Impact of symptom-to-surgery time and malperfusion on mortality in patients with acute type A aortic dissection

Xun E. Zhang, Chao Fu, Jun Shao, Bo Wang, Changming Niu, Hao Yao, Qing-Guo Li

The 2nd Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China

Background

- **Malperfusion is a well recognized mortality risk factor in patients with acute type A aortic dissection (ATAAD)**

- **How symptom-to-surgery time impacts survival is less well understood**

- **The optimal timing of surgery remains undefined and delayed repair is believed to worsen survival, particularly in those with malperfusion**

- **<u>Objective</u>: to determine the impact of symptom-to-surgery time on operative and mid-term mortalities in ATAAD patients with and without malperfusion**

Methods

- **Design: single-centered retrospective cohort study**

- **Time: Jan. 2016 to Dec. 2020**

- **Participants: patients with ATAAD underwent surgical treatment at our center, excluding deaths before the operation**

- **Symptom-to-surgery time: reliably established from medical history**

- **Surgical strategy**
  - **Total arch repair + frozen elephant trunk: type I dissection, arch (vessel) involved, Marfan syndrome**
  - **Ascending / hemiarch repair: type II dissection**
  - **Right axillary/Femoral artery cannulation**
  - **Antegrade/retrograde cerebral perfusion with hypothermic circulatory arrest at 20-25℃**

- **Outcomes**
  - **Operative death: deaths within 30 days of surgery, or before final hospital discharge, including transfers**
  - **Late death: all-cause mortality occurring after discharge until last follow-up, excluding operative deaths**

- **Statistical Analysis**
  - **Grouping: median symptom-to-surgery time used to separate participants into two groups**
  - **Univariate analysis and multivariable logistic regression used for operative and mid-term mortality**
  - **Kaplan-Meier analysis of time-to-event outcomes**

Results

- **288 patients participated in the study**

- **Mean (standard deviation) follow-up time was 4.3 $\pm$ 1.6 years**

- **Symptom-to-surgery time**
  - **Median: 10 hour**
  - **Mean: 20.4 hour**
  - **Range: 1 ~ 97 hour (IQR 6 - 21.8 hour)**

- **Two study groups defined by median symptom-to-surgery time**
  - **Late ≥ 10 h, n = 138 (48%)**
  - **Early < 10 h, n = 150 (52%)**

- **Surgical re-intervention: 19 patients at median 1.7 years (interquartile range 1.4 ~ 4.4)**

Results - Demographics

- **Baseline characteristics were comparable between groups**

- **Male gender was significantly different between late group [91 (66%)] and early group: [121 (81%)], *p* = 0.005**

- **Prior aortic dissection was significantly different between late group [11 (8%)] vs early group [2 (1%)], *p* = 0.007**

Variables	Timing of presentation		P-value
	Late, N = 138 (48%)	Early, N = 150 (52%)	
Age (Year, mean ± SD)	53 ± 13	54 ± 12	0.590
BMI (kg/m^2, mean ± SD)	25.4 ± 3.8	25.7 ± 3.3	0.422
Symptom to surgery time (hour, mean ± SD)	35 ± 25	7 ± 2	**<0.001**
Male gender	91 (66%)	121 (81%)	**0.005**
Presentation			
Chest pain	106 (77%)	117 (78%)	0.810
Back pain	88 (64%)	82 (55%)	0.117
Abdominal pain	23 (17%)	36 (24%)	0.123
History			
Hypertension	96 (70%)	113 (75%)	0.273
Type 2 diabetes mellitus	4 (3%)	1 (1%)	0.197
Prior aortic dissection	11 (8%)	2 (1%)	**0.007**
Marfan syndrome	4 (3%)	2 (1%)	0.431
Smoking history	25 (18%)	37 (25%)	0.177
Chronic obstructive lung disease	2 (1%)	1 (1%)	0.609

SD: standard deviation

Results - Malperfusion

- **Malperfusion: 107 (37%) of 288**
  - ➢ **By organ systems**
    - Temponade: 21 (7%)
    - Cerebral: 34 (12%)
    - Cardiac: 53 (18%)
    - Renal: 35 (12%)
    - Mesenteric: 5 (2%)
    - Limb: 22 (8%)
    - Spinal: 1 (0%)
  - ➢ **By total malperfused organ number**
    - One: 59 (20%)
    - Two: 29 (10%)
    - Three: 11 (4%)
  - ➢ **By Penn Classification system**
    - Penn B: 86 (30%)
    - Penn C: 8 (3%)
    - Penn B-C: 13 (5%)
- **No statistic significant between groups differences**

Variables	Overall N=288 (100%)	Timing of presentation		P-value
		Late N = 138 (48%)	**Early** N = 150 (52%)	
Malperfusion	107 (37%)	46 (33%)	61 (41%)	0.198
Tamponade	21 (7%)	12 (9%)	9 (6%)	0.379
Cerebral	34 (12%)	17 (12%)	17 (11%)	0.796
Cardiac	53 (18%)	20 (14%)	33 (22%)	0.100
Renal	35 (12%)	14 (10%)	21 (14%)	0.317
Mesenteric	5 (2%)	1 (1%)	4 (3%)	0.373
Limb	22 (8%)	10 (7%)	12 (8%)	0.810
Spinal	1 (0%)	1 (1%)	0 (0%)	0.479
Number of malperfused organs (Tamponade not included)				0.539
One organ	59 (20%)	26 (19%)	33 (22%)	
Two organs	29 (10%)	11 (8%)	18 (12%)	
Three organs	11 (4%)	5 (4%)	6 (4%)	
Penn classification				0.251
Penn B	86 (30%)	34 (25%)	52 (35%)	
Penn C	8 (3%)	4 (3%)	4 (3%)	
Penn B-C	13 (5%)	8 (6%)	5 (3%)	

Results – Operative Data and Outcomes

- **Total operative death 14 (6%)**

  - **Late group: 20 (14%)**

  - **Early group: 32 (21%)**

  - ***p* = 0.132**

- **Total late death 14 (6%)**

  - **Late group: 20 (14%)**

  - **Early group: 32 (21%)**

  - ***p* = 1.000**

- **Total mid-term mortality 66 (23%)**

 - **Late group: 27 (20%)**

  - **Early group: 39 (26%)**

  - ***p* = 0.194**

| Variables | Overall N (%) | Timing of presentation | | P-value |
		Late N = 138 (48%)	Early N = 150 (52%)	
Operative procedures				
Total arch replacement	227 (79%)	108 (78%)	119 (79%)	0.824
Bentall	116 (40%)	50 (36%)	66 (44%)	0.179
CABG	52 (18%)	22 (16%)	30 (20%)	0.371
ECMO	13 (5%)	5 (4%)	8 (5%)	0.485
Operative times, min, mean ± SD				
Cardiopulmonary bypass	186 ± 61	185 ± 62	187 ± 59	0.767
Cross-clamp	125 ± 51	124 ± 54	126 ± 47	0.701
Hypothermic circulatory arrest	24 ± 9	23 ± 8	25 ± 9	0.057
Postoperative complications				
Renal failure requiring dialysis	51 (18%)	25 (18%)	26 (17%)	0.862
Stroke	30 (10%)	15 (11%)	15 (10%)	0.809
Reintubation	20 (7%)	8 (6%)	12 (8%)	0.463
Tracheostomy	18 (6%)	5 (4%)	13 (9%)	0.077
Paraplegia	4 (1%)	0 (0%)	4 (3%)	0.124
Re-exploration for bleeding	22 (8%)	9 (7%)	13 (9%)	0.494
Delayed wound healing	9 (3%)	5 (4%)	4 (3%)	0.742
Operative death	52 (18%)	20 (14%)	32 (21%)	0.132
Late death	14 (6%)	7 (6%)	7 (6%)	1.000
Mid-term mortality	66 (23%)	27 (20%)	39 (26%)	0.194

Results – Univariate and Multivariable Logistic Regression Analyses for Operative Mortality

Variables	Univariate Analysis			Multivariable Analysis (model 1)			Multivariable Analysis (model 2)			Multivariable Analysis (model 3)			Multivariable Analysis (model 4)		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Age	1.04	1.02-1.07	0.001	1.09	1.06-1.14	<0.001	1.10	1.06-1.14	<0.001	1.10	1.06-1.14	<0.001	1.09	1.06-1.14	<0.001
Cardiopulmonary bypass time	1.01	1.01-1.02	<0.001	1.01	1.00-1.02	0.159							1.01	1.00-1.02	0.150
Cross-clamp time	1.02	1.01-1.02	<0.001	1.01	1.00-1.03	0.100	1.02	1.01-1.03	<0.001	1.02	1.01-1.03	<0.001	1.01	1.00-1.03	0.073
Bentall procedure	0.83	0.44-1.52	0.544	0.46	0.19-1.02	0.064	0.41	0.16-0.94	0.043	0.43	0.17-1.00	0.058	0.48	0.20-1.09	0.090
CABG	2.79	1.39-5.48	0.003				0.24	0.06-0.90	0.046	0.31	0.08-1.01	0.071	0.48	0.17-1.28	0.158
ECMO	12.14	3.77-46.46	<0.001	10.61	2.50-51.61	0.002	19.38	3.71-127.07	0.001	22.15	3.97-160.86	0.001	17.67	3.57-107.11	<0.001
Malperfusion	5.23	2.77-10.26	<0.001	7.06	3.11-17.19	<0.001									
Tamponade	2.47	0.89-6.29	0.066												
Cerebral	3.41	1.55-7.33	0.002				3.18	1.08-9.11	0.032						
Cardiac	4.32	2.21-8.43	<0.001				6.13	1.33-27.43	0.018						
Visceral (renal + mesenteric)	6.38	3.02-13.57	<0.001				2.99	0.81-11.90	0.107						
Limb	2.29	0.83-5.77	0.088				6.41	1.79-22.76	0.004						
Malperfused organ numbers															
1	3.45	1.59-7.47	0.002							6.48	2.51-17.58	<0.001			
2	8.22	3.38-20.13	<0.001							13.46	3.08-67.22	0.001			
3	17.71	4.86-73.60	<0.001							49.09	8.23-322.71	<0.001			
Penn Classification															
Penn B	5.25	2.69-10.57	<0.001										8.26	3.28-22.32	<0.001
Penn C	1.47	0.08-9.05	0.725										2.30	0.11-17.66	0.480
Penn B-C	8.84	2.57-29.93	<0.001										13.26	2.81-63.75	0.001

model 1: Malperfusion status was used; model 2: individual organ malperfusion status was used; model 3: malperfused organ numbers were used; Penn classification systems were used. CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation

Results – Survival for Preoperative Malperfusion Status vs Symptom-to-Surgery Time
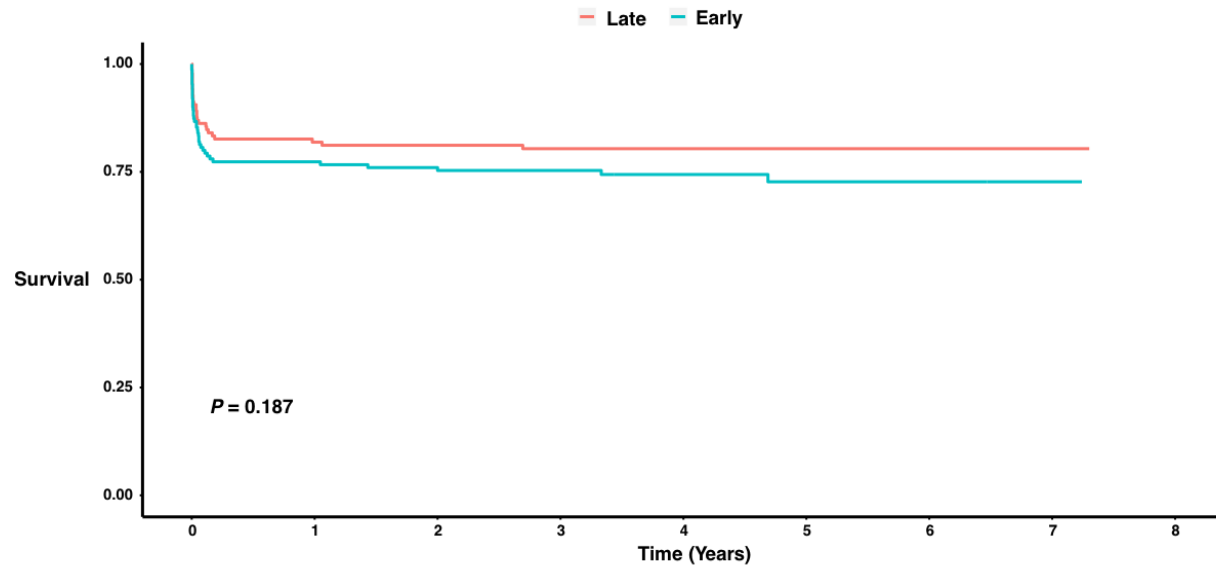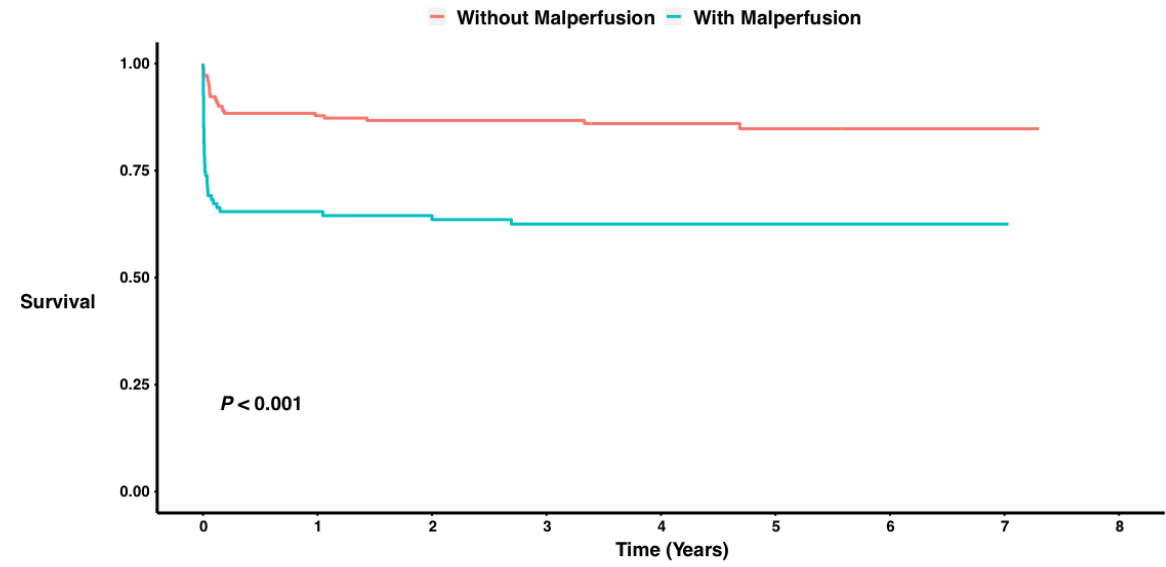
Preoperative malperfusion status, rather than symptom-to-surgery time significantly affected mid-term mortality

Results - Operative and Mid-term Mortalities Separately Analyzed by Symptom-to-Surgery Time

Operative mortality

Groups	Without Malperfusion	With Malperfusion	Adjusted OR (95% CI)[*]	P value	P for interaction
All	16/181 (8.8)	36/107 (33.6)	7.06 (3.11-17.19)	<0.001	
Late	6/92 (6.5)	14/46 (30.4)	12.54 (3.07-70.85)	0.001	0.189
Early	10/89 (11.2)	22/61 (36.1)	5.40 (1.77-18.31)	0.004	

[*] Adjusted for Age, Cardiopulmonary bypass time, Cross-clamp time, Bentall, ECMO

Mid-term mortality

Groups	Without Malperfusion	With Malperfusion	Adjusted HR (95% CI)[*]	P value	P for interaction
All	26/181 (14.4)	40/107 (37.4)	3.38 (1.97-5.77)	<0.001	
Late	11/92 (12.0)	16/46 (34.8)	4.16 (1.77-9.81)	0.001	0.342
Early	15/89 (16.9)	24/61 (39.3)	4.07 (1.84-8.98)	<0.001	

[*] Adjusted for Age, Cardiopulmonary bypass time, Cross-clamp time, Bentall, ECMO

Conclusions

- In this series of patients with acute type A dissection, preoperative malperfusion, rather than symptom-to-surgery time determines operative and mid-term mortality

- In patients presenting with malperfusion syndrome, the symptom-to-surgery time did not significantly affect operative or mid-term mortality

- The results of this study highlight the significant impact of malperfusion on mortality risk and call for continued efforts to improve survival in patients with ATAAD complicated by malperfusion