SOPHIEN- UND HUFELAND-KLINIKUM gGMBH WEIMAR

10. Kardiologie-Symposium, Herzzentrum Hirslanden Zentralschweiz, 10. November 2016

Das Akute AortenSyndrom

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Einleitung

Das **AAS** ist der moderne Oberbegriff für akute Erkrankungen der Aortenwand und umfasst die Dissektion, intramurale Einblutung, Ulcusbildung und Traumatisierung.

Nach klinischen Erhebungen liegt die Inzidenz bei 3 – 5/100.000 pro Jahr.
Die wahre Inzidenz ist allerdings höher, da Fehldiagnosen, Codierfehler und Todesfälle vor Hospitalisierung nicht berücksichtigt werden.

Häufig entsteht ein AAS, ohne vorangehende ***aneurysmatische*** Degeneration.

Die Pathophysiologie ist komplex – zum Entstehen der Erkrankung tragen unter anderem langjährige Mikrotraumatisierungen der Media-Schicht (z.B. durch inflammatorische Prozesse) und eventuell genetische Dispositionen bei.

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Risikofaktoren für akute Aortensyndrome

lange bestehender Hypertonus: Rauchen, Dyslipoproteinämie, Cocain/Crack
Bindegewebserkrankungen: erbliche Fibrillinopathien wie annuloaortale Ektasie, Marfan-Syndrom oder Ehlers-Danlos-Syndrom (Typ 4)
erbliche Vaskulopathien: Aortenisthmusstenose, bikuspidale Aortenklappe
entzündliche Gefäßerkrankungen: ▪ Riesenzellarteritis ▪ Takayasu-Arteriitis ▪ rheumatische Aortitis ▪ systemischer Lupus erythematodes ▪ Morbus Behçet ▪ Syphilis ▪ mykotische Aortitis ▪ Morbus Ormond (retroperitoneale Fibrose)
Dezelerationstrauma (Autounfall, Sturz aus der Höhe)
Iatrogen: ▪ Instrumente/Kathetereingriffe ▪ Aortenklappen-/Aortenoperation: Clamping, Aortotomie, Graft-Anastomose, Patch-Aortoplasty, Aortenwandfragilität

Rehders TC et al. Kardiologie up2date 2006:75-88

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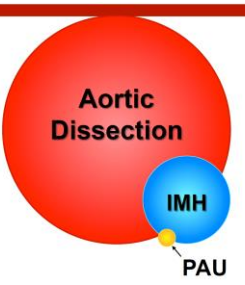
Häufigkeitsverteilung

Klassische Aortendissektion

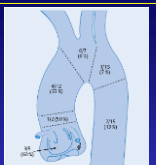
IntraMurales Hämatom

Penetrierendes Atherosklerotisches Ulkus

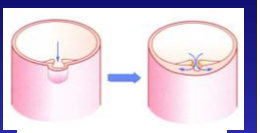


Vorläufer der Aortendissektion

Intramurales Hämatom



InHospital-Mortalität in Abhängigkeit vom betroffenen Aortensegment
Evangelista A et al. Circulation 2005;111:1063-70



Penetrierendes atherosklerotisches Ulkus

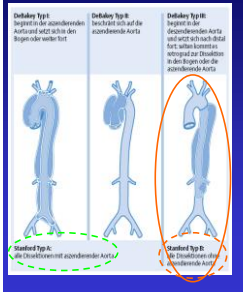
Lokalisation: ubiquitär in thorakaler Aorta
Ausdehnung: sehr variabel (fokal bis langstreckig)
Krankheitsverlauf: alles möglich (Spontankonsolidierung bis Dissektion)
Prädiktoren für Progression*: Ascendens >50mm, Wanddicke >10mm
Therapie: bei proximalez (Typ A-) IMH eher dringliche Aorten-OP bei Typ B-IMH zunächst „wait-and-watch"-Strategie

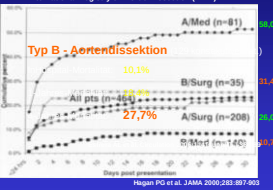
*Song JK et al. Circulation 2009;120:2046-52

: meist thorakale Aorta descendens (Bogen/Ascendens aber möglich)
: ganz umschrieben (nur mm) bis wenige cm
: Neigung zu Pseudoaneurysmen und transmuraler Ruptur
: **Longitudinale Ausdehnung >20mm u./o. Ulcus-Tiefe >10mm**
: bei Pseudoaneurysma / symptomatischem PAU
→ bevorzugt **endovaskuläre Therapie***

*Botta L et al. Ann Thorac Surg 2008;85:987-92

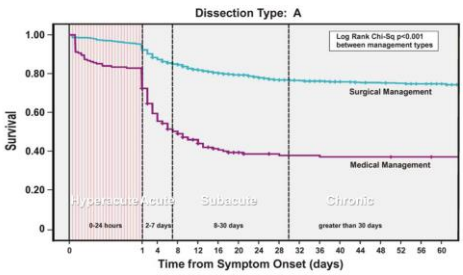
Aortendissektion
Klassifikationen und Mortalität





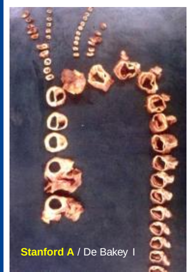
Hagan PG et al. JAMA 2000;283:897-903

Prognose der Typ A -Aortendissektion



Booher AM, et al. Am J Med 2013;26:e19-24.

Akutes Aortensyndrom: Fulminante Komplikationen



- Cerebrale / spinale Ischämie: Insult, Paraplegie
- Kardial: ACS, aMI
  Aorteninsuffizienz, Perikardtamponade
- Aortenruptur
- Viszeralischämie / Nierenversagen
- Extremitäten - Malperfusion

Demographie und Vorgeschichte bei Dissektion

Variable	All	Type A	Type B	p-value
	(n=3037)	(n=1924)	*(n=1113)*	
Age (yrs)	61.9	61.3	63.0	0.003
Male	67.1%	67.2%	67.1%	NS
HTN	75.2%	72.0%	80.7%	<0.001
Marfan	4.3%	4.5%	3.8%	NS
Prior Heart Surgery	**16.9%**	**15.3%**	**19.8%**	**0.002**
Iatrogenic	3.3%	3.8%	2.6%	0.09

IRAD Investigators

Klinische Präsentation bei Aortendissektion

Table 4 Main clinical presentations and complications of patients with acute aortic dissection

	Type A	Type B
Chest pain	80%	70%
Back pain	40%	70%
Abrupt onset of pain	85%	85%
Migrating pain	<15%	20%
Aortic regurgitation	40–75%	N/A
Cardiac tamponade	<20%	N/A
Myocardial ischaemia or infarction	10–15%	10%
Heart failure	<10%	<5%
Pleural effusion	15%	20%
Syncope	15%	<5%
Major neurological deficit (coma/stroke)	<10%	<5%
Spinal cord injury	<1%	NR
Mesenteric ischaemia	<5%	NR
Acute renal failure	<20%	10%
Lower limb ischaemia	<10%	<10%

NR = not reported; NA = not applicable. Percentages are approximated.

ESC Guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J 2014;35:2873-2926

Laborchemie bei Verdacht auf AAS

Table 5 Laboratory tests required for patients with acute aortic dissection

Laboratory tests	To detect signs of:
Red blood cell count	Blood loss, bleeding, anaemia
White blood cell count	Infection, inflammation (SIRS)
C-reactive protein	Inflammatory response
ProCalcitonin	Differential diagnosis between SIRS and sepsis
Creatine kinase	Reperfusion injury, rhabdomyolysis
Troponin I or T	Myocardial ischaemia, myocardial infarction
D-dimer	Aortic dissection, pulmonary embolism, thrombosis
Creatinine	Renal failure (existing or developing)
Aspartate transaminase/ alanine aminotransferase	Liver ischaemia, liver disease
Lactate	Bowel ischaemia, metabolic disorder
Glucose	Diabetes mellitus
Blood gases	Metabolic disorder, oxygenation

SIRS = systemic inflammatory response syndrome.

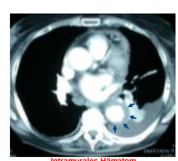
ESC Guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J 2014;35:2873-2926

Bildgebende Diagnostik bei Verdacht auf AAS

Comparison of methods for imaging the aorta

Advantages/disadvantages	TTE	TOE	CT[c]	MRI[c]	AORTOGRAPHY
Ease of use	+++	++	+++	++	+
Diagnostic reliability	+	+++	+++	+++	++
Bedside/interventional use[a]	++	++	–	–	++
Serial examinations	++	+	++(+)[b]	+++	
Aortic wall visualization[c]	+	+++	+++	+++	–
Cost	–	–	– –	– – –	– – –
Radiation	0	0	– – –	–	– –
Nephrotoxicity	0	0	– – –	– –	– – –

CT = computed tomography; MRI = magnetic resonance imaging; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.
+ means a positive aspect and – means a negative point. The number of signs indicates the estimated potential value.
[a]IVUS can be used to guide interventions (see web addenda at www.escardio.org/guidelines).
[b]+++ only for follow-up after aortic stenting (metallic struts), otherwise limit radiation.
[c]PET can be used to visualize suspected aortic inflammatory disease.



Intramurales Hämatom

Table 9 Diagnostic value of different imaging modalities in acute aortic syndromes

Lesion	TTE	TOE	CT	MRI
Ascending aortic dissection	++	+++	+++	+++
Aortic arch dissection	+	+	+++	+++
Descending aortic dissection	+	+++	+++	+++
Size	++	+++	+++	+++
Mural thrombus	+	+++	+++	+++
Intramural haematoma	+	+++	++	+++
Penetrating aortic ulcer	++	++	+++	+++
Involvement of aortic branches	+[a]	(+)	+++	+++

[a]Can be improved when combined by vascular ultrasound (carotid, subclavian, vertebral, celiac, mesenteric and renal arteries).
+++ = excellent; ++ = moderate; + = poor; (+) = poor and inconstant; CT = computed tomography; MRI = magnetic resonance imaging; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

ESC Guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J 2014;35:2873-2926

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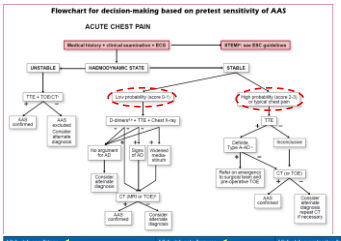
Diagnostisches Vorgehen bei Verdacht auf AAS



ESC Guidelines on the diagnosis and treatment of aortic diseases. Eur Heart J 2014;35:2873-2926

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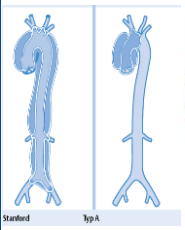
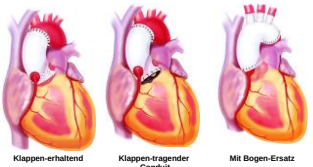
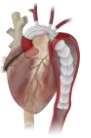
Therapie der Typ A -Aortendissektion





Nach Einleitung von Analgesie und RR-Optimierung
→ umgehende Verlegung in cardiochirurgisches Zentrum


„elephant-trunk"-Technik

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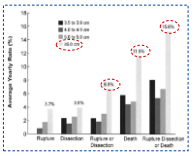
Typ B - Aortendissektion

Kriterien für komplizierte Dissektion:
- Aneurysmatische Expansion mit Aortendiametern > 5.5 cm
- Rascher Diameter-Progress (> 0.5 cm / Jahr)
- Drohende Aortenruptur
- Malperfusion (Mesenterial / Beine)
- Therapie-resistente Schmerzen / RR-Entgleisung



Invasive Therapieoptionen:
- **Offene Aortenchirurgie**
  - Sterblichkeitsrate im Krankenhaus: 3 - 15 %
  - Querschnittslähmung: 2 - 5 % *(ältere Studien 13 – 17 %)*

  Svensson LG et al. Ann Thorac Surg 2008;85:S1-45
- **EndoVaskuläre AortenRekonstruktion (EVAR)**: weniger invasive Therapiealternative

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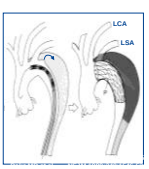
Technisches Prinzip der Thorakalen EndoVaskulären AortenRekonstruktion (TEVAR)



Ziele:
- Proximale Intimaeinrisse (Entries) verschließen
- Thrombosierung im falschen Lumen induzieren
- Obstruktion des ***wahren Lumens*** durch das unter Systemdruck stehende **falsche Lumen** beseitigen
- nach fibrotischem Umbau des Thrombus die dissezierte Aorta im Sinne des „aortic remodelling" zu rekonstruieren

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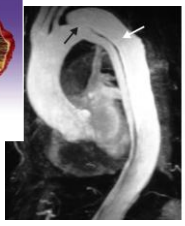
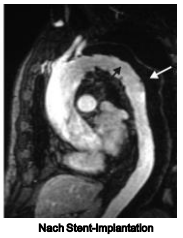
Erfolgreiche TEVAR bei Typ B -Aortendissektion


Freisetzung des Stent-Grafts


Ausgangsbefund


Nach Stent-Implantation

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„Take-home" Messages

Klinisch lassen sich IMH, PAU bzw. Dissektion **nicht** sicher voneinander unterscheiden. Bei klinischem Verdacht ist **immer** eine Schnittbilddiagnostik der **gesamten** Aorta indiziert.

Die **Differentialdiagnose AAS** sollte immer bei Patienten mit ungeklärter Synkope, akuten Brust- oder Rückenschmerzen, akuten Bauchschmerzen, Schlaganfall oder akuter Herzinsuffizienz erwogen werden.

Seitendifferente Pulse oder Zeichen von Malperfusion sind besondere Verdachtsmomente.

Mit den modernen Bildgebungstechniken sind diagnostische Fehler heute weniger ein Problem, sondern eher Verzögerungen bei der Veranlassung einer bildgebenden Diagnostik.

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„Take-home“ Messages II

Die Prognose des AAS wird schlechter, je **proximaler** die Aorta ein entsprechendes pathoanatomisches Substrat aufweist.
Hieraus ergibt sich, dass tendenziell ein **IMH der ascendierenden Aorta** eine ähnlich ungünstige Prognose wie eine **Typ A -Dissektion** hat, während ein ***IMH der deszendierenden Aorta*** eine Prognose wie eine ***Typ B -Dissektion*** aufweist.

Bei allen Patienten, die ein AAS überstanden haben, ist eine **konsequente Nachsorge** notwendig, da insuffiziente Blutdruck-Einstellung und Expansion der Aortendiameter relativ häufig vorkommen und in aller Regel **asymptomatisch** verlaufen.

→ serielle Untersuchungen mit RR-Monitoring und Bildgebungen der Aorta (z.B. MRA)
→ da sonst Gefahr für **weitere aortale Komplikationen !!**

Σ Erhöhung der Sensibilität für Akutes Aorten Syndrom

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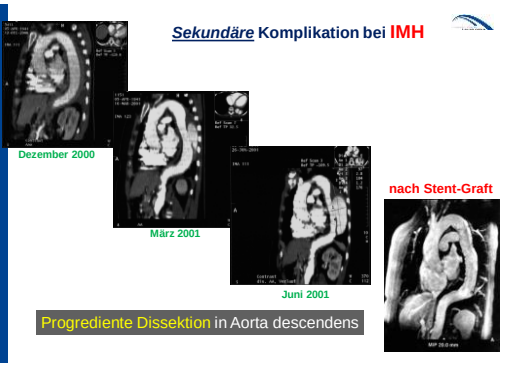
Sekundäre Komplikation bei IMH



Progrediente Dissektion in Aorta descendens

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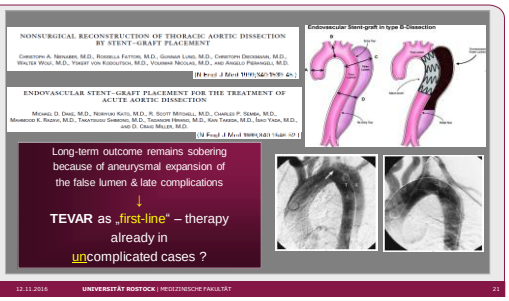
Steps towards **INSTEAD**


NONSURGICAL RECONSTRUCTION OF THORACIC AORTIC DISSECTION BY STENT-GRAFT PLACEMENT

ENDOVASCULAR STENT-GRAFT PLACEMENT FOR THE TREATMENT OF ACUTE AORTIC DISSECTION

Endovascular Stent-graft in type B-Dissection

Long-term outcome remains sobering because of aneurysmal expansion of the false lumen & late complications

↓

TEVAR as „first-line“ – therapy already in uncomplicated cases ?

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INSTEAD: Trial design

INvestigation of STEnt grafts in patients with type B Aortic Dissection: Design of the INSTEAD trial—a prospective, multicenter, European randomized trial

Christoph A. Nienaber, MD,[a] Simona Zannetti, MD,[a] Barbara Barbieri, MD,[b] Stephan Kische, MD,[a] Wolfgang Schareck, MD,[a] and Tim C. Rehders, MD,[a] on behalf of the INSTEAD study collaborators[1]
Rostock, Germany, and Maastricht, The Netherlands

- Background: Persistent false-lumen perfusion = risk factor for adverse outcome
  Complete false-lumen thrombosis is associated with improved outcome
  → Hypothesis: Nonsurgical TEVAR might improve prognosis for pat. with uncomplicated type B-AD
- Patients: Chronic type B-dissection (2 weeks - 1 year)
- Randomization: Optimal Medical Treatment vs. OMT + Stent-Graft (only *Talent*)
- Aim: Evaluation of 1- and 2-year outcome (F-U: Baseline, 3 months, 1 year, 2 years)
- 02/2002: Start → 05/2005: Enrollment completed (140 patients in Germany, France, Italy & Austria)

Nienaber CA et al. Am Heart J 2005;149:592-9

INSTEAD: European Multicenter-Study

- Initially 7 centers
  - Rostock
  - Essen
  - Toulouse
  - Bologna
  - Berlin
  - Hannover
  - Lille
- 5 additional centers for accelerated enrollment
  - Leipzig
  - Bordeaux
  - Wien
  - Ludwigshafen
  - Bari

05/2005: Enrollment completed (136 patients)

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INSTEAD: Patient selection

Further Inclusion Criteria
- Total aortic diameter ≤ 6.0 cm
- Aortic kinking < 75 °
- No contraindication for general anesthesia
- Written informed consent form
- Availability for follow-up visits

Exclusion Criteria
- Complete thrombosis of false lumen
- Need for oral anticoagulation
- Thrombocytopenia (< 50.000/µl)
- Age < 18 a, Pregnancy
- Participation in other trials
- Creatinine > 2,5 mg/dl
- Ongoing infection
- Cancer with life-expectancy < 2 a

Nienaber CA et al. Am Heart J 2005;149:592-9

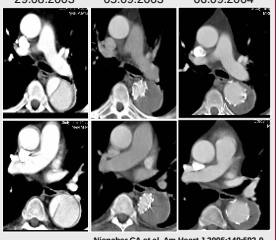
INSTEAD: Endpoints

Primary endpoint

- All-cause mortality at 1- & 2-year follow-up

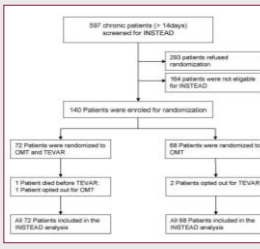
Secondary endpoints

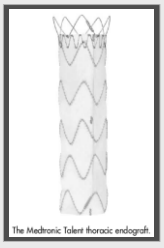
- Cardiovascular morbidity
- Conversion to stent and/or open surgery
- Thrombosis of false lumen
- Degree of aortic expansion
- Quality of life (SF 12-questionnaire)
- Length of ICU and hospital stay



Nienaber CA et al. Am Heart J 2005;149:592-9

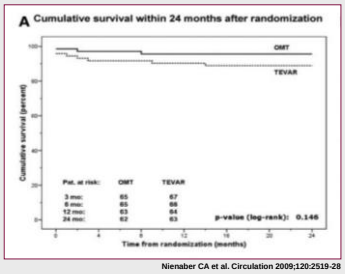
INSTEAD: Trial enrollment





Nienaber CA et al. Circulation 2009;120:2519-28

INSTEAD: Results I



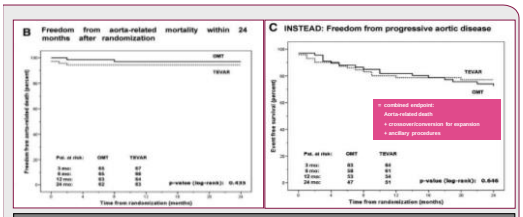
95.6 ± 2.5 %

88.9 ± 3.7 %

The trial turned out to be underpowered

Nienaber CA et al. Circulation 2009;120:2519-28

INSTEAD: Results II



@ I year: crossover rate 14% (p=0.02)
@ 2 years: crossover rate 20% (p=0.02)

Nienaber CA et al. Circulation 2009;120:2519-28

August 2013: INSTEAD-XL

Endovascular Repair of Type B Aortic Dissection
Long-Term Results of the Randomized Investigation of Stent Grafts in Aortic Dissection Trial

Christoph A. Nienaber, MD, PhD; Stephan Kische, MD; Hervé Rousseau, MD, PhD; Holger Eggebrecht, MD; Tim C. Rehders, MD; Guenther Kundt, MD, PhD; Aenne Glass, MA; Dierk Scheinert, MD, PhD; Martin Czerny, MD, PhD; Tilo Kleinfeldt, MD; Burkhart Zipfel, MD; Louis Labrousse, MD; Rossella Fattori, MD, PhD; Hüseyin Ince, MD, PhD; for the INSTEAD-XL trial

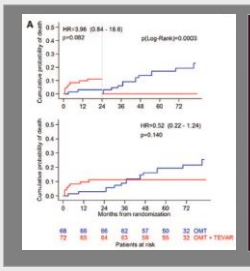
Circ Cardiovasc Interv 2013;6:407-16

The rationale was to compare medical management alone with additional TEVAR for long-term outcomes in uncomplicated type B aortic dissection.

INSTEAD was fully approved by an Institutional Review Committee and Human Rights and Ethics Committee at each participating center, including an amendment for 5 years follow-up (INSTEAD-XL).

The INSTEAD-XL study aimed for annual computed tomography and clinical visits for surveillance, with adjustment of antihypertensive medication if needed; with access to all images and charts, complete clinical follow-up was available in all patients.

INSTEAD-XL: Landmark analysis



Cumulative probability of all-cause death at 5 years with landmark analysis at 2 years breakpoint

>5 years all-cause mortality trended lower in patients randomized to TEVAR than with OMT alone

11.1 ± 3.7% vs. 19.3 ± 4.8%; *P=0.14*

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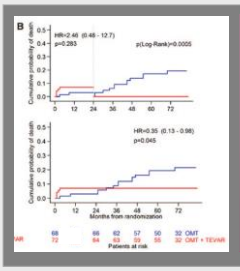
INSTEAD-XL: Landmark analysis



Cumulative aorta-specific mortality
at 5 years
with landmark analysis at 2 years breakpoint

At 5 years the aorta-specific mortality was
6.9 ± 3.0% with TEVAR vs.
19.3 ± 4.8% with OMT alone (*P=0.045*)

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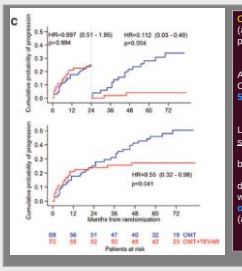
INSTEAD-XL: Landmark analysis



Combined end point of disease progression
(aorta-specific death, crossover/conversion and secondary procedures) and aorta-specific events

At 5 years of follow-up:
Cumulative freedom from this cluster end point was
53.8 ± 6.1% with OMT alone vs. 73.0 ± 5.3% with TEVAR

Landmark analysis (top left) revealed for TEVAR and OMT similar pattern of freedom from progression until 2 years

but

diverging survival estimates after 2 years
with plateauing course after TEVAR vs.
ongoing events with OMT alone
(attributed to crossover/conversion and aorta-specific death)

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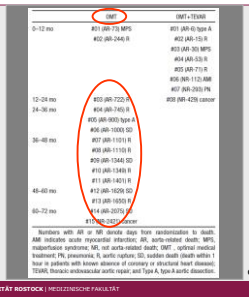
INSTEAD-XL: Causes of death since randomization



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INSTEAD-XL: Aortic morphology at 5 years

	OMT	OMT+TEVAR	*P* Value
FL thrombosis	11/50 (22.0%)	48/53 (90.6%)	<0.0001
Partial FL/no FL thrombosis	39/50 (78.0%)	5/53 (9.4%)	<0.0001
Remodeling of thoracic aorta*	5/50 (10.0%)	42/53 (79.2%)	<0.0001
Critical expansion of thoracic aorta†	33/50 (66.0%)	11/53 (20.8%)	<0.0001

FL indicates false lumen; OMT, optimal medical treatment; and TEVAR, thoracic endovascular aortic repair.
*Based on aortic morphology as assessed vs baseline.
†Occurring within long-term follow-up.

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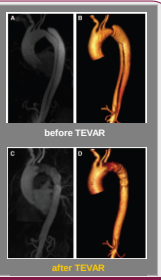

INSTEAD-XL: Conclusions I

- In this study of survivors of uncomplicated type B aortic dissection, TEVAR in addition to optimal medical treatment is associated with improved 5-year aorta-specific survival and delayed disease progression.
- Long-term results of INSTEAD-XL challenge the current consensus on treatment of uncomplicated type B aortic dissection, for example, default medical management with focus on blood pressure and surveillance.
- Although preemptive TEVAR was associated with an excess early mortality (attributable to periprocedural hazards), the procedure turned beneficial at 5 years of follow-up with a NNT of 13. Thus, INSTEAD-XL corroborates recent observational evidence, suggesting long-term beneficial results of TEVAR in subacute and chronic dissection.

INSTEAD-XL: Conclusions II

- With safer procedures attributable to improved operator skills and better technology, TEVAR may emerge as first-line therapy of type B dissection

  → the attempt to heal and remodel dissected aorta may replace the current complication-specific strategy

- Moreover, INSTEAD-XL suggests medical management and surveillance were associated with failure to prevent late complications, such as expansion, rupture, and late crossover/conversion to emergent TEVAR, conveying a higher aorta-specific mortality.

Σ In stable (uncomplicated) type B aortic dissection with suitable anatomy, preemptive TEVAR should be considered to improve late outcome.