QRS Duration Predicts Prognosis in Heart Failure with Mildly Reduced Ejection Fraction

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Introduction - Epidemiology

Heart-failure (HF)

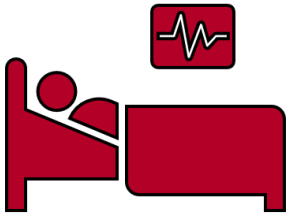
Continuously increasing prevalence[1] due to:

→ Demographic changes

→ Better health care supply

→ Improved medical management of HF

>64 million people worldwide affected by HF[2]



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LVEF ≥50%	LVEF ≤40%
Heart failure with **preserved** ejection fraction	Heart failure with **reduced** ejection fraction
HFpEF	HFrEF

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LVEF ≥50%

LVEF ≤40%

Heart failure with **reserved** ejection fraction

Heart failure with mildly reduced ejection fraction

Heart failure wit**h** **reduced** ejectio**n** fraction

FpEF

LVEF 41-49%

2013: ACCF/AHA – „HFpEF borderline“[3]

2016: ESC – „HFmrEF“ („mid range“)[4]

HFr

21 & 2022: ESC + ACC/AHA/HFSA – HFmrEF („mildly reduced“)

Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure. Circulation. 2013;128(16):e240-e327.
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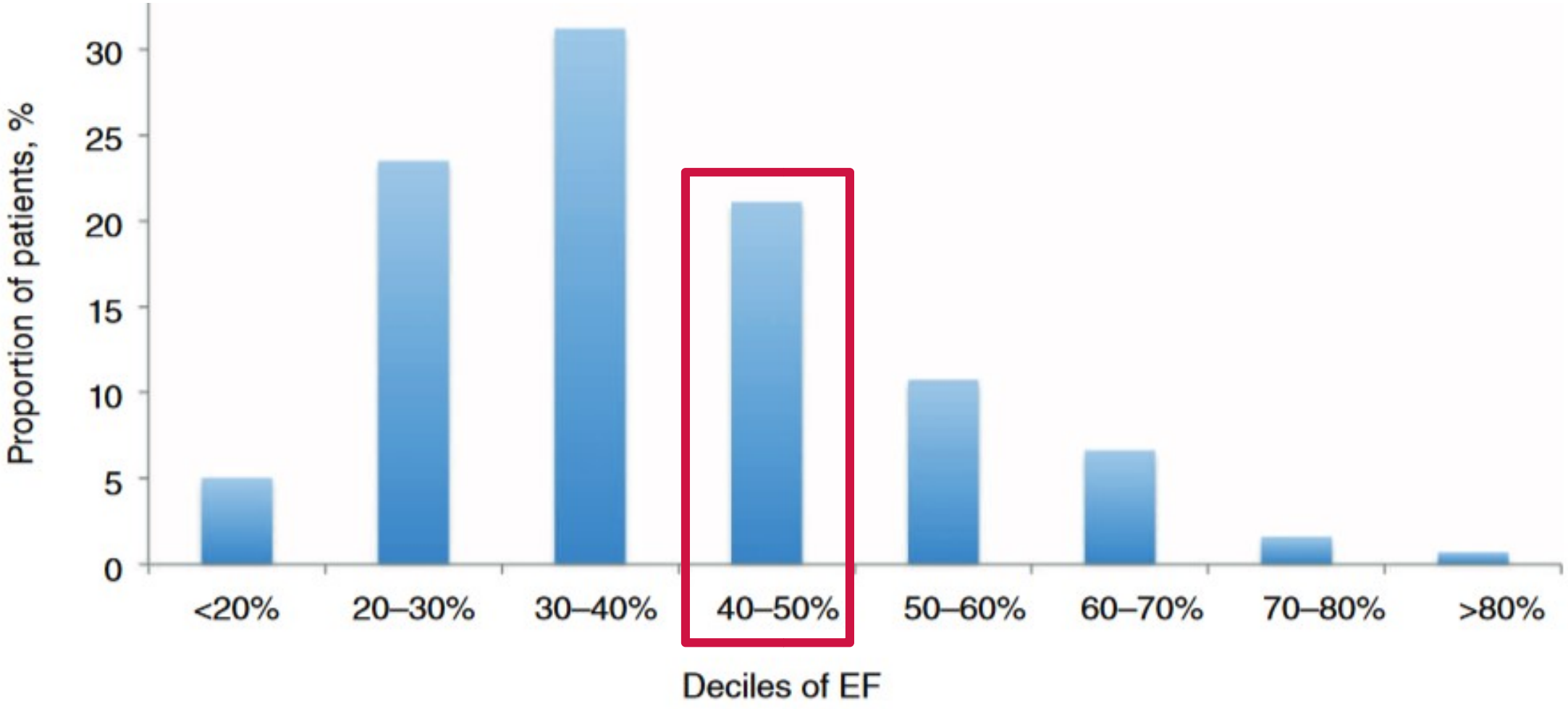
Heart failure with mildly reduced ejection fraction - epidemiology



- ¼ of the HF spectrum is classified as heart failure with mildly reduced ejection fraction (HFmrEF)

Chioncel O et al.; Eur J Heart Fa

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Heart failure with mildly reduced ejection fraction – similarite to HFrEF and HFpEF

le 1 Baseline characteristics in chronic heart failure patients stratified by ejection fraction

	All ($n = 9134$)	EF <40% ($n = 5460$)	EF 40–50% ($n = 2212$)	EF >50% ($n = 1462$)	*P*-value
graphic distribution, *n* (%)					
stern	1607 (17.6)	1014 (18.6)	384 (17.4)	209 (14.3)	
orthern	665 (7.3)	444 (8.1)	151 (6.8)	70 (4.8)	
outhern	5174 (56.6)	2995 (54.8)	1226 (55.4)	953 (65.2)	
Vestern	721 (7.9)	492 (9.0)	148 (6.7)	81 (5.5)	
orth Africa	559 (6.1)	227 (4.2)	255 (11.5)	77 (5.3)	
iddle East	408 (4.5)	288 (5.3)	48 (2.2)	72 (4.9)	
years, mean ± SD	64.8 ± 13.3	64.0 ± 12.6	64.2 ± 14.2	68.6 ± 13.7	<0.001
≥75 years, %	25.7	21.9	26.4	38.9	<0.001
ale gender, %	28.2	21.6	31.5	47.9	<0.001
kg/m^2, mean ± SD	28.1 ± 5.1	27.8 ± 4.9	28.6 ± 5.4	28.4 ± 5.4	<0.001
mmHg, mean ± SD	124.3 ± 20.8	121.6 ± 20.0	126.5 ± 21.1	130.98 ± 21.4	<0.001
≤110 mmHg, %	30.3	34.4	27.0	19.9	<0.001
rt rate, b.p.m., mean ± SD	72.9 ± 15.4	72.9 ± 15.1	73.2 ± 15.9	72.5 ± 15.5	0.344
rt rate ≥70 b.p.m., %	55.7	56.4	55.6	53.5	0.108
HA class III/IV, %	26.0	30.6	18.4	20.3	<0.001
ary aetiology, %					
chaemic heart disease	42.9	48.6	41.8	23.7	<0.001
ypertension	7.9	4.5	9.6	18.1	<0.001
ypertension treatment	58.5	55.6	60.1	67.0	<0.001
iopathic dilated cardiomyopathy	29.5	35.1	27.6	11.6	<0.001
lve disease	8.2	4.4	10.0	19.5	<0.001
chycardia-related cardiomyopathy	1.4	1.1	1.5	2.4	<0.001
ther	8.4	6.1	8.4	17.0	<0.001

HFmrEF has parallels with heart failu preserved ejection fraction (HFpEF) as with heart failure with reduced fraction (HFrEF).

Regarding the effect of pharmacotherapies, HFmrEF may be linked to HFpEF.

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Heart failure with mildly reduced ejection fraction – all-cause mortality predictors from the ESC-HF-LT Registry

Table 3 Predictors for all-cause mortality within 1 year by ejection fraction category

Variables	EF <40% OR (95% CI)	*P*-value	EF 40–50% OR (95% CI)	*P*-value	EF >50% OR (95% CI)	*P*-value
Age	1.026 (1.017–1.035)	<0.0001	1.035 (1.021–1.049)	<0.0001	1.021(1.012–1.029)	0.021
Sex (ref = male)	—	—	0.587 (0.393–0.877)	0.0094	—	—
Body mass index	0.958 (0.937–0.979)	0.0001	—	—	0.938 (0.896–0.983)	0.0071
Systolic blood pressure	0.983 (0.978–0.988)	<0.0001	0.977 (0.968–0.985)	<0.0001	—	—
Heart rate	1.007 (1.001–1.012)	0.0276	1.011 (1.001–1.020)	0.0316	—	—
NYHA class III/IV	2.023 (1.664–2.4				2.722 (1.746–4.244)	<0.0001
Ischaemic heart disease	—				—	—
Pulmonary congestion	—				0.993 (0.989–0.998)	0.0049
S3 gallop	1.437 (1.076–1.				—	—
Mitral regurgitation	—				—	—
Aortic stenosis	1.886 (1.288–2.				2.144 (1.261–3.647)	0.0049
Diabetes	1.419 (1.160–1.				—	—
Atrial fibrillation	—	—	—	—	2.158 (1.360–3.422)	0.0011
Peripheral artery disease	1.422 (1.115–1.815)	0.0046	—	—	3.234 (1.947–5.371)	<0.0001
Chronic kidney disease	1.781 (1.452–2.185)	<0.0001	1.601 (1.108–2.314)	0.0122	1.981 (1.251–3.136)	0.0035
Hepatic dysfunction	—	—	2.370 (1.282–4.381)	0.0059	—	—
Depression	1.504 (1.113–2.032)	0.0078	—	—	—	—

CI, confidence interval; EF, ejection fraction; NYHA, New York Heart Association; OR, odds ratio.

QRS??

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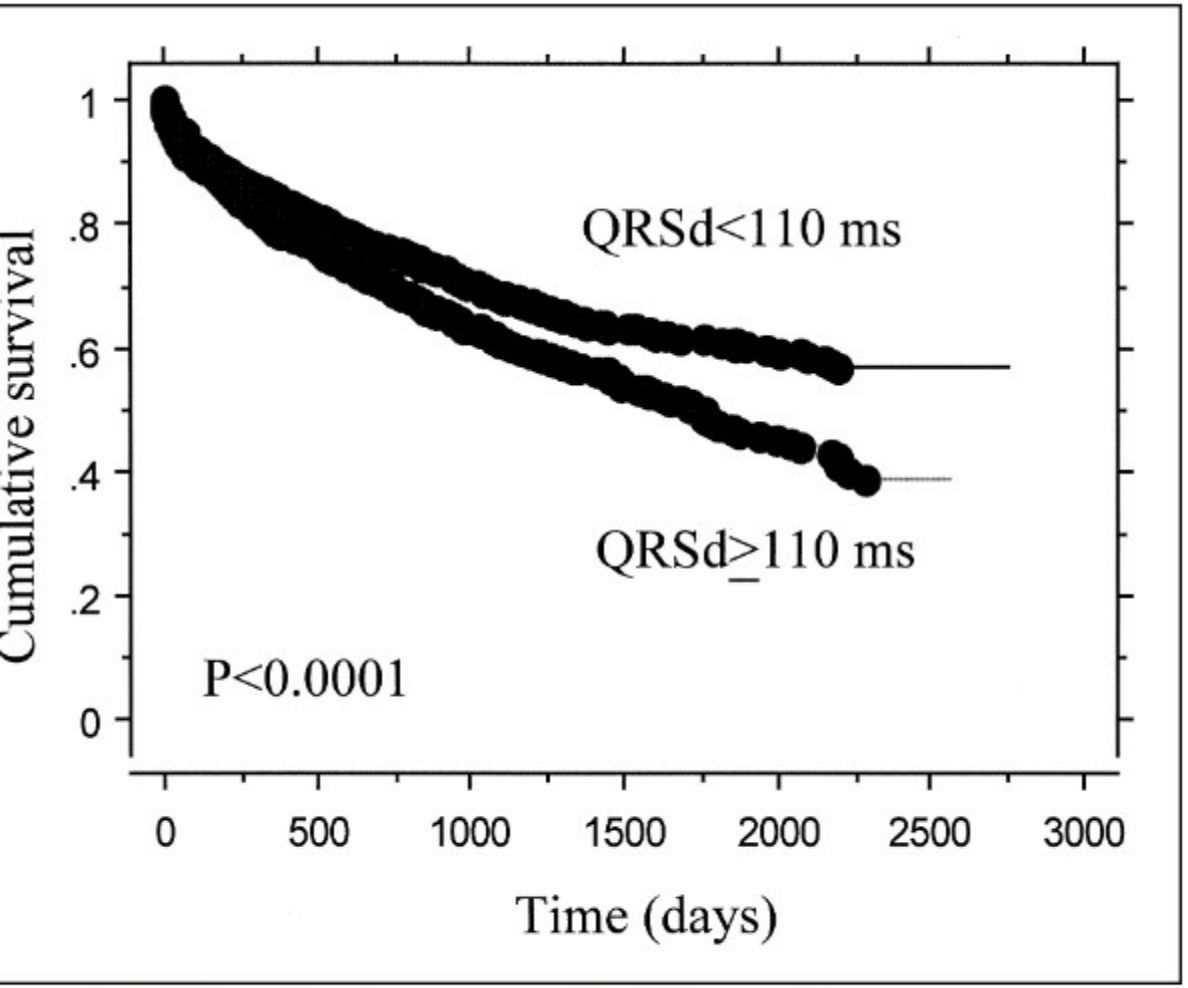
Heart failure with reduced ejection fraction – QRS duration ar mortality



GURE 1. Effect of QRS duration (QRSd) on all-cause mortality. RS prolongation significantly increased the mortality in patients th moderate and severe LV dysfunction.[1]

- In HFrEF, a prolonged QRS duration is a recogniz factor for adverse events and potentially treatab cardiac resynchronization therapy.[2]
- Most studies investigating the impact of the QRS c were restricted to HFrEF or post-AMI patients.

[1]Silvet H et al.: Am J Cardiol. 2001
[2]McDonagh TA et al.: Eur Heart J. 2021

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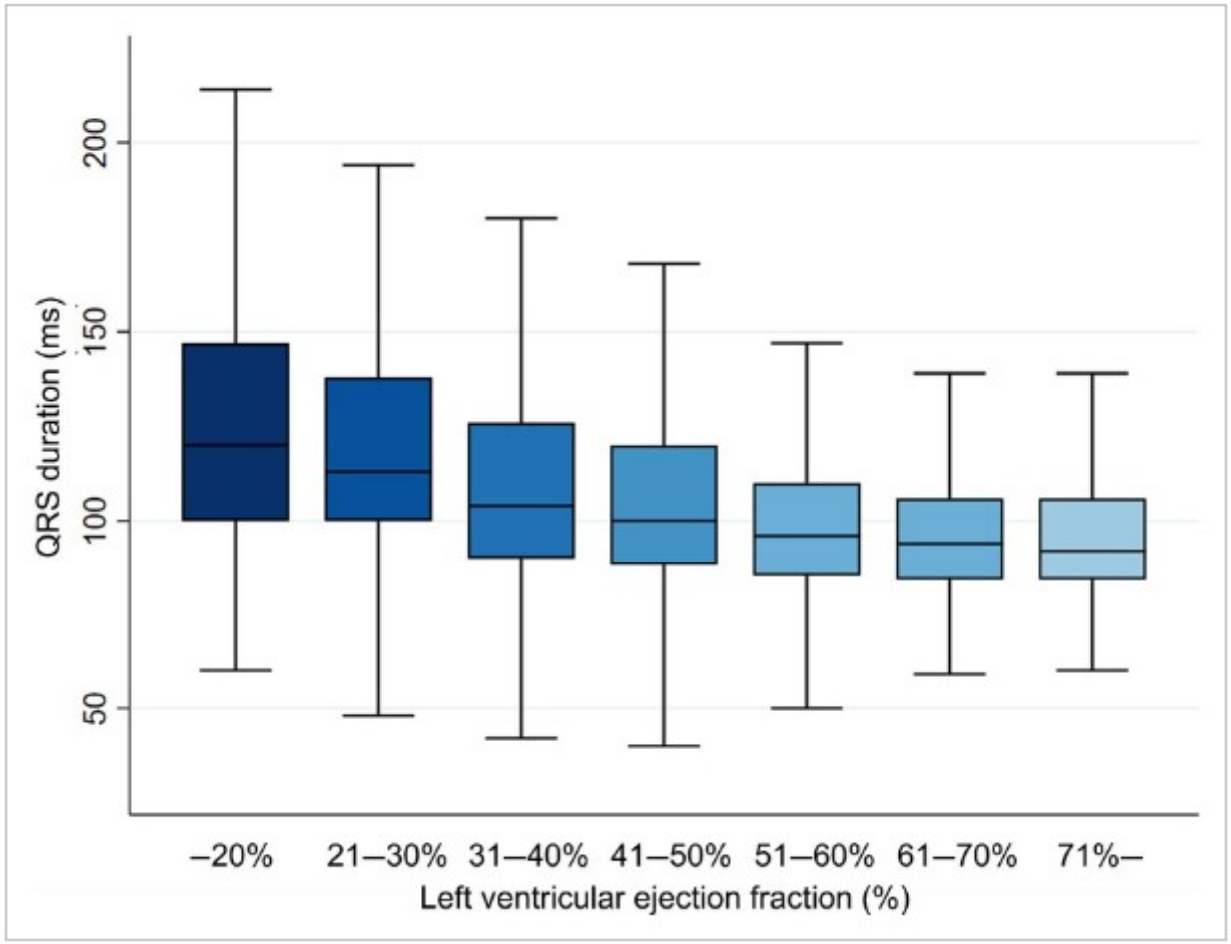
QRS duration across the spectrum of HF



QRS duration increases with lowering LVEF.
QRS prolongation in HFmrEF is common.

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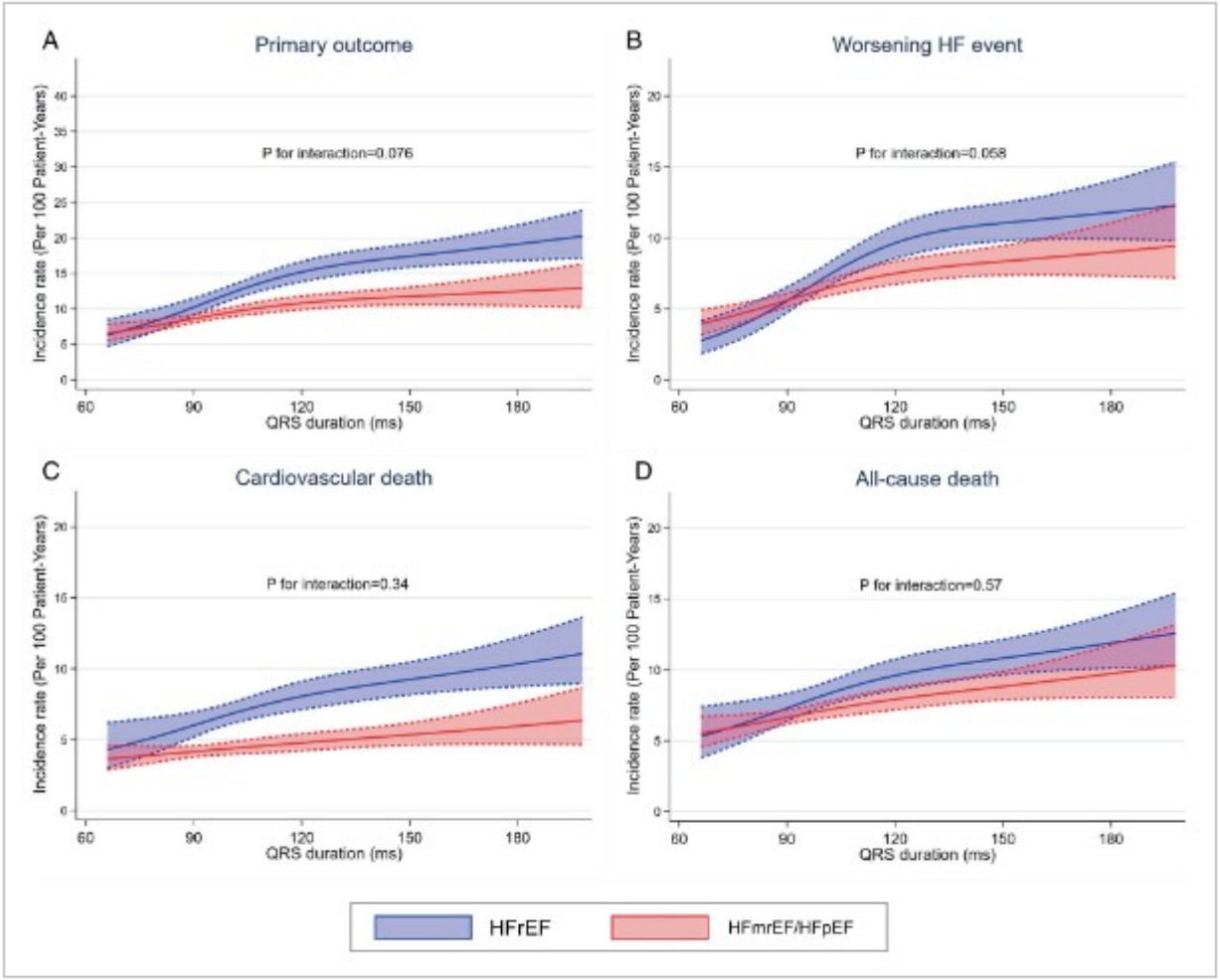
Results from DAPA-HF and DELIVER trials



Higher risk of the composite of CV death and HF-hospitalizations even in HFmrEF/HFpEF.
No further stratification by HFmrEF/HFpEF.

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Heart Failure With Mildly Reduced Ejection Fraction Registry (HARME

Consecutive patients with HFmrEF according to current European guidelines (i.e., LVEF 41 – 49%) with additional sign
and/or symptoms of heart failure.

n = 2.184 consecutive patients admitted to the University Medical Center Mannheim from 2016 to 2022 we
retrospectivly included.

Patients with native QRS duration <120 ms were compared to patients with prolonged QRS duration ≥120 ms.

primary endpoint: all-cause mortality during median follow-up (i.e., 30 months).

secondary endpoints: heart failure related rehospitalization, cardiac rehospitalization, revascularization, stroke, maj
adverse cardiac and cerebrovascular events (MACCE) (i.e., composite of all-cause mortality, acute myocardi
infarction, stroke).

ClinicalTrials.gov Identifier: NCT05603390

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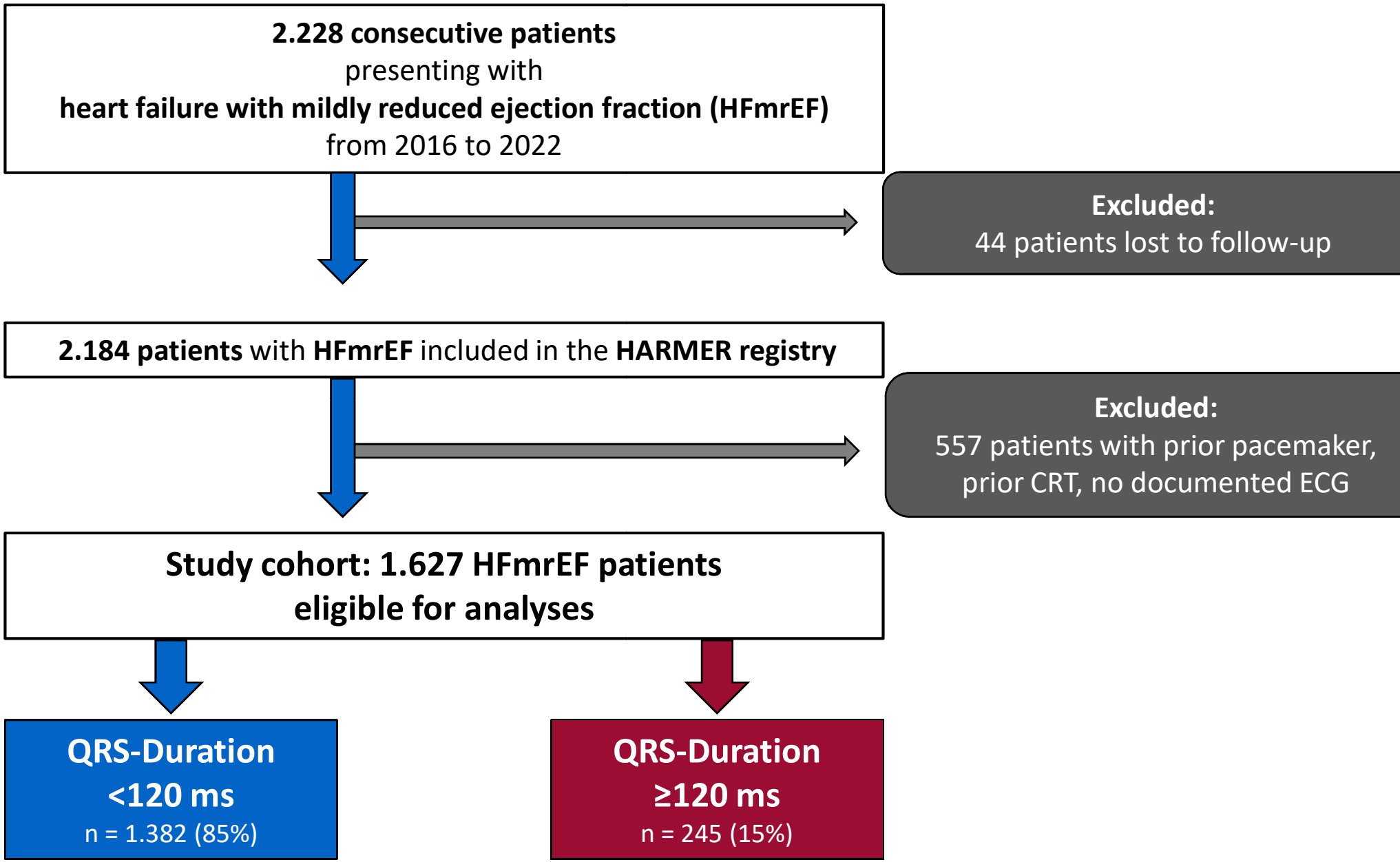
Study flow chart



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Baseline characteristics

Table 1. Baseline characteristics.

	QRS <120 ms (*n* = 1382)		QRS ≥120 ms (*n* = 245)		p value
Age, median (IQR)	73	(62-81)	80	(72-85)	**0.001**
Male sex, n (%)	892	(64.5)	176	(71.8)	**0.027**
Body mass index, kg/m², median (IQR)	26.8	(23.8-30.9)	26.5	(24.0-30.5)	0.790
SBP, mmHg, median (IQR)	143	(125-161)	140	(122-160)	0.438
DBP, mmHg, median (IQR)	80	(70-92)	74	(63-87)	**0.001**
Heart rate, bpm, median (IQR)	83	(70-99)	76	(65-89)	**0.001**
Medical history, n (%)					
Coronary artery disease	544	(39.4)	113	(46.1)	**0.047**
Prior myocardial infarction	337	(24.4)	63	(25.7)	0.656
Prior PCI	393	(28.4)	77	(31.4)	0.341
Prior CABG	120	(8.7)	35	(14.3)	**0.006**
Prior valvular surgery	39	(2.8)	16	(6.5)	**0.003**
Congestive heart failure	415	(30.0)	100	(40.8)	**0.001**
Decompensated heart failure < 12 months	137	(9.9)	37	(15.1)	**0.015**
Chronic kidney disease (1er)	380	(27.5)	85	(34.7)	**0.022**
Peripheral artery disease	155	(11.2)	36	(14.7)	0.119
Stroke	194	(14.0)	37	(15.1)	0.660
Liver cirrhosis	18	(1.3)	7	(2.9)	0.068
Malignancy	218	(15.8)	36	(14.7)	0.668
Cardiovascular risk factors, n (%)					
Arterial hypertension	1063	(76.9)	201	(82.0)	0.076
Diabetes mellitus	485	(35.1)	93	(38.0)	0.388
Hyperlipidaemia	403	(29.2)	86	(35.1)	0.062
Smoking					
Current	282	(20.4)	31	(12.7)	**0.005**
Former	248	(17.9)	51	(20.8)	0.285
Family history	145	(10.5)	23	(9.4)	0.601
Comorbidities at index hospitalization, n (%)					
Acute coronary syndrome					
Unstable angina	68	(4.9)	15	(6.1)	0.431
STEMI	149	(10.8)	11	(4.5)	**0.002**
NSTEMI	195	(14.1)	35	(14.3)	0.942
Acute decompensated heart failure	309	(22.4)	66	(26.9)	0.117
Cardiogenic shock	33	(2.4)	10	(4.1)	0.128
Atrial fibrillation	553	(40.0)	103	(42.0)	0.551
Cardiopulmonary resuscitation	36	(2.6)	8	(3.3)	0.557
Out-of-hospital	15	(1.1)	3	(1.2)	0.848
In-hospital	21	(1.5)	5	(2.0)	0.549
Stroke	160	(11.6)	31	(12.7)	0.630
COPD	164	(11.9)	29	(11.8)	0.989

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Heart failure related and procedural data

Table 2. Heart-failure related and procedural data.

	QRS <120 ms (*n* = 1382)	QRS ≥120 ms (*n* = 245)	p value
Heart failure etiology, n (%)			
Ischemic cardiomyopathy	827 (59.8)	152 (62.0)	
Non-ischemic cardiomyopathy	88 (6.4)	14 (5.7)	
Hypertensive cardiomyopathy	104 (7.5)	22 (9.0)	
Congenital heart disease	1 (0.1)	0 (0.0)	0.408
Valvular heart disease	53 (3.8)	10 (4.1)	
Tachycardia-associated Tachymyopathy	67 (4.8) / 32 (2.3)	5 (2.0) / 2 (0.8)	
Unknown	210 (15.2)	40 (16.3)	
NYHA functional class, n (%)			
I/II	1014 (73.4)	161 (65.7)	
III	242 (17.5)	67 (27.3)	**0.001**
IV	126 (9.1)	17 (6.9)	
Electrocardiographic data			
Heart rate, bpm, median (IQR)	78 (66-93)	73 (63-86)	**0.001**
PQ-interval, ms, median (IQR)	160 (140-180)	170 (150-200)	**0.001**
QRS-interval, ms, median (IQR)	90 (80-100)	140 (130-150)	**0.001**
QT-interval, ms, median (IQR)	360 (340-400)	400 (375-440)	**0.001**
Echocardiographic data			
LVEF, %, median (IQR)	45 (45-47)	45 (45-47)	0.434
IVSd, mm, median (IQR)	12 (10-13)	12 (11-13)	**0.001**
LVEDD, mm, median (IQR)	49 (44-54)	50 (45-54)	0.156
TAPSE, mm, median (IQR)	20 (18-23)	21 (18-24)	**0.040**
LA diameter, mm, median (IQR)	41 (36-47)	42 (38-49)	**0.048**
LA surface, cm^2, median (IQR)	21.0 (17.0-25.0)	22.0 (17.0-26.0)	0.312
E/A, median (IQR)	0.8 (0.7-1.2)	0.7 (0.6-1.1)	0.075
E/E', median (IQR)	9.0 (6.3-13.5)	10.0 (6.0-15.2)	0.453
Diastolic dysfunction, n (%)	989 (71.6)	185 (75.5)	0.204
Moderate-severe aortic stenosis, n (%)	124 (9.0)	34 (13.9)	**0.017**
Moderate-severe aortic regurgitation, n (%)	57 (4.1)	8 (3.3)	0.527
Moderate-severe mitral regurgitation, n (%)	156 (11.3)	43 (17.6)	**0.006**
Moderate-severe tricuspid regurgitation, n (%)	190 (13.7)	42 (17.1)	0.161
VCI, mm, median (IQR)	19 (15-25)	21 (17-25)	0.257
Aortic root, mm, median (IQR)	33 (30-36)	33 (30-37)	0.571
Coronary angiography, n (%)	657 (47.5)	110 (44.9)	0.445
No evidence of coronary artery disease	124 (18.9)	22 (20.0)	
1-vessel disease	121 (18.4)	19 (17.3)	0.057
2-vessel disease	153 (23.3)	14 (12.7)	
3-vessel disease	259 (39.4)	55 (50.0)	
CABG	46 (7.0)	17 (15.5)	**0.003**
Chronic total occlusion	87 (13.2)	14 (12.7)	0.883
PCI, n (%)	368 (56.0)	48 (43.6)	**0.016**
Sent to CABG, n (%)	37 (5.6)	4 (3.6)	0.389
Baseline laboratory values, median (IQR)			
Potassium, mmol/L	3.9 (3.6-4.2)	3.9 (3.6-4.2)	0.869
Sodium, mmol/L	139 (137-141)	139 (137-142)	0.421
Creatinine, mg/dL	1.04 (0.85-1.37)	1.19 (0.88-1.54)	**0.001**
eGFR, mL/min/1.73 m^2	68 (48-88)	59 (43-77)	**0.001**
Haemoglobin, g/dL	12.5 (10.5-14)	12.0 (10.3-13.6)	0.085
WBC count, x 10^9/L	8.37 (6.56-10.32)	7.85 (6.25-9.42)	**0.006**
Platelet count, x 10^9/L	228 (180-289)	224 (176-275)	0.250
HbA1c, %	5.9 (5.5-6.7)	6.1 (5.5-7.1)	0.172
LDL- cholesterol, mg/dL	99 (76-128)	91 (71-128)	0.259
HDL- cholesterol, mgl/dL	42 (34-51)	42 (35-50)	0.956
C-reactive protein, mg/L	14 (3-46)	13 (4-48)	0.990
NT-pro BNP, pg/mL	2607 (947-6828)	2607 (1140-5777)	0.125
Cardiac troponin I, µg/L	0.03 (0.02-0.29)	0.03 (0.02-0.12)	0.334

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Primary and secondary endpoints

Table 4. Follow-up data, primary and secondary endpoints.

	QRS <120 ms (*n* = 1382)	QRS ≥120 ms (*n* = 245)	HR	95% CI	p value
Primary endpoint, n (%)					
All-cause mortality, at 30 months	397 (28.7)	86 (35.1)	1.254	0.993-1.583	0.057
Secondary endpoints, n (%)					
Heart-failure related rehospitalization, at 30 months	159 (11.9)	43 (18.2)	1.574	1.124-2.204	**0.008**
Cardiac rehospitalization, at 30 months	297 (22.2)	67 (28.4)	1.299	0.997-1.694	0.053
Coronary revascularization, at 30 months	108 (8.1)	18 (7.6)	0.926	0.562-1.525	0.763
Stroke, at 30 months	32 (2.4)	6 (2.5)	1.048	0.438-2.506	0.916
MACCE, at 30 months	514 (37.2)	106 (43.3)	1.186	0.963-1.462	0.109
Follow-up data, median (IQR)					
Hospitalization time, days	8 (5-15)	10 (6-15)	-	-	0.221
ICU time, days	0 (0-1)	0 (0-1)	-	-	0.625
Follow-up time, days	884 (378-1556)	857 (362-1467)	-	-	0.263

CI, confidence interval; HF, heart failure; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; MACCE, major adverse cardiac and cerebrovascular events;.Level of significance p≤0.05. Bold type indicates statistical significance.

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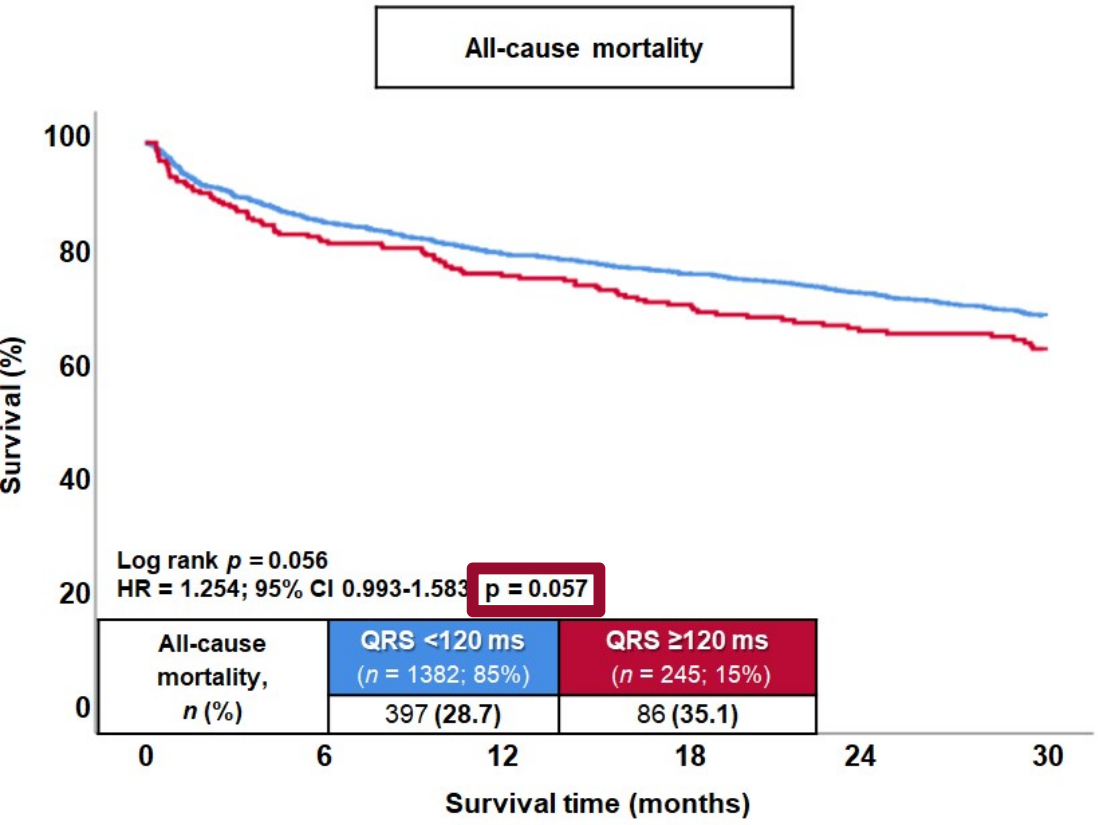
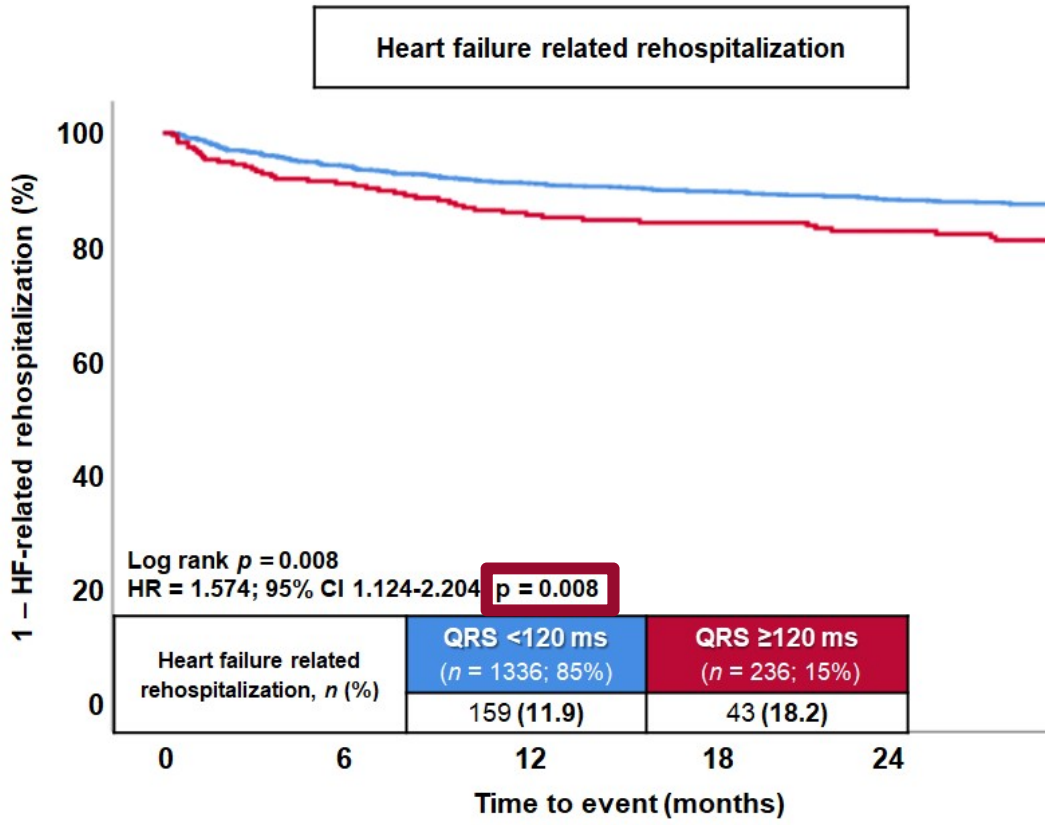
Primary and secondary endpoint: Kaplan-Meier analysis





at risk:						
0 ms	1382	1186	1048	920	795	680
0 ms	245	202	184	159	135	115

Patients at risk:					
QRS <120 ms	1336	1258	1155	1036	915
QRS ≥ 120 ms	236	215	198	178	159

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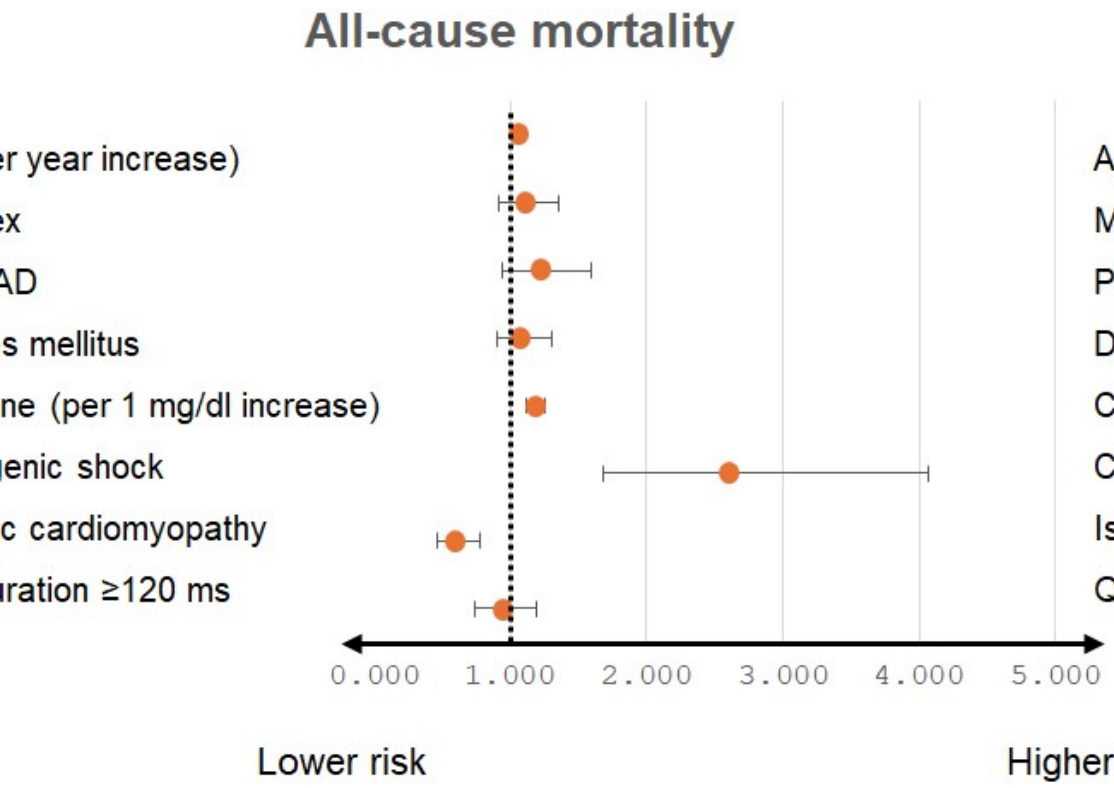
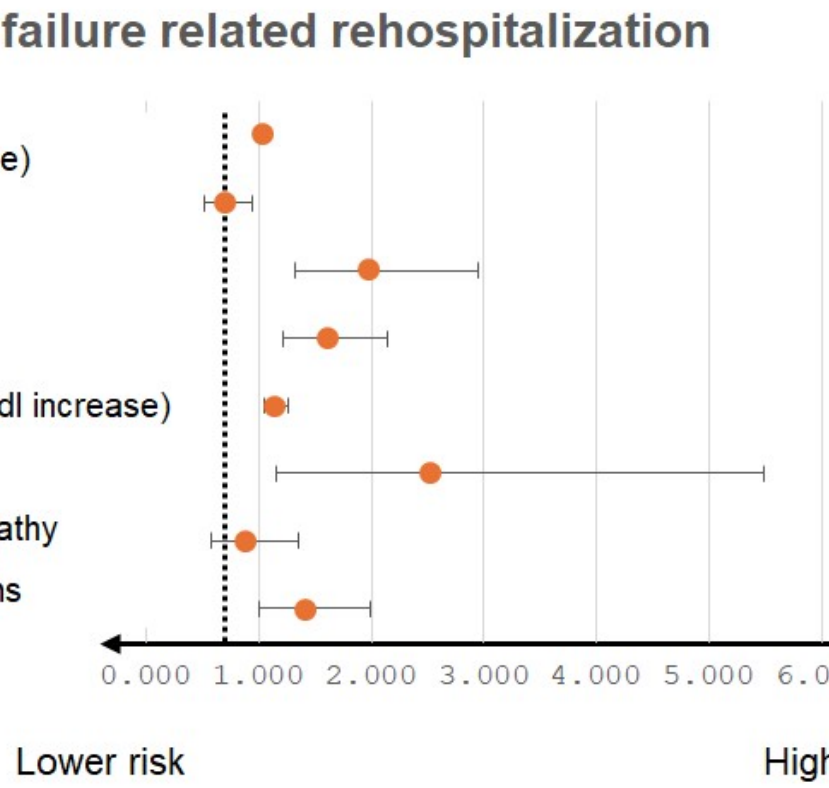
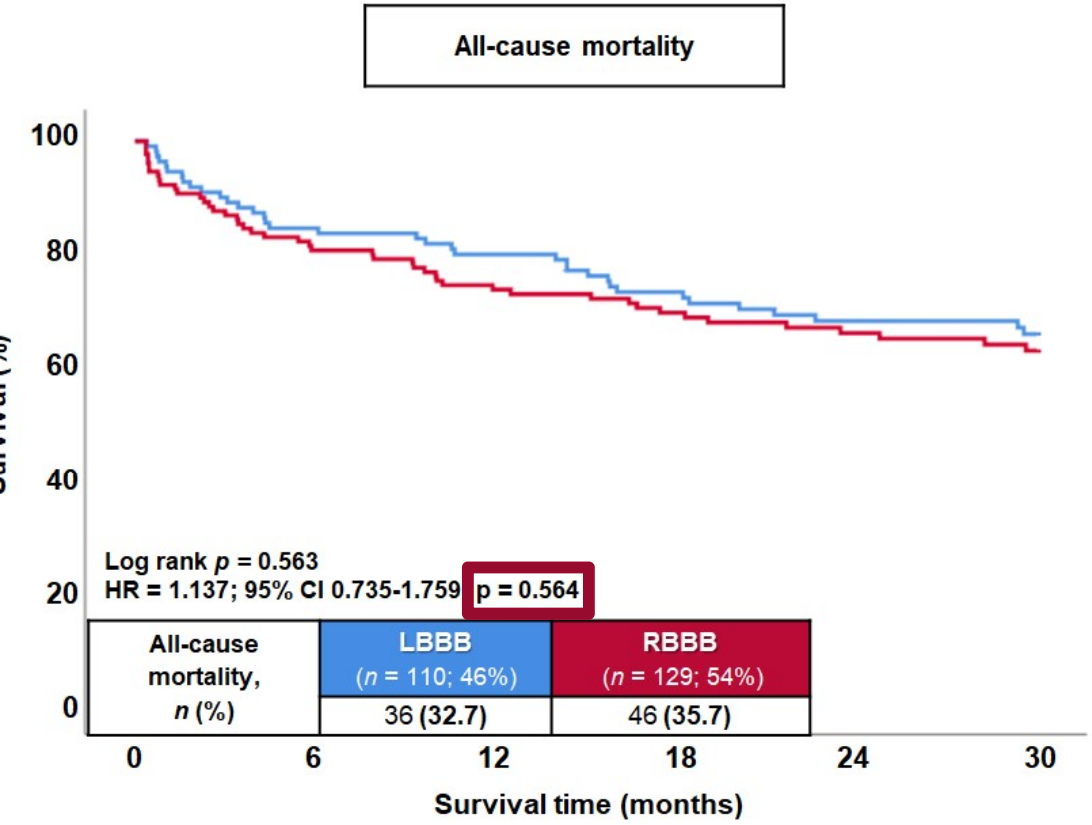
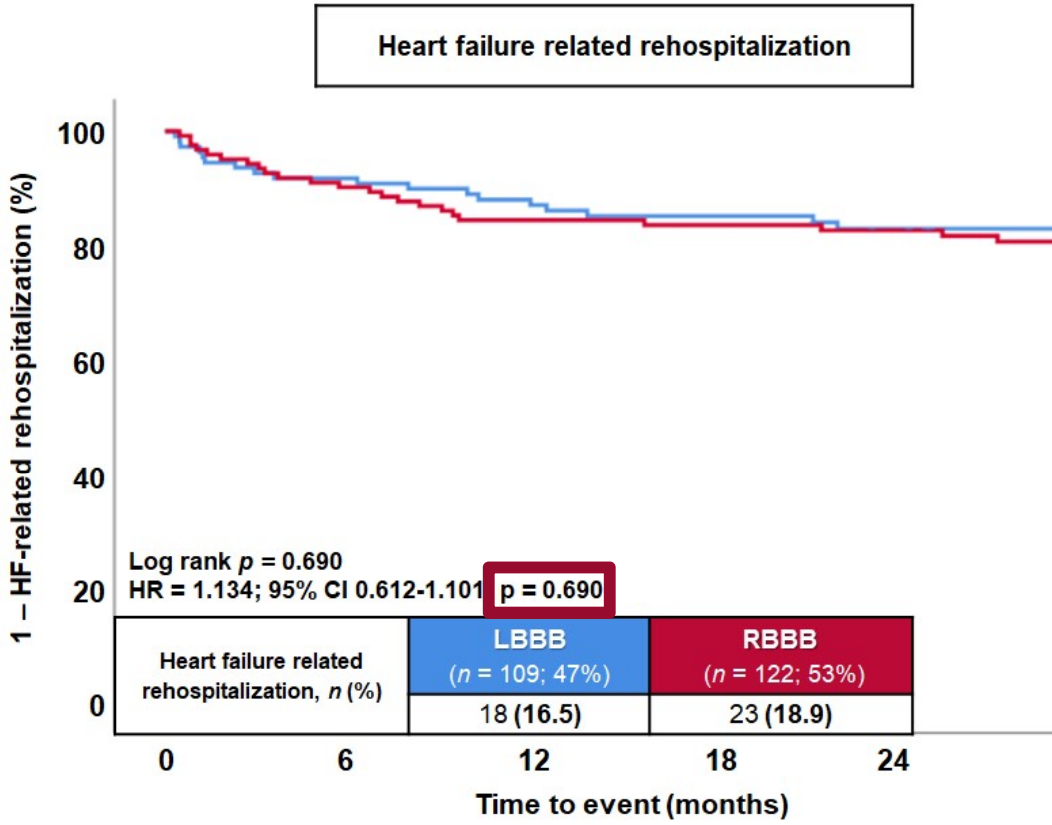
Multivariable risk prediction models





Left vs. right bundle branch block





t risk:

	110	93	85	73	64	55
	129	104	95	82	68	58

Patients at risk:

LBBB	109	100	91	79	72
RBBB	122	110	103	95	84

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Key messages

A prolonged QRS duration was observed in 15% of consecutive patients with HFmrEF.

In HFmrEF patients, a prolonged QRS duration is associated with a higher HF related rehospitalization rate at 30 month
even after multivariable adjustment.

In contrast, the risk of long-term all-cause mortality was not affected by the QRS duration.

Prognosis of patients with LBBB and RBBB was comparable.

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Thank you for your attention!



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