

SUPPLEMENTAL MATERIAL

Table S1. Details of endovascular interventions in 135* patients with suspected malperfusion syndrome

Level of aortic fenestration/stenting	Aortic fenestration (n=93)	Aortic stenting (n=90)	Branch vessel fenestration (n=1)	Branch vessel stenting (n=95)
Head vessels**	-	-	0	2
Descending thoracic	0	1	-	-
Supraceliac	21	23	-	-
Celiac	16	0	0	4
Supramesenteric	38	52	-	-
Mesenteric	11	0	0	42
Suprarenal	4	4	-	-
Renal	14	6	0	30
Infrarenal	40	62	-	-
Iliac	-	-	1	57

* Only 112/135 patients underwent fenestration and/or stenting in interventional radiology (IR); 23 patients had non-therapeutic IR.

** We performed innominate artery and carotid artery stenting in two patients, of whom, one had concurrent right upper extremity MPS and the other one had renal MPS. MPS = malperfusion syndrome.

Table S2. Pre-existing comorbidities and admission data (all patients)

	Both decades (n = 597)	1 st decade (n = 243)	2 nd decade (n = 354)	p value (1 st vs. 2 nd decade)
<u>Demographics and chronic comorbidities</u>				
Age on admission (years)	59 (49-68)	59 (47.5-69)	59.5 (51-68)	0.69
Female gender	181 (30)	67 (28)	114 (32)	0.26
Body mass index (kg/m ²)	28.1 (24.9-32.0)	28.2 (24.7-31.2)	28.0 (25.0-32.1)	0.76
Body surface area (m ²)	2.04 (1.88-2.20)	2.06 (1.89-2.20)	2.04 (1.87-2.19)	0.46
NYHA class				
I or II	418 (77)	106 (52)	312 (92)	< 0.001
III or IV	122 (23)	96 (48)	26 (7.7)	
CAD	104 (18)	51 (22)	53 (16)	0.08
History of MI	34 (5.7)	16 (6.7)	18 (5.1)	0.53
Previous cardiac surgery	64 (11)	35 (14)	29 (8.2)	0.02
Hypertension	426 (72)	173 (72)	253 (71)	1
COPD	54 (9.1)	21 (8.7)	33 (9.3)	0.90
Smoking status				

Never smoker	267 (45)	101 (42)	166 (47)	0.01
Former smoker	153 (26)	77 (32)	76 (22)	
Current smoker	170 (29)	60 (25)	110 (31)	
History of CVA	16 (2.7)	5 (2.1)	11 (3.1)	0.60
Diabetes	36 (6.2)	10 (4.3)	26 (7.4)	0.18
Chronic kidney disease	28 (4.7)	14 (5.8)	14 (4.0)	0.39
End-stage renal disease on chronic dialysis	13 (2.2)	8 (3.3)	5 (1.4)	0.20
PVOD	70 (12)	24 (9.9)	46 (13)	0.30
Connective tissue disorder	32 (5.4)	16 (6.6)	16 (4.5)	0.36
<u>Clinical condition on admission</u>				
Cardiogenic shock	51 (8.8)	13 (5.7)	38 (11)	0.053
Acute MI	19 (3.2)	5 (2.1)	14 (4.0)	0.29
Tamponade	48 (8.1)	12 (5.0)	36 (10)	0.03
Pre-operative CPR	16 (2.7)	11 (4.5)	5 (1.4)	0.04
Aortic insufficiency				
None	158 (28)	73 (31)	85 (26)	< 0.001

Trace/trivial	64 (11)	22 (9.4)	42 (13)	
Mild	108 (19)	28 (12)	80 (25)	
Moderate	95 (17)	37 (16)	58 (18)	
Severe	134 (24)	74 (32)	60 (18)	
Acute stroke	34 (5.7)	9 (3.7)	25 (7.1)	0.12
Acute paralysis	15 (2.5)	7 (2.9)	8 (2.3)	0.83
Serum creatinine on admission (mg/dL) *	1.0 (0.8-1.4)	1.1 (0.9-1.4)	1.0 (0.8-1.3)	0.04
GFR on admission (mL/min/1.73 m ²)	87 (64-117)	89 (62-120)	86 (65-115)	0.81
Pre-operative AKI	125 (21)	62 (26)	63 (18)	0.03
Pre-operative AKI requiring new dialysis	5 (0.8)	2 (0.8)	3 (0.8)	1

Data expressed as number (percentage) or median (interquartile range).

AKI = acute kidney injury; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CPR = cardiopulmonary resuscitation; CVA = cerebrovascular accident; GFR = glomerular filtration rate as estimated using the Cockcroft-Gault formula; MI = myocardial infarction; NYHA = New York Heart Association; PVOD = peripheral vascular occlusive disease.

* 1 mg/dL = 88.42 μ mol/L

Table S3. Intra-operative variables (only patients who underwent open repair)

	Both decades (n = 545)	1 st decade (n = 213)	2 nd decade (n = 332)	p value (1 st vs. 2 nd decade)
Previous cardiac surgery (reoperation)	54 (9.9)	29 (14)	25 (7.5)	0.03
Aortic root procedure				0.34
None	55 (10)	26 (12)	29 (8.7)	
Aortic root replacement	185 (34)	77 (36)	108 (33)	
Aortic root repair	295 (54)	107 (50)	188 (57)	
Aortic valve replacement only	10 (1.8)	3 (1.4)	7 (2.1)	
Arch procedure (branch vessel reimplantation)				0.03
None	37 (6.8)	15 (7.0)	22 (6.6)	
Transverse arch (0 branch vessels)	318 (58)	116 (54)	202 (61)	
Zone 1 arch (1-2 branch vessels)	40 (7.3)	11 (5.2)	29 (8.7)	
Zone 2 arch (2-3 branch vessels)	109 (20)	47 (22)	62 (19)	
Zone 3 arch (3-4 branch vessels)	41 (7.5)	24 (11)	17 (5.1)	

Frozen elephant trunk	33 (6.1)	6 (2.8)	27 (8.1)	0.02
CPB time (minutes)	222 (181-272)	226 (180-275)	219 (181-271)	0.86
Cross clamp time (minutes)	156 (115-201)	170 (125-213)	142 (111-192)	0.002
HCA used	515 (94)	199 (93)	316 (95)	0.49
HCA time (minutes)	35 (28-45)	42 (33-51)	31 (25-39)	< 0.001
Type of cerebral perfusion				
ACP only	169 (32)	11 (5.5)	158 (48)	< 0.001
RCP only	191 (36)	84 (42)	107 (32)	
Both ACP and RCP	139 (26)	89 (45)	50 (15)	
Neither	31 (5.8)	15 (7.5)	16 (4.8)	
Concomitant procedures				
CABG	32 (5.9)	16 (7.5)	16 (5.1)	0.26
Mitral valve procedure	3 (0.6)	1 (0.5)	2 (0.6)	1
Tricuspid valve procedure	7 (1.3)	2 (0.9)	5 (1.5)	0.71
Intra-operative PRBC transfusion	414 (80)	178 (95)	236 (72)	< 0.001
PRBC units transfused	4 (1-8)	6 (4-10)	3 (0-6)	< 0.001

Data expressed as number (percentage) or median (interquartile range).

ACP = antegrade cerebral perfusion; CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; HCA = hypothermic circulatory arrest; PRBC = packed red blood cells; RCP = retrograde cerebral perfusion.

Table S4. Post-operative outcomes (only patients who underwent open repair)

	Both decades (n = 545)	1 st decade (n = 213)	2 nd decade (n = 332)	p value (1 st vs. 2 nd decade)
Reoperation for bleeding	48 (8.8)	24 (11)	24 (7.3)	0.15
Post-operative tamponade	11 (2.0)	4 (1.9)	7 (2.1)	1
Myocardial infarction	6 (1.1)	3 (1.4)	3 (0.9)	0.68
Atrial fibrillation	193 (35)	74 (35)	119 (36)	0.84
DSWI	13 (2.4)	11 (5.2)	2 (0.6)	0.002
New-onset CVA	38 (7.0)	10 (4.7)	28 (8.4)	0.13
New-onset paraplegia	4 (0.7)	1 (0.5)	3 (0.9)	1
Prolonged ventilation	84 (15)	76 (36)	8 (2.4)	< 0.001
Pneumonia	97 (18)	43 (20)	54 (16)	0.30
Reintubation	36 (6.6)	14 (6.6)	22 (6.6)	1
Tracheostomy	19 (3.5)	13 (6.1)	6 (1.8)	0.02
Post-operative renal failure	94 (17)	42 (20)	52 (16)	0.28
Requiring dialysis	52 (9.6)	23 (11)	29 (8.8)	0.52
Post-operative LOS (days)	10 (7-17)	12 (7-20)	10 (7-15)	0.02

Intraoperative death	7 (1.3)	6 (2.8)	1 (0.3)	0.02
In-hospital mortality	44 (8.1)	21 (9.9)	23 (6.9)	0.29
30-day mortality (after open repair)	35 (6.4)	17 (8.0)	18 (5.4)	0.31
Operative mortality*	47 (8.6)	22 (10)	25 (7.5)	0.33

Data expressed as number (percentage) or median (interquartile range).

CVA = cerebrovascular accident; DSWI = deep sternal wound infection; LOS = length of stay.

* Operative mortality was defined as in-hospital mortality or mortality within 30 days after open repair.

Table S5. Detailed cause of death in patients with organ failure after endovascular procedures by interventional radiology (IR), but before open repair or discharge

Case	Year of Treatment	Type of Malperfusion	Cause of Death
		<i>First Decade</i>	
1	1996	Cerebral, Spinal, Renal, Lower Extremity	Brain death
2	1997	Celiac/hepatic, Renal	Unarousable; withdrawal of care
3	1997	Renal	Respiratory failure; withdrawal of care
4	2000	Mesenteric, Renal, Lower Extremity	Renal failure, lower extremity necrosis
5	2002	Mesenteric, Renal, Lower Extremity	Extensive necrotic bowel
6	2003	Cerebral, Mesenteric, Renal, Lower Extremity	Fixed and dilated pupil, renal failure, respiratory failure, shock
7	2003	Mesenteric, Celiac/hepatic, Renal, Lower Extremity	Necrotic lower extremity, shock, acidosis, renal failure, respiratory failure, hepatic failure

8	2003	Celiac/hepatic, Renal, Lower Extremity	Global cerebral ischemia, brain death
9	2004	Cerebral, Lower Extremity	Diffuse cerebral edema, brain herniation, brain death
10	2005	Spinal, Mesenteric, Renal, Lower Extremity	Shock; withdrawal of care
11	2005	Lower Extremity	Respiratory failure, withdrawal of care
12	2006	Mesenteric	Inoperable necrotic bowel
13	2006	Cerebral, Mesenteric	Stroke, arrhythmia
14	2006	Mesenteric, Lower Extremity	Extensive bowel necrosis, severe acidosis and hyperkalemia
15	2007	Mesenteric, Celiac/hepatic, Renal	Renal failure, respiratory failure, pneumonia, withdrawal of care
16	2007	Cerebral, Mesenteric, Celiac/hepatic, Renal, Lower Extremity	Large cerebral infarction, cerebral edema, brain herniation, withdrawal of care
		<u>Second decade</u>	
17	2008	Cerebral, Spinal, Mesenteric, Renal, Lower Extremity	Large stroke, withdrawal of care

18	2008	Cerebral, Mesenteric, Renal	Extensive stroke, withdrawal of care
19	2009	Mesenteric, Celiac/hepatic	Renal failure, liver failure, shock
20	2009	Cerebral, Upper Extremity	Large stroke, respiratory failure, withdrawal of care
21	2011	Mesenteric, Renal, Lower Extremity	Respiratory failure, renal failure, sepsis, necrotic bowel, shock
22	2011	Cerebral, Mesenteric, Renal	Severe large stroke, necrotic bowel, renal failure, brain herniation, withdrawal of care
23	2012	Cerebral, Mesenteric, Renal	Liver injury, sepsis, shock, diffuse brain infarction
24	2015	Mesenteric	Shock, acidosis, renal failure
25	2016	Renal, Lower Extremity	Arrhythmia; withdrawal of care
26	2016	Renal, Lower Extremity	Renal failure, extremity ischemia, respiratory failure; withdrawal of care
27	2016	Mesenteric, Renal, Lower Extremity	Respiratory failure, renal failure, liver failure, necrotic bowel
28	2016	Cerebral, Mesenteric, Renal	Necrotic bowel, lower extremity ischemia, arrhythmia

29	2016	Mesenteric, Renal, Lower Extremity	Bilateral lower extremity necrosis, refused amputation
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IR = interventional radiology (endovascular treatment).

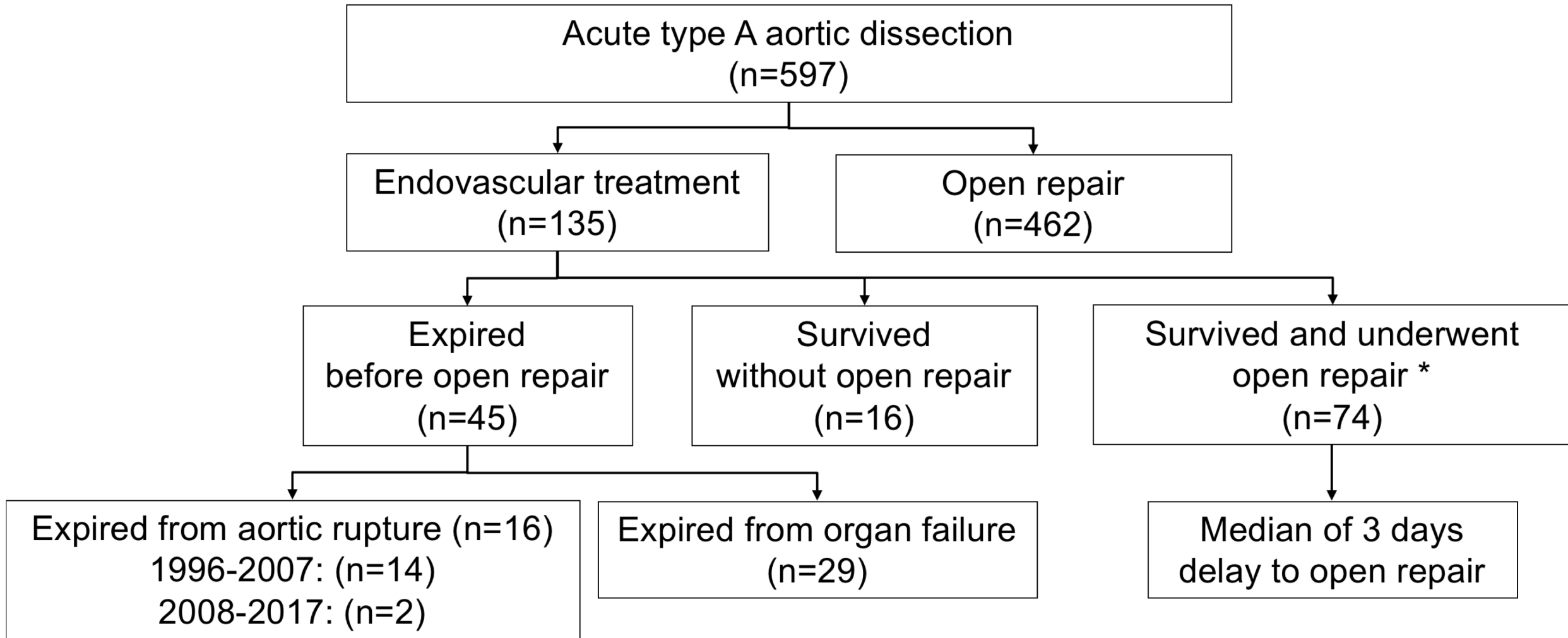
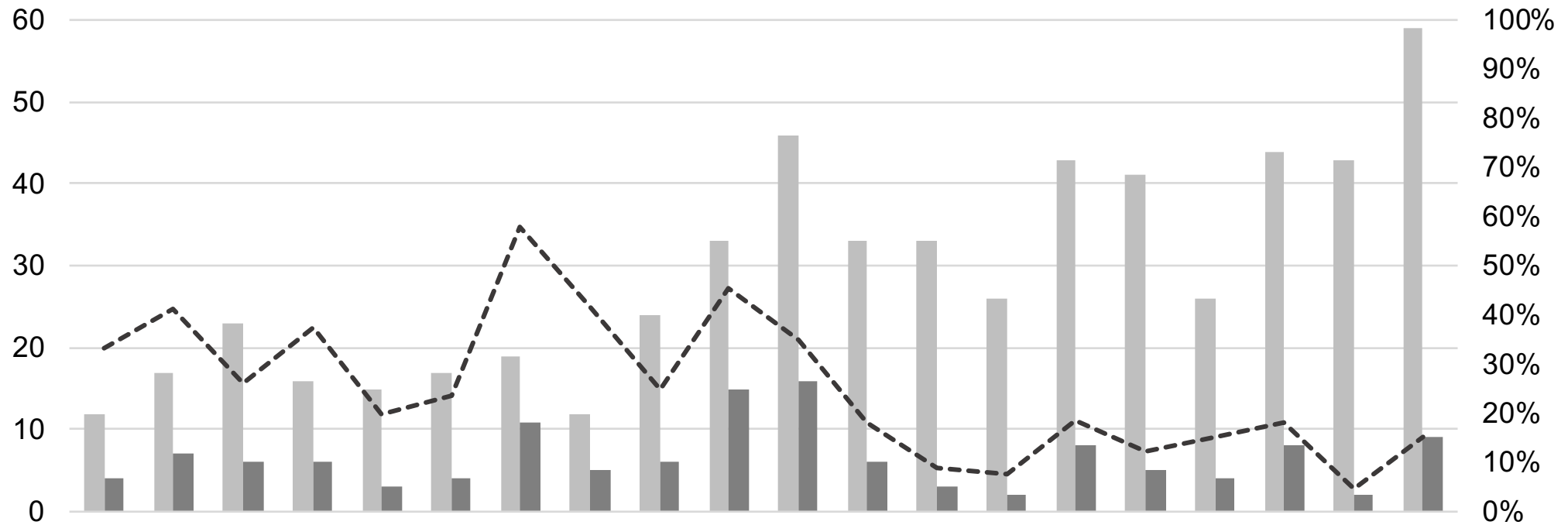


Figure S1. Actual clinical experience. Total 597 patients with acute type A aortic dissection treated at the University of Michigan from 1996-2017.

All patients with ATAAD (n)
 Patients with IR-amenable MPS (upfront IR) (n)
 Patients with IR-amenable MPS (upfront IR) (% of all)



Year
 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
 Non-therapeutic IR/all IR 4/4 2/7 0/6 2/6 0/3 1/4 2/11 3/5 1/6 1/15 1/16 0/6 0/3 1/2 2/8 0/5 1/4 0/8 0/2 0/9

Figure S2. Clinical volume and patient selection over time. *Light gray bars:* number of patients of acute type A aortic dissection (ATAAD) per year. *Dark gray bars:* number of ATAAD patients who underwent upfront IR for visceral and/or extremity malperfusion syndrome (MPS) per year. *Dotted line:* % of MPS patients treated by IR over all ATAAD patients. ATAAD = acute type A aortic dissection; IR = interventional radiology (for endovascular treatment); MPS = malperfusion syndrome.

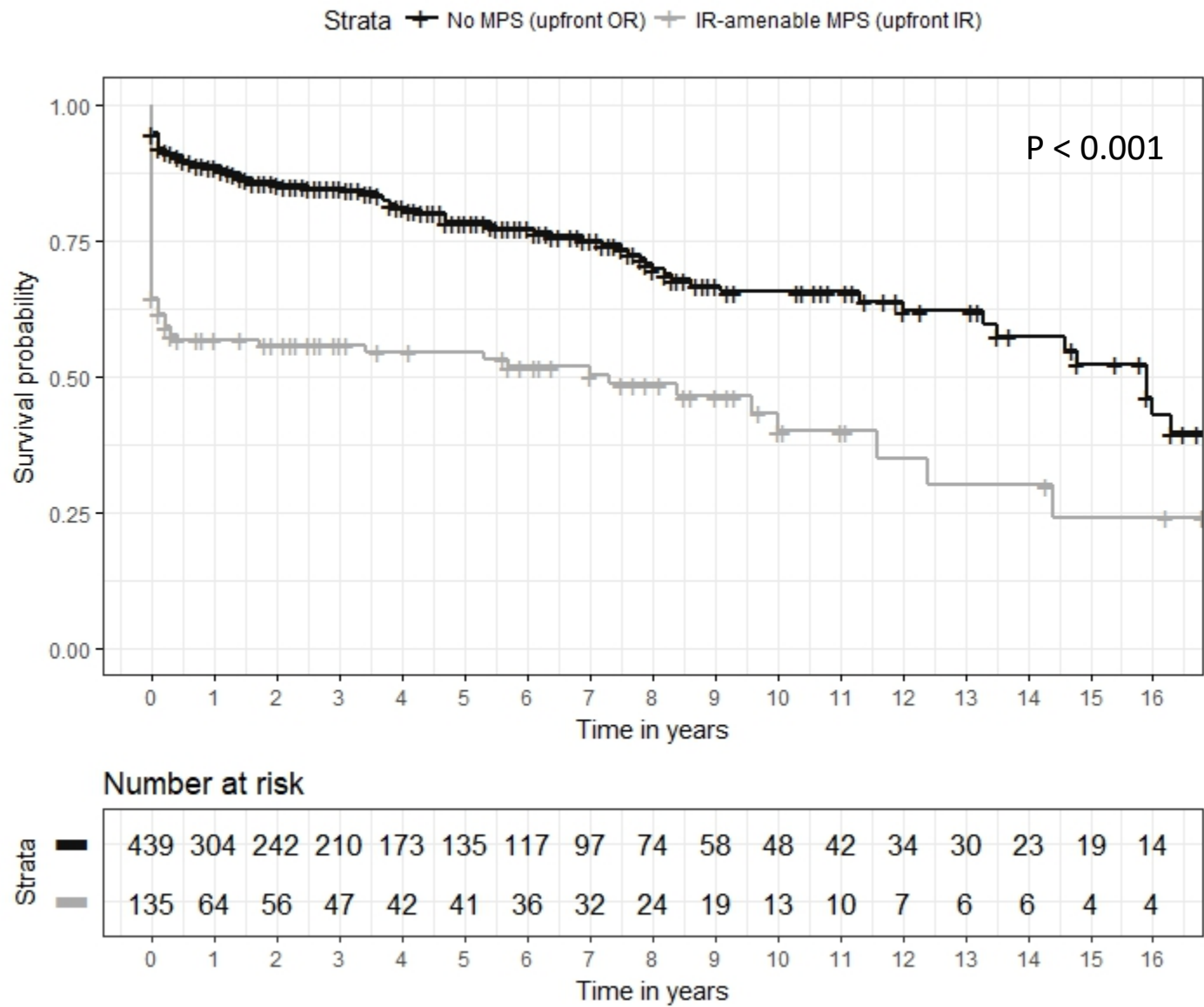


Figure S3. Long-term survival of patients with acute type A aortic dissection with or without malperfusion syndrome (MPS). Overall Kaplan-Meier survival since hospital admission for patients without any MPS who underwent upfront open repair (OR) (*black*) vs. patients who underwent upfront interventional radiology (IR) for IR-amenable (i.e. visceral and/or extremity) MPS (*gray*). Survival curves are truncated at 16 years. MPS = malperfusion syndrome.