DESCRIBING OCCURRENCE OF CORONARY EVENTS AND TREATMENT IN HAEMOPHILIACS (DOCETH REGISTRY): REPORT OF 30 PATIENTS

A. Coppola[1], S. Linari[2], G.F. Rivolta[3], M.R. Fasulo[4], M.E. Mancuso[4], P. Radossi[5], I. Cantori[6], L. Valdrè[7], E. Zanon[8], M. Franchini[9], R. Santoro[10], A. Tagliaferri[3]

Haemophilia Centres of [1]Naples, Federico II University, [2]Florence, [3]Parma, [4]Milan, [5]Castelfranco Veneto, [6]Macerata, [7]Bologna, [8]Padova, [8]Mantova, [10]Catanzaro; Italy

Introduction and Methods

* The prolonged life expectancy and the growing impact of some cardiovascular risk factors in persons with haemophilia (PWH) raise concerns on the occurrence and, particularly, management of cardiovascular events in these patients. Few literature clinical data are available (most reviews and expert opinions).

* A retrospective-prospective registry of coronary artery disease (CAD) in PWH (the DOCETH Registry) has been estabilished in Italy in September 2009, for collecting data on clinical manifestations, risk factors and treatment approaches of such previously unusual events.

Patients and events

At May 2012 30 patients from 17 Centres registered.

Occasional diagnosis = 3*

Symptomatic patients = 27

- 6 **Stable angina**

- 21 (70%) **Acute** → 7 **Unstable angina** 14 **Miocardial infarction**

coronary syndrome (ACS) 9 **STEMI** 5 **NSTEMI** **Cerebral ischemic events** also reported in **2 cases** 12 patients (40%) were **younger than 60 yrs**

Patients' clinical features and risk factors

	n (%)
Haemophilia A^	26 (87)
Severe (<1%) Moderate/Mild	15 (50) 3/12
Age at CAD diagnosis, yrs, median [range]	63 [22-81]
Treatament On-demand Second. Prophilaxis	 27 (90) 3 (10)
Type of concentrate Plasma-derived Recombinant*	 17 (57) 13 (43)*
HCV pos	28 (93)
HIV pos	4^ (13)

*including 2 patients with inhibitors, treated with rFVIIa
^2/4 on highly-active antiretroviral therapy (HAART)
NSTEMI: non ST-elevation myocardial infarction
STEMI: ST-elevation myocardial infarction

Risk factors	All pts, n=30 n (%)	Severe pts, n=15 n (%)
Concentrate infusion (<24 hrs)	4 (17%)	4 (44%)
Hypertension*	20 (87%)	9 (100%)
Overweight/ obesity*	14 (61%)	6 (67%)
Dyslipidemia*	11 (48%)	3 (33%)
Diabetes mellitus*	5 (22%)	2 (22%)
Active smoking*	9 (39%)	4 (44%)
*Estabilished risk factors (RF)		
1-2 RF	11 (36%)	3 (20%)
3 RF	13 (43%)	8 (53%)
4-5 RF	6 (20%)	4 (27%)
≥ 3 RF	19 (63%)	12 (80%)

Treatment approaches

Coronary angiography in 21 patients (17/21 ACS), receiving heparin and antiplatelet agents with replacement treatment (30-70 IU/Kg; continuous infusion in 1), bleeding complications in 3 (14%). Severe 3-vessel disease in 11 patients (50%), leading to CABG in 7. **PTCA** in 11 patients (4 severe), with **stenting** in 10, followed by antiplatelet agents (double in 6 with drug eluting stents). 19 patients (7 severe) on prolonged antiplatelet therapy, 10 (53%, 7 mild) had bleeding complications. No bleeds in 6 patients receiving concomitant concentrate prophylaxis. Such regimens enabled to continue antiplatelet agents in further 3 mild patients. **Five fatal cases** were reported, 4 not receiving antiplatelet agent at all.

Type, severity	Event	PCA (coronary stenosis)^	Treatment	Anti-platelet agent(s)	Bleeding complications
A, severe	Asymptomatic	YES (IVA, diagonals)	**CABG**	ASA	NO (prophylaxis)
A, severe	Stable Angina	No	Anti-ischemic drugs	No	
A, severe	Stable Angina	No	Anti-ischemic drugs	No	
A, severe	Stable Angina	No	Anti-ischemic drugs	No	
A, severe, inhib.	Unstable Angina	YES (IVA, Cx, Rx)	Anti-ischemic drugs	No	
A, severe	Unstable Angina	YES (IVA, Cx, Rx)	**CABG**	Clop	NO (prophylaxis)
A, severe	Unstable Angina	YES (IVA, Cx, Rx)	**CABG**	No	
A, severe	NSTEMI	No	Anti-ischemic drugs	No	
A, severe	NSTEMI	YES (IVA, Cx)	PTCA + **DES**	ASA + Clop	NO (prophylaxis)
A, severe, inhib.	NSTEMI	No	Anti-ischemic drugs	ASA	**YES**
A, severe	STEMI	YES (CT, Rx)	**CABG**	No	
A, severe	STEMI	YES (IVA, Rx)	PTCA + BMS	ASA	**YES**
A, severe	STEMI	YES (IVA)	PTCA + BMS	ASA	NO (prophylaxis)
A, severe	STEMI	No	Anti-ischemic drugs	No	
B, severe	STEMI	YES (IVA)	PTCA + BMS	ASA	NO
A, moderate	STEMI	YES (IVA)	PTCA + BMS	ASA	**YES**
B, moderate	NSTEMI	No	Anti-ischemic drugs	ASA	NO (prophylaxis)
B, moderate	STEMI	Yes (IVA, Cx, Rx)	**CABG**	ASA	NO (prophylaxis)
A, mild	Asymptomatic	Yes (IVA, Cx, Rx)	Anti-ischemic drugs	ASA	NO
A, mild	Asymptomatic	No	Anti-ischemic drugs	No	
A, mild	Stable Angina	YES (IVA)	Anti-ischemic drugs	No	
A, mild	Stable Angina	YES (IVA, Rx)	PTCA + **DES**	ASA + Clop	**YES, severe**
A, mild	Stable Angina	YES (IVA, Cx, Rx)	**CABG**	ASA	**YES**
A, mild	Unstable Angina	YES (IVA, Cx, Rx)	**CABG**	No	
A, mild	Unstable Angina	YES (IVA, Cx, Rx)	**CABG**	No	
A, mild	Unstable Angina	YES (IVA, Cx, Rx)	PTCA + **DES**	ASA + Clop	**YES**
B , mild	Unstable Angina	YES (IVA, Cx, Rx)	PTCA + **DES**	ASA + Clop	**YES, severe**
A, mild	Unstable Angina	YES (IVA)	PTCA + **DES**	ASA + Clop	NO
A, mild	NSTEMI	YES (IVA, Rx)	PTCA	ASA	**YES**
A, mild	STEMI	YES (IVA, Cx, Rx)	PTCA + **DES**	ASA + Clop	**YES, severe**
A, mild	STEMI	No	Anti-ischemic drugs	ASA	**YES**

^PCA: Percutaneous Coronary Angiography; in parenthesis critical coronary stenosis: CT: common trunk; IVA: Inter-ventricular; Cx: circumflex; Rx: right.
CABG: coronary artery by-pass grafting; PTCA: percutaneous transluminal coronary angioplasty; BMS: bare-metal stent; DES: drug-eluting stent; ASA: aspirin; Clop: clopidogrel

Conclusions

- Irrespective of severity of coagulation defect, PWH may develop clinically significant coronary atherosclerosis and experience all pictures of coronary artery disease, even before the age of 60 years.
- Multiple cardiovascular risk factors are shown in the majority of patients. The role of primary and secondary prevention strategies is crucial by correcting modifiable risk factors.
- Reported treatment approaches are heterogeneous, with risk of undertreatment because of concerns of bleeding complications. However, coronary interventions and antiplatelet treatment are feasibile and safe, balancing the bleeding risk with 'individualized' prophylaxis regimens.

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Antonio Coppola
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