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Poisoning with Carbon Monoxide and Importance of Monitoring of Patients after CO Poisoning

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Abstract. Carbon monoxide is known to be a highly dangerous indoor pollutant leading to severe health outcomes. However, CO-related mortality data are not available through standard reporting schemes, and therefore, the magnitude of CO-related mortality has always been subject to estimation. Along with the diagnosis of poisoning by carbon monoxide poisoning, forecast has a great importance for the consequences of monitoring. It is to necessary in observe during a certain time health status of persons poisoned, as carbon monoxide poisoning can cause damage to tissues and organs such as the cardiovascular and respiratory systems, muscles, liver, and kidneys. The study identifies the problems that exist with the suggests actions for better monitoring.

Key Words and Phrases: carbon monoxide, monitoring, nervous and cardiovascular systems

2010 Mathematics Subject Classifications: Primary 68N19, 68P10, 68T20

1. Introduction

Indoor air pollution sources from outdoor diffusion and indoor human activities have become the leading cause of the disease burden. Numerous poisons, from natural toxins to synthetic chemicals existing in our environment, can produce a wide variety of deleterious effects in living organisms. Usually, indoor air has the same pollutants as outdoor and could cause the same disease effects, such as particulate matter (PM), sulphur dioxide (SO2), nitrogen dioxide (NO2), and carbon monoxide (CO). However, the health effect and the emergency poisoning event caused by ambient CO were rare, while this usually occurred in an indoor environment with limited space and high concentration has become an urgent public health problem worldwide. This review article discusses carbon monoxide poisoning from a clinical point of view. CO sometimes termed a "silent killer" is a colourless, odorless, and non-irritable gas. As the specific gravity of CO is 0.97, it is slightly lighter than air. CO normally present in the atmosphere at a concentration of approximately 0.03–0.20 parts per million. This gas can be generated by natural or anthropogenic sources, especially by incomplete combustion of fossil fuels and biomasses. The toxicity of CO is mostly attributable to its capability to diffuse into the erythrocytes and bind to haemoglobin, for which CO has a nearly 200-fold higher affinity than oxygen.

In poisoned patients, both oxygen and CO compete for binding to haemoglobin, but even small volumes of CO dissolved in the blood may be effective to largely displace oxygen binding (i.e. the so-called Haldane effect) [1]. The severity of symptoms is conventionally determined by the exposure values of CO and the consequent carboxyhaemoglobin (COHb) level, whose normal concentration in blood is typically comprised between 0.5% and 1.5% in non-smokers [2]. A CO concentration between 10% and 20% is usually accompanied by nausea, fatigue, tachypnoea, emotionality, confusion, and clumsiness, CO levels between 21% and 30% is accompanied with headache, exertional dyspnoea, angina, visual impairment, and decreased sensory perception, and that between 31% and 50% is accompanied with dizziness, fainting, confusion, nausea, vomiting, visual impairment, and problematic decision-making, while CO values >51% typically trigger seizures, coma, severe acidosis, and death [3]. Toxic exposures more frequently occur from faulty heaters, fires, industrial accidents, and car exhausts.

2. Worldwide epidemiology of carbon monoxide poisoning

This article presents updated information on the worldwide burden of carbon monoxide (CO) poisoning. The worldwide epidemiologic data were obtained from the Global Health Data Exchange registry, a large database of health-related data maintained by the Institute for Health Metrics and Evaluation. The worldwide cumulative incidence and mortality of CO poisoning are currently estimated at 137 cases and 4.6 deaths per million, respectively. The worldwide incidence has remained stable during the last 25 years, while both mortality and percentage of patients who died have declined by 36% and 40%, respectively. The incidence of CO poisoning does not differ between sexes, whilst mortality is double in men. The incidence shows two apparent peaks, between 0–14 years and 20–39 years. The percentage of patients who died constantly increases in parallel with aging, peaking in patients aged 80 years or older. The number of CO poisoning grows in parallel with the socio-demographic index (SDI), though more detailed analyses would be needed to confirm our findings. Mortality displays a similar trend, being approximately 2.1- and 3.6-fold higher in middle and middle-to-high than in low-to-middle SDI countries [4].

Carbon monoxide (CO) poisoning is a public health concern in developing countries especially in China with a high disease burden. A total of 27 855 non-occupational CO poisoning cases were reported between 2017 and 2021 in China [5]. In the recent 5 years, 90% of the CO poisoning cases of China occurred in the northern region, and Shandong Province got the first with nearly half cases reported [5, 6]. Jinan city with a 10 million population is the capital of Shandong province. In Jinan between 2007 and 2021 among total of 6588 CO poisoning, 5616 cases (85.25%) and 180 deaths caused by household coal heating was identified during study period. The cumulative incidence rate was 5.78 per 100,000 person-years and the mortality rate was 0.19 per 100,000 person-years. The incidence in urban areas (6.55 per 100,000 person-years) was higher than rural areas (5.04 per 100,000 person-years), and there was a statistical difference between urban and rural ($P < 0.001$) ($P < 0.001$). The poisoning time point mainly occurs in the sleep stage [7].

Since the mid-1950s, Korean society started to use coal briquettes as fuel for cooking

and heating. According to a survey of the leading causes of accidental CO poisoning between 1965 and 1976, gas leaking from ondol structures accounted for 54.2% of accidents, while gas leaking from a fireplace such as a coal fuel hole accounted for 26.3%. Overall, about 80% of CO poisoning cases could be attributed to ondol heating facilities [8]. CO poisoning incidence increased during the 1960s. This trend had continued until the 1980s. The number of victims of CO poisoning peaked at approximately 1 million people in 1980. The number of mild cases in 1980 at approximately 0.86 million cases, while severe cases numbered approximately 134,000 that year. The number of fatal cases first exceeded 1,000 in 1964, and it was estimated that at least 1,000 annual deaths continued during the subsequent 30 years, until 1993. The number of fatal cases peaked in 1980, with approximately 2,400 deaths [9].

In the 1990s, CO poisoning was dramatically reduced as coal briquettes were replaced by oil. However, in Korea CO poisoning using burning coal briquettes during suicide attempts has recently increased. The number of suicides associated with CO poisoning were 34 among the total 10,653 suicide cases (0.3%) in 2006, but 1125 was observed among the total 14,159 suicidal cases (7.9%) in 2012 [10]. We estimated that, from 1951 to 2018, the cumulative number of CO poisoning victims comprised approximately 22,830,000 mild cases, 3,570,000 severe cases, and 65,000 deaths.

Carbon monoxide (CO) is the leading cause of poisoning deaths in many countries, including Japan. Annually, CO poisoning claims about 2000-5000 lives in Japan (Fig. 1), which is over half of the total number of poisoning deaths. However, deaths from CO poisoning doubled in 2003 compared to that for 2001 in Japan. This may be attributable to an increase of suicides by means of CO inhalation [11]. We estimated that, in Japan, 42339 persons died from the toxic effects of CO between 1997 and 2009. Eighty-three percent of the deaths occurred in males [12].

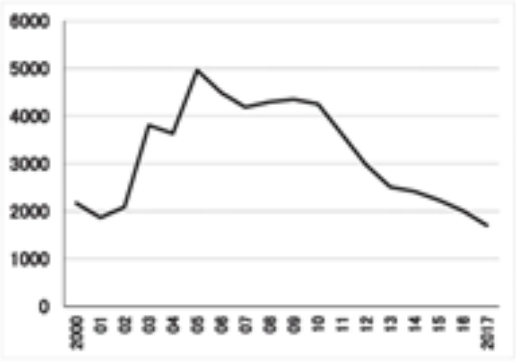


Fig. 1. Statistics on annual numbers of death by CO poisoning in Japan (2000–2015).

In England, unintentional non-fire related poisoning (UNFR) is the most common cause of CO poisoning, with an average of 25 deaths per year being reported between 2015 and 2016 by the Office of National Statistics (ONS) (Fig. 2) [13, 14] and a hospitalization rate of 0.49/100,000 between 2001 and 2010 [15]. Between 2002 and 2016 were identified 6643 hospital admissions for CO poisoning in England, excluding fire-related cases (n = 408; 5.9%) (Fig. 3). Of these, 1782 (52.5%) were unintentional, which represented 47.5% (n =

1617) and 52.5% (n = 1782) of female and male hospitalizations, respectively (p = 0.091). Overall, this is equivalent on average to 227 unintentional non-fire related CO poisoning hospital admissions per year (min. 2013 = 166; max. 2010 = 326). There was clear seasonality in the admissions, with the largest proportion of hospitalisations occurring during winter months (November to February) [16].

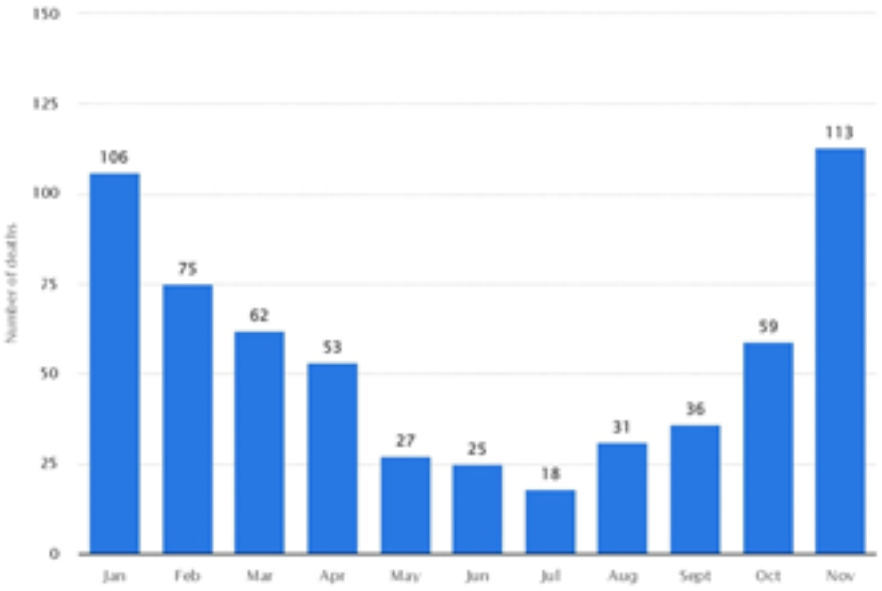


Fig. 2. Number of deaths from unintentional carbon monoxide poisoning in the United Kingdom (UK) from 1995 to 2021, by month

The highest age-specific crude rates were found in poisoning with carbon monoxide among those aged over 85 years. Crude rates among children aged < 10 years were slightly higher than those found in older children, aged from 10 to 24 and young adult groups, aged from 25 to 29. Here were found higher age-standardized rates in rural areas compared to urban areas. These patterns were observed both overall and by gender. Age-standardized rates were slightly higher among males than females, respectively [16].

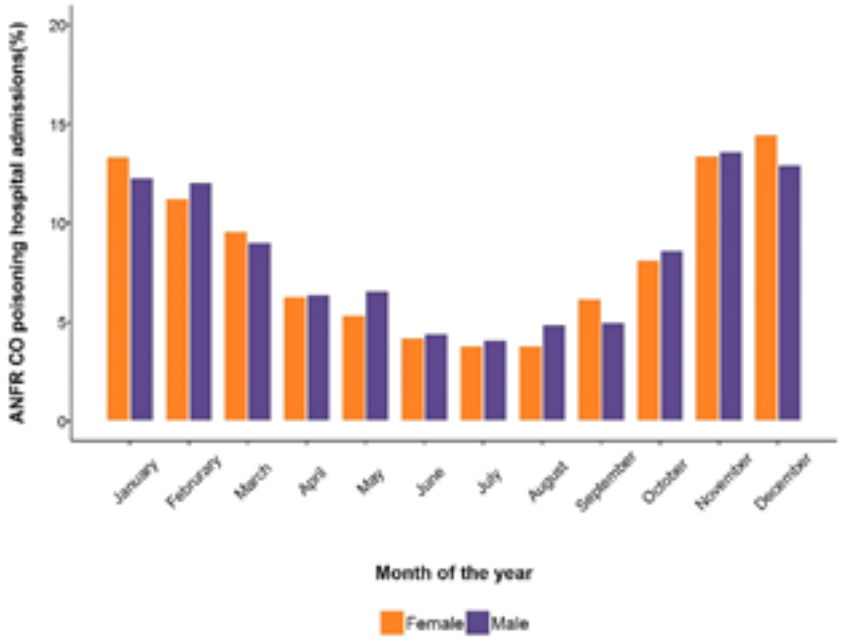


Fig. 3. Percentage of ANFR CO poisoning hospital admissions among males (purple) and females (orange) by calendar month, England, 2002–2016.

In England, temporal trends were analysed using piecewise log-linear models and comparing them to analogous data obtained for Canada, France, Spain, and the US. Here were estimated age-standardized rates per 100,000 inhabitants by area-level characteristics using the WHO standard population (2000–2025). Temporal trends showed significant decreases after 2010. Decreasing trends were also observed across all countries studied, yet France had a 5-fold higher risk. Based on 3399 unintentional non-fire related CO poisoning hospitalizations, is found an increased risk in areas classified as rural, highly deprived or with the largest proportion of Asian or Black population [16].

According to Statistics Canada, between 2000 and 2013, in Canada, there were 4,990 deaths associated to CO poisoning. This number included 1,125 deaths where there were no other underlying causes of death and 3,865 where there were other underlying causes of death. In terms of the total number of deaths, 34.8% were registered for people between the ages of 25 and 44, and an additional 40% were reported for those between the ages of 45 and 64. Quebec had the highest total number of carbon monoxide-related deaths (n = 1,445) followed by Ontario (27.5 per cent), the Prairies (24.6 per cent), British Columbia and the Territories (13.3 per cent), and the Maritimes (5.6 per cent). In total, there were 3,027 hospitalizations related to CO poisoning in Canada between 2002 and 2016, and 14.3% of CO-related hospitalizations in Canada were for people of 65 years of age or older. When missing data or unspecified data were removed from the analysis, 75% of CO-related hospitalizations occurred as a result of CO poisoning originating at home. Ontario, Alberta, and British Columbia had the highest number of CO-related hospitalizations, while the largest increases in per capita hospitalization between 2002

and 2016 were in Saskatchewan (34.7 per cent), Manitoba (19.2 per cent), and British Columbia (7.6 per cent). There are more than 300 CO-related deaths per year in Canada, and more than 200 hospitalizations per year in Canada [17].

In the United States, 50,000 patients with carbon monoxide poisoning are admitted to the emergency departments of hospitals annually, resulting in 1,500 deaths [18, 19]. Most of poisoning events are observed and reported in the state of Nebraska in January [20, 21]. In the period between 2000 and 2009, the number of carbon monoxide poisoning patients estimated was about 68,316; 30,798 (45.1%) were provided on-site aid, and 36,691 (53.7%) patients were treated in hospitals. 34,386 of poisoned patients are women, 30,257 are men. Most of poisoning events are related to the living conditions, and here, a special place have women, children less than 17 years of age, and persons aged between 18 and 44. In spite of these factors the quantity of poisoned persons has decreased: in 2006 - 0.31%, in 2009 - 0.24%. Between 2000 and 2009, 16,447 death events are registered [22, 23]. In 2015, according to data from the Centers for Disease Control and Prevention (CDC) in the United States, there were 393 deaths from accidental carbon monoxide poisoning (Fig. 4) [24].

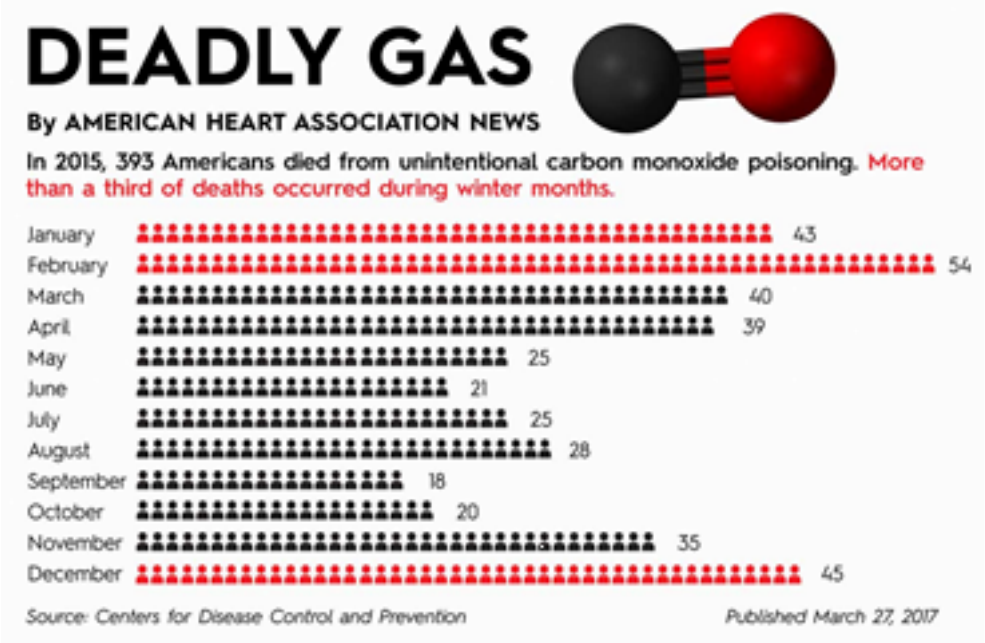


Fig. 4. Statistical information on carbon monoxide poisoning in USA

Between January 2008 to December 2017, the risk of CO-related death in Turkey was 0.35/100000. There were 2667 deaths from CO poisoning in the 10-year period. 1371 (51.4%) of the victims were male, 1178 (44.2%) of them were female and there were 118 (4.4%) victims whose genders were unknown. The median age of the patients was 45 years (range, 15 days-108 years). Most of the deaths occurred in cases of $\geq$50 years of age. 2545 (95.4%) of the incidents were heating related, 50 (1.9%) of them were work related and 72 (2.7%) of them were for unknown cause. There was a stagnating trend of CO-related deaths. Most of the incidents occurred in winter. The Middle Anatolian region was of the

highest risk in CO-related mortality [25]. Figure 5. shows mapping of carbon monoxide related death risk in Turkey.

Fig. 5. CO-related death risks in the provinces of Turkey

According to statistical data, a considerable increase in the number of acute poisonings with carbon monoxide has been observed in Azerbaijan too. Between 2010 and 2022, in Baku (the capital of Azerbaijan), the number of carbon monoxide poisoning patients estimated is 21,404. Reliable Information on poisonings within Baku during the period between 2010 and 2022 is given in Table 1.

Table 1.

Statistical information on carbon monoxide poisoning in the districts of Baku

Baku city, districts	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Narimanov	69	121	127	118	105	137	77	42	56	46	41	32	43
Khatai	106	135	192	126	161	201	177	139	138	152	98	104	104
Sabayil	42	85	109	88	139	74	94	84	57	75	65	59	57
Yasamal	118	137	151	132	76	116	183	195	202	188	162	130	173
Nasimi	129	221	237	178	187	185	100	71	86	95	75	68	71
Nizami	64	123	171	200	197	175	159	100	112	154	112	80	129
Binegedi	190	316	395	378	371	419	493	352	345	393	322	277	293
Khazar	17	26	36	63	78	91	106	94	89	147	157	148	142
Surakhani	70	141	141	193	185	185	199	156	162	186	137	198	132
Sabunchi	107	147	221	202	158	177	271	189	241	229	201	238	196
Garadag	98	115	232	145	206	166	139	110	114	105	79	78	77
Total	1010	1567	2012	1823	1863	1949	1998	1532	1602	1770	1449	1412	1417

Most of poisoning events are observed in Baku in winter. Rates of poisoned with CO were higher among females. The cases of poisoned with carbon monoxide among children aged < 10 years old were slightly lower than those found in older children, 10 to 24 years old and young adult groups, 25 to 29 years old. Epidemiology of CO poisoning in different age groups during the period between 2020 and 2022 in Baku is shown in Table 2.

Table 2.

Age-standardized rates of the number of cases of poisoned with CO in Baku (2020–2022) by population characteristics

		2020		**2021**		**2022**	
Age groups (years old)							
	Total	Male	Female	Male	Female	Male	Female
<10	147	18	27	27	30	20	25
10 to 24	1190	144	285	124	213	178	246
25 to 39	1463	210	313	204	335	161	240
40 to 54	751	117	120	117	110	120	167
55 to 69	672	90	105	113	125	112	127
70 to 84	53	3	17	1	13	2	17
>85	2	-	-	-	-	-	2

3. The importance of monitoring by carbon monoxide poisoning

Along with the diagnosis of poisoning by carbon monoxide poisoning in order to forecast has a great importance for the consequences of monitoring. It is to be observed during a certain time health status of persons poisoned. Because we know CO binds to haemoglobin with a higher affinity than oxygen. By interfering with oxygen binding, it induces tissue hypoxia, which is thought to affect the organs that heavily depend on oxygen utilization, including the cardiovascular system [26]. Major causes of tissue and organ damage is not only hypoxia, but also oxidative stress, formation of oxygen reactive species, neuron necrosis, apoptosis, and abnormal inflammation.

The heart is extremely susceptible to CO-induced hypoxia, due to its high oxygen demand. Cardiac involvement manifests mainly as ischemic insult, with elevated enzyme levels and ECG changes ranging from ST-segment depression to transmural infarction. Conduction abnormalities, atrial fibrillation, prolonged QT interval [27] and ventricular arrhythmia have been demonstrated. There have been few studies of CO-induced cardiopulmonary compromise in children. Known is a case of severe cardiopulmonary compromise without overt neuropsychiatric sequelae in a 15-year-old boy [28].

Satran et al. performed a research with 230 patients from 1994 to 2002. They reported that myocardial injury, defined as the elevation of cardiac enzyme levels or ischemic changes indicated in electrocardiography, was observed in 37% of patients with CO poisoning requiring hyperbaric oxygen therapy. When this patient group was followed up until 2005, the hazard ratio (HR) of long-term mortality was significantly higher in the group with myocardial infarction (MI) at 2.1 (95% confidence interval [CI], 1.2–3.7) compared to the group without MI [29]. Additionally, there have been reports of MI after CO poisoning [30–32], and among them, there were cases that occurred at low exposure levels [32]. Therefore, the possibility that the risk of ischemic heart disease (IHD) may increase due

to CO poisoning can be considered. However, only a few case reports have confirmed the effects of CO toxicity on the cardiovascular system. Moreover, in a large epidemiological study performed in Taiwan based on a nationwide health database, no increased risk of IHD was found [33]. No large-scale epidemiological studies have explored the relationship between CO poisoning and IHD development other than the study in Taiwan. Therefore, further epidemiological research is needed.

Therefore to investigate the association between CO poisoning and IHD, a nested case-control study of 28,113 patients who experienced CO poisoning and 28,113 controls matched by sex and age was performed using the nationwide health database of South Korea. Based on a conditional logistic regression, there was a significantly higher risk of IHD among the CO poisoning group than among the control group (adjusted hazard ratio [HR], 2.16; 95% confidence interval [CI], 1.87–2.49). IHD risk was the highest within 2 years after CO poisoning. The risk of IHD after CO poisoning was higher among the younger age group under 40 years (adjusted HR, 4.85; 95% CI, 3.20–7.35), and it was much greater among those with comorbidities (adjusted HR, 10.69; 95% CI, 2.41–47.51). The risk of IHD was the highest within the first two years after CO poisoning (adjusted HR, 11.12; 95% CI, 4.54–27.22). Even if more than six years had passed, the risk was still significantly higher than among the control group (adjusted HR, 1.55; 95% CI, 1.27–1.89). The analyses imply that CO poisoning is associated with an increased risk of IHD. Although they observed increased IHD risk after CO poisoning, the exact mechanism of this association remains unclear. Further studies of the long-term effects of CO poisoning on the cardiovascular system and the underlying mechanisms are thus required [34].

There is limited information regarding cardiac imaging after CO poisoning. One case report involving the use of cardiac magnetic resonance imaging (CMRI) detected late gadolinium enhancement (LGE) during the 4-month follow-up of a patient with severe CO poisoning [35]. Figure 6 shows a representative CMRI image of injury patterns and changes. Another report described a patient with acute subendocardial injury after CO poisoning [36].

The symptoms of poisoning with carbon monoxide resolves in most patients following normobaric or hyperbaric oxygen therapy, but a minority of patients experience persistent neuropsychiatric abnormalities or delayed encephalopathy. The carboxyhaemoglobin (COHb) level on admission after CO inhalation does not always correlate with clinical findings or prognosis. Chronic CO exposure may present itself with loss of dentition, gradual-onset neuropsychiatric symptoms, or recent impairment of cognitive ability inconsistent with delayed neurological sequelae (DNS) [37-39]. Increasing evidence indicates that the brain damage caused by CO intoxication results from mitochondrial oxidative stress in the central nervous system, white matter demyelination resulting from the immune response, abnormal inflammatory responses, and apoptosis. Free radicals activate a cascade responsible for the appearance of the delayed effects seen in an estimated 1%-47% of patients with CO intoxication [38, 40].

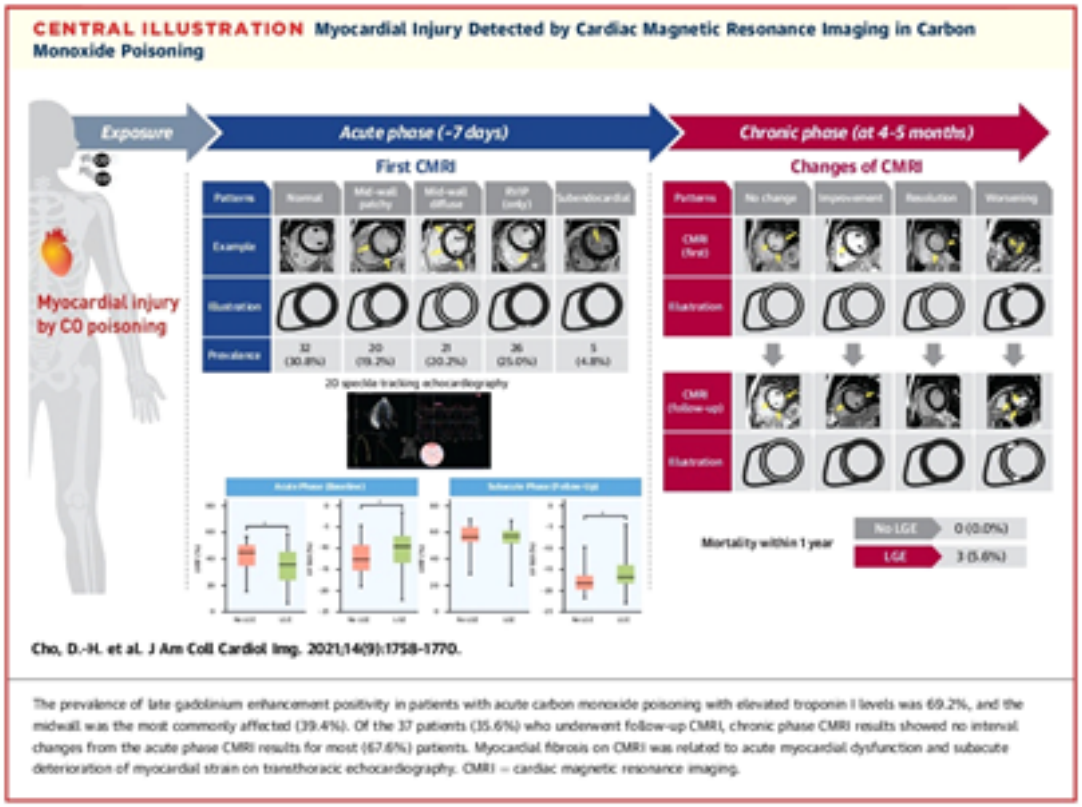


Fig. 6. Representative CMRI image of injury patterns and changes.

DNS includes a broad spectrum of symptoms. The sequelae may vary from mild to severe headache, seizures, alteration in consciousness, lethargy, concentration problems, cognitive disturbances, emotional liability, personality changes, amnestic syndromes, dementia, psychosis, gait disturbances, movement disorders (e.g., parkinsonism), chorea, apraxia, agnosia, inaction, peripheral neuropathy, urinary incontinence, and even vegetative state [38, 40-42]. Delayed CO intoxication is diagnosed by the presence of a clinically silent period or lucid interval lasting for 2-40 days after acute intoxication followed by recurrent neuropsychiatric symptoms [40]. It should also be noted neurological symptoms of CO poisoning can manifest not only immediately but also as late as 2 to 6 weeks.

The diagnosis of DNS is primarily made on the basis of the clinical features and radiological findings of CT and conventional MRI. MRI have shown that particularly vulnerable areas of the brain include the cerebral cortex, hippocampus, basal ganglia, and cerebellum [43]. These include newly formed hyperintense white matter lesions on T2-weighted images and fluid-attenuated inversion recovery (FLAIR), but they may be absent even in cases with chronic neurological symptoms [44, 45]. Cerebrospinal fluid (CSF) analysis is a valuable diagnostic tool, but it is highly invasive and time-consuming.

4. Organization of monitoring, investigation of the dynamics of changes in indicators

Eventually monitoring is advisable for both once poisoned also for persons affected by chronic intoxication.

Monitoring needs to be conducted after successful treatment in hospital. Therefore, starting time of monitoring should coincide with the end of the treatment. Functional parameters and biochemical analysis of carbon monoxide victim needs to be examined from time to time during the monitoring (fixed time interval). Particularly, type of poisoning, more affected poisoning of the body and more nervous and cardiovascular systems, mainly due to the majority of these indicators are checked by selecting among the more specific ones. In most cases, the determination of patient treatment verification of indicators reflecting the health of people is selected in the process of stationar treatment. Analysis in the selected interval of time should be checked for prevention and prognose of consequences after poisoning.

Time changes in carbon monoxide poisoning should be controlled after receiving treatment in order to avoid the consequences of toxication. Time series method is used in those situations. The basis of time series analysis is that former happenings have important indications for future happenings. Time series data is a sequence of successive moments of time, which reflects to the situation. In contrast to randomly selected analysis, time series based on observation data of equal times. Time series can be often found in medicine. Time series analysis has two goals: determination the nature of queue and prognosis. In both cases, the model must be specified before the turn to the interpretation of the data.

According to the analysis of time series, data consists of systematic component and a random voice complication detection components arranged in a regular variable. Majority of research methods allow to observe the change in the index on a regular basis using a variety of methods for filtering noise. Routine variables of time series have two classes: either the trend or seasonal components.

Change dynamics reflects the trend. Trend consists of the variable components changed through the time organized in a systematic linear or non-linear. The seasonal component is repeated periodically [46].

Time series process used to identify prognostic factors of data in the past, today linked to a similar effect in the near future.Analysis of observations is a continuous process estimated in a certain discrete moments of time (when you can evenly across the distribution). For that reason indications which can cause a dangerous development in near future should be selected (months, sometimes years).

There is not “automate” methods for detection of time series. If the trend (increasing or decreasing) is monotone, the queue is not difficult to analyze. If the time series has enough offense in that case smoothing process should be conducted primarily as a method of filtration. Smoothing process is a kind of moderation of data. In this case, the non-systematic errors repel each other. The most common method of smoothing method is moving average, when m members of the neighboring row of each member shall be replaced by a simple average, m is a price of intervals. Also, the trend is to be used for the

detection of exponential smoothing. Many monotone time series is described by linear to express analytically. If there is non-linear component, set of data needs to be carried out to remove it. For this reason, most of the time logarithmic, exponential, or polynomial transformations can be used. In some cases, the least squares method is carried out in the smoothing. All of these methods are given the relatively smooth line noise filtering, transforms to circle.

Moving average method determine the start of a new trend, also warns of the end or return. This method allows you to keep track of the development process, it can be viewed as trend lines. However, this method is not used for making predictions, because it follows a trend, but it can't predict, it only shows the start of a new trend. Smoothed curve and the trend observed during the performance of the simplified average, short-term floating-average rate reflect dynamics more accurately for long intervals calculation.

Moving average is defined as follows:

$$y_t = 1/m \tag{1}$$

where y_i, is the value of the i-th level; m is the number of levels from smooth intervals -$(m = 2p + 1)$; y_t dynamic row of the current level; i is the number smooth level range; p is m single range value $p = (m - 1)/2$

Smooth change interval depends on the determination of the indicators. Thus, indicators of irregular, small changes smooth interval assumed to be more. If you are required to take into account changes in smoothing, small gap becomes smaller.

Moving average method is used if time series is organized in straight lines. Because this time does not misrepresent the dynamics of the index. If the range is non-linear, usage of this method can cause distortion of indicators . It is used when smooth is exponential [47].

Analytical smoothing method is an identification of development trends as time series function.

$$\widehat{y}_t = f(t), \tag{2}$$

where $\widehat{y}_t$ is theoretical value of time series with analytical expression for the time, t is time.

Theoretical values are derived from the mathematical model.

Indicating the trend of development, the following features are implemented:

- The linear function with straight line graphs:

$$\widehat{y}_t = a_0 + a_1 t,$$

- Exponential function

$$\widehat{y}_t = a_0 * a_1',$$

- Exponential function second degree (parabola)

$$\widehat{y}_t = a_0 + a_1 * t + a_2 t^2,$$

- Logarithmic function:

$$\widehat{y}_t = a_0 + a_1 lnt$$

Estimation of functions parameters are carried out by least squares method. In this case, the solution is the minimum value of the sum of theoretical and empirical level squares:

$$\sum (\widehat{y}_t - y_i)^2 \to min, \tag{3}$$

where $\widehat{y}$ is calculated, y_t are real levels.

Smooth on a straight line is used in cases where the increments are fixed.

Smooth with exponential function is applied in geometric changes when there is a steady increase in the ratios.

Secondary exponential function smooth is used to change dynamic range and stable chain increases.

The smooth on logarithmic function reflects growth of the number of decrease, the recent increase in the time series.

Counting accuracy of the analytical expressions is defined as follows: sum of empirical series of price must coincide with the sum of the smoothed series levels. In this case, small errors can occur due to the calculated values:

$$\sum y = \sum \widehat{y}_t \tag{4}$$

Autocorrelation is used to determine patterns of additional data change in time series smooth method. Autocorrelation function, determine indication whether it is increasing or decreasing based on seasonal fluctuations.

Determination model is used to assess the trend model accuracy:

$$R^2 = \frac{\sigma^2_{\widehat{y}}}{\sigma^2_y}, \tag{5}$$

where, $\sigma^2_{\widehat{y}}$ is theoretical model dispersion of the data variance, σ^2_y is empirical dispersion of the data.

Trend model shows development tendency of R^2 close to 1 indicators in values.

According to the time series method, data processing is carried out in three stages:

In the first phase filtering is carried out not taking into consideration distortions resulting from seasonal or other changes. The main goal of filtration is to find out y-changes affected from x-changes, eliminate factors that will affect that relationship further. A few known methods for filtering floating above the average value is the most widely used.

According to the moving average price at the time of moving to and from in the price index is calculated by determining the average number. In this situation, the long-term periods doesn't show accurate value compared to the changes in the short-term periods. However, filiration should be conducted carefully. Important information may be lost as a result of the smoothing filter. Therefore, filtration should be carried out in several ways, the results should be verified with the help of correlation analysis.

The second stage is a conduction of the forecast index. For this reason regression model selection and installation is carried out.

Regression analysis is used for two reasons:

1. Detection of relationship between the measured parameters;

2. Prognose of the value of a variable based on the value of regression equation.

Monitoring with carbon monoxide poisoning shows interesting facts according to the method of time series in the monitoring of indicators to determine whether certain moments of time, but also forecast the change indicators. Time series method is using to show the changed indicators of regression equation by time to time. Single regression equation shows the variation of the moments and observation of a person poisoned by a factor. Changes of signs in time creates time series of dynamic rows. The characteristics of that rows is time factor (x), and dependant variable (y) factor, the sign of the value changes. The dependence between them can be shown as a regression equation.

The changes indications by using the method of time series depend on single factor regression equation or multivariate factor of regression equation. In addition, the figure forecast in a single-factor regression equation is given by:

$$y = a + b * x \tag{6}$$

where a is the free member; b determines the slope of the regression line of rectangular axes. According to the least squares method, to determine the parameters, the equations will be as follows:

$$a * n + b \sum x = \sum y \tag{7}$$

$$a \sum x + b \sum x^2 = \sum y * x \tag{8}$$

Formulas given for determination of parameters:

$$a = y - b * x \tag{9}$$

$$b = \frac{y * x - \overline{y} * \overline{x}}{x^2 - \overline{x}^2} \tag{10}$$

Multivariate regression equation is used to monitor and predict the dynamics of change of many traits at the same time:

$$\widehat{y}_x = a + b_1 x_1 + b_2 x_2 + ... + b_m x_m \tag{11}$$

Based on the assumption multivariate regression testing is not possible, dependents become more obvious on the basis of the probabilities. Because the regression coefficients for the various tendencies traits values cause a shift in the regression line, and can change direction. Even one trait value in the presence causes a change in the outcome. Despite it is necessary to monitor the observation of a large number of indicators in carbon monoxide poisoning, more realistic indication of each individual was considered more appropriate to the forecast by the factorial regression. This has been confirmed in numerous experiments. The prognosis by regression equation is given for a certain time after the end of the monitoring period.

In the third stage, the quality of the model should be estimated.

The regression is carried out by adequacy of the model determination:

$$R^2 = \sum_{i=1}^{N} (\widehat{y}_i - \bar{y})^2 / \sum_{i=1}^{N} (y_i - \bar{y})^2. \tag{12}$$

where $\overline{y}_i$ is relevant to x_i the theoretical or estimated value y_i.

Determination coefficient shows variables depending on the degree of compared dispersion. The adequacy of the regression equation is increasing in respect to R^2 high value. Determination coefficient regression model is useful for prediction. The regression equation for the determination of a criteria of Fisher is used:

$$F = \frac{R^2}{1` - R^2} * \frac{n - m - 1}{m} \tag{13}$$

where R is determination coefficient, n is the number of observations, m is the number of parameters in x variables (the number of factors in linear regression model).

This criterion assesses the significance factors included in the regression equation. Calculated F-value of the significance level αup, are compared with 1 and $n - m - 1$ in table value. If the calculated F value exceeds the value of the table, $F \geq F_{table}$, then x factor included in the model is of statistical significance. If the calculated F is less than table value, x variable doesn't affect to y variables changes and the inclusion in the model is inappropriate.

Determination coefficient with the help of correlation is defined as follows:

$$r = \sqrt{R^2} \tag{14}$$

Determination coefficiency, $-1, +1$ varies in correlation coefficient. Determination coefficiency close $+1$ shows close relation of y variables with x factor to prove that indicator is the most significant factor for formalization of consequences. In this regard, the regression model can be used to forecast the indicator.

The indicators selected for monitoring medicine will be:

$$x_i \in X, i = \overline{1, n}$$

where x_i is an indicator.

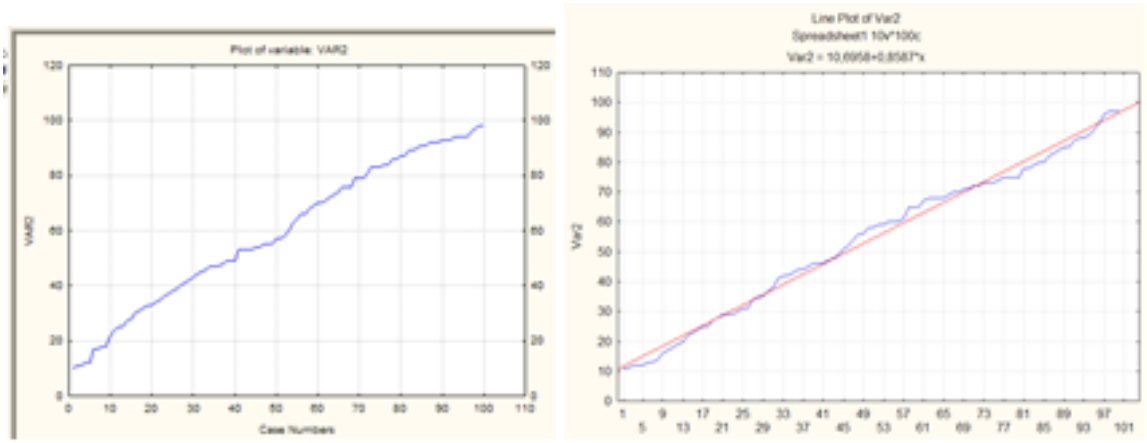
There are ending regulatory values for given parameters. Based on this, there is specific change interval for $\forall x_i$ (in some cases, the standards are different for men and women). Standards in accordance with the upper and lower boundaries is y_i and z_i. Then

$$y_i < x_i < z_i$$

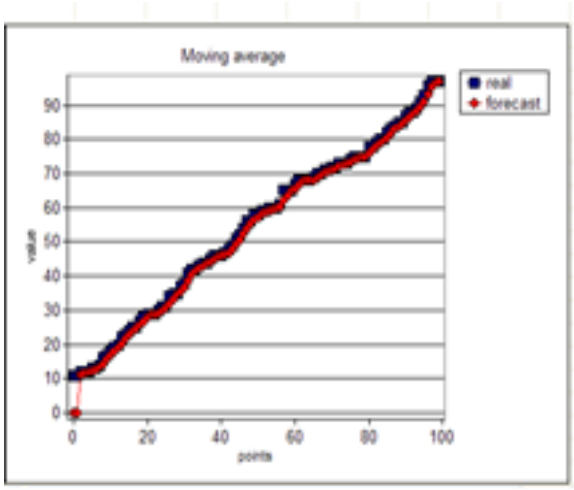
should be. Each x_i is observed in $T = t_1, t_2, ..., t_k$ time. k is the number of measurements. Then v_i^j can be described as an arbitrary parameter, where $i = 1, 2, ..., n, j = 1, 2, ..., k$. Lower and upper variables can be considered as pathology:

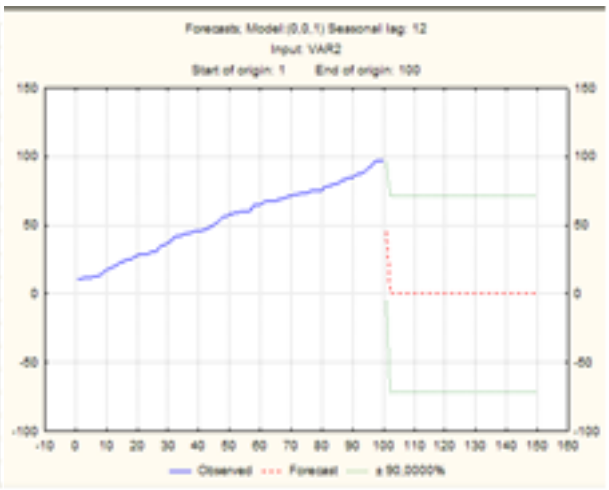
$$x_1^j < y_i \mathrm{x}_1^j > z_i$$

Autocorrelation functions are established for observation of any change of variable x_1^j in $T = t_1, t_2, ..., t_k$ time. It should be noted that the numbers do not reflect the cost of health indicators, the random number generator has been used. K as the number of points used in the determination during the observation period, sometimes it means the number of years or monthes. For example, 100-point numbers with a given distribution (fig. 7a), trend (fig. 7b), smoothing curve (moving average) (fig. 7c), forecasting (fig. 7d), shown a certain time autocorrelation (fig. 7e) and partial autocorrelation function (fig. 7d). This series show ascending value of numbers.

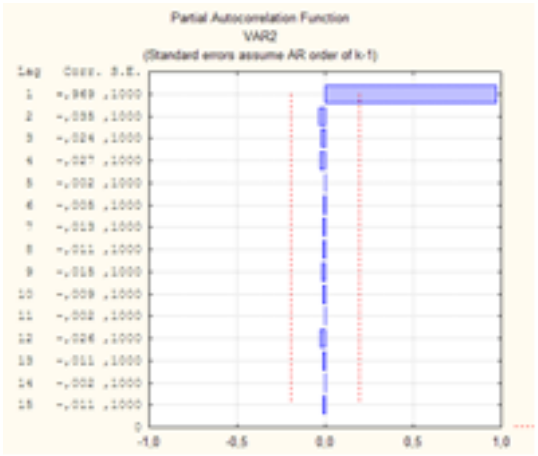


1. b)





1. d)

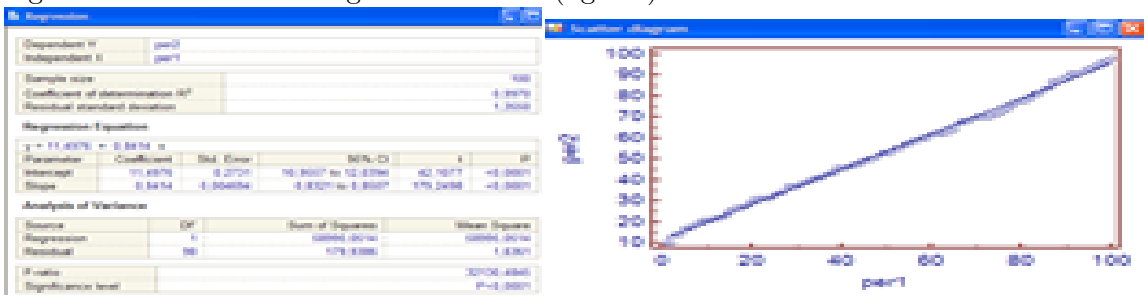


1. f)

Fig.7. Characteristic of time series with ascending numbers

Partial correlation shows variables between two random variables, when taken the effect of internal values of autocorrelation doesn't take into account. Partial autocorrelation is almost same with simple autocorrelation in small moving. In practice, the periodic dependence of the specific autocorrelation is showing as "clean". The appearance of autocorrelation and partial autocorrelation depends on the length of the time series. Autocorrelation function shows the model accurately when the series is long. When the range is short, correlogram loses its accuracy and autocorrelation and autocorrelation estimation degree is decreasing. Meanwhile, the trend shows that there is not a periodic function in autocorrelation changes.

Regression equation for distribution, coefficient of determination (fig. 8a), scatter regression of the order are given as follows (fig. 8b):

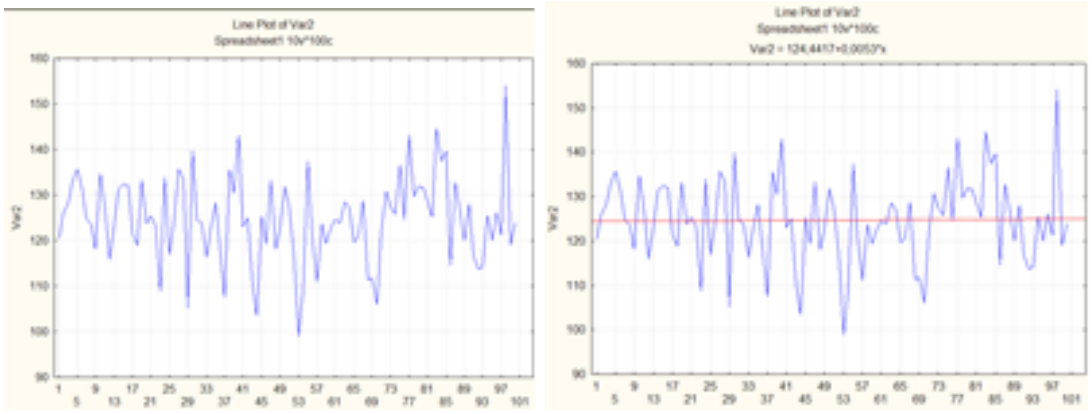


1. b)

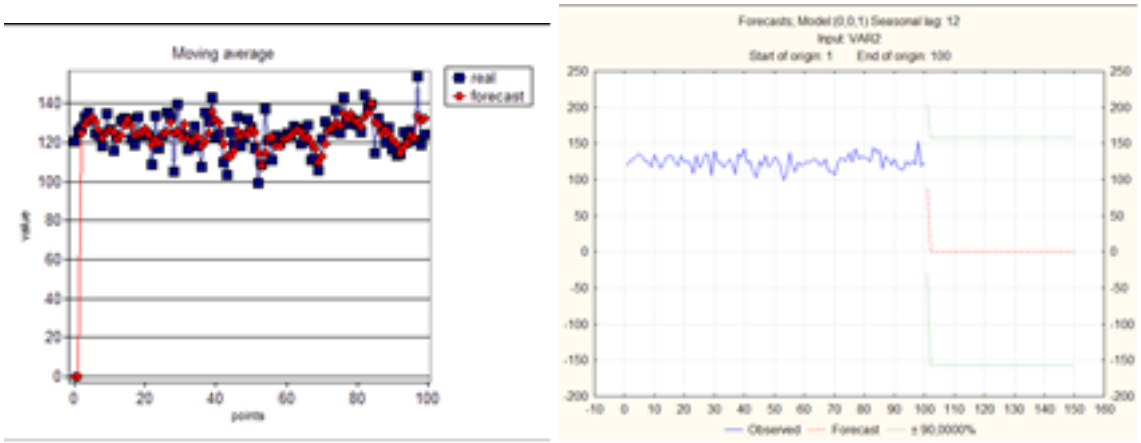
Fig. 8. Regression equation for distribution, coefficient of determination

According to Fisher criteria, this statistics is significant.

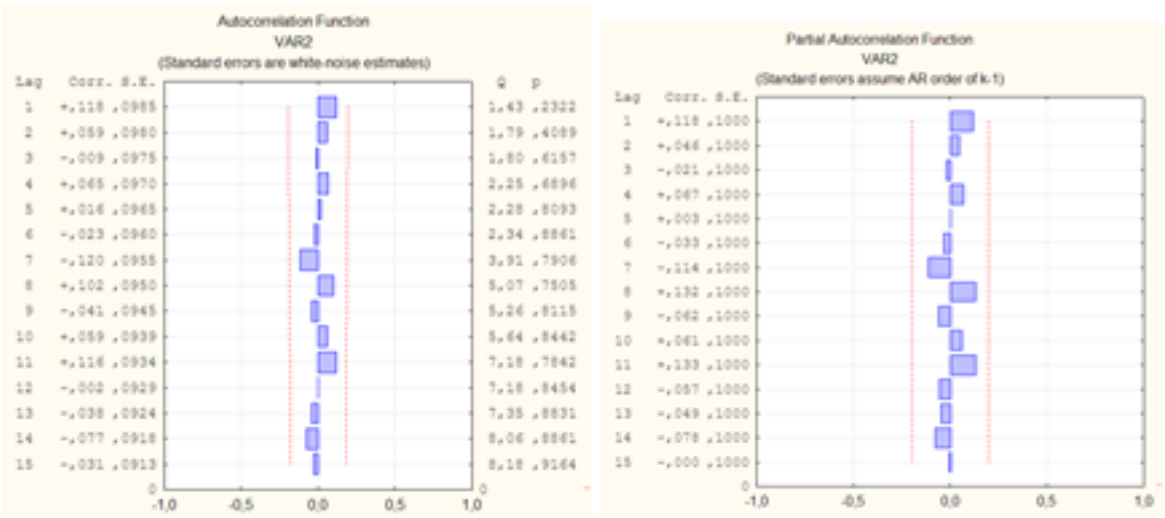
Another example for number of shows with normal distribution in fig. 9 a, b, c, d, e, f.



1. b)



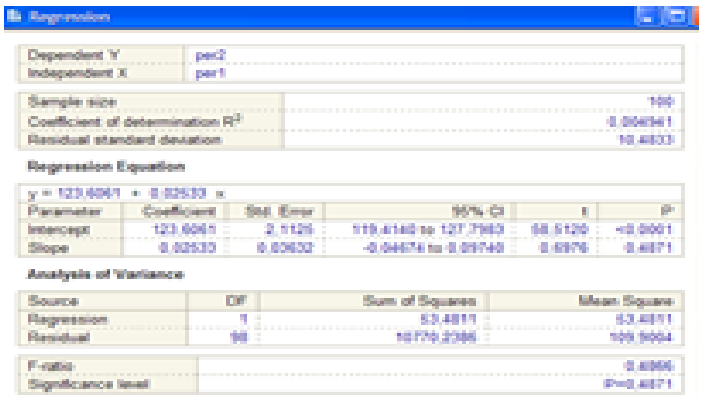
c) d)



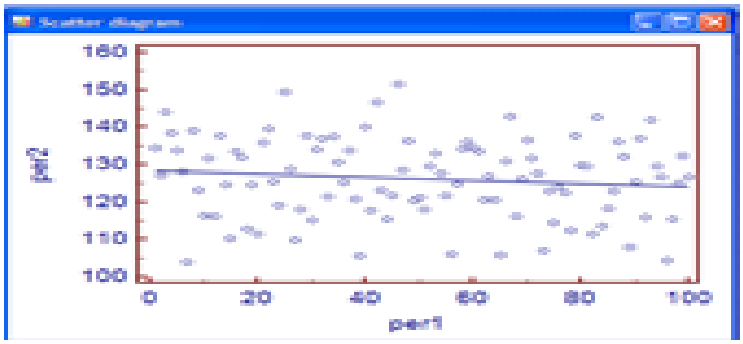
e) f)

Fig. 9. Characteristic of time series with normal distribution numbers

Regression equation for distribution, coefficient of determination, scatter and regression of the order are given as follows (fig. 10 a, b):



a)



b)

Fig. 10. Regression equation for distribution, coefficient of determination

Smoothing curve, autocorrelation and special autocorrelation functions shows that there is trend in that range. Determination coefficient value shows that forecast is impossibe. According to Fisher theory, the value of indication is not significant.

During the course of the monitoring indicators of each time interval along with the observation of one or several indicators needs to be found observed. Mann-Whitney criteria is used for the evaluation of the difference between two independent indicators, Wilcoxon T-criterion is used for evaluation of monitoring from treatment period, any indication of a change in a certain time, Friedman method is used to measure the difference between double monitoring difference evaluation and Kruskal-Wallis criterion is applied for assessment of presence of indicators in several measurements.

5. Conclusion

In different scientific studies we can see people with carbon monoxide poisoning later suffer from cardiovascular and nervous system diseases. For this reason, patients should be under medical supervision after receiving appropriate treatment. This means conducting a large number of analyses and examinations from time to time.

This work proposes a time series method for monitoring the state of a patient after treatment of carbon monoxide poisoning. The said method allows to trace dynamics of indices in time intervals and detect a more important index for observation of treatment resistant symptoms and elimination of excessive checks. For comparison of the indices in time intervals, parametric and non-parametric criteria of biostatistics are employed.

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