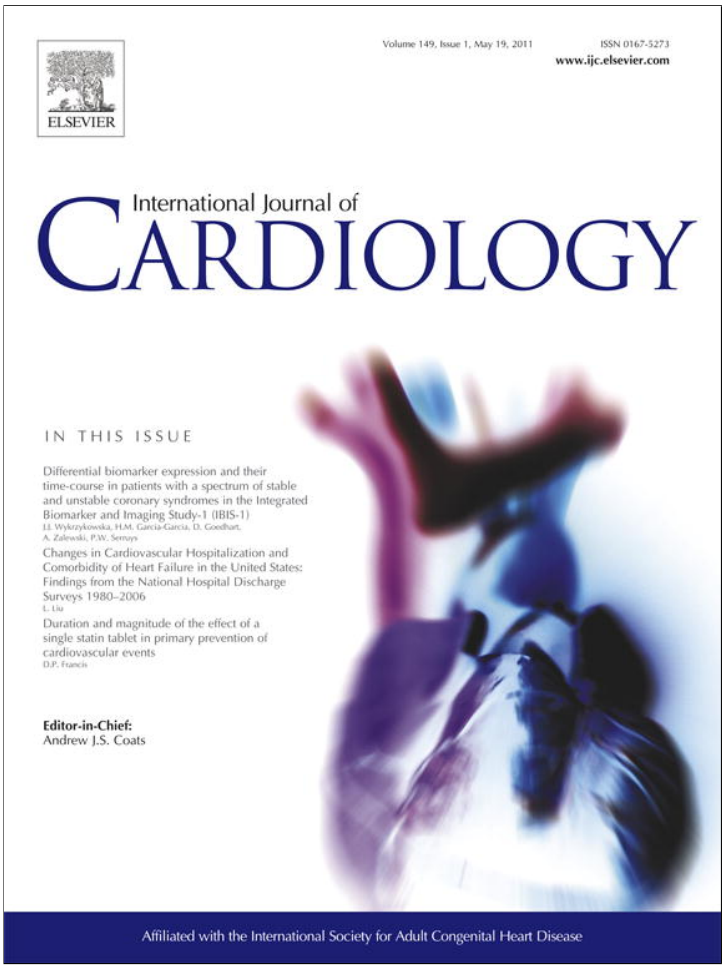

Table 2
Multivariate analysis of factors related with mortality in the Global Surgical Group (Group A + Group B1).

	OR	HF 95%	*p*
EF <40%	2.4	1–5.79	0.05
Mitral regurgitation	2.02	0.93–4.39	0.07
Post CoreValve AVR	0.41	0.092–1.83	0.24
Low output	4.04	1.86–8.76	<0.01

AVR: aortic valve replacement; EF: ejection fraction.

previously treated with surgery, the most outstanding characteristic of the new group is the increase in morbidity, factors that have been seen to increase perioperative mortality [2–4], with an objective increase in Group B's logistic EuroSCORE, despite a significant decrease in peri-interventional mortality and complications. This reduction in mortality is observed not only in patients treated with TAVI [1,5], but also of patients who undergo surgery. This morbi-mortality reduction in comparison of the exclusively surgical patients of both groups (A vs. B1) can be due to the profile changes; there are a lower incidence of mitral insufficiency, COPD, patients with EF < 40%, a significant reduction of the number of 19 mm aortic prosthesis implanted (a factor associated with low output and a high post operative transvalvular gradient) [6], a lower percentage of patients with high NYHA functional class and also factors that are not assessed by the EuroSCORE [7].

In conclusion, the TAVI in our hospital has allowed us to increase the number of patients treated for severe aortic stenosis, at the expense of high surgical risk patients, modifying the profile of those undergoing valve replacement surgery. Despite this, there has been a significant reduction in the global mortality of patients treated for AS.

None declared.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [8].

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Rationale and design for a cardiovascular screening and prevention study with telecardiology in Mediterranean Italy: The CAPITAL study (CArdiovascular Prevention wIth Telecardiology in ApuLia)

Natale Daniele Brunetti [a,*], Luisa De Gennaro [a], Giulia Dellegrottaglie [b], Ernesto Straziota [c], Vito Novielli [c], Gianfranco Antonelli [d], Matteo Di Biase [a]

[a] *University of Foggia, Cardiology Department, Foggia, Italy*
[b] *Cardio on Line Europe S.R.L., Bari, Italy*
[c] *FARPAS (FARmacisti Pugliesi ASsociati, Associated Pharmacists of Apulia) Modugno (Bari), Italy*
[d] *Cardiology Department, Azienda Ospedaliera Policlinico, Bari, Italy*

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Cardiovascular diseases are the main cause of death in middle-aged and older adults in most European countries [1]. Despite recent advance in treatment, leading to a considerable reduction in cardiovascular mortality the number of cardiovascular disease patients may actually be increasing because of aging populations, and the improving prognosis of coronary patients due to more effective treatments for acute coronary heart disease, revascularization and use of prophylactic drug therapies [2]. All these factors are contributing to an enlarging pool of coronary patients, who are at high risk of myocardial reinfarction and heart failure, bearing heavily on medical costs.

There is substantial scientific evidence showing that lifestyle interventions and risk factor modification can reduce cardiovascular morbidity and mortality [3]. In coronary patients lifestyle interventions (smoking cessation, healthy food choices and increased physical activity), control of blood pressure, cholesterol and diabetes, and the selective use of prophylactic drug therapies (aspirin, beta-blockers,

* Corresponding author at: Viale Pinto 1, 71100 Foggia, Italy. Tel.: +39 3389112358; fax: +39 0881745424.
E-mail address: nd.brunetti@unifg.it (N.D. Brunetti).

ACE inhibitors, lipid-lowering drugs and anticoagulants) will reduce the risk of recurrent non-fatal and fatal disease and improve survival. The main goals of cardiovascular prevention are to reduce morbidity and mortality, improve quality of life, and increase the chances of a longer life expectancy [4].

Any intervention of cardiovascular risk reduction needs to be based on a preliminary assessment of individual cardiovascular risk [5]. Cardiovascular prevention strategies yield better results within high risk patients [5,6]. Several cardiovascular risk score tools are available in order to assess the individual cardiovascular score [7–10]. These are usually based on the presence of main cardiovascular risk factors (hypertension, diabetes, hypercholesterolemia, and smoke habit) [8].

In 1994–1995, a survey assessing risk factor recording and management in patients with coronary heart disease, called ASPIRE (Action on Secondary Prevention through Intervention to Reduce Events), was therefore carried out in the United Kingdom [11]. The study revealed that risk factor control, particularly cholesterol, was inadequate. A few years later, a European survey (EUROASPIRE I), based on the U.K. ASPIRE study, was undertaken by the ESC in nine European countries [12] and also showed a high prevalence of modifiable risk factors in coronary heart disease patients, with a real potential to further reduce coronary heart disease morbidity and mortality and improve survival chances. A second EUROASPIRE survey (EUROASPIRE II) was undertaken in order to verify the applicability of European guidelines on the treatment and prevention of cardiovascular diseases, to facilitate their implementation, to investigate the applicability of the results of clinical trials in everyday practice, to analyze the outcome of different disease management strategies [13]. Also this survey showed a high prevalence of unhealthy lifestyles, modifiable risk factors and inadequate use of drug therapies to achieve blood pressure and lipid goals.

However, evidence coming from these surveys is somehow limited in numerical and geographical significance. Mediterranean countries are represented only by France and Italy and even reports from these countries come from “non-bare Mediterranean” zones such as Northern France and North-Eastern Italy (Fig. 1) [14]. Less is known with regards to “bare Mediterranean” contexts such as Southern Italy. Mediterranean countries seem to share a lower cardiovascular risk [8], probably related to beneficial effects of Mediterranean life-style and diet [15].

Also the number of the patients enrolled in these studies does not usually exceed few thousands of subjects.

Even pivotal epidemiologic studies such as those coming from the Framingham cohort do not really represent the “Mediterranean” scenario [16], although main cardiovascular risk score is actually derived from Framingham database analysis [7]. This study therefore aimed to investigate the prevalence of cardiovascular risk factors, the entity of cardiovascular prevention strategies in a Mediterranean region and to compare this Mediterranean reality to other “non-Mediterranean” realities.

The CAPITAL study (CArdiovascular Prevention wIth Telecardiology in ApuLia) (Fig. 2) originates from the joint effort of two dynamic actors of health care assistance in Apulia, a 4 million inhabitants region in South-Eastern Italy: FARPAS and Cardio-On-Line Europe s.r.l.. FARPAS (FARmacisti Pugliesi ASsociati, Associated Pharmacists of Apulia) is a pharmaceutical commercial distribution firm devoted to improvement of local quality of pharmaceutical assistance with scientific and cultural initiatives. Cardio-On-Line Europe s.r.l is a telecardiology services provider, supporting regional public free emergency medical service of Apulia (telephone number “118”) since 2004 [17–19]. A scientific grant by FARPAS and the active collaboration of 100 pharmacies scattered all over Apulia territory (Fig. 3) allowed the realization of this cardiovascular prevention program, involving 10 thousand people in primary and secondary prevention. Telecardiology support will enable all the recruited patients to be on-time screened with a 12-lead ECG reported by a cardiologist, wherever they will access the pharmacy-based study network.

Based on the above mentioned rationale, the objectives of CAPITAL study are:

1. To determine either in patients with established heart disease (acute myocardial infarction and ischaemia and patients following revascularization by angioplasty or coronary artery surgery, patients with heart failure) or in primary prevention whether the European recommendations on cardiovascular prevention of heart disease are being followed.
2. To compare prevalence of cardiovascular risk factors and the practice of preventive cardiology in a region of Mediterranean Southern Italy with results from the rest of Europe and North America.
3. To determine whether screening for risk factors has occurred and, if so, to describe their management by lifestyle and drug therapies.
4. To ascertain the incidence of cardiovascular adverse events in a 5-year follow up in relation with baseline prevalence of cardiovascular risk factors, then comparing these results with those from other cardiovascular risk stratification analysis [7–10].
5. To provide an epidemiological snapshot of a region-wide real world reality suitable for public health care policy makers for planning future interventions of cardiovascular primary and secondary prevention or sensibilization.

The study will enroll 10 thousand consecutive subjects either in primary or secondary cardiovascular prevention with an age comprised between 30 and 90 years living in Apulia territory. Patients will be recruited, after a written informed consent, and administrated with an apposite study information form when accessing their usual pharmacy.

Participants were deemed to be at high cardiovascular (CV) risk if there was confirmed evidence of at least one of (a) a prior myocardial infarction (MI), or stroke, or revascularization; (b) angina with documented ischemia; (c) evidence of left ventricular hypertrophy; and (d) diabetes.

The data collection will be based on an interview of the patients, conducted by trained research staff who will review patient forms, interview and examine the patients at the pharmacy or their home using standardized methods and instruments.

All statistical analyses will be undertaken using Statistica statistical software by the Cardiology Department of the University of Foggia, Italy. Descriptive statistics will be used to estimate the prevalence of risk factor recording and management. In order to assess prevalence of risk factors, it was calculated that a sample of 400 patients, who attended for interview, was sufficient to estimate prevalences with precision of at least 5%, and with a confidence interval of 95% [13]. As this was a descriptive survey, with emphasis on estimation of prevalences, no formal hypothesis testing was done.

The relationships between either subject characteristics, parameters or cardiovascular risk factors and the incidence of major adverse events will be evaluated by univariate and multivariate linear regression models. Subgroup analysis will be performed only when the added interaction term will be significant in the multivariate model and if a biological plausible mechanism will be present.

The predictive capacity of each condition (risk factors, drug therapy, and medical prevention) to identify between the presence and absence of major cardiac adverse events in a 5-year follow up will be quantified using univariate logistic regression analyses and estimated as logistic regression coefficients with their 95% confidence intervals. The prognostic ability to discriminate between subjects with and without risk factors will be assessed using the receiver operation characteristic curve (ROC area). Time-to event curves will be constructed for each primary outcome and compared with log-rank tests; hazard ratios and 95% CIs will be estimated using

Fig. 1. EUROASPIRE II participating centers map: no center is available from southern "bare-Mediterranean" areas of Italy (and Western Mediterranean basin).

Cox regression. Statistical significance will be claimed if the overall P value is ≤.05.

All data will be stored electronically onto notebook computers using a unique identification number for center and individual. Patients' forms will be sent on a weekly basis by each center to the Coordinating Center where they will be checked for completeness, internal consistency and accuracy. All data will be stored under the provisions of the Italian Privacy and Personal Information Protection Act (D. Lgs. 196/2003).

All participants will be followed until the scheduled study end, regardless of adherence to or discontinuation of medications for any reason. Clinical outcomes and adverse events will be ascertained at 1, 2 and 5 years. Major cardiovascular adverse events will be considered (a) incident CV death (i.e., any death for which no non-cardiovascular cause has been identified), nonfatal MI diagnosed on the basis of the clinical presentation, nonfatal stroke diagnosed on the basis of clinical presentation; (b) a revascularization procedure; (c) hospitalization for angina or heart failure. Secondary outcomes include (a) each component of the primary outcomes; (b) all-cause mortality; (c) new type 2 diabetes in participants without diabetes at baseline.

All outcomes will be ascertained direct or telephone contact with the recruited subject or, in the event of death, the next of kin and adjudication will be based on the information provided and supporting documentation. It is done by an adjudication committee whose members are unaware of participant allocation and who assess all of the available data and documentation with reference to pre-established criteria developed and finalized by this committee.

The CAPITAL Study was designed by the CAPITAL Steering Committee. This committee is responsible for all aspects of study management including collecting and cleaning all data, dealing with all protocol-related issues, monitoring and optimizing adjudicating outcomes, auditing the progress of the study, identifying and providing logistical support and determining, executing, and publishing the final study analysis. Funding, regulatory support, site monitoring, form distribution and collection will be provided by Far.P.As. and Cardio-on-line Europe s.r.l.. Each sponsor has 1 representative on the Steering Committee.

The following information will be obtained from the participating form during interview held within the pharmacy:

(a) Personal and demographic details.
(b) Personal cardiac history.
(c) Risk factor recordings:
  i. Medical history of cigarette smoking, hypertension, hyperlipidaemia, and diabetes.
  ii. Recorded measurements of smoking status, blood pressure, lipids, and diabetes.
(e) Medication (generic and commercial name and total daily dose).The following measurements will be performed:
  (a) Height and weight measured in light indoor clothes without shoes. The body mass index will then be calculated.
  (b) Waist circumference
  (c) Blood pressure measured twice in a sitting position on the right upper arm and the mean of the two measurements will be used in data analyses.

Fig. 2. a. Capital with Four Heads, ca. 1230. Southern Italy, Apulia, probably Troia. Limestone. The capital depicts four people representing Medieval population of Apulia (a man, a woman, a black man, and a moor), the study acronym (CArdiovascular Prevention wIth Telecardiology in ApuLia) and logo (b).

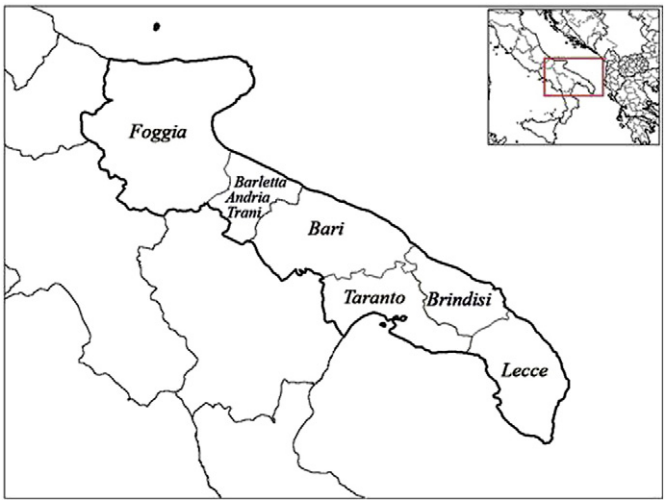

Fig. 3. Mediterranean Italy, Apulia and its administrative districts.

(d) Measurement of serum total cholesterol, HDL cholesterol and triglycerides, and plasma glucose.

(e) ECG with telecardiology support by Cardio-on-line Europe s.r.l. with CardioVox P12 ECG recording device. The ECG will be immediately transmitted to the tele-cardiology regional "hub" active 24/7, where a cardiologist will promptly read the ECG, highlighting within the report the presence of any significant arrhythmia, left ventricular hypertrophy, myocardial ischemia or cardiomyopathy. Subjects with evidence of any suspected heart disease will be immediately addressed to further cardiology examination (emergency room, cardiologist consultation, and echocardiograph).

All patients recruited will receive an estimation of 10-year cardiovascular risk according to main available risk calculator scores [7–10].

All participating subjects will preliminarily give a written informed consent of participation. The study will be held according to the principle of Helsinki Declaration and was approved by local ethic committees.

The CAPITAL study will investigate the prevalence and the prognostic relevance of main cardiovascular risk factor in a "Mediterranean" reality of 10 thousand subjects in primary and secondary prevention. All patients, recruited and interviewed within their usual pharmacy, will be screened with an ECG performed with telecardiology support. The study results will be compared with other epidemiologic study from "non-Mediterranean" areas.

The study will be held thanks to a grant by FARPAS, Modugno (Bari), Italy.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [20].

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