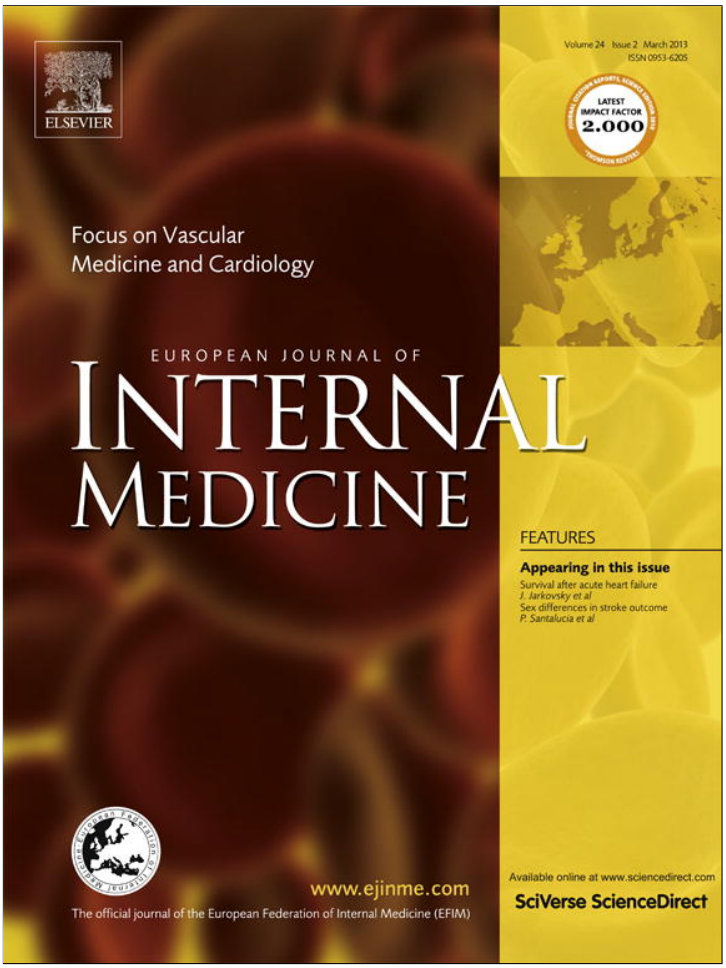

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Original article

Concomitant renal and hepatic dysfunctions in chronic heart failure: Clinical implications and prognostic significance ☆

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ABSTRACT

Background: The cardio-renal syndrome is common and eGFR is an established biomarker in chronic heart failure (CHF). Recent findings also indicate a predictive role of liver function abnormalities such as GGT in CHF. We aimed to jointly investigate the characteristics and importance of renal and hepatic failure in CHF.
Methods: Clinical and laboratory parameters of 1290 ambulatory patients (NYHA class I 25%, II 47%, III/IV 27%; median LV-EF 29%) were evaluated. Hemodynamics was available in 253 patients. The endpoint was defined as death from any cause or heart transplantation.
Results: eGFR <60 mL/min and GGT elevations were highly prevalent (25% and 44%, respectively; 12.8% for both). Renal and hepatic dysfunctions were correlated with disease severity and independently associated with adverse outcome in univariate ($p<0.001$) and multivariate analyses ($p=0.012$ and $p<0.001$, respectively). Signs of congestion and elevated CVP but not CI were independent predictors of changes in eGFR and GGT. In patients with concurrent impairment of both organs estimated five-year event rate was 46% as compared to 25% in patients with eGFR and GGT in the normal ranges (HR 3.12, 95% CI 2.33–4.18; $p<0.001$).
Conclusions: Impairment of renal and hepatic function is related to functional status and a poor prognosis in patients with mild to moderate heart failure. Concurrent involvement of both organs indicates disease progression and further elevates the hazard for adverse outcomes. Moreover, our data suggest that venous congestion rather than forward failure accounts for the development of renal and hepatic dysfunctions in these patients.

1. Introduction

Chronic heart failure (CHF) is a systemic clinical syndrome characterized by the involvement of multiple organ systems. In recent years, the cardiorenal syndrome (CRS) has received increasing recognition [1,2]. Renal dysfunction is highly prevalent in HF and is one of the most important independent risk factors for poor outcome and all-cause mortality in these patients [3–6]. CRS type II comprises the complex and bidirectional nature of pathophysiological interactions between the failing heart and the kidneys in CHF [1]. By contrast, until recently perception of secondary liver dysfunction was basically restricted to acute and advanced heart failure (ischemic hepatitis, shock liver) [7]. This is remarkable since liver function abnormalities are frequently found in patients with chronic heart failure [8–11]. Recent studies indicate that liver dysfunction in this setting is characterized by a predominantly cholestatic enzyme pattern, whereas in acute heart failure elevation of transaminases prevails [7,11–13]. In particular, γ-glutamyltransferase (GGT) proved to be an independent predictor of transplant-free survival in CHF [14,15].

In many cases of CHF, coexisting renal and liver dysfunctions may complicate the treatment course. Also, recent findings indicate that both renal and liver dysfunctions in CHF may be attributed primarily to venous congestion rather than arterial blood flow [16–18].

Given the high frequency and the predictive potential of impaired glomerular filtration rate (GFR) and GGT elevation in CHF along with the inexpensive and easily accessible availability, both markers are clearly of interest as potential biomarkers in CHF. However, data on characteristics and adverse effects of concomitant organ dysfunction on patient outcome are not yet available.

The present study therefore aimed to jointly investigate the characteristics and importance of renal and hepatic failure in CHF.

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2. Methods

2.1. Study population

This retrospective analysis made use of a dataset consisting of 1325 consecutive Caucasian heart failure patients. Patients were recruited between April 2000 and December 2010 on occasion of first presentation at the specialized heart failure clinic of a tertiary referral center. Eligible patients were ≥18 years of age. The diagnosis of CHF was based on the presence of current or previous symptoms or characteristic clinical signs, and evidence of left ventricular systolic and/or diastolic dysfunction. Patients were included irrespective of the underlying cause of heart failure and were treated according to prevailing CHF guidelines. All patients were followed up to July 2011 (time point of data censoring) or to the occurrence of death or heart transplantation. Death events were retrieved from the local mortality registry and personal contacts with members of patient families. Thirty-five (2.6%) patients were excluded from the present study because of incomplete baseline data. Hence, the present analysis comprises 1290 participants. Of those, follow-up information was available in 1228 patients (95.2%).

The study conformed to the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee.

2.2. Measurements

All laboratory variables were measured by a central laboratory that undergoes regular internal and external quality audits. Measurements were performed in fasting blood samples on the day of blood collection and are given as milliliters per minute per standardized body surface area (mL/min/1.73 m^2) for eGFR and as units per liter (U/L) for GGT. The upper laboratory reference limits differed by sex for GGT (65 U/L in men, 38 U/L in women). Glomerular filtration rate (GFR) was estimated by using the simplified modification of diet in renal disease equation (estimated glomerular filtration rate [eGFR] [mL/min/1.73 m^2] = $186.3 \times [\text{serum creatinine}]^{-1.154} \times \text{age}^{-0.203}$ [×0.742 if female]) [19]. Estimated GFR values >200 mL/min/1.73 m^2 were set equal to 200 mL/min/1.73 m^2, according to Coresh et al. [20].

Hemodynamic variables obtained during catheterization included cardiac output (thermodilution, L/min) and right atrial pressure as an indicator of central venous pressure (CVP, mm Hg). Cardiac index (CI) (L/min/m^2) was determined as cardiac output divided by the body surface area. Measurements were obtained from patients at rest.

2.3. Statistical analysis

Cross-sectional associations between eGFR and GGT and established heart failure variables were assessed for all patients and for a subgroup of patients with hemodynamic measurements available by univariate correlation and multiple linear regression analyses; Pearson's correlation coefficients and standardized beta coefficients are presented. Assessment of the prognostic relevance of eGFR and GGT for transplant-free survival was performed using sex-stratified Cox proportional hazards regression analyses, again in both univariate and multivariable manner. Selection of variables for Cox proportional hazards regression analyses was based on clinical relevance and data from the literature. All parametric analyses were performed on natural logarithm-transformed data for eGFR and GGT due to their skewed distribution. Results of endpoint and sex-stratified Kolmogorov–Smirnov testing for normality as well as inspection of Q–Q plots indicated approximately normal distribution for all log-transformed variables. p-Values <0.05 were considered to indicate statistical significance. Statistical analysis was performed using the SPSS software package (SPSS 18.0 for Windows, SPSS Corp.).

3. Results

Table 1a shows the baseline characteristics of the total population (n = 1290) and a subgroup of 253 patients for whom hemodynamic measurements were available. eGFR and GGT levels were skewed distributed for both sexes. Median estimates and serum levels, respectively, of eGFR and GGT were 72 mL/min (IQR 56–90) and 36 U/L (IQR 21–69) in women, and 78 mL/min (IQR 62–97) and 53 U/L (IQR 30–112) in men. Prevalence of reduced eGFR (≤60 mL/min) was 29.9% in women and 22.8% in men, overall 24.6%. Corresponding numbers for elevated GGT levels (>38 U/L, and >65 U/L, respectively) were 47% and 42%, overall 44%. Table 1b gives the characteristics of patients classified according to gender-specific cut-off values for eGFR (60 mL/min) and GGT. Prevalence of concurrent impairment of eGFR and GGT elevation (eGFR↓/GGT↑) was 12.8%.

3.1. Cross-sectional relations between eGFR/GGT and heart failure severity/duration

A weak but significant correlation was observed between eGFR and GGT (r = −0.11, p = 0.005). eGFR and GGT were significantly associated with NYHA class (r = −0.197, and r = 0.215; p<0.001). Also, in a subgroup of 764 patients with NT-proBNP available both

Table 1a
Baseline characteristics and medication for the entire cohort and a subgroup of 253 patients with hemodynamic measurements available.

	All patients		Patients with hemodynamics	
	n = 1290		n = 253	
	Median or %	IQR	Median or %	IQR
Demographic and clinical characteristics				
Age (years)	61	51–69	51	43–60
Gender (male)	74.3		76.6	
LV-EF (%)	29	22–38	25	19–32
Heart rate (bpm)	75	65–86	73	63–86
Systolic BP (mm Hg)	120	110–140	120	100–130
BMI	25.4	23.0–28.4	25.0	23.0–28.1
NYHA class I	25.4		18.0	
NYHA class II	47.2		49.8	
NYHA class III/IV	27.4		32.2	
Signs of congestion	26.6		27.0	
Duration of heart failure (>6 months)	64.4		50.7	
Ischemic etiology	29.3		18.1	
A-Fib	25.8		17.6	
Medical history				
Hypertension	48.1		32.0	
Diabetes	19.4		13.7	
Reported alcohol consumption	14.7		7.7	
Laboratory testing (serum)				
eGFR (mL/min/1.73 m^2)	**77.0**	**60.6–95.3**	**79.6**	**65.5–96.3**
GGT (U/L)	**48**	**27–95**	**50**	**31–100**
NT-proBNP (ng/L)	1181	377–2967	1254	372–3107
Hemodynamic measurements				
CVP (mm Hg)			**10**	**7–14**
CI (L/min per m^2)			**2.1**	**1.7–2.5**
Medication				
ACE inhibitor/ARB	81.6		86.0	
Beta-blocker	62.3		69.9	
Aldosterone antagonist	28.3		36.8	
Diuretic	70.5		68.9	

Data are reported as number (percentage) or median (interquartile range). Data for NT-proBNP were available in 764 patients. eGFR, GGT, CVP, and CI are presented in boldface.

LV-EF, left ventricular ejection fraction; SBP, systolic blood pressure; BMI, body mass index; NYHA, New York Heart Association class; signs of congestion, peripheral edema a/o jugular venous distension; A-Fib, atrial fibrillation; eGFR, estimated glomerular filtration rate; GGT, γ-glutamyltransferase; NT-proBNP, amino-terminal pro-B-type natriuretic peptide; CVP, central venous pressure; CI, cardiac index; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

Table 1b
Baseline characteristics and medication for patients classified according to gender-specific cut-off values for eGFR (60 mL/min in both sexes) and GGT (65 U/L in men, 38 U/L in women).

	eGFR⊥/GGT⊥		eGFR⊥/GGT↑		eGFR↓/GGT⊥		eGFR↓/GGT↑		p-Value
	n = 583 (45.2%)		n = 391 (30.3%)		n = 151 (11.7%)		n = 165 (12.8%)		
	Median or %	IQR	Median or %	IQR	Median or %	IQR	Median or %	IQR	
Demographic and clinical characteristics									
Age (years)	59	47–67	60	51–67	68	62–75	66	60–74	<0.001
Gender (male)	76.7		75.4		71.5		65.5		0.025
LV-EF (%)	30	24–43	27	21–37	26	20–33	27	22–36	<0.001
Heart rate (bpm)	72	62–84	77	67–89	75	65–85	76	66–87	<0.001
SBP (mm Hg)	123	110–140	120	110–140	120	110–138	120	105–140	0.046
BMI (kg/m^2)	25.0	23.0–28.1	25.4	23.0–28.5	26.0	23.0–29.0	26.0	23.0–28.4	0.890
NYHA class I	36.6		22.8		7.9		7.9		
NYHA class II	46.4		46.7		57.0		42.4		<0.001
NYHA class III/IV	17.0		30.5		35.1		49.7		
Signs of congestion	15.9		28.1		34.3		51.6		<0.001
Duration of heart failure (>6 months)	60.7		66.3		64.2		70.8		0.178
Ischemic etiology	25.2		27.2		42.7		36.8		<0.001
A-Fib	18.3		31.2		25.7		39.4		<0.001
Medical history									
Hypertension	45.2		44.2		59.3		57.8		<0.001
Diabetes	15.7		21.3		22.7		24.8		0.017
Reported alcohol consumption	11.5		20.4		8.9		15.3		0.002
Laboratory testing (serum)									
eGFR (mL/min/1.73 m^2)	**84.2**	**73.1–100.0**	**84.0**	**71.9–103.0**	**48.2**	**38.3–54.8**	**47.2**	**40.0–54.8**	<0.001
GGT (U/L)	**29**	**21–42**	**105**	**77–162**	**28**	**21–38**	**113**	**81–192**	<0.001
NT-proBNP (ng/L)	706	153–1785	1556	559–3227	2148	928–4854	3005	1352–5534	<0.001
Medication									
ACE inhibitor/ARB	77.7		87.0		79.4		83.3		0.004
Beta-blocker	58.5		62.4		70.2		67.3		0.036
Aldosterone antagonist	21.2		30.9		30.0		44.2		<0.001
Diuretic	55.5		77.0		84.3		92.9		<0.001

eGFR and GGT are presented in boldface.
eGFR⊥/GGT⊥, eGFR >60 mL/min/GGT in the normal range; eGFR⊥/GGT↑, eGFR >60 mL/min/GGT elevated; eGFR↓/GGT⊥, eGFR ≤60 mL/min/GGT in the normal range; eGFR↓/GGT↑, eGFR ≤60 mL/min/GGT elevated; LV-EF, left ventricular ejection fraction; SBP, systolic blood pressure; BMI, body mass index; NYHA, New York Heart Association; signs of congestion, peripheral edema a/o jugular venous distension; A-Fib, atrial fibrillation; eGFR, estimated glomerular filtration rate; GGT, γ-glutamyltransferase; NT-proBNP, amino-terminal pro-B-type natriuretic peptide; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

parameters were related to NT-proBNP (r = −0.330, and r = 0.287; p<0.001) in age- and sex-adjusted correlation analysis. Increasing NYHA classes were related to a significant stepwise decrease in eGFR and an increase in GGT levels. When patients were categorized according to gender-specific cut-off levels for eGFR and GGT, a stepwise increase was seen in heart failure severity with either one and all the more with both parameters in the pathologic range (Table 2).

Prevalence and serum levels of GGT significantly increased with heart failure duration ≥6 months (42.9% to 49.4%; p = 0.035, and 49.0 U/L [28–94] vs. 52.5 U/L [30–118]; p = 0.04, respectively). By contrast, prevalence and levels of eGFR did not change significantly with advanced disease duration (22.5% vs. 26.1%; p = 0.124, and 78.8 mL/min [63.7–98.7] vs. 74.5 mL/min [59–93]; p = 0.66, respectively).

Table 2
Relationship between eGFR/GGT and heart failure severity (n = 1290) and CVP (n = 253), respectively (numbers in brackets denote percentage of patients in NYHA class III/IV).

	eGFR⊥/GGT⊥	eGFR⊥/GGT↑	eGFR↓/GGT⊥	eGFR↓/GGT↑	p-Value
NYHA class	1.8 ± 0.7 (17)	2.1 ± 0.8 (30.5)	2.3 ± 0.6 (35.1)	2.5 ± 0.7 (49.7)	<0.001
CVP	9.6 ± 4.3	12.3 ± 6.1	10.3 ± 5.0	14.1 ± 6.6	<0.001

eGFR⊥/GGT⊥, eGFR >60 mL/min/GGT in the normal range; eGFR⊥/GGT↑, eGFR >60 mL/min/GGT elevated; eGFR↓/GGT⊥, eGFR ≤60 mL/min/GGT in the normal range; eGFR↓/GGT↑, eGFR ≤60 mL/min/GGT elevated; NYHA, New York Heart Association; CVP, central venous pressure.

3.2. Relationship between eGFR/GGT and venous congestion/hemodynamics

Cross-sectional correlates of eGFR and GGT with venous congestion as assessed in multiple linear regression analysis are given in Table 3a and – for a subgroup of 253 patients – with hemodynamic variables in Table 3b. The presence of jugular venous distension and/or peripheral edema and CVP elevation showed a significant association with renal and hepatic function. By contrast, CI was an independent predictor of perturbations in neither eGFR nor GGT. Table 2 shows the close correlation between eGFR/GGT and CVP.

Table 3a
Determinants of impaired renal and hepatic function (n = 1290).

	eGFR		GGT	
	Standardized regression coefficient beta	p-Value	Standardized regression coefficient beta	p-Value
Male gender	0.058	0.06	0.121	<0.001
Age ≥65a	−0.233	<0.001	−0.057	0.079
Ischemic etiology	−0.093	0.003	0.034	0.299
Diabetes	−0.034	0.279	0.037	0.259
Hypertension	−0.062	0.041	−0.040	0.206
Alcohol consumption	0.026	0.403	0.118	<0.001
LV-EF ≤35%	−0.032	0.291	0.038	0.234
NYHA III/IV	−0.103	0.001	0.087	0.010
Signs of congestion	**−0.158**	**<0.001**	**0.145**	**<0.001**

Table 3b
Determinants of impaired renal and hepatic function in patients with hemodynamic measurements available (n = 253).

	eGFR		GGT	
	Standardized regression coefficient beta	p-Value	Standardized regression coefficient beta	p-Value
Male gender	0.189	0.051	0.239	0.009
Age ≥65a	−0.089	0.356	−0.069	0.438
Ischemic etiology	−0.189	0.073	0.228	0.021
Diabetes	−0.062	0.546	0.242	0.012
Hypertension	−0.251	0.012	−0.169	0.068
Alcohol consumption	−0.017	0.866	0.032	0.731
LV-EF ≤35%	−0.143	0.156	−0.038	0.685
NYHA III/IV	−0.045	0.682	0.108	0.293
CVP	**−0.236**	**0.027**	**0.372**	**<0.001**
CI	**0.045**	**0.660**	**0.103**	**0.277**

eGFR, estimated glomerular filtration rate; GGT, γ-glutamyltransferase; LV-EF, left ventricular ejection fraction; NYHA, New York Heart association class; CVP, central venous pressure; CI, cardiac index. Signs of congestion, CVP and CI are presented in boldface.

3.3. Relations between reduced renal and hepatic function and heart failure outcome

Follow-up (mean 42.6 months [95% CI 40.8–44.4]) showed that 323 (25.3%) patients (71 women) had died, and 96 (7.8%) (22 women) had undergone heart transplantation as their first event.

In univariate sex-stratified Cox regression analysis, eGFR*(−1) (HR 2.15 [95% CI 1.79–2.58]; p<0.001) and GGT (HR 1.49 [95% CI 1.34–1.66]; p<0.001) were associated with increased risk for death or heart transplantation. The relation between eGFR and GGT levels and the endpoint remained robust, even in a sex-stratified multivariate model that included relevant clinical predictors (Fig. 1). A statistical test for interaction between eGFR and the risk for death or heart transplantation associated with elevated GGT levels was negative (p = 0.10), which suggests an additive association between renal and hepatic dysfunctions with poor outcome.

Unadjusted receiver operating characteristic (ROC) analysis of eGFR*(−1) and GGT to predict transplant-free survival revealed comparable prognostic accuracy. The area under the curve generated for 1/eGFR was 0.60 (95% CI 0.57–0.64; p<0.001) and for GGT 0.64 (95% CI 0.61–0.67; p<0.001).

To test for a potential additive effect of impaired renal and hepatic function to predict transplant-free survival, patients were classified according to cut-off level for eGFR (60 mL/min) and GGT (68 U/L in men, 35 U/L in women). Event rates were calculated with the Kaplan–Meier method and compared with the log-rank test. The estimated five-year event rate in patients with both enzymes in the normal range was 25% as compared with 46% when both markers were deflected (HR 3.12, 95% CI 2.33–4.18; p<0.001; Fig. 2). The relation between impaired renal and liver function and adverse outcome was independent of age, gender and NYHA class. In patients with preserved renal function elevated GGT levels raised the estimated five-year event rate from 25% to 35% (HR 2.04, 95% CI 1.60–2.60; p<0.001). The additive predictive value of GGT elevation in patients with impaired renal function was not significant (HR 1.25, 95% CI 0.88–1.76; p = 0.211). By contrast, in patients with GGT elevations concomitant eGFR reduction further increased the hazard for worse outcome by 53% (HR 1.53 [1.16–2.01]; p = 0.002). Patients with isolated changes in eGFR or GGT showed no difference in outcome (HR 1.23, 95% CI 0.90–1.67; p = 0.191).

4. Discussion

The present study is the first to jointly investigate the importance of impaired function of critical organs such as the kidneys and the liver in patients with mild to moderate heart failure. Renal and hepatic dysfunctions are related to disease severity and independently correlated with adverse prognosis. Venous congestion rather than forward failure appears to be the hemodynamic factor that drives secondary organ involvement. Coexisting organ dysfunction indicates disease progression and further limits outcome of patients with CHF.

In chronic heart failure impairment of renal and hepatic function exhibits remarkable analogies. Dysfunctions of both organs are highly prevalent. In this study, 24.6% and 44% of the patients exhibit some impairment of renal and hepatic function, respectively, which is similar to the data reported in the literature [6,9,10]. Impairment of both renal and hepatic function is associated with disease severity. eGFR and GGT show a significant stepwise increase with increasing NYHA classes and – in a subgroup of patients – are significantly correlated with NT-proBNP. Also, signs of congestion such as peripheral edema and/or jugular venous distension were independently correlated with renal and hepatic dysfunctions. Likewise, in a subgroup of 253 patients with hemodynamic measurements available, CVP but not CI

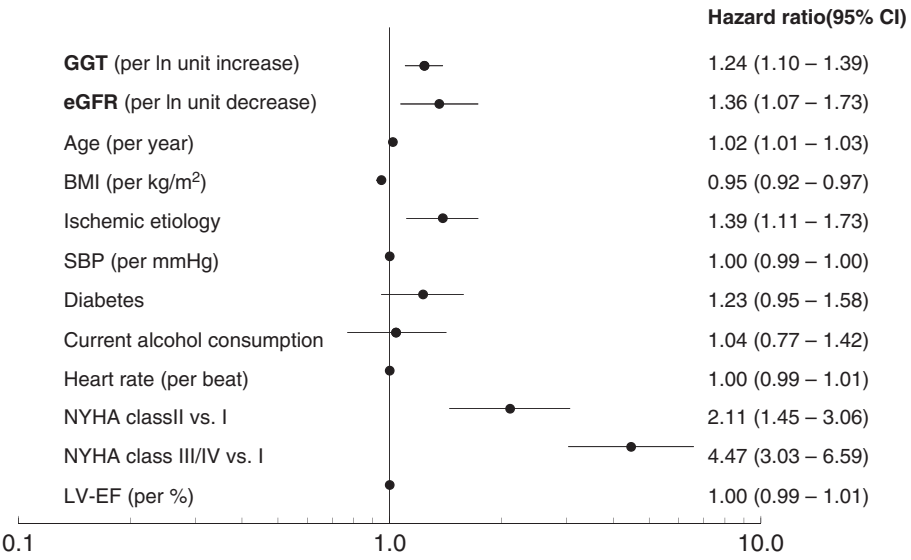
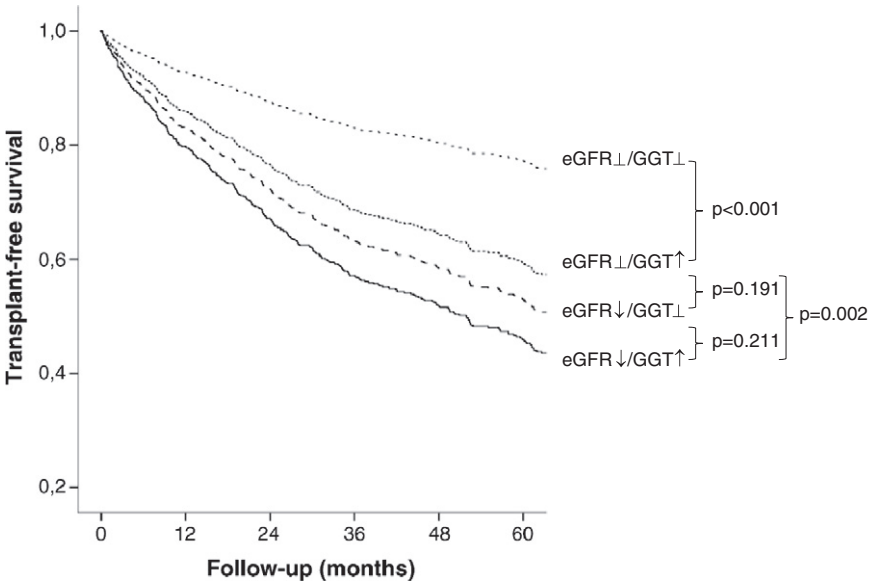


Fig. 1. Multivariate sex-stratified Cox regression analysis for death and heart transplantation. Hazard ratios and 95% confidence intervals are shown in a forest plot. GGT, γ-glutamyltransferase; eGFR, estimated glomerular filtration rate; BMI, body mass index; SBP, systolic blood pressure; NYHA, New York Heart Association; LV-EF, left-ventricular ejection fraction.



Number of patients at risk

eGFR⊥/GGT⊥	553	438	356	287	229	179
eGFR⊥/GGT↑	375	299	245	194	163	126
eGFR↓/GGT⊥	146	106	80	58	36	24
eGFR↓/GGT↑	154	117	85	64	46	31

Fig. 2. Separate and additive value of eGFR and GGT in predicting outcome. Kaplan–Meier transplant-free survival curves adjusted for age, gender and NYHA class for patients stratified according to sex-specific cut-off levels of eGFR and GGT are shown and compared with the log-rank test. eGFR⊥, eGFR >60 mL/min; GGT⊥, GGT in the normal ranges; eGFR, eGFT ≤60 mL/min; GGT↑, GGT (65 U/L in men, 38 U/L in women).

was an independent predictor of changes in eGFR and GGT in a multiple regression model including a variety of clinical variables. These findings are supported by previous reports showing that in chronic heart failure primarily venous congestion rather than arterial blood flow is an important mediator of both renal [21] and hepatic failure in CHF [16–18,21]. It is believed that hypervolemia and transmission of venous congestion to the renal veins impair glomerular filtration rate by reducing glomerular net filtration pressure [22]. Similarly, hyperemia and congestion are the histopathological substrates of non-ischemic cardiac hepatopathy [18,23].

The present results also confirm prior studies that demonstrated renal and hepatic dysfunctions to be strongly associated with poor outcome in heart failure [3,4,8,14,15]. In our study, eGFR and GGT independently predict transplant-free survival with comparable accuracy as assessed by ROC curve analyses. When patients were categorized according to sex-specific cut-off levels, concurrent organ dysfunction was present in 12.8%. Coexisting perturbation of both organs was indicative for an increase in disease severity and further elevated the hazard for adverse outcomes. The additive prognostic information on GGT elevation and renal failure was independent of age, gender, and heart failure severity. Appreciation of hepatic function was of particular importance in patients with preserved renal function. In this group of patients GGT elevation was associated with a 2-fold increased risk for death or heart transplantation.

We therefore conclude that in patients with CHF the occurrence of concomitant renal and hepatic disease indicates disease progression and poor outcome. Consequently, these patients deserve special attention and close follow-up. Clearly, a randomized clinical trial is needed to show whether meticulous fluid management can improve prognosis.

Interestingly, in patients with a long-lasting history of heart failure elevation of GGT serum levels was highly prevalent and GGT levels were significantly higher as compared to patients with a short duration of disease. By contrast, no such differences were seen for eGFR, which suggests that hepatic impairment may occur later in the course of the syndrome. This may be attributed to the liver's complex dual blood supply that makes it relatively resistant to hepatocyte necrosis and thus functional impairment. Clearly, this interesting finding needs to be confirmed elsewhere.

4.1. Strengths and limitations

We investigated a large unselected cohort of well-defined patients with CHF using a longitudinal design with a long follow-up time and comprehensive adjustment for covariates at baseline. However, several limitations must be noted. This is a single-center study from a tertiary referral center. Accordingly, characterization of included patients, who were predominantly young and male, does not exactly match the general heart failure population. Hence, results of the study have to be confirmed in a different patient population. Other than a thorough medical history and baseline function tests, no additional information on renal and liver pathology such as proteinuria and hepatitis serology or imaging studies and on drugs with potential liver toxicity was available.

5. Conclusion

In patients with mild to moderate heart failure impairment of renal and hepatic function is related to disease severity and a poor prognosis. Venous congestion rather than forward failure appears to be the hemodynamic factor that drives secondary organ involvement. Concurrent organ involvement indicates disease progression and poor outcome. Thus, consideration of easily available and inexpensive parameters of renal and hepatic function such as eGFR and GGT improves the assessment of patients with CHF and enhances a holistic appreciation of the complex syndrome.

Learning points

- The present work suggests that in chronic heart failure a worsening of renal and hepatic function shares a common hemodynamic pathomechanism, which is venous congestion rather than low output.
- Both, renal and hepatic dysfunctions are related to disease severity.
- Concurrent involvement of both organs indicates disease progression and poor outcome.
- These results clearly support the holistic appreciation of the complex heart failure syndrome.

Conflict of interests

The authors state that they have no conflicts of interest.

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