± 11	67 ± 11	70 ± 12	68 ± 11	69 ± 13	70 ± 13	69 ± 11	71.7 ± 13	71 ± 12	73 ± 12	<.0001
<b>VO<sub>2</sub> AT (mL)</b>	n = 3058 802 (628;1031)	1124 (906;1420)	1004 (805;1213)	946 (771;1115)	900 (725;1060)	826 (668;1001)	782 (624;915)	703 (590;833)	683 (552;796)	618 (512;756)	553 (454;673)	<.0001
<b>Workload AT (Watt)</b>	n = 2873 52 ± 24	75 ± 32	63 ± 23	59 ± 21	56 ± 21	52 ± 21	48 ± 19	43 ± 18	40 ± 17	39 ± 16	33 ± 17	<.0001
<b>VO<sub>2</sub> peak (mL/min)</b>	n = 3865 1185 ± 453	1731 ± 556	1490 ± 439	1376 ± 402	1305 ± 352	1207 ± 346	1121 ± 320	1025 ± 279	952 ± 256	892 ± 248	755 ± 215	<.0001
<b>VE/VO<sub>2</sub> slope</b>	n = 3865 33 ± 8	27 ± 5	28 ± 4	29 ± 5	30 ± 6	31 ± 5	32 ± 6	349 ± 6	36 ± 6	39 ± 7	45 ± 9	<.0001
<b>RER</b>	n = 3807 1.11 ± 0.12	1.11 ± 0.11	1.11 ± 0.11	1.11 ± 0.11	1.11 ± 0.11	1.11 ± 0.12	1.1 ± 0.12	1.11 ± 0.13	1.1 ± 0.12	1.11 ± 0.12	1.1 ± 0.14	0.8450
<b>Hb (m/dL)</b>	n = 3865 13.5 ± 1.7	13.9 ± 1.6	14.0 ± 1.6	13.9 ± 1.7	13.9 ± 1.5	13.6 ± 1.6	13.5 ± 1.6	13.2 ± 1.7	13.2 ± 1.7	13.1 ± 1.7	12.6 ± 1.7	<.0001
<b>Na<sup>+</sup> (mmol/L)</b>	n = 3865 139 ± 3	140 ± 23	140 ± 3	140 ± 3	140 ± 3	140 ± 3	139 ± 3	139 ± 3	139 ± 3	139 ± 3	138 ± 4	<.0001
<b>K<sup>+</sup> (mmol/L)</b>	n = 3853 4.3 ± 0.5	4.2 ± 0.4	4.2 ± 0.4	4.3 ± 0.4	4.3 ± 0.4	4.3 ± 0.2	4.3 ± 0.5	4.4 ± 0.5	4.3 ± 0.5	4.3 ± 0.5	4.3 ± 0.5	<.0001
<b>BNP (pg/mL)</b>	n = 2105 237 (91;631)	79 (40;135)	100 (53;186)	130 (70;296)	206 (87;428)	206.5 (100;476)	233.1 (150;487)	385.5 (171;798.5)	504 (269;1003)	641 ( (345;1257)	992 (585;2180)	<.0001
<b>NT pro BNP (pg/mL)</b>	n = 1068 1151 (481;2416)	199 (47;711)	411 (181;835)	598 (315;1138)	609 (373;1086)	750 (401;1576)	924 (502;1973)	1287 (613;2260)	1508 (778;2865)	2276 (1172;3866)	3558 (1925;5037)	<.0001
<b>MDRD (mL/min/1.73 m<sup>2</sup>)</b>	n = 3865 73 ± 26	92 ± 28	86 ± 24	82 ± 22	79 ± 22	77 ± 22	73 ± 23	67 ± 23	66 ± 22	59 ± 22	51 ± 20	<.0001
<b>VO<sub>2</sub> peak (mL/min/kg)</b>	n = 3865 15.1 ± 5.1	21.3 ± 5.9	18.7 ± 5.0	16.9 ± 4.5	16.2 ± 4.0	15.2 ± 3.6	14.4 ± 3.5	13.5 ± 3.3	12.7 ± 3.1	12.0 ± 3.0	10.2 ± 2.6	<.0001
<b>VO<sub>2</sub> peak (%)</b>	n = 3865 58 ± 18	83 ± 18	73 ± 15	67 ± 13	63 ± 12	59 ± 13	55 ± 12	52 ± 11	48 ± 11	44 ± 10	37 ± 10	<.0001
<b>MECKI score (%)</b>	n = 3865 0.05 (0.02;0.11)	0.01 (0.01;0.01)	0.01 (0.02;0.02)	0.02 (0.02;0.03)	0.03 (0.02;0.03)	0.04 (0.04;0.04)	0.05 (0.05;0.06)	0.08 (0.07;0.08)	0.11 (0.10;0.13)	0.17 (0.15;0.2)	0.32 (0.26;0.43)	<.0001

Patient baseline characteristics are presented for the entire study population (All) and stratified by MECKI score deciles (Dec. from 1 to 10). The table includes demographic, clinical, and laboratory variables to describe the cohort's profile across risk groups. Data are reported as mean ± standard deviation or median (interquartile range, IQR), as appropriate.

**Table 2** Number of events and event rates at 2 and 5 years in the all population and by MECKI score deciles

	At 2 years			At 5 years		
	N	Events	%	N	Events	%
<b>ALL</b>	2333	273	11.7%	933	105	11.3%
<b>Deciles (min-max of MECKI score)</b>						
0.0005–0.0082	258	12	4.7%	116	9	7.8%
0.0083–0.0156	245	12	4.9%	109	9	8.3%
0.0156–0.0229	237	19	8.0%	96	8	8.3%
0.0230–0.0321	234	17	7.3%	93	8	8.6%
0.0321–0.0458	267	25	9.4%	121	12	9.9%
0.0458–0.0650	242	30	12.4%	103	9	8.7%
0.0651–0.0942	213	22	10.3%	81	10	12.3%
0.0944–0.1368	242	38	15.7%	96	15	15.6%
0.1368–0.2240	216	54	25.0%	74	17	23.0%
0.2240–0.8505	179	44	24.6%	44	8	18.2%

This table summarizes the number of patients (N), number of events, and corresponding event rates (%) at 2-year and 5-year follow-up across the entire cohort (ALL) and stratified by deciles of the MECKI score. Each decile is labelled according to the minimum and maximum values of its MECKI score range, from the lowest risk (0.0005–0.0082) to the highest risk (0.2240–0.8505).

Among the available tools, the Metabolic Exercise Cardiac Kidney Indexes (MECKI) score is easy to calculate and likely offers the best prognostic accuracy. It has undergone multiple validations<sup>1,5–8</sup> and has been successfully compared with other scores, such as the Seattle Heart Failure Model, Meta-Analysis Global Group in Chronic Heart Failure, and Heart Failure Survival Score.<sup>5,6,9</sup> The MECKI score was developed using a Cox proportional hazards regression with stepwise variable selection and cross-validation, and it incorporates six parameters: peak oxygen uptake ( $\text{VO}_2$ ), ventilatory efficiency measured by the ventilation over  $\text{CO}_2$  production ( $\text{VE}/\text{VCO}_2$ ) slope—both obtained from symptom-limited maximal cardiopulmonary exercise testing (CPET)—haemoglobin (Hb), serum sodium concentration ( $\text{Na}^+$ ), left ventricular ejection fraction (LVEF), and estimated glomerular filtration rate (eGFR), calculated using the Modification of Diet in Renal Disease (MDRD) formula.<sup>10</sup>

In the present study we want to compare MECKI score-based survival with that of HTX recipients from the International Society of Heart and Lung Transplantation registry<sup>11</sup> and to identify a MECKI score threshold above which survival is inferior to that of HTX recipients at 5-year follow-up. This may allow a more precise allocation of ambulatory HF patients in the HTX list.

## Methods

The study population belongs to the multicentre MECKI registry, which includes patients with previous or current heart failure symptoms (NYHA Class I–IV, ACC/AHA Stages B–C) and a documented LVEF <40%, clinically stable for at least three months, able to perform a CPET, and without major cardiovascular interventions planned.<sup>10</sup> From a population of 8060 ambulatory HF patients, we selected those enrolled between January 2010 and January 2022 ( $n = 4209$ ). A total of 344 patients were excluded due to incomplete data required to compute the MECKI score. Inclusion and exclusion criteria have been described previously.<sup>10</sup> In brief major inclusion criteria were current or prior HF symptoms, history of prior or current LVEF <40%, and stable HF treatment for at least 3 months. Major exclusion criteria were history of pulmonary embolism, moderate-to-severe primitive valvular heart disease, pericardial disease, severe obstructive lung disease, exercise-induced angina, significant electrocardiographic abnormalities, or

any clinical comorbidity that could interfere with exercise performance. A requisite for MECKI score data base inclusion was a cycle-ergometer symptoms limited CPET performed with a ramp exercise protocol. Cardiopulmonary exercise testing data were collected and analysed using standardized procedures.<sup>12</sup> Predicted peak  $\text{VO}_2$  ( $\%\text{VO}_2$ ) was calculated using Hansen et al.'s equations.<sup>13</sup>

In addition to CPET variables, the MECKI registry collects clinical, echocardiographic, ECG, therapeutic, and laboratory data at baseline. The primary endpoint was a composite of cardiovascular death, urgent HTX, or left ventricular assist device (LVAD) implantation. For patients who died outside the hospital, cause of death and medical documentation were reviewed. Treatments were updated during follow-up according to clinical need and guideline recommendations.

The MECKI score was calculated using the formula:

$$e^c / (1 + e^c)$$

where:

$$c = 10.3464 + (-0.0262 \times \%\text{predicted peak } \text{VO}_2) \\ + (0.0472 \times \text{VE}/\text{VCO}_2 \text{ slope}) + (-0.1086 \times \text{Hb}) + (-0.0615 \times \text{Na}^+) \\ + (-0.0699 \times \text{LVEF}) + (-0.0136 \times \text{eGFR})$$

Heart transplant survival data were obtained from the International Society of Heart and Lung Transplantation registry<sup>11</sup> updated through 2023. To identify the MECKI score threshold beyond which prognosis is worse than that of HTX recipients, patients were stratified by deciles of MECKI score. MECKI score was calculated at study run in.

The study was approved by the local ethics committee (protocol number: CCM04\_21 PA).

## Statistical analysis

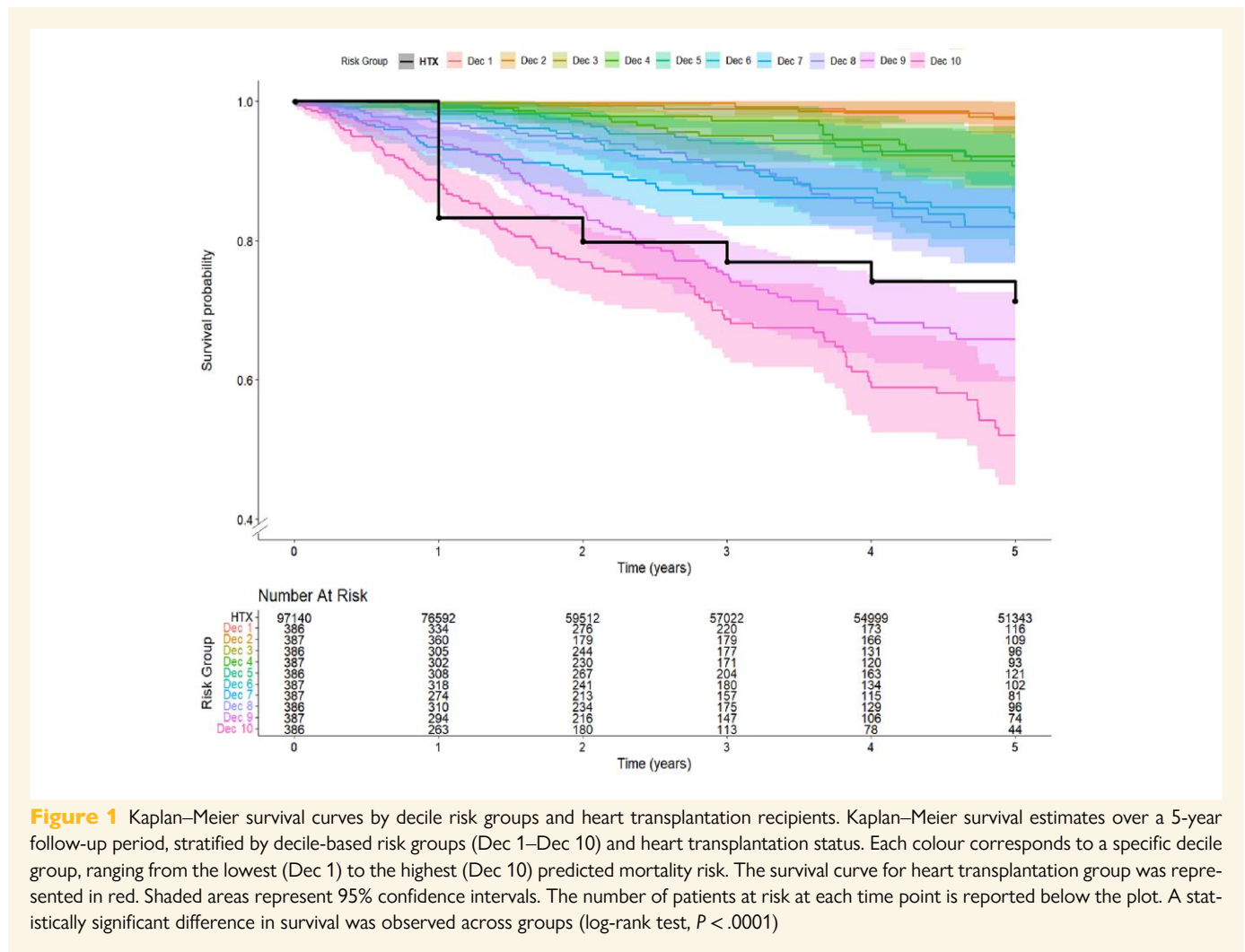
Continuous variables were reported as mean  $\pm$  standard deviation (SD) or median and interquartile range (IQR), as appropriate. Categorical variables were expressed as counts and percentages. Differences in continuous variables across MECKI score deciles were tested using one-way ANOVA or Kruskal–Wallis tests, as appropriate. Trends were assessed using linear regression or non-parametric equivalents. Kaplan–Meier curves were used for survival analysis. Heart transplant recipient survival curves were reconstructed from aggregate data using the 'KM\_reconstruct' function from the reconstruct KM package in R (v4.3.1). Survival curves were compared using log-rank tests. All tests were two-sided, and  $P$ -values <.05 were considered statistically significant. Analyses were performed using SAS v9.4 (SAS Institute, Cary, NC, USA) and R v4.3.1.

## Results

We analysed 3865 adult and Caucasian HF patients (mean age  $62.4 \pm 12.6$  years; 81.1% male, NYHA class I = 16.1%, II 56.7%, III 25.9%, IV 1.3%) with reduced LVEF (HF<sub>r</sub>EF,  $n = 2937$ ; 76%) or improved LVEF (HF<sub>imp</sub>EF,  $n = 928$ ; 24%). At enrolment, most patients were treated with  $\beta$ -blockers (91.2%), ARNI/ACEi/ARBs (88.1%), MRAs (58.5%), and diuretics (80.1%). Mean peak  $\text{VO}_2$  was  $15.1 \pm 5.1$  mL/min/kg ( $58.2 \pm 18.3\%$  predicted);  $\text{VE}/\text{VCO}_2$  slope, Hb,  $\text{Na}^+$ , LVEF, and eGFR were  $33.2 \pm 8.2$ ,  $13.5 \pm 1.7$  g/dL,  $139 \pm 3$  mmol/L,  $33.7 \pm 10.4\%$ , and  $73 \pm 26$  mL/min/ $1.73 \text{ m}^2$ , respectively. Periodic breathing occurred in 15.8% of patients; 43.4% had ICDs and 18.4% had CRT devices. Baseline characteristics of the entire population and clustered by decile are shown in Table 1.

Median follow-up was 2.59 (1.08–4.88) years. A total of 372 (9.6%) events occurred over 5 years: 286 cardiac deaths, 28 LVAD implantations, and 58 HTXs. Event rates by decile are reported in Table 2. Specifically, the event rate was calculated using as denominator the total number of subjects at risk at each yearly interval. A total of 933 cases were alive and actively followed at 5 years.

At 2 years, mean survival was 93.4% (ranging from 99.3% in decile 1 to 76.9% in decile 10). At 5 years, mean survival was 83.7% (from 97.5% in decile 1 to 52.0% in decile 10). Kaplan–Meier curves are presented in



**Figure 1** Kaplan–Meier survival curves by decile risk groups and heart transplantation recipients. Kaplan–Meier survival estimates over a 5-year follow-up period, stratified by decile-based risk groups (Dec 1–Dec 10) and heart transplantation status. Each colour corresponds to a specific decile group, ranging from the lowest (Dec 1) to the highest (Dec 10) predicted mortality risk. The survival curve for heart transplantation group was represented in red. Shaded areas represent 95% confidence intervals. The number of patients at risk at each time point is reported below the plot. A statistically significant difference in survival was observed across groups (log-rank test,  $P < .0001$ )

**Figure 1.** Heart transplant survival at 2 and 5 years was 79.8% and 71.2%, respectively.

Patients in the two highest MECKI score deciles had worse 5-year outcomes compared with HTX recipients. Specifically, patients with a median MECKI score of 0.17 (IQR: 0.15–0.20) had 2- and 5-year survival rates of 84.9% and 65.9%, respectively, and those with a median score of 0.32 (IQR: 0.26–0.43) had survival of 76.9% and 52.0%. Results were similar when excluding 928 cases with improved LVEF or after adjusting for the years of enrolment to take into account treatment strategy changes and guidelines evolution.

## Discussion

In the present study we showed that a MECKI score  $\geq 0.1368$  may warrant HTX listing. Indeed, the average 5-year survival of HTX recipients (71.2%) lies between the 8th and 9th MECKI score deciles (score range: 0.11–0.17). Therefore, patients with a MECKI score  $\geq 0.1368$  (the upper bound of the 8th and lower bound of the 9th decile) should be considered for HTX listing. Conversely, HTX may be postponed in those with lower scores, if clinically appropriate. Given the dynamic nature of HF, regular reassessment of the MECKI score is essential.<sup>14</sup>

The MECKI score was first introduced in 2013<sup>10</sup> with ongoing data collection since 1993. This study focused on patients enrolled between January 2010 and January 2022, to avoid historical biases in survival while allowing for adequate follow-up.<sup>15</sup> It is acknowledged that, during

this observation period, HF guidelines were progressively updated and introduced into clinical practice. Treatment reported refers to enrolment time but it was already with a great percentage of  $\beta$ -blockers, ACE/AT1/ARNI, and MRA. In any case treatment of MECKI score population has progressively changed and updated. The MECKI score provides a holistic assessment of HF considering, LVEF, kidney function, Hb and  $\text{Na}^+$  values, and two exercise-derived measurements (peak  $\text{VO}_2$  and  $\text{VE}/\text{VCO}_2$  slope), all of which are considered among the most powerful HF prognostic parameters. Kidney function, i.e. eGFR, in the original MECKI score report was calculated based on MDRD formula.<sup>16</sup> However, similar results are obtained using different formulas as eGFR calculations including Cockcroft-Gault (CG), Chronic Kidney Disease Epidemiology Collaboration, modified versions of the CG and MDRD (MDRDm) equations, as well as the European Kidney Function Consortium equation.<sup>17–21</sup> MECKI score prognostic capability at 2 years has been found to be in a range between 0.79 (first report) and 0.85 (international validation).<sup>8,10</sup>

The data we present provides actionable information to optimize timing of referral for HTX in ambulatory HF patients. However, it must be underlined that HTX recipient data were reconstructed based solely on published survival curves and the number of patients at risk at yearly intervals.<sup>22</sup> Due to the lack of additional patient-level clinical information, the reconstructed dataset may not fully account for the presence of high-risk individuals or comorbid conditions that could have significantly influenced outcomes. Moreover, the 0.1368 MECKI

score cut-off value should not be used to risk stratify HF patient populations who were not well represented in this cohort including patients with non-Caucasian ethnicity, patients with HF due to congenital heart disease, patients with preserved EF or with valvular HF. Similarly, the present data should be considered with caution in women who only represent 19% of our study population, albeit a recent report suggests the good performance of MECKI score in women.<sup>23</sup>

Further study limitations must be acknowledged: first, we can only provide an approximate MECKI score value above which patients survival is worst of that of the HTX cases; indeed, the 0.1368 is the upper/lower limit of the eighth and ninth deciles, respectively and a definite cut-off cannot be assessed with the available data. Moreover, it must be emphasized that  $\geq 0.1368$  is a statistical boundary, not a validated clinical cut-off. Accordingly there is a need for a prospective validation of the present findings. Second, we arbitrarily selected 5 years as the time interval to define the appropriate HTX follow-up; however, from [Figure 1](#) shorter time intervals can be evaluated. Third, MECKI score value changes during the follow-up were not regularly assessed. Indeed, in HF trajectory events that influence patients prognosis including worsening HF or treatment changes may occur.<sup>4</sup> As a matter of facts, we previously reported the importance of re-evaluation of MECKI score at least yearly.<sup>14</sup> Fourth, SGLT2i were introduced by ESC guideline in 2021 and likely prescribed during the follow-up only in a limited number of patients within this cohort. Finally, we must re-emphasize that we studied a population of adult Caucasian low LVEF HF patients so that our findings cannot be extended to different HF population as paediatric patients, patients of different ethnicity or with preserved LVEF.

In summary, after a validation of the present data with a prospective study we believe that MECKI score must be implemented into the clinical practice and guide the HF decision making process. At present MECKI score can only help to guide patients referral, listing, or prioritization. Indeed, a MECKI score  $\geq 0.1368$  may warrant HTX listing, while lower scores support clinical deferral. Regular MECKI score assessment remains crucial.

## Author contributions

A.P., A.L.: Conceptualization; Project administration; Supervision; Data interpretation; Writing—original draft; Writing—review and editing. G.A., S.E.: Data curation; Formal analysis; Writing—original draft; Writing—review and editing. Visualization. M.M., E.M., P.M., P.A., S.G., M.D., P.S., P.A., C.J., C.U., R.R., C.A., I.A., S.A., B.R., S.M., P.F.P., C.M., P.E., M.M., V.C., C.M., B.N., C.G., G.M., L.G., P.G., P.B., W.R., P.P., A.A., M.M.V., B.F., B.M., R.F., S.A.B., S.S., G.D., P.C., L.V.F., P.F.: Writing—review and editing; Critical review of the manuscript; Critical discussion of results, revision of the text. All authors: Validation; Final approval of the manuscript; Agreement to be accountable for all aspects of the work.

## Declarations

### Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

### Data Availability

Repository of raw data will be available after acceptance at [www.zenodo.org](http://www.zenodo.org)

### Funding

This research was supported by the Italian Ministry of Health-Ricerca Corrente to Centro Cardiologico Monzino IRCCS (CUP= B43C2400090001).

## Ethical Approval

The study was approved by the local ethics committee (protocol number: CCM04\_21 PA).

## Pre-registered Clinical Trial Number

None supplied.

## Appendix

Other participants to the MECKI score group to be acknowledged:

- Centro Cardiologico Monzino, IRCCS, Milan, Italy  
Irene Mattavelli, Stefania Farina, Paola Gugliandolo
- Department of Clinical and Molecular Medicine, Azienda Ospedaliera Sant'Andrea, 'Sapienza' Università degli Studi di Roma, Roma, Italy  
Giovanna Gallo; Emiliano Fiori
- Dipartimento di Scienze Cardiovascolari, Respiratorie, Nefrologiche, Anestesiologiche e Geriatriche, 'Sapienza', Rome University, Rome, Italy:  
Federica Moscucci
- UOC Cardiologia, G da Saliceto Hospital, Piacenza, Italy  
Geza Halasz, Bruno Capelli
- Cardiologia SUN, Ospedale Monaldi (Azienda dei Colli), Seconda Università di Napoli, Napoli  
Giuseppe Pacileo, Fabio Valente, Rossella Vastarella, Rita Gravino
- Cardiovascular Department, Ospedali Riuniti and University of Trieste, Trieste, Italy:  
Cosimo Carriere, Nikita Baracchini, Teresa Capovilla, Maddalena Rossi, Marco Masè, Andrea Di Lenarda
- Istituto Auxologico Italiano, Milan, Italy:  
Sergio Caravita, Elena Viganò
- Cardiac Rehabilitation Unit, Istituti Clinici Scientifici Maugeri, Scientific Institute of Milan, Milan, Italy:  
Giovanni Marchese
- Cardiology Division, Santo Spirito Hospital, Roma, Italy:  
Roberto Ricci, Luca Arcari
- Division of Cardiology, Istituti Clinici Scientifici Maugeri, Institute of Cassano Murge, Bari, Italy: Domenico Scrutinio
- U.O. Cardiologia, S. Chiara Hospital, Trento, Italy:  
Elisa Battaia, Michele Moretti
- Ospedali Riuniti, Ancona, Italy:  
Matilda Shkoza
- Federico II, Naples, Italy:  
Alberto Maria Marra, Roberta D'Assante, Giulia Crisci
- Ospedale di Foggia, Italy:  
Armando Ferraretti
- Cardiologia Riabilitativa, Ospedali Riuniti, Ancona:  
Francesca Pietrucci
- Cardiology, Department of Medical and Surgical Specialities, Radiological Sciences, and Public Health, Brescia, Brescia, Italy: Carlo M. Lombardi, Cristina Gussago
- Mater Dei hospital, Bari: Rocco Lagioia
- Ospedale Ca' Granda, A. O. Niguarda, Milano: Caterina Santolamazza.

## References

1. Siddiqi TJ, Ahmed A, Greene SJ, Shahid I, Usman MS, Oshunbade A, et al. Performance of current risk stratification models for predicting mortality in patients with heart failure: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2022;**29**:2027–48. <https://doi.org/10.1093/eurjpc/zwac148>
2. Peled Y, Ducharme A, Kittleson M, Bansal N, Stehlik J, Amdani S, et al. International society for heart and lung transplantation guidelines for the evaluation and care of cardiac transplant candidates-2024. *J Heart Lung Transplant* 2024;**43**:1529–628 e1554. <https://doi.org/10.1016/j.healun.2024.05.010>
3. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;**42**:3599–726. <https://doi.org/10.1093/eurheartj/ehab368>

4. Agostoni P, Chiesa M, Salvioni E, Emdin M, Piepoli M, Sinagra G, et al. The chronic heart failure evolutions: different fates and routes. *ESC Heart Fail* 2025;**12**:418–33. <https://doi.org/10.1002/ehf2.14966>
5. Freitas P, Aguiar C, Ferreira A, Tralhao A, Ventosa A, Mendes M. Comparative analysis of four scores to stratify patients with heart failure and reduced ejection fraction. *Am J Cardiol* 2017;**120**:443–9. <https://doi.org/10.1016/j.amjcard.2017.04.047>
6. Kouwert IJ, Bakker EA, Cramer MJ, Snoek JA, Eijsvogels TM. Comparison of MAGGIC and MECKI risk scores to predict mortality after cardiac rehabilitation among Dutch heart failure patients. *Eur J Prev Cardiol* 2020;**27**:2126–30. <https://doi.org/10.1177/2047487319865730>
7. Corra U, Agostoni P, Giordano A, Cattadori G, Battaia E, La Gioia R, et al. The metabolic exercise test data combined with Cardiac And Kidney Indexes (MECKI) score and prognosis in heart failure. A validation study. *Int J Cardiol* 2016;**203**:1067–72. <https://doi.org/10.1016/j.ijcard.2015.11.075>
8. Adamopoulos S, Miliopoulos D, Piotrowicz E, Snoek JA, Panagopoulou N, Nanas S, et al. International validation of the metabolic exercise test data combined with cardiac and kidney indexes (MECKI) score in heart failure. *Eur J Prev Cardiol* 2023;**30**:1371–9. <https://doi.org/10.1093/eurjpc/zwad191>
9. Agostoni P, Paolillo S, Mapelli M, Gentile P, Salvioni E, Veglia F, et al. Multiparametric prognostic scores in chronic heart failure with reduced ejection fraction: a long-term comparison. *Eur J Heart Fail* 2018;**20**:700–10. <https://doi.org/10.1002/ehf.989>
10. Agostoni P, Corra U, Cattadori G, Veglia F, Gioia RL, Scardovi AB, et al. Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: a multiparametric approach to heart failure prognosis. *Int J Cardiol* 2013;**167**:2710–8. <https://doi.org/10.1016/j.ijcard.2012.06.113>
11. UNOS 2023 four year monitoring report for adult heart allocation. Available from: <https://unos.org/news/four-year-monitoring-report-for-adult-heart-allocation-now-available/>.
12. Agostoni P, Dumitrescu D. How to perform and report a cardiopulmonary exercise test in patients with chronic heart failure. *Int J Cardiol* 2019;**288**:107–13. <https://doi.org/10.1016/j.ijcard.2019.04.053>
13. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. *Am Rev Respir Dis* 1984;**129**:S49–55. <https://doi.org/10.1164/arrd.1984.129.2P2.S49>
14. Pezzuto B, Piepoli M, Galotta A, Sciomer S, Zaffalon D, Filomena D, et al. The importance of re-evaluating the risk score in heart failure patients: an analysis from the Metabolic Exercise Cardiac Kidney Indexes (MECKI) score database. *Int J Cardiol* 2023;**376**:90–6. <https://doi.org/10.1016/j.ijcard.2023.01.069>
15. Paolillo S, Veglia F, Salvioni E, Corra U, Piepoli M, Lagioia R, et al. Heart failure prognosis over time: how the prognostic role of oxygen consumption and ventilatory efficiency during exercise has changed in the last 20 years. *Eur J Heart Fail* 2019;**21**:208–17. <https://doi.org/10.1002/ehf.1364>
16. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in renal disease study group. *Ann Intern Med* 1999;**130**:461–70. <https://doi.org/10.7326/0003-4819-130-6-199903160-00002>
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;**16**:31–41. <https://doi.org/10.1159/000180580>
18. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;**150**:604–12. <https://doi.org/10.7326/0003-4819-150-9-200905050-00006>
19. Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek JW, et al. Expressing the modification of diet in renal disease study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem* 2007;**53**:766–72. <https://doi.org/10.1373/clinchem.2006.077180>
20. Rostoker G, Andrivet P, Pham I, Griuncelli M, Adnot S. A modified cockcroft-gault formula taking into account the body surface area gives a more accurate estimation of the glomerular filtration rate. *J Nephrol* 2007;**20**:576–85. PMID: 17918143.
21. Pottel H, Bjork J, Courbebaisse M, Couzi L, Ebert N, Eriksen BO, et al. Development and validation of a modified full age Spectrum creatinine-based equation to estimate glomerular filtration rate: a cross-sectional analysis of pooled data. *Ann Intern Med* 2021;**174**:183–91. <https://doi.org/10.7326/M20-4366>
22. Khush KK, Hsich E, Potena L, Cherikh WS, Chambers DC, Harhay MO, et al. The international thoracic organ transplant registry of the international society for heart and lung transplantation: thirty-eighth adult heart transplantation report—2021; focus on recipient characteristics. *J Heart Lung Transplant* 2021;**40**:1035–49. <https://doi.org/10.1016/j.healun.2021.07.015>
23. Grilli G, Salvioni E, Moscucci F, Bonomi A, Sinagra G, Schaeffer M, et al. A matter of sex-persistent predictive value of MECKI score prognostic power in men and women with heart failure and reduced ejection fraction: a multicenter study. *Front Cardiovasc Med* 2024;**11**:1390544. <https://doi.org/10.3389/fcvm.2024.1390544>