

# Time Course of the Occurrences of Acute Cardiovascular Events in the Italian City of Brindisi

Rita Balocchi<sup>1</sup>, Alberto Macerata<sup>1,2</sup>, Emilio Antonio Luca Gianicolo<sup>3</sup>, Cristina Mangia<sup>4</sup>, Marco Cervino<sup>5</sup>, Clara Carpeggiani<sup>1</sup>

<sup>1</sup>Institute of Clinical Physiology, National Research Council, Pisa, Italy

<sup>2</sup>Department of Physiological Sciences, University of Pisa, Italy

<sup>3</sup>Institute of Clinical Physiology, National Research Council, Lecce, Italy

<sup>4</sup>Institute of Atmospheric Sciences and Climate, National Research Council, Lecce, Italy

<sup>5</sup>Institute of Atmospheric Sciences and Climate, National Research Council, Bologna, Italy

## Abstract

*In a recent study on mortality on municipalities at high risk of environment crisis, significant excesses concerning all causes of death have been localized in the municipality of Brindisi. Focusing on cardiac pathology, we investigated the time course of the daily occurrences of acute cardiovascular events (OCE) leading to unscheduled hospitalization of subjects residents in Brindisi, during years 2001-2008. OCE series was analyzed by Detrended Fluctuation Analysis.*

*The results indicate presence of long-term positive correlation, suggesting a role of atmospheric agents and air quality effects: increase/decrease of OCE following persistent high/low levels of air pollution.*

## 1. Introduction

The area of Brindisi is one of the most industrialized regions in southern Italy, with several polluted emission activities which include two power plants, a petrochemical plant and several other pharmaceutical, metallurgical, manufacturing and cement industries. Two other large industrial emissions outside the border of the town may affect the area: a big coal power plant one of the largest European iron producers.

An epidemiological study in the high-risk area of Brindisi for the period 1990-1994 was conducted by the World Health Organization (WHO). A significant excess of mortality from all causes, all cancers, lung cancers, respiratory and ischemic diseases was estimated for both males and females [1]. Gender differences were pointed out and ascribed to professional exposure. These results have been recently confirmed by a descriptive geographical study conducted in the municipalities of the province of Brindisi [2]. Using a different point of view and focusing only on cardiovascular events, we analyzed

the time series of the daily occurrences of acute events: any apparent behavior different from a white noise random process would be a further confirmation of the role played by the influence of external agents, namely atmospheric and air quality factors.

## 2. Methods

Hospital discharge data of residents in Brindisi in the period 2001-2008 were analyzed. Three series of the daily occurrences of unscheduled hospitalization for cardiac (ICD-9 390-429) causes (OCE) were considered: OCE concerning only male population (OCE\_M), OCE concerning only female population (OCE\_F) and OCE concerning the entire population (OCE\_All). All the series were analyzed by Detrended Fluctuation Analysis (DFA).

DFA [3] is a widely used tool of time series analysis which provides the relationship between the root mean square fluctuations  $F(n)$  and the scale  $n$ . This relationship is characterized by a scaling exponent  $\alpha$ ,  $0 < \alpha \leq 1.5$ , related to the correlation properties of the underlying process. Values of  $\alpha$  lower than 0.5 indicate a process characterized by *antipersistence*: low values are likely to be followed by high values and vice versa. Values of  $\alpha$  higher than 0.5 indicate a process characterized by *persistence*: low/high values are likely to be followed by low/high values respectively. A value of  $\alpha$  equal to 0.5 characterizes a *random process* (white noise). For a correct interpretation of the DFA results, it is common to repeat the analysis on a new series obtained by the original one after selectively destroying some specific property such as nonlinearity, determinism or other (method of *surrogate data*); in this study we decided to destroy the temporal structure of the data, the unique characteristic of interest, to reject spurious results if falsely suggesting non-random behavior of the data.

For OCE\_All the DFA was then repeated over a set of thousand realizations of the randomly shuffled series; the 95th percentile of the distribution of their alpha exponents (alpha95) was computed and compared to the value of alpha of the original OCE.

### 3. Results

Figure 1 shows the DFA curve of OCE\_All. Two scaling regions are clearly visible, with a crossover located at approximately  $n_x=32$  days. The first region, i.e.  $n < n_x$ , scales with the exponent  $\alpha_1=0.51$  and the second, i.e.  $n > n_x$ , scales with the exponent  $\alpha_2=0.77$ . This behavior would indicate the presence of two different dynamics: a white noise process at short-term and a long-term persistency. After shuffling the data, the crossover disappears and the scaling is characterized by only one exponent  $\alpha_{95}=0.53$ , significantly ( $p < 0.05$ ) different from the value of  $\alpha_2$ .

Figure 2 and Figure 3 show the DFA curves of OCE\_F and OCE\_M, respectively. They both show a similar behavior, that is a double regimen with the same crossover, yet with different values of the exponents  $\alpha_2$ , both between them and with respect to OCE\_All. In particular, OCE\_F exhibits a lower level of persistence ( $\alpha_2=0.64$ ), while the behavior of OCE\_M, with  $\alpha_2=0.72$ , is much similar to that of OCE\_All.

The slopes  $\alpha_1$  and  $\alpha_2$  (before and after crossover respectively) are reported in Table 1.

Since the OCE\_All series showed higher evidence of the two regimens, we decided to test its behavior against spurious results through the analysis of its surrogate data. Two results were obtained: disappearance of the crossover and therefore a unique values of the slope,  $\alpha_{95}=0.53$ , significantly ( $p < 0.05$ ) different from the value of  $\alpha_2$ .

Figure 1. DFA curves of OCE\_All in double log scale. A crossover phenomenon is visible at approximately  $n_x=32$  days, separating a region characterized by a white noise behavior ( $n < n_x$ ) from a region of persistency ( $n > n_x$ ).

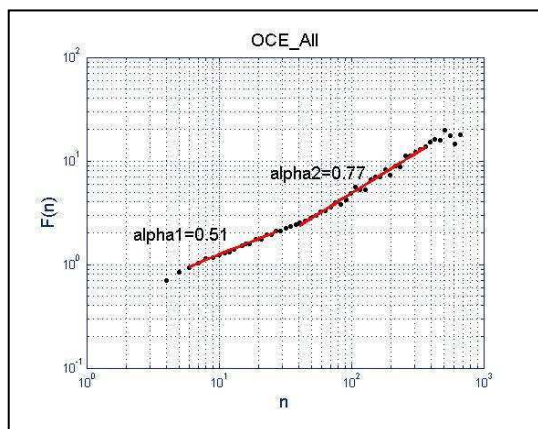


Figure 2. DFA curves of OCE\_F. A crossover similar to the one detected in OCE\_All is still present. The two regions are characterized by a white noise behavior ( $n < n_x$ ) and a region of persistency ( $n > n_x$ ).

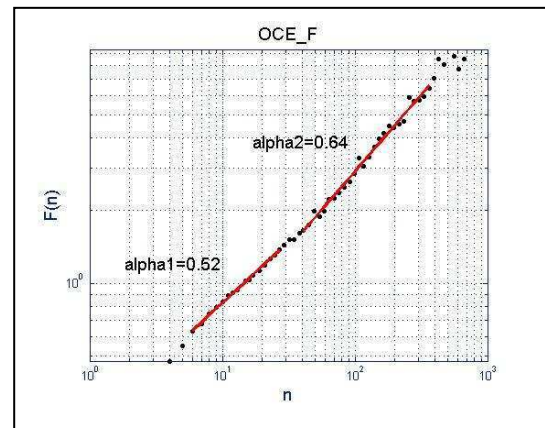


Figure 3. DFA curves of OCE\_M. A crossover separating the two regions of white noise and persistency is still present.

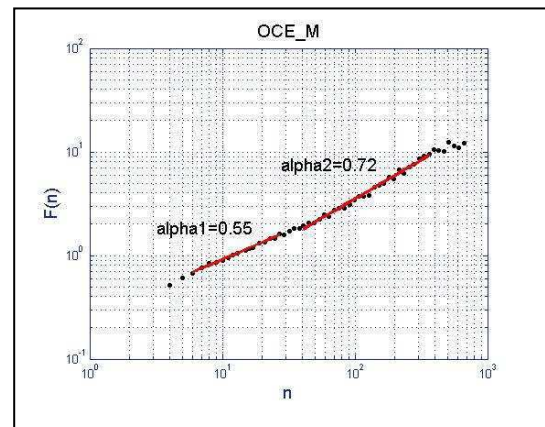


Table 1. Values of DFA exponents before ( $\alpha_1$ ) and after ( $\alpha_2$ ) crossover.

	$\alpha_1$	$\alpha_2$
All	0.51	0.77
Females	0.52	0.64
Males	0.55	0.72

### 4. Discussion and conclusions

The DFA analysis of the three series evidenced a common distinctive trait, that is the presence of two scaling regions separated by a crossover located approximately at  $n_x=32$  days. The phenomenon of crossovers detected by DFA analysis is often encountered in many different time series: physiologic, atmospheric,

financial, to cite a few. This phenomenon can be caused by different factors: it can be the expression of a real change on the dynamics of the series, and in this case we are in presence of a process characterized by multiple scaling laws (multifractality). There are conditions, however, that give raise to a crossover separating apparently different processes, and which is not belonging to the real dynamics of the series. This can happen when trends are superposed to correlated noise: DFA indicates two scaling regions, one relative to the noise and the other to the trend. A complete treatment of this topic can be found in [4-6].

Another condition, mostly encountered in real world data, is a long-range correlated process with additive random noise. This condition can be easily identified because the DFA curve has a crossover from a slope  $\alpha_1=0.5$  to a different value of  $\alpha_2$ . This topic is detailed in [7]. Our results strictly resemble this second condition: a first regimen dominated by noise and then the emerging of the correlated process. In our data the process emerging from noise exhibits a persistent behavior. A possible explanation, in agreement with a recent case crossover study in which the association between OCE and air pollution in Brindisi was analyzed [8], is the role of air pollutants concentrations: increase/decrease of the number of cardiovascular events following high/low levels of air pollution.

Another point of interest is the slight difference in persistency between OCE\_M and OCE\_F: all our series suffer from a low range of variability, particularly for the data concerning females. This sort of 'discretization' can affect the DFA method. The higher persistence shown by OCE\_All, having the highest occurrences of events, seems to support this explanation.

However, at present, we cannot exclude other interpretations, as, for instance, a difference of gender response to external adverse factors.

To give answers to the questions opened by this preliminary study, we are currently investigating the behavior of both atmospheric and air pollution factors recorded for the same period of time in the city of Brindisi.

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Address for correspondence.

Rita Balocchi  
 Institute of Clinical Physiology  
 CNR, National Research Council  
 Area della Ricerca San Cataldo, via Moruzzi,1  
 56124-Pisa, ITALY.  
[balocchi@ifc.cnr.it](mailto:balocchi@ifc.cnr.it).