胸部外科この１０年の進歩

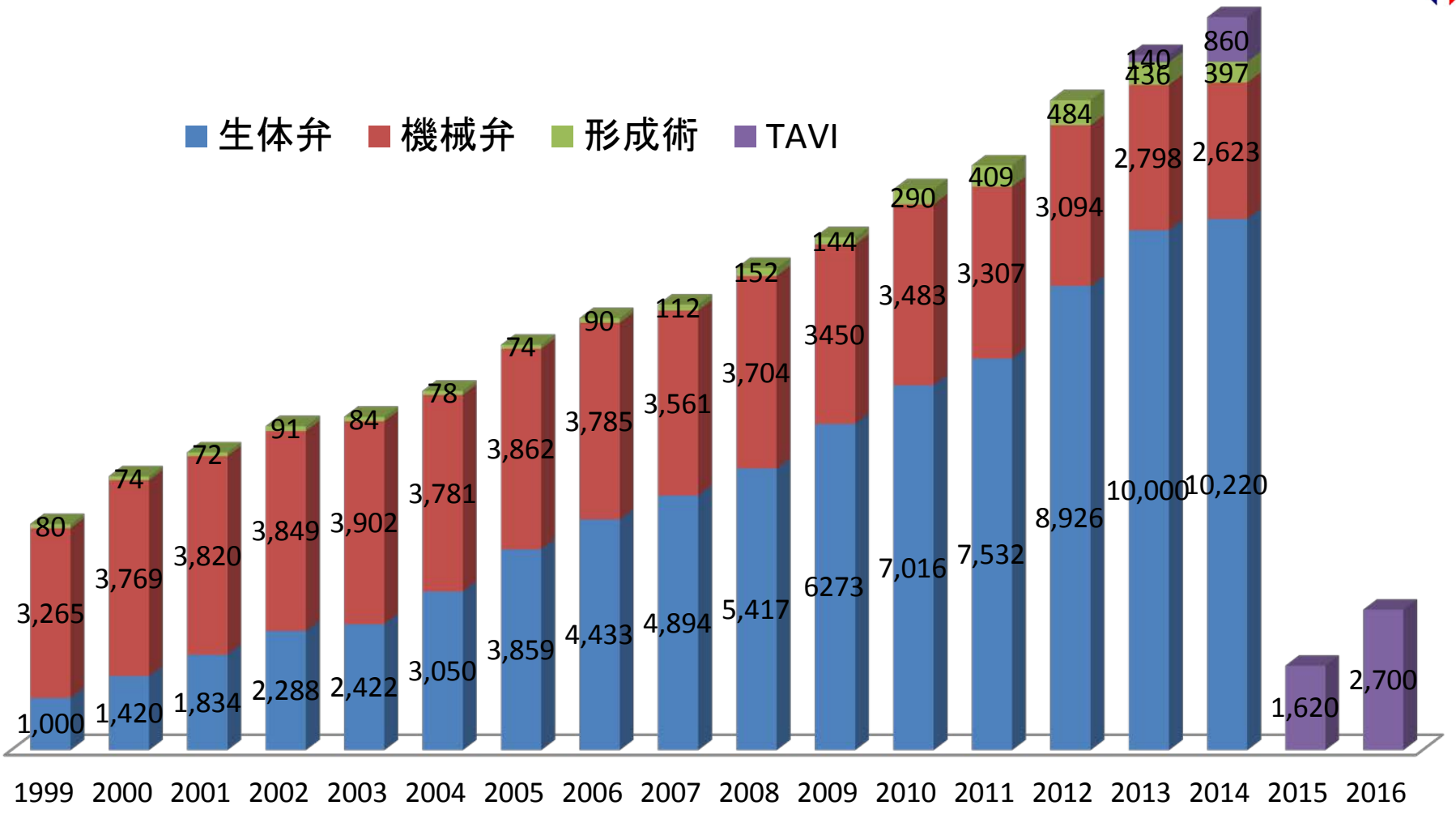
ー大動脈弁疾患ー

心臓病センターー榊原病院

坂口太一

2017.6.22. 第60回関西胸部外科学会教育講演

日本における大動脈弁手術症例の推移



Annual report by the JATS. Gen Thorac Cardiovasc Surg.02 September2016 .

この10年の大動脈弁治療の進歩

- 生体弁の良好な長期成績（>20年）の報告
- 生体弁 vs 機械弁
- 新しい生体弁の登場
  - 外巻き弁
  - Stentless valve
  - Sutureless valve
- 低侵襲治療
  - TAVR
  - MICS
- 大動脈弁形成
  - Remodeling or Reimplantation
  - 尾崎法

第二世代（国内販売開始年）

CEP Magna (2008)

Epic (2011)

Trifecta/GT (2012/2016)

Crown PRT (2015)

第三世代

Mosaic Ultra (2007)

Magna Ease (2011)

Carpentier-Edwards Pericardial Valve in the Aortic Position: 25-Years Experience

Jessica Forcillo, MD, MS, Michel Pellerin, MD, Louis P. Perrault, MD, PhD, Raymond Cartier, MD, Denis Bouchard, MD, MS, Philippe Demers, MD, MS, and Michel Carrier, MD, MBA

(Ann Thorac Surg 2013;96:486–93)

Freedom from reoperation for SVD

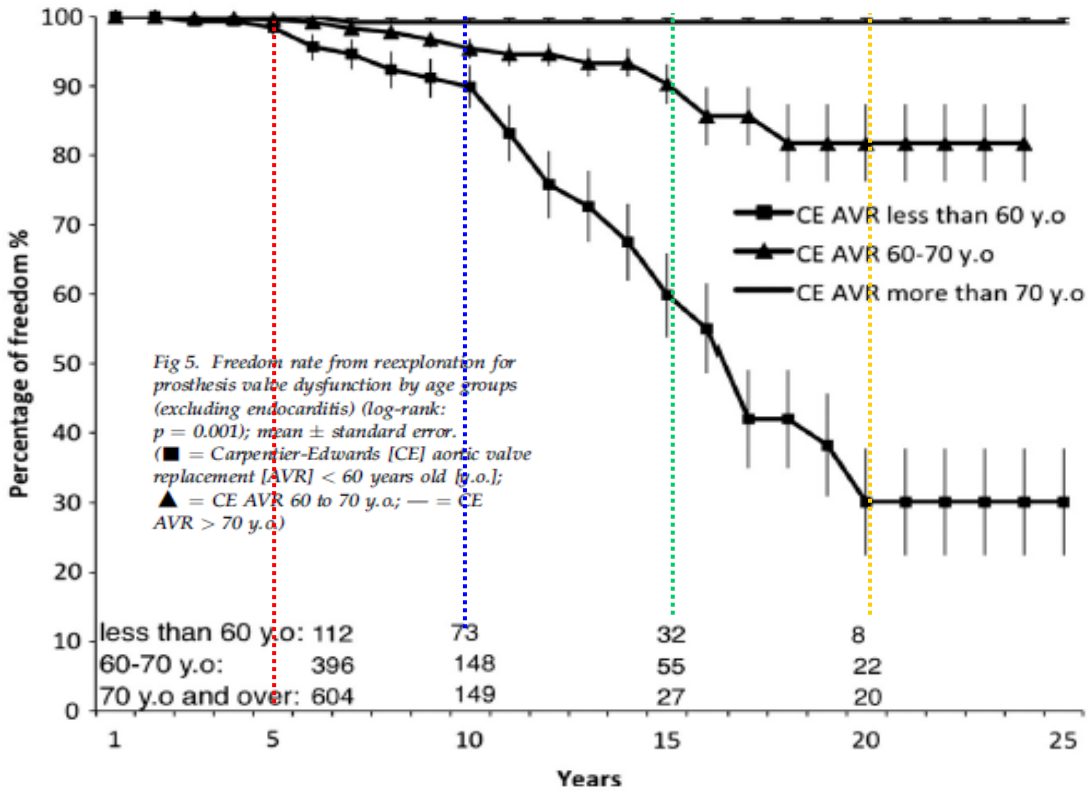


Fig 5. Freedom rate from reexploration for prosthesis valve dysfunction by age groups (excluding endocarditis) (log-rank: p = 0.001); mean ± standard error. (■ = Carpentier-Edwards [CE] aortic valve replacement [AVR] < 60 years old [y.o.]; ▲ = CE AVR 60 to 70 y.o; — = CE AVR > 70 y.o)

＞ 70 y

60～70 y

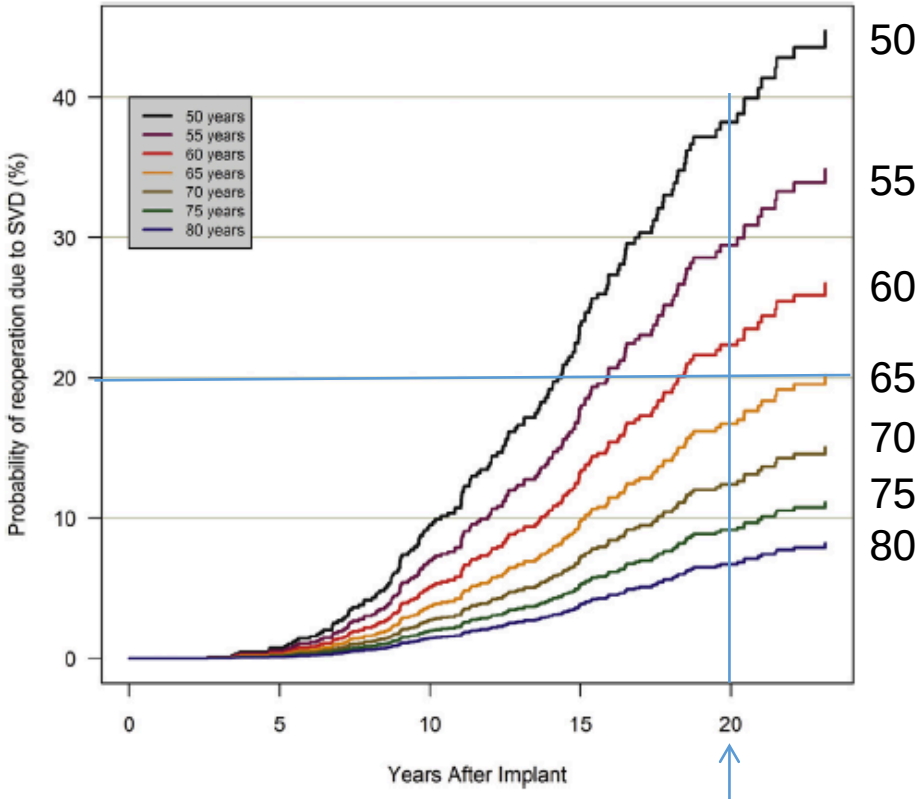
＜ 60 y

SVD回避率（15年）は70代で100%, 60代で90%以上

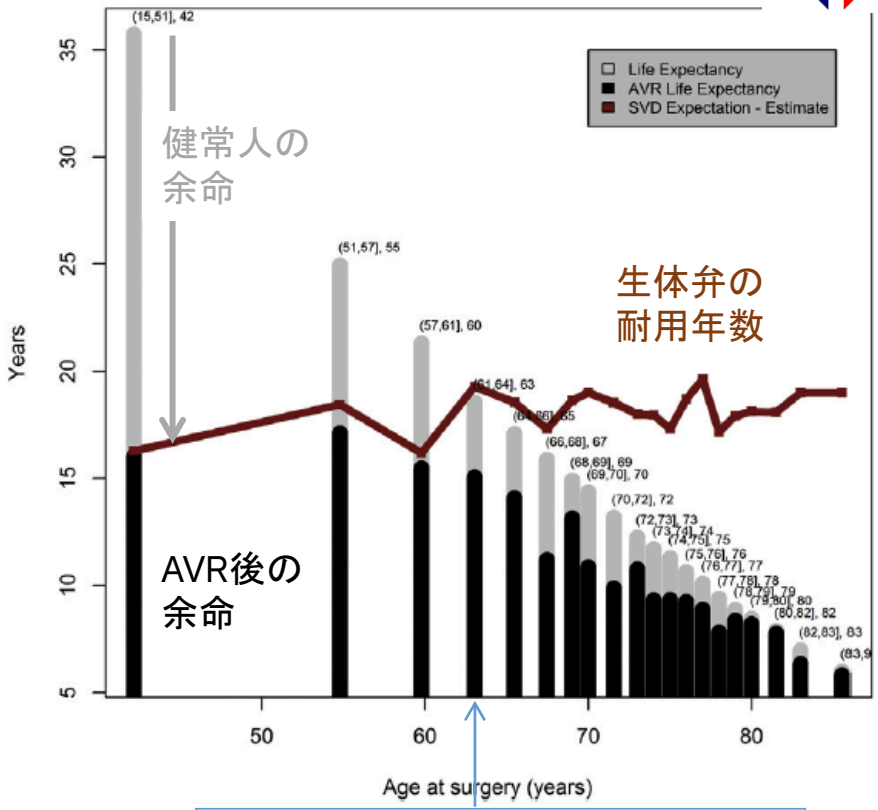
Very Long-Term Outcomes of the Carpentier-Edwards Perimount Valve in Aortic Position

Thierry Bourguignon, MD, Anne-Lorraine Bouquiaux-Stablo, MD, Pascal Candolfi, PhD, Alain Mirza, MD, Claudia Loardi, MD, Marc-Antoine May, MD, Rym El-Khoury, MD, Michel Marchand, MD, and Michel Aupart, MD

(Ann Thorac Surg 2015;99:831–7)



60-65歳の患者は約20%の確率で20年後にSVDによる再手術が発生する

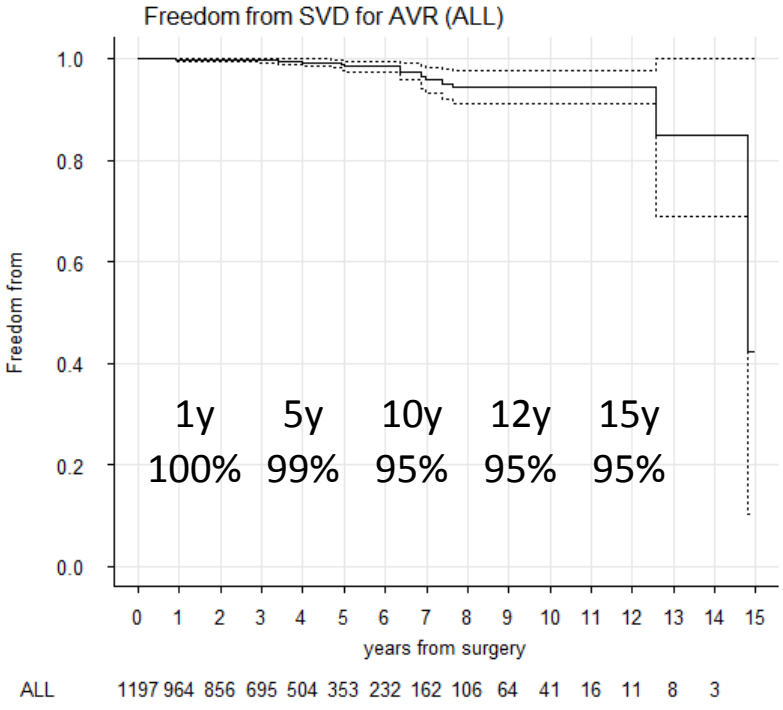


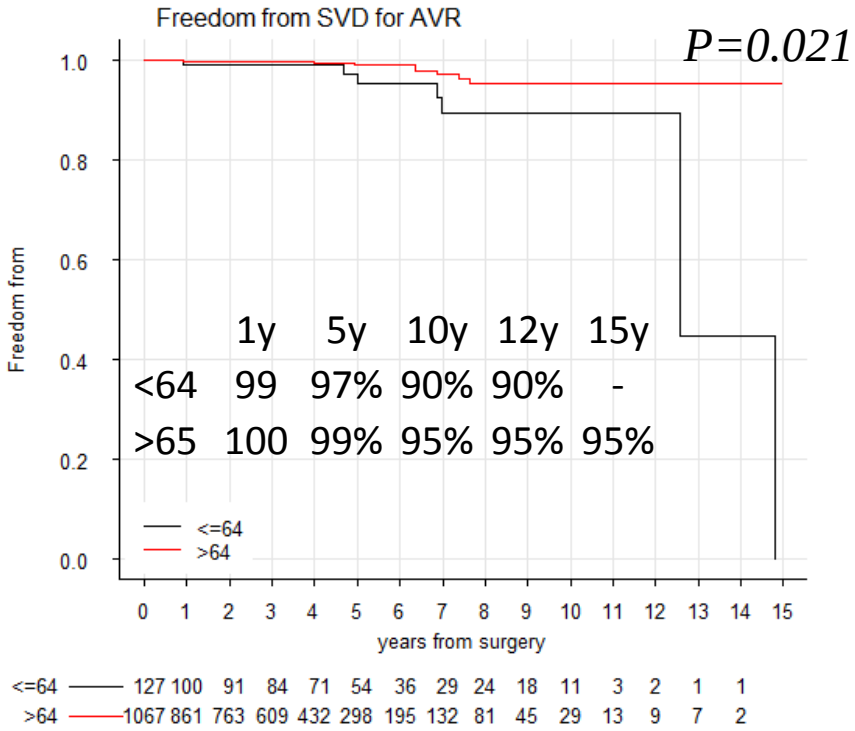
61-64歳で生体弁の耐用年数が健常人の平均余命を上回る

MOSAIC AVR SVD回避率

（国内10施設による多施設共同研究　N=1202）

平均年齢76歳　AS 78%





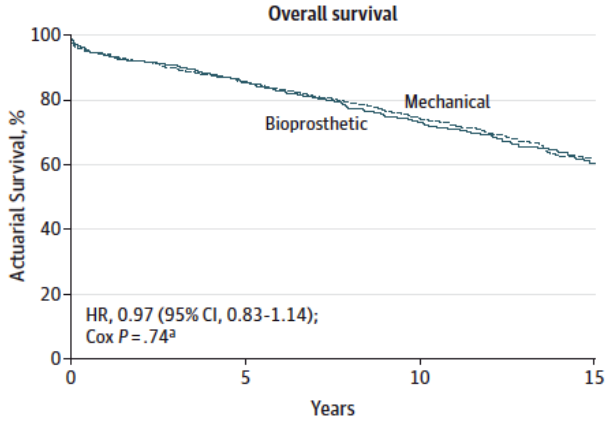
SVD回避率は15年で95%で65歳未満の群で有意に低かったが、65歳未満の群においても12年で90%と良好であった。

(Courtesy to Dr. Yoshikawa, Osaka Univ.)

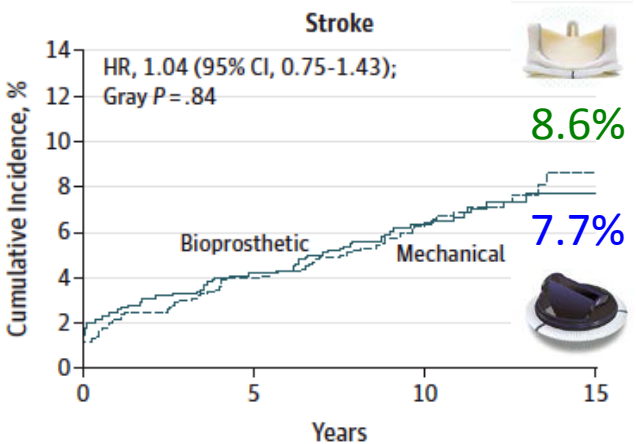
Survival and Long-term Outcomes Following Bioprosthetic vs Mechanical Aortic Valve Replacement in Patients Aged 50 to 69 Years

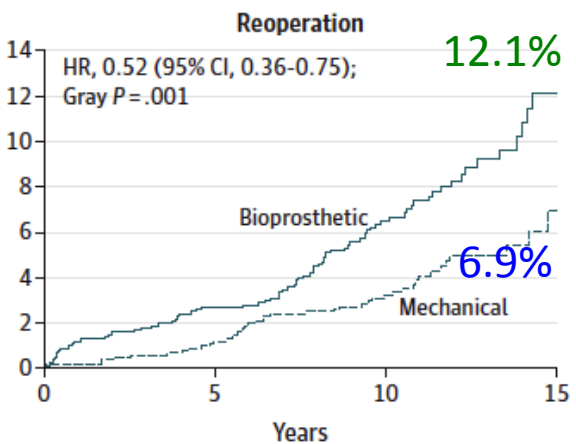
Yuting P. Chiang, BA; Joanna Chikwe, MD; Alan J. Moskowitz, MD; Shinobu Itagaki, MD; David H. Adams, MD; Natalia N. Egorova, PhD

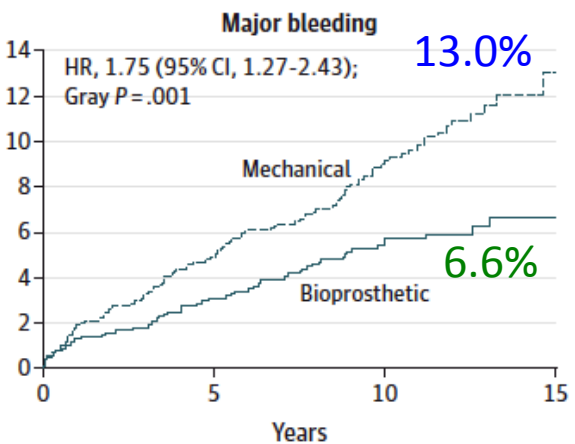
JAMA. 2014;312(13):1323-1329.



- 50–69歳までのAVR in NY (1997–2004, N=4253)
- 生体弁と機械弁の15年までの成績を比較
- 全生存率、脳梗塞（死亡率18.7%)に有意差なし
- 再手術（死亡率9%)は生体弁が多い
- 出血合併症（死亡率13.2%)が機械弁に多い
- 50–69歳の生体弁は理にかなった選択だろう







Circ J
doi:10.1253/circj.CJ-17-0154

Circ J 2017;81:1198-1206.

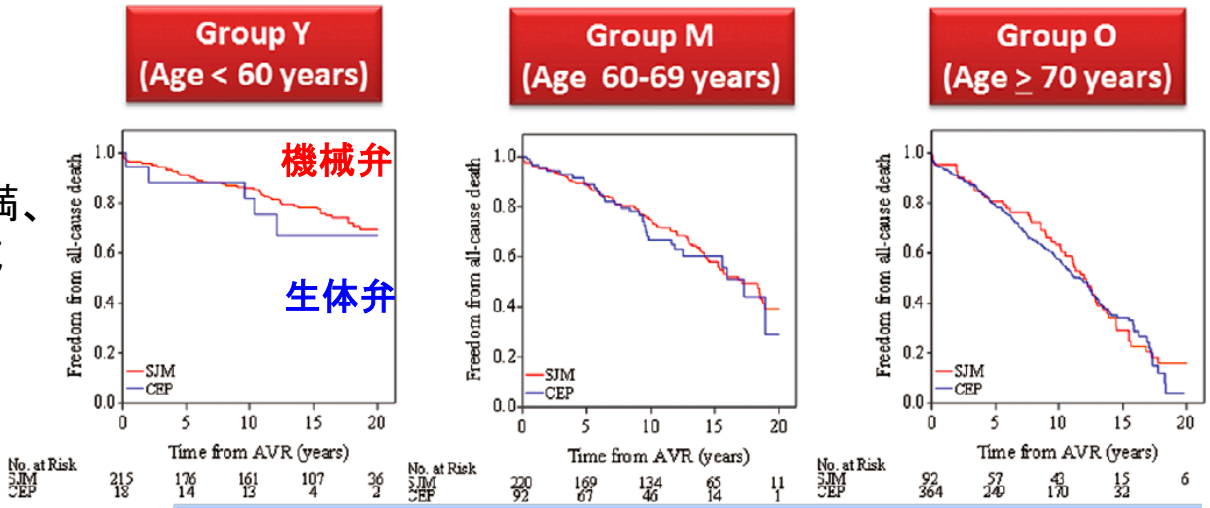
Comparison of the Long-Term Outcomes of Mechanical and Bioprosthetic Aortic Valves

— A Propensity Score Analysis —

Kenji Minakata, MD, PhD; Shiro Tanaka, PhD; Nobushige Tamura, MD, PhD; Shigeki Yanagi, MD, PhD; Yohei Ohkawa, MD, PhD; Shuichi Okonogi, MD; Tatsuo Kaneko, MD, PhD; Akihiko Usui, MD, PhD; Tomonobu Abe, MD, PhD; Mitsuomi Shimamoto, MD, PhD; Yoshiharu Takahara, MD, PhD; Kazuo Yamanaka, MD, PhD; Hitoshi Yaku, MD, PhD; Ryuzo Sakata, MD, PhD

- 第二世代生体弁(CEP:n=395) vs 機械弁(SJM: n=441)
- 国内9施設のMulti-center study
- 3グループの年齢層（60歳未満、60-69歳、70歳以上）で遠隔成績を比較 (propensity score analysis)

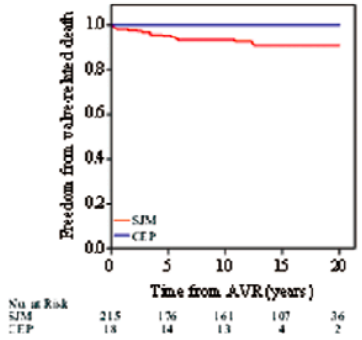
Freedom from All-Cause Death



生存率はどの年齢層でも有意差なし

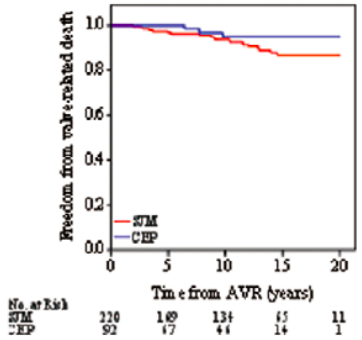
Freedom from Valve-Related Death

Group Y (Age < 60 years)



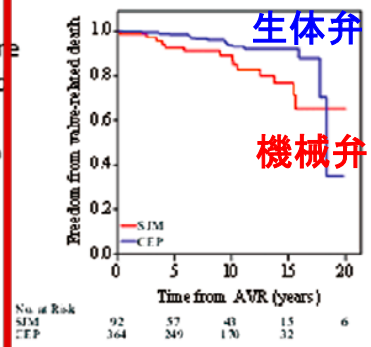
Hazard ratio was not estimatable

Group M (Age 60-69 years)



Propensity score adjusted hazard ratio=1.97 (95%CI: 0.54 to 7.18, p=0.31)

Group O (Age ≥ 70 years)

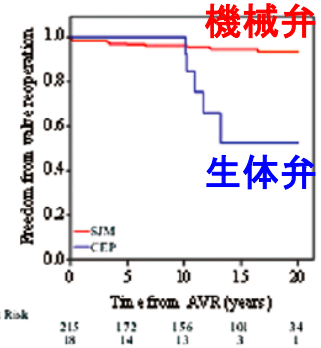


Propensity score adjusted hazard ratio=2.36 (95%CI: 1.07 to 5.23, p=0.03)

弁関連死亡は70歳以上で機械弁に多い

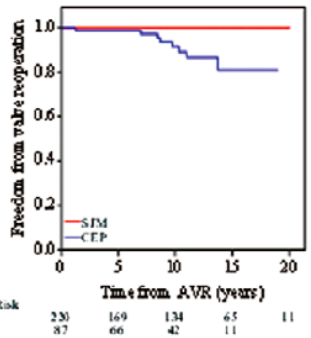
Freedom from Reoperation

Group Y (Age < 60 years)



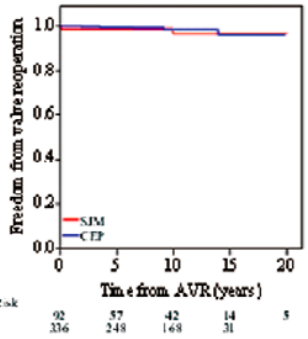
Propensity score adjusted hazard ratio=**0.16** (95%CI: 0.06 to 0.46, **p<0.01**)

Group M (Age 60-69 years)



Hazard ratio was not estimatable

Group O (Age ≥ 70 years)

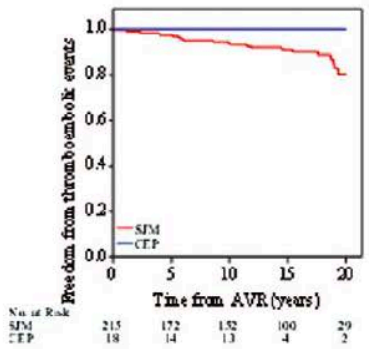


Propensity score adjusted hazard ratio=1.71 (95%CI: 0.29 to 10.13, p=0.56)

再手術は70歳未満で生体弁に多い

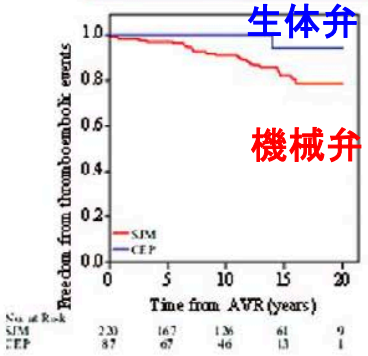
Freedom from Thromboembolic Event

Group Y (Age < 60 years)



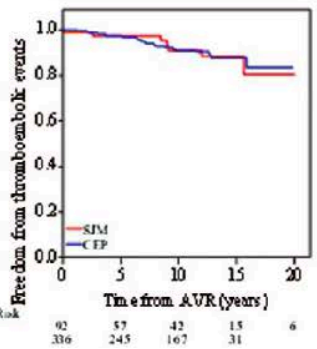
Hazard ratio was not estimatable

Group M (Age 60-69 years)



Propensity score adjusted hazard ratio=7.55 (95%CI: 0.98 to 58.0, p=0.05)

Group O (Age ≥ 70 years)



Propensity score adjusted hazard ratio=1.32 (95%CI: 0.55to 3.20, p=0.54)

血栓塞栓症は70歳未満で機械弁に多い

Conclusions

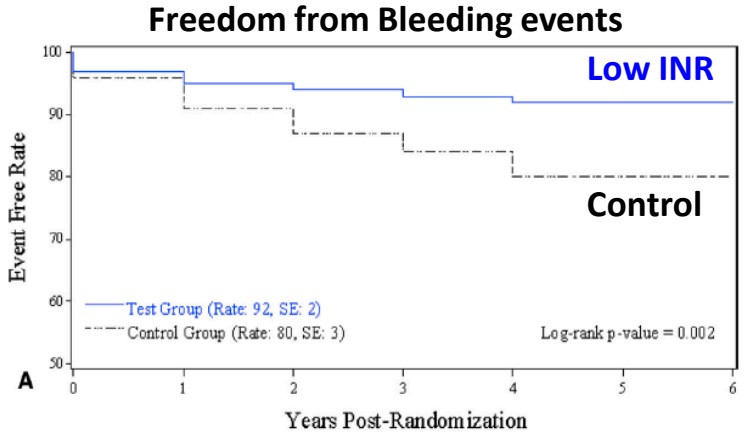
Although there were no differences in overall survival between bioprosthetic and mechanical valves in all age groups, bioprosthetic valves may provide better freedom from valve-related mortality and thromboembolic events in elderly patients. Mechanical valves should be the choice in patients <70 years of age who wish to avoid reoperation.

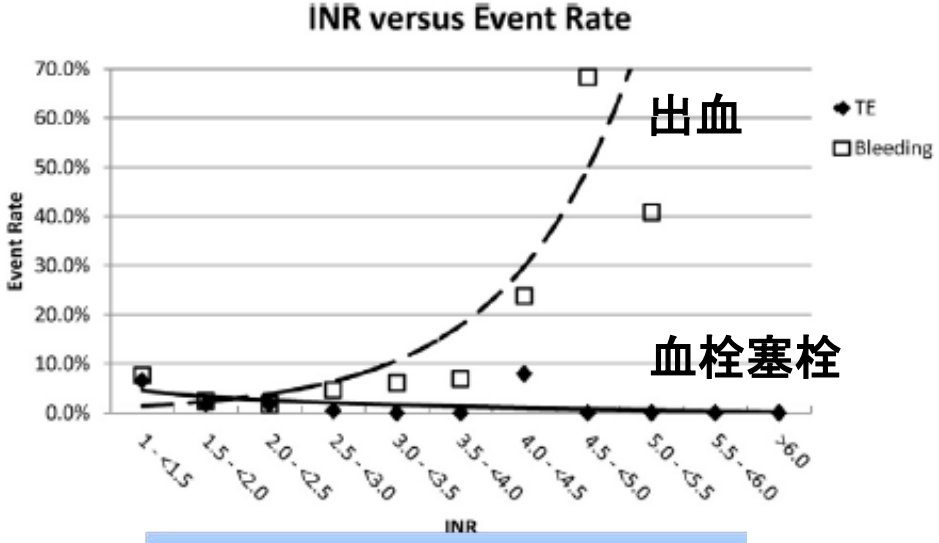
Reduced anticoagulation after mechanical aortic valve replacement: Interim results from the Prospective Randomized On-X Valve Anticoagulation Clinical Trial randomized Food and Drug Administration investigational device exemption trial

John Puskas, MD, MSc, FACS, FACC,[a] Marc Gerdisch, MD,[b] Dennis Nichols, MD,[c] Reed Quinn, MD,[d]

(J Thorac Cardiovasc Surg 2014;147:1202-11)

- PROACT study, elevated risk factor for thromboembolism
  - **Low-dose warfarin** (INR **1.5-2.0**; mean 1.89±0.49) N=185
  - **Control** (INR **2.0-3.0**; mean 2.50±0.63) N=190
- Age 55±13 years





Low-dose群で出血合併症が低い
血栓塞栓症は両群間に有意差なし。

INR=1.5で出血と塞栓の
リスク曲線が交差する

2017年AHA/ACC弁膜症ガイドライン改訂

- 抗凝固療法が禁忌ではない50歳未満の患者に対し、機械弁を選択する（クラスⅡa）
- 50歳～70歳の患者に対して、良く話し合った上で、生体弁と機械弁の選択をする（クラスⅡa）
- 生体弁（A弁）が狭窄あるいは逆流のために重度の症状があり、再手術のリスクが高い、 もしくは禁忌であり、血行動態改善の見込みがあるとハートチームで判断した場合、「Valve in Valve」を行う (クラスⅡa: 新規追加）

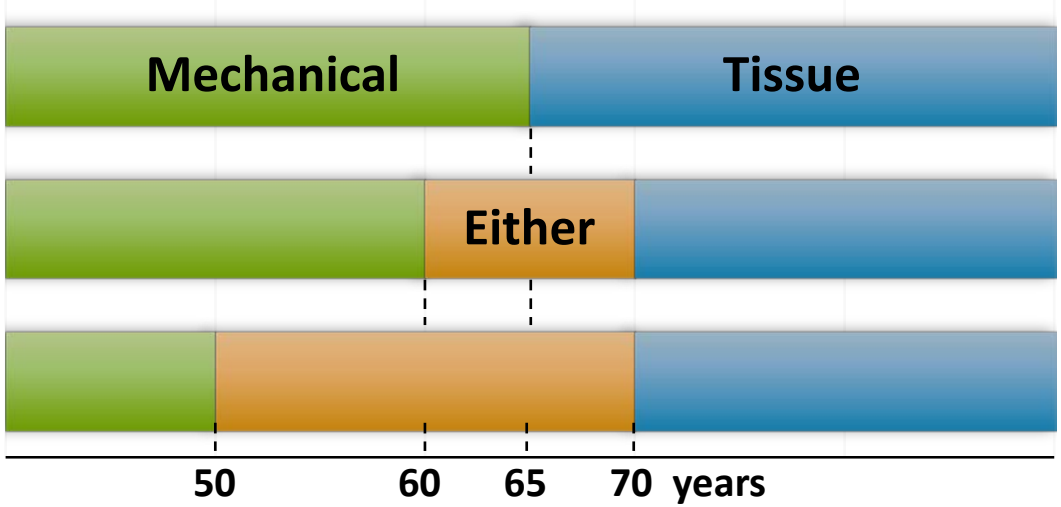
ACC/AHA弁膜症ガイドライン
生体弁 vs 機械弁

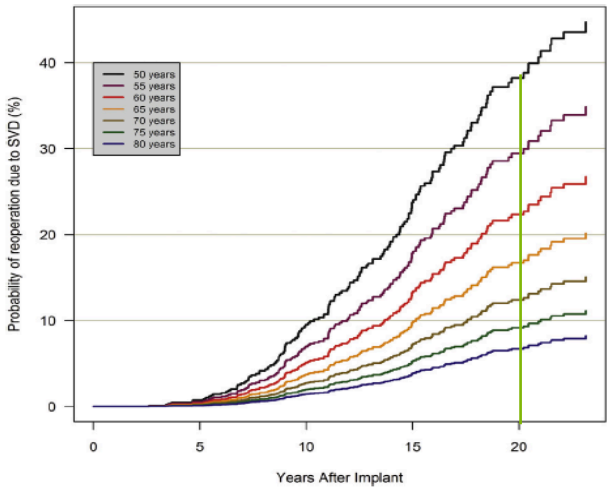
クラスIIa推奨

2006 ACC/AHA
(2012 JCS)

2014 ACC/AHA

2017 ACC/AHA





50y

60y

70y

Redoは2回までOK?
50歳のSVD回避率は20年で60%
→ Redo　with SAVR (70歳）
→ 2nd Redo with VIV

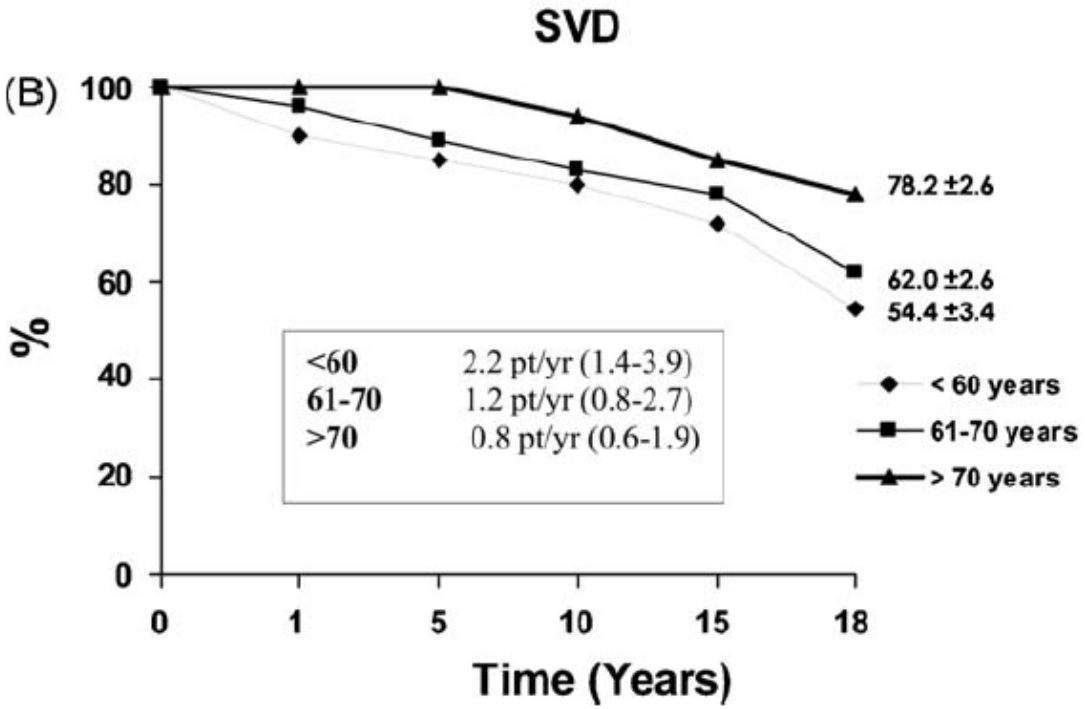
日本人は狭小弁輪が多いのでVIVを見越した生体弁の適応は慎重に

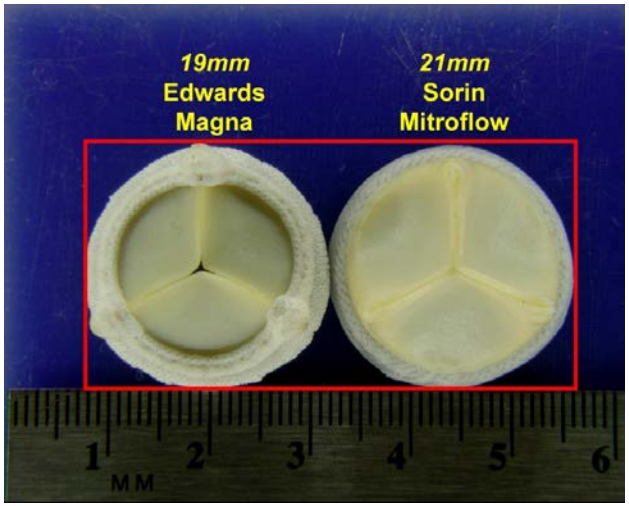
外巻き弁- CROWN PRT

The Italian study on the Mitroflow postoperative results (ISTHMUS): a 20-year, multicentre evaluation of Mitroflow pericardial bioprosthesis☆

The ISTHMUS Investigators[a,b,c,d,e,f,g,h,i,j,k,l,m,1]

European Journal of Cardio-thoracic Surgery 39 (2011) 18–26





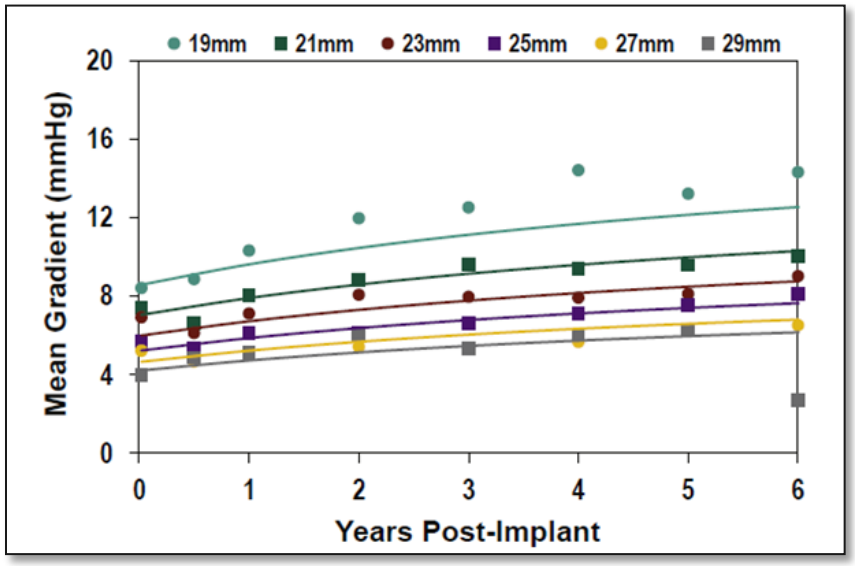
７０代のSVD回避率は10年で90%以上

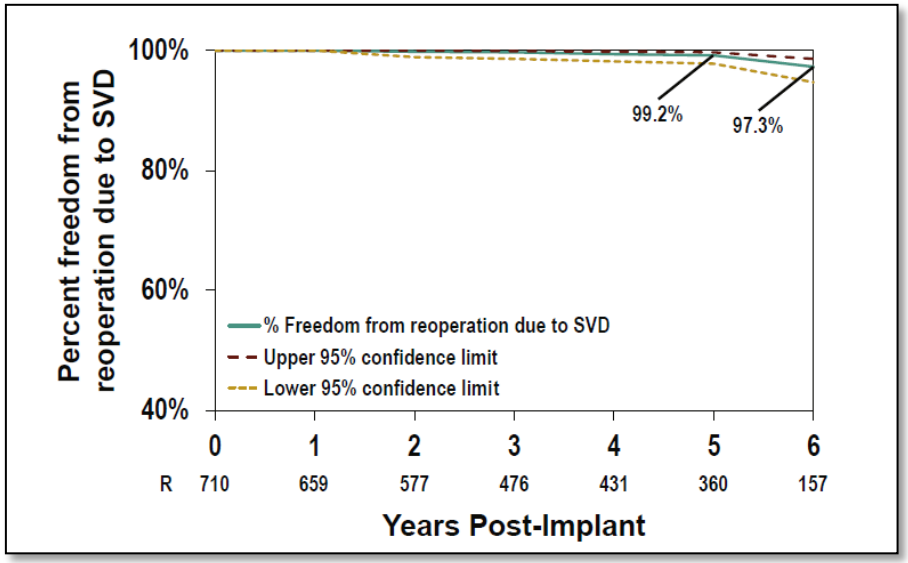
外巻き弁- Trifecta

Midterm, multicenter clinical and hemodynamic results for the Trifecta aortic pericardial valve

Scott Goldman, MD,[a] Anson Cheung, MD,[b] Joseph E. Bavaria, MD,[c] Michael R. Petracek, MD,[d] Mark A. Groh, MD,[e] and Hartzell V. Schaff, MD[f]

J Thorac Cardiovasc Surg 2017;153:561-9

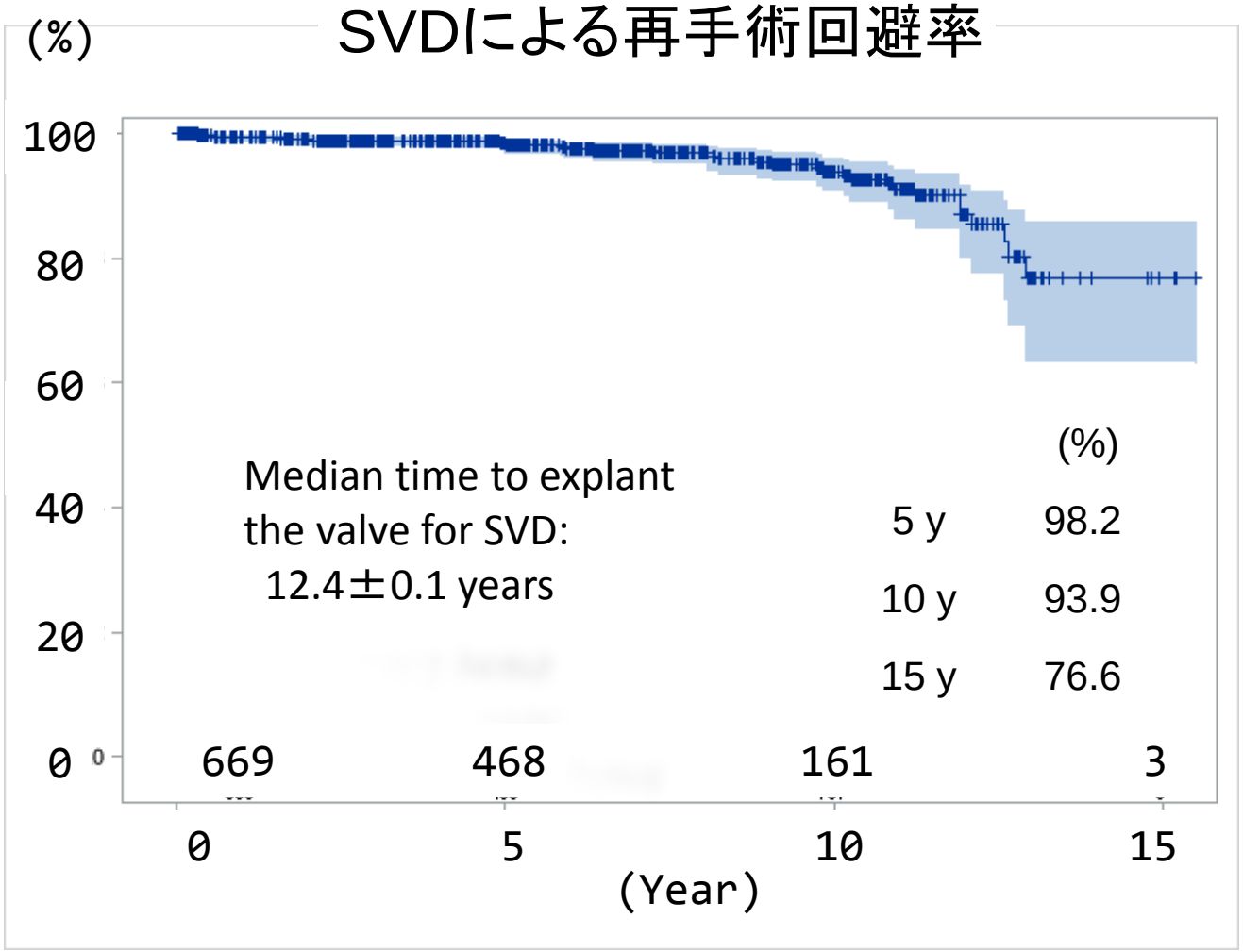




- 2007年～2009年の11施設の710名(平均年齢: 72.4±9.3歳)を対象
- 6年時のSVDによる再手術回避率: 97.3%(95%CI: 98.6-94.7)

ステントレス弁- Freestyle弁

（国内10施設による多施設共同研究　1996-2009, N=938)

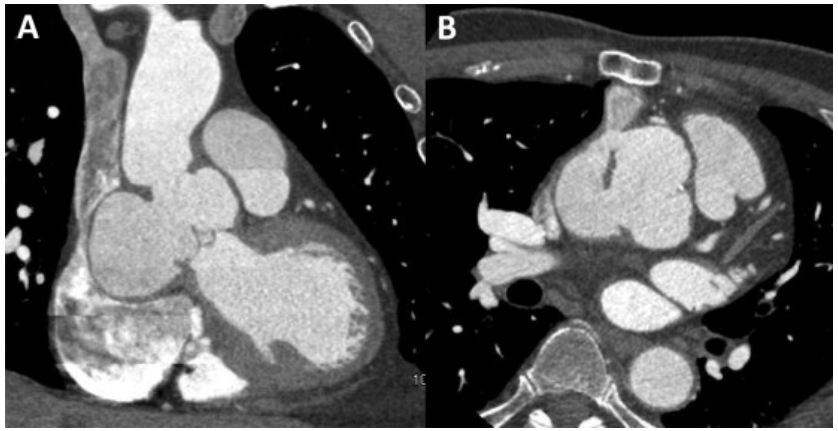


Available in Japan
in 1996

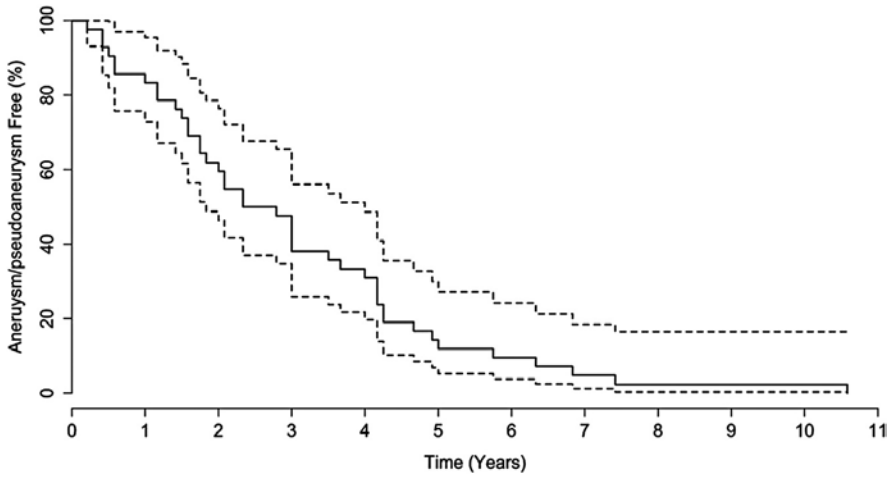
(Courtesy to Dr. Yoshikawa, Osaka Univ.)

Freestyle弁full root症例の遠隔期仮性瘤

- 2005年頃から症例報告が散見
- 4.7% (US), 3.2% (Japan)
- 術後5年までconstantに発生。5年以降も続く
- 23mm以上しか発生していない
  - 大きなサイズの弁では不十分な圧固定になる可能性がある



(Sakaguchi et al. Ann Thorac Surg 2013;95:1074)



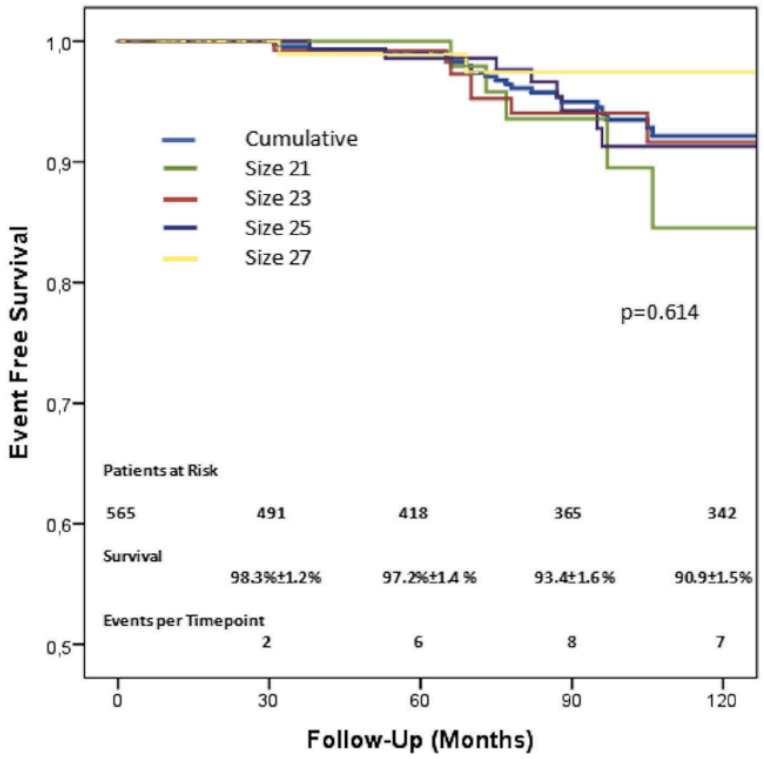
(Englum et al. Ann Thorac Surg 2014;98:2061)

Freedom Solo / Solo Smart

Pericardial Stentless Valve for Aortic Valve Replacement: Long-Term Results

Alberto Repossini, MD, Theodor Fischlein, MD, Giuseppe Santarpino, MD, Christina Schäfer, MD, Benjamin Claus, MD, Bruno Passaretti, MD, Lorenzo Di Bacco, MD, Laura Giroletti, MD, Gianluigi Bisleri, MD, Claudio Muneretto, MD, and Herko Grubitzsch, MD

Ann Thorac Surg 2016;102:1956-65.



Freedom Solo

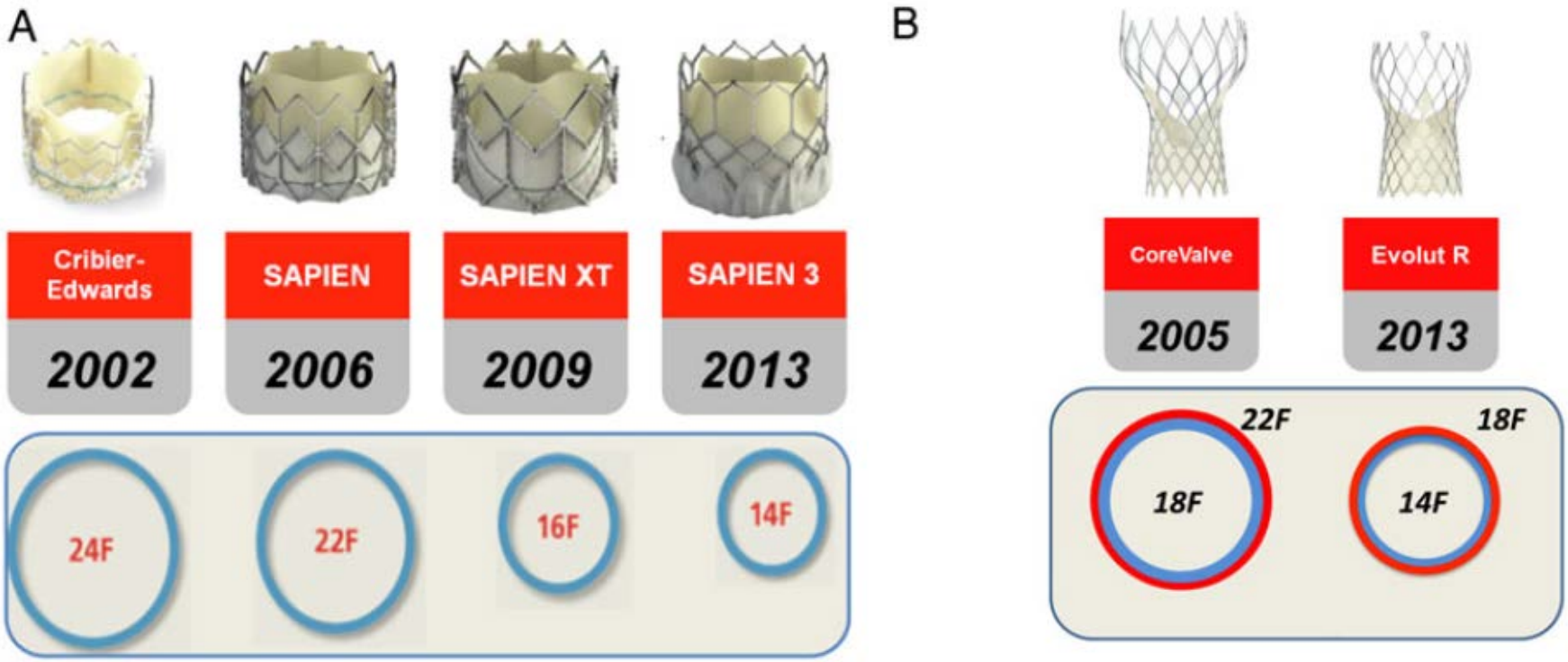
(2004～)

Sutureless Valve (1 year results)

	Perceval (CE Mark 2011)	**Intuity (CE Mark 2014)**
Study (n)	Multicenter (658)	Single center (150)
Patient profile	78 years, STS 7.2%	77 years, Euro II 3.8%
Isolated AVR (%) MICS (%)	71% 33%	69% 33%
Implant success	95.4%	97.3%
Mortality Stroke	4.5% 3%	2.9% 3.3%
PVL Endocarditis	**1.1%** 1.4%	**3.2%** 0.7%
Valve thrombosis SVD, migration	0	0
Pacemaker	**9.6%**	**5.6%**

Fischlein T, et al. J Thorac Cardiovasc Surg 2016;151:1617-26.
Theron A, et al. Interact Cardiovasc Thorac Surg 2017;25:68-74.

TAVI　Deviceの進化



European Heart Journal (2016) 37, 803–810

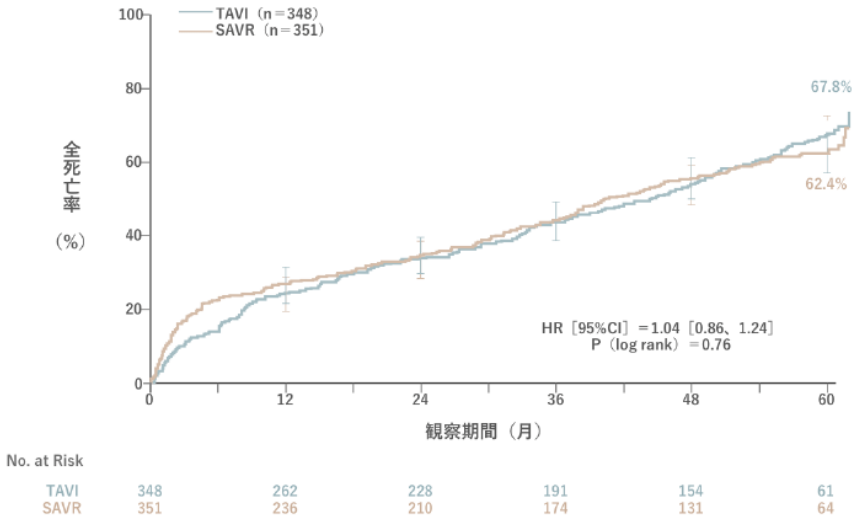
PARTNER Trial

Cohort A: high risk patients

Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

AVR VS TAVI



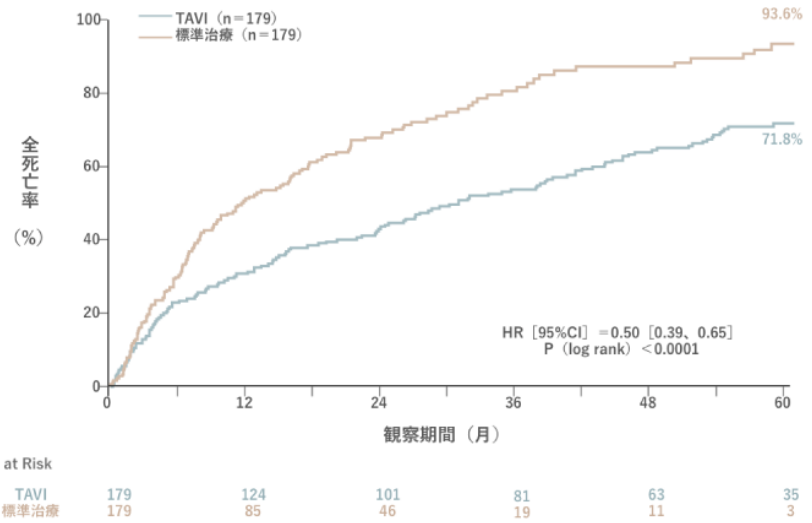
5年での全死亡および脳卒中はTAVRはSAVRと同等

Cohort B: inoperable patients

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

一般内科治療 VS TAVI

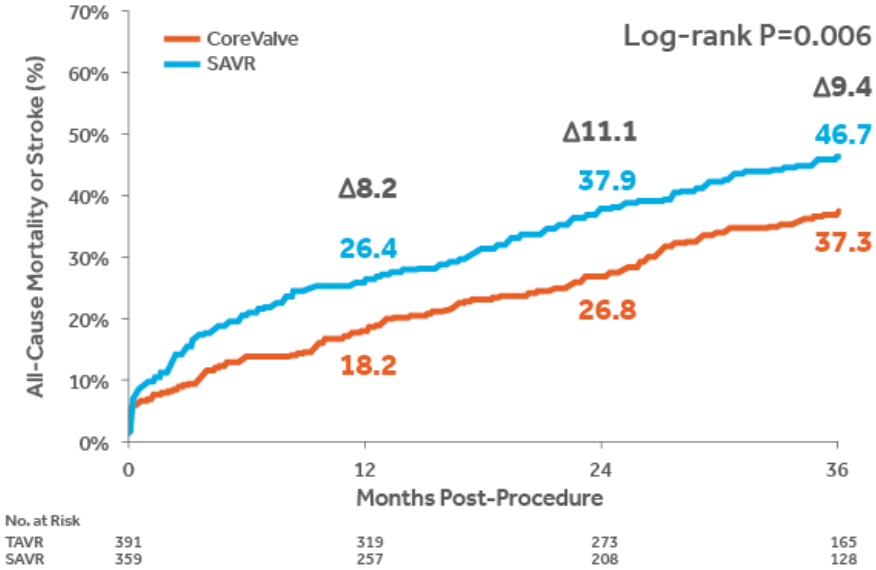


5年での全死亡においてTAVRは標準治療より優れる

3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement

(J Am Coll Cardiol 2016;67:2565-74)

- CoreValve US Pivotal High Risk Study
- TAVR N=390, STS 7.3% vs SAVR, N=357, STS 7.5%



3年での全死亡および脳卒中はTAVRがSAVRより少ない

Intermediate RiskのTAVIの成績 (SURTAVI)

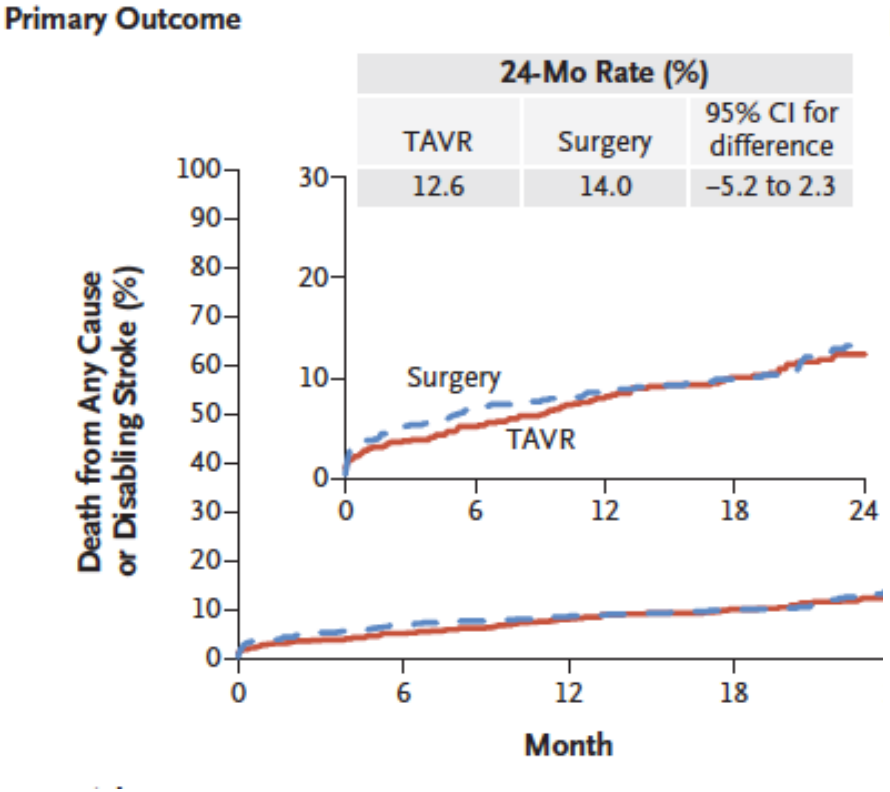
The NEW ENGLAND JOURNAL of MEDICINE

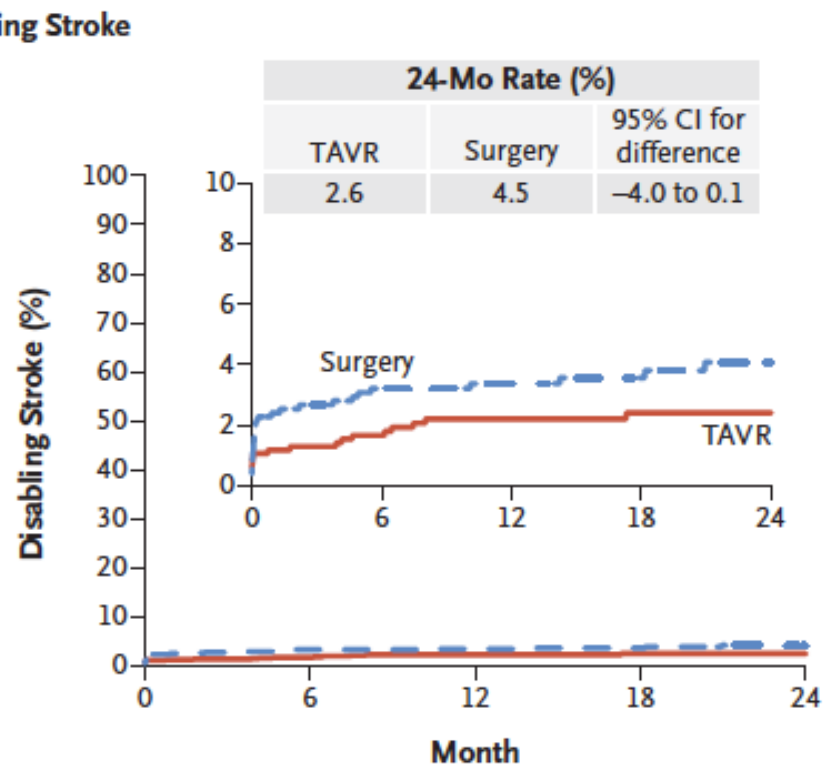
Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

M.J. Reardon, N.M. Van Mieghem, J.J. Popma, N.S. Kleiman, L. Søndergaard, M. Mumtaz, D.H. Adams, G.M. Deeb, B. Maini, H. Gada, S. Chetcuti, T. Gleason, J. Heiser, R. Lange, W. Merhi, J.K. Oh, P.S. Olsen, N. Piazza, M. Williams, S. Windecker, S.J. Yakubov, E. Grube, R. Makkar, J.S. Lee, J. Conte, E. Vang, H. Nguyen, Y. Chang, A.S. Mugglin, P.W.J.C. Serruys, and A.P. Kappetein, for the SURTAVI Investigators*

- SURTAVI registry, 1660 patients
- mean age 79.8±6.2 years, STS score 4.5±1.6%
- 2-year outcomes

New England Journal of Medicine 2017





2年の全死亡および脳卒中は
TAVRはSAVRと同等

2年の脳卒中発生率に有意差はないが、TAVRで少ない傾向

TAVRで弁周囲逆流が多い。mPGが低い。
TAVRで術後AKI, Afib, 輸血が少ない。

Valve In Valve (現在保険適応外)

CoreValve / CoreValve Evolut

2013 CE approval

Aortic VIV

SAPIEN XT

2014 CE approval

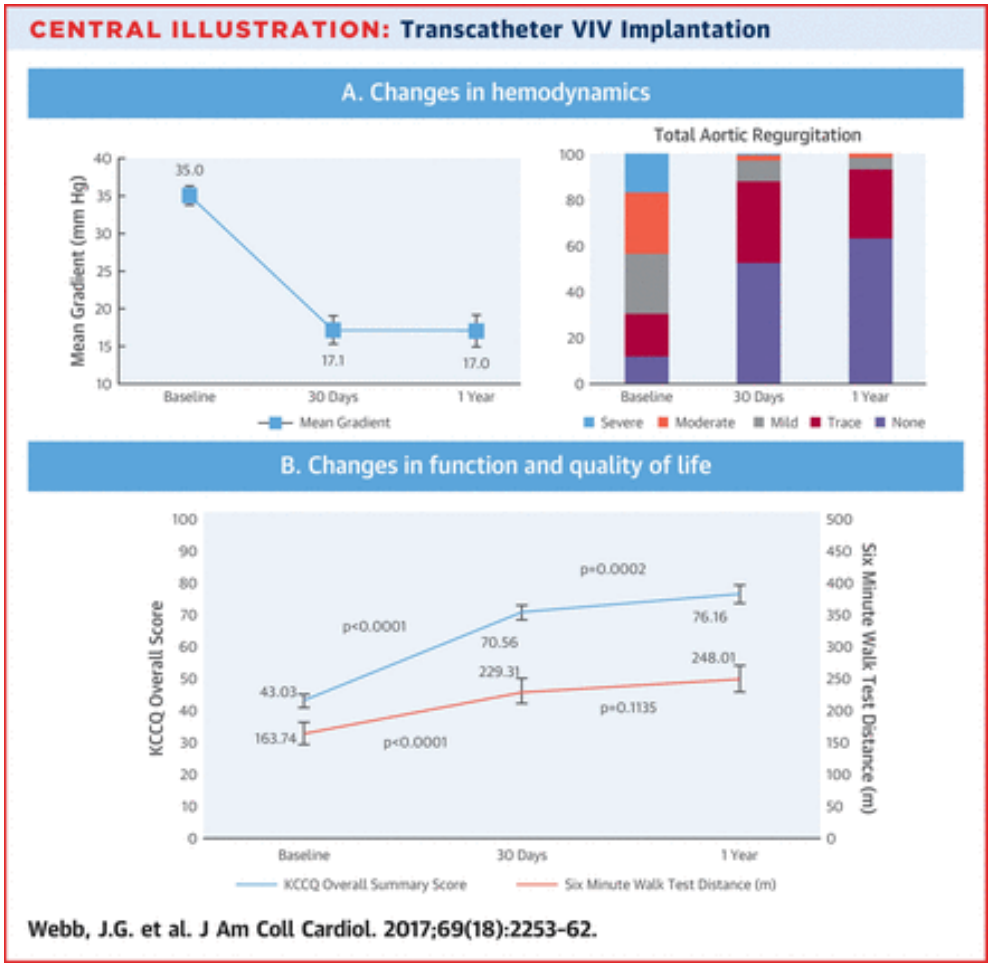
Aortic / Mitral VIV

2015 FDA approval

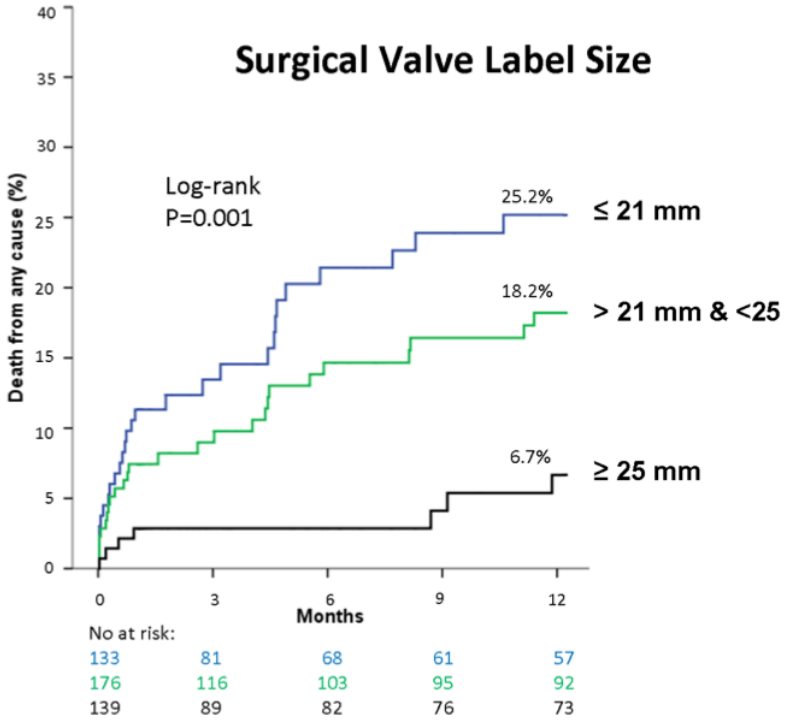
Aortic VIV

現在適応外だが Valve-in-Valve見据え大きな弁を

PARTNER 2 VIV Registry



Webb, J.G. et al. J Am Coll Cardiol. 2017;69(18):2253-62.

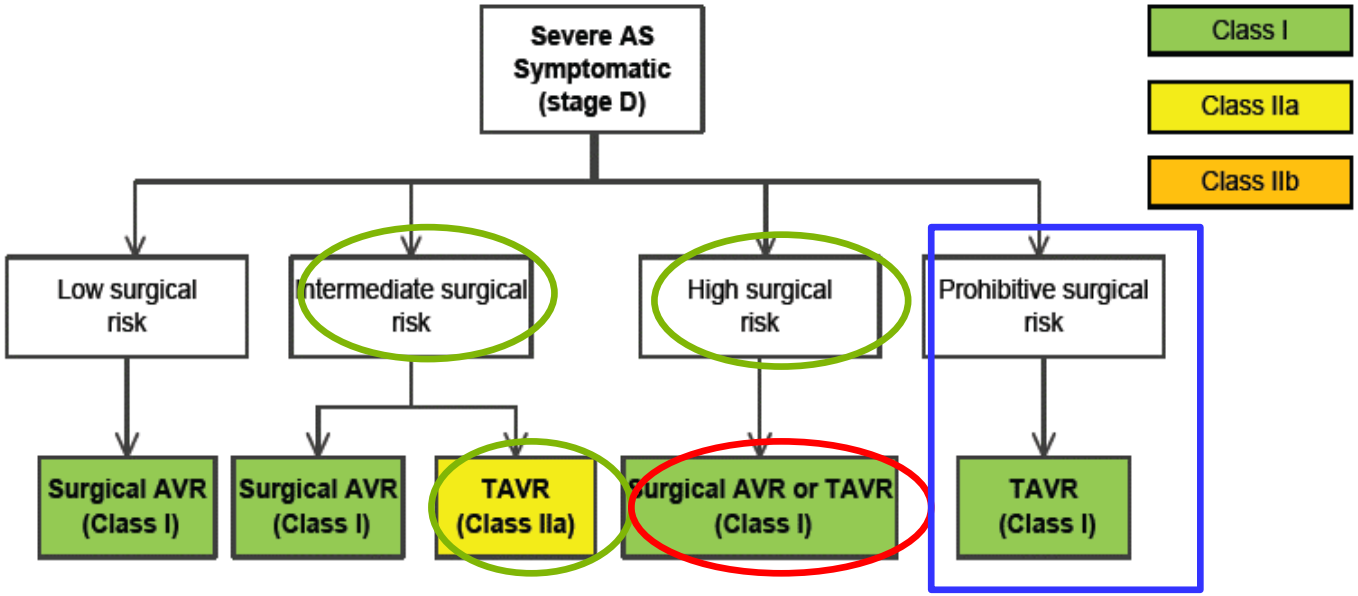


Dvir D,et al. JAMA 2014;312:162-70

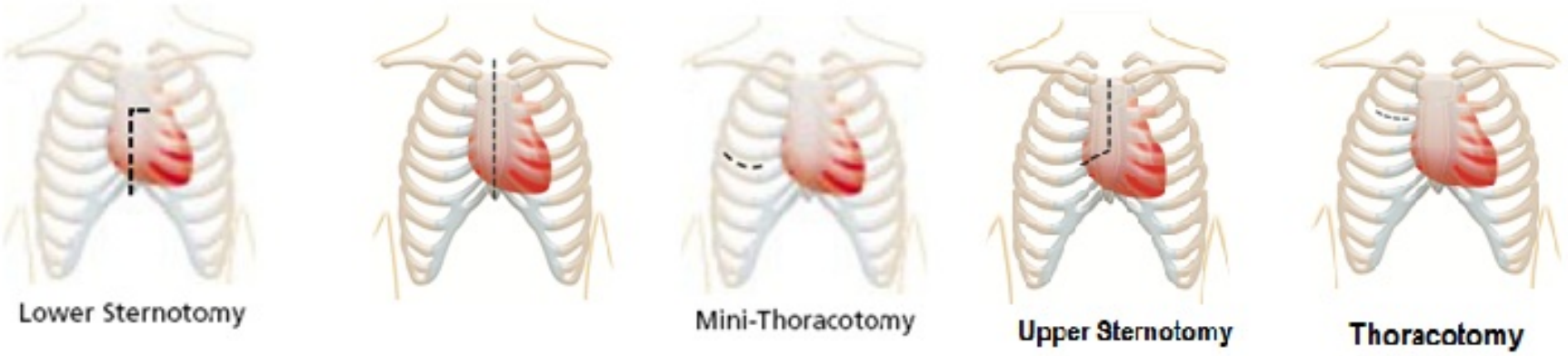
初回AVRでは23mm以上がインプラントされていることが推奨される

2017年AHA/ACC弁膜症ガイドライン改訂

- High Riskな症候性重度AS患者（StageD)に、ハートチームで話し合った結果、AVRもしくはTAVRを選択する。クラスⅠ（Ⅱaから変更）
- Intermediate Riskな症候性重度AS患者(Stage D)に、ハートチームで話し合った結果、AVRの替わりにTAVRを選択する 。クラスⅡa（新規追加）



MICS AVRのアプローチ



Propensity Score-Matched Analysis of Minimally Invasive Aortic Valve Replacement

Arudo Hiraoka, MD; Toshinori Totsugawa, MD, PhD; Masahiko Kuinose, MD, PhD; Kosuke Nakajima; Genta Chikazawa, MD, PhD; Kentaro Tamura, MD; Hidenori Yoshitaka, MD, PhD; Taichi Sakaguchi, MD, PhD

(*Circ J* 2014; **78:** 2876–2881)

- Full sternotomy , Partial Sternotomy, Mini thoracotomyの3群間でAVRの成績を比較 (N=194, 26, 62)
- Minithoracotomy群で手術時間、輸血率、ICU/Hospital stayがFull sternotomyより有意に短かった。
- Partial SternotomyはFull sternotomyと差は認めなかった。

Comparison of Two Minimally Invasive Techniques and Median Sternotomy in Aortic Valve Replacement

Severin Semsroth, MD, PhD, Raffaela Matteucci Gothe, Yvonne Rodríguez Raith, Kristof de Brabandere, Esther Hanspeter, Juliane Kilo, Markus Kofler, Ludwig Müller, Elfriede Ruttman-Ulmer, and Michael Grimm

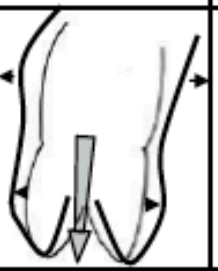
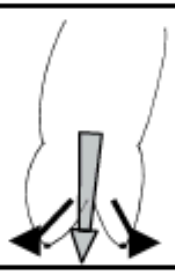
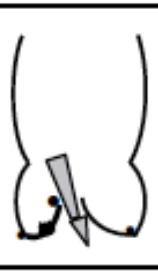
(Ann Thorac Surg 2017;■:■–■)

- Full sternotomy, Partial Sternotomy, Mini thoracotomyの比較 (N=328, 315, 167)
- Mini thoracotomyは正中conversion (14.4%)、再ポンプ (5.1%)、再遮断 (10.2%)がFull sternotomyより多い。
- Mini thoracotomyは遮断時間、ポンプ時間がFull sternotomyより長い。
- Mini thoracotomyは鼠径部合併症(14.4%)がFull sternotomyより多い。
- Partial stenrotomyは合併症発生率は正中切開と同等。
- １年後の生存率は同じ。

多くの施設ではPartial SternotomyによるMICSが推奨される

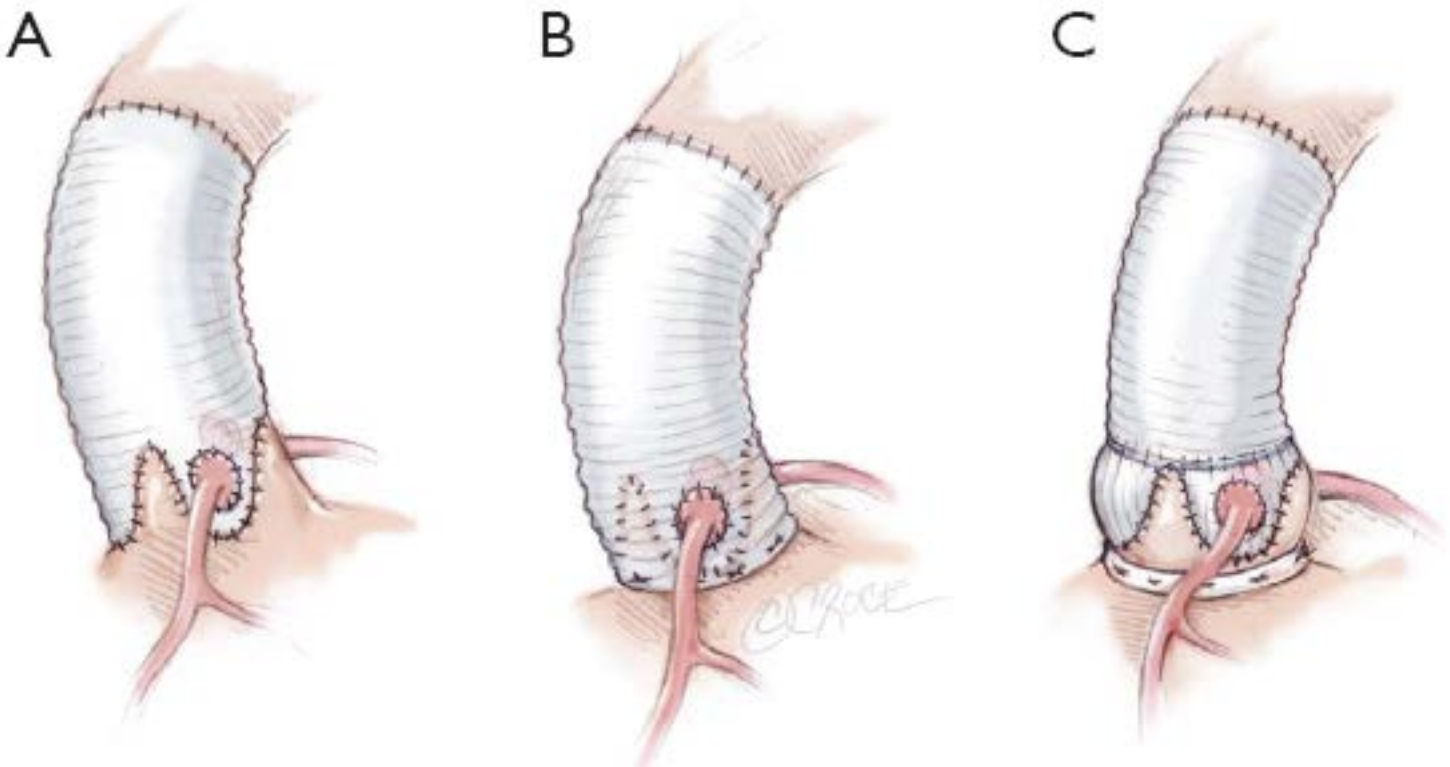
Repair-oriented classification of aortic insufficiency: Impact on surgical techniques and clinical outcomes

Munir Boodhwani, MD, MMSc, Laurent de Kerchove, MD, David Glineur, MD, Alain Poncelet, MD, Jean Rubay, MD, Parla Astarci, MD, Robert Verhelst, MD, Philippe Noirhomme, MD, and Gébrine El Khoury, MD

AI Class	Type I Normal cusp motion with FAA dilatation or cusp perforation				Type II Cusp Prolapse	Type III Cusp Restriction
	Ia	Ib	Ic	Id		
Mechanism						
Repair Techniques (Primary)	STJ remodeling *Ascending aortic graft*	Aortic Valve sparing: *Reimplantation or Remodeling with SCA*	SCA	Patch Repair *Autologous or bovine pericardium*	Prolapse Repair *Plication* *Triangular resection* *Free margin Resuspension* *Patch*	Leaflet Repair *Shaving* *Decalcificatio* *Patch*
(Secondary)	SCA		STJ Annuloplasty	SCA	SCA	SCA

(JTCVS 2009;137:186-94)

Valve Sparing Root Replacement

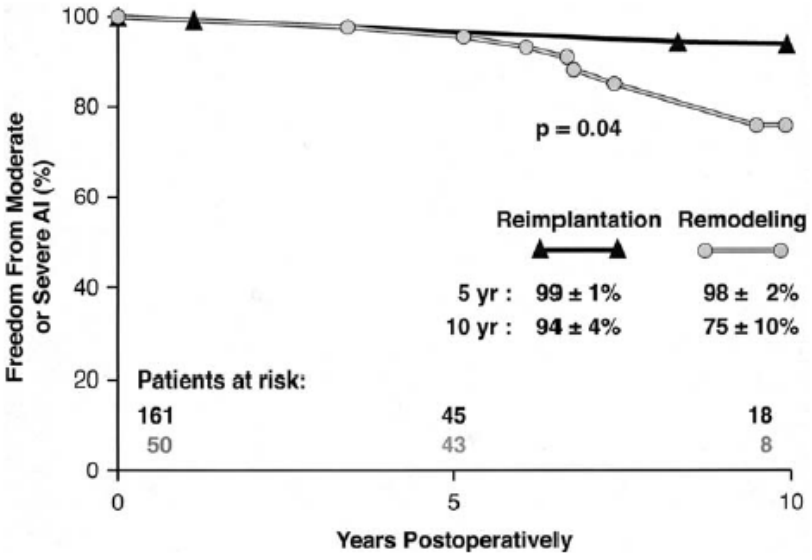


Remodeling (Yacoub)

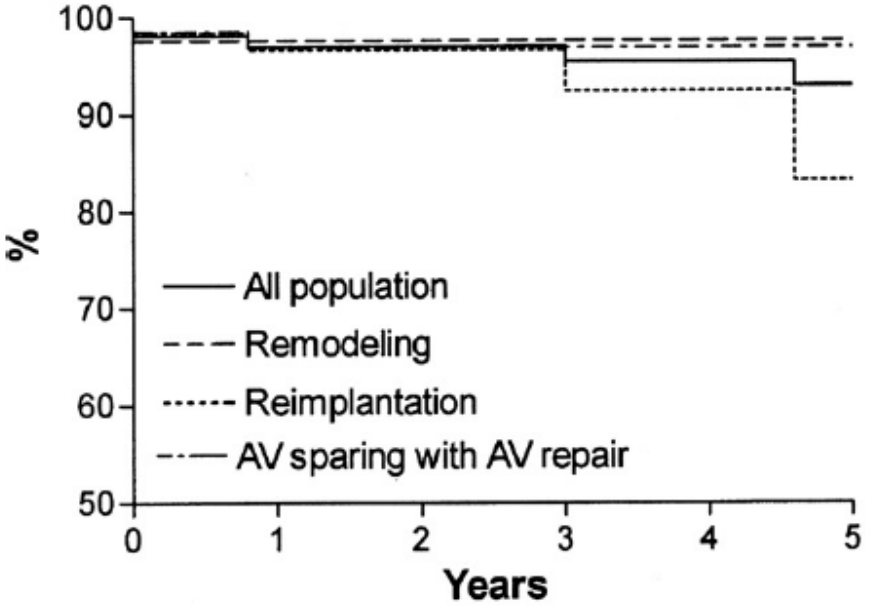
Reimplantation (David)

Remodeling+Annuloplasty (Lansac etc)

Remodeling or Reimplantation? Freedom from AR



(David TE, et al
JTCVS 2006;132:347)

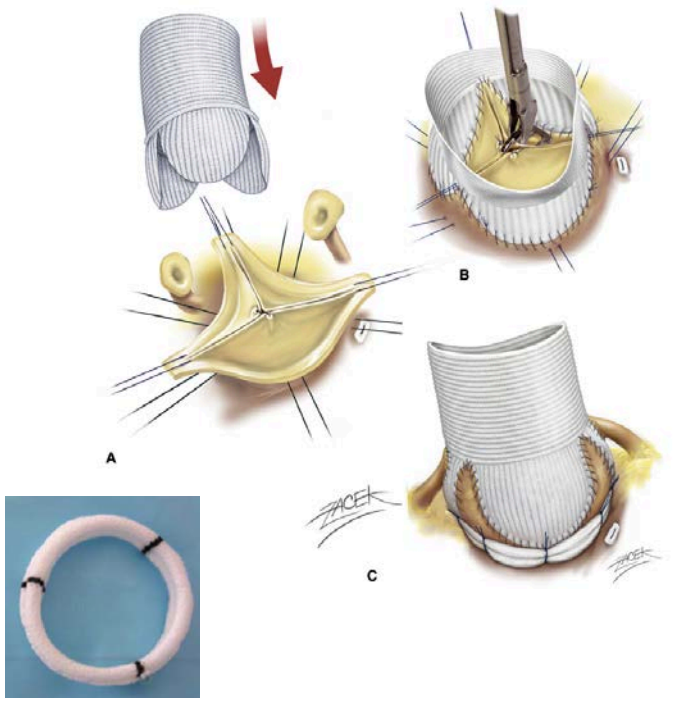


(Jeanmart, El Khoury, et al
Ann Thorac Surg 2007;83:S746)

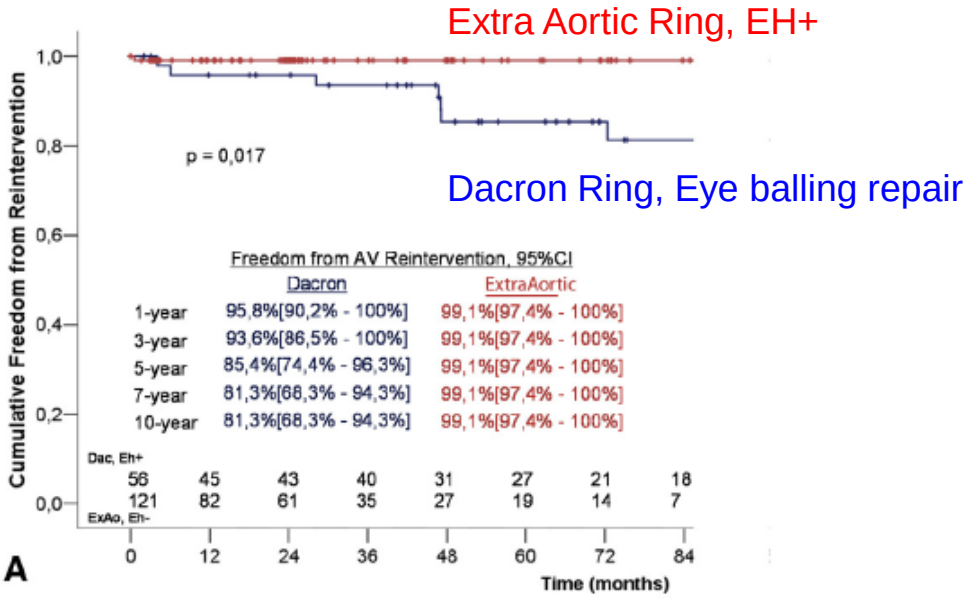
Remodelingにおいてannuloplastyがあまりされていなかった。

Remodeling法の標準化による遠隔成績の改善

(Lansac, et al JTCVS 2017;153:1033-42)



	Aortic annular base diameter (Hegar dilators, mm)				
	25-27	28-30	31-33	34-39	>40
Valsalva tube graft diameter (mm)	26	28	30	32	34
Extra-Aortic ring annuloplasty diameter (mm)	25	27	29	31	33



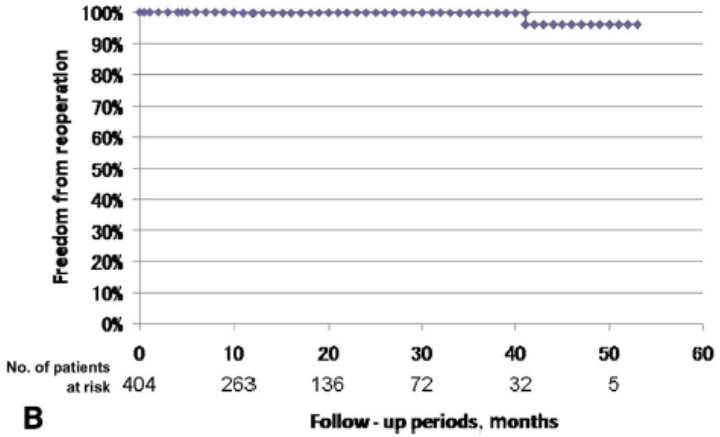
1) 実測弁輪径に合ったValsalva graftとringを選択
2) 1 st Valve repair (central plication / cusp resection)
3) Root reconstruction
4) 2 nd Valve repair (EH≥9mm）
5) Ring annuloplasty (expansible ring)

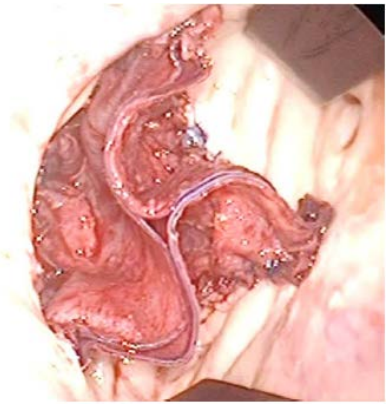
尾崎法（AVNeo）

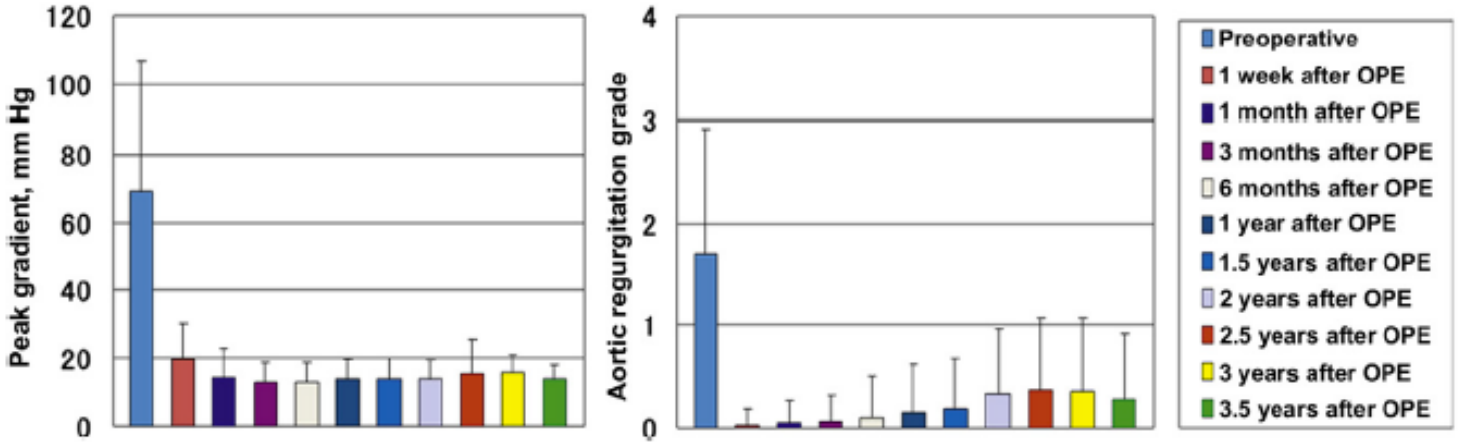
A total of 404 cases of aortic valve reconstruction with glutaraldehyde-treated autologous pericardium

Shigeyuki Ozaki, MD, PhD, Isamu Kawase, MD, Hiromasa Yamashita, MD, Shin Uchida, MD, Yukinari Nozawa, MD, Mikio Takatoh, MD, and So Hagiwara, MD

(J Thorac Cardiovasc Surg 2014;147:301-6)







まとめ
この10年の大動脈弁治療の進歩と今後の展望

- 生体弁の長期成績は極めて優れており、ガイドライン上50代でも生体弁を考慮しても良いとなった。
- 新しい生体弁(外巻き弁, Stentless, Sutureless valve)の短期成績は満足しうるものであり、長期成績が待たれる。
- 中等度リスク患者に対してもTAVIの短期成績はSAVRと同等であることが証明され、低侵襲手術のさらなる普及が予想される。
- 大動脈弁形成の標準化が進んだが、安定した長期成績とAVRとの比較が今後の課題である。