Nordic I, 10 years follow up –

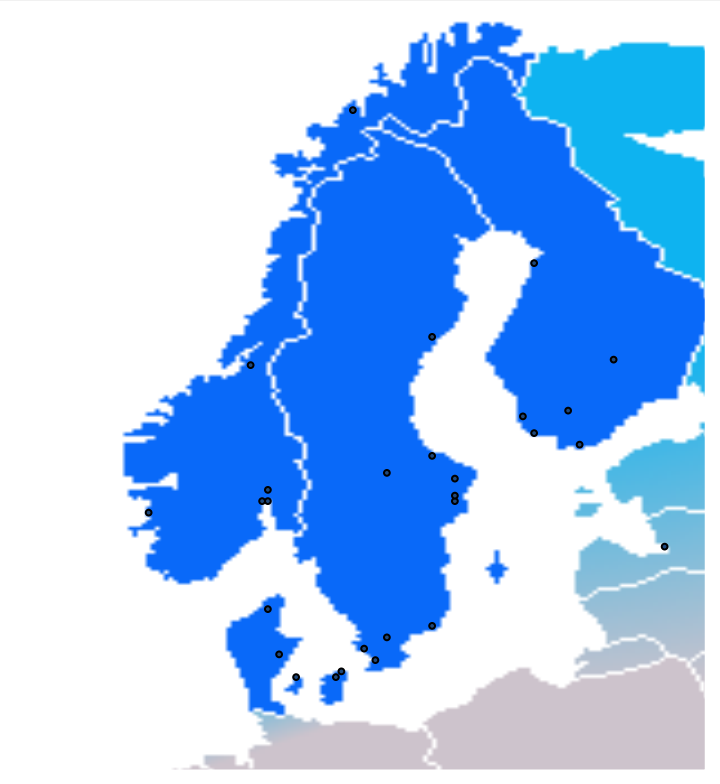
What have we learned from the early randomized bifurcation studies?

Terje Steigen

What have we learned from the early randomized bifurcation studies?

- «Nordic one» started in the early days of PCI and bifurcation stenting
- We had high expectations to 1. generation DES
- **Leif Thuesen and Jens Lassen and the whole** Skejby group, *invited us all in*…
- Leif had a vision: With united efforts we could match the scientific impact we so far only observed from the US.
- We would gain experience and knowledge from more «peripheral bifurcations» to move proximally to the LEFT MAIN
- AND WE DID GOOD!

Nordic Bifurcation Study
Participating Centers



Nordic Bifurcation Study
Participating Centers

Nordic I, BIF I

This nonblinded, randomized, multicenter trial was conducted at 28 cardiology centers in Denmark, Sweden, Finland, Norway, and Latvia. From September 2004 to May 2005, a total of 413 patients were enrolled. A flow diagram of the study is shown in Figure 1. The

Randomized Study on Simple Versus Complex Stenting of Coronary Artery Bifurcation Lesions

The Nordic Bifurcation Study

Terje K. Steigen, MD; Michael Maeng, MD; Rune Wiseth, MD; Andrejs Erglis, MD; Indulis Kumsars, MD; Inga Narbute, MD; Pål Gunnes, MD; Jan Mannsverk, MD; Oliver Meyerdierks, MD; Svein Rotevatn, MD; Matti Niemelä, MD; Kari Kervinen, MD; Jan S. Jensen, MD; Anders Galløe, MD; Kjell Nikus, MD; Saila Vikman, MD; Jan Ravkilde, MD; Stefan James, MD; Jens Aarøe, MD; Antti Ylitalo, MD; Steffen Helqvist, MD; Iwar Sjögren, MD; Per Thayssen, MD; Kari Virtanen, MD; Mikko Puhakka, MD; Juhani Airaksinen, MD; Jens F. Lassen, MD; Leif Thuesen, MD; for the Nordic PCI Study Group

Conclusions—Independent of stenting strategy, excellent clinical and angiographic results were obtained with percutaneous treatment of de novo coronary artery bifurcation lesions with sirolimus-eluting stents. The simple stenting strategy used in the MV group was associated with reduced procedure and fluoroscopy times and lower rates of procedure-related biomarker elevation. Therefore, this strategy can be recommended as the routine bifurcation stenting technique. (***Circulation***. 2006;114:1955-1961.)

Safety

Safety in simple versus complex stenting of coronary artery bifurcation lesions. The Nordic Bifurcation Study 14-month follow-up results

Jan S. Jensen[1]; Anders Galløe[1], MD; Jens F. Lassen[2], MD; Andrejs Erglis[3], MD; Indulis Kumsars[3]; Terje K. Steigen[4], MD; Rune Wiseth[5], MD; Inga Narbute[3], MD; Pål Gunnes[6], MD; Jan Mannsverk[4], MD; Oliver Meyerdierks[7], MD; Svein Rotevatn[8], MD; Matti Niemelä[9], MD; Kari Kervinen[9], MD; Kjell Nikus[10], MD; Saila Vikman[10], MD; Jan Ravkilde[12], MD; Stefan James[11], MD; Jens Aarøe[12], MD; Antti Ylitalo[13], MD; Steffen Helqvist[14], MD; Iwar Sjögren[15], MD; Per Thayssen[16], MD; Kari Virtanen[17], MD; Mikko Puhakka[18], MD; Juhani Airaksinen[19], MD; Leif Thuesen[2]*, MD for the Nordic-Baltic PCI Study Group

Conclusions: After 14 months, two months after recommended cessation of dual antiplatelet therapy, the rates of stent thrombosis and major adverse cardiac events were low and independent of treatment complexity in patients treated with SES for coronary artery bifurcation lesions.

EuroInterv.2008;4:**229-233**

BBC one and Nordic I pooled analysis

Simple or Complex Stenting for Bifurcation Coronary Lesions

A Patient-Level Pooled-Analysis of the Nordic Bifurcation Study and the British Bifurcation Coronary Study

Miles W. Behan, DM, MRCP; Niels R. Holm, MD; Nicholas P. Curzen, PhD, FRCP; Andrejs Erglis, MD; Rodney H. Stables, MD, FRCP; Adam J. de Belder, MD, FRCP; Matti Niemelä, MD; Nina Cooter, MSc; Derek P. Chew, MPH, FRACP; Terje K. Steigen, MD; Keith G. Oldroyd, MD, FRCP; Jan S. Jensen, MD; Jens Flensted Lassen, MD; Leif Thuesen, MD; David Hildick-Smith, MD, FRCP

Conclusions—For bifurcation lesions, a provisional single-stent approach is superior to systematic dual stenting techniques in terms of safety and efficacy. A complex approach does not appear to be beneficial in more anatomically complicated lesions.
Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT 00376571 and NCT 00351260.
(***Circ Cardiovasc Interv***. 2011;4:57-64.)

Crush vs. Culotte BIF-II

Randomized Comparison of Coronary Bifurcation Stenting With the Crush Versus the Culotte Technique Using Sirolimus Eluting Stents

The Nordic Stent Technique Study

Andrejs Erglis, MD; Indulis Kumsars, MD; Matti Niemelä, MD; Kari Kervinen, MD; Michael Maeng, MD; Jens F. Lassen, MD; Pål Gunnes, MD; Sindre Stavnes, MD; Jan S. Jensen, MD; Anders Galløe, MD; Inga Narbute, MD; Dace Sondore, MD; Timo Mäkikallio, MD; Kari Ylitalo, MD; Evald H. Christiansen, MD; Jan Ravkilde, MD; Terje K. Steigen, MD; Jan Mannsverk, MD; Per Thayssen, MD; Knud Nørregaard Hansen, MD; Mikko Syvänne, MD; Steffen Helqvist, MD; Nikus Kjell, MD; Rune Wiseth, MD; Jens Aarøe, MD; Mikko Puhakka, MD; Leif Thuesen, MD; for the Nordic PCI Study Group

Conclusions—Both the crush and the culotte bifurcation stenting techniques were associated with similar and excellent clinical and angiographic results. Angiographically, there was a trend toward less in-segment restenosis and significantly reduced in-stent restenosis following culotte stenting. (***Circ Cardiovasc Intervent.*** **2009;2:27-34.)**

Crush vs. Culotte BIF-II, 36 months

Clinical Outcome After Crush Versus Culotte Stenting of Coronary Artery Bifurcation Lesions

The Nordic Stent Technique Study 36-Month Follow-Up Results

Kari Kervinen, MD,* Matti Niemelä, MD,* Hannu Romppanen, MD,*†
Andrejs Erglis, MD,‡ Indulis Kumsars, MD,‡ Michael Maeng, MD,§ Niels R. Holm, MD,§
Jens F. Lassen, MD,§ Pål Gunnes, MD,|| Sindre Stavnes, MD,|| Jan S. Jensen, MD,¶
Anders Galløe, MD,¶ Inga Narbute, MD,‡ Dace Sondore, MD,‡
Evald H. Christiansen, MD,§ Jan Ravkilde, MD,§ Terje K. Steigen, MD,#
Jan Mannsverk, MD,# Per Thayssen, MD,** Knud Nørregaard Hansen, MD,**††
Steffen Helqvist, MD,‡‡ Saila Vikman, MD,§§ Rune Wiseth, MD,|||| Jens Aarøe, MD,¶¶
Jari Jokelainen, MSc,##*** Leif Thuesen, MD,§ for the Nordic PCI Study Group

Conclusions At 36-month follow-up, the clinical outcomes were similar for patients with coronary bifurcation lesions treated with the culotte or the crush stent technique. (Nordic Bifurcation Study. How to Use Drug Eluting Stents [DES] in Bifurcation Lesions? NCT00376571) (J Am Coll Cardiol Intv 2013;6:1160–5) © 2013 by the American College of Cardiology Foundation

KISS OR NOT, «Nordic- Baltic III»

Randomized Comparison of Final Kissing Balloon Dilatation Versus No Final Kissing Balloon Dilatation in Patients With Coronary Bifurcation Lesions Treated With Main Vessel Stenting

The Nordic-Baltic Bifurcation Study III

Matti Niemelä, MD; Kari Kervinen, MD; Andrejs Erglis, MD; Niels R. Holm, MD; Michael Maeng, MD; Evald H. Christiansen, MD; Indulis Kumsars, MD; Sanda Jegere, MD; Andis Dombrovskis, MD; Pål Gunnes, MD; Sindre Stavnes, MD; Terje K. Steigen, MD; Thor Trovik, MD; Markku Eskola, MD; Saila Vikman, MD; Hannu Romppanen, MD; Timo Mäkikallio, MD; Knud N. Hansen, MD; Per Thayssen, MD; Lars Åberge, MD; Lisette O. Jensen, MD; Anders Hervold, MD; Juhani Airaksinen, MD; Mikko Pietilä, MD; Ole Frobert, MD; Thomas Kellerth, MD; Jan Ravkilde, MD; Jens Aarøe, MD; Jan S. Jensen, MD; Steffen Helqvist, MD; Iwar Sjögren, MD; Stefan James, MD; Heikki Miettinen, MD; Jens F. Lassen, MD; Leif Thuesen, MD; for the Nordic-Baltic PCI Study Group

Conclusions—MV stenting strategies with and without FKBD were associated with similar clinical outcomes. FKBD reduced angiographic side branch (re)stenosis, especially in patients with true bifurcation lesions. The simple no-FKBD procedures resulted in reduced use of contrast media and shorter procedure and fluoroscopy times. Long-term data on stent thrombosis are needed.

Clinical Trial Registration—URL: http://clinicaltrials.gov. Unique identifier: NCT00914199. (***Circulation***. 2011;123:79-86.)

KISS OR NOT BY FFR

Side branch fractional flow reserve measurements after main vessel stenting: a Nordic-Baltic Bifurcation Study III substudy

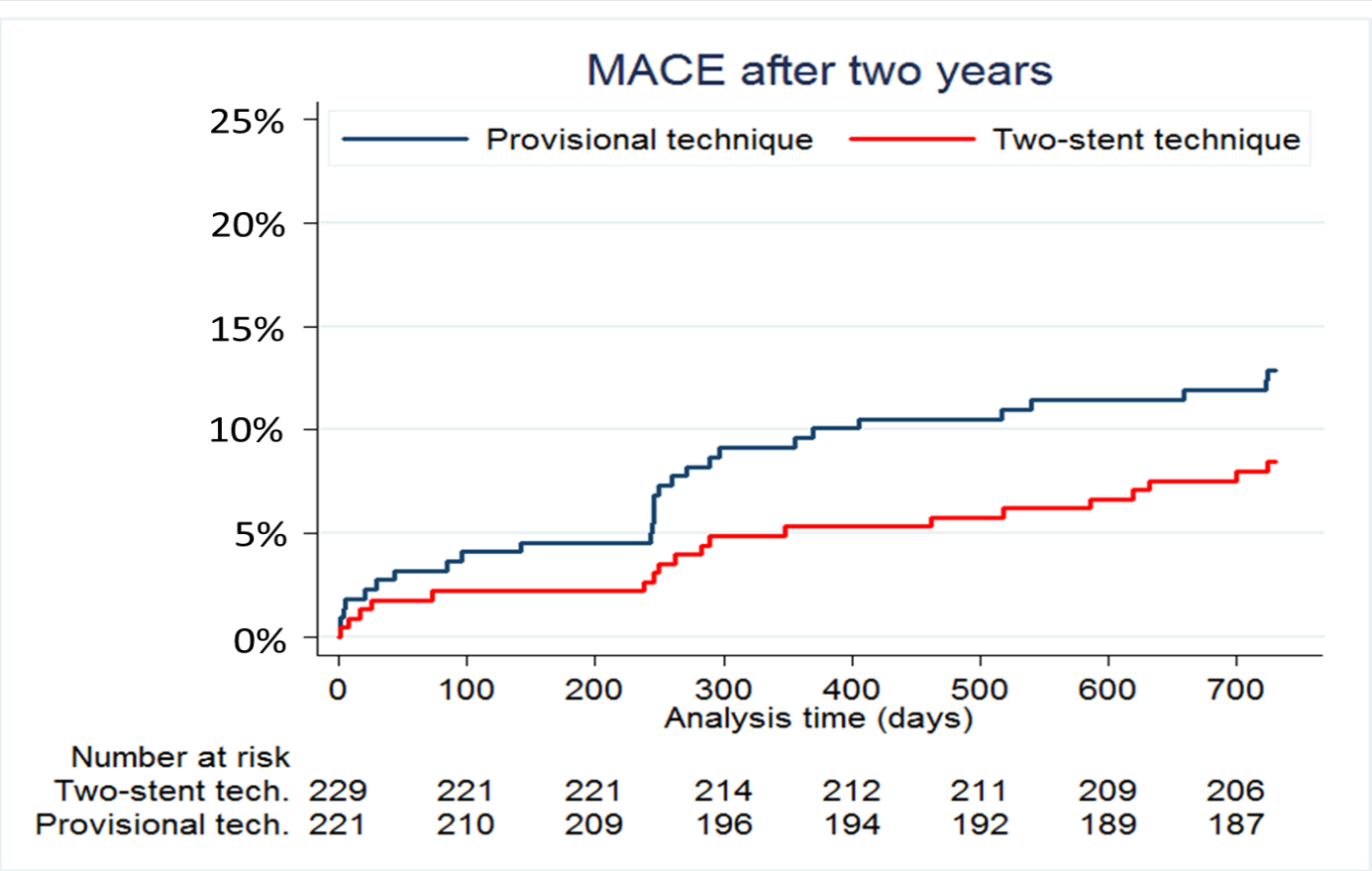
Indulis Kumsars[1]*, MD; Inga Narbute[1], MD; Leif Thuesen[2], MD; Matti Niemelä[3], MD; Terje K. Steigen[4], MD, PhD; Kari Kervinen[3], MD; Dace Sondore[1], MD; Niels R. Holm[2], MD; Jens F. Lassen[2], MD, PhD; Evald H. Christiansen[2], MD, PhD; Michael Maeng[2], MD, PhD; Sanda Jegere[1], MD; Dace Juhnevica[1], MD; Andrejs Erglis[1], MD, PhD; for the Nordic-Baltic PCI Study Group

Conclusions: FKBD in simple stenting of bifurcation lesions improved acute functional outcome in SB compared to leaving the SB jailed. No significant difference was detected at follow-up. In both groups there was no significant functional late loss during follow-up. Thus, both strategies were equally effective in ensuring that side branch jailing would not cause ischaemia in the long term.

Randomized comparison of provisional side branch stenting versus a two-stent strategy for treatment of true coronary bifurcation lesions involving a large side branch.

The Nordic-Baltic bifurcation study IV

Indulis Kumsars, Niels R. Holm, Matti Niemelä, Andrejs Erglis, Kari Kervinen, Evald H. Christiansen, Michael Maeng, Andis Dombrovskis, Vytautas Abraitis, Aleksandras Kibarskis, Thor Trovik, Gustavs Latkovskis, Dace Sondore, Inga Narbute, Christian Juhl Terkelsen, Markku Eskola, Hannu Romppanen, Mika Laine, Lisette Okkels Jensen, Mikko Pietilä, Pål Gunnes, Lasse Hebsgaard, Ole Frobert, Fredrik Calais, Juha Hartikainen, Jens Aarøe, Jan Ravkilde, Thomas Engstrøm, Terje K. Steigen, Leif Thuesen and Jens F. Lassen



Nordic I, BIF I, 5 Y follow up

Long-Term Results After Simple Versus Complex Stenting of Coronary Artery Bifurcation Lesions

Nordic Bifurcation Study 5-Year Follow-Up Results

Michael Maeng, MD,* Niels R. Holm, MD,* Andrejs Erglis, MD,† Indulis Kumsars, MD,† Matti Niemelä, MD,‡ Kari Kervinen, MD,‡ Jan S. Jensen, MD,§ Anders Galløe, MD,§ Terje K. Steigen, MD,‖ Rune Wiseth, MD,¶ Inga Narbute, MD,† Pål Gunnes, MD,# Jan Mannsverk, MD,** Oliver Meyerdierks, MD,†† Svein Rotevatn, MD,‡‡ Kjell Nikus, MD,§§ Saila Vikman, MD,§§ Jan Ravkilde, MD,‖‖ Stefan James, MD,¶¶ Jens Aarøe, MD,‖‖ Antti Ylitalo, MD,## Steffen Helqvist, MD,*** Iwar Sjögren, MD,††† Per Thayssen, MD,‡‡‡ Kari Virtanen, MD,§§§ Mikko Puhakka, MD,‖‖‖ Juhani Airaksinen, MD,¶¶¶ Evald H. Christiansen, MD,* Jens F. Lassen, MD,* Leif Thuesen, MD,* for the Nordic-Baltic Percutaneous Coronary Intervention Study Group

Conclusions At 5-year follow-up in the Nordic Bifurcation Study, the clinical outcomes after simple optional side branch stenting remained at least equal to the more complex strategy of planned stenting of both the main vessel and the side branch. (J Am Coll Cardiol 2013;62:30–4)

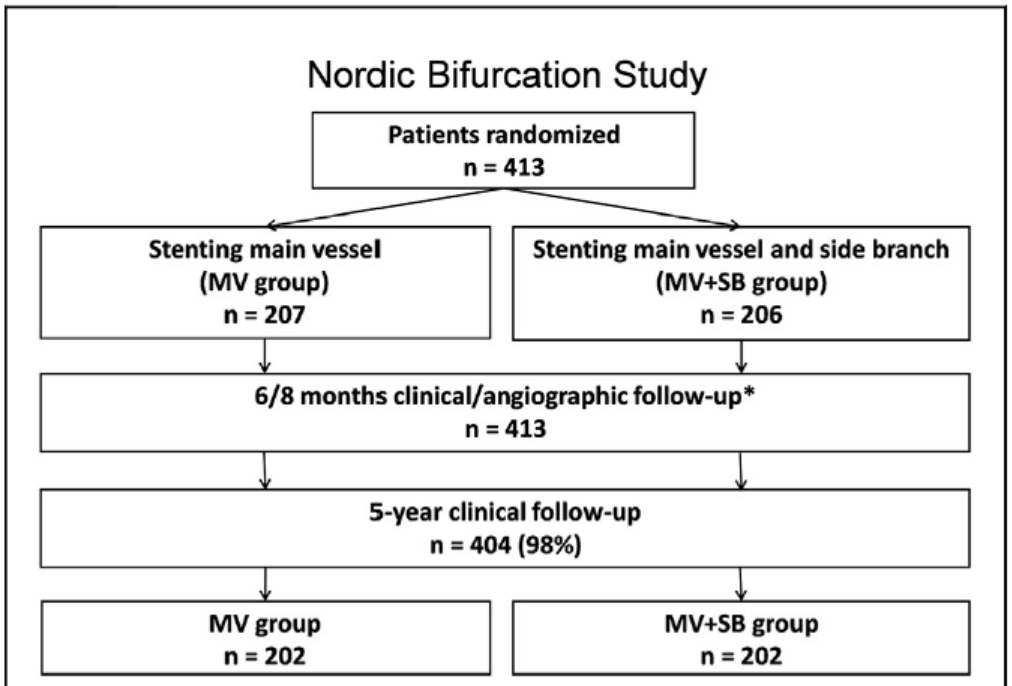


Figure 1 **5-Year Follow-Up Patient Flow Chart of the Nordic Bifurcation Study**

*A total of 307 patients had a quantitative coronary assessment at the index procedure and after 8 months. MV = main vessel; SB = side branch.

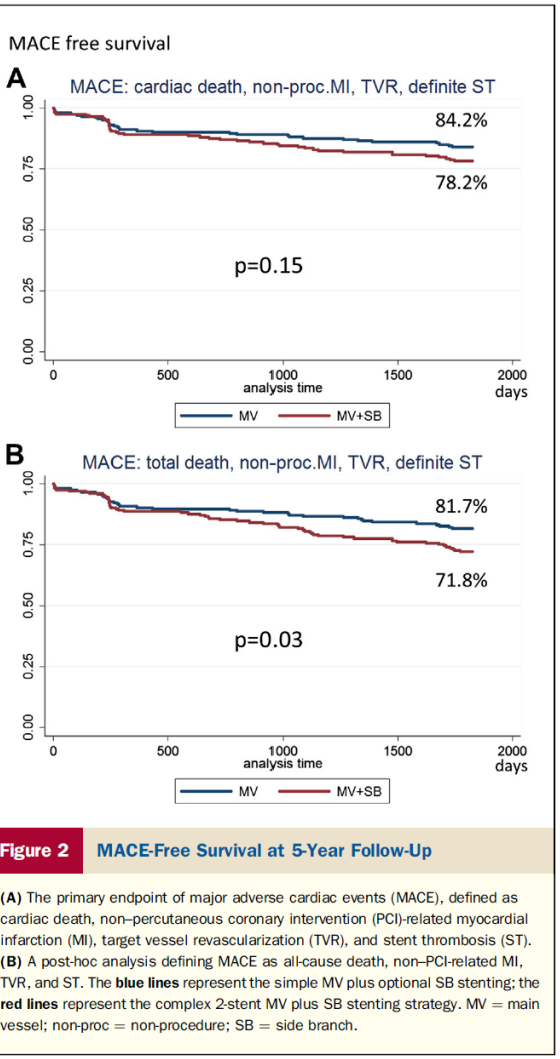


Figure 2 **MACE-Free Survival at 5-Year Follow-Up**

(A) The primary endpoint of major adverse cardiac events (MACE), defined as cardiac death, non–percutaneous coronary intervention (PCI)-related myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis (ST). **(B)** A post-hoc analysis defining MACE as all-cause death, non–PCI-related MI, TVR, and ST. The **blue lines** represent the simple MV plus optional SB stenting; the **red lines** represent the complex 2-stent MV plus SB stenting strategy. MV = main vessel; non-proc = non-procedure; SB = side branch.

Although the Kaplan-Meier curves of the combined safety and efficacy endpoint (MACE) separated over time, showing an absolute 6% difference in favor of the simple strategy at 5-year follow-up, this difference was not statistically different. However, a post-hoc analysis, substituting cardiac death with all-cause death in the MACE analysis, resulted in significantly more events in the MV plus SB group and added further support to the simple MV stenting plus optional SB stenting approach. Using all-cause death instead of cardiac death may be relevant, as late-occurring fatal events in elderly patients may be difficult to classify correctly.

BBC one and Nordic I pooled analysis,

Coronary bifurcation lesions treated with simple or complex stenting: 5-year survival from patient-level pooled analysis of the Nordic Bifurcation Study and the British Bifurcation Coronary Study

5-year survival

Miles W. Behan[1*], Niels R. Holm[2], Adam J. de Belder[3], James Cockburn[3], Andrejs Erglis[4], Nicholas P. Curzen[5], Matti Niemelä[6], Keith G. Oldroyd[7], Kari Kervinen[6], Indulis Kumsars[4], Paal Gunnes[8], Rodney H. Stables[9], Michael Maeng[2], Jan Ravkilde[10], Jan Skov Jensen[11], Evald H. Christiansen[2], Nina Cooter[3], Terje K. Steigen[12], Saila Vikman[13], Leif Thuesen[10], Jens Flensted Lassen[2], and David Hildick-Smith[3]

Conclusion For coronary bifurcation lesions, a provisional single-stent approach appears to be associated with lower long-term mortality than a systematic dual stenting technique.

Eur Heart J. 2016 Jun 21;37(24):1923-8. doi: 10.1093/eurheartj/ehw170. Epub 2016 May 8

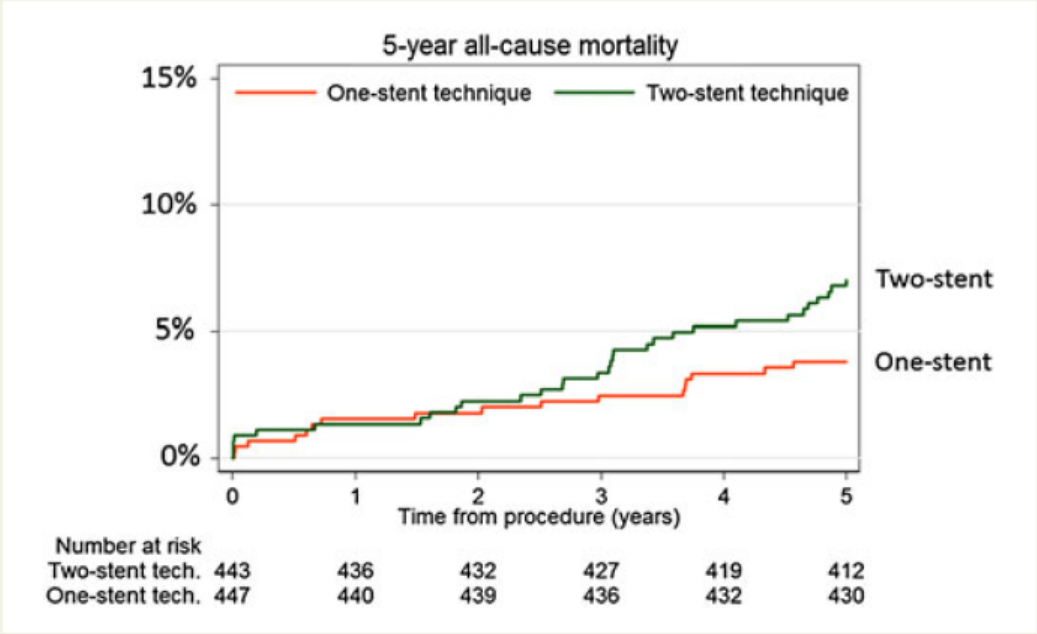


Figure 2 Five-year survival.

All-cause death was lower in the Simple group in comparison to the complex group [17 patients (3.8%) vs. 31 patients (7.0%); $P = 0.04$]. The Kaplan–Meier curve for survival is shown in *Figure 2*.

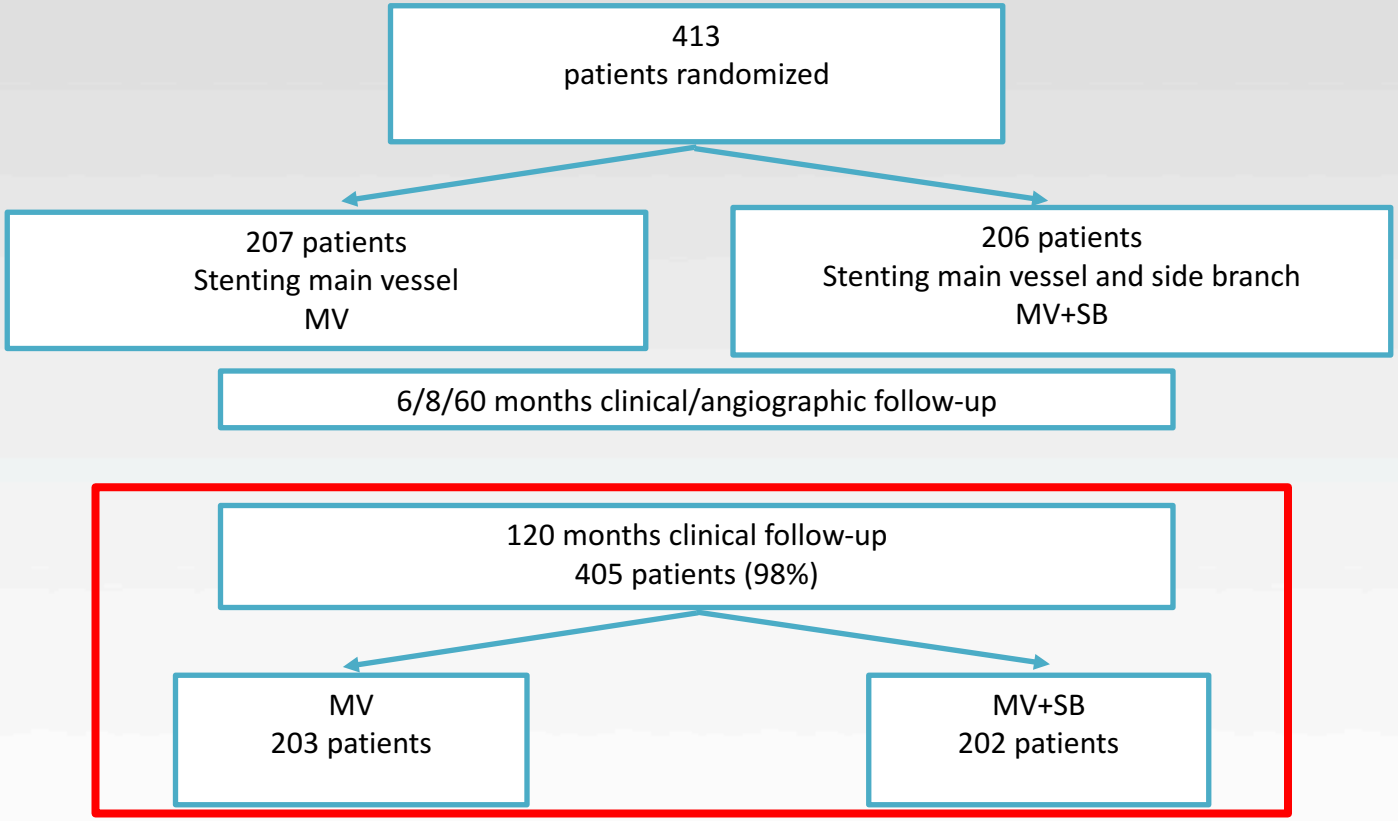
Ten-year All-cause Mortality after

Simple versus Complex Stenting of Coronary Artery Bifurcation Lesions in the Randomized Nordic Bifurcation Study

Introduction

- Patients with stable or unstable angina pectoris, or stabilized myocardial infarction, and a coronary bifurcation lesion with a reference diameter in the main vessel ≥3.0 mm and side branch ≥2.25 mm were eligible.
- The study stent was the sirolimus eluting Cypher® stent (Cordis, US). First generation DES.
- Follow-up for all-cause mortality after 10 y was obtained by national or local health registries, patient files, or by clinically follow-up, as applicable

Nordic Bifurcation Study 10 y

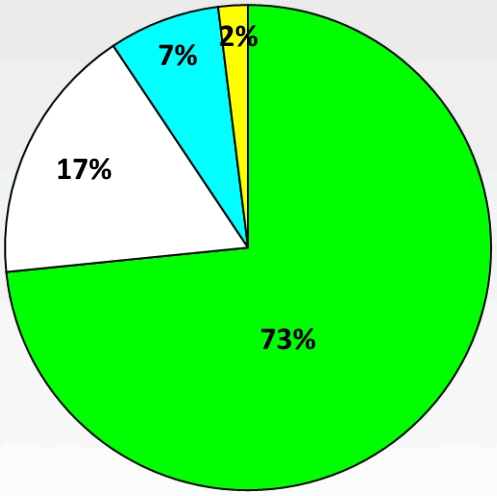


Baseline demographics

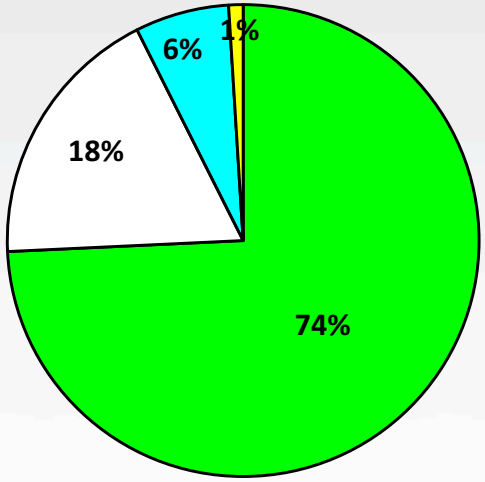
	MV (n=202)	MV+SB (n=203)	P-value
Age (yrs)	63±10	63±10	0.49
Male sex (%)	76	78	0.72
Diabetes (%)	13	12	0.76
Smoker (%)	28	22	0.27
Hypertension (%)	54	58	0.42
Statin Tx (%)	78	72	0.17
Family history (%)	58	54	0.56
History of PCI (%)	25	25	1.00
History of CABG (%)	4	3	0.79

Vessels treated

MV



MV+SB



LAD
Cx
RCA
LM

Angiography

Visual assessment

	MV (n=201)	MV+SB (n=196)	P-value
MV les. length (mm)	17.9±8.2	17.4±7.4	0.44
MV stent length (mm)	23.4±8.6	23.1±8.2	0.77
SB les. length (mm)	6.0±4.9	6.3±4.7	0.47
MV ref. diam. (mm)	3.3±0.4	3.3±0.4	0.89
SB ref. diam. (mm)	2.6±0.6	2.6±0.3	0.97

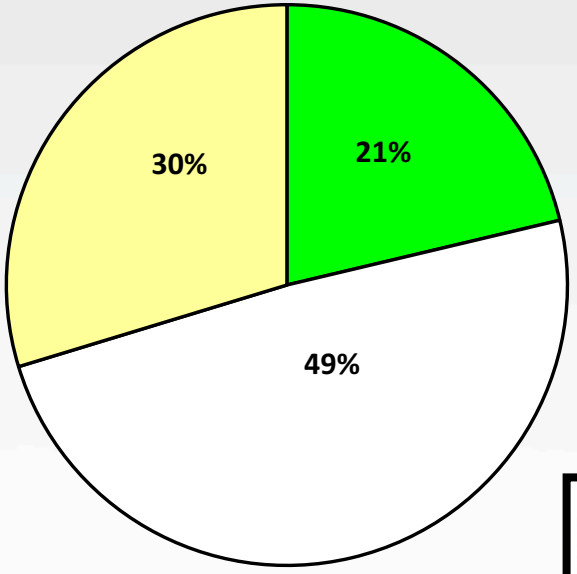
Procedural data II

	MV (n=203)	MV+SB (n=202)	P-value
MV stented (%)	99.5	98.5	0.37
SB stented (%)	4.4	95.0	<0.0001
Kissing balloon (%)	32	74	<0.0001
Tx successful (%)	97	94	0.25

(Residual stenosis <30% of MV + TIMI flow III in SB)

Procedural data III

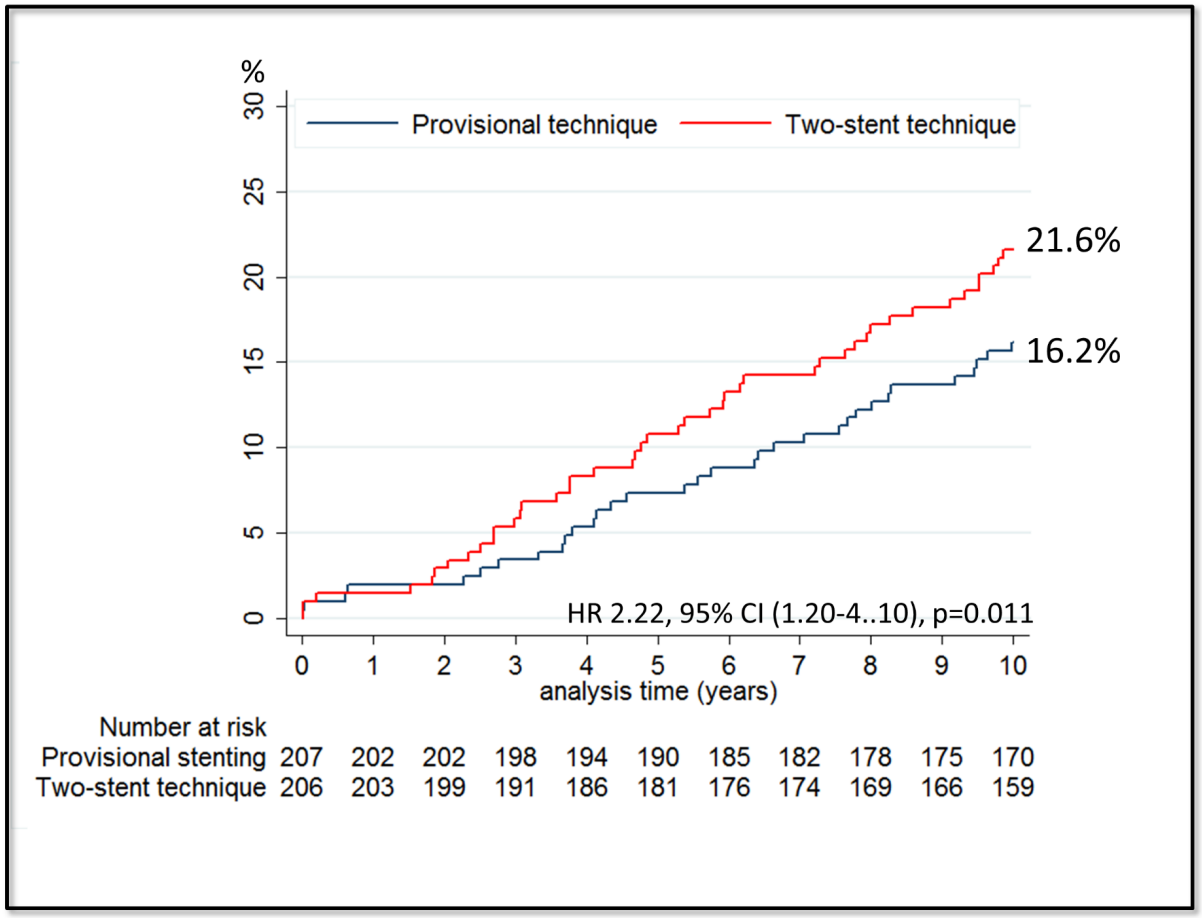
Stent technique in the MV+SB treatment group



- Culotte
- Crush
- Other

The Nordic-Baltic PCI Study Group

10-year all-cause mortality in the Nordic Bifurcation Study



p= 0.011

Conclusion

Very long-term all-cause mortality was significantly increased in patients treated with planned two-stent techniques compared to simple provisional stenting in the randomized Nordic Bifurcation Study.

BIFURCATIONS IN «NORSTENT»

- 9013 patients who had stable or unstable coronary artery disease randomly assigned PCI with either contemporary drug-eluting stents or bare-metal stents. In the DES group, 96% of the patients received either everolimus- or zotarolimus-eluting stents.
- We have identified 1400 bifurcations where a single stent strategy was planned in the NORSTENT trial. Randomized to BMS or DES, 700 in each group of stents.

- I hope to present the data in 2018.

Thank You!


Tromsø ,
The Northernmost
University in the World
UiT, the Arctic University
of Norway

NORSTENT

- The primary outcome was a composite of death from any cause and nonfatal spontaneous myocardial infarction after a median of 5 years of follow-up. Secondary outcomes included repeat revascularization, stent thrombosis, and quality of life.