blood flow is derived from the portal system while only 30% is delivered by the hepatic artery and oxygen delivery can be maintained by increasing oxygen extraction when hepatic blood flow is decreased. This is in line with our findings, in which transaminases were much rarely elevated and correlated with other HF-related variables. However, under profound hypotension or hypoxemia, as in severe AHF, the above protective mechanism may be overwhelmed, resulting in shock liver.

It seems that GGT is not a simple bystander in HF, but it may be involved in the pathophysiology of the syndrome. It plays an important role in glutathione synthesis and may induce production of superoxide anion and hydrogen peroxide, thus leading to systemic inflammation and oxidative stress that are crucial mechanisms in HF pathophysiology. GGT may also be considered a "pro-atherogenic" marker, given its relationship with low-density lipoprotein cholesterol oxidation and its presence in atherosclerotic plaques.

Renal dysfunction frequently coexists with HF and hepatic dysfunction [3]. Venous congestion, hypoperfusion and neurohormonal activation may affect renal function, which in turn accentuates the pathogenetic processes involved in cardiac and hepatic dysfunction [5]. Therefore, there is not a simple concomitance of comorbidities, but rather a pathogenetic interaction between the three organs, involving a systemic hemodynamic, neurohormonal, and biochemical process that propagates a vicious circle of progressive failure. In addition, the fact that GGT is also synthesized by the kidneys may explain further its close relationship with renal function and WRF beyond the expected cardio–reno–hepatic interaction.

In conclusion, GGT is related to left and right ventricular function, neurohormonal activation and renal function in AHF, while it is also an independent predictor of WRF and long-term all-cause mortality. This widely available and inexpensive biomarker may merit further investigation as a potential marker in AHF.

References

[1] Allen LA, Felker GM, Pocock S, et al. Liver function abnormalities and outcome in patients with chronic heart failure: data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Eur J Heart Fail 2009;11:170–7.

[2] Ruttmann E, Brant LJ, Concin H, et al. Gammaglutamyltransferase as a risk factor for cardiovascular disease mortality: an epidemiological investigation in a cohort of 163,944 Austrian adults. Circulation 2005;112:2130–7.

[3] Poelzl G, Ess M, Von der Heidt A, et al. Concomitant renal and hepatic dysfunctions in chronic heart failure: clinical implications and prognostic significance. Eur J Intern Med 2013;24:177–82.

[4] van Deursen VM, Damman K, Hillege HL, et al. Abnormal liver function in relation to hemodynamic profile in heart failure patients. J Card Fail 2010;16:84–90.

[5] Filippatos G, Farmakis D, Parissis J. Renal dysfunction and heart failure: things are seldom what they seem like. Eur Heart J 2014;35:416–8.

http://dx.doi.org/10.1016/j.ijcard.2014.03.127

Comparative effectiveness of disease-modifying-drugs in elderly patients after incident hospitalization for heart failure ☆

Andrea Barbieri [a,*], Elena Berti [b], Massimiliano Marino [b], Letizia Reggianini [a], Francesco Grigioni [c], Rossana De Palma [b]

[a] Department of Cardiology, Policlinico Hospital, Modena and Reggio Emilia University, Modena, Italy
[b] Healthcare and Social Agency, Regione Emilia Romagna, Bologna Italy
[c] Institute of Cardiology, University of Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy

ARTICLE INFO

Article history:
Received 2 February 2014
Accepted 14 March 2014
Available online 21 March 2014

Keywords:
Heart failure
Drugs
Elderly
Hospitalization

Beta-blockers (BB), ACE inhibitors/angiotensin receptor blockers (ACEi/ARBs) and aldosterone antagonists (AA) do represent disease modifying drugs and have become the cornerstone of heart failure (HF) pharmacological therapy [1]. However, it is never safe to assume that treatments of proven efficacy in younger, healthier patients will provide equivalent benefit in older patients [2] but current guidelines rarely distinguish the use of these therapies on the basis of age [3].

To help clarify these issues a retrospective cohort study was undertaken by identifying all patients hospitalized for HF and never hospitalized for HF in the previous 10 years, discharged from 1 January 2009 to 31 December 2010 in the Emilia–Romagna, 4.3 million resident inhabitants in the Italian region. Inclusion criteria were one of the following ICD9-CM codes as principal discharge diagnosis: 428.0, 428.1, 428.2x, 428.3x, 428.4x, 428.9x, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 398.91. Exclusion criteria were: age ≤75 years, residence outside Emilia–Romagna region and death within 90 days of discharge. Accordingly, the eventual HF disease-modifying drug was prescribed away from the known clinically "vulnerable" phase regardless of standard medical therapy [4].

The eligible cohort was categorized in 6 groups of patients based on a drug prescription within 90 days from hospital discharge: 1) no BB/ACEi/ARBs/AA ("*No drug*"); 2) single ACEi/ARBs ("*only ACEi/ARBs*"); 3) single BB ("*only BB*"); 4) ACEi/ARBs plus BB ("*double therapy*"); 5) BB plus ACEi/ARBs plus AA ("*triple therapy*"); and 6) other different combinations between BB and/or ACEi/ARBs and/or AA ("*other combinations*").

Data were collected from the Emilia–Romagna Region administrative healthcare databases, which capture information about health service utilization from the entire region. Patients' information was retrieved from the regional database of hospital discharges, the regional outpatient and inpatient drug prescription database and the regional mortality registry. The following ATC classes were used: C07 class (BB); C09A' 'C09B' 'C09C' 'C09D class (ACEi/ARBs); and C03DA class (AA).

☆ Author conflict of interest disclosure: F. Grigioni has received honoraria and travel grants from Edwards Lifesciences, Sorin, St Jude Medical and Novartis. All the other authors declare no conflict of interest.

* Corresponding author at: Department of Cardiology, Policlinico Hospital, Modena and Reggio Emilia University, Via del Pozzo 71, 41100 Modena, Italy. Tel.: +39 059 4223145.
E-mail address: olmoberg@libero.it (A. Barbieri).