and 12 presented a HF-driven readmission, which resulted in 10 primary cardiovascular events. The combined primary endpoint occurred more frequently in patients with mvPA ≤8 cm/s, as indicated in Kaplan-Meier survival curve; Log Rank 4.905, p=0.027 (Figure 1).

Table 1

	mvPA≤8 cm/s (n=16)	mvPA >8 cm/s (n=32)	p-value
Trolox concentration (mM/ml)	0.32±0.18	0.44±0.14	0.040
	No primary combined event (n=37)	Primary combined event (n=11)	p-value
IL-10 concentration (pg/ml)	73.6±57.4	41.2±25.8	0.012

mvPA: mean velocity pulmonary artery.

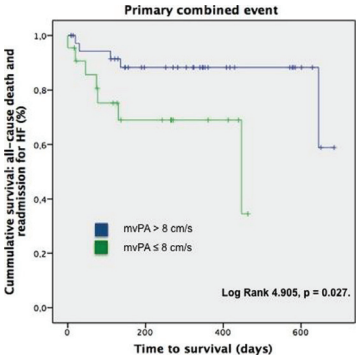

Figure 1. Kaplan-Meier survival analysis

Conclusion: MvPA acts as a simple non-invasive prognostic indicator in HFrEF. Trolox presented higher expression among patients with mvPA >8cm/s, thus confirming lower oxidative stress levels in these patients. Higher IL-10 concentration among patients not presenting any cardiovascular event could be a reflection of its anti-inflammatory and thus protective role in disease.

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P2801
Prognostic value of galectin-3 in patients with heart failure and reduced ejection fraction

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Background and introduction: Galectin-3, as a biomarker of fibrosis and inflammation has been implicated in the development and progression of heart failure (HF) and may predict increased morbidity.
Purpose: We sought to determine the prognostic role of galectin-3 in patients with heart failure and reduced ejection fraction (Left Ventricular Ejection Fraction<40%) (HFREF) and to assess the association between galectin-3 and clinical outcomes.
Methods: Clinical, echocardiographic and laboratory parameters were assessed in 87 consecutive patients with HFREF (age: 65.01±9.58years, 56% ischemic HF) visiting our outpatient clinic. Galectin-3 concentrations in serum were determined by an automated quantitative test using the ELFA technique. Statistical analysis was performed using SPSS 19.
Results: Serum galectin-3 levels were 21.77±13.12ng/ml. During follow-up (median: 17.5 months), 30 (35%) HF patients died. In univariate Cox regression analysis age (B=0.046, Exp(B)=1.047, 95% CI: 1.008–1.087, p=0.018), NYHA III-IV vs I-II (B= 1.369, Exp(B)=3.932, 95% CI: 1.165–13.279, p=0.027), ischemic HF vs. DCM (B= 1.432, Exp(B)=4.186, 95% CI: 1.659–10.564, p=0.002), right ventricular diameter (B=0.062, Exp(B)=1.064, 95% CI: 1.004–1.128, p=0.037), pulmonary artery systolic pressure (B=0.044, Exp(B)=1.045, 95% CI: 1.011–1.080, p=0.008), logNT-proBNP (B=1.698, Exp(B)= 5.466, 95% CI: 2.043–14.625, p=0.001), urea (B=0.012, Exp(B)=1.012, 95% CI: 1.005–1.019, p=0.001) and galectin-3 (B=0.031, Exp(B)=1.031, 95% CI: 1.013–1.050, p=0.001) were positively associated with all-cause mortality, whereas serum Na (B= -0.260, Exp(B)=0.771, 95% CI: 0.665–0.894, p=0.001) was negatively associated with it. In ROC curve analyses, the optimal cutoff point for galectin-3 as a predictor for all-cause mortality was 15.75ng/ml, associated with a 90% sensitivity and 62.5% specificity (AUC:0.782, 95% CI: 0.672–0.893, p<0.001), whereas the cut-off for logNT-proBNP was 3.25 associated with a 91% sensitivity and 50% specificity (AUC:0.784, 95% CI: 0.653–0.915, p=0.001). The combination of these 2 biomarkers slightly improved the AUC (AUC:0.795, 95% CI: 0.668–0.922, P=0.001). Kaplan-Meier survival analysis showed that galectin-3 >15.75 combined with logNT-proBNP >3.25 significantly predicted all-cause mortality (Log-rank=0.029). In multivariate Cox regression analysis, galectin-3>15.75 as a dichotomous variable independently predicted all-cause mortality after adjusting for age, NYHA, right ventricular diameter, PASP, creatinine and Na. However, when logNT-proBNP was added to the model, the association of galectin-3>15.75 with all-cause mortality was markedly attenuated and no longer significant.

Conclusion: Serum galectin-3>15.75 predicted all-cause mortality independently of age, NYHA, right ventricular diameter, PASP, creatinine and Na, but not when logNT-proBNP was included in the model.

CHRONIC HEART FAILURE – TREATMENT

P2802
Vertebral fractures and bone metabolism impairment after heart transplant: results from a prospective cohort study

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Background: Osteoporosis (OP) and fragility fractures are known complications of heart transplant (HTx). Despite avoiding bone mass loss, previous studies with bisphosphonates did not show consistent results on prevention of fractures. Therefore, better knowledge of the effects of HTx on bone and identification of patients with higher risk of fractures, can help identifying those that may benefit from more aggressive therapies for OP.
Purpose: To evaluate bone mass loss, bone metabolism and incidence of vertebral fractures (VF) after HTx.
Methods: Adult patients submitted to HTx between June 2013 and September 2015 and discharged from intensive care unit (ICU) were prospectively followed for 1 year. Clinical, laboratorial parameters, daily physical activity, bone mineral density (BMD) and VF were assessed at baseline (ICU discharge), after 6 and 12 months. BMD and VF were evaluated with DXA. OP was defined as T-score≤-2.5. All patients received dietary recommendations for adequate calcium intake and oral supplementation of vitamin D (50,000U/week for 3 months, followed by 7,000U/week) after HTx.
Results: Seventy patients were included but 5 died during the follow up. We found a high prevalence of OP (27.1%) at baseline, which was associated with time of hospitalization before HTx (p=0.009). Mean BMD decreased in the first 6 months, with partial recovery later (Figure). At baseline, 92.9% of patients had vitamin D<30ng/dL, associated with low calcium, high alkaline phosphatase and high bone resorption biomarker (CTX) serum levels. These abnormalities were suggestive of bone mineralization impairment and were corrected with vitamin D supplementation (Table). VF was found in 23.5% of patients at first evaluation, 29.7% at 6m and 29.0% at 12m. Multivariate analyses showed that low fat mass was the only variable correlated with VF (OR 0.80, 95% CI 0.67–0.95, p=0.01).

Table. Laboratorial parameters

	Initial	6m	12m	p
Calcium (mg/dL)	8.5±0.7	9.3±0.5	9.2±0.5	<0.001
Alkaline phosphatase (U/mL)	138.7±87.5	116.0±58.2	106.3±47.7	0.006
25-OH vitamin D (ng/mL)	15.5±9.1	33.8±11.6	34.7±11.4	<0.001
P1NP (μg/mL)	72.1±37.8	114.8±75.2	92.1±69.3	<0.001
CTX (ng/mL)	0.79±0.39	0.59±0.33	0.52±0.30	<0.001

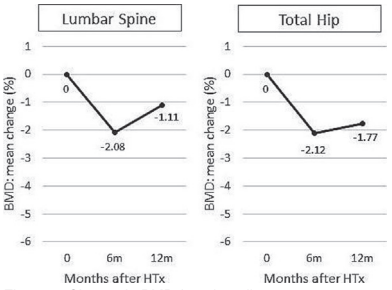

Figure 1. Change in BMD from baseline

Conclusion: Present study showed high prevalence of OP and VF right after HTx, associated with significant vitamin D deficiency and biomarkers abnormalities suggestive of bone mineralization impairment. In this way, correction of vitamin D deficiency should be the first step in OP management and may be considered even before HTx.

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P2803
Rejection diagnostics with digital droplet PCR measuring donor-derived cell-free DNA: A retrospective proof-of-concept study in heart-transplanted patients

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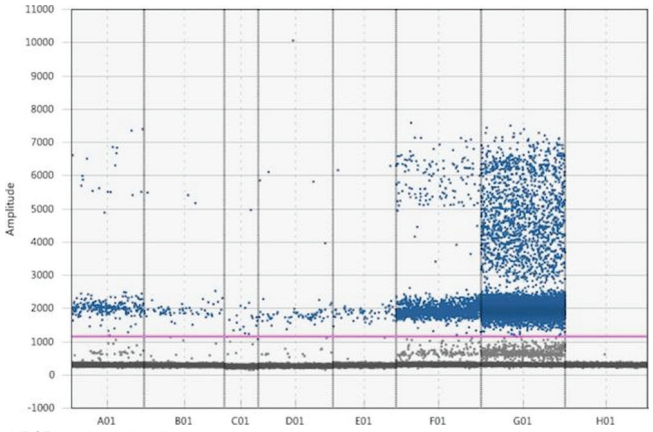
Purpose: Donor-derived cell-free DNA (dd-cfDNA) as a highly sensitive and spe-

cific marker of rejection after heart transplantation (HTx) has gained emerging interest. However, the method is not established, in part due to technical issues: Sequencing techniques come with high cost and long turn-around time while real-time PCR-based methods struggle with the low yield of cfDNA-harvest. In this proof-of-concept study, we used digital droplet PCR as a new diagnostic tool to analyze minimal amounts of dd-cfDNA against the background noise of recipient-derived cfDNA.

Patients and methods: Frozen serum samples from sex-mismatched donor-recipient pairs (female recipient, male donor) were selected, and a Y-chromosome-based assay was used to identify dd-cfDNA. This approach allowed measurements without the access to donor blood. 30 serum samples from 6 patients were analyzed in total. The samples had been taken at pre-defined time points after HTx, without correlation to the clinical state of the patient, but at the same time as scheduled heart biopsies were obtained. The samples hat been stored between 1–7 years. Measurements were done using a digital droplet auto droplet-generator PCR System, with fluorescein (FAM) as dye. Correlations were calculated between biopsy results and levels of dd-cfDNA.

Results: Of the 30 patient samples, the biopsy results were ISHLT 0R in 19 cases, ISHLT 1R in 8, and ISHLT 2R in 1 case. 2 samples were taken before HTx. It was possible to detect and quantify dd-cfDNA in all post-HTx samples, with a broad yield between 0.17 - 17.73 copies/mikroliter. The two samples taken before HTx showed negative results and could, thus, serve as negative controls. There was no correlation between biopsy grading and the levels of dd-cfDNA (correlation coefficient -0,07).



ddPCR-results patient A

Conclusion: A Y-chromosome-based approach for the retrospective design of this study detected dd-cfDNA but showed no correlation between heart biopsies and dd-cfDNA. This may be explained by sample management, since samples had not been frozen and stored according to protocols for the harvest of cfDNA. It is also known that stored cfDNA degrades over time. The lack of more severe rejections in the biopsies contributes to difficulties in interpretation of the results. Even more important, in the lowest levels of dd-cfDNA, the background noise of recipient-derived cfDNA becomes more obvious, lowering sensitivity of the method in this range. In the future, pre-amplification of regions of interest before ddPCR may allow to reduce background noise. Different SNP-based (single nucleotide-polymorphism) assays will allow for the analysis of any possible recipient-donor pairs in upcoming, prospective studies. Digital Droplet PCR-based assays hold the potential for a fast and feasible approach to rejection diagnostics after HTx.

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P2804
Quality of life in recipients after heart transplantation

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Objective: To estimate the dynamic of quality of life (QoL) and define factors which impact on it in heart transplanted patients.

Methods: From 2010 to 2017 we performed 96 orthotopic heart transplantation (HTx) (mean age - 46±14 yrs; 70 – male, 26 – female). Causes of heart failure were ischemic heart disease (IHD) (50%, n=48), dilated cardiomyopathy (32,3%, n=31), non-compacted myocardium (8,3%, n=8) and others (9,4%, n=9). QoL was defined by questionnaire – SF-36, physical activity (PA) – by IPAQ. According to IPAQ, recipients were divided into 2 groups: with PA (n=26) and sedentary lifestyle ones. Physical component summary (PCS) and mental component summary (MCS) were measured by SF-36. Moreover, Lazarus coping strategies questionnaire was completed by patients. Results of all questionnaires were estimated before, 3 months, 1 yr and 3 yrs after HTx.

Results: After HTx PCS increased (3 months – 42,6±8,2, $p<0,001$; 1 yr – 46,9±9,4, $p<0,001$; 3 yrs – 47,7±8,6, $p>0,05$). At the same time in 3 months after HTx MCS improved (48,0±6,6, $p<0,05$) and stayed stable in 1 yr ($p>0,05$), but 3 yrs after HTx it decreased (44,3±7,4, $p<0,05$). Following 1 yr after HTx physically active patients achieved higher level of QoL than sedentary lifestyle ones (PCS – 50,0±7,3 vs. 45,5±9,9, respectively, $p<0,05$; MCS - 48,0±6,9 vs. 46,7±8,0, respectively, $p>0,05$). In fact, 3 months and 1 yr after HTx non-IHD recipients showed higher level of MCS ($p<0,05$). In 3 months after HTx patients who had spent less than 6 months in HTx waiting list had lower MCS than those who were waiting more time (47,3±7,4 vs. 51,2±4,2, respectively, $p<0,05$). There was no dynamics in coping strategies in early and long-term follow-up ($p>0,05$). But in 3 months after HTx IHD patients had higher levels of distancing (56,7±14,9 vs. 51,3±21,9, respectively, $p<0,05$) and in 6 months – of self-controlling (68,1±22,8 vs. 64,3±11,2, respectively, $p<0,001$). In addition, 3 yrs after HTx male patients showed less seeking of social support (56,6±23,9 vs. 63,7±15,9, respectively, $p<0,05$) and confrontive coping (42,2±22,4 vs. 43,6±11,5, respectively, $p<0,05$). There were positive correlations between duration of the surgery and MCS 1 yr after HTx ($r=0,261$, $p<0,05$), posttransplant survival and distancing 3 yrs after HTx ($r=0,390$, $p<0,05$) and negative correlations between time on inotropes in ICU and self-controlling 3 months after HTx ($r=-0,342$, $p<0,05$), PCS and distancing 3 months after HTx ($r=-0,309$, $p=0,024$), days in ICU during early follow-up and distancing in 3 yrs ($r=-0,305$, $p<0,05$), MCS and escape-avoidance 3 yrs after HTx ($r=-0,430$, $p<00,5$).

Conclusion: After heart transplantation most of recipients increase their quality of life. Physical activity, male gender is a factor that influences on quality of life improving, the same as non-IHD patients can show better results. There is an impact of intraoperative and early-term results on quality of life in long-term follow-up.

P2805
Elevated PCSK9 levels may contribute to dyslipidemia early after cardiac trasplantation

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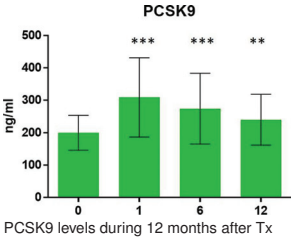
Background: Dyslipidemia after heart transplantation (HTx) contributes to early intimal thickening and development of coronary allograft vasculopathy which is the main reason for late graft loss. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an enzyme that regulates low density lipoprotein cholesterol (LDL-C) levels by affecting stability of LDL-C receptor, that is targetable by novel drug therapy.

Purpose: To analyze the dynamics and the determinants of PCSK9 levels prior and during the first year after HTx.

Methods: We investigated 25 patients with advanced heart failure (16 males, age 53±13 years) who underwent heart transplantation in 2015–2016. Blood samples were obtained immediately prior HTx, 1, 6 and 12 months after HTx. After HTx, all received induction with thymoglobulin, followed by standard immunosuppression with tacrolimus (TAC), mycophenolate and prednisone that was partially tapered over time. PCSK9 was measured by ELISA. Blood lipids and TAC through levels were measured by conventional assays.

Results: In the first month after Tx, PCSK9 level significantly increased from pretransplant level by 54.5%. At 6 and 12 months, PCSK9 levels dropped, but were still 39% and 21% above the pretransplant level. Similar dynamics at pretransplant, 1 6 and 12 month sample was also observed in total cholesterol (C) (3.9±0.9; 5.3±1.3; 5.0±1.3; 4.3±0.9 mmol/l), LDL-C (2.4±0.6; 3.0±0.9; 2.6±0.8; 2.3±0.7 mmol/L) and HDL-C (0.8±0.3; 1.5±0.4; 1.4±0.6; 1.2±0.3 mmol/L). In pooled data, PCSK9 correlated ($p<0.01$) with total-Ch ($r=0.33$), LDL-C ($r=0.21$) and HDL-C ($r=0.31$), but not with triglycerides. The increase in PCSK9 after Tx was not related to change in body weight, but was likely related to immunosupressive drugs. In the pooled data, PCSK9 correlated with TAC levels ($r=0.32$, $p=0.001$) and even stronger with prednisone daily dose ($r=0.42$, $p<0.0001$).



PCSK9 levels during 12 months after Tx

Conclusion: Increased PCSK9 after heart transplantation contributes to dyslipidemia after HTx. The strongest determinant of PCSK9 level was the daily steroid dose. Potential benefits of PCKSK9 inhibitors on postransplant dyslipidemia and coronary allograft vasculopathy should be examined in patients after HTx.