Impact of Functional Warm Ischemia Time on Donation After Circulatory Death Heart Transplant

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Introduction

Donation after circulatory death heart transplantation (DCD HT) has emerged as a viable strategy for expanding the cardiac donor pool by enabling the use of hearts from donors who do not meet traditional brain death criteria.

In DCD HT, donor hearts are subjected to mandatory agonal hypoxia known as functional warm ischemia time (FWIT).[1]

The maximum safe duration of FWIT remains an ongoing debate. **Historically, safe FWIT has been regarded as less than 30 minutes**, yet some studies have reported successful short-term outcomes for DCD HT with FWIT extending beyond this threshold.[2,3]

The objective of this study was to examine the impact of donor FWIT on long-term survival among DCD HT recipients.

Methods

Using the UNOS database, adults undergoing DCD HT between 2019 and 2024 were stratified into **nine subgroups** based on FWIT: <15, 15-20, 20-25, 25-30, 30-35, 35-40, 40-50, 50-60, and >60 minutes.

FWIT was defined as agonal start time (mean arterial pressure <80 mmHg and O2 saturation <80%) to cross-clamp for DPP and agonal time to death +10 minutes for NRP.

30 day, 1 year, and 3 year survival were compared using the Kaplan-Meier method.

Multivariate Cox proportional hazard models were used to assess predictors of overall mortality risk.

A secondary analysis using the same statistical methods was performed by categorizing FWIT into two groups: <30 minutes and ≥30 minutes.

Results

Variables	<15, N= 63[1]	15-20, N = 194[1]	20-25, N = 358[1]	25-30, N = 254[1]	30-35, N = 105[1]	35-40, N = 56[1]	40-50, N = 55[1]	50-60, N = 41[1]	≥60, N = 87[1]	p-value[2]
Age	52.38 (12.83)	53.59 (12.44)	54.36 (12.13)	54.06 (12.91)	53.56 (11.87)	50.02 (12.39)	53.65 (11.64)	55.27 (12.45)	54.74 (13.11)	0.4
Sex										
Female	10 (16%)	43 (22%)	75 (21%)	50 (20%)	30 (29%)	10 (18%)	8 (15%)	11 (27%)	15 (17%)	0.4
Male	53 (84%)	151 (78%)	283 (79%)	204 (80%)	75 (71%)	46 (82%)	47 (85%)	30 (73%)	72 (83%)	
Race										
White	40 (63%)	130 (67%)	230 (64%)	164 (65%)	78 (74%)	30 (54%)	37 (67%)	21 (51%)	58 (67%)	0.012
Black	17 (27%)	43 (22%)	84 (23%)	65 (26%)	10 (9.5%)	17 (30%)	6 (11%)	10 (24%)	20 (23%)	
Other	6 (9.5%)	21 (11%)	44 (12%)	25 (9.8%)	17 (16%)	9 (16%)	12 (22%)	10 (24%)	9 (10%)	
Diabetes	26 (41%)	62 (32%)	111 (31%)	81 (32%)	41 (39%)	11 (20%)	21 (38%)	14 (35%)	21 (24%)	0.2
Cigarette Use	28 (44%)	80 (41%)	161 (45%)	99 (39%)	47 (45%)	25 (45%)	28 (51%)	14 (35%)	41 (48%)	0.7
BMI										
<=30	44 (70%)	125 (64%)	225 (63%)	159 (63%)	65 (62%)	36 (64%)	39 (71%)	26 (63%)	59 (68%)	>0.9
>30	19 (30%)	69 (36%)	132 (37%)	95 (37%)	40 (38%)	20 (36%)	16 (29%)	15 (37%)	28 (32%)	
LVAD at Transplant	25 (41%)	63 (34%)	140 (40%)	93 (38%)	38 (37%)	18 (34%)	25 (47%)	12 (32%)	42 (51%)	0.2
DPP vs. NRP										<0.001
NRP	10 (16%)	43 (22%)	92 (26%)	105 (41%)	52 (50%)	26 (46%)	25 (45%)	18 (44%)	38 (44%)	
DPP	53 (84%)	151 (78%)	266 (74%)	149 (59%)	53 (50%)	30 (54%)	30 (55%)	23 (56%)	49 (56%)	

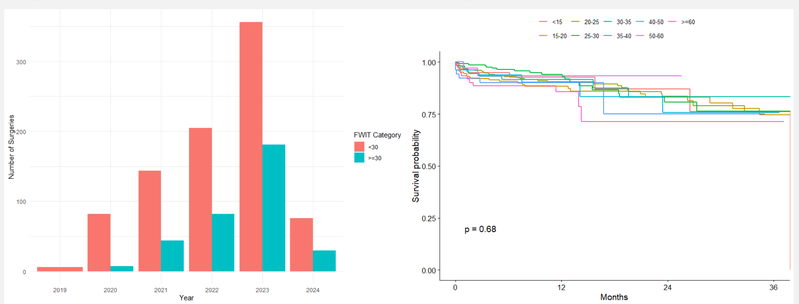
[1] Mean (SD); n (%)

[2] One-way ANOVA; Pearson's Chi-squared test; Fisher's exact test

We analyzed 1,213 recipients: 869 (72%) had a FWIT < 30 min and 344 (28%) had a FWIT ≥ 30 min.

409 patients (34%) received normothermic regional perfusion (NRP) hearts and 804 (66%) received direct procurement and preservation (DPP) hearts.

In baseline characteristics, only procurement method (DPP vs. NRP, p<0.001) and race (p=0.012) demonstrated statistically significant variation across FWIT subgroups.



We found no significant differences in 30d, 1y, and 3y survival between FWIT groups (p=0.68). The <15-minute FWIT group had survival rates of 96.6%, 92.7%, and 76.1% at 30 days, 1 year, and 3 years, respectively, while the ≥60-minute FWIT group had survival rates of 93.3%, 85.7%, and 71.4% at the same time points.

Results

Covariates	Hazard Ratios	95 % Confidence Intervals	p-value
Functional Warm Ischemia Time			
≤ 15 min	REF		
15-20 min	1.19	0.52 – 2.74	0.687
20-25 min	1.02	0.45 – 2.29	0.970
25-30 min	0.95	0.40 – 2.27	0.911
30-35 min	1.19	0.44 – 3.24	0.729
35-40 min	1.35	0.45 – 4.09	0.590
40-50 min	1.80	0.60 – 5.44	0.297
50-60 min	0.82	0.17 – 4.00	0.808
≥ 60min	2.14	0.82 – 5.58	0.119
Black race	1.67	1.12 – 2.49	0.012
Other race	1.08	0.60 – 1.96	0.794
DPP	1.61	1.04 – 2.47	0.032

After adjusting for covariates, Black race (HR 1.67, p=0.012) and the use of direct procurement and preservation (HR 1.61, p=0.032) were independently associated with increased mortality risk.

Notably, FWIT >60 minutes was not associated with worse survival (HR 2.14, p=0.119)

Conclusions

These findings challenge the traditional 30-minute FWIT cutoff, which we believe should be cautiously re-evaluated. While more research is needed to clarify the role of NRP and other strategies in mitigating potential risks, our results support broader use of DCD hearts with prolonged FWIT in select patients.

References

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