Acute Aortic Dissection: Lessons Learned from 9000 Patients

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On Behalf of the IRAD Investigators

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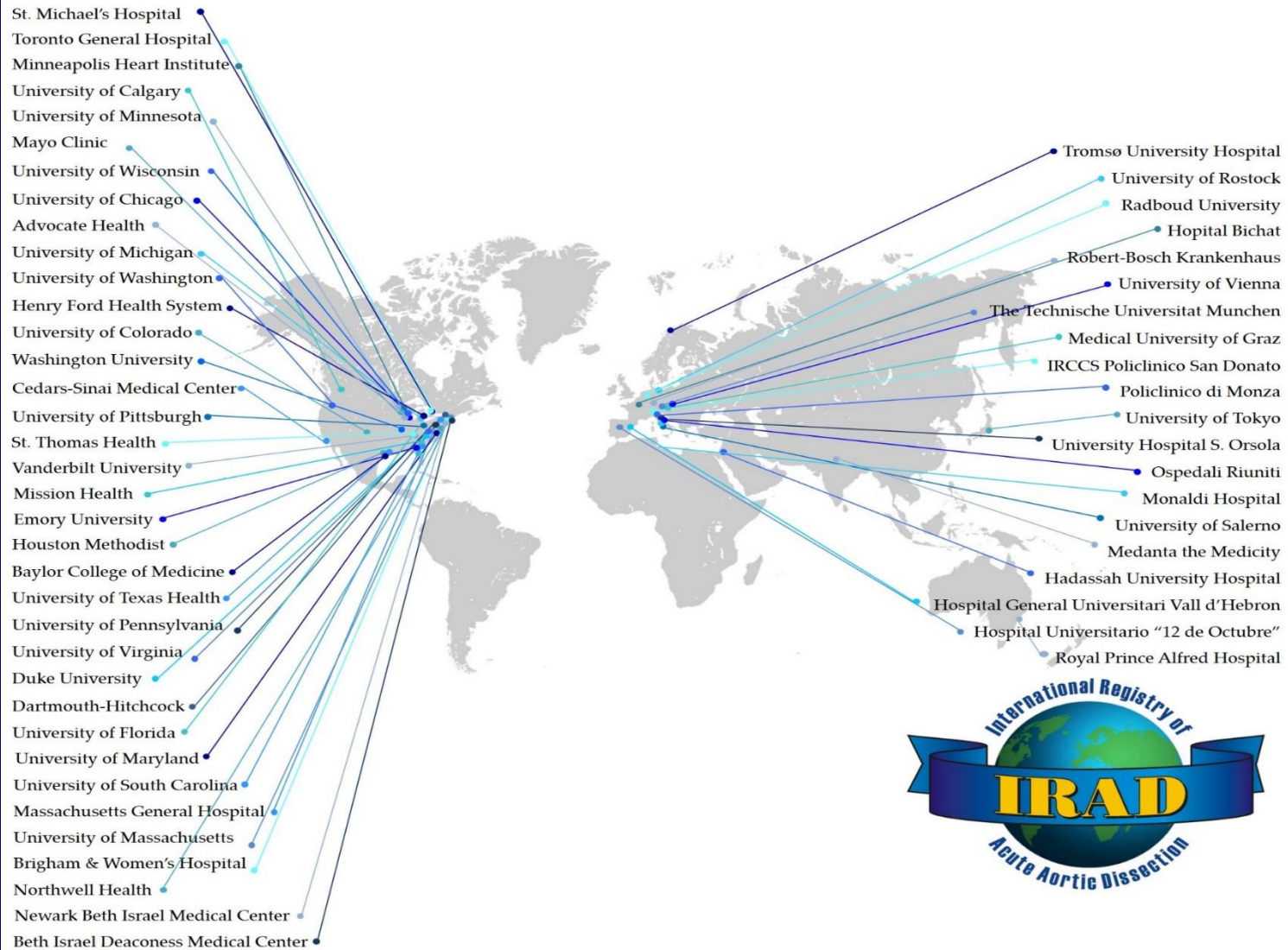 - Terumo
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Background

Over the past 25 years, the approach to diagnosis, treatment, and outcomes of acute aortic dissection has evolved.

- What have we learned?
- Where do we need to go?

Methods: IRAD

Methods

- 9000 patients enrolled from 1996-2019

- 55 active centers in 13 countries

  - 12 participating sites in 1996

- Divided cohort into 3 tertiles of patients comparing:

  - Diagnosis
  - Treatment
  - In-hospital and 5 year mortality

Methods

- Patients are identified both prospectively and retrospectively from medical records, imaging databases, emergency departments, and operating room and procedure logs
  - Every effort is made to enroll consecutive patients
- Ethics board approval is required from all participating sites
  - The consent process is determined locally by each IRB
- Data is submitted to an online database housed at the IRAD coordinating center
- Case report forms are reviewed for consistency, face validity, and completeness

Methods: Statistical

- Continuous variables: Analysis of Variance or Kruskal-Wallis for variables with skewed distributions.
  - Linear contrasts and Jonckheere-Terpstra respectively were used to determine trends across time groups
- Categorical variables: Chi-Square analysis
  - The Mantel-Haenszel test was used to determine linear trends across the time periods.
- 5-year survival: Kaplan-Meier analysis with log-rank Chi-Square test
- Missing numbers were not defaulted to zero; percentages reflect cases with information available for each variable.

Results: Demographics, History

	Tertile 1 Dec. 1995- Aug. 2007	Tertile 2 Aug. 2007- Aug. 2013	Tertile 3 Aug. 2013- Nov. 2018	p-value	Trend p-value
N	3037 (33.3%)	3036 (33.3%)	3037 (33.3%)	-	-
Age (mean±SD)	61.9±14.5	62.0±14.2	62.0±14.6	0.948	0.754
Gender – male	2056 (67.7%)	1974 (65.0%)	1957 (64.4%)	0.017	0.007
Type A aortic dissection	1966 (64.7%)	2032 (66.9%)	1988 (65.5%)	0.185	0.552
Type B aortic dissection	1071 (35.3%)	1004 (33.1%)	1049 (34.5%)	0.185	0.552
Hypertension	2209 (76.8%)	2261 (80.3%)	2273 (81.5%)	<0.001	<0.001
Atherosclerosis	762 (27.8%)	546 (21.3%)	390 (16.5%)	<0.001	<0.001
Bicuspid aortic valve	83 (3.7%)	76 (3.0%)	66 (2.8%)	0.196	0.082
Marfan Syndrome	128 (4.7%)	89 (3.5%)	81 (3.5%)	0.038	0.027
Cocaine abuse	40 (1.5%)	79 (3.2%)	69 (2.9%)	<0.001	<0.001
Peripartum state	8 (0.9%)	10 (1.1%)	7 (0.8%)	0.757	0.907
Family history aortic disease	60 (11.0%)	235 (10.9%)	203 (9.1%)	0.118	0.063
Current smoker	205 (31.4%)	773 (35.6%)	784 (32.1%)	0.022	0.389

Results: 1st Diagnostic Imaging

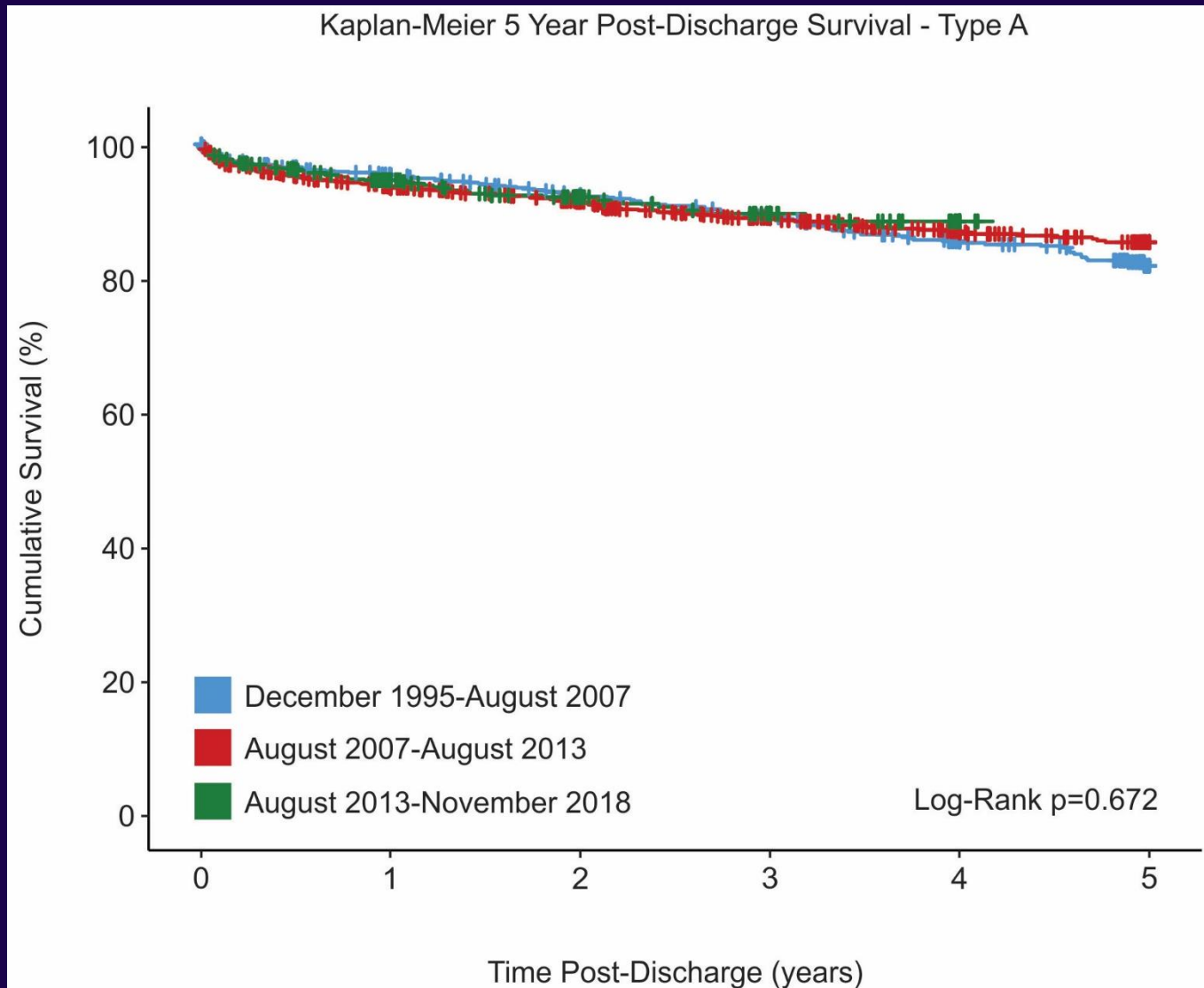|	Tertile 1 Dec. 1995-Aug. 2007	Tertile 2 Aug. 2007-Aug. 2013	Tertile 3 Aug. 2013-Nov. 2018	p-value	Trend p-value
MRI	38 (1.4%)	25 (1.0%)	20 (0.9%)	0.160	0.062
TEE	794 (29.6%)	406 (16.7%)	184 (8.0%)	<0.001	<0.001
CT Scan	1785 (66.5%)	1956 (80.4%)	2095 (90.6%)	<0.001	<0.001

Results: Type A Management

	Tertile 1 Dec. 1995- Aug. 2007	Tertile 2 Aug. 2007- Aug. 2013	Tertile 3 Aug. 2013- Nov. 2018	p-value	Trend p-value
N	1966	2032	1988	-	-
Surgical management	1670 (85.0%)	1802 (88.7%)	1762 (88.6%)	<0.001	0.001
Surgery within 24 hours	1033 (73.9%)	1005 (78.6%)	897 (76.4%)	0.017	0.114
Surgery with arch tear	65 (73.9%)	67 (88.2%)	52 (83.9%)	0.054	0.084
Surgery with proximal arch extent	63 (26.1%)	35 (21.0%)	31 (21.4%)	0.387	0.238
Pre-operative coma/stroke	122 (7.4%)	100 (5.8%)	65 (3.9%)	<0.001	<0.001
Surgical management	85 (69.7%)	72 (72.0%)	48 (73.8%)	0.824	0.764
Surgical in-hospital mortality	28 (32.9%)	25 (34.7%)	17 (35.4%)	0.951	0.760
Overall in-hospital mortality	60 (49.2%)	45 (45.0%)	31 (47.7%)	0.824	0.764

Results: Type A Outcomes

	Tertile 1 Dec. 1995- Aug. 2007	Tertile 2 Aug. 2007- Aug. 2013	Tertile 3 Aug. 2013- Nov. 2018	p-value	Trend p-value
In-hospital mortality					
Overall mortality	516 (26.2%)	353 (17.4%)	325 (16.3%)	<0.001	<0.001
Surgical management	352 (21.1%)	267 (14.8%)	229 (13.0%)	<0.001	<0.001
Medical management	143 (57.4%)	68 (46.3%)	73 (50.7%)	0.086	0.126
5 year post-discharge survival (Kaplan-Meier estimates)					
Overall 5 year survival	81.9%	85.4%	88.5%	0.672	-
Surgical management	84.7%	86.6%	90.2%	0.772	-
Medical management	49.6%	53.5%	55.1%	0.460	-

Results: Type A 5 Year Outcomes

Kaplan-Meier 5 Year Post-Discharge Survival - Type A

Results: Type A 5 Year Mortality Model

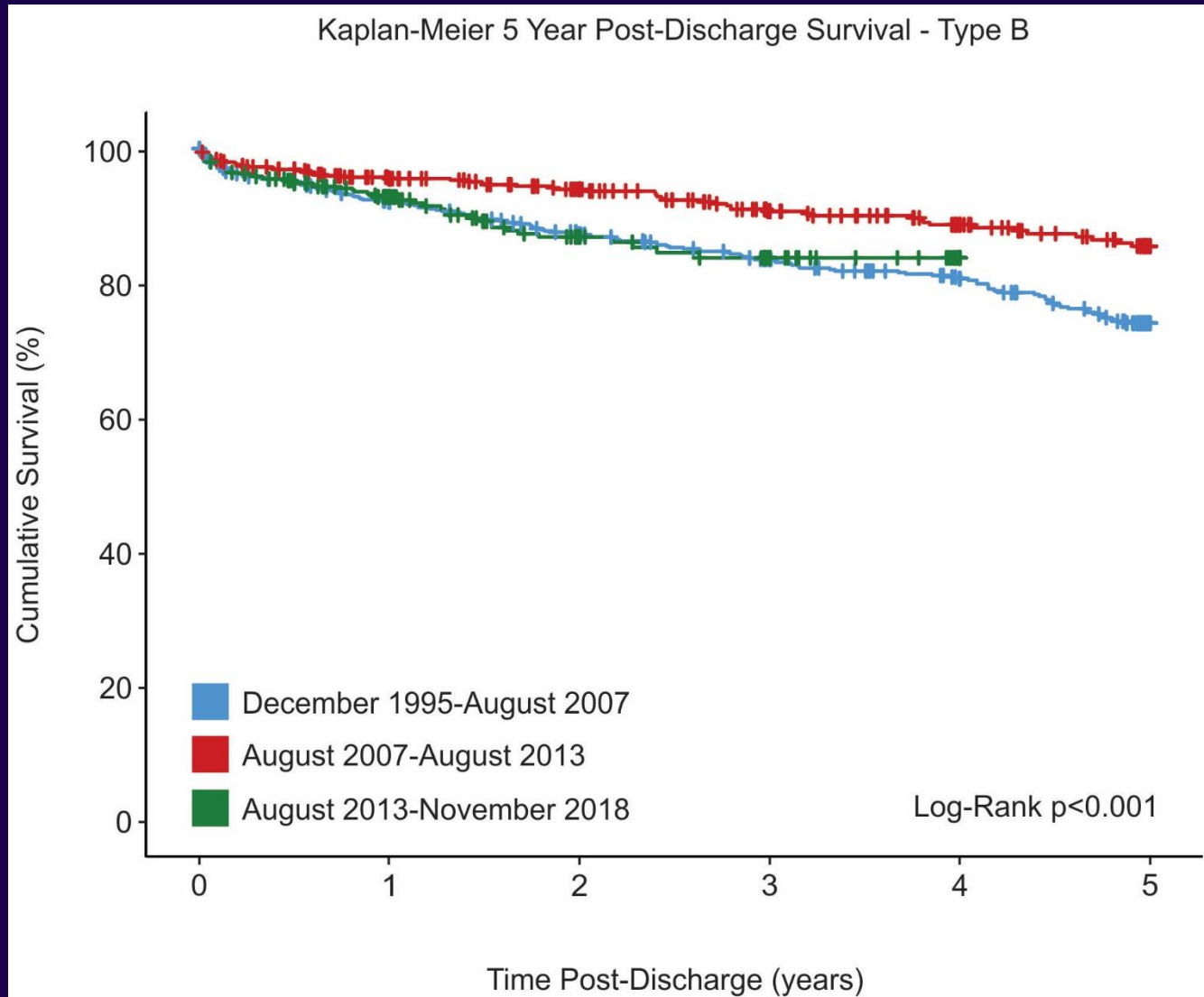|	Hazard Ratio	p-value	95% Confidence Interval	
			Lower	Upper
Tertile 2 Aug. 2007-Aug. 2013	0.878	0.403	0.648	1.191
Tertile 3 Aug. 2013-Nov. 2018	0.760	0.179	0.508	1.135
Age ≥70	2.945	<0.001	2.229	3.891
Post-procedure coma	2.437	0.052	0.991	5.989
Post-procedure stroke	3.242	<0.001	2.222	4.730
Post-procedure cardiac tamponade	1.718	0.026	1.068	2.764

Results: Type B Management

	Tertile 1 Dec. 1995- Aug. 2007	Tertile 2 Aug. 2007- Aug. 2013	Tertile 3 Aug. 2013- Nov. 2018	p-value	Trend p-value
N	1071	1004	1049	-	-
Medical management	694 (64.8%)	547 (54.5%)	637 (60.7%)	<0.001	<0.001
Endovascular management	209 (19.5%)	348 (34.7%)	327 (31.2%)	<0.001	<0.001
Surgical management	161 (15.0%)	64 (6.4%)	64 (6.1%)	<0.001	<0.001

Results: Type B Outcomes

	Tertile 1 Dec. 1995- Aug. 2007	Tertile 2 Aug. 2007- Aug. 2013	Tertile 3 Aug. 2013- Nov. 2018	p-value	Trend p-value
In-hospital mortality					
Overall mortality	109 (10.2%)	92 (9.2%)	78 (7.4%)	0.082	0.027
Medical management	56 (8.1%)	41 (7.5%)	37 (5.8%)	0.258	0.112
Surgical management	30 (18.6%)	8 (12.5%)	6 (9.4%)	0.173	0.064
Endovascular management	22 (10.5%)	37 (10.6%)	29 (8.9%)	0.710	0.487
5 year post-discharge survival (Kaplan-Meier estimates)					
Overall 5 year survival	74.0%	85.5%	83.7%	<0.001	-
Medical management	71.8%	84.9%	82.7%	0.001	-
Surgical management	67.2%	78.5%	88.9%	0.698	-
Endovascular management	84.0%	87.9%	84.3%	0.161	-

Results: Type B 5 Year Outcomes

Kaplan-Meier 5 Year Post-Discharge Survival - Type B

December 1995-August 2007
August 2007-August 2013
August 2013-November 2018

Log-Rank p<0.001

Results: Type B 5 Year Mortality Model

	Hazard Ratio	p-value	95% Confidence Interval	
			Lower	Upper
Tertile 2 Aug. 2007-Aug. 2013	0.705	0.143	0.441	1.126
Tertile 3 Aug. 2013-Nov. 2018	1.112	0.681	0.669	1.849
Age ≥70	3.240	<0.001	2.226	4.718
Pre- or post-procedure spinal cord ischemia	3.502	0.008	1.380	8.882
Pre- or post-procedure renal failure	1.683	0.023	1.074	2.637
History of chronic obstructive pulmonary disease	1.932	0.002	1.265	2.949

Results: Diagnosis, Aortic Size

	Tertile 1 Dec. 1995- Aug. 2007	Tertile 2 Aug. 2007- Aug. 2013	Tertile 3 Aug. 2013- Nov. 2018	p-value	Trend p-value
Time from admission to diagnosis, hours (median, Q1-Q3)	2.8 (1.2-6.8)	2.7 (1.4-5.5)	2.7 (1.4-5.2)	0.733	0.493
Type A	2.5 (1.1-6.5)	2.6 (1.3-5.5)	2.7 (1.4-5.4)	0.503	0.233
Type B	3.3 (1.5-7.2)	3.0 (1.5-5.2)	2.5 (1.5-4.6)	0.006	0.002
Time from admission to surgery, hours (median, Q1-Q3)					
Type A	7.0 (4.0-20.0)	7.0 (4.0-15.0)	6.0 (4.0-15.0)	0.925	0.694
Type A: Diameter ≤ 5 cm	573 (51.9%)	518 (59.2%)	151 (59.2%)	0.002	0.002
Type B: Diameter ≤ 6 cm	594 (89.5%)	376 (91.0%)	51 (86.4%)	0.470	0.901

Conclusions

- Hypertension, smoking, and atherosclerosis are the most common risk factors for aortic dissection.

- CT imaging is by far the dominant initial imaging test.

- Surgical management has increased for Type A dissection to nearly 90%.

- For Type A dissection overall in-hospital mortality (16.3%) and surgical mortality (13.0%) have fallen. 5-year survival is steady at 85%.

Conclusions

- Endovascular therapy has increased for Type B dissection to above 30%, and open surgery has dropped to 6%.

- Overall in-hospital mortality for Type B dissection is now 7.4% with 5-year survival at 85%.

- Delays in time to diagnosis and time to surgery for Type A dissection remain substantial.

- Most patients dissect at an aortic diameter below current recommendations for prophylactic repair.

Where Do We Need To Go?

- Genetic testing along with development of "aortic" biomarkers offer possible in-roads into identifying "at-risk" patients earlier, before dissection occurs.

- An accurate biomarker platform might allow speedier acute diagnosis and treatment.

- Continued evolution of endovascular therapies for Type A and Type B dissection offers potential for less invasive and potentially more efficacious treatments for patients requiring an intervention.

- Optimal medical therapy and imaging surveillance protocols need to be better defined for long-term survivors.

Reflection

The study of rare disorders requires persistence, large numbers of centers and investigators, steady funding, passionate, investigative teams, and above all, willing patients who by consenting to participate in research give a face and a voice to their struggles which ultimately allow better care for future generations. This talk is dedicated to the first 9000 IRAD enrollees and their families.