

# Comparative efficacy of empagliflozin and drugs of baseline therapy in post-infarct heart failure in normoglycemic rats

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## Purpose

The experimental comparative study on empagliflozin efficacy in CHF in normoglycemic settings with the drugs which are generally accepted agents for CHF treatment: angiotensin-converting enzyme inhibitor,  $\beta$ -blocker and aldosterone antagonist.

## Methods

CHF in 50 rats was simulated via permanent ligation of the left coronary artery. 1 month later, the operated animals were randomized under echocardiographic (echoCG) control to 5 equal groups of 10 animals: a group that did not receive any treatment, groups which took empagliflozin, fosi-nopril, bisoprolol and spironolactone as monotherapy, respectively. 3 months of the therapy, echoCG and treadmill exercise time were analyzed.

## Results

**Vehicle treated** animals exhibited an increase of LVEDD, LVESD, LVID and LVIDS and a decrease of FS, EF(T) and EF(C) as compared with baseline, one-month post MI measurements. Moreover, the atrium dimensions were increased: LAs, LAI, RAI (Tab.1). These changes characterize progression of heart failure (Fig.1).

**The empagliflozin treated** animals had only increased left atrial anterior-posterior dimension and left atrium long axis dimension as compared to baseline. Neither LV sizes nor ejection fraction were changed. Moreover, the minute volume was significantly increased (61,2 $\pm$ 21,2 sec vs. 52,0 $\pm$ 15,5 sec) (Tab.1).

**In fosi-nopril treated** group, the left atrial anterior-posterior dimension and right atrium long axis dimension were increased (Table 1), although LV sizes and LV ejection fraction did not differ.

In bisoprolol group, we found a deterioration of LV dysfunction exhibited by decreased FS, EF(T) and MAPSE (Tab.1).

The animals treated with **spironolactone** did not have any echocardiographic changes in comparison with vehicle, except for thickening of the interventricular septum (p<0.05) (Tab.1).

The tolerance during the treadmill exercise was evidently decreased in 3 months in all study groups compared with baseline (Figure 1). Hereby the maximal changes were shown in vehicle, fosi-nopril, bisoprolol and spironolactone groups.

The maximum activity time was the highest in the rats treated with empagliflozin (Fig. 2). It was significantly higher than in the sham group (289  $\pm$  27 sec. vs. 180  $\pm$  53 sec; p<0.05), fosi-nopril (183  $\pm$  61 sec; p<0.05), bisoprolol (197  $\pm$  95 sec; p<0,05) and spironolactone group (47  $\pm$  46 sec; p<0.05).

## Conclusions

Sodium-glucose co-transporter 2 inhibitor empagliflozin reduced progression of left ventricular dysfunction and improved tolerance of physical exercise in normoglycemic rats with HF. Empagliflozin treatment was superior in respect of physical tolerance compared with fosi-nopril, bisoprolol and spironolactone.

## Results

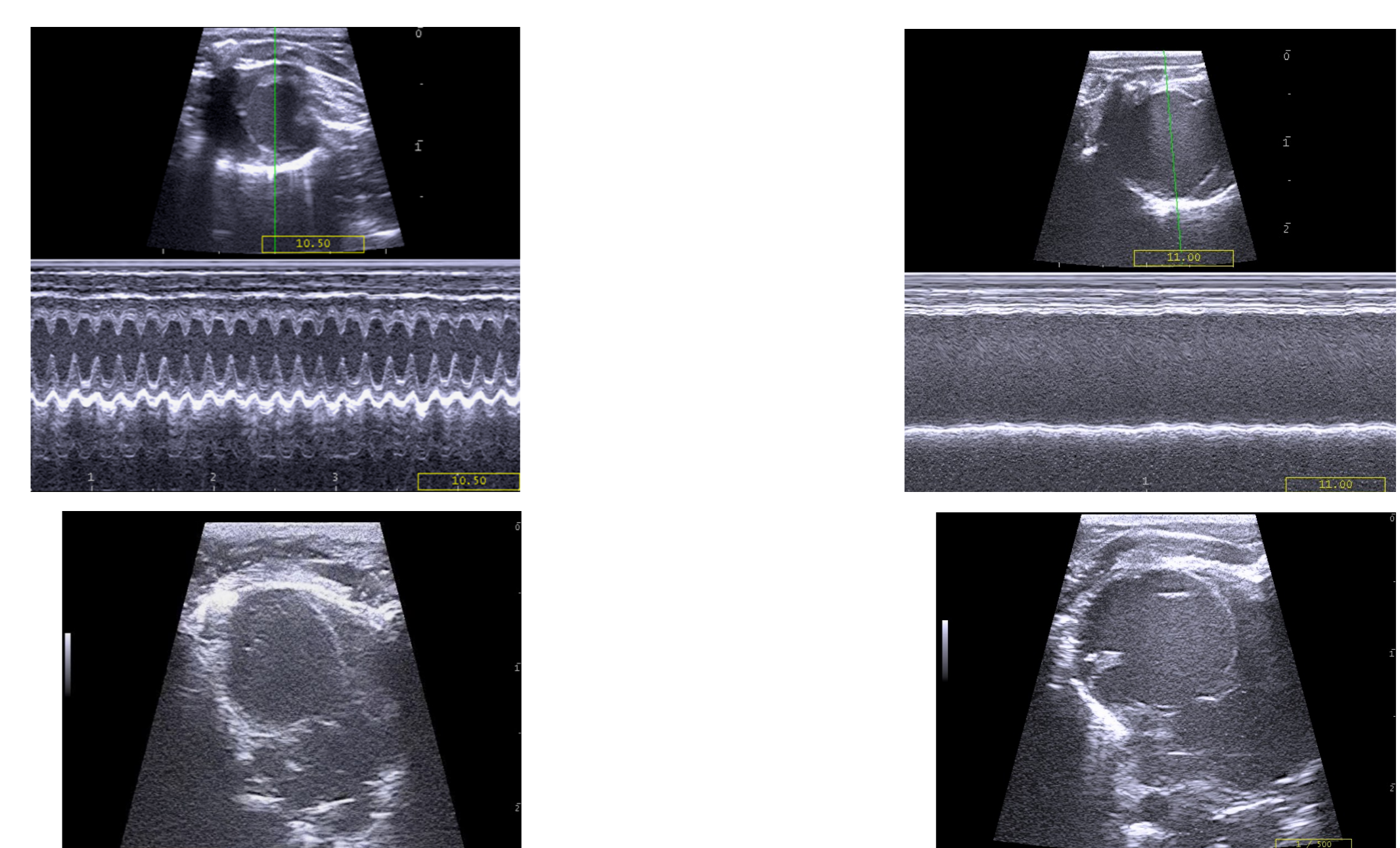


Fig. 1. Examples of M-mode echoCG of the rat before (left) and after the operation (right). On the right picture one can note dilated LV with low amplitude of wall motion and the line of effusion behind the posterior wall – it is a good model of CHF

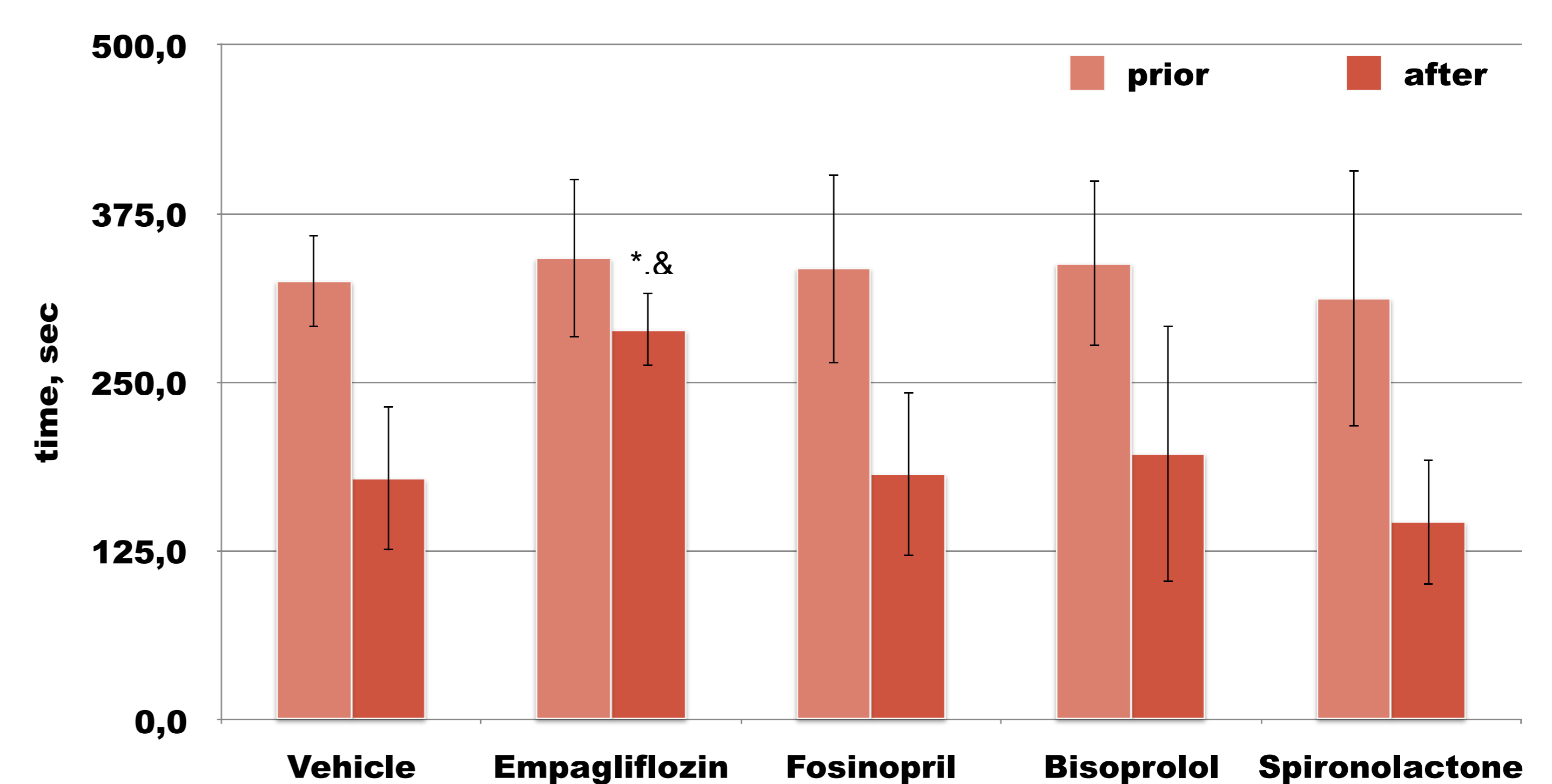


Fig. 2. Maximum activity time at the treadmill in the test groups of animals at the baseline and in 3 months of the observation  
Remarks: \* - significant difference to vehicle (p<0.05), & - significant difference to others groups (p<0.05)

Variable	Vehicle	Empagliflozin	Fosi-nopril	Bisoprolol	Spironolactone
LVEDD, mm	+				
LVESD, mm	+				
IVSEs, mm					+
SF, %	-			+	
EF(T), %	-			+	
LVvolD, ml	+				
LVvolS, ml	+				
SV, ml					
MV, ml/min		+			
EF(S), %	-				
MAPSE, mm				+	
LAap, mm		+	+	+	
LAs, mm	+				
LAI, mm	+	+			
RAI, mm	+		+		

Table 1. Significant changes of echocardiographic values after induction of myocardial infarction, n =10 in the group in the test groups of animals in 3 months of the observation  
Remarks: «+» - increase of dynamics (p<0.05), «-» - decrease of dynamics (p<0.05).