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Lékařská fakulta
Univerzita Palackého v Olomouci

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

# PARAGON-HF - jak interpretovat výsledky?

Martin Hutyra

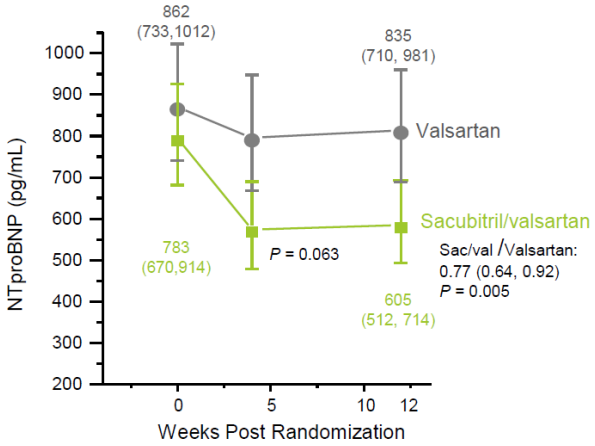
# Úvod

- Currently, no therapy has been shown to reduce morbidity and mortality in patients with HFpEF and no therapy has received regulatory approval [1,2]
- In the PARADIGM-HF trial, sacubitril/valsartan reduced morbidity and mortality in patients with HFrEF compared with enalapril[3]
- In PARAMOUNT, a Phase II trial in patients with HFpEF, sacubitril/valsartan reduced NT-proBNP at 12 weeks, reduced left atrial volume, and improved NYHA class at 36 weeks, compared with valsartan[4]
- PARAGON-HF has been designed to determine the efficacy and safety of sacubitril/valsartan compared with valsartan in patients with chronic HFpEF (LVEF ≥45%)[5]

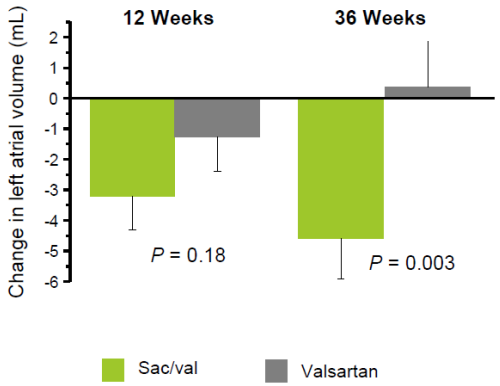
1. Ponikowski P et al. *Eur Heart J* 2016; 37:2129-2200; 2. Redfield MM. *N Engl J Med* 2016;375:1868-1877; 3. McMurray JJ et al. *N Engl J Med*. 2014;371:993-1004; 4. Solomon SD et al. *Lancet*. 2012;380:1387-1395; 5. Solomon SD et al. *JACC Heart Fail*. 2017;5:471-482

# Sakubitril/valsartan u HFpEF (studie PARAMOUNT)

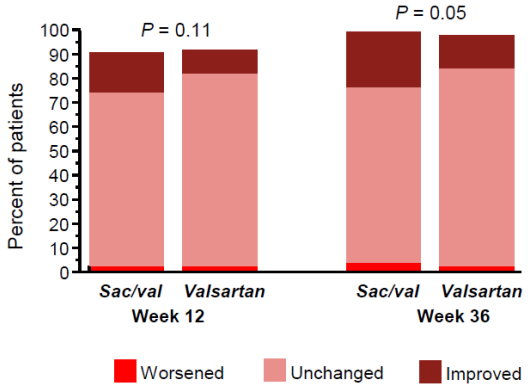
## Improvement in NT-proBNP




## Improvement in left atrial size




## Improvement in NYHA class




HFpEF, heart failure with preserved ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; sac/val, sacubitril/valsartan

Solomon et al. Lancet 2012 380(9851):1387-1395

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

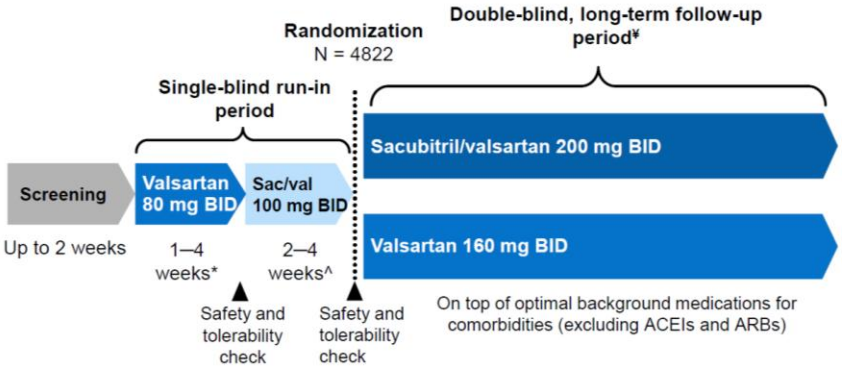
S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiva, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON-HF Investigators and Committees

This article was published on September 1, 2019, at NEJM.org.

DOI: 10.1056/NEJMoa1908655

# PARAGON-HF –design studie

| Parameter | Description |
|---|---|
| Study description | A phase III, randomized, double-blind, parallel group, active-controlled, 2-arm event-driven trial |
| Target population | 4,822 symptomatic HFpEF patients (NYHA Class II–IV) in 43 countries requiring diuretic treatment ≥30 days prior to screening, and LVEF ≥45%. |
| Treatment arms | Sacubitril/valsartan 200 mg BID versus valsartan 160 mg BID |
| Study initiation | July 2014 |
| Number of patients | Screened: 10,359<br>Randomized: 4822<br>Final analysis set: 4796 (ITT population) |
| Number of events accrued | 1487/416 hospitalizations/CV deaths |
| Follow-up for ITT analysis | Median follow-up 35 months<br>All participants were followed until April 30 2019 |



# Kritéria k zařazení do studie

## Key inclusion criteria

- Age ≥50 years; LVEF ≥45%
- Symptoms of HF requiring treatment with diuretic(s) for ≥30 days prior to screening
- Current symptomatic HF (NYHA class II–IV)
- Structural heart disease within the 6 months prior to screening (LAE and/or LVH)
- Patients with at least 1 of the following:
  - HF hospitalization within 9 months prior to screening and NT-proBNP >200 pg/mL for patients without AF or >600 pg/mL for patients with AF*

    OR
  - NT-proBNP >300 pg/mL for patients without AF or >900 pg/mL for patients with AF*

## Key exclusion criteria

- History of LVEF <40%
- MI, CABG or any event within the 6 months prior to screening that could have reduced the LVEF (unless LVEF confirmed as ≥45%)
- Current acute decompensated HF requiring therapy
- Requirement for treatment with two or more of the following: ACEi, ARB or renin inhibitor
- SBP <110 mmHg OR SBP ≥180 mmHg at screening^
- Serum potassium >5.2 mmol/L at screening, or >5.4 mmol/L at the end of each run-in period
- eGFR <30 mL/min/1.73m$^2$ at screening, OR at the end of each run-in period eGFR <25 mL/min/1.73m$^2$ or eGFR reduction of >35% compared to that at screening

ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; AF, atrial fibrillation; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; HF, heart failure; LAE, left atrial enlargement; LVH, left ventricular hypertrophy; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure.

Solomon SD et al. JACC Heart Fail. 2017;5:471-482

| | |
|---|---|
| **Aged ≥50 years with LVEF ≥45%** | • HFpEF is a disease of old age<br>• Almost all HFpEF trials designed to date use a LVEF cut-off of 40–45% |
| **NYHA class II-IV HF treated with diuretics for ≥30 days; no other diseases to explain symptoms** | • Diuretics are the only therapy recommended by HF guidelines<br>• Excludes patients with symptoms due to other conditions, such as severe lung disease, obesity, and others |
| **Elevated NT-proBNP (300 pg/mL or 200 pg/mL if hospitalised for HF in last 9 months)*** | • Rules out symptoms of non-cardiac origin (e.g., severe COPD)<br>• Predicts poor outcomes |
| **Structural heart disease (LAE or LVH)** | • Physical evidence of the HFpEF syndrome mandated by Guidelines<br>• Predicts poor outcomes |

Afib, atrial fibrillation; COPD, chronic obstructive pulmonary disease; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; LAE, left atrial enlargement; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association

Solomon SD et al. JACC Heart Fail. 2017;5:471-482

# Výsledné ukazatele – endpointy studie

## Primary objective

- To evaluate the efficacy of sacubitril/valsartan compared with valsartan in reducing the rate of the composite endpoint of CV death and total (first and recurrent) HF hospitalizations in HF patients (NYHA class II to IV) with preserved ejection fraction (LVEF ≥45%)

## Secondary objectives

- To compare the effects of sacubitril/valsartan vs. valsartan on:
  - improvement in the KCCQ clinical summary score for HF symptoms and physical limitations at 8 months
  - improvement in NYHA functional classification at 8 months
  - delay in the time to the first occurrence of a composite renal endpoint*
  - delay in the time to all-cause mortality

CV, cardiovascular; HF, heart failure; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B type natriuretic peptide; NYHA, New York Heart Association

Solomon SD et al. JACC Heart Fail. 2017;5:471-482

# Základní charakteristiky

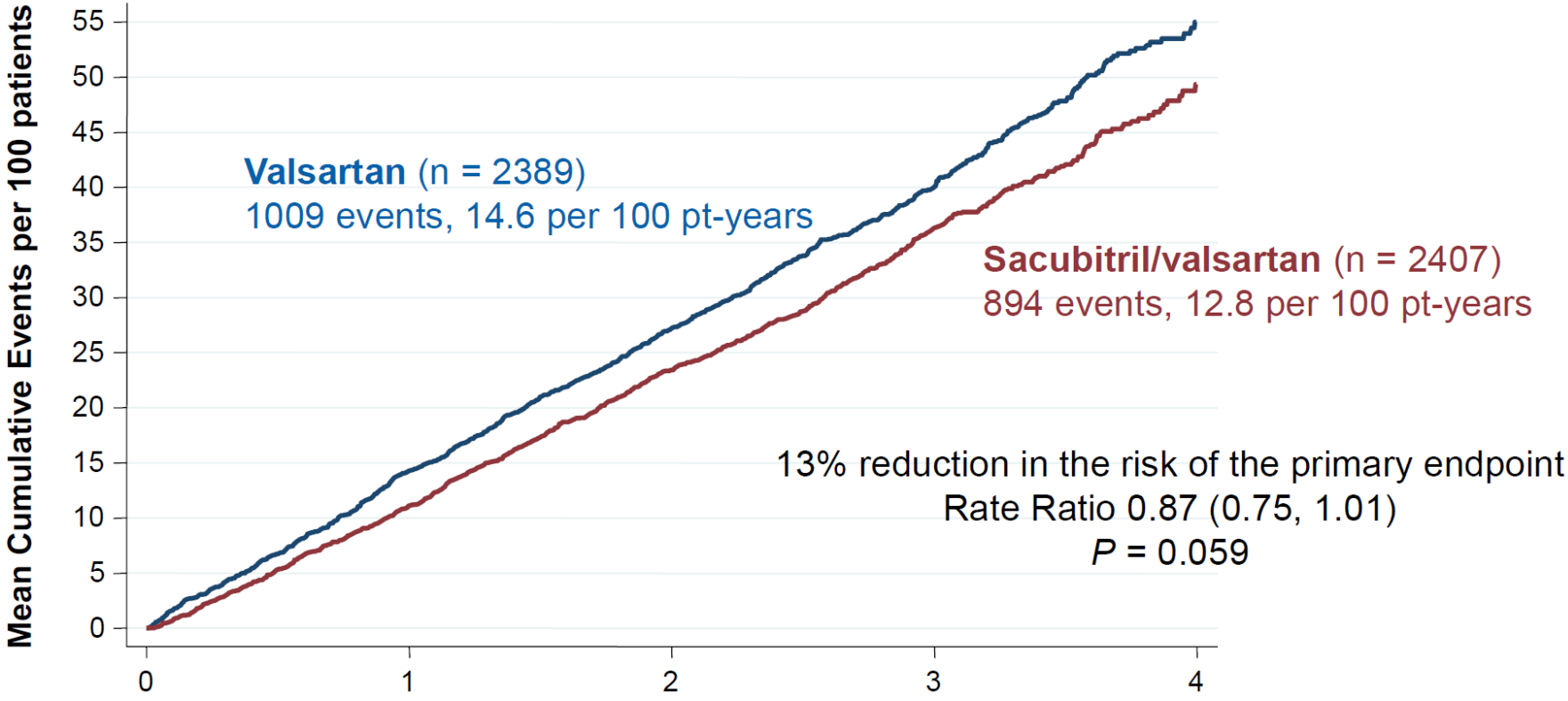
| Characteristic | | Sacubitril/valsartan (n=2407) | Valsartan (n=2389) |
|---|---|---|---|
| **Age, years (SD)** | | 72.7 (8.3) | 72.8 (8.5) |
| **Female sex, n (%)** | | 1241 (51.6) | 1238 (51.8) |
| **Race or ethnic group, n (%)†** | White | 1963 (81.6) | 1944 (81.4) |
| | Black | 52 (2.2) | 50 (2.1) |
| | Asian | 297 (12.3) | 310 (13.0) |
| | Other | 95 (4.0) | 85 (3.6) |
| **Region, n (%)** | North America | 288 (12.0) | 271 (11.3) |
| | Latin America | 191 (7.9) | 179 (7.5) |
| | Western Europe | 699 (29.0) | 691 (28.9) |
| | Central Europe | 856 (35.6) | 859 (36.0) |
| | Asia–Pacific | 373 (15.5) | 389 (16.3) |
| **Mean systolic blood pressure, mm Hg (SD)†** | | 130.5 (15.6)/74.3 (10.6) | 130.6 (15.3)/74.3 (10.4) |
| **Heart rate, beats/min (SD) )†** | | 70.6 (12.3) | 70.3 (12.2) |
| **Mean body mass index, kg/m$^2$ (SD)** | | 30.2 (4.9) | 30.3 (5.1) |
| **Serum creatinine, mg/dL (SD)†** | | 96.2 (27.2) | 96.6 (27.4) |
| **Mean estimated glomerular filtration rate, ml/min/1.73 m$^2$ (SD)** | | 63 (19) | 62 (19) |

SD, standard deviation

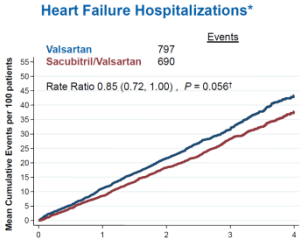
†Baseline characteristics measured at randomization visit (all others from screening visit). 1 missing value for each of the following: ischemic etiology, creatinine, body mass index, systolic blood pressure, heart rate. All other baseline data is complete unless otherwise noted.

| Characteristic | | | Sacubitril/valsartan (n = 2407) | Valsartan (n = 2389) |
|---|---|---|---|---|
| **Ischemic etiology, n (%)** | | | 899 (37.4) | 824 (34.5)* |
| **Mean left ventricular ejection fraction,% (SD)** | | | 57.6 (7.8) | 57.5 (8.0) |
| **Median NT-proBNP, pg/ml (IQR)** | | | 904 (475,1596) | 915 (453,1625) |
| **NYHA functional class, n (%)†** | | I | 73 (3.0) | 64 (2.7) |
| | | II | 1866 (77.5) | 1840 (77.0) |
| | | III | 458 (19.0) | 474 (19.8) |
| | | IV | 8 (0.3) | 11 (0.5) |
| | | Missing | 2 (0.1) | 0 (0.0) |
| **Medical history** | Hypertension, n (%) | | 2304 (95.7) | 2280 (95.4) |
| | Diabetes, n (%) | | 1046 (43.5) | 1016 (42.5) |
| | Atrial fibrillation/flutter at screening, n (%) | | 775 (32.2) | 777 (32.5) |
| | Hospitalization for heart failure, n (%) | | 1135 (47.2) | 1171 (49.0) |
| | Myocardial infarction, n (%) | | 561 (23.3) | 522 (21.9) |
| | Stroke, n (%) | | 266 (11.1) | 242 (10.1) |
| **Treatments at Randomization, n (%)** | Diuretics† | | 2294 (95.3) | 2291 (95.9) |
| | ACEIs/ARBs | | 2074 (86.2) | 2065 (86.4) |
| | MRAs† | | 592 (24.6) | 647 (27.1) |
| | Beta-Blockers† | | 1922 (79.9) | 1899 (79.5%) |

# Primární endpoint



| | Sacubitril/valsartan (n = 2407) | Valsartan (n = 2389) | Rate ratio | p-value |
|---|---|---|---|---|
| **Primary endpoint** | | | | |
| Total (first and recurrent) hospitalizations for heart failure or death from cardiovascular causes (total number of events)* | 894 (37.1)<br><br>12.8 per 100-patient years | 1009 (42.2)<br><br>14.6 per 100-patient years | 0.87 (0.75, 1.01) | 0.059 |
| **Components** | | | | |
| Total hospitalizations for worsening of HF, n (%) | 690 (28.7) | 797 (33.4) | 0.85 (0.72, 1.00) | 0.056† |
| Death from CV causes, n (%) | 204 (8.5%) | 212 (8.9%) | 0.95 (0.79, 1.16) | 0.62† |



# Sekundární endpointy

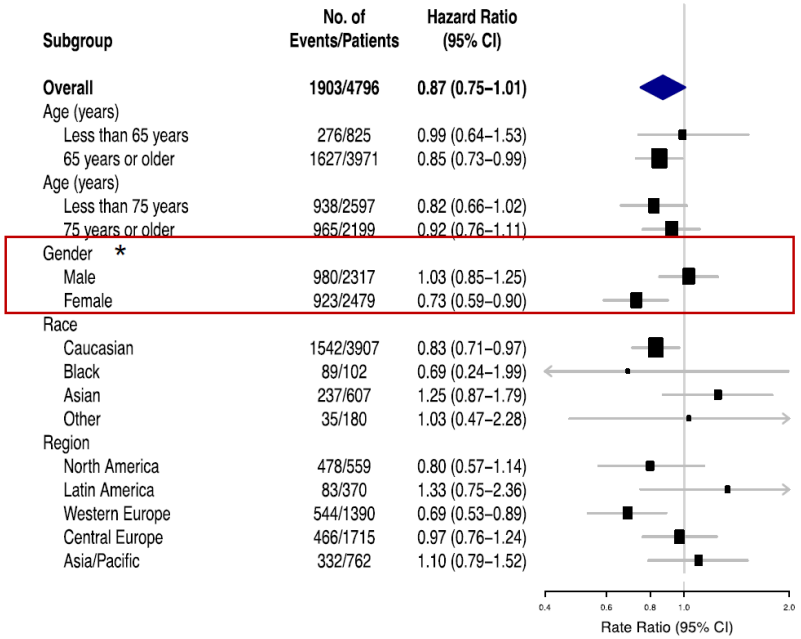
| | Sacubitril/valsartan (n = 2407) | Valsartan (n = 2389) | Hazard ratio/ Odds ratio/ Difference | Nominal p-value |
|---|---|---|---|---|
| **NYHA functional classification at 8 months, n (%)** | | | | |
| **Improved** | 347 (15.0) | 289 (12.6) | Odds ratio for improvement 1.45 (1.13, 1.86)‡ | 0.0035 |
| **Unchanged** | 1767 (76.3) | 1792 (77.9) | | |
| **Worsened** | 202 (8.7) | 221 (9.6) | | |
| **LSM change from baseline in KCCQ clinical summary score at 8 months*** | -1.6 (0.4) | -2.6 (0.4) | LSM of difference 1.03 (0.00 to 2.1) | 0.051 |
| **KCCQ responder (>5 points)** | 33.0% | 29.6% | Odds ratio 1.30 (1.04 to 1.61) | 0.019 |
| **Renal Composite Endpoint†** | 1.4% | 2.7% | Hazard ratio 0.50 (0.33 to 0.77) | 0.002 |
| **All-cause mortality – n/N (%)** | 14.2% | 14.6% | Hazard ratio 0.97 (0.84 to 1.13) | 0.68 |

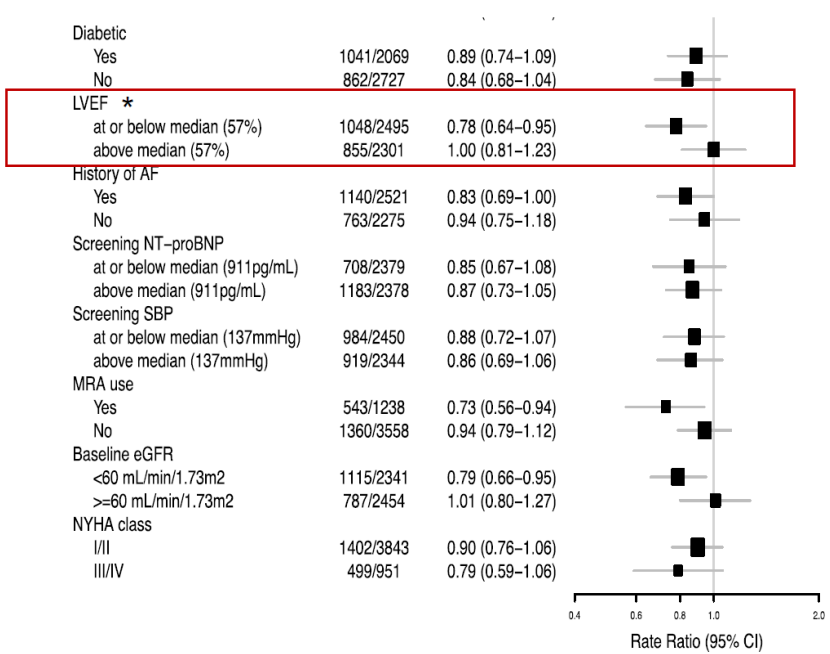
KCCQ, Kansas City Cardiomyopathy Questionnaire; LSM, least square means; NYHA, New York Heart Association

*A higher score indicated better quality of life

† Defined as renal death, reaching end stage renal disease (ESRD), or ≥50% decline in estimated glomerular filtration rate (eGFR) relative to baseline

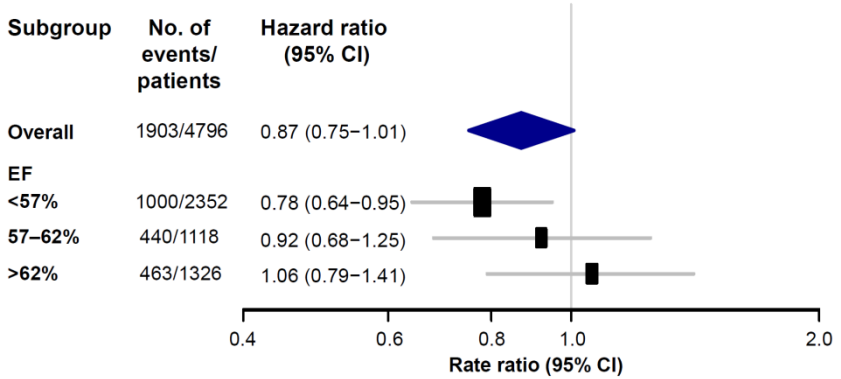
# Subanalýzy



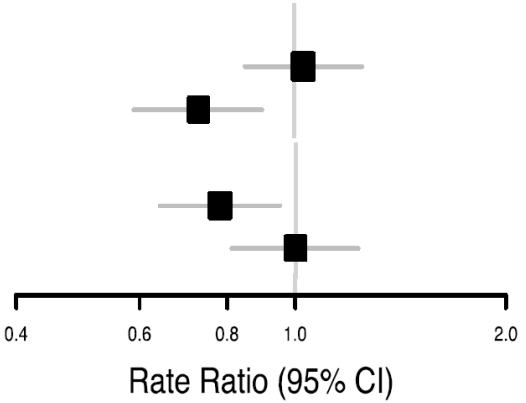




AF, atrial fibrillation; IQR, interquartile range; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor blocker; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New Yok Heart Association; SBP, systolic blood pressure; SD, standard deviation

*Multivariate p-interaction < 0.003

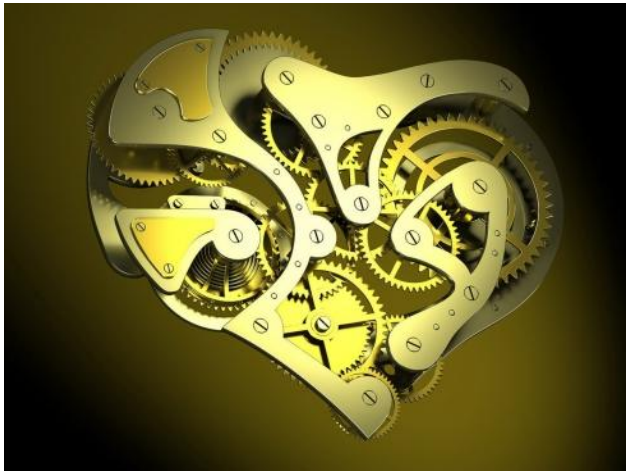



| | | |
|---|---|---|
| Gender | | |
| Male | 980/2317 | 1.03 (0.85–1.25) |
| Female | 923/2479 | 0.73 (0.59–0.90) |
| LVEF | | |
| at or below median (57%) | 1048/2495 | 0.78 (0.64–0.95) |
| above median (57%) | 855/2301 | 1.00 (0.81–1.23) |




In a multivariable model incorporating all interaction terms and covariates, only interactions for sex and ejection fraction remained nominally significant ($p < 0.003$ for both)

# PARAGON-HF - jak interpretovat výsledky studie?



# Hodnota p ≤0.05 – „zlatý“ endpoint každé studie?


1. P-values can indicate how incompatible the data are with a specified statistical model.
2. P-values do not measure the probability that the studied hypothesis is true, or the probability that the data were produced by random chance alone.
3. Scientific conclusions and business or policy decisions should not be based only on whether a p-value passes a specific threshold.
4. Proper inference requires full reporting and transparency.
5. A p-value, or statistical significance, does not measure the size of an effect or the importance of a result.
6. By itself, a p-value does not provide a good measure of evidence regarding a model or hypothesis.

# Pohlaví a jeho vliv na výsledky studie PARAGON-HF

10.1161/CIRCULATIONAHA.119.044491

**Effects of Sacubitril-Valsartan, versus Valsartan, in Women Compared to Men with Heart Failure and Preserved Ejection Fraction: Insights from PARAGON-HF**

**Running Title:** *McMurray & Jackson, et al.; Women and Men in PARAGON-HF*

John J.V. McMurray* & Alice M. Jackson*, et al.

| | Women (n=2479) | Men (n=2317) | P value |
|---|---|---|---|
| Age – years | 73.6±8.0 | 71.8±8.7 | <0.001 |
| Age category | | | <0.001 |
| 50-59 | 143 (5.8) | 232 (10.0) | |
| 60-69 | 562 (22.7) | 676 (29.2) | |
| 70-79 | 1168 (47.1) | 942 (40.7) | |
| ≥80 | 606 (24.4) | 467 (20.2) | |
| Region | | | 0.003 |
| Asia-Pacific and other | 379 (15.3) | 383 (16.5) | |
| Central Europe | 885 (35.7) | 830 (35.8) | |
| Latin America | 222 (9.0) | 148 (6.4) | |
| North America | 264 (10.6) | 295 (12.7) | |
| Western Europe | 729 (29.4) | 661 (28.5) | |
| Race | | | <0.001 |
| Asian | 287 (11.6) | 320 (13.8) | |
| Black | 61 (2.5) | 41 (1.8) | |
| Other | 124 (5.0) | 56 (2.4) | |
| White | 2007 (81.0) | 1900 (82.0) | |
| Duration of heart failure | | | 0.41 |
| 0-3 months | 417 (16.9) | 356 (15.4) | |
| 3-6 months | 319 (12.9) | 267 (11.5) | |
| 6-12 months | 309 (12.5) | 307 (13.3) | |
| 1-2 years | 340 (13.8) | 339 (14.7) | |
| 2-5 years | 508 (20.6) | 485 (21.0) | |
| >5 years | 578 (23.4) | 559 (24.2) | |
| Systolic blood pressure – mmHg | 131±16 | 130±15 | 0.04 |
| Diastolic blood pressure – mmHg | 74±11 | 74±10 | 0.99 |
| Pulse pressure – mmHg | 57±15 | 56±14 | 0.029 |
| Heart rate – beats/min | 71±12 | 70±12 | 0.047 |
| Left ventricular ejection fraction – % | 58.9±7.9 | 56.0±7.6 | <0.001 |
| Body mass index – kg/m$^2$ | 30.4±5.2 | 30.0±4.8 | 0.001 |
| Body mass index >30 kg/m$^2$ | 1272 (51.3) | 1082 (46.7) | 0.001 |
| Waist circumference – cm | 101.8±14.5 | 107.6±14.7 | <0.001 |
| Abnormal* | 1953 (82.8) | 1339 (61.6) | <0.001 |
| Waist/hip ratio | 0.93±0.12 | 1.00±0.11 | <0.001 |
| Estimated GFR – mL/min/1.73m2 | 60±18 | 65±20 | <0.001 |
| Estimated GFR <60 mL/min/1.73m2 | 1320 (53.2) | 1021 (44.1) | <0.001 |
| N-terminal-pro B-type natriuretic peptide – pg/ml | 836 (446-1601) | 954 (496-1631) | 0.002 |
| In patients with atrial fibrillation† | 1712 (1252-2360) | 1508 (1124-2210) | <0.001 |
| In patients without atrial fibrillation† | 575 (378-1018) | 625 (381-1103) | 0.022 |
| Urinary cGMP/creatinine | 129±70 | 120±61 | 0.013 |
| NYHA functional class | | | <0.001 |
| I | 49 (2.0) | 88 (3.8) | |
| II | 1865 (75.3) | 1841 (79.5) | |
| III | 554 (22.4) | 378 (16.3) | |
| IV | 10 (0.4) | 9 (0.4) | |



**Background:** Unlike heart failure with reduced ejection fraction, there is no approved treatment for heart failure with preserved ejection fraction (HFpEF), the predominant phenotype in women. Therefore, there is a greater heart failure therapeutic deficit in women, compared with men.
**Methods:** In a pre-specified subgroup analysis, we examined outcomes according to sex in the PARAGON-HF trial which compared sacubitril-valsartan and valsartan in patients with HFpEF. The primary outcome was a composite of first and recurrent hospitalizations for heart failure and death from cardiovascular causes. We also report secondary efficacy and safety outcomes.
**Results:** Overall, 2479 women (51.7%) and 2317 men (48.3%) were randomized. Women were older, had more obesity, less coronary disease, and lower estimated glomerular filtration rate and NT-proBNP levels than men. For the primary outcome, the rate ratio for sacubitril-valsartan versus valsartan was 0.73 (95% CI 0.59-0.90) in women and 1.03 (0.84-1.25) in men; P interaction=0.017. The benefit from sacubitril-valsartan was due to reduction in heart failure hospitalization. The improvement in NYHA class and renal function with sacubitril-valsartan was similar in women and men, whereas the improvement in KCCQ-CSS was less in women than in men. The difference in adverse events, between sacubitril-valsartan and valsartan, was similar in women and men.
**Conclusions:** As compared with valsartan, sacubitril-valsartan seemed to reduce the risk of heart failure hospitalization more in women than in men. While the possible sex-related modification of the effect of treatment has several potential explanations, the present study does not provide a definite mechanistic basis for this finding.

## What is new?

1. Women represent approximately a quarter of people with HF and reduced EF (HFrEF) and over half of those with HF and preserved EF (HFpEF).
2. There are multiple effective drug and device therapies for HFrEF, but none approved for HFpEF; thus, there is a greater heart failure “therapeutic deficit” in women, compared with men.
3. In PARAGON-HF, sex and LVEF appeared to modify the effect of sacubitril-valsartan, versus valsartan, on the primary outcome (total heart failure hospitalizations and cardiovascular death), with a more favorable treatment effect in women than in men (rate ratio 0.73 (0.59-0.90) in women, 1.03 (0.84-1.25) in men; P interaction=0.017).

## What are the clinical implications?

1. While the apparent sex-related modification of the effect of sacubitril-valsartan has several potential explanations, the present study does not provide a definite mechanistic basis for this finding.
2. Our findings raise the possibility that the effects of pharmacological treatments for HFpEF may differ between men and women.
3. This hypothesis should be investigated further, given the therapeutic deficit in this heart failure phenotype in general and, particularly, in women.

# Ejekční frakce LK

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association. Learn and Live.

Assessment of left ventricular ejection fraction and volumes by real- time, two-dimensional echocardiography. A comparison of cineangiographic and radionuclide techniques
ED Folland, AF Parisi, PF Moynihan, DR Jones, CL Feldman and DE Tow

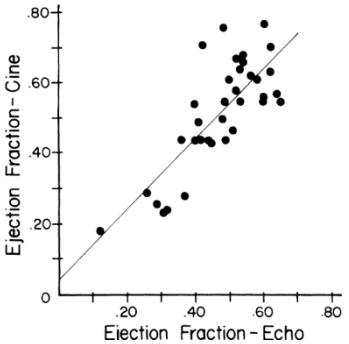
Circulation 1979; 60:760-766
doi: 10.1161/01.CIR.60.4.760
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 72514

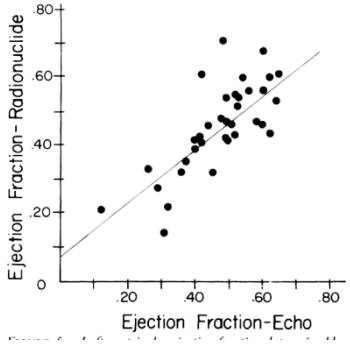
## Assessment of Left Ventricular Ejection Fraction and Volumes by Real-time, Two-dimensional Echocardiography

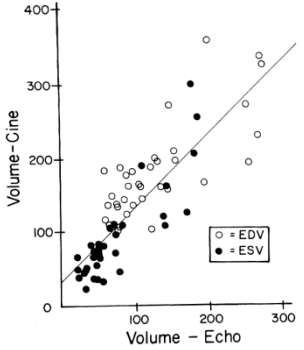
### A Comparison of Cineangiographic and Radionuclide Techniques

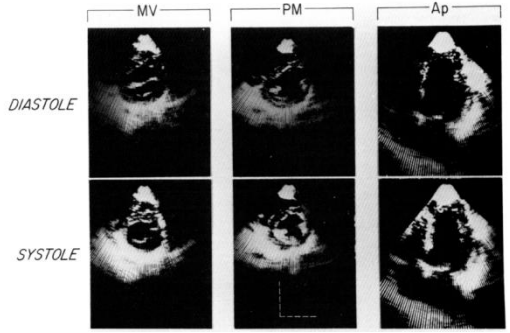
EDWARD D. FOLLAND, M.D., ALFRED F. PARISI, M.D., PAUL F. MOYNIHAN, B.S., D. RAY JONES, M.S., CHARLES L. FELDMAN, D.SC., AND DONALD E. TOW, M.D.

**SUMMARY** Five different algorithms for determining left ventricular (LV) ejection fraction (EF) and volumes from two-dimensional echocardiographic examination (TDE) were compared with standard methods for obtaining EF and volume from x-ray cineangiography (cine) and EF from radionuclide ventriculography (RVG) in 35 patients. Although all methods correlated positively, the degree of correlation varied with the algorithm used. For EF determination, TDE algorithms (especially those using multiple planes of section) were superior to unidimensional algorithms commonly used with M-mode echocardiography. The best algorithm (modified Simpson's rule) correlated well enough with cine EF ($r$ = 0.78; SEE 0.097) and RVG EF ($r$ = 0.75; SEE 0.087) to make clinically useful estimates. TDE volumes also correlated meaningfully with cine end-diastolic and end-systolic volumes ($r$ = 0.84; n = 70) but were associated with a large standard error of the estimate (43 ml) and offered less advantage over unidimensional volume estimations. Quantitative application of TDE appears to be a useful noninvasive method of evaluating LVEF, but is not as useful for estimating LV volumes.



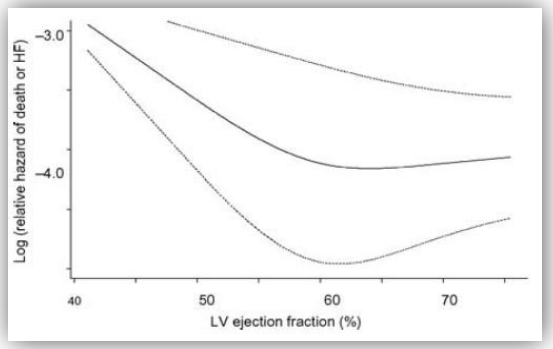



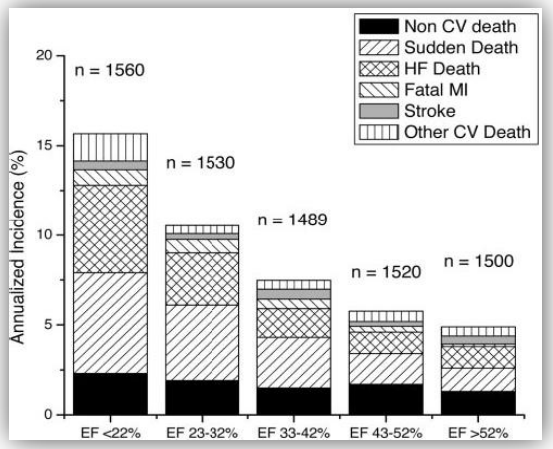




| Algorithm | Formulation | Geometric Model |
|---|---|---|
| Simpson's Rule | $V=(A_m)\frac{L}{3}+(\frac{A_m+A_b}{2})\frac{L}{3}+\frac{1}{3}(A_b)\frac{L}{3}$ | |
| Ellipsoid – Biplane | $V=\frac{\pi}{6}L(\frac{4A_m}{\pi D})(\frac{4A_l}{\pi L})$ | |
| Ellipsoid – Single Plane | $V=\frac{8(A_l)^2}{3\pi L}$ | |
| Hemisphere – Cylinder | $V=(A_m)\frac{L}{2}+\frac{2}{3}(A_m)\frac{L}{2}$ | |
| Modified Ellipsoid | $V=(\frac{7O}{2.4+O})D^3$ | |

| Echo algorithm | Cine* $r$ | Cine* (SEE) | RVG $r$ | RVG (SEE) |
|---|---|---|---|---|
| Modified Simpson's rule | 0.78 | (0.097) | 0.75 | (0.087) |
| Ellipsoid biplane | 0.78 | (0.098) | 0.73 | (0.089) |
| Ellipsoid single plane | 0.76 | (0.101) | 0.71 | (0.092) |
| Hemisphere-cylinder | 0.66 | (0.116) | 0.58 | (0.107) |
| Modified ellipsoid (Teichholz) | 0.55 | (0.130) | 0.46 | (0.117) |

*X-ray cineangiographic vs RVG ejection fractions (linear regression): $r$ = 0.88; SEE = 0.073.
Abbreviations: Cine = x-ray contrast cineangiography; RVG = radionuclide ventriculography.

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Learn and Live

Results of the Predictors of Response to CRT (PROSPECT) Trial
Eugene S. Chung, Angel R. Leon, Luigi Tavazzi, Jing-Ping Sun, Petros Nihoyannopoulos, John Merlino, William T. Abraham, Stefano Ghio, Christophe Leclercq, Jeroen J. Bax, Cheuk-Man Yu, John Gorcsan, III, Martin St John Sutton, Johan De Sutter and Jaime Murillo
*Circulation* 2008;117:2608-2616; originally published online May 5, 2008.

Interindividual **variability ESV** (CV 14.5%) and **LVEF** (mean LVEF 23.6±7%, corlab 29.3±10%)

20% patients indicated for CRT implantation have **corlab LVEF >35%**

1/3 suboptimal 2D **image quality** for ESV estimation

No **QC**

40%: old ultrasound machines

37% GE, 50% Philips, 12% Siemens

Nicolosi JL. Et al. European Heart Journal (2009) 30, 1656–1665
Solomon SD et al. Influence of Ejection Fraction on Cardiovascular Outcomes in a Broad Spectrum of Heart Failure Patients Circ 2005; 112; 3738-44
Chung, E. S. et al. Circulation 2008;117:2608-2616

# RT-3D EF LK a...

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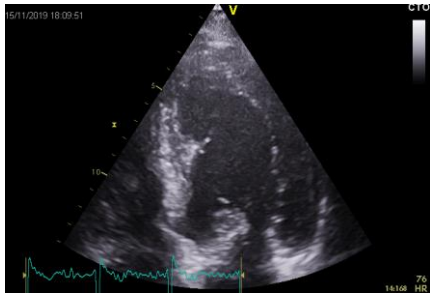
**Echocardiography**

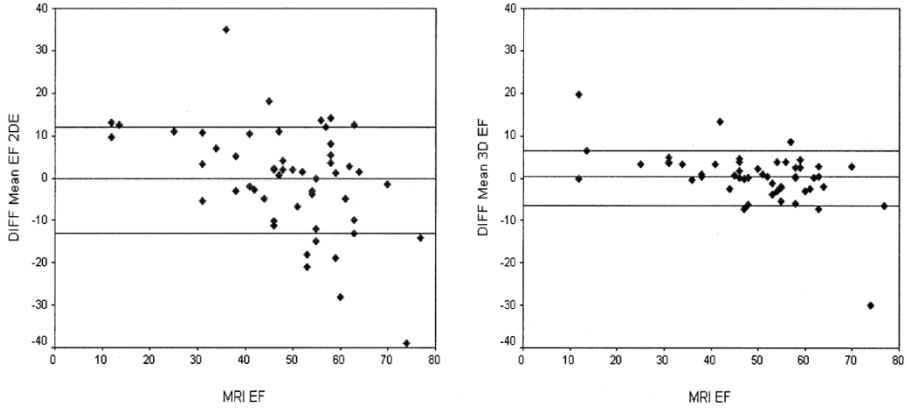
## Reproducibility and Accuracy of Echocardiographic Measurements of Left Ventricular Parameters Using Real-Time Three-Dimensional Echocardiography

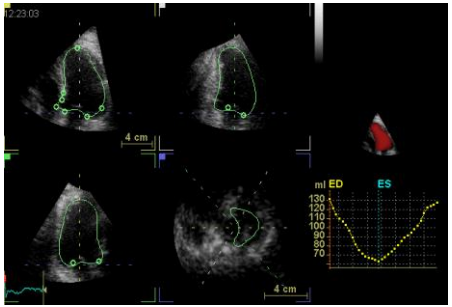
Carly Jenkins, BS, Kristen Bricknell, BS, Lizelle Hanekom, MD, Thomas H. Marwick, MD, PhD, FACC

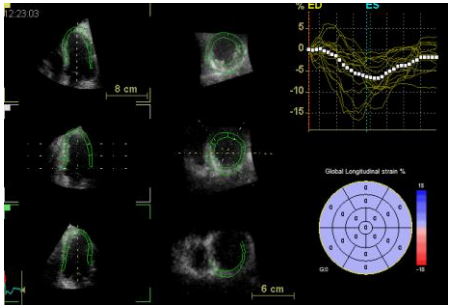
**Table 5.** Mean Difference Between Echocardiographic and MRI Measurements (n = 50)

| | RT-3DE | | 2DE | | Difference in Variance Between MRI and RT-3DE or 2DE | |
|---|---|---|---|---|---|---|
| End-diastolic volume (172 ± 53 ml) | −4 ± 29 | p = 0.31 | −54 ± 33 | p < 0.01 | F = 1.31 | p = 0.17 |
| End-diastolic volume (91 ± 53 ml) | −3 ± 18 | p = 0.23 | −28 ± 28 | p < 0.01 | F = 2.38 | p = 0.001 |
| Ejection fraction (50 ± 14%) | 0 ± 7 | p = 0.74 | −1 ± 13 | p = 0.76 | F = 3.82 | p < 0.0001 |
| LV mass (183 ± 50 g) | 0 ± 38 | p = 0.94 | 16 ± 57 | p = 0.04 | F = 2.25 | p < 0.003 |






Jenkins C. et al. Reproducibility and Accuracy of Echocardiographic Measurements of Left Ventricular Parameters Using Real-Time Three-Dimensional Echocardiography. J Am Coll Cardiol 2004;44:878–86

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