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Long-term monitoring of 340 patients with a cardiac resynchronization therapy: Evaluation of responders, super-responders and non-responders

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The main objective of this retrospective study is to analyze the future of heart failure patients, refractory to optimal pharmacological treatment, implanted by a bi-ventricular pacemaker (CRT-P) or defibrillator (CRT-D).

Methods: 340 patients were implanted between the 1st January 1999 and 31 December 2007, aged 69 +/-10 years mainly men (80%). The total population presented in part ischemic heart disease (56%), NYHA class III (79%) and an indication of primary prevention (76%). The number of hospitalization in the 6 months prior to implantation is an average of 1 +/- 1. The population was divided into 3 groups:
Group 1: 194 patients responders [R] (decrease of NYHA class, or stable NYHA and decreasing hospitalization, or the latter stable and increasing the LVEF of more than 10%, 6 months after implantation),
Group 2: 84 patients not responders [NR] (do any of the above criteria),
Group 3: 62 patients very good responders [SR] with the increasing LVEF greater than 15%.

Results: The comparison between the 3 groups showed a significant difference for the follow parameters: the NYHA class ([NR] 2.8 +/- 0.6 vs [R] 2.0 +/- 0.4 vs [SR] 1.8 +/- 0.5), the number of hospitalization ([NR] 1.1 +/- 1.3 vs [R] 0.2 +/- 0.5 vs [SR] 0.1 +/-0.3), LVEF ([NR] 29 +/- 9 vs [R] 33 +/- 8 vs [SR] 47 +/- 8). The curves of Kaplan-Meyer show a significant difference in survival rates for non-responders, responders and good responders (Logrank p <0.001).

Discussion: Treatment with bi-ventricular stimulation shows that 75% of patients are improved compared to the criteria usually measured. The study reveals a group of very good responders representing 18% of the total population with a survival rate at 5 years over 65%.

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Oxidative stress implication in cardiogenic shock with ischemic or idiopathic severe left ventricular dysfunction: role of etiologies of cardiomyopathies

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Background: Oxidative stress (OS) implication is paramount in pathology: ischemia reperfusion sequence (acute coronary syndrome, cardiac surgery, transplantation). Involvement of OS in heart failure (HF) is less known but is increased in the failing heart, and this might contribute to the pathogenesis of myocardial remodeling and HF.

Aim: Prospective study to identify OS in plasma from patients with a cardiogenic shock and to evaluate the role of etiologies of cardiomyopathy: ischemia or no.

Methods: Consecutive patients hospitalized in the cardiology unit with a first cardiogenic shock that complicated an idiopathic or ischemic dilated cardiomyopathy (DCM) with left ventricular (LV) dysfunction.

Exclusion criteria: known cardiomyopathy, acute coronary syndrome, septic or anaphylactic or hypovolemic shock, treatment with angiotensin converting enzyme inhibitors (ACEI) or angiotensin II antagonists (AA II).

OS was evaluated in blood samples at the admission (T_0) and one month later: thiobarbituric acid-reactive substances (TBARS), total antioxidant status (TAS), protein carbonyls (PC) and LDL oxidized; superoxide dismutase (SOD), glutathione peroxidase(GSH and GSSG/GSH) and catalase activities; plasma α tocopherol, vitamin A and β carotene.

Results: 23 consecutive patients (90% men), mean age 59±11y. Follow-up of 15 months. The aetiologies of CMD were ischemic (n=6), idiopathic (n=15), toxic (n=1) or restrictive (n=1). The mean LV ejection fraction was 23.3±8%. The NT-proBNP level was 9600±2000ng/ml.

	T_0	1 MONTH	NORMAL VALUE
PC (µmol/g prot)	0.16 (0.05-0.41)	0.14 (0.07-0.29)	< 0.10
TBARS (nmol/gHb)	2.2 (1.3-17.3)	2.5 (1.1-6.5)	0.7-1.6
LDLox (UI/L)	48 (20-83)	49 (26-98)	16-18
GSH (µmol/g Hb)	2.1 (0.8-3.1)	2.2 (1.7-4)	3.3-6.9
GSSG/GSH	0.19 (0.09-0.93)	0.13 (0.07-0.29)	< 0.08

Acute heart failure was associated with an increased OS. OS was more important in patients with arrhythmia.

Conclusion: Acute heart failure increased the level of oxygen free radicals. We hypothetized that modifications of OS could be implied in arrhythmias and complications of acute heart failure.

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Prescription of beta blockers at hospital discharge and beyond, in patients with heart failure. Results from the DEVENIR study

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Rationale: Beta blockers are a corner stone treatment of heart failure (HF) in patients with altered systolic function (LVEF<40%). Guidelines are less clear for HF patients with preserved systolic function (LVEF>50%) or for patients belonging to the "grey zone" (LVEF 40-50%).

Objectives: to describe the prescription rate of beta-blockers in HF patients.

Methods: Cross sectional observational survey with retrospective collection of data at hospital discharge. Patients must have been diagnosed with CHF and have been hospitalised for CHF within the previous 18 months. Patients are classified according to the LVEF at hospital discharge.

Results: 1 452 patients were included by 412 French outhospital cardiologists. 1137 with known LVEF at hospital discharge have had at least one visit by the cardiologist between hospital discharge (mean delay 5.76±4.51 months). In a multivariate model, BB prescription was more frequent in HF from ischemic origin (OR=1.39) or with dilated cardiomyopathy (OR=1.44) and less frequent in older patients (OR=0.97 per year) and in case of asthma/COPD (OR=0.31 and if FEVG was >50% (OR=0.62).

	LVEF < 40% N=661	LVEF 40-50% N=282	LVEF > 50% N=194	Total N=1137
At hospital discharge/*at entry in the survey*				
BB	78%/***83%***	78%/***85%***	62%/***70%***	76%/***82%***
Recommended BB†	75%/***77%***	72%/***74%***	54%/***62%***	71%/***74%***
Reaching the target dose	8%/***16%***	7%/***16%***	7%/***13%***	7%/***15%***
Changes since discharge				
BB added*	28%	34%	25%	28%
BB stopped**	1%	1%	2%	1%
BB dose increased*	27%	27%	17%	25%
BB dose decreased	4%	1%	3%	3%

†metoprolol, nebivolol, bisoprolol, carvedilol ;
****percentage calculated in patients without BB at hospital discharge (N=278);***
***** percentage calculated in patients with BB at hospital discharge (N=859).***

Conclusion: Rate of betablockers prescription is high at hospital discharge. Outhospital cardiologists not only pursue but also amplify the care strategies defined during hospitalisation increasing the proportion of patients receiving BB and the percentage reaching the target dose.

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Heart Failure management in ambulatory care: what happens beyond hospital discharge? Results from the DEVENIR study

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Rationale: Heart failure (HF) treatment is often started during hospitalisation and patients are generally taken over after discharge by outhospital cardiologists.

Objectives: To describe changes in HF treatment implemented by the outhospital cardiologist after hospital discharge.

Methods: Cross sectional observational survey with retrospective collection of data at hospital discharge. Patients must have been diagnosed with HF and hospitalized for HF within the previous 18 months.

Results: 1 452 patients were included by 412 French outhospital cardiologists. 1170 have had at least one visit by the cardiologist between hospital discharge (mean delay 5.76±4.51 months). At hospital discharge, target doses were reached in 10.5% of patients receiving betablockers, 50.9% of patients with ACEI and in 4.1% of patients with ARB. Doses were increased in 25.3% of patients receiving betablockers, in 11.7% of patients receiving ACEI and in 10.3% of patients treated with ARB enabling a target dose in 20.4% of patients with betablockers, and in 83.2% of patients with ACEI or an ARB.

Table. Evolution of treatment after discharge

	At hospital discharge	At start of the survey	Medication prescribed after discharge	Medication discontinued after discharge
Betablocker	826 (70,6%)	863 (73,8%)	87 (25,3%)*	50 (6,1%)*
ACEI††	807 (69,0%)	788 (67,4%)	46 (12,7%)*	65 (8,1%)**
ARB‡	170 (14,5%)	210 (18,0%)	56 (5,6%)*	16 (9,4%)**
ACEI or ARB	961 (82,1%)	973 (83,2%)	-	-

percentages calculated on the number of patients without the treatment at hospital discharge;
****percentages calculated on the number of patients without the treatment at hospital discharge;†metoprolol, nebivolol, bisoprolol, carvedilol;††captopril, enalapril, lisinopril, trandolapril, ramipril, perindopril (at an accepted target dose of 4mg);‡candesartan, valsartan***

Conclusion: Outhospital cardiologists play a critical role in care management of HF patients. Not only do they implement but they also amplify the care strategies defined during hospitalisation.

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Direct involvement of Bortezomib in the occurrence of heart failure

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Bortezomib is an antitumor therapy for Multiple Myeloma and Non Hodgkin Lymphoma which incidence is dramatically growing up. This drug inhibits proteasome activity through action on the 26 S proteasome in mammalian cells and leads to apoptosis of tumoral cells. Cardiac toxicity of this drug is not clearly established and its mechanistic poorly understood. Moreover, the few reports in the update literature are unable to prove a direct involvement of bortezomib in the occurrence of Acute or Chronic Heart Failure.

We report the first clinical observation of chronic heart failure which can be directly related to administration of bortezomib. This relationship is strongly suggested by the pharmacological Begaud's score for drug adverse events with a high degree of imputability. This observation is further supported by the report of all other cases of cardiac failure associated with bortezomib, reported in the French pharmacovigilance database (table 1).

These reports, the largest cohort available in the international literature, should lead to a systematically screening for asymptomatic cardiac diseases as well as a rigorous follow up of patients exposed to bortezomib. The strength of our report is i/ the identification of a case for which the direct role of bortezomib was demonstrated, ii/ to emphasize with our case series that this effect occurs more frequently than suspected with a serious outcome.

Table 1. (090)

Patients	Age (Year)	Gender	Disease	Cardiac Risk Factor	Prior Chemotherpy regimens	N°bortezomib containing cycles	Cumulated Dose (mg/m^2)	Cardiac complication	death	Imputability
#1	79	F	MM	HTA	0	1	2,64	Acute Heart Failure	yes	I3
#2	79	F	MM	0	1	6	31,2	Acute Heart Failure	No	I1
#3	71	F	MM	0	0	6	31,2	Acute Heart Failure	No	I1
#4	54	F	MM	0	2	1	4,45	Cardiogenic Shock	Yes	I1
#5	74	M	MM	0	0	1	3,9	Acute Heart Failure	Yes	I4
#6	61	F	MM	HTA	4	10	54,3	Acute Heart Failure	No	I1
#7	69	F	MM	0	0	3	15,6	Acute Heart Failure	No	I1
#8	54	M	MM	0	5	3	15 ,6	Acute Heart Failure	No	I1

Data from the French Pharmacovigilance Database