

Favorable Impact of a Multidisciplinary Team Approach on Heart Transplantation Outcomes: A 14-Year Experience in a Mid-Volume Center

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Research Article

Keywords: Multidisciplinary team, Critical care, Heart failure, Heart transplantation, Extracorporeal life support, Online information sharing

Posted Date: May 25th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-526489/v1>

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Abstract

Although a multidisciplinary team (MDT) approach is recommended in advanced heart failure and heart transplantation (HTx), no studies have discussed the impact of the team approach on the clinical outcomes of HTx. In 2014, we established an MDT approach in our HTx program with active involvement of teams for critical care and extracorporeal life support (ECLS) using a real-time online information sharing system. We hypothesized that this MDT approach improved the survival of patients who have undergone HTx. In this study, we enrolled 250 adult patients who underwent HTx between December 2003 and June 2018; they were divided into non-MDT (n = 120; before 2014) and MDT (n = 130; since 2014) groups, with the primary outcome being overall mortality. The mean age of HTx recipients was 51.0 ± 13.7 years, and 77 recipients (30.8%) were female. The MDT group had more high-risk patients in terms of age of donors, diabetes, dialysis, ECLS, and waiting time. Various multivariable analytic methods, including inverse-probability-of-treatment-weighting analysis, revealed that the MDT approach was an independent predictor of overall survival. Therefore, collaboration of an HF team, a critical care team, and an ECLS team may improve survival after HTx.

Introduction

The guideline of the American College of Cardiology Foundation and American Heart Association strongly recommend the use of the team approach for treating heart failure (HF)¹. The International Society for Heart and Lung Transplantation has stated that a multidisciplinary team (MDT) should include nearly all teams and health care workers related to the heart transplantation (HTx) procedure². Several studies have reported that the team approach is considered the gold standard model for treating patients with HF³⁻¹¹. Although many HF centers have developed and operated their own HF teams^{6,8}, no studies have reported on the impact of the team approach, such as the survival of patients following HTx. In the recent decade, it has been challenging for HF centers to perform high-risk transplantation such as HTx for recipients in intensive care units (ICUs) owing to the need for mechanical life support. We believe that strong cooperation with teams for intensive care and extracorporeal life support (ECLS) can improve the outcomes of high-risk HTx.

However, communication between many team members from different departments, teams, and centers poses a significant problem. To overcome this, we have introduced a real-time online information sharing system using a social network service (SNS) to be utilized by the HF team. We then analyzed the impact of our MDT approach on certain clinical outcomes including survival in patients after HTx.

Methods

MDT approach. Our HF team began collaborating with the center for intensive care in 2014, which has cardiac, pulmonary, and surgical intensive care specialists and an ECLS team. As more members were added to the HF team, it became necessary to introduce an online information sharing tool to enhance the efficacy of the MDT approach. Although person-to-person discussions through physical meetings and phones were consistently used in MDTs, we have also decided to use a secure online group chat room provided by an SNS. In the online chat room for patients with advanced HF and cardiogenic shock,

approximately 15 key persons were added, including HF cardiologists, a chief cardiac intensivist, the surgical director of HTx, HF nurses, ECLS specialists, a cardiologist, and the cardiac surgeon on in-house duty. Anyone can post concerns regarding any patient who requires the attention of the HF team in the online group chat room (**Supplementary Fig. S1**). The MDT approach was defined as a combination of a traditional HF team, an intensive care team, and an ECLS team utilizing a real-time online information sharing system as a means of communication. A summary of the features of an MDT are compared with those of a non-MDT in **Supplementary Table S1**.

Study population, data collection, and endpoints. A total of 259 adult patients underwent HTx at Samsung Medical Center from December 2003 to June 2018 (Fig. 1). All patients were on the waiting list for HTx in the Korean Network for Organ Sharing. We excluded nine patients who underwent repeated HTx. In the final cohort of 250 patients, 130 (52.0%) were treated and monitored postoperatively with the MDT approach (MDT group), whereas patients who underwent HTx before 2014 were assigned to the non-MDT group.

The primary outcome of this study was overall mortality. The baseline characteristics of the clinical and laboratory data of the patients were collected from electronic medical records and databases. A trained coordinator collected follow-up clinical data, including vital status by reviewing the medical records and telephone interviews. This information was confirmed by the National Registry of Births and Deaths using a unique personal identification number for each patient to complete data on mortality. The study protocol was approved by the Institutional Review Board of Samsung Medical Center (IRB No. SMC 2020-07-139). All data were anonymized before analysis and informed consent from the study participants was waived due to the retrospective nature of this study. The current study was carried out in accordance with the Declaration of Helsinki.

Statistical analysis. The baseline and clinical characteristics of the study population were presented as mean \pm standard deviation, median with interquartile range, or frequency and proportion. Wilcoxon rank-sum tests were used to compare skewed continuous variables. The Chi-square test was used to compare categorical variables between the two groups. The Cox proportional hazards regression model for univariable and multivariable analyses and the forest plot based on the results of multivariable analysis were used to determine the independent predictors of overall mortality. Multivariable analyses were performed on the significant variables in the univariable analyses. To estimate the survival curves during the follow-up period, we used the Kaplan–Meier method, whereas the log rank test was used to compare survival rates between the two groups.

We adjusted for the differences in baseline characteristics using weighted Cox proportional hazards regression models with inverse-probability-of-treatment-weighting (IPTW) to reduce potential confounding factors¹². The adjusted variables are summarized in **Supplementary Table S2**. The standardized difference was calculated from the mean and prevalence for the continuous and dichotomous variables, respectively (Table 1).

Table 1. Baseline characteristics of all patients.

	Overall cohort				IPTW		
	Total (n = 250)	Non- MDT (n = 120)	MDT (n = 130)	<i>p</i> value	Standardized difference	<i>p</i> value	Standardized difference
Age of recipient (years)	54.0 (43.8–61.0)	52.5 (40.3–61.0)	55.0 (45.0–61.0)	0.121	0.217	0.312	0.060
Female recipients	77 (30.8)	41 (34.2)	36 (27.7)	0.268	-0.140	<0.001	-0.559
Age of donor (years)	43.0 (34.0–50.0)	41.0 (34.0–48.0)	44.5 (33.8–51.3)	0.012	0.271	0.146	0.235
Female donors	64 (25.6)	31 (25.8)	33 (25.4)	0.935	-0.010	<0.001	-0.449
Gender mismatch	81 (32.4)	38 (31.7)	43 (33.1)	0.812	0.030	0.204	0.109
Same ABO type matching	191 (78.3)	90 (78.9)	101 (77.7)	0.812	-0.031	0.242	-0.100
Hypertension	88 (35.2)	43 (35.8)	45 (34.6)	0.840	-0.026	<0.001	-0.399
Diabetes	56 (22.4)	20 (16.7)	36 (27.7)	0.037	0.268	0.160	0.120
Stroke	21 (8.4)	11 (9.2)	10 (7.7)	0.675	-0.053	0.618	0.043
Previous cardiac surgery	52 (20.8)	23 (19.2)	29 (22.3)	0.541	0.078	<0.001	0.331
LVAD	14 (5.6)	4 (3.3)	10 (7.7)	0.134	0.192	0.179	0.114
Dialysis	38 (15.3)	16 (13.3)	22 (17.2)	0.400	0.107	0.006	0.235
CRRT	30 (12.1)	9 (7.5)	21 (16.4)	0.032	0.277	0.091	0.144
History of PCI	43 (17.2)	14 (11.7)	29 (22.3)	0.026	0.286	0.238	0.101
LVEF (%)	21.0 (17.0–27.0)	21.5 (17.0–27.8)	21.0 (17.0–27.0)	0.613	-0.122	0.953	0.088
HFpEF	28 (11.2)	16 (13.3)	12 (9.2)	0.304	-0.130	0.007	0.230
ICMP	56 (22.4)	21 (17.5)	35 (26.9)	0.074	0.228	0.032	0.183
SOFA score	7.0 (4.0–11.0)	6.0 (4.0–10.0)	8.0 (5.0–12.0)	0.052	0.244	0.087	0.258

Waiting period for HTx (days)	49.0 (18.0–124.5)	36.0 (14.3–80.8)	72.5 (22.0–167.0)	0.002	0.300	0.683	-0.449
Pre-HTx ECLS	92 (36.8)	28 (23.3)	64 (49.2)	< 0.001	0.559	0.006	0.234
Pre-HTx ECLS duration (days)	10.0 (6.0–17.0)	8.0 (2.0–14.5)	11.0 (7.0–18.8)	0.050	0.394	0.101	0.270
Hemoglobin (g/dL)	10.8 (9.6–12.5)	11.3 (9.7–12.9)	10.5 (9.4–12.1)	0.019	-0.308	0.044	-0.324
Platelet count (10 ³ /mm ³)	149.0 (100.0–214.0)	158.0 (111.0–216.3)	143.0 (93.3–214.0)	0.157	-0.203	0.265	-0.166
Creatinine (mg/dL)	1.1 (0.9–1.5)	1.2 (0.9–1.5)	1.1 (0.9–1.5)	0.381	0.093	0.504	0.205
Total bilirubin (mg/dL)	1.7 (0.9–2.9)	1.6 (0.9–3.0)	1.7 (0.8–2.8)	0.879	0.120	0.185	0.106
Albumin (g/dL)	3.6 (3.1–4.1)	3.6 (3.0–4.2)	3.6 (3.1–4.1)	0.836	0.007	0.349	-0.181
NT-proBNP (pg/mL)	8058.0 (3799.5–18433.5)	7792.0 (3813.0–21543.0)	8105.0 (3742.8–16024.8)	0.640	-0.149	0.105	-0.137

Non-normally distributed numerical variables are presented as medians (interquartile ranges) and were analyzed using the Wilcoxon rank-sum test. Categorical variables are presented as numbers (percentages) and were analyzed using the Chi-square test.

IPTW, inverse-probability-of-treatment-weighting; MDT, multidisciplinary team; LVAD, left ventricular assist device; CRRT, continuous renal replacement therapy; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; HFpEF, heart failure with preserved ejection fraction; ICMP, ischemic cardiomyopathy; SOFA, Sequential Organ Failure Assessment; HTx, heart transplantation; ECLS, extracorporeal life support; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

Values in bold typeface indicate statistically significant findings.

All tests were two-tailed. *P* values of less than 0.05 were considered statistically significant. Statistical analysis was performed using R (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria) and Statistical Analysis System (version 9.4; SAS Institute Inc., Cary, NC, USA).

Results

Baseline characteristics. The mean age of the HTx recipients was 51.0 ± 13.7 years, while the median age was 54 years (range: 18–78 years). Of the 250 patients, 77 (30.8%) were female. Patients in the MDT group were more likely to have diabetes, continuous renal replacement therapy, history of percutaneous coronary intervention, longer waiting time for HTx, and more frequent use of pre-HTx ECLS than those in the non-MDT group. The mean duration of ECLS before HTx was 15.2 ± 18.9 days, while the median duration was 10.0 days (range: 1–126 days, interquartile range: 6–17 days). The frequency of pre-HTx ECLS was significantly different between the two groups (non-MDT group: 23.3% vs. MDT group: 49.2%; $p < 0.001$). We also observed significant inter-group differences in the baseline covariates of hypertension, previous cardiac surgery, dialysis, HF with preserved ejection fraction, ischemic cardiomyopathy, and the frequency of pre-HTx ECLS after adjusting for the baseline profiles using IPTW. The baseline characteristics of the patients in the non-MDT and MDT groups are summarized in Table 1.

Early clinical outcomes. Although cold ischemic time was longer in the MDT group than in the non-MDT group, the total ischemic time was similar between both groups because of the shorter warm ischemic time and aortic cross-clamping time in the MDT group. Post-HTx ICU stay and total ICU stay were longer in the MDT group than in the non-MDT group, but post-HTx hospital stay was similar between both groups ($p = 0.993$). The frequency of post-HTx ECLS did not differ between the two groups (non-MDT group: 10.0% vs. MDT group: 13.8%; $p = 0.350$). There was no significant difference regarding the frequency of new ECLS after HTx between both groups ($p = 0.069$). The operative and postoperative data are summarized in Table 2. The immunosuppression strategy at three months after HTx is described in Fig. 2. Tacrolimus and mycophenolate were commonly used during the study period, whereas everolimus was used only in the MDT group.

Table 2
Operative and postoperative characteristics of all patients.

	Total (n = 250)	Non-MDT (n = 120)	MDT (n = 130)	p value
CPB time (minutes)	147.0 (126.0–177.0)	159.0 (135.0–190.5)	139.0 (121.0–161.0)	< 0.001
ACC time (minutes)	86.0 (68.0–105.0)	97.0 (86.0–112.0)	70.0 (60.0–87.0)	< 0.001
Total ischemic time (minutes)	181.0 (147.0–235.0)	173.0 (143.0–237.0)	187.0 (150.0–235.0)	0.383
Cold ischemic time (minutes)	116.0 (82.0–169.0)	100.0 (70.0–163.0)	120.0 (96.0–174.0)	0.003
Warm ischemic time (minutes)	65.0 (54.0–76.0)	70.0 (63.0–82.0)	56.0 (47.0–68.0)	< 0.001
Post-HTx ECLS	30 (12.0)	12 (10.0)	18 (13.8)	0.350
Post-HTx new ECLS	8 (5.1)	2 (2.2)	6 (9.1)	0.069
Post-HTx ICU stay (days)	10.0 (6.0–16.0)	7.0 (5.0–14.0)	12.0 (8.0–20.0)	< 0.001
Total ICU stay (days)	14.0 (7.0–28.3)	10.5 (5.3–21.8)	17.0 (9.0–35.0)	< 0.001
Post-HTx hospital stay (days)	30.0 (23.0–50.0)	30.5 (24.0–41.0)	30.0 (22.0–59.3)	0.993

Non-normally distributed numerical variables are presented as medians (interquartile ranges) and were analyzed using the Wilcoxon rank-sum test. Categorical variables are presented as numbers (percentages) and were analyzed using the Chi-square test or Fisher's exact test.

MDT, multidisciplinary team; CPB, cardiopulmonary bypass; ACC, aorta cross-clamping; HTx, heart transplantation; ECLS, extracorporeal life support; ICU, intensive care unit.

Values in bold typeface indicate statistically significant findings.

In all patients, the 30-day and 1-year mortality rates were 4.4% (n = 11) and 13.6% (n = 34), respectively. There was no significant difference in the 30-day mortality rate between both groups (non-MDT group: 5.8% vs. MDT group: 3.1%; $p = 0.288$). However, the 1-year mortality rate was significantly higher in the non-MDT group (non-MDT group: 18.3% vs. MDT group: 9.2%; $p = 0.036$). Kaplan–Meier survival analysis also revealed a difference in 1-year survival after HTx (log rank $p = 0.040$) (**Supplementary Fig. S2**).

Impact of the MDT and predictors of overall mortality. Kaplan–Meier survival analysis revealed an intergroup difference in overall survival after HTx (log rank $p = 0.012$) (Fig. 3). Additionally, the cardiac-related survival after HTx was different between the two groups (log rank $p = 0.012$) (**Supplementary Fig. S3**). The MDT approach was an independent predictor of survival ($p = 0.001$; hazard ratio: 0.341; 95% confidence

interval: 0.182–0.637) in the multivariable analysis before IPTW for overall mortality. The age of HTx recipients (analyzed 10 years increases; $p = 0.002$; hazard ratio: 1.371; 95% confidence interval: 1.128–1.666) and the level of total bilirubin ($p = 0.024$; hazard ratio: 1.040; 95% confidence interval: 1.005–1.076) were observed to be independent predictors of death. The results of the Cox proportional hazards regression model for univariable and multivariable analyses of overall mortality are summarized in Fig. 4A and **Supplementary Table S3**.

The MDT approach was found to be an independent predictor of survival ($p < 0.001$; hazard ratio: 0.312; 95% confidence interval: 0.198–0.491) after adjustment using IPTW. Additionally, the age of the HTx recipients (analyzed 10 years increases; $p < 0.001$; hazard ratio: 1.408; 95% confidence interval: 1.207–1.642) and the level of total bilirubin ($p < 0.001$; hazard ratio: 1.050; 95% confidence interval: 1.022–1.078) were also found to be independent predictors of death after adjustment using IPTW (Fig. 4B and **Supplementary Table S3**, right columns). In contrast, the duration of waiting for HTx was an independent predictor of survival ($p = 0.011$; hazard ratio: 0.982; 95% confidence interval: 0.968–0.996). The adjusted outcomes of various statistical methods are detailed in Table 3. A lower risk of overall mortality was observed in the MDT group compared to the non-MDT group ($p < 0.001$) when the adjustment using IPTW was further augmented by the multivariable analyses (IPTW + multivariable analyses).

Table 3
Adjusted hazard ratios for overall mortality following the MDT group compared with the non-MDT group.

Outcomes	<i>p</i> value	Hazard Ratio	95% Confidence Interval	
			Lower .95	Upper .95
Crude	0.001	0.341	0.182	0.637
IPTW	0.002	0.506	0.327	0.783
IPTW + multivariable*	< 0.001	0.396	0.253	0.621

*Baseline variables that were significantly different after IPTW: hypertension, previous cardiac surgery, previous dialysis, heart failure with preserved ejection fraction, ischemic cardiomyopathy, and the frequency of pre-HTx ECLS.

MDT, multidisciplinary team; IPTW, inverse-probability-of-treatment-weighting; HTx, heart transplantation; ECLS, extracorporeal life support.

Values in bold typeface indicate statistically significant findings.

Discussion

In the study, we found that (a) the MDT approach positively affected the outcomes of patients after HTx, (b) the MDT group had an increased use of pre-HTx ECLS, (c) the MDT group had more high-risk HTx patients, and (d) both surgical and medical management markedly changed after using the MDT approach. Although most large HTx programs are already using the team approach in their HF programs³⁻¹¹, no studies have discussed its effect on the survival of patients who underwent HTx. Although one study has reviewed a change in outcomes after the deployment of the team approach in their HTx program, they reported no notable changes in the survival or changes of their pre/post-HTx management¹³. Aside from the formation of an HF team, we believe that it is also important to know how to properly operate an HF team. We developed a large-scale MDT that included a critical care team and an ECLS team. We also used a secure online chat room provided by an SNS, which can be used as a tool to improve the efficiency of our MDT.

In our results, the baseline covariates of hypertension, previous cardiac surgery, dialysis, ischemic cardiomyopathy, and the use of pre-HTx ECLS was significantly higher in the MDT group than in the non-MDT group after adjusting for baseline profiles using IPTW. Moreover, the use of pre-HTx ECLS had a significant inter-group difference between the two groups both before ($p < 0.001$) and after ($p = 0.006$) adjustment using IPTW (Table 1). Therefore, HTx has progressed in recipients with higher risk in the MDT group. Furthermore, the Sequential Organ Failure Assessment score tended to be higher in the MDT group as well. Since patients in the MDT group had worse preoperative conditions, the duration of post-HTx ICU stay was significantly longer, and the frequency of post-HTx ECLS and new post-HTx ECLS tended to be higher as well. Nevertheless, the 1-year, cardiac-related, and overall survival rates in the MDT group were significantly better than those in the non-MDT group, suggesting that the post-HTx care was well performed through the MDT approach. The favorable response could be explained by the positive effect of having a cardiac and general critical care team and an ECLS team in the MDT approach¹⁴.

We aimed to use the MDT approach to overcome the increasing number of high-risk HTx patients. We collaborated with a critical care team and an ECLS team. Majority of the significant changes in the patients' conditions were immediately shared in our secure online chat room. We also tried deploying the ECLS system before the occurrence of severe end-organ damage or sudden cardiac arrest. Interventional or surgical left heart decompression and distal limb protection procedures were performed prophylactically or during an exceedingly early stage of ECLS. The principles of modern critical care, including light/no sedation, adequate pain control, and active rehabilitation, among others, were applied to all patients in our service.

Additionally, prioritizing a patient for ECLS or other temporary mechanical circulatory support methods was an important approach in our team. Donors in the extended criteria were accepted to reduce the waiting time of HTx recipients. Donors older than 50 years or expecting a cold ischemic time of up to four hours were accepted for HTx patients on temporary mechanical circulatory support. This was done by modifying the surgical technique to decrease the warm ischemic time. Postoperative medical management, including infection prevention and control, immune suppression, and monitoring protocols for acute and chronic rejection were all revised. The postoperative concerns of HTx patients were also shared during the regular physical meetings between the physicians and surgeons, as well as in the secure online chat room.

Limitations

We also recognize several limitations of this study. First, this was a single-center study involving 250 patients, and thus, the results in our cohort may not be generalizable to all HTx patients. Second, there may be residual confounding factors even after statistical adjustments because this was a retrospective observational study comparing two periods. Aside from the effect of the MDT approach, the outcomes may have also been influenced by the cumulative experience in performing surgical techniques and perioperative management. These changes in the MDT group were unavoidable, and so we performed various adjustments to control for confounders and reduce this limitation, including IPTW and a regression modeling including several risk factors. A randomized multicenter trial is needed to further investigate the impact of the MDT approach, but this may be exceedingly difficult. Third, the duration of ECLS before HTx was shorter in this study (median: 10.0 days, mean: 15.2 ± 18.9 days) than in some reports with ECLS in the United States^{15,16} but was comparable or longer compared to other previous publications^{17,18}.

Conclusion

The MDT approach was an independent predictor of overall survival. Collaboration of an HF team, a critical care team, and an ECLS team may improve survival after HTx. We suggest the use of a real-time online information sharing system to enhance the efficiency of the MDT approach.

Abbreviations

ECLS Extracorporeal life support

HF Heart failure

HTx Heart transplantation

IPTW Inverse-probability-of-treatment-weighting

MDT Multidisciplinary team

SNS Social network service

Declarations

Data availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Acknowledgement

The authors would like to thank Yun Jin Kim, Nayeon Choi, and Han-Pyo Hong (Biostatistical Consulting and Research Lab in Medical Research Collaborating Center at Hanyang University) for providing statistical

support.

Author contributions

J.H.L, J.Y.K, and Y.H.C conceived and designed the study. J.H.L, J.Y.K, and I.P performed the statistical analyses and wrote the manuscript. K.S, W.S.K, D.K, J.H.Y, E.S.J, J.O.C, and Y.H.C revised the manuscript. All authors participated in drafting the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

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Figures

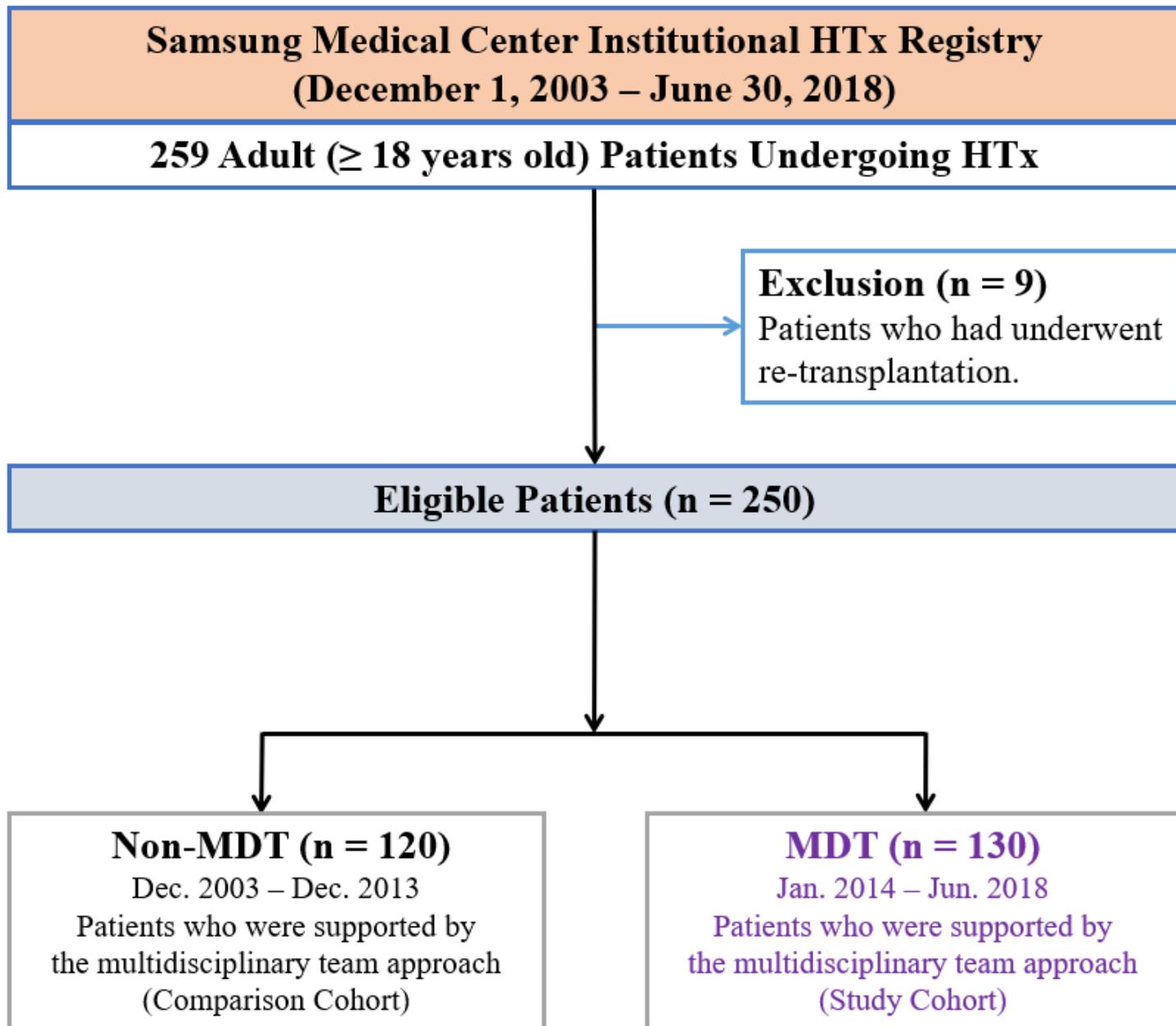
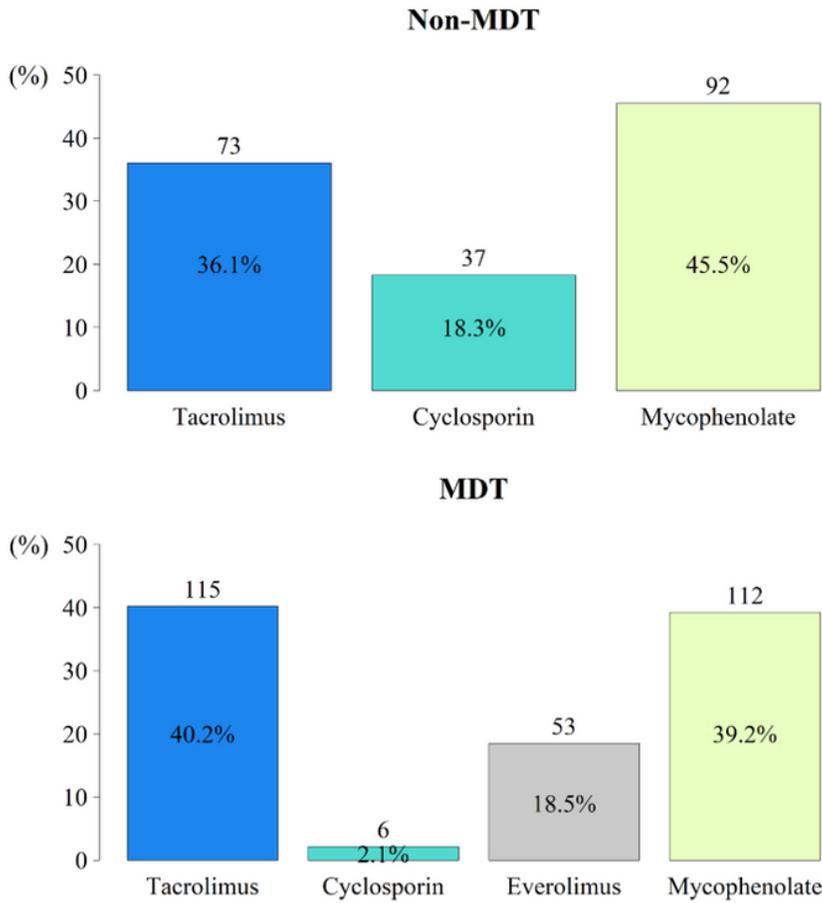


Figure 1

Flow diagram of patient recruitment. HTx, heart transplantation; MDT, multidisciplinary team.



Variables	Non-MDT (n = 202)	MDT (n = 286)
Tacrolimus	73 (36.1)	115 (40.2)
Cyclosporin	37 (18.3)	6 (2.1)
Everolimus	0 (0.0)	53 (18.5)
Mycophenolate	92 (45.5)	112 (39.2)

Variables	Non-MDT (n = 202)	MDT (n = 286)
Tacrolimus	Yes	73 (36.1)
	No	129 (63.9)
Cyclosporin	Yes	6 (2.1)
	No	280 (97.9)
Everolimus	Yes	53 (18.5)
	No	233 (81.5)
Mycophenolate	Yes	112 (39.2)
	No	174 (60.8)

Figure 2

Use of immunosuppressive agents at three months after heart transplantation. MDT, multidisciplinary team.

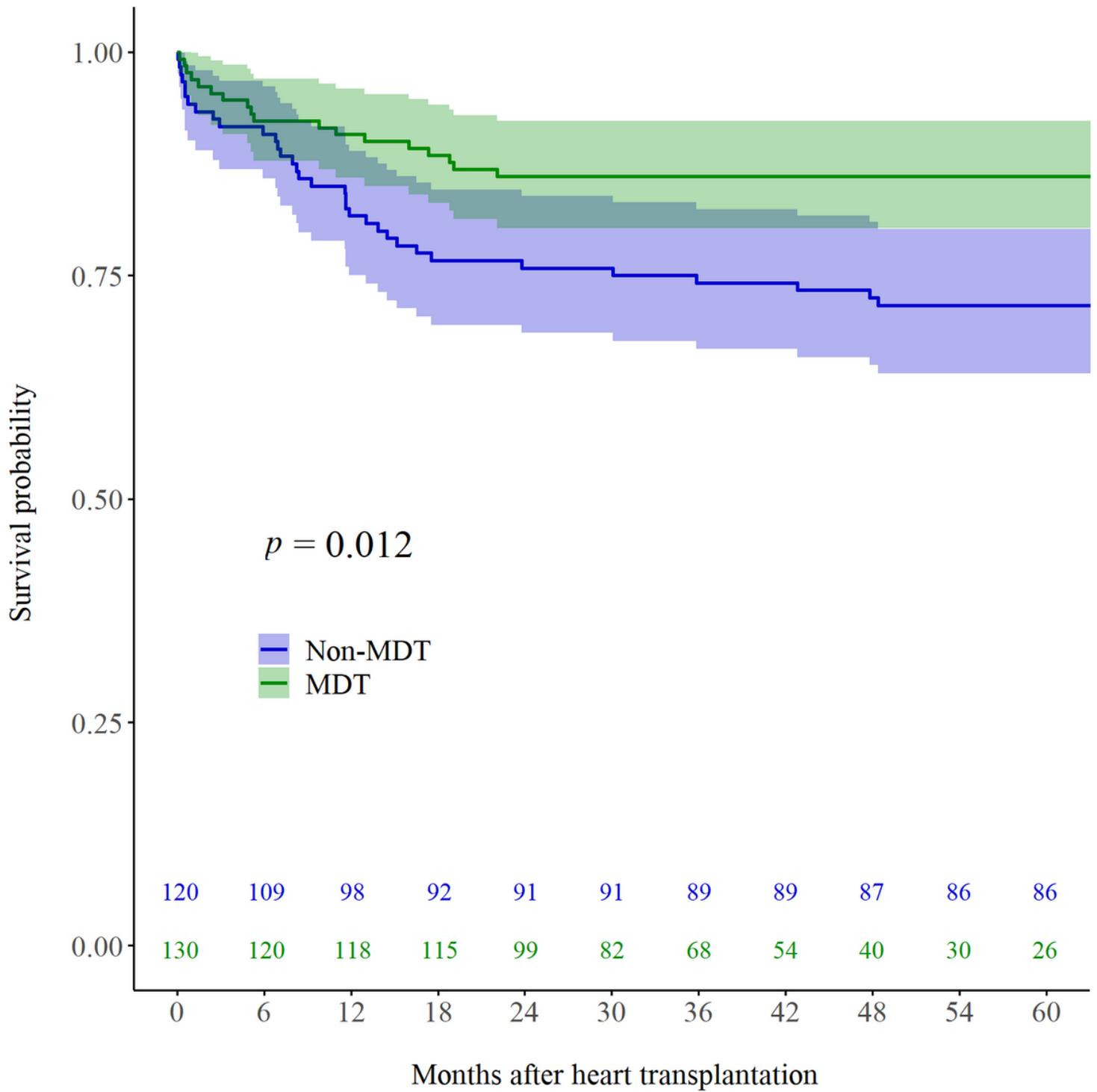
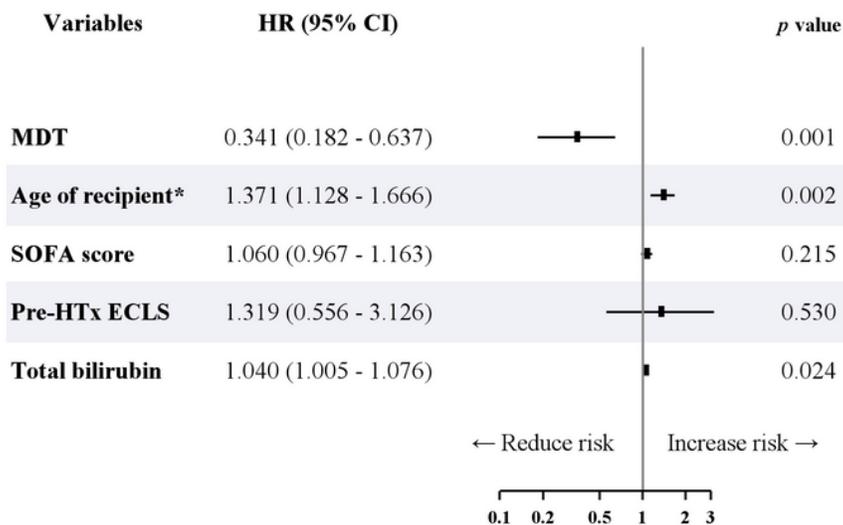


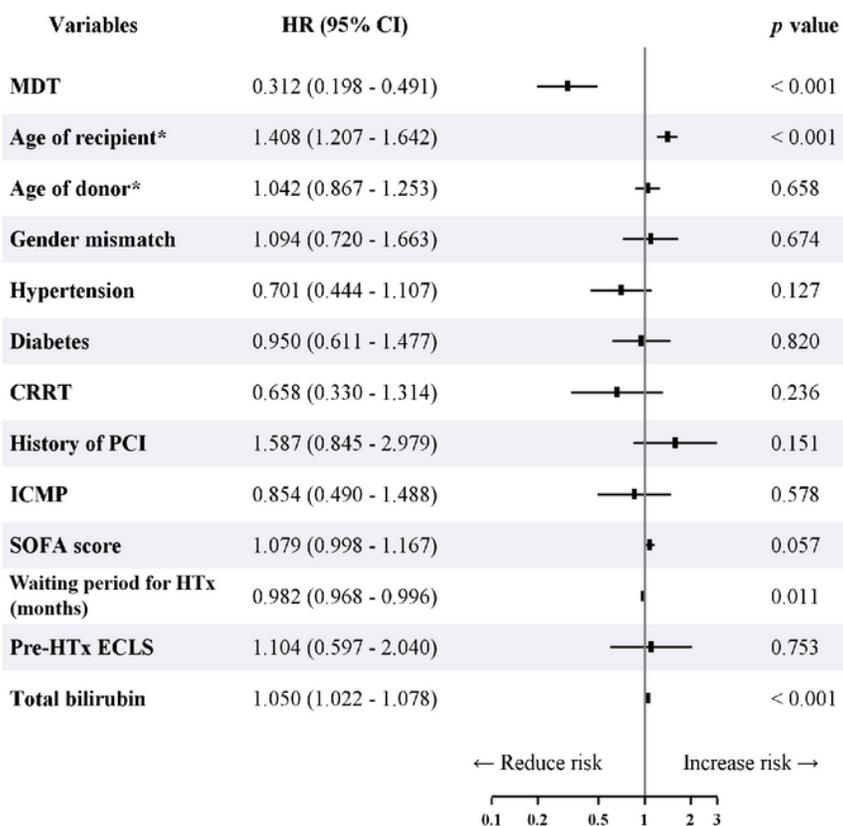
Figure 3

Kaplan–Meier post-heart transplantation survival curves for overall survival in patients who underwent heart transplantation with the multidisciplinary team approach (MDT group; green line) and without the multidisciplinary team approach (Non-MDT group; blue line). MDT, multidisciplinary team.

(A) Before adjustment with IPTW



(B) After adjustment using IPTW



* Analyzed 10 years increases

Figure 4

Forest plot based on the results of multivariable analysis of overall mortality (A) before adjustment using IPTW and (B) after adjustment using IPTW. IPTW, inverse-probability-of-treatment-weighting; HR, hazard ratio; CI, confidence interval; MDT, multidisciplinary team; SOFA, Sequential Organ Failure Assessment; HTx, heart transplantation; ECLS, extracorporeal life support; CRRT, continuous renal replacement therapy; PCI, percutaneous coronary intervention; ICMP, ischemic cardiomyopathy.

Supplementary Files

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