Unfallkrankenhaus Berlin

Berliner Erfahrungen mit der REDUCE LAP-HF II Studie

und der Post Market Studie

Sebastian Winkler

Unfallkrankenhaus Berlin

ukb

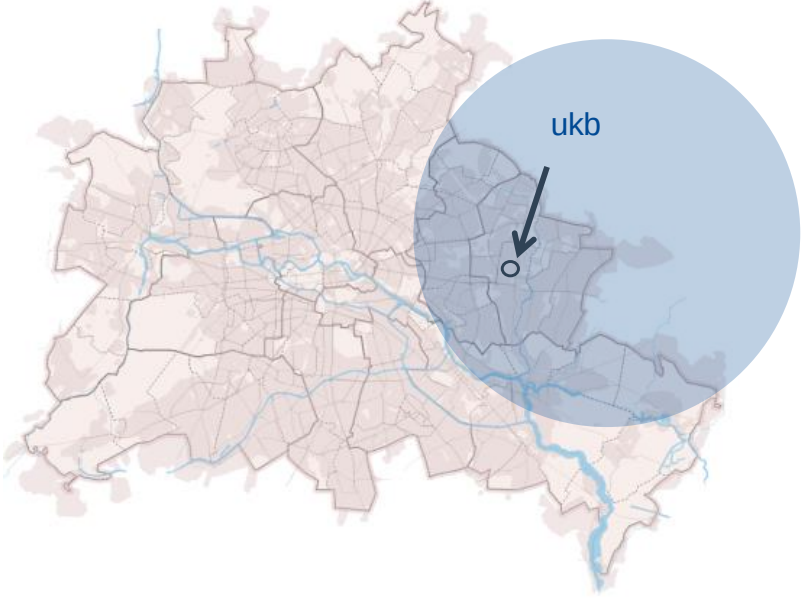
Krankenhaus der Maximalversorgung, 600 Betten

Klinik für Innere Medizin/ Kardiologie

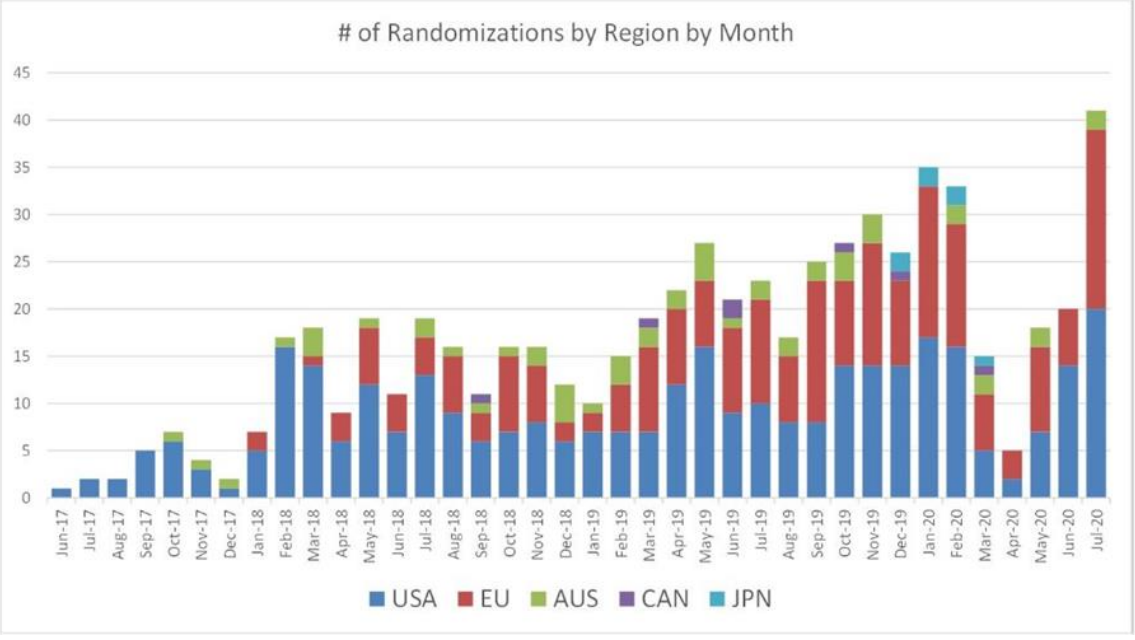
2 Stationen

3 HK-Labore

große Herzinsuffizienz-Ambulanz



REDUCE LAP HF II - Rekrutierung ist beendet



Top randomizing sites

Site #	Principal Investigator	Hospital/University	City	# Enrolled	# Randomized
0171	Dr. Vijay Swarup	Arizona Heart Rhythm Center	Phoenix, AZ	60	41
1408	Dr. Sebastian Winkler	Unfallkrankenhaus Berlin (UKB)	Berlin, Germany	31	30
1401	Dr. Gerd Hasenfuß	Georg-August Universität Göttingen	Göttingen, Germany	38	27
0135	Dr. Rajeev Mohan	Scripps Health	La Jolla, CA	38	23
0114	Dr. Barry Borlaug	Mayo Clinic - Saint Mary's Hospital	Rochester, MN,	34	23

Unfallkrankenhaus Berlin

Studienprotokoll REDUCE LAP HF II

5.1.1 Inclusion Criteria

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   a. Symptoms of HF requiring current treatment with diuretics for ≥ 30 days **AND**
   b. New York Heart Association (NYHA) class II if a prior history of > NYHA class II; ***OR*** NYHA class III, or ambulatory NYHA class IV symptoms (paroxysmal nocturnal dyspnea, orthopnea, dyspnea on mild or moderate exertion) at screening visit; or signs (any rales post cough, chest x-ray demonstrating pulmonary congestion,) within past 12 months; **AND**
   c. ≥ 1 HF hospital admission (with HF as the primary, or secondary diagnosis); or treatment with intravenous (IV); or the need for intensification of oral diuresis for HF in a healthcare facility within the 12 months prior to study entry; ***OR*** an NT-pro BNP value > 150 pg./ml in normal sinus rhythm, > 450 pg./ml in atrial fibrillation, or a BNP value > 50 pg./ml in normal sinus rhythm, > 150 pg./ml in atrial fibrillation within the past 6 months
2. Ongoing stable GDMT HF management and management of potential comorbidities according to the 2017 ACC/AHA Guidelines for the Management of Heart Failure with no significant changes (>100% increase or 50% decrease, excluding diuretic dose changes for a minimum of 4 weeks prior to enrollment which is expected to be maintained for 6 months. Stable management includes a minimum period of 4 weeks post hospitalization for any cause, including treatment with IV diuretics.
3. Age ≥ 40 years old
4. Site determined echocardiographic LV ejection fraction ≥ 40% within the past 6 months, without documented ejection fraction <30% in the 5 years prior to study entry
5. Site determined elevated PCWP with a gradient compared to right atrial pressure (RAP) documented by
   a. End-expiratory PCWP during supine ergometer exercise ≥ 25mm Hg, and greater than RAP by ≥ 5 mm Hg.
6. Site determined echocardiographic evidence of diastolic dysfunction documented by **one or more** of the following:
   a. LA diameter > 4 cm; *or*
   b. Diastolic LA volume > 50 *or* LA volume index > 28 ml/m² *or*
   c. Lateral e' < 10 cm/s; *or*
   d. Septal e' < 8 cm/s; *or*
   e. Lateral E/e' > 10; *or*
   f. Septal E/e' > 15
7. Subject has been informed of the nature of the study, agrees to its provisions and has provided written informed consent, approved by the IRB or EC
8. Subject is willing to comply with clinical investigation procedures and agrees to return for all required follow-up visits, tests, and exams
9. Trans-septal catheterization and femoral vein access is determined to be feasible by site interventional cardiology investigator.

9 + 33

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3. Advanced heart failure defined as one or more of the below:
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   b. Cardiac Index < 2.0 L/min/m²
   c. Inotropic infusion (continuous or intermittent) for EF < 40% within the past 6 months
   d. Patient is on the cardiac transplant waiting list.
4. Inability to perform 6 minute walk test (distance < 50 m), OR 6 minute walk test > 600m
5. The patient has verified that the ability to walk 6 minutes is limited primarily by joint, foot, leg, hip or back pain; unsteadiness or dizziness or lifestyle (*and not* by shortness of breath and/or fatigue and/or chest pain).
6. Unwilling or unable (per PhysIQ protocol) to wear telemonitoring patch, unless cell-phone based monitoring device is not available in that region.
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22. Life expectancy less than 12 months for known non-cardiovascular reasons
23. Echocardiographic evidence of intra-cardiac mass, thrombus or vegetation
24. Known or suspected allergy to nickel
25. Women of child bearing potential
26. Currently requiring dialysis; or estimated-GFR <25ml/min/1.73 m2 by CKD-Epi equation
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29. Subjects on significant immunosuppressive treatment or on systemic steroid treatment (>10 mg prednisone/day).
30. Severe obstructive sleep apnea not treated with CPAP or other measures
31. Severe depression and/or anxiety
32. In the opinion of the Investigator, the subject is not an appropriate candidate for the study
33. BMI >45. BMI 40 - 45 is also excluded unless in the opinion of the investigator, vascular access can be obtained safely.

Unfallkrankenhaus Berlin

Studienprotokoll REDUCE LAP HF II

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…mic steroid treatment (>10

…easures

…e candidate for the study

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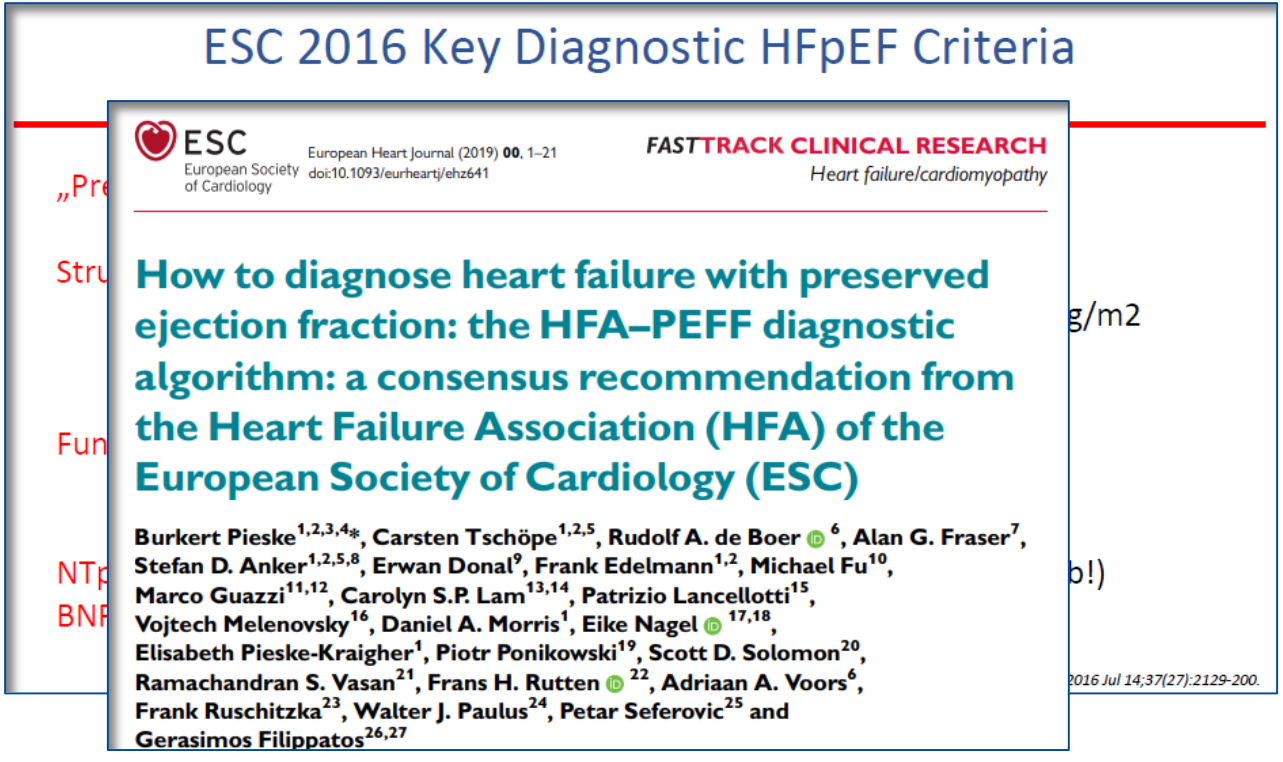
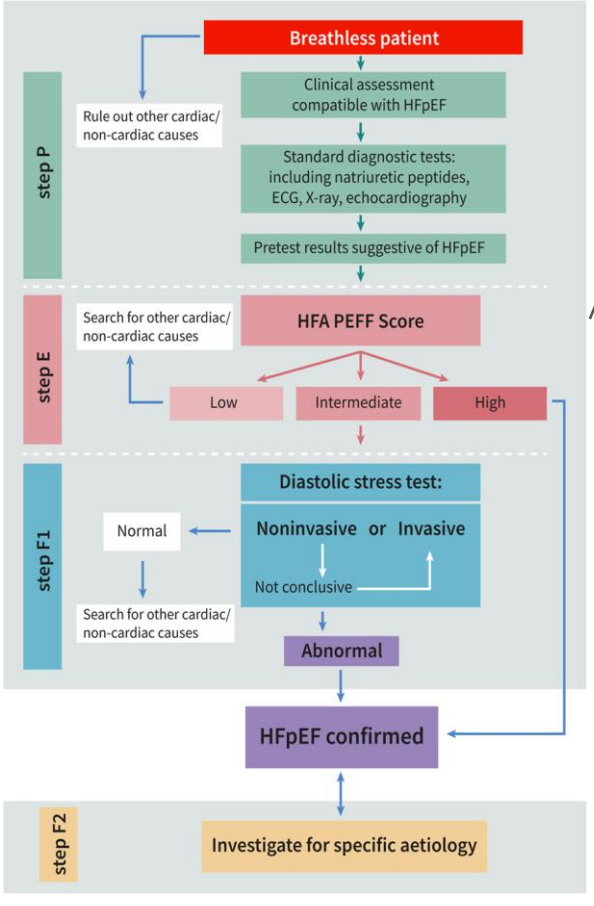
Rekrutierung

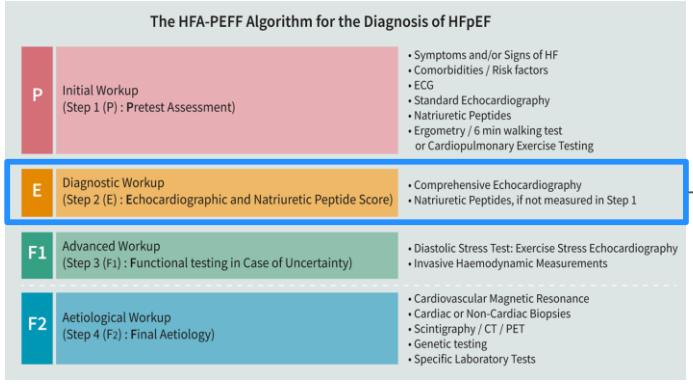
- HFpEF diagnostizieren (lernen)



Eur Heart J 2019

HFpEF diagnostizieren





	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	septal e' < 7 cm/s or lateral e' < 10 cm/s or Average E/e' ≥ 15 or TR velocity > 2.8 m/s (PASP > 35 mmHg)	LAVI > 34 ml/m² or LVMI ≥ 149/122 g/m² (m/w) and RWT > 0,42 #	NT-proBNP > 220 pg/ml or BNP > 80 pg/ml	NT-proBNP > 660 pg/ml or BNP > 240 pg/ml
Minor	Average E/e' 9 -14 or GLS < 16 %	LAVI 29-34 ml/m² or LVMI > 115/95 g/m² (m/w) or RWT > 0,42 or LV wall thickness ≥ 12 mm	NT-proBNP 125-220 pg/ml or BNP 35-80 pg/ml	NT-proBNP 365-660 pg/ml or BNP 105-240 pg/ml

Major Criteria: 2 points	≥ 5 points: HFpEF
Minor Criteria: 1 point	2-4 points: Diastolic Stress Test or Invasive Haemodynamic Measurements

Pieske et al, Eur Heart J 2019

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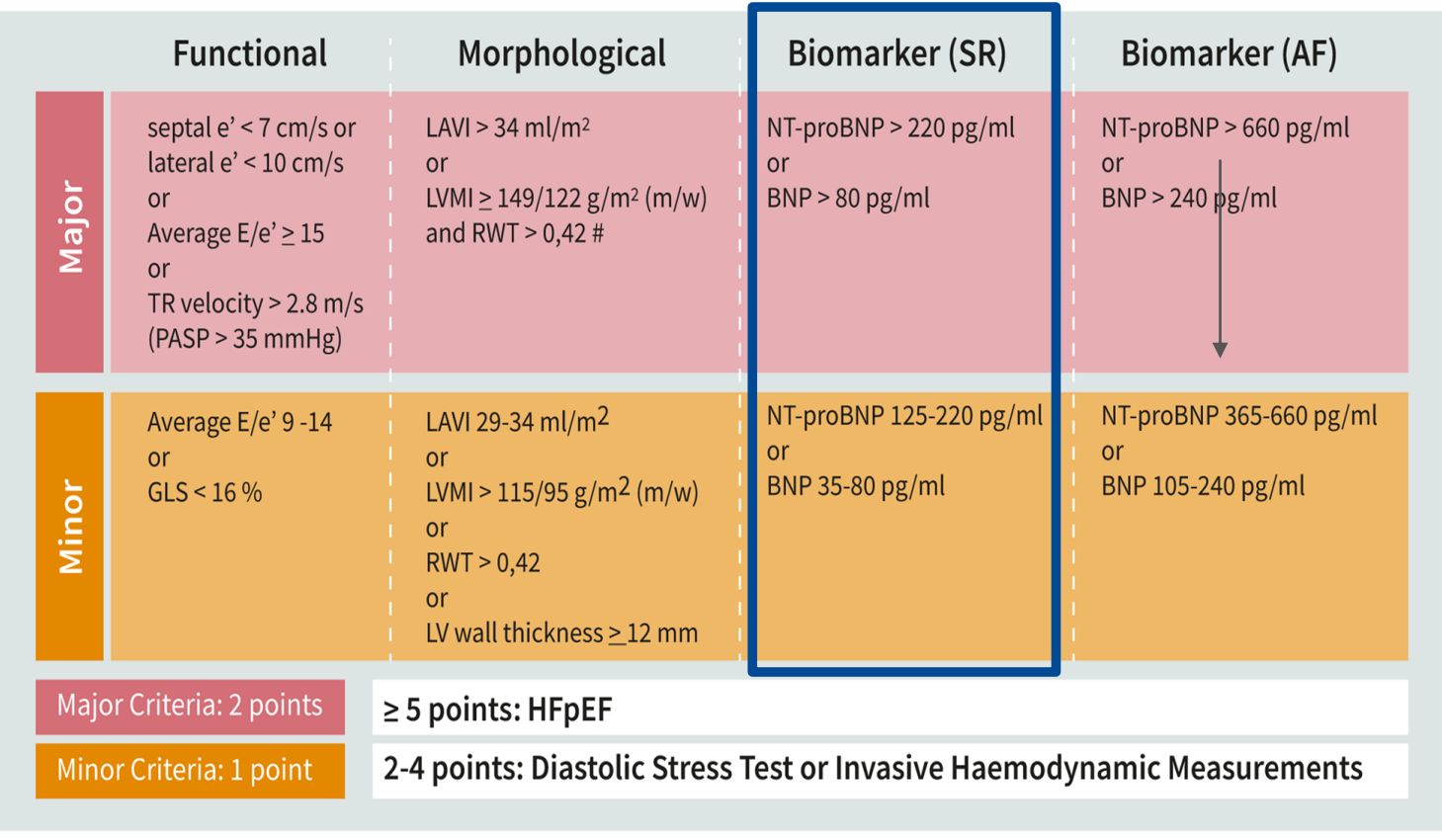
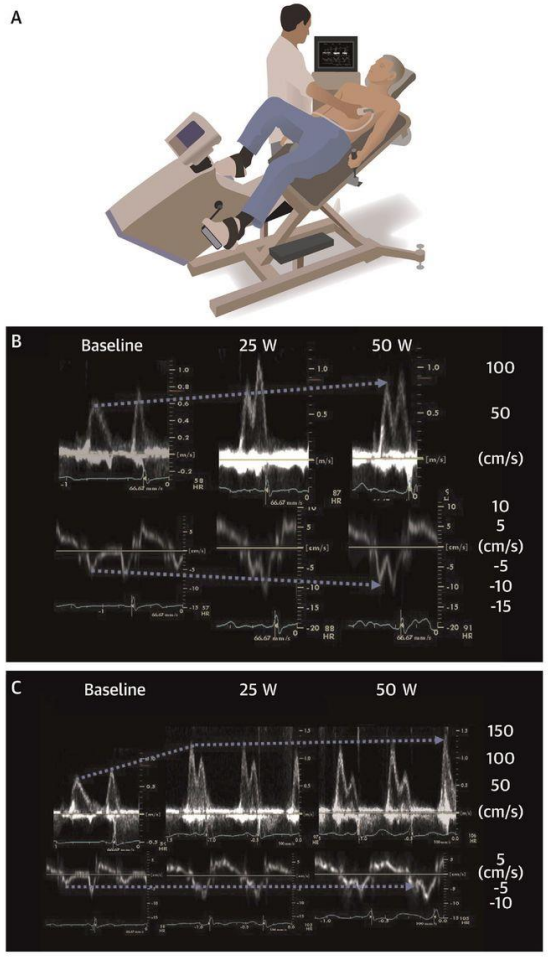
HFpEF diagnostizieren



Pieske et al, Eur Heart J 2019

HFpEF diagnostizieren

CENTRAL ILLUSTRATION: Noninvasive Diastolic Stress Test



Ha, J.-W. et al. J Am Coll Cardiol Img. 2020;13(1):272-82.

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HFpEF diagnostizieren

Hämodynamik:
Stufe: Baseline

Größe	174 cm	Herzfrequenz	64 1/min
Gewicht	102,00 kg	Hämoglobin	15,10 g/dL
BSA	2,16		

Drücke

Vorhöfe

	A Welle (mmHG)	V Welle (mmHG)	Mittel (mmHG)	SO2 (%)
RA	11	9	8	
PCW	17	15	10	
LA				

Kammern

	Systolisch (mmHG)	Diastolisch (mmHG)	End-Diastolisch (mmHG)	SO2 (%)
RV	32	7	15	
LV	150	-22	11	

Große Gefäße

	Systolisch (mmHG)	Diastolisch (mmHG)	Mittel (mmHG)	SO2 (%)
AO	146	89	111	95,00
PA	23	10	16	66,00

Herzzeitvolumen
HZV: 4,80 l/min, HI: 2,20 l/min/m².
SV: 75,60 ml/Schlag, SVI: 35,00 ml/Schlag/m².

Widerstände
SVR: 1716,70 (dyn*s)/cm⁵, SVRI: 3708,00 (dyn*s)/cm⁵/m².
PVR: 100,00 (dyn*s)/cm⁵, PVRI: 216,00 (dyn*s)/cm⁵/m².

HFpEF diagnostizieren

Stufe: nach 500 ml SF

Größe	174 cm	Herzfrequenz	67 1/min
Gewicht	102,00 kg	Hämoglobin	15,10 g/dL
BSA	2,16		

Drücke

Vorhöfe

	A Welle (mmHG)	V Welle (mmHG)	Mittel (mmHG)	SO2 (%)
RA	18	18	15	
PCW	24	25	23	
LA				

Kammern

	Systolisch (mmHG)	Diastolisch (mmHG)	End-Diastolisch (mmHG)	SO2 (%)
RV	32	10	16	
LV	136	-7	20	

Große Gefäße

	Systolisch (mmHG)	Diastolisch (mmHG)	Mittel (mmHG)	SO2 (%)
AO	136	86	106	94,00
PA	32	21	25	66,00

Herzzeitvolumen
HZV: 5,00 l/min, HI: 2,30 l/min/m².
SV: 74,80 ml/Schlag, SVI: 34,60 ml/Schlag/m².

Widerstände
SVR: 1456,00 (dyn*s)/cm⁵, SVRI: 3145,00 (dyn*s)/cm⁵/m².
PVR: 32,00 (dyn*s)/cm⁵, PVRI: 69,10 (dyn*s)/cm⁵/m².

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HFpEF diagnostizieren

-Das Fehlen struktureller Veränderungen des Herzens („normales Echo“) schließt HFpEF nicht aus

-Normale Füllungsdrücke in Ruhe (LVEDP, PCWP) schließen HFpEF nicht aus

-Natriuretische Peptide richtig interpretieren

Ein niedriges oder normales BNP/ NTproBNP schließt HFpEF nicht aus

-Belastungs-Echokardiografie (Diastolic Stresstest) oder Belastungs-Hämodynamik durchführen

-Invasive Diagnostik unter Beachtung des Volumenstatus

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Studienprotokoll REDUCE LAP HF II

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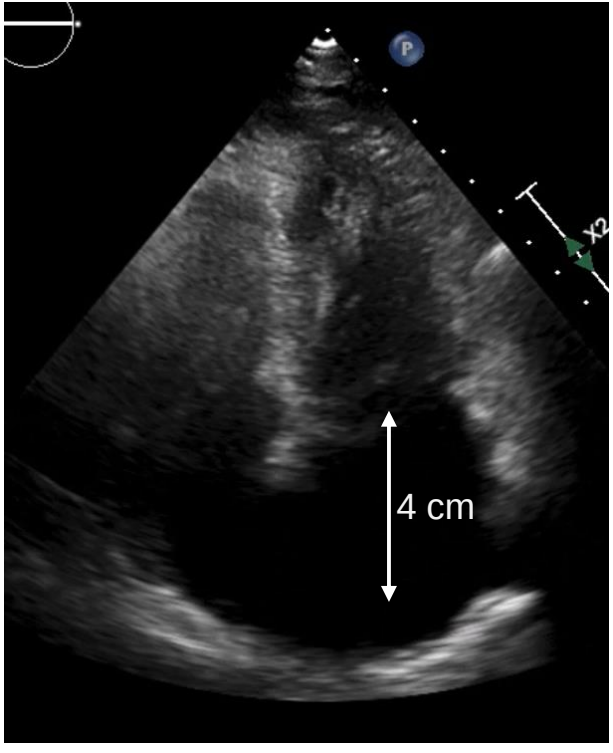
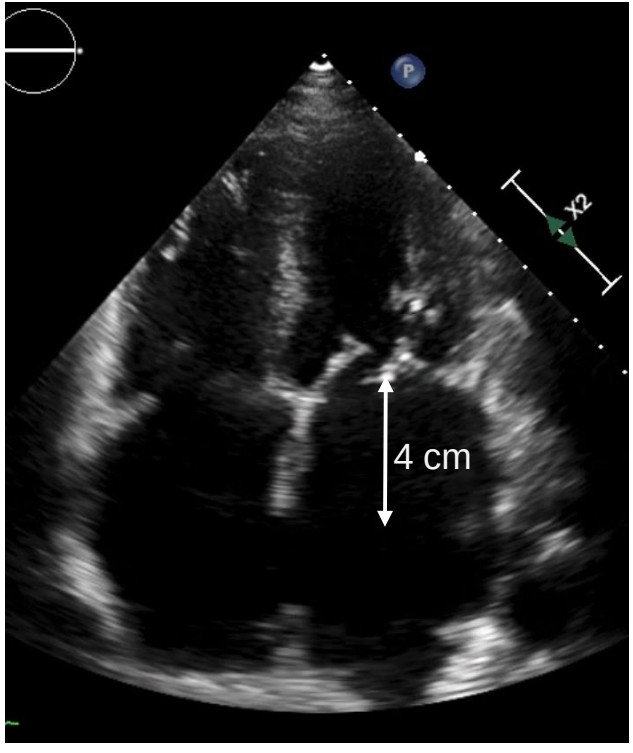
Studienprotokoll REDUCE LAP HF II



kleine hypertrophierte Ventrikel



VHF-Herzen mit großen Vorhöfen

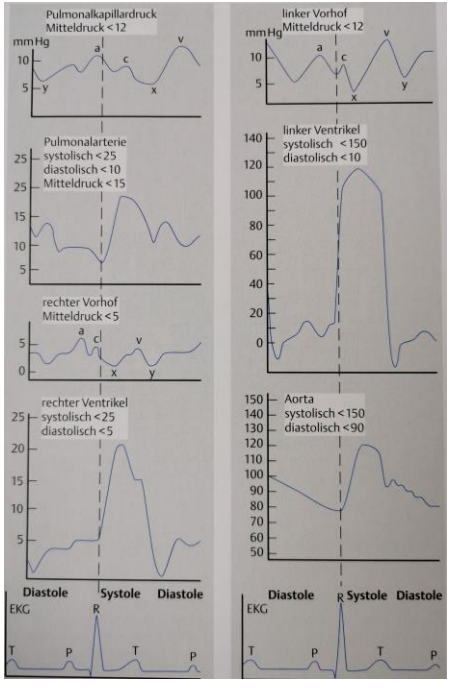
Invasive Hämodynamik

Setting und Ablauf ist maximal standardisiert – Messung ist aber eine stark variable Momentaufnahme

$$HMV = \frac{VO_2\ (ml/min)}{AVDO_2\ (ml/100ml)\ x\ 10}\ \text{in l/min}$$

$$PVR = \frac{PAP_m - LAP_m}{Q}\ x\ 80\ \text{in dyn·s·cm}^{-5}$$

wobei



Pathologische Hämodynamik = kranker Patient (Diagnose beweisend)

Normale Hämodynamik = gesunder Patient

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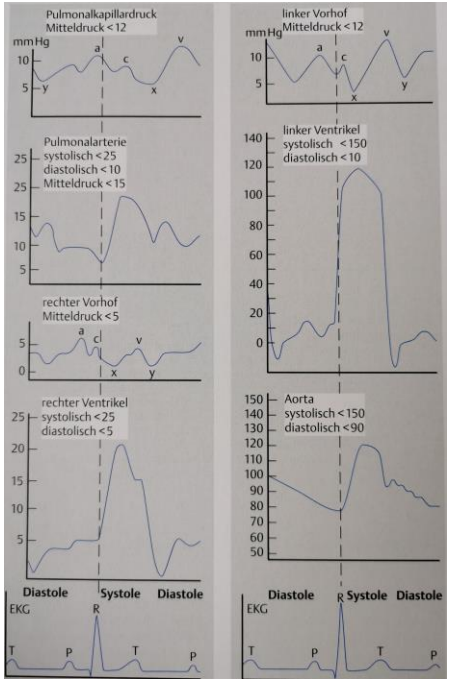


Pathologische Hämodynamik = kranker Patient (Diagnose beweisend)

~~Normale Hämodynamik = gesunder Patient~~

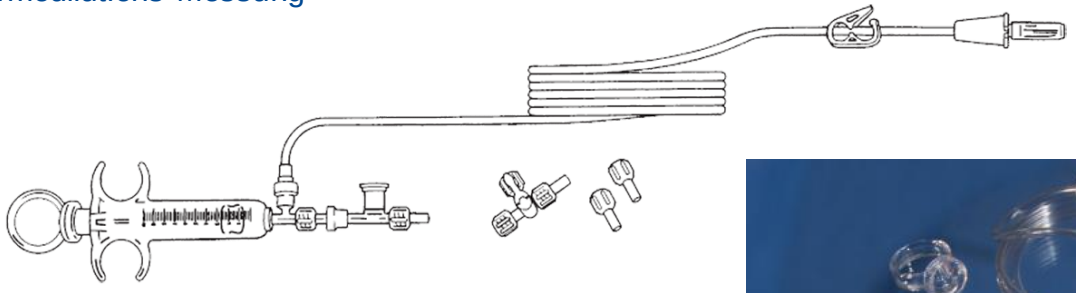
Normale Hämodynamik = kranker Patient, falsch untersucht

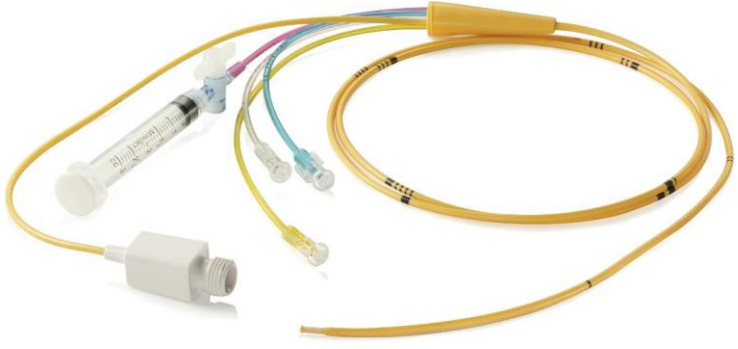
HFpEF erfordert in vielen Fällen eine Belastungs-Hämodynamik

Studienprozedur und Implantation des Corvia IASD

Rechtsherzkatheter mit Belastung über linkscubitalen Zugang

Thermodilutions-Messung





Studienprozedur und Implantation des Corvia IASD

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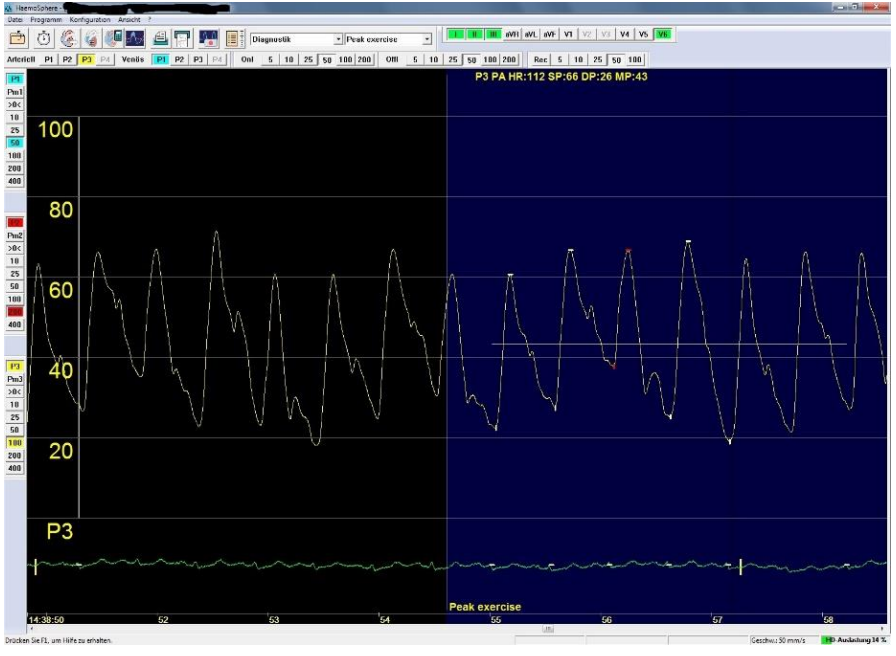
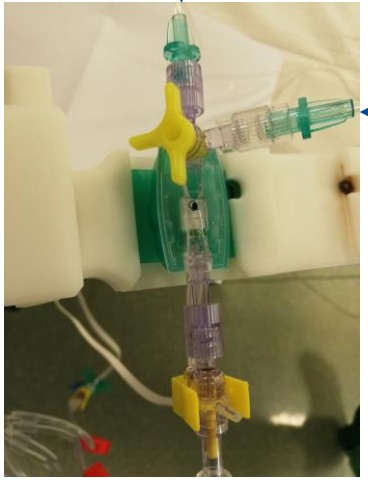
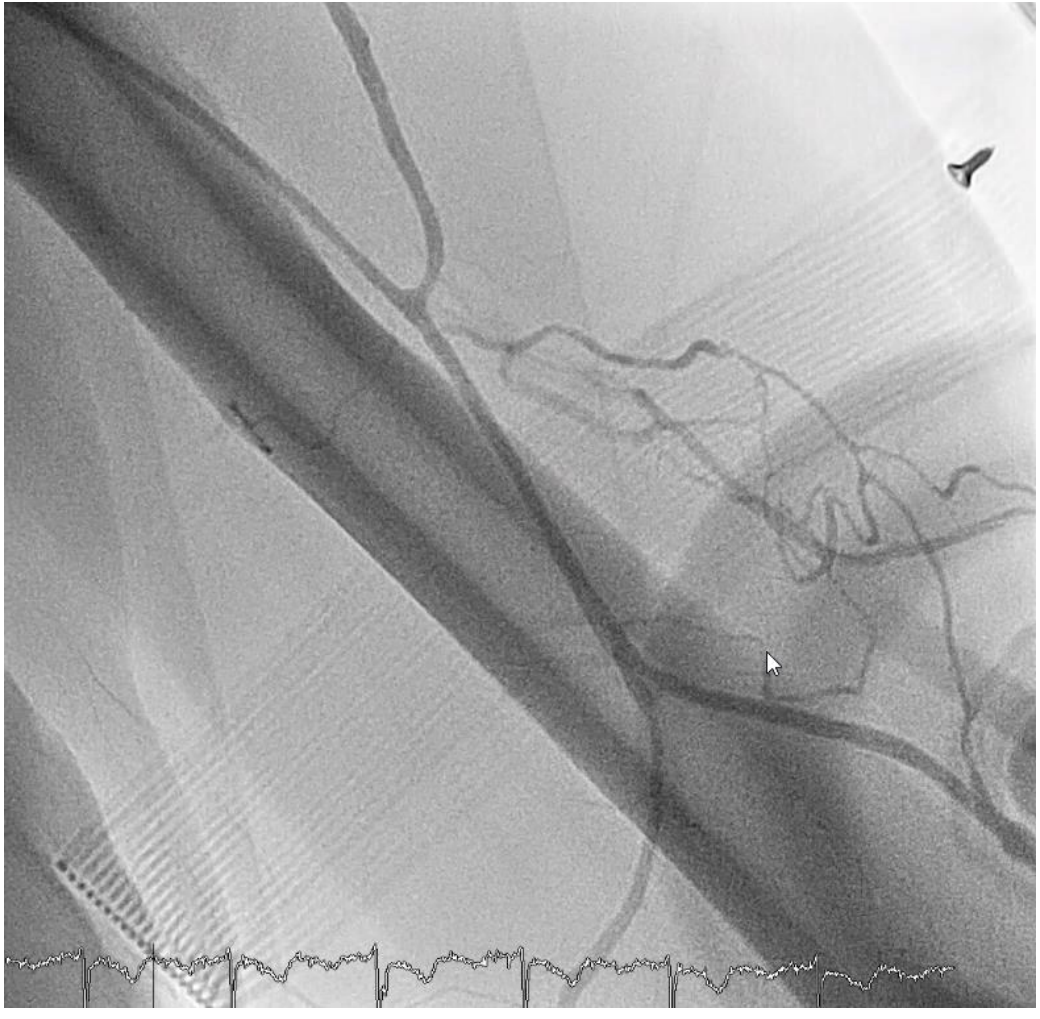




Unfallkrankenhaus Berlin

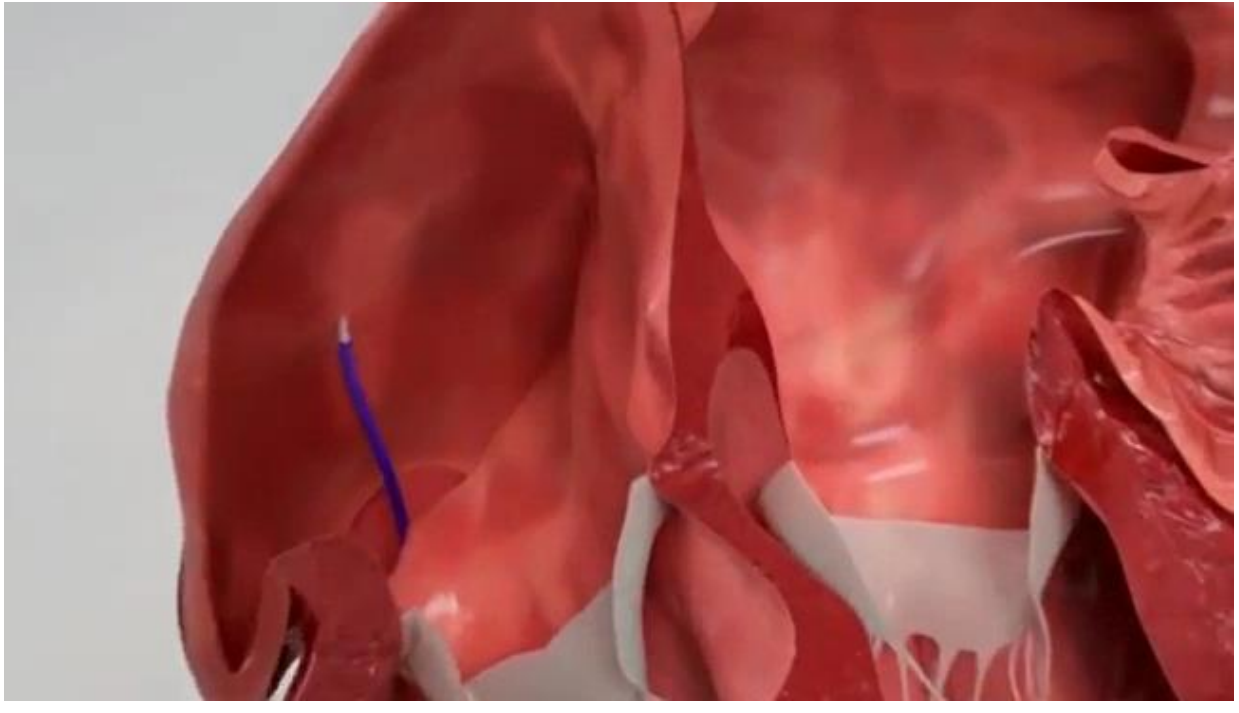
Cubitaler Zugang für Rechtsherzkatheter



Unfallkrankenhaus Berlin

IASD-Implantation

1. Transseptale Punktion – Draht in LUPV
2. Wechseln auf 16F Schleuse
3. ACT > 250s
4. Einbringen des Delivery-Systems und Implantation in 2 Schritten



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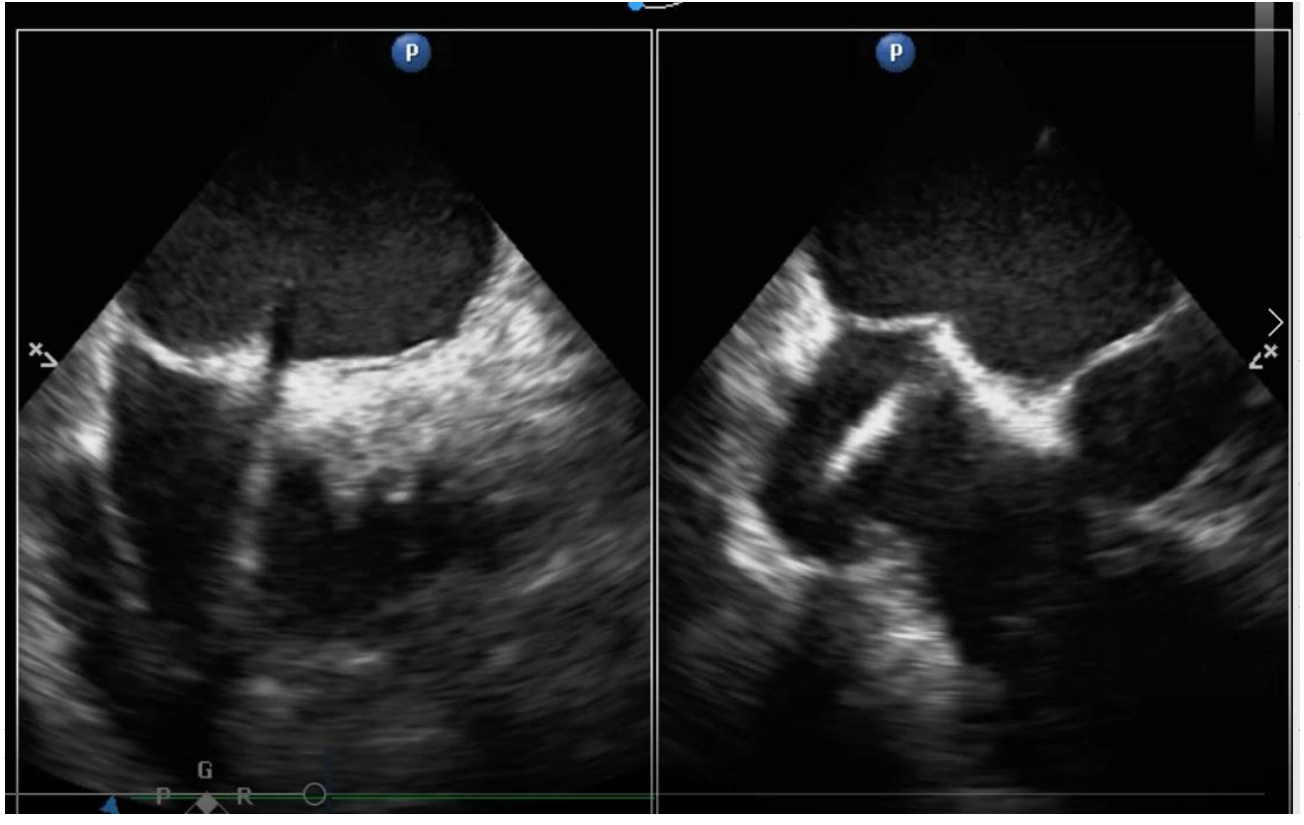
1. Problem: Ort der transseptalen Punktion

Außendurchmesser IASD 19mm



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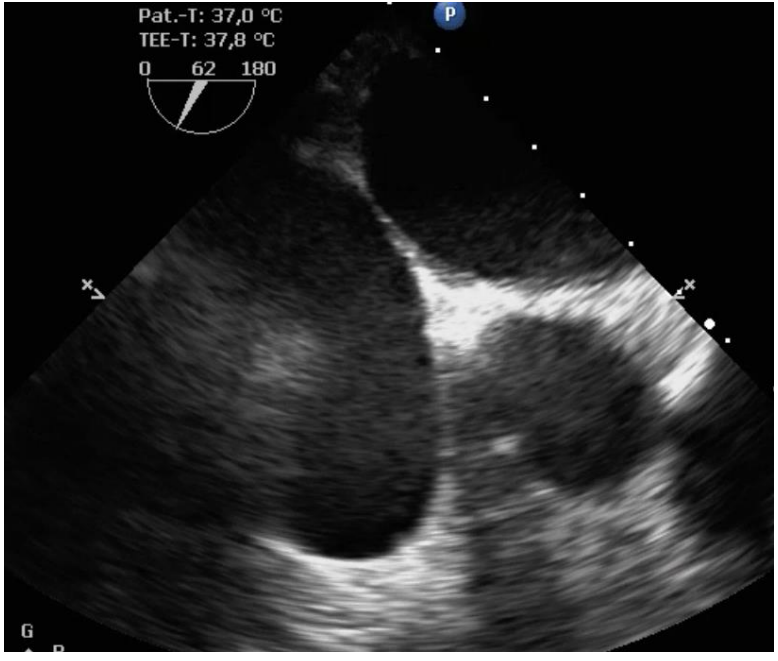
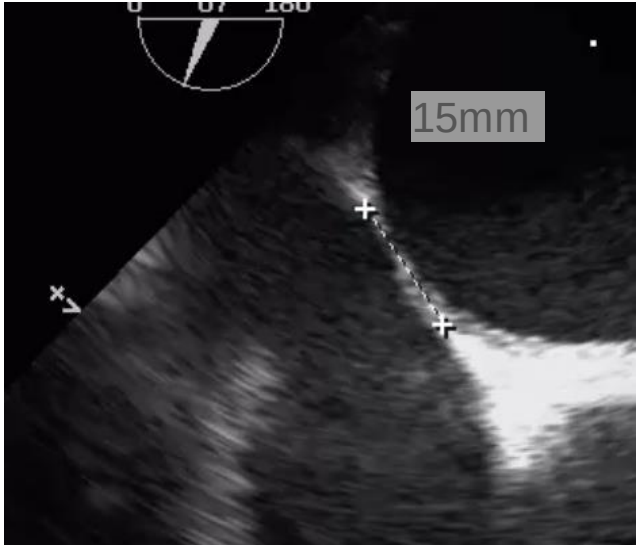
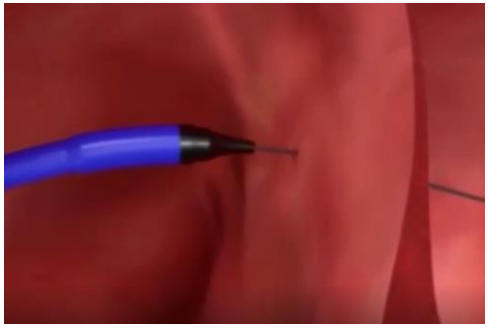


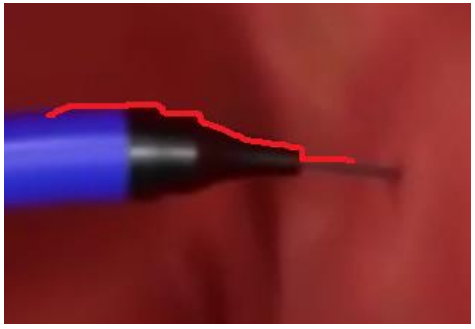


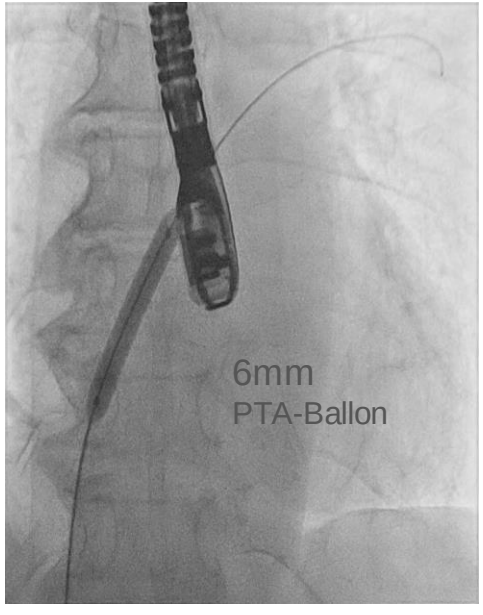
Ungünstiger Winkel

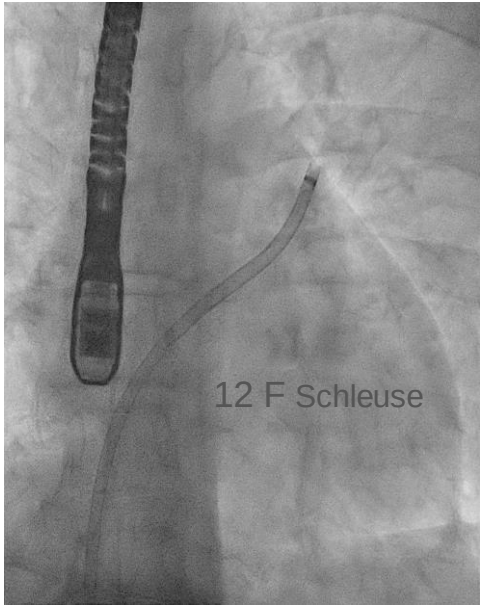
-steuerbare Schleuse (Agilis)

2. Problem: Passage des Systems über das IAS

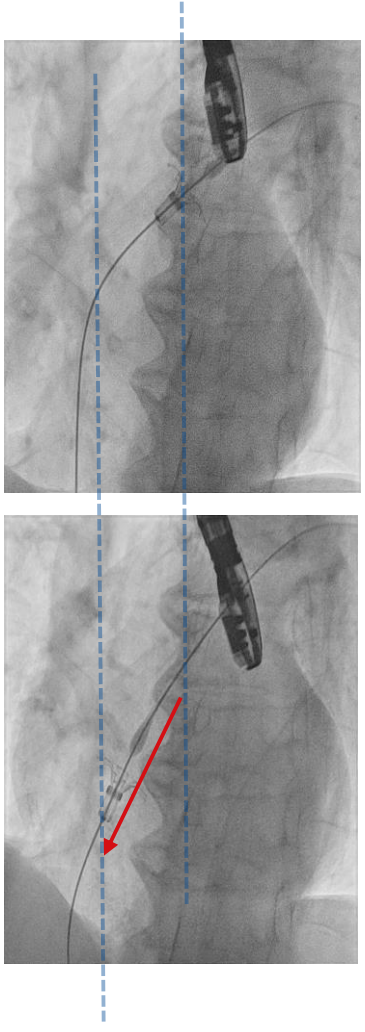






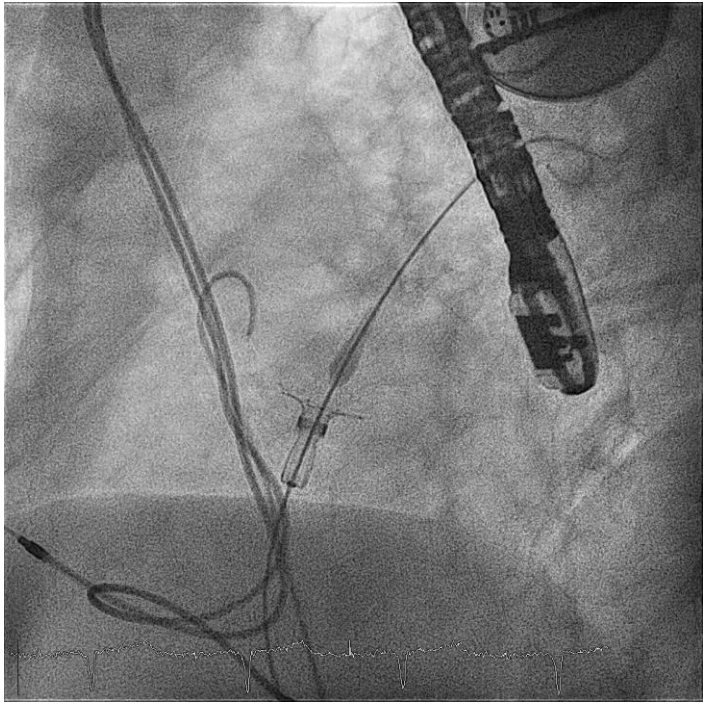


3. Problem: Mobilität des IAS

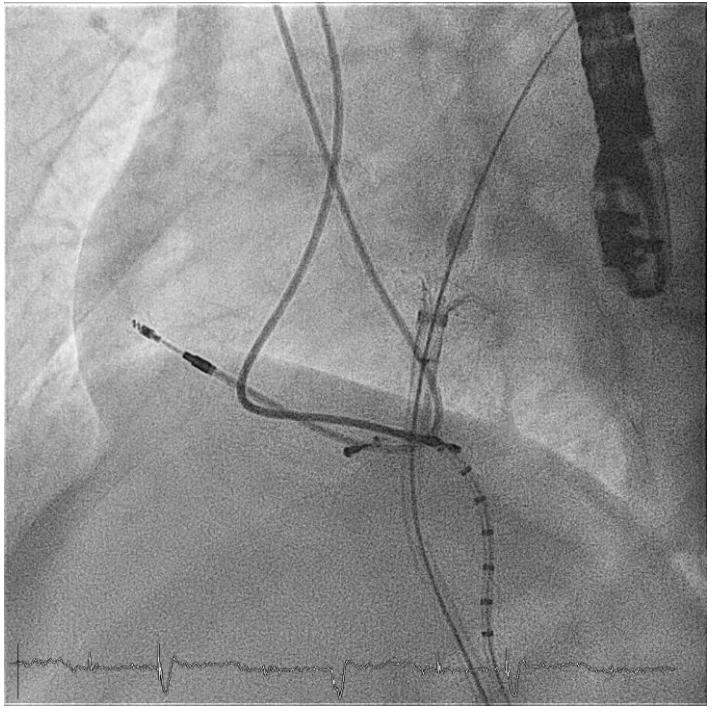


mehrere Zentimeter Rückzug

4. Problem: Schrittmacher-Sonden im RA



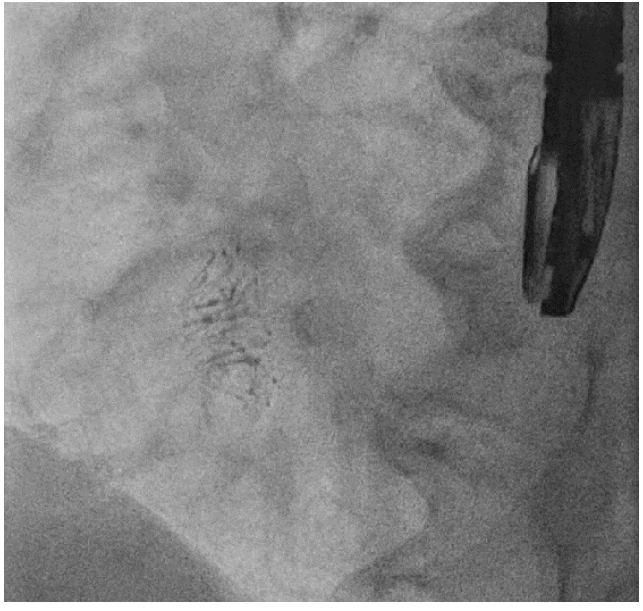
Pigtail (5F)

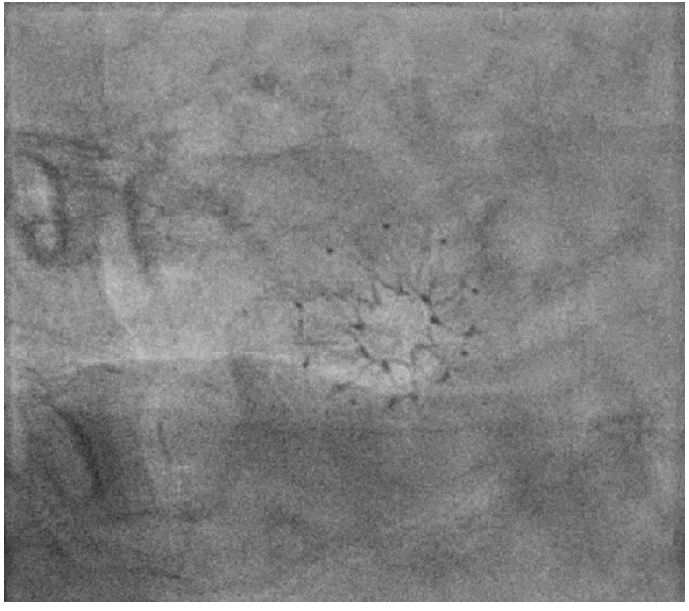


steuerbarer EP-Katheter

Unfallkrankenhaus Berlin

Lagekontrolle





REDUCE LAP-HF III (Postmarket-Studie)

observational, multi-center, prospective, single-arm, bis 500 Pat., bis 50 Zenten in Europa

Follow up 5 Jahre

Germany

Klinikum Lippe GmbH Detmold, Germany Contact: Stephan Gielen, MD	**Recruiting**
Elisabeth-Krankenhaus Essen Essen, Germany Contact: Oliver Bruder, MD	**Recruiting**
Universitäts Klinikum Halle Halle, Germany Contact: Michel Noutsias, MD	**Recruiting**
St Vincenz-Kranenhaus Paderborn, Germany Contact: Andreas Goette, MD	**Recruiting**
Evangelisches Krankenhaus Paul Gerhardt Stift - Unfallstation Wittenberg, Germany Contact: Franz Kleber, Prof	**Recruiting**

Switzerland

Bürgelspital Solothurn Solothurn, Switzerland Contact: Rolf Vogel, Prof	**Recruiting**

REDUCE LAP-HF III (postmarket-Studie)

Problem Reembursement – NUB

Protokoll

-ähnlich REDUCE LAP-HF II,

-eine Belastungs-Hämodynamik ist nicht zwingend erforderlich, wenn bereits in Ruhe Grenzwerte überschritten werden

Unfallkrankenhaus Berlin

Zusammenfassung

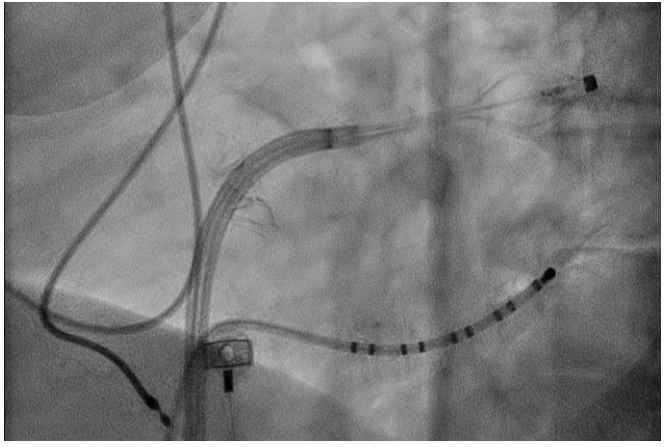
1. HFpEF ist häufig, kann leicht übersehen werden und wird oft erst spät diagnostiziert

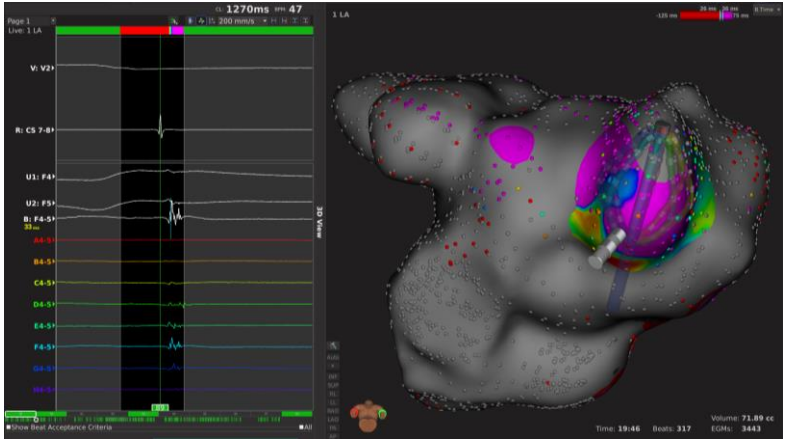
2. Zur Diagnostik von HFpEF ist oft eine ergometrische Untersuchung (invasiv, Echo) nötig

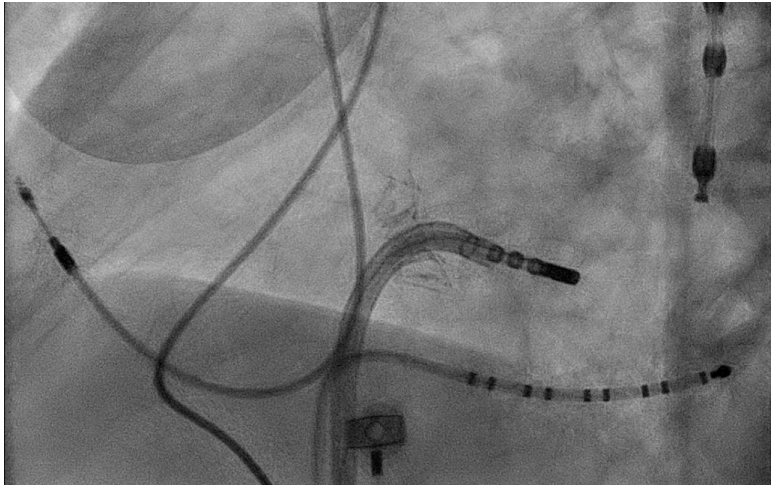
3. Interatriales Shunting ist ein vielversprechender therapeutischer Ansatz

4. Das CORVIA IASD ist gut zu implantieren, mögliche prozedurale Probleme sind lösbar

Linksatriale Prozeduren durch das Corvia IASD sind möglich







Unfallkrankenhaus Berlin

Vielen Dank