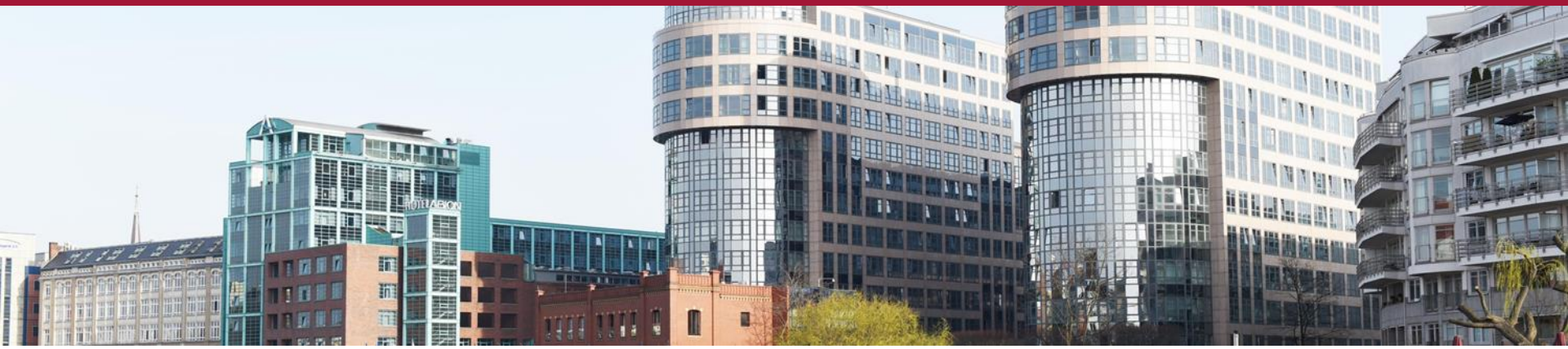

Klinischer und praktischer Einsatz von ARNI- was sagen die Leitlinien zum Stellenwert

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Gesunde Probanden

Eur J Clin Pharmacol (2017) 73:409–416
DOI 10.1007/s00228-016-2189-8

REVIEW

Who is a 'healthy subject'?—consensus results on pivotal eligibility criteria for clinical trials

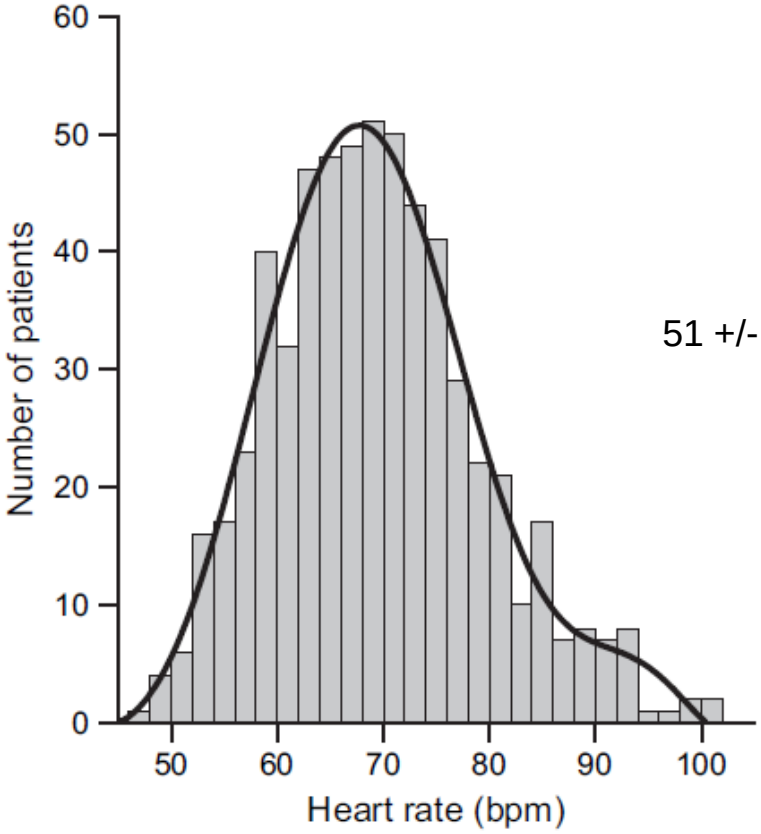
Kerstin Breithaupt-Groegler[1] · Christoph Coch[2] · Martin Coenen[2] · Frank Donath[3] · Katharina Erb-Zohar[4] · Klaus Francke[5] · Karin Goehler[6] · Mario Iovino[7] · Klaus Peter Kammerer[7] · Gerd Mikus[8] · Jens Rengelshausen[9] · Hildegard Sourgens[10] · Reinhard Schinzel[11] · Thomas Sudhop[12] · Georg Wensing[13]

Herzfrequenz bei gesunden Probanden

First-in-human trials: A resting heart rate **between 50 and 90** beats per minute (bpm) is recommended as inclusion criterion. Subjects with heart rate values **between 45 and 50 bpm may be enrolled** in case they have a normal thyroid function, no clinical symptoms associated with the bradycardia and no apparent signs of other diseases causing bradycardia (e.g. hypothyroidism).

Breithaupt-Groegler et al. 2017

Normale Herzfrequenz in Ruhe

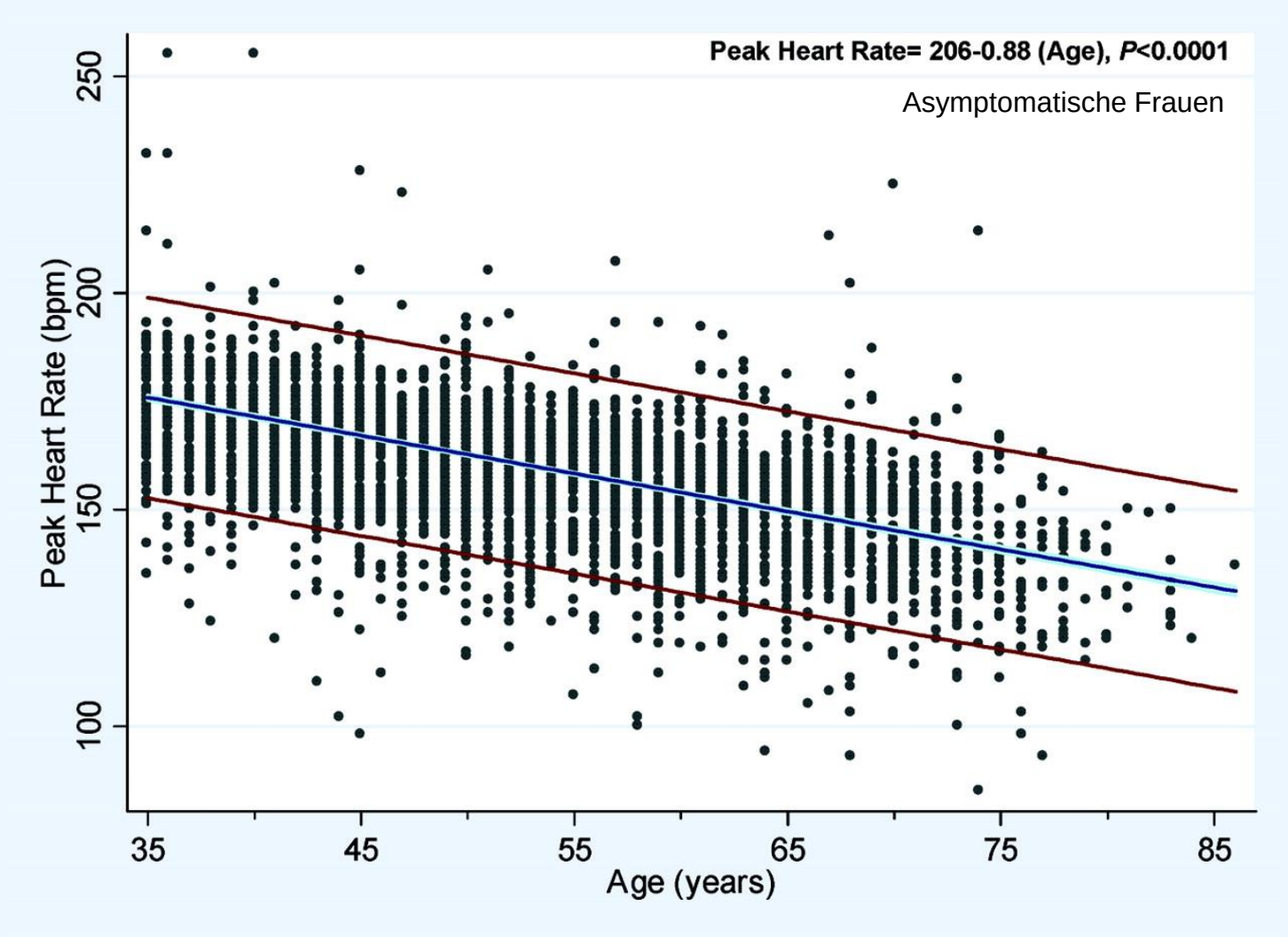


51 +/- 6 Jahre

Figure 1 Distribution of heart rate in random sample of middle-aged subjects.

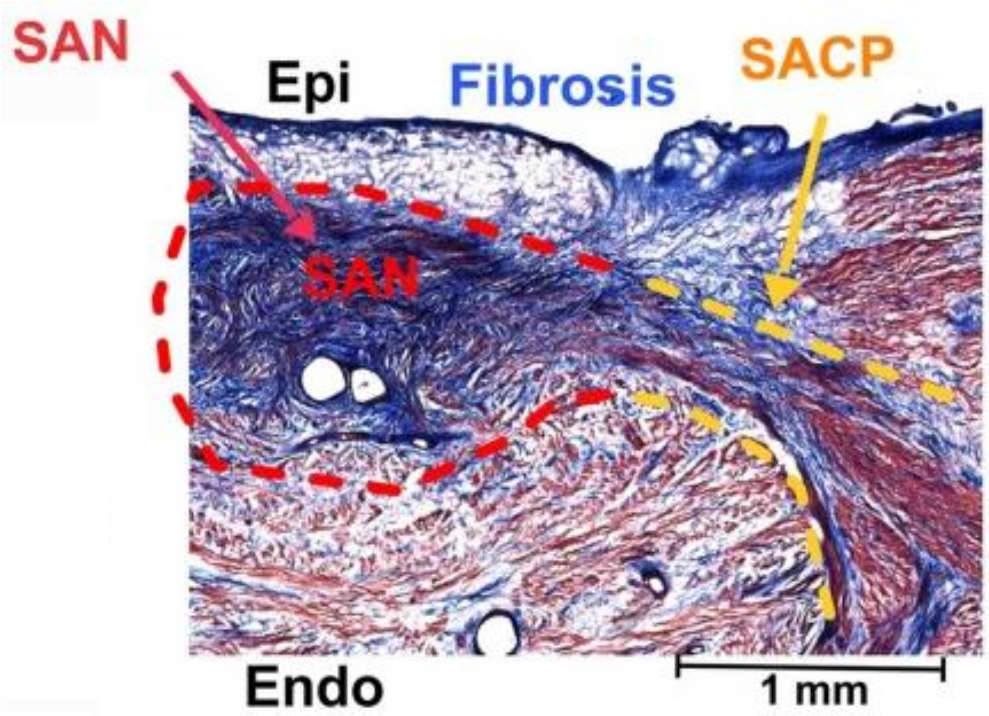
Still et al. 2005

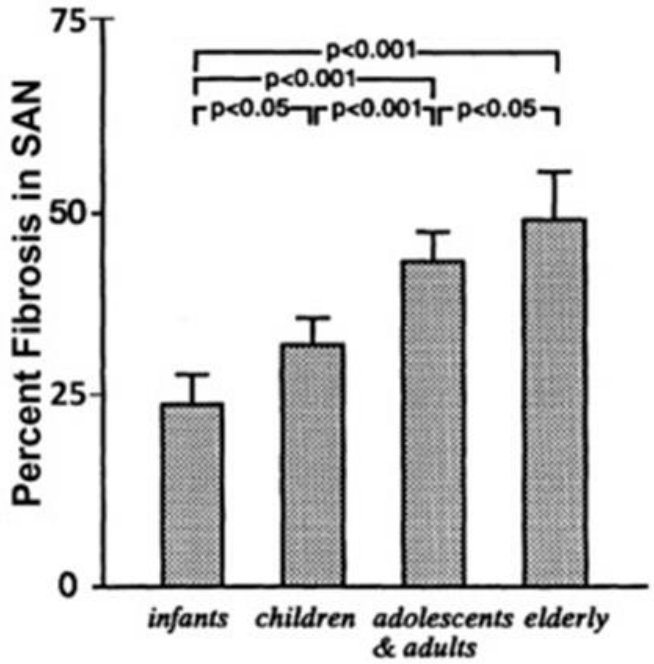
Maximale Herzfrequenz und Alter



Gulati et al. 2010

Sinuatriale Fibrose

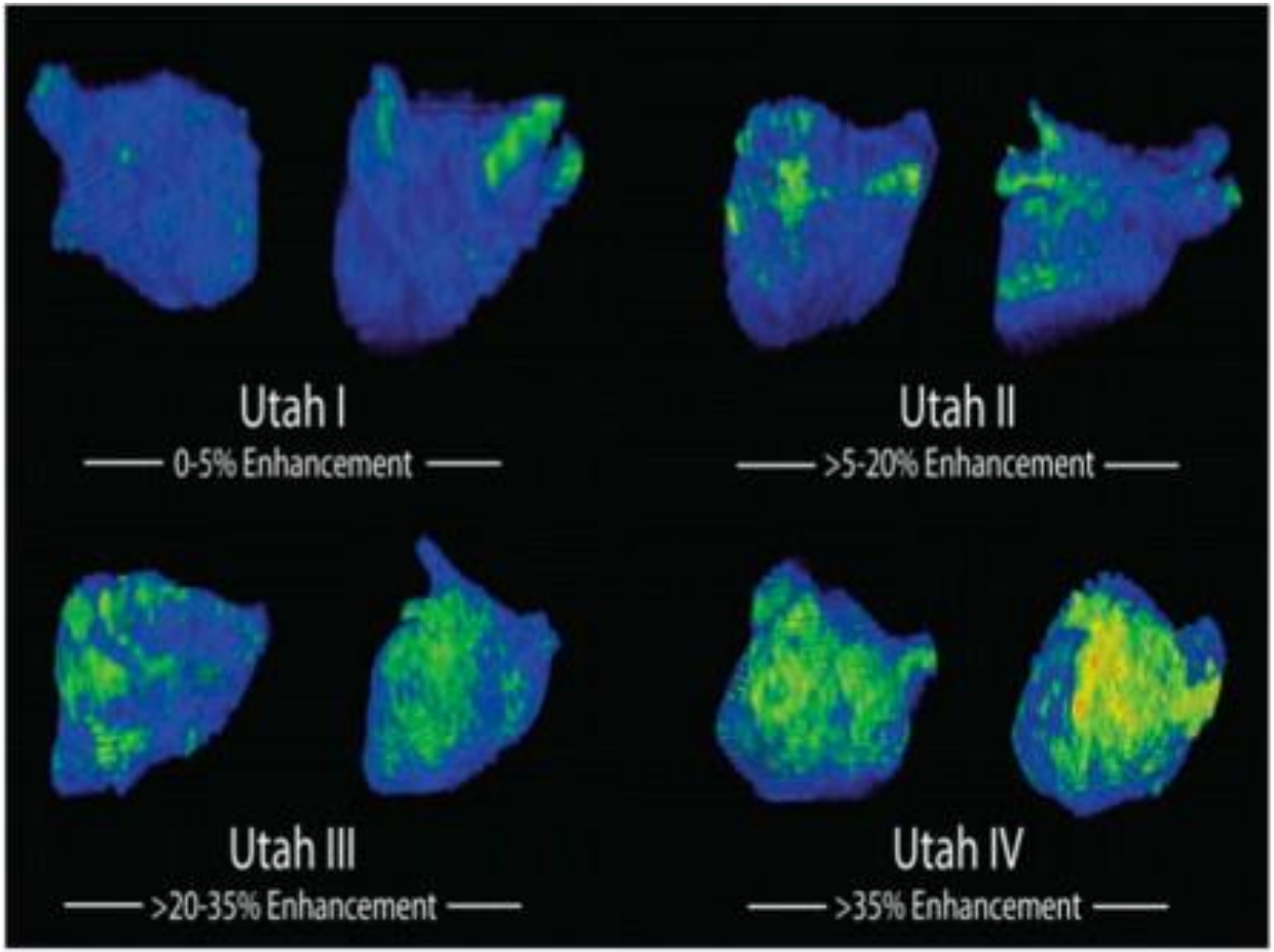




SAN: Sinusknoten (sinuatrial node)
SACP: sinuatriale Leitungswege (sinuatrial conduction pathways)

Csepe et al, 2015

Atriale Fibrose und Vorhofflimmern



Marrouche et al. 2014

Sport und Rhythmusstörungen

Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists

Sylvette Baldesberger[1], Urs Bauersfeld[2], Reto Candinas[1], Burkhardt Seifert[3], Michel Zuber[4], Manfred Ritter[5], Rolf Jenni[6], Erwin Oechslin[6], Pia Luthi[1], Christop Scharf[1], Bernhard Marti[7], and Christine H. Attenhofer Jost[1]*

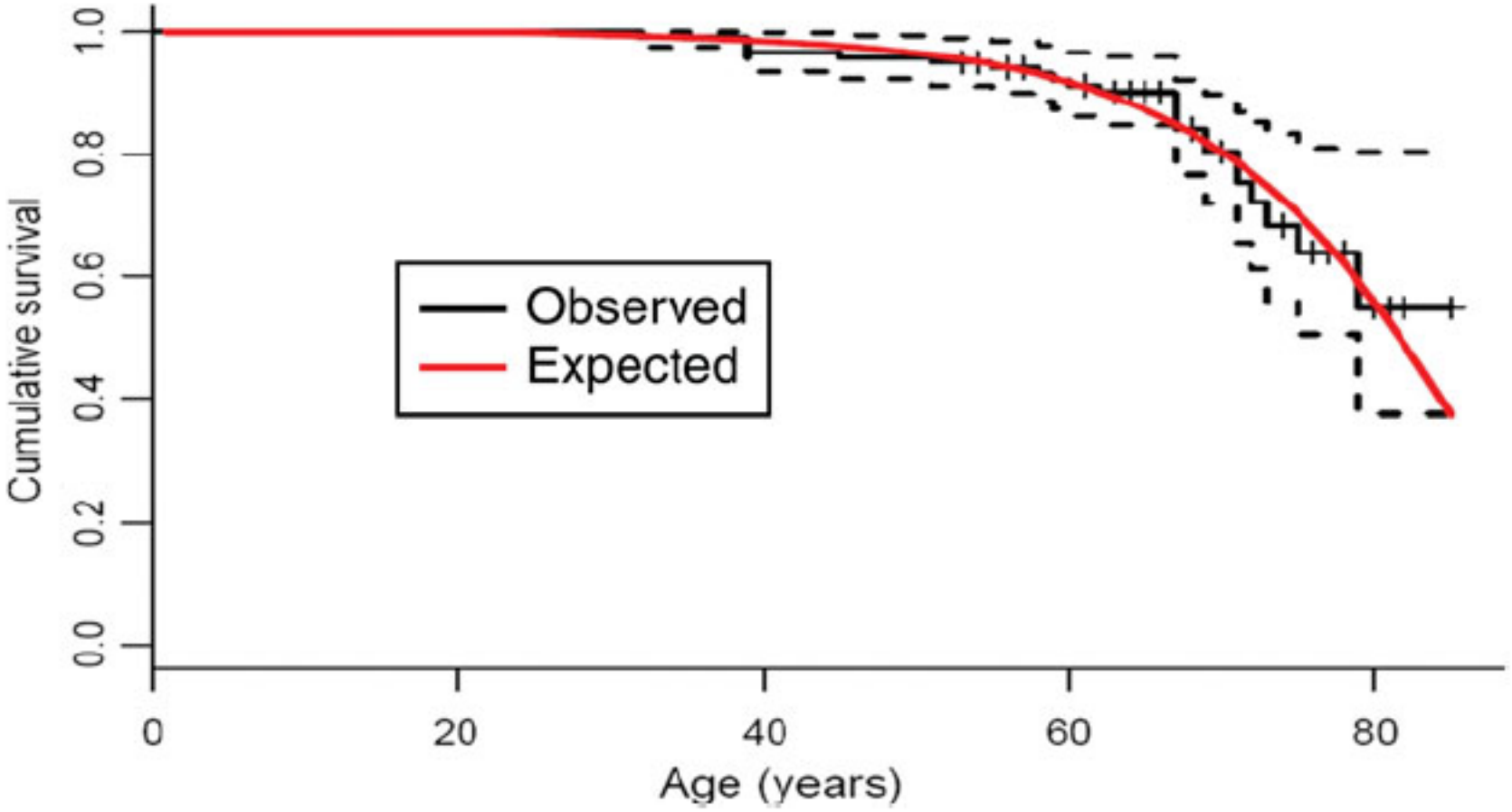
[1]Cardiovascular Center Zurich, Klinik Im Park, Seestr. 220, 8027 Zurich, Switzerland; [2]Division of Cardiology, University Children's Hospital, Zurich, Switzerland; [3]Department of Biostatistics University of Zurich, Zurich, Switzerland; [4]Outpatient Clinic Othmarsingen, Zurich, Switzerland; [5]HerzZentrum Hirslanden, Zurich, Switzerland; [6]Division of Cardiology, University Hospital Zurich, Zurich, Switzerland; [7]Institute of Sports Science Magglingen, Zurich, Switzerland

Received 6 February 2007; revised 16 October 2007; accepted 5 November 2007; Online publish-ahead-of-print 7 December 2007

Among all 134 former Swiss professional cyclists [hereafter, former athletes (FAs)] participating at least once in the professional bicycle race Tour de Suisse in 1955–1975, 62 (46%) were recruited for the study. The control group consisted of 62 male golfers matched for age, weight, hypertension, and cardiac medication. All participants were screened with history, clinical and echocardiographic examination, ECG, and 24 h ECG. The time for the last bicycle race of FAs was 38 ± 6 years. The mean age at examination was 66 ± 6 years in controls and 66 ± 7 years in FAs ($P = 0.47$). The percentage of study participants with >4 h current cardiovascular training

Baldesberger et al. 2008

Lebenserwartung (Radrennfahrer)



Baldesberger et al. 2008

Befund im Ruhe-EKG bei früheren Athleten

	FAs ($n = 62$)	Controls ($n = 62$)	*P*-value
Heart rate, b.p.m.	58 ± 10	63 ± 9	0.01
PR interval, ms	186 ± 37	177 ± 24	0.14
QRS duration, ms	102 ± 20	95 ± 13	0.027
Corrected QT interval, ms	416 ± 27	404 ± 18	0.004
Left bundle branch block	0	0	
Left anterior hemiblock, *n* (%)	3 (5)	3 (5)	1.0
Left posterior hemiblock, *n* (%)	0	1 (2)	1.0
RBBB complete, *n* (%)	0	3 (5)	0.24
RBBB incomplete, *n* (%)	2 (3)	1 (2)	1.0
AV block, *n* (%)	8 (13)	9 (15)	1.0
First degree	7 (11)	8 (13)	
Second degree	0	1 (2)	
Third degree, *n* (%)	1 (2)	0	
Atrial flutter or fibrillation, *n* (%)	6 (10)	0	0.028

Baldesberger et al. 2008

Holter-Befunde bei früheren Athleten

	FAs ($n = 62$)	Controls ($n = 62$)	*P*-value
Heart rate, mean, b.p.m.	66 ± 9	70 ± 8	0.004
Heart rate, minimal, b.p.m.	49 ± 8	51 ± 6	0.05
Heart rate, maximal, b.p.m.	124 ± 26	124 ± 17	0.97
Heart rate <50 b.p.m. during the day, *n* (%)	20 (32)	6 (10)	0.004
Heart rate <40 b.p.m.			
Ever, *n* (%)	6 (10)	1 (2)	0.11
During the day, *n* (%)	2 (3)	0	0.49
During the night, *n* (%)	6 (10)	1 (2)	0.11
Maximal RR interval, ms (mean)	1761 ± 702	1499 ± 223	0.007
median (range)	1565 (1031–5300)	1500 (1100–2160)	
Maximal RR interval >2.5 s	4 (6%)	0	0.12

Baldesberger et al. 2008

Supraventrikuläre Arrhythmien bei früheren Athleten

	FAs ($n = 62$)	Controls ($n = 62$)	*P*-value
Atrial premature complexes per 24 h			
Median (range)	18 (0–2616)	17 (1–6135)	0.35
Atrial premature complexes			
None <1/h, *n* (%)	35 (56)	39 (63)	
Rare, *n* (%)	23 (37)	19 (31)	
Occasional, *n* (%)	3 (5)	2 (3)	
Frequent, *n* (%)	1 (2)	2 (3)	
Number of subjects with SVT, *n* (%)	21 (34)	19 (31)	0.82
Number of runs of SVT			
Mean	0.7 ± 1.3	0.7 ± 1.4	0.88
Median (range)	0 (0–7)	0 (0–7)	

Baldesberger et al. 2008

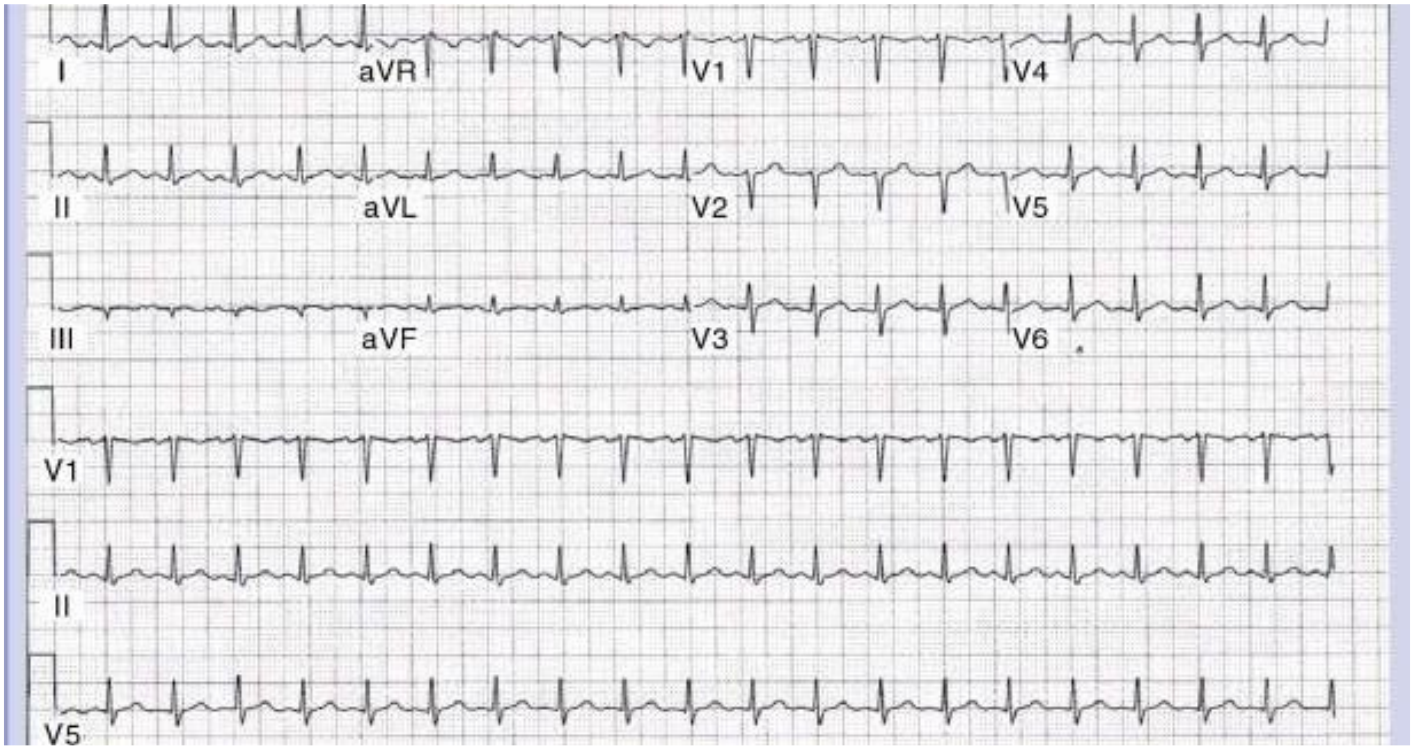
Ventrikuläre Arrhythmien bei früheren Athleten

	FAs ($n = 62$)	Controls ($n = 62$)	*P*-value
Number of subjects with VPCs, *n* (%)	28 (45)	22 (35)	0.12
Number of VPCs per 24 h			
Total	337 ± 1054	390 ± 1211	0.59[a]
Median (range)	32 (0–7780)	67 (0–7792)	
None/rare VPCs	49	48	
Occasional VPCs	10	10	
Frequent VPCs	3	4	
Couplets of VPC			
Mean	12 ± 72	8 ± 33	0.70*
Median (range)	0 (0–569)	0 (0–222)	
Subjects with VT	9 (15%)	2 (3%)	0.05

Baldesberger et al. 2008

Sport ist Mord?

Sinustachykardie



115/min; 38-jährige Patientin mit Palpitationen seit 3 Wochen

Inadäquate Sinustachykardie

Inadäquate Sinustachykardie

Definition: Sinusfrequenz > 100/min tragsüber und > 90/min im 24h-EKG

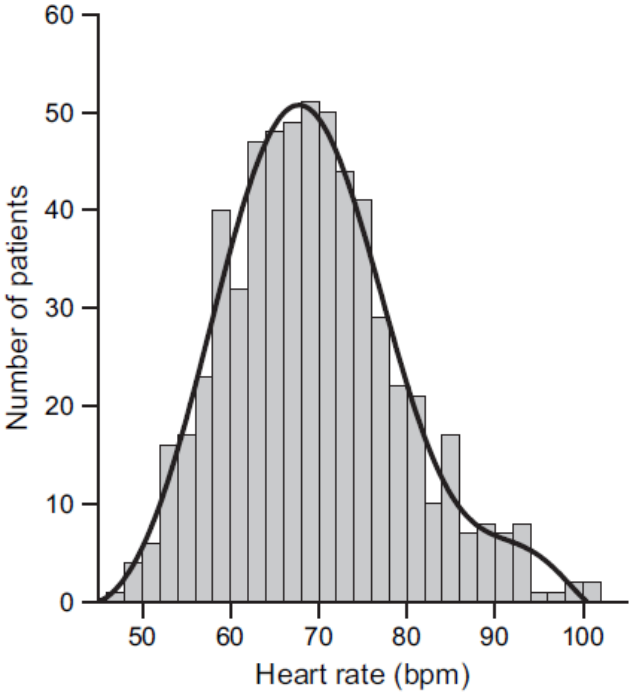
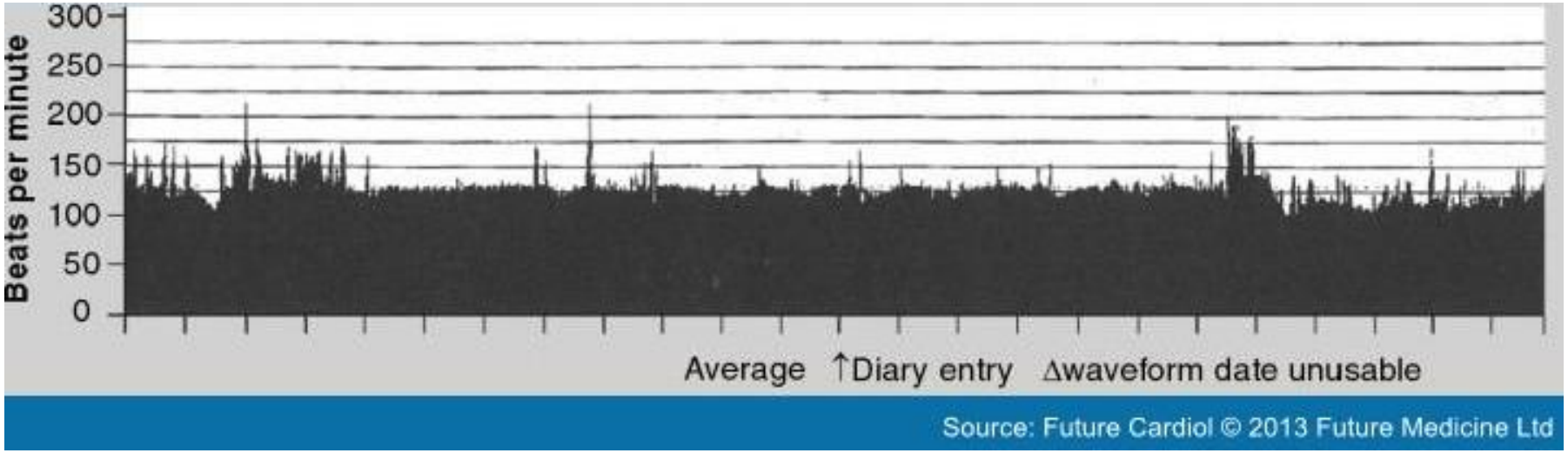


Figure 1 Distribution of heart rate in random sample of middle-aged subjects.

Still et al. 2005

Inadäquate Sinustachykardien



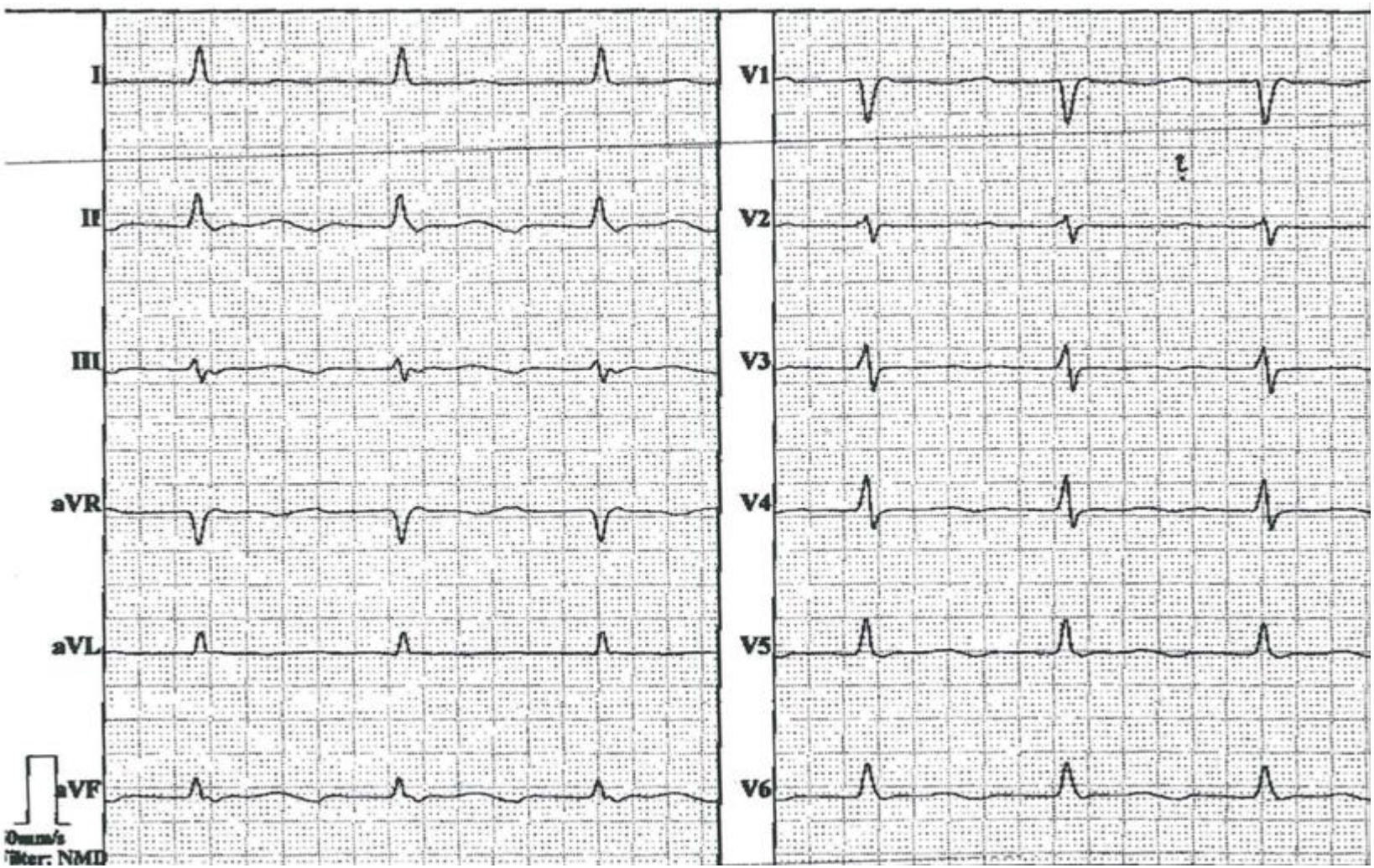
Mittlere Herzfreqeunz 130/min (102 – 213/min)

Inadäquate Sinustachykardie

- Definition: Sinusfrequenz > 100/min tragsüber und > 90/min im 24h-EKG
- Prävalenz: bis zu 1,2% in Stichproben* (mittleres Lebensalter)
- Klinik
  - Symptamtik steht im Vporedergrund
    Prognoseverschlachterung bislang nicht nachgeweisen
  - im Langzeitverlauf oft spontane Frequenzabnahme

*Still et al. 2005

Fall: 12-Kanal-EKG



Frequenz 104/min; 66-jährige Patientin

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Fall: Belastungs-EKG

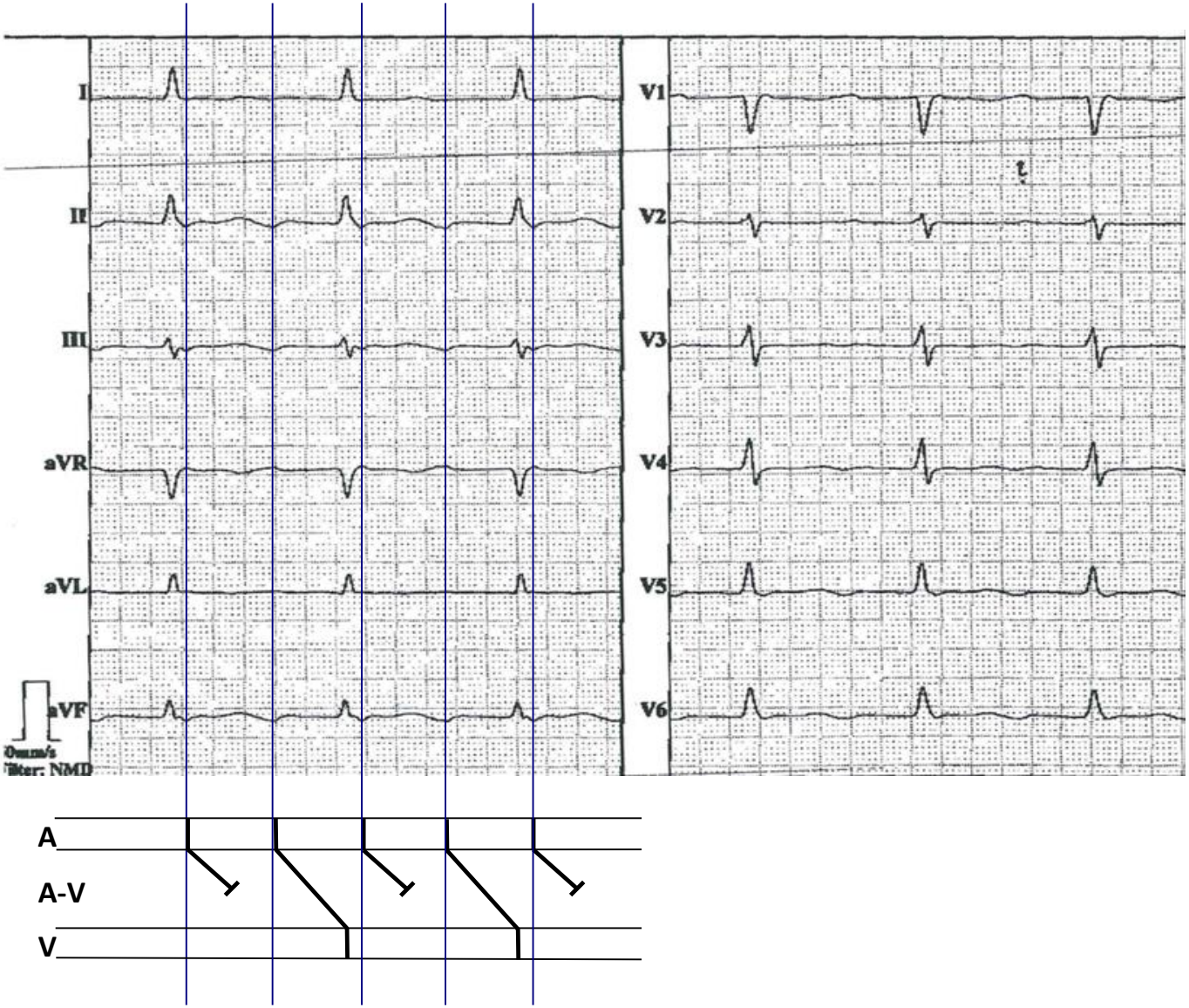
Stufe	Zeit	Dauer		Last [Watt]	Drehz. [/min]	METs	Blutdruck [mmHg]	Herzfrequ. [/min]	ST-Ampl. aVL, J+80ms [mm]	ST-Anstieg aVL [mm/ms]	Anz. VES	Bemerkungen
Referenz							115/85	100	-0.15	-0.08		Q-Zk 98%
Belastung 1	0:00	2:00		25	15	2.5					0	
	1:35						110/85					98%
	2:00			50	39	3.9		88	-0.26	-0.04		
Belastung 2	2:00	1:49		50	41	3.9					3	
	3:29						115/85					
	3:49			25	28	2.5		107	-0.30	0.00		99%
Erholung 1	3:49	1:58		25	28	2.5					0	
	4:35						130/85					
	5:47			25	0	2.5		104	-0.21	-0.11		99%
Erholung 2	5:47	0:40		25	0	2.5					0	
	6:06						100/80					
	6:27			25	0	2.5		103	-0.26	-0.13		99%

www.fokus-ekg.de

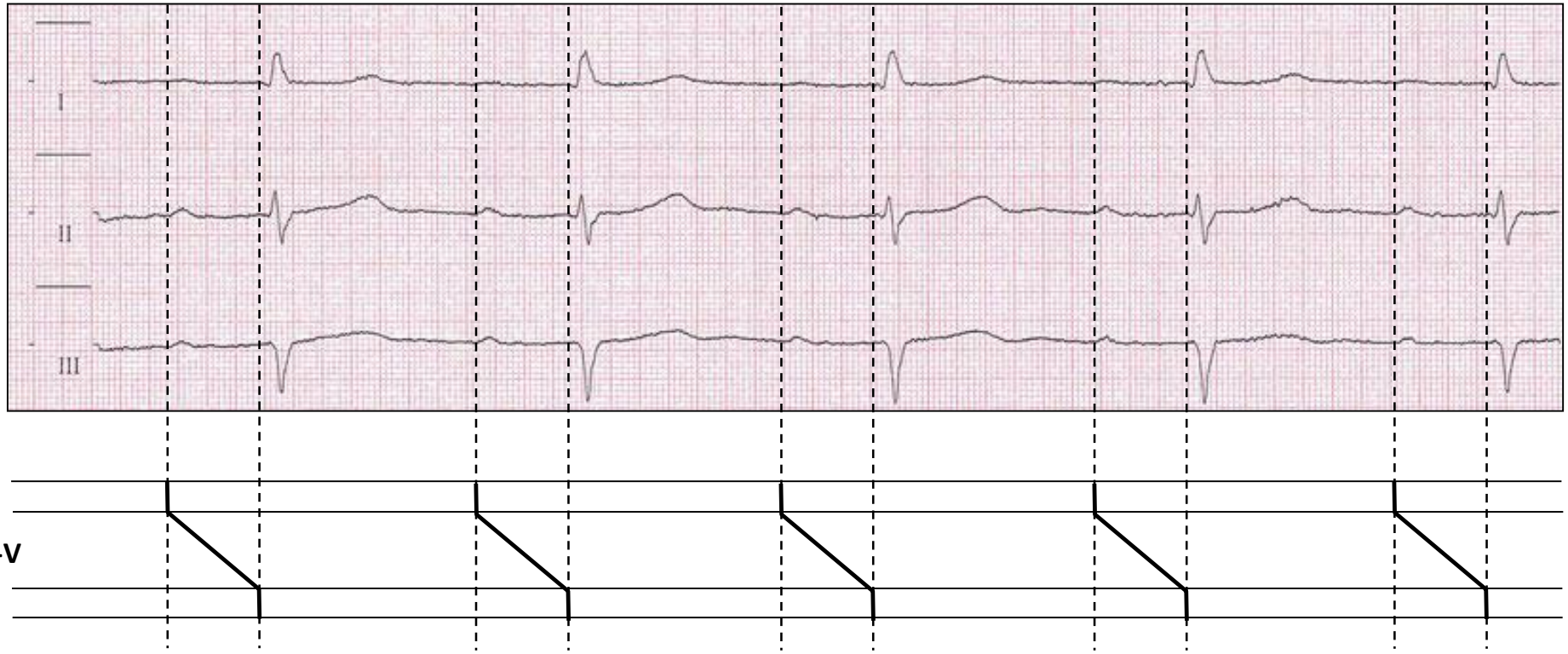
?

www.fokus-ekg.de

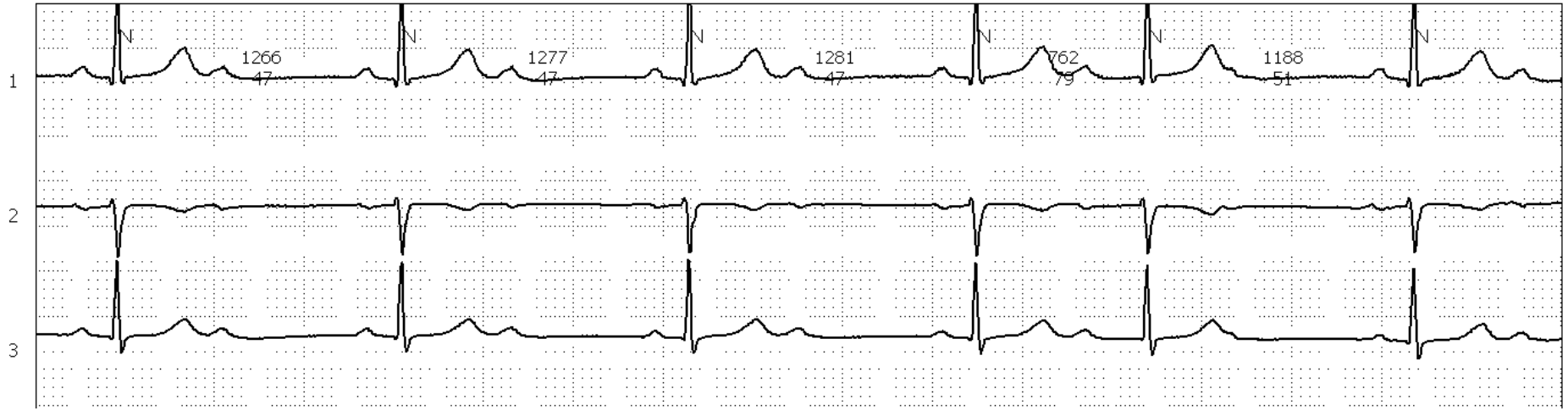
Fall: Atriale Tachykardie (104/min)



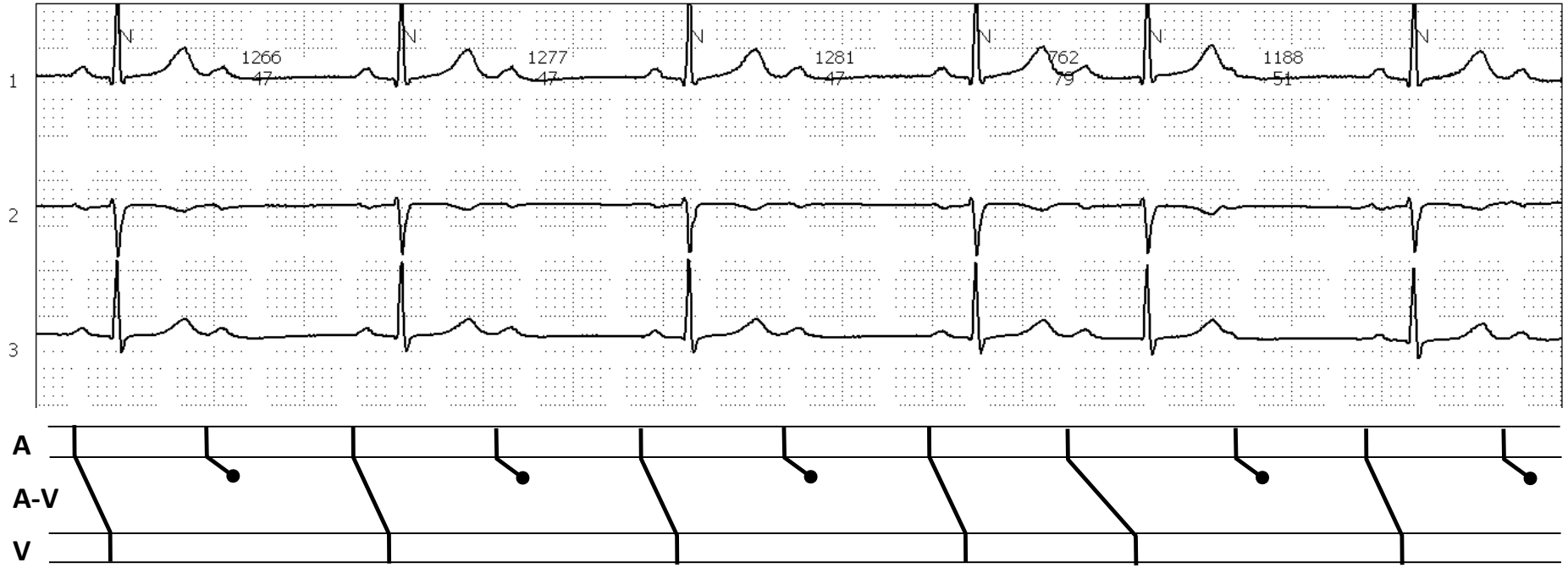
Leiterdiagramm bei Sinusrhythmus



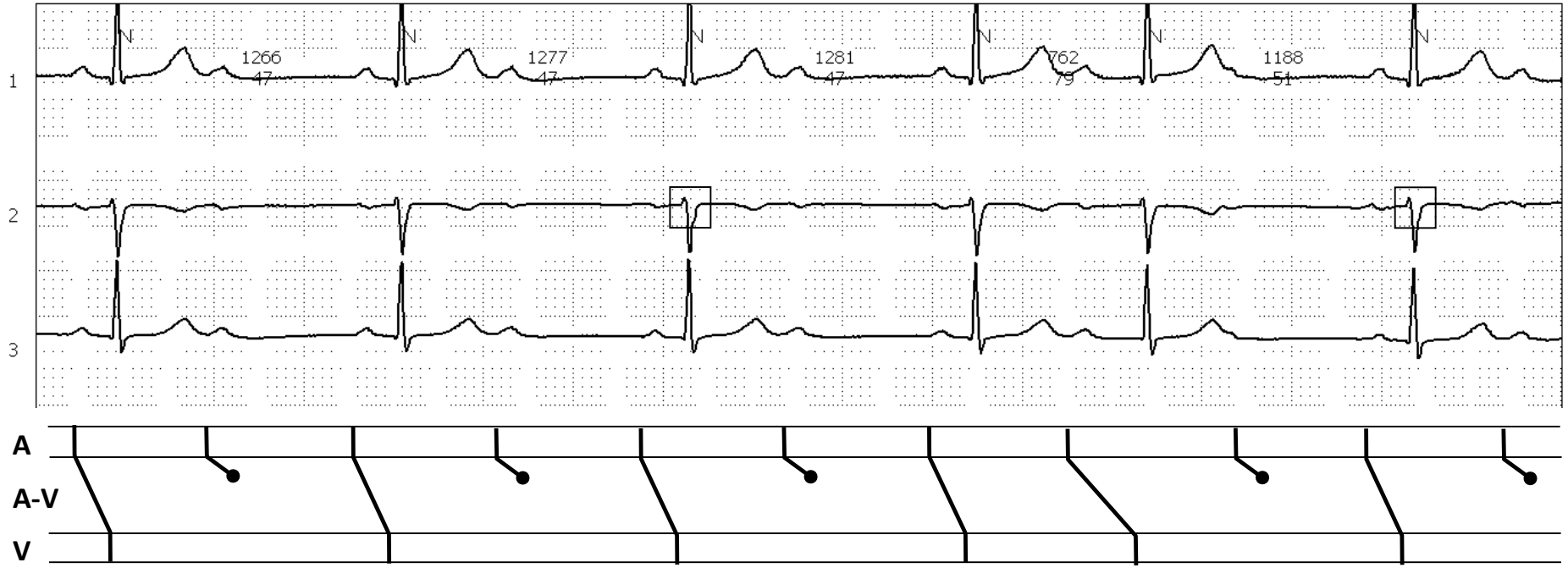
?


1
2
3
N
1266
47
N
1277
47
N
1281
47
N
762
79
N
1188
51
N

?

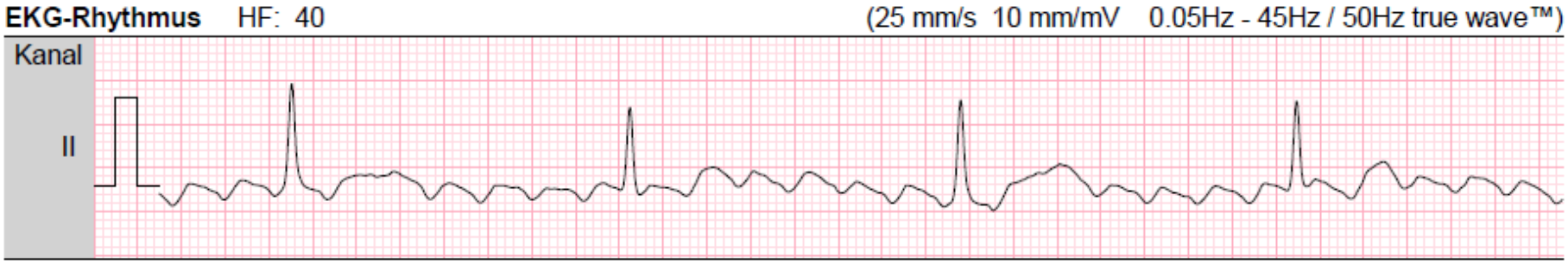

1
2
3
N
1266
47
1277
47
1281
47
762
79
1188
51
A
A-V
V

AV-Block II. Grades Typ Wenkebach und 2:1



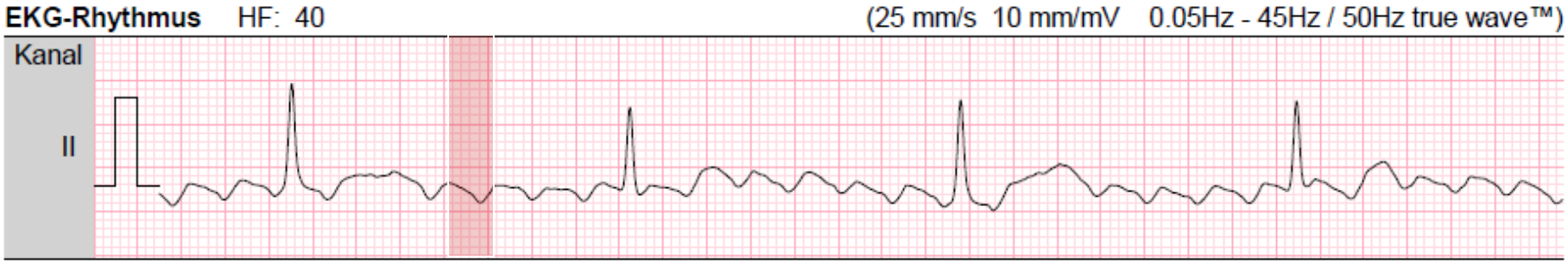
Vorhofflattern

Langsame Überleitung oder AV-Block III. Grades?



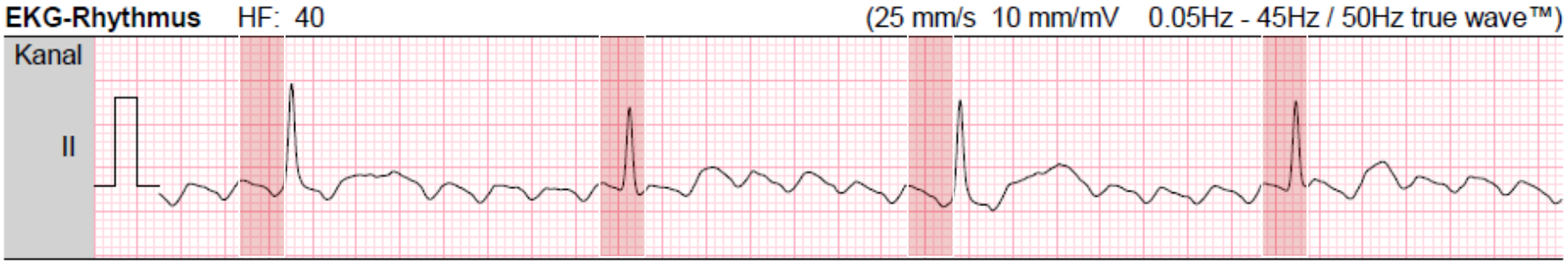
Vorhofflattern

Langsame Überleitung oder AV-Block III. Grades?



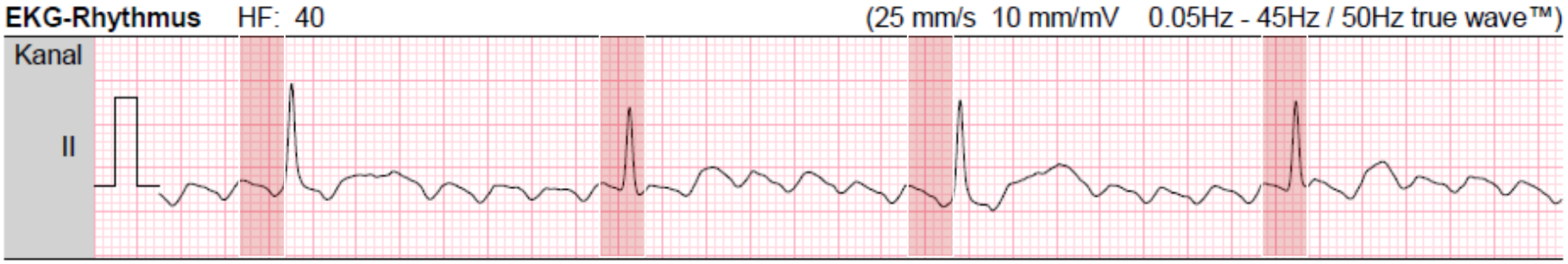
Vorhofflattern

Langsame Überleitung oder AV-Block III. Grades?

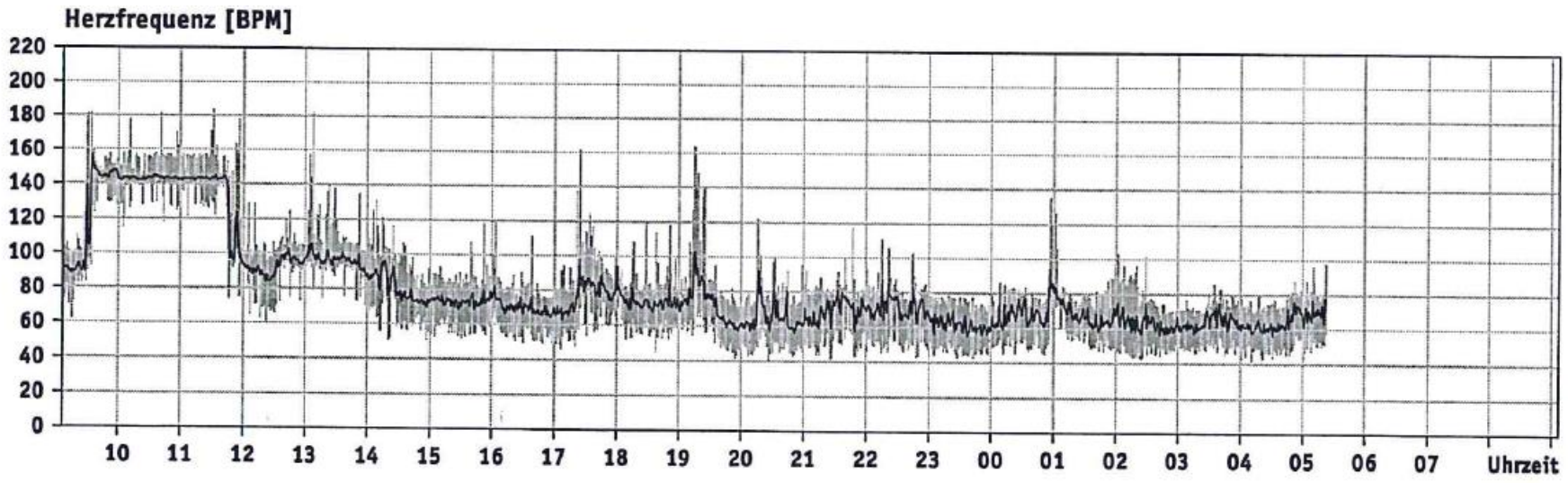


Vorhofflattern

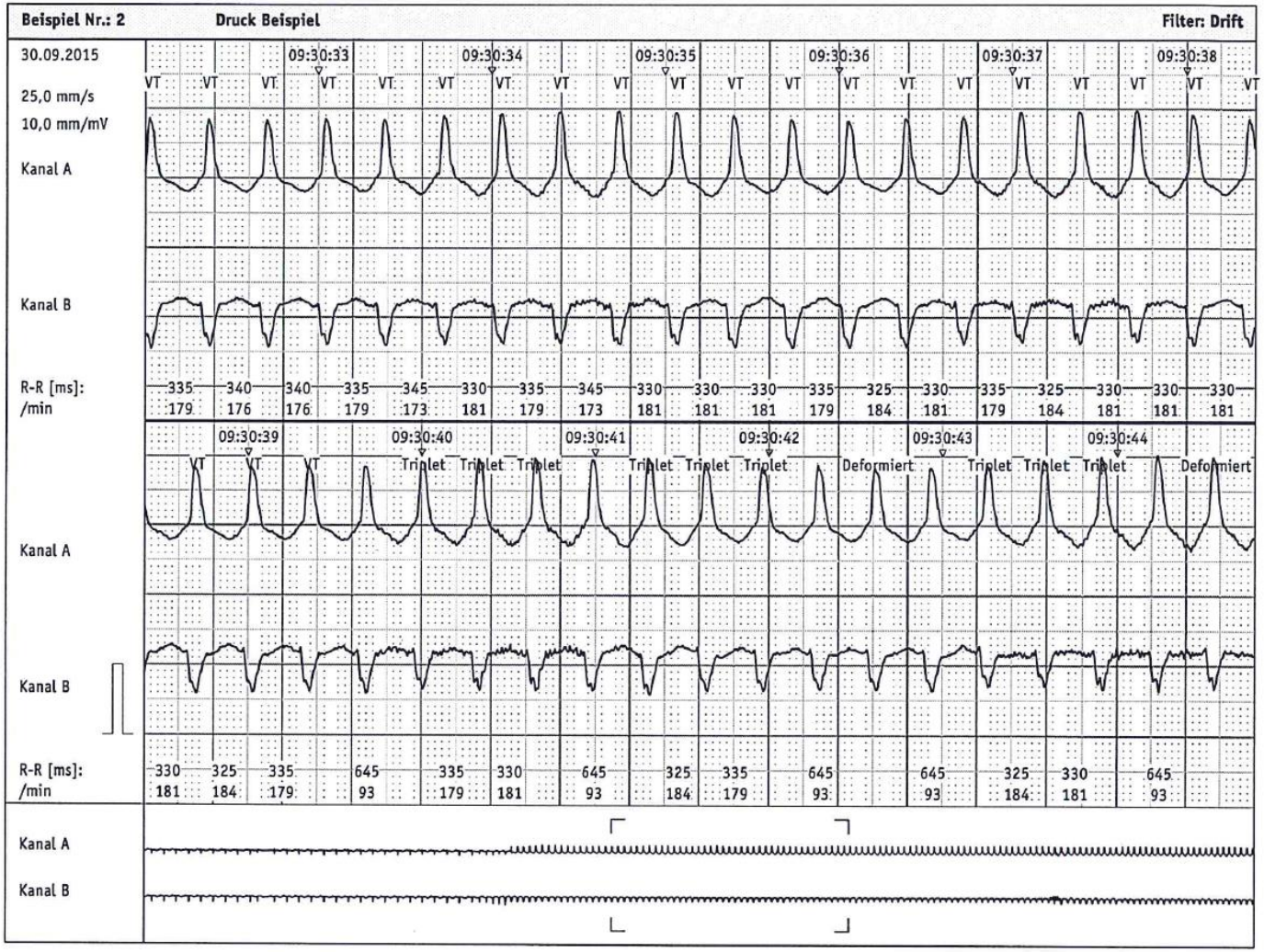
III. Grades



Unklare Arrhythmie



VHF



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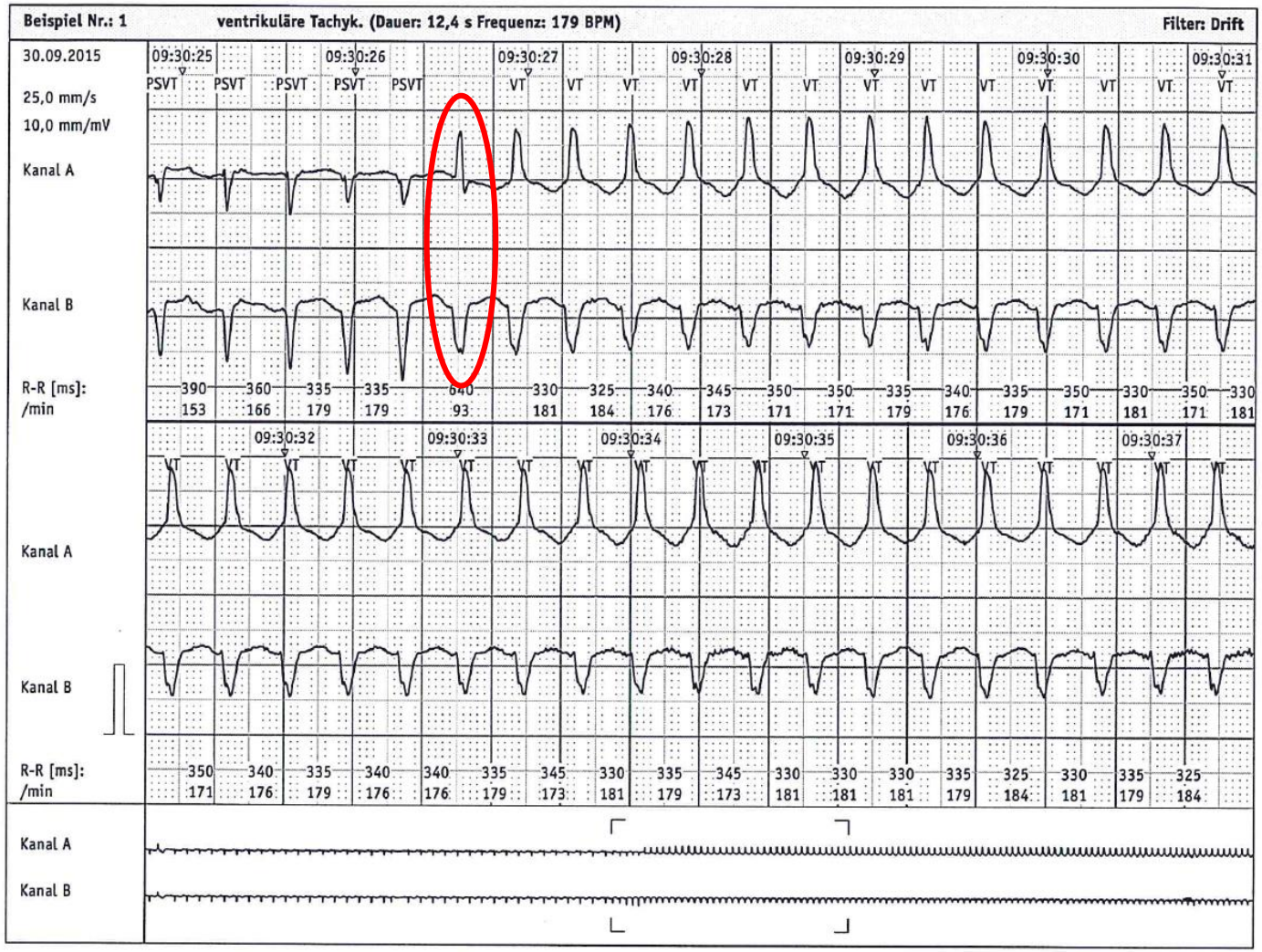
VT bei VHF


Beispiel Nr.: 1
ventrikuläre Tachyk. (Dauer: 12,4 s Frequenz: 179 BPM)
Filter: Drift
30.09.2015
25,0 mm/s
10,0 mm/mV
Kanal A
Kanal B
R-R [ms]:
/min
09:30:25
09:30:26
09:30:27
09:30:28
09:30:29
09:30:30
09:30:31
PSVT
VT
390 360 335 335 640 330 325 340 345 350 350 335 340 335 350 330 350 330
153 166 179 179 93 181 184 176 173 171 171 179 176 179 171 181 171 181
09:30:32
09:30:33
09:30:34
09:30:35
09:30:36
09:30:37
350 340 335 340 340 335 345 330 335 345 330 330 330 335 325 330 335 325
171 176 179 176 176 179 173 181 179 173 181 181 181 179 184 181 179 184

Breitkomplex-Tachykardien bei VHF als Grundrhythmus

- Bei Arrhythmien mit einem breiten QRS-Komplex bei VHF als Grundrhythmus
  - handelt es sich meistens um Aktionen mit einem **ventrikulären Ursprung** und
  - nur selten um aberrierende Leitung (d.h. funktionelle Schenkelblockierungen)

Lown-Klassifikation

Finding	Grade
No ventricular premature beats	0
Less than 30 ventricular premature beats per hour	1
30 or more ventricular premature beats per hour	2
Multiform/polymorphic ventricular premature beats	3
Repetitive ventricular premature beats • couplets (2 consecutive ventricular extrasystoles) • monomorphic ventricular tachycardia runs (salvos, 3 or more consecutive ventricular extrasystoles)	 4a 4b
R on T phenomenon (ventricular premature beat on receding T wave)	5

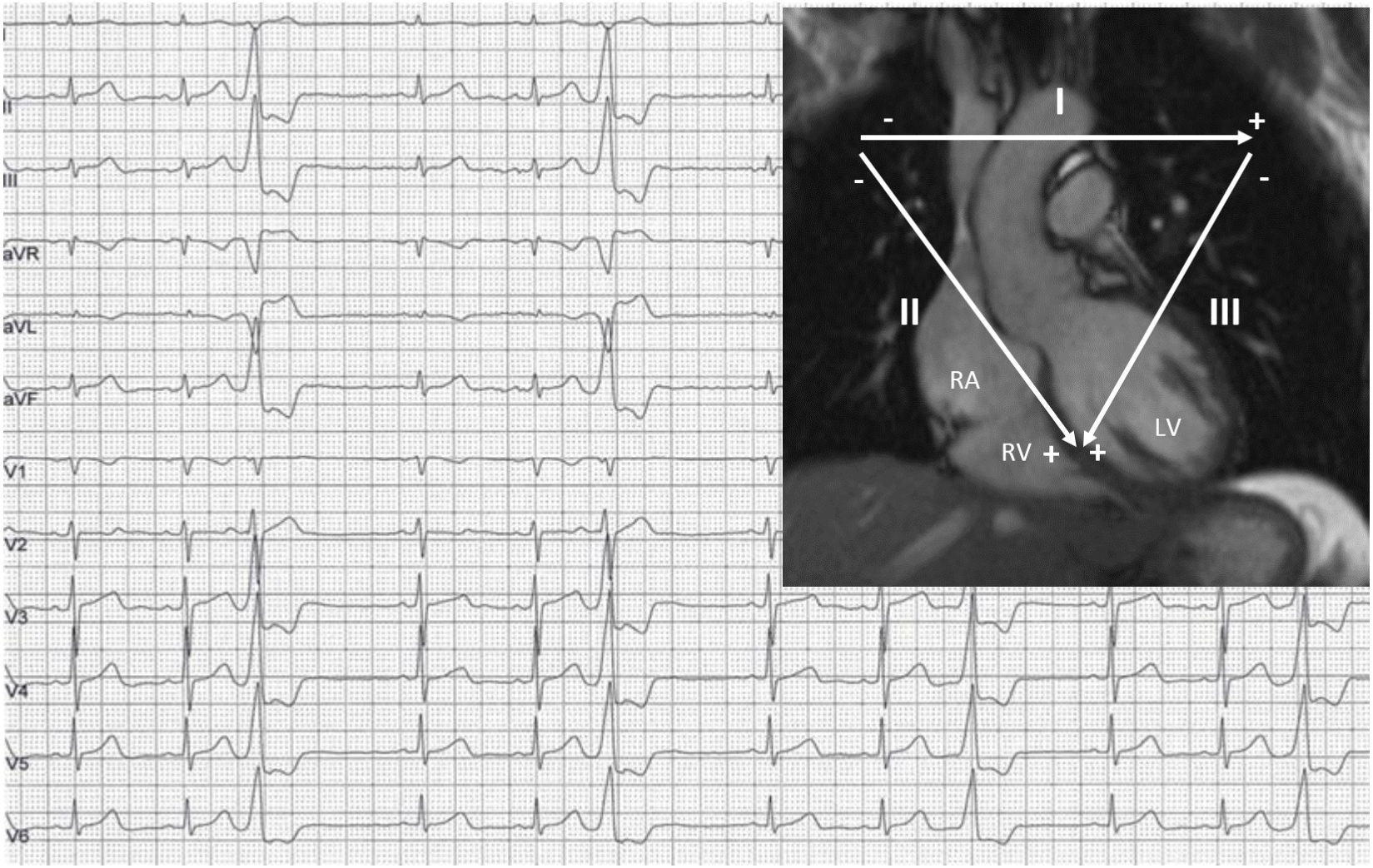
Lown-Klassifikation: Prognostische Bedeutung

Grade	Mortality Rate
0	14%
1	11%
2	0%
3	15%
4A	20%
4B	33%
5	29%

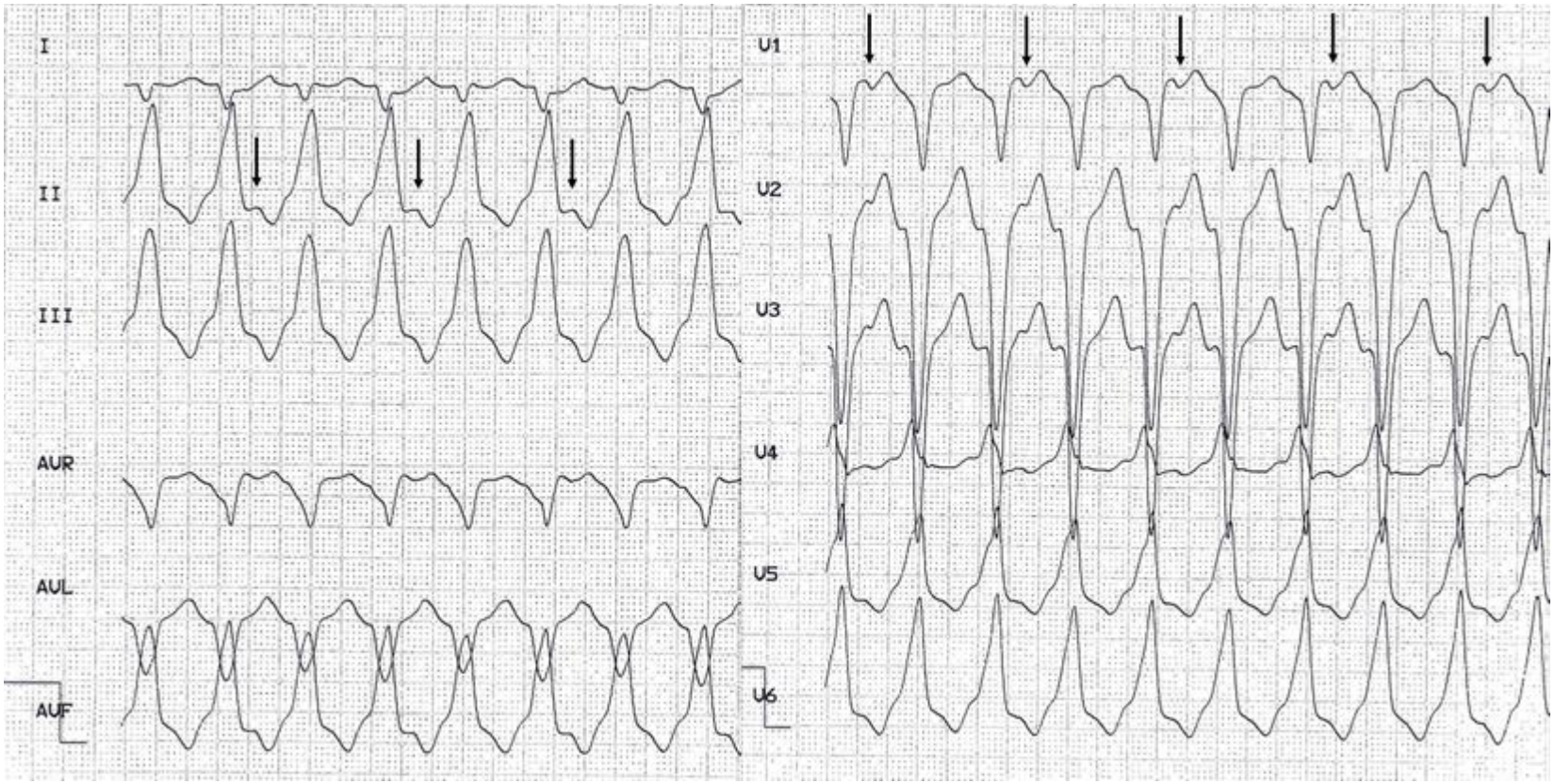
Bigger JT Jr, Weld FM. Analysis of prognostic significance of ventricular arrhythmias after myocardial infarction. Shortcomings of the Lown grading system. Br Heart J. 1981; 45: 717-724.

Ventrikulärer Trigeminus

VES aus dem RV-Ausflußtrakt



Kammertachykardie (RVOT)



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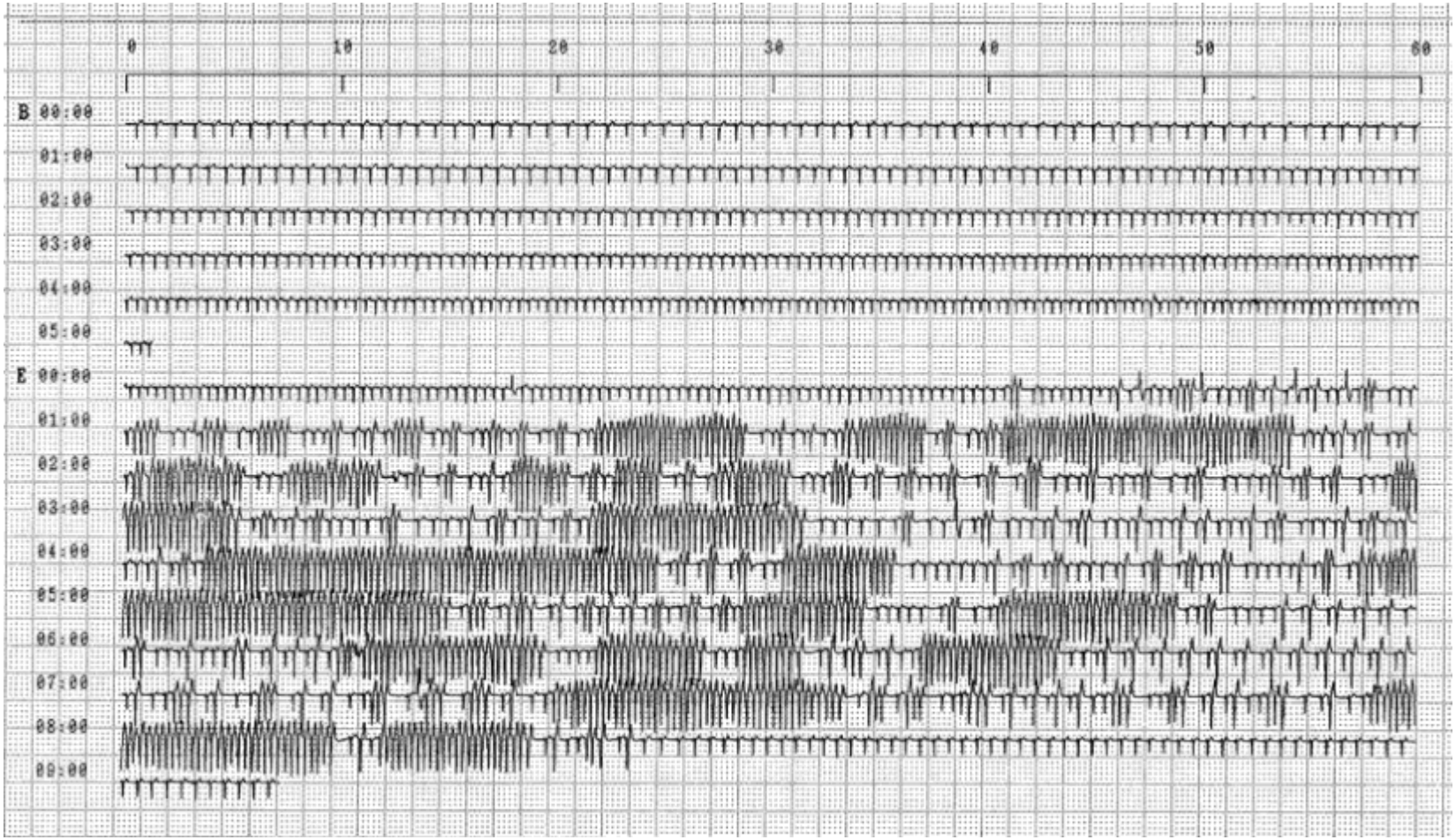
nsVT nach Belastung



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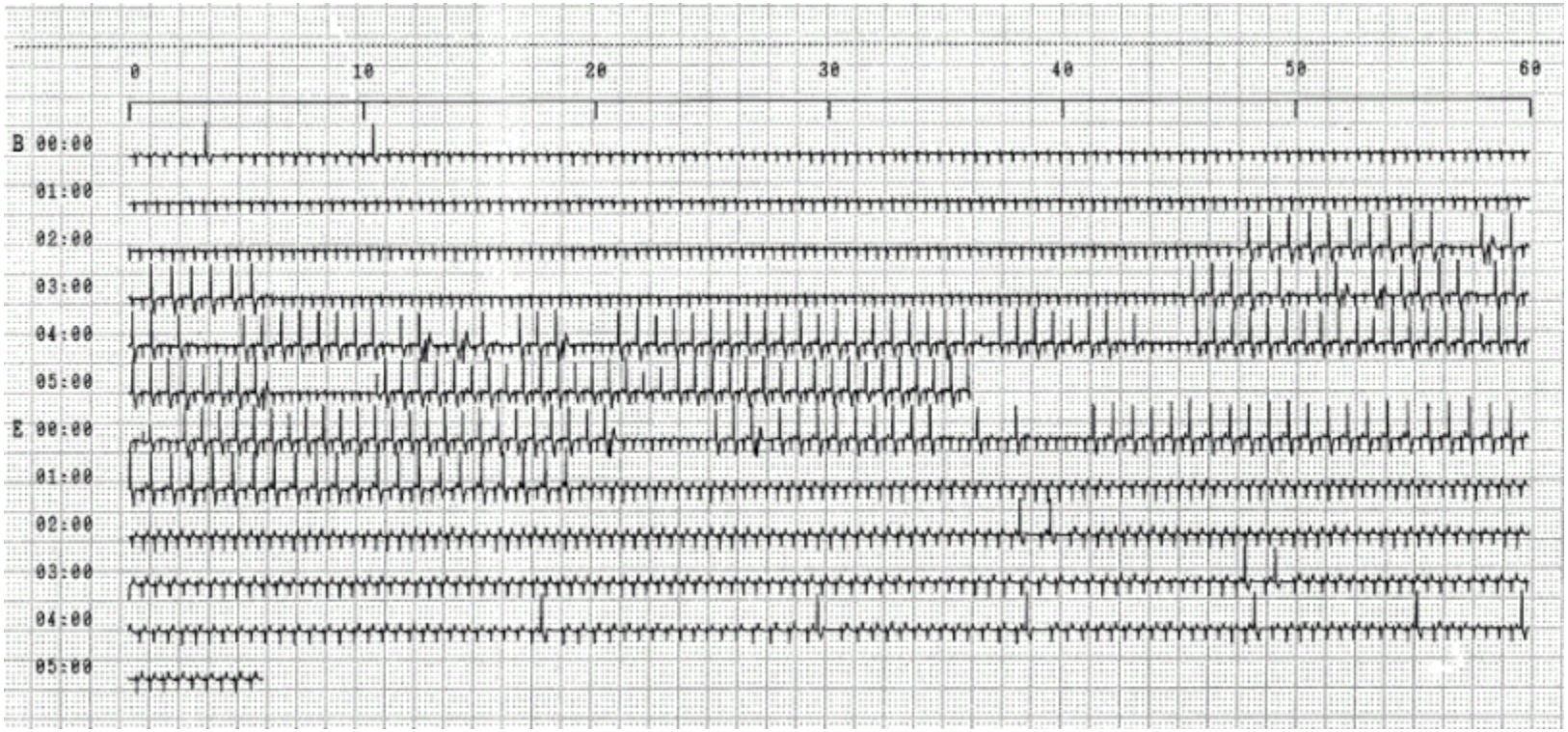
VES nach Belastung



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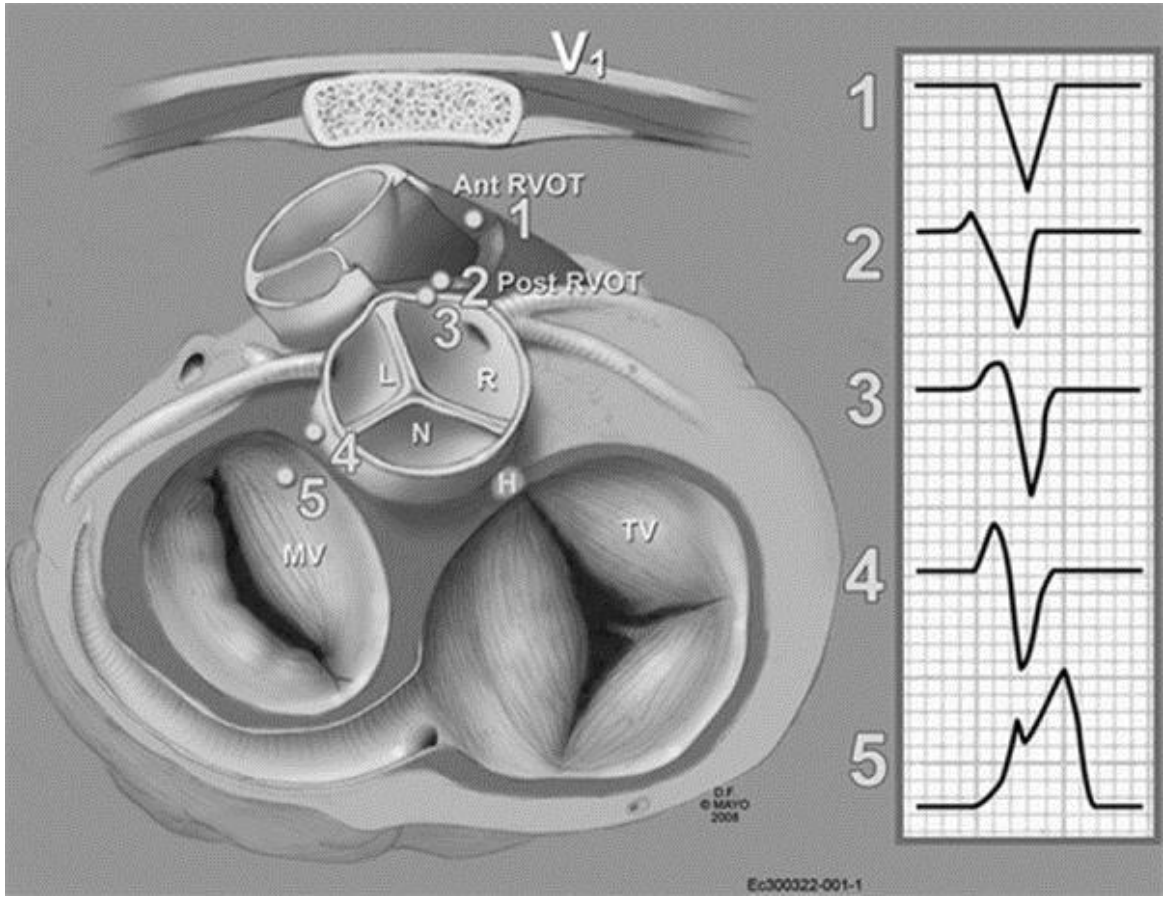
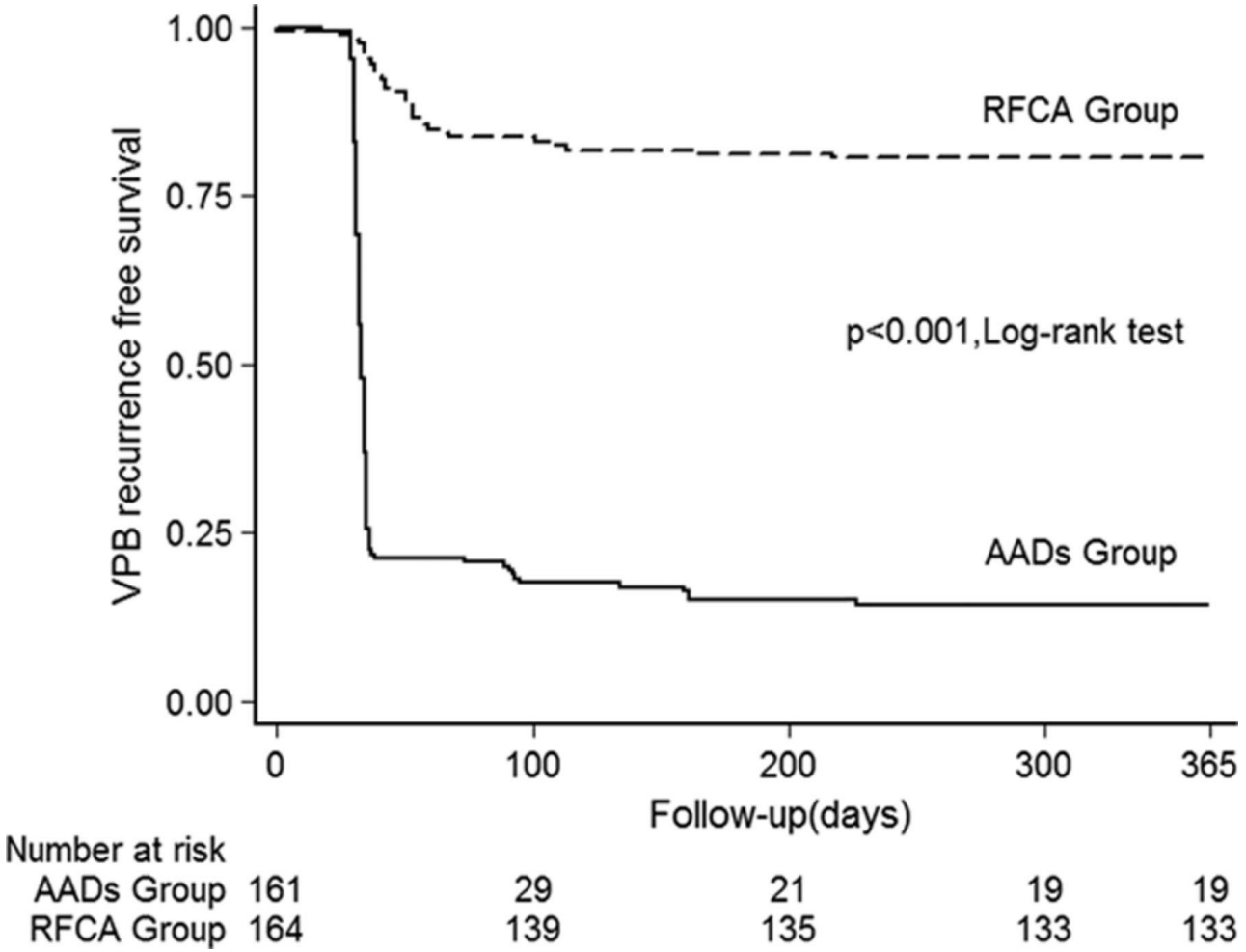
Idiopathische VES: Lokalisationsdiagnostik



RVOT-VES/nsVT

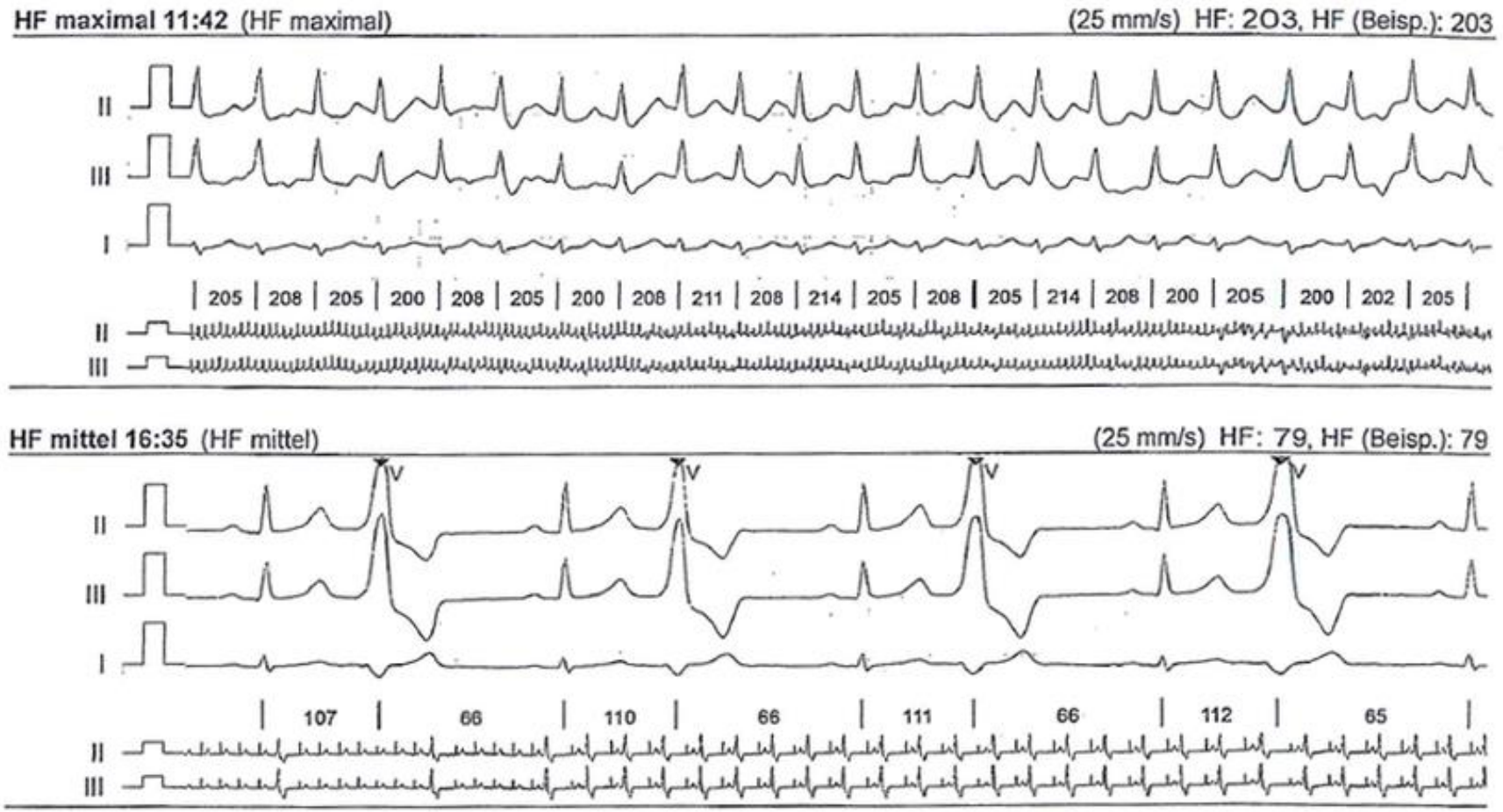
- Therapie:
  - **Beta-Blocker** um Symptome zu lindern
  - **Katheterablation** bei symptomatischen Arrhythmien (Anzahl sollte ca. 10.000/24h übersteigen) oder Verschlechterung der LV-Funktion (meist erst bei großer VES-Last von >20.000/24h)

Idiopathische VES: Ablation im Vergleich zu AA



Ling et al. 2014

RVO-VES und AVNRT: Läuse und Flöhe



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