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- Traumatic Stress Syndrome
- Chromosomal Aberrations
- Intracranial Meningioma
- Dilated Cardiomyopathy

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Analysis of the Type of Tragedies Inducing Post Traumatic Stress Syndrome and evaluating PTSD in relation to our Species' Social Construct and Norms.

By Manoj Jagtiani
Rutgers University

Abstract – The goal of this paper is to understand why some tragedies induce PTSD and other tragedies that may be of the same magnitude do not induce Post Traumatic Stress Syndrome. Furthermore, to understand and assess the common link of PTSD tragedies and effects in helping one understand PTSD in relation to our society's social construct.

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The phenomenon of normalcy is an interesting one pertaining to the field of psychology because it is a subjective notion created by the norms of one's environment and population. Consequently, the notion of Post Traumatic Stress Disorder severely affecting individuals involved in wars, assaults, rapes, and other "unnatural" notions, rather than affecting individuals with common but nonetheless extremely tragic circumstances such as a failed relationship or death, therein establishes a point in itself. If PTSD affects only certain types of tragic instances, are those instances thus not natural or "normal?" The issue within the latter phenomena is to differentiate why PTSD affects certain tragic situations rather than others of the same magnitude, and what this consequently establishes about what is socially psychologically acceptable. Through analysis of the physiological changes of Post Traumatic Stress Disorder, analysis of the DSM-IV criteria in diagnosing the latter illness, and lastly the difference between a "trauma" and being "traumatized, one should consequently be able to deduce what makes such an illness affect some individuals with catastrophic life instances and not others with different ones but one certainly of the same threshold and furthermore the connection of the notion to social normalcy and order.

Establishing the fact that PTSD is an actual illness and a disease, asserts the fact that it affects an individual physiologically. The physiological effect created on a patient with PTSD is what makes an individual different from another individual who might have suffered through a tragedy and is merely exhibiting normal signs of grief. Moreover, the PTSD patient has dysfunction in the amygdala, the structure in the brain that is involved in autonomic responses. Consequently, PTSD patients have issues with such autonomic responses such as increased hear rate, blood pressure, and the startle response. Furthermore, a PTSD inducing tragedy will also cause physiological changes such as the following, "hyperarousal, numbing, sleep disturbance, irritability, intrusive emotions and memories, flashbacks, outbursts, and memory impairment."(Swierzewski,6) The pituitary gland is affected as well and stress hormones are released including norepinephrine and epinephrine. And, to add on, since PTSD inducing tragedies are so traumatic, when such stress is activated within the body, opiates such as endorphin and enkephalins are constantly released to bring the patient's mental structure to a type of homeostatic order. This then consequently leads to emotional nonresponsiveness, numbing, or amnesia. Moreover, serotonin depletion also results from the latter "opiate concept," as it results from repeated exposure to tradegy, trauma, and stress. This consequently, can lead to development or irritability, violence, schizophrenic type behavior, and etc. Conclusively, it is evident that PTSD involves major biological changes in a patient that results in a number of not only physiological changes but illness and psychiatric problems. One can definitely deduce that something that would cause the latter issues is not something that is "normal," or in other words, is not something that, evolutionarily speaking, humans have been adapted for. Consequently, tragedies that induce the latter phenomena must not have been widespread, popular, and significant among a population since we have not adapted to deal with them. In other words, such tragedies must be in some way, "unnatural." (Swierzewski,3)

So far, we have concluded that PTSD is definitely not a natural way in coping with trauma and consequently that the PTSD inducing trauma is different than other trauma, but how and why is it different? Analysis of the governmentally approved handbook that professionals use for diagnosing this disease, DSM-IV, should provide enough insight that through deductive reasoning will allow one to understand the difference between the aforementioned different type of tragedies. "The diagnostic features within the DSM-IV sections indicates that the following specific tragedies are usually linked to the illness: military combat, violent personal assault (sexual assault, physical attack, robbery,

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mugging), being kidnapped, being taken hostage, terrorist attack, torture, incarceration as a prisoner of war or in a concentration camp, natural or manmade disasters, severe automobile accidents, or being diagnosed with a life-threatening illness."(A.P.A.,5) More interestingly, the DSM-IV specifies that " individuals who have recently emigrated from areas of considerable social unrest and civil conflicts," have elevated levels of PTSD. (A .P.A., 5)In the latter excerpt from the manual there seems to be one continuous theme in each of the PTSD inducing traumas. With military combat, one is going against the macrocosmical social norm of "thou shall not kill," but following the microcosmical norm of " it is your duty to protect and serve (via killing). Thus there is a great cognitive dissonance established. Not following and coexisting with social rules has extreme psychologicalconsequences,as our species evolved dependent on one another to continue our lineage. In other words, we are social creatures of the highest order and social norms are considerably significant. Violent personal attacks, sexual assaults, and physical attacks not only socially deem the victim as in a sense, "dirty," but place a cognitivedissonance within the victim since the victim's caregivers help the victim in an "unrelating" way , since not everyone gets raped, assaulted, and etc. Moreover, the latter explanation goes for the rest of the DSM-IV examples. Since an individual is experiencing something not everyone experiences, but still experiences notions that have been in man's history since the "dawn of time," they are in a sense outcasts since the majority of the population is "lucky" enough to not have unfortunate traumas happen to them and hence the victims are outcasts because the majority cannot relate and so they are "different." One can thus deduce being so different causes the utmost cognitive dissonance imaginable, and that being PTSD. Another example, of how PTSD is thus social disease is evident in the following quote from a male individual, age twenty-nine, "I was going to Alcoholics Anonymous and people were saying they didn't know why they were alcoholics, but I knew. Men don't get raped do they? I felt so ashamed. My dirty secret. I had never told anyone. In fact I completely blocked it out for years. Then I saw something on TV and the flashbacks began. After that I kept reliving the rape, sometimes hundreds of times a day. I started drinking. You know, to try and shut it out. I was going to the surgery with all sorts of aches and pains and the practice nurse asked me one day if anything bad had happened to me and it just spilled out. I got help after that." (McDonald, 11) The significant line in this individual's quote is that he felt so ashamed because it is not "normal" for a man to get raped. This individual feels alienated, he feels different, and consequently he feels ashamed, thus PTSD has ensued. Once again, it is evident social traumas are responsible for Lastly, the issue of trauma versus traumatization is how professionals decipherif a tragedy has caused normal grief or PTSD. Dr. Cathrell of the Chicago institute establishes the difference in the following excerpt: "Most of us have had trauma experiences in our lives. Usually, we're upset for a while, but eventually we get over them and life continues. But occasionally, some of us run into events that are so traumatic that we can't get over them with-out help. We still hurt and reexperience the trauma long after normal grieving should have ended. When this happens, we've not only been exposed to a painful experience, we've been *traumatized* by it. We feel decidedly abnormal and it may be quite some time before we come to feel normal again." (Cathrell, 1) Essentially, Dr. Cathrell deems that events such as deaths and romantic breakups are tragedies that produce trauma, whereas events such as a war or a rape produces traumatization. The reason being is that "traumatization based events" make us feel "abnormal." Dr. Cathrell then goes on the establish how else to understand the difference between "trauma"(not inducing PTSD) events and "traumatic" (inducing PTSD) events. He asserts, PTSD (traumatized) individuals , "cannot trust people, are socially withdrawn, are hostile towards people, are obsessive compulsive over the situation, live isolated, feel different from people."(Cathrell, 2) Once again, Dr. Cathrell has allowed one to establish that the difference between the different types of trauma is that PTSD emerges from tragedies which go against social norms, are not popular, are different, are not accepted, and that are "abnormal," to produces a grief that involves a very "clinically" antisocial experience. Hostility, isolation, and mistrust are all forms of anti-social behavior. Therein, it is established PTSD is a social disease not a disease from the actual trauma itself, rather the social after effects; instead trauma not involving social effects can be dealt with via normal grief (the inevitable outcome of death, or a "broken heart"). (Cathrell, 1- 9)

Conclusively through the analysis of the physiological effects of PTSD, one has learned that the tragedies that induce such an illness are ones that are not normal and we as a species do not seem adapted for dealing with the stresses of these certain types of, as Cathrell states, " traumatizations." The DSM-IV guide maintained by professionals has furthermore allowed one to elicit the true cause of PTSD through assessment of the type of specific scenarios that induce it and assessment of other extraneous information extracted from it. Dr. Cathrell , a specialist in PTSD, in his book, *Back from the Brink: A Family Guide to Overcoming Traumatic Stress,* establishes the difference between the concept of "trauma," and "traumatizations," involved in the causation of PTSD. He furthermore establishes psychological rather than the aforementioned assessment of physiological results of PTSD, allowing one to furthermore deduce the relationship of PTSD in subjectively affecting certain types of tragedies rather than others of the same magnitude. The overall

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assessment via analysis of information surrounding PTSD can lead one to believe that PTSD is a social sickness rather than one created directly from the tragedy itself. PTSD selectively occurs from certain tragedies rather than others, if the specific tragedy can affect the individual in a negatively social way and establishes clinically antisocial behavior in the aforementioned victim.

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The effect of spraying vegetable oil and elevating relative humidity during incubation on the hatchability of Rhode Island Red (RIR) eggs

By Shiferaw Muluget, Tadelle Dessie, Alemu Yami
Jimma University, College of Agriculture and Veterinary Medicine

Abstract – In Ethiopia, Rhode Island Red (RIR) breed of chickens acclimatize very well to the existing production environment with fairly reasonable level of production. Unfortunately however, there is a serious complaint about the poor hatchability of their eggs. This study was conducted at Debre Zeit Agricultural Research Center (DZARC) to study the effect of oil spraying and elevated Relative Humidity (RH) on hatchability of RIR eggs. Five treatments comprising of 80-85%RH, 80-85%RH plus oil spraying, 90%RH, 90%RH starting from 12th day of incubation and 90%RH during hatching were studied in CRD with four replications. The results obtained revealed that there was no statistically significant difference ($P<0.05$) between the treatments in percent fertility and hatchability. Spraying with vegetable oil negatively affected fertility, whereas, oil spraying as well as elevated relative humidity of 90% during the larger segment of the incubation period were found to be equally depressive in hatchability. More over the weight loss recorded from the eggs sprayed with oil was lower than the others indicating that oil spraying prevented the recommended level of weight loss through water evaporation, which in turn resulted in lower hatchability. On the contrary increasing of relative humidity from 80-85% to 90% during hatching period seem to increase hatchability of RIR eggs.

Keywords : *Chicken, DZARC, Evaporation of water, Fertility, Incubation of eggs, Weight loss*

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Shiferaw Muluget [α], Tadelle Dessie [Ω], Alemu Yami [β]

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I. Introduction

Chicken population of Ethiopia is estimated to be 56.5 million (4), which is about 60% of the total chicken population of east Africa subcontinent (6). To exploit this national genetic resource in the development process Ethiopia launched a short and long-term plans of food self-sufficiency and poverty reduction program starting from 1995, placing special emphasis on the introduction of exotic chickens. The extension service of the Ministry of Agriculture and Rural Development (MoARD) promoted a scheme in which cockerels and pullets from selected strains mainly Rhode Island Red and to some extent White Leghorn are distributed from the government Poultry Breeding and Multiplication Centers (PBMC) to subsistence farmers in order to "upgrade" the genetic potential of the local breeds (15) and benefit from increased productivity of exotic birds. These extension approaches have been practiced for more than forty-five years (1). However, the impact of this strategy on the genetic makeup of indigenous birds has not been assessed carefully. Some empirical evidences, however, suggest that these approaches did not meet the desired target due to high mortality rate of exotic breeds (15). A study report by (16) in the central highlands of Ethiopia revealed that there has been an introduction of exotic breeds to three study villages at various times and in different forms through the introduction of cockerels, pullets, and fertile eggs, but their impact in upgrading the genetic potential of local chickens found to be less significant.

A study report based on the averages of five years fertility and hatchability of RIR chickens of the Poultry Breeding and Multiplication Centers was found to be 88% and 69% at Nazareth, 86.6% and 54.4% at Kombolcha and 82.89% and 62.36% at Andassa, respectively, which is below the recommended level. The information obtained from Amhara Rural Development Bureau of Agriculture (BoARD) in association with RIR breeding performance also indicated that the farming community by and large facing problems as a result of poor fertility and hatchability levels (5). However, (2) indicated that the fertility and hatchability percentage of commercial layers is recommended to be around 97% and 90%, respectively.

In Ethiopia, it was reported that RIR breed acclimatize well to the existing production environment with a reasonable level of production under smallholder management systems. Unfortunately however, there is a serious complaint about the poor hatchability of RIR egg under natural incubation. This is a very critical issue for sustainability and multiplication of the breed in the rural farming system. (5) reported fertility level of RIR is influenced by both male and female whereas, poor hatchability performance is primarily due to higher egg weight, weight loss during incubation and high embryonic mortality. The best hatchability results were obtained when egg weight loss is 12 percent of their fresh weight from the time of lay to the time of embryo pipe out of the shell. Weight loss smaller than 10 percent and greater than 15 percent of their fresh weight decreases hatchability (13); (7) and (17). Excess moisture loss of up to 20% was reported from RIR eggs incubated, during the first 18 days of incubation by (5), who recommended minimizing the loss to the normal level to improve the hatchability. (8) reported that the coating of the eggshell with mineral oil results in the

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sealing of the majority of the pores aimed at reducing moisture loss from the eggs. Improving fertility and hatchability of any breeding stock is essential factor to determine success of poultry operation, as fertility and hatchability are the most important determinant factors in the reproductive efficiency of poultry. The objectives of the study were to determine the effect of spraying vegetable oil and elevating relative humidity during incubation on the hatchability of RIR eggs.

II. Materials and Methods

a) Experimental site

The experiment was conducted at Debre Zeit Agricultural Research Center (DZARC) located at 45 km south east of Addis Ababa, at an altitude of 1900 m.a.s.l and between 8.44°N latitude and 39.02°E l ongitude. The average annual rainfall is 845 mm and the annual minimum and maximum temperatures are 10°C and 22°C, respectively (11).

b) Management of the experimental eggs

A total of 1500 RIR eggs were obtained from Kombolcha Poultry Breeding and Multiplication Center (PBMC), which is 385 km North East of the capital Addis Ababa. The eggs were collected from RIR flock kept under intensive management system and kept on floor and large spacious shed surrounded by half wall in lower portion and above it was surrounded by solid wall up to door level, above which mesh wire is fitted. Complete feed was supplied in circular type feeder with sufficient feeding space. Adequate clean drinking water also supplied to the flock. The flocks were vaccinated against New Castle Disease (NCD) and Fowl Pox. Hatching eggs were collected, fumigated and stored in cold-humid storage for five days at 12-18°C and 75% RH, with small end down position until transportation. The hatching eggs reached DZARC poultry farm after 12 hrs of transportation. Soon after arrival (before setting), the eggs were allowed to rest for 36 h. The eggs were fumigated aimed at minimizing the introduction of disease to the DZARC poultry farm. They were also fumigated before incubation at DZARC poultry farm.

c) Incubation of eggs

The incubators were cleaned, disinfected and fumigated properly and the incubation temperature, ventilation and turning devices were checked and adjusted according to the recommendation of the manufacturer in advance of setting the eggs. The eggs were selected against large and small size, abnormal shape, undesirable shell structure and broken eggs during transportation in each treatments. The remaining eggs in five treatment groups were further sub-divided in to 4 groups each with average 72 to 74 eggs and individually weighed. Finally each group were randomly allocated to the five treatments shown in below in completely randomized Design with four replications

Trt-1 = 80-85% RH through out the incubation period with a total number of 298 eggs.

Trt-2 = Trt-1 + spraying vegetable oil on the surface eggs with a total number of 298 eggs.

Trt-3 = 90% RH through out the incubation period with a total number of 291 eggs.

Trt-4 = 80-85% RH from the 1st day incubation to 11th day and 90% RH from 12th day to the hatching period with a total number of 292 eggs.

Trt-5 = 90% RH during the hatching period only (18-21st days) with a total number of 294 eggs.

The eggs were candled on the 18th days of incubation and at the end of each hatch the unhatched eggs were broken to confirm day on which embryos died (break out analysis). Hatchability was calculated on the basis of set and fertile eggs in the incubator and the number of chicks hatched. Moreover, fertility was also calculated during candling using the following formulae:

$$\text{Percent fertility} = \frac{\text{Total fertile eggs}}{\text{Total eggs set}} \times 100$$

Percent hatchability was calculated from two points of view:

i. Percent hatchability on fertile egg basis =

$$\frac{\text{Number of chicks hatched}}{\text{Total fertile eggs}} \times 100$$

ii. Percent hatchability on total eggs set basis =

$$\frac{\text{Number of chiks hatched}}{\text{Total eggs set}} \times 100$$

d) Weight loss of the eggs during incubation

The initial weight of egg from all treatment groups were taken before the eggs were set for incubation and an average individual initial weight of the eggs from each treatment were calculated. On the 18th days of incubation, the final weight of each egg from all treatment groups were taken before the eggs were set in the hatchery and the average individual final weight of the eggs from each treatment were calculated. Finally, percent weight loss was calculated with the following formula:

$$\%\, wt\ loss = \frac{average\ initial\ wt\ of\ x(before\ incubation) - average\ final\ wt\ of\ eggs(on\ 18\ days)}{average\ initial\ wt\ of\ eggs(before\ incubation)} * 100$$

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e) Statistical analysis

The collected data were summarized and analyzed using a Statistical Analytical System (SAS) computer software (14)

III. Results and Discussions

Mean percent fertility and hatchability of the experimental eggs are presented in Table 1. There was significant difference ($P<0.05$) between treatments in fertility and hatchability. Treatment 1 and treatment 5 were significantly higher than the others in both fertility and hatchability ($P<0.05$).

Even though there is no significant difference ($P>0.05$) between Treatment 1 and 5 in mean total number of hatched chicks, mean percent hatchability on both total set and fertile eggs, there is a slight increase in mean total number of hatched chicks, mean percent hatchability on both total set and fertile eggs for Treatment 5 compared to Treatment 1. Increasing 5% more RH during the hatching period than Treatment-1 contributed to the observed slight increase in above parameters. High humidity towards hatching time might be necessary for better hatchability of RIR eggs. Similarly (3) reported that high humidity towards hatching time will be necessary if sufficient evaporation from the eggs has occurred previously but detrimental if the humidity was high at all the times. (12) also reported that an increase of the RH by 10% after 18th days of incubation i.e. in the hatchery improved the hatchability of chicken eggs. From Table 1 it can also be seen that the low mean total number of hatched chicks, the low mean percent hatchability on both total set and fertile eggs in Treatment 2 might be due to the addition of vegetable oil on the incubated eggs, which may prevent sufficient evaporation of moisture from the eggs. The optimum levels of weight loss due to dehydration (loss of water from the eggs) during incubation may be important to have optimum hatchability of eggs but from Table 2 it can be clearly seen that only 4% weight loss was observed on the oil treated eggs (Treatment 2) as compared to the other treatments. The smaller weight loss might have resulted in low hatchability of eggs from the oil treated eggs. Different researchers concluded from their research that the best hatchabilities are obtained with poultry species when eggs loss 12% of their fresh weight from the time of lay to the time the embryo pips the shell (10), (7) and hatchability decreases for eggs losing less than 10% or greater than 15% of their fresh egg weight. (5) reported that low hatchability of eggs from RIR might be due the higher loss of the weight eggs during incubation as result of loss of excess water through the pores. However, in this study no much extra loss of weight is observed.

Apart from lower amount of weight loss from the oil treated eggs, the low hatchability of eggs from the oil treated eggs might be related with the closing effect oil on the pores of the shell and reduce exchange of respiratory gasses.

a) Breakout analysis result

Break out analysis result (Table 3) clearly indicates that late embryonic mortality (18-21 days) accounts the major loss of chicks followed by percent infertility, death at middle stage (8-18 days) and death at early stage. (9) reported that an increase in deaths during middle period (8-18 days in chickens) usually ascribed to nutritional problems, notably vitamins or minerals deficiency. He also reported that the causes of clear eggs (infertile eggs) usually related with undernourished males, too few males, competition among breeding males, and diseased flock. He again reported that the causes of chicks fully formed, but dead without pipping (death at later stage) are low average humidity, improper incubation temperature, improper ventilation in the incubator, improper turning of eggs and diseased or poorly conditioned breeder flock. Immature males, male with abnormal sperm, too few males, resulting in infrequent mating; too many males, resulting in fighting or interference, breeder flock disease, nutritional deficiencies or excess: severe feed restriction, parasites such as mites and decreased mating frequency or no mating was indicated for the major causes of clear or infertile eggs (19). It has also been indicated that the improper incubator temperature, humidity, turning, ventilation, contamination, nutritional deficiencies and lethal genes are the major causes of deaths between 8–18 days (19). Finally improper incubator temperature, humidity, turning, ventilation, improper hatcher temperature, humidity, ventilation, contamination especially from molds (aspergillis), too severe or too prolonged fumigation and nutritional deficiencies are reported be the major causes of death at later stage (>18 day) (19).

Since the incubator temperature for the incubation period was between 32^{0}C and 37.7^{0}C and the metabolic heat production of the developing embryo is sufficient to raise the internal egg temperature by 1.5^{0}C to 2^{0}C (17) that is above the incubator temperature. This may contribute the high percent of death at later stage. (18) indicated that chickens eggs don't survive continuously in an incubator at a temperature less than 35^{0}C or greater than 39.5^{0}C.

IV. Summary and Conclusions

This study was conducted at DZARC to determine the effect of spraying vegetable oil and elevating relative humidity during incubation to control water loss of fertile eggs. Increasing the relative humidity by 5% (90% RH) than the recommended level (80-85%) during the hatching period only caused the increase in hatchability of RIR eggs. Oil treatment of eggs drastically reduced the hatchability than the recommended level (<10% and >15%) of weight loss were observed for all treatments except for oil treatment and 90% relative humidity for 21 days.

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Table 1 : Multiple comparisons of means of percent fertility and hatchability on total eggs set, hatchability on fertile eggs and total number of hatched chicks among treatments.

Treatment	Mean percent fertility (%)	Mean hatchability on fertile eggs (%)	Mean hatchability on total set eggs (%)
T_1 =(80-85%RH) for 21 day	80.90[a]	61.40[a]	49.70[a]
T_2= (T_1 + spraying vegetable oil)	50.30[b]	2.00[b]	1.00[b]
T_3=(90%RH) for 21 days	85.90[a]	23.20[b]	19.90[b]
T_4 =(90%RH) after 11th days	79.50[a]	25.00[b]	19.90[b]
T_5=(90%RH) in hatching period	90.10[a]	71.30[a]	64.30[a]

[ab] means in the same column for each parameter with different superscripts are different at P<0.5

Table 2 : Average weight of eggs before setting (g), average weight of eggs at 18th day (g) and % weight loss.

Treatment	Weight of the eggs before setting (g)	Weight of the eggs on 18th day (g)	Weight loss (%)
T_1 =(80-85%RH) for 21 day	58.2	50.2	13.5
T_2= (T_1 + spraying vegetable oil)	59.4	57.0	4.0
T_3=(90%RH) for 21 days	58.1	52.5	9.6
T_4 =(90%RH) after 11th days	59.4	51.5	13.3
T_5=(90%RH) in hatching period	58.2	50.2	13.5

Table 3 : Breakout analysis result from unhatched eggs

Treatment	Infertile eggs (%)	Early period death (%)	Middle period death (%)	Late period death (%)
T_1 =(80-85%RH) for 21 day	32.4	17.6	0	50.0
T_2= (T_1 + spraying vegetable oil)	50.0	13.2	7.9	28.9
T_3=(90%RH) for 21 days	20.0	0	14.3	65.7
T_4 =(90%RH) after 11th days	23.5	0	17.6	58.8
T_5=(90%RH) in hatching period	25.7	0	5.7	68.6

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Is there a relationship between intraoperative bispectral index and cognitive impairment after coronary artery surgery?

By Judith A. Hudetz,PhD, Zafar Iqbal, MD , Sweeta D. Gandhi, MD, Kathleen M. Patterson, PhD , Paul S. Pagel, MD, PhD

Department of Anesthesiology, Medical College of Wisconsin,USA.

Abstract – We examined the relationship between short- and medium-term POCD and anesthetic depth using bispectral index (BIS) values in patients undergoing coronary artery bypass graft (CABG) surgery using cardiopulmonary bypass (CPB). We identified 89 patients in whom BIS monitoring was used. Memory and executive functions were assessed before, one week, and three months after surgery. Two cognitive tests showed at least two standard deviation (SD) decrease from baseline in patients one week after surgery. After three months, six tests showed at least one SD decrease from baseline. BIS scores were significantly higher after CPB in patients with versus without POCD one week after surgery. The BIS scores during and after CPB and throughout the surgery were also higher in patients with versus without POCD three months after surgery. The results suggest that there may be a relationship between POCD and anesthetic depth in patients undergoing CABG.

Keywords : coronary artery surgery, cardiopulmonary bypass, postoperative cognitive dysfunction, bispectral index monitoring.

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Is there a relationship between intraoperative bispectral index and cognitive impairment after coronary artery surgery?

Judith A. Hudetz,PhD,[α] Zafar Iqbal, MD[Ω], Sweeta D. Gandhi, MD,[β] Kathleen M. Patterson, PhD[ψ], Paul S. Pagel, MD, PhD[¥]

Abstract - We examined the relationship between short- and medium-term **POCD** and anesthetic depth using bispectral index **(BIS)** values in patients undergoing coronary artery bypass graft **(CABG)** surgery using cardiopulmonary bypass **(CPB)**. We identified 89 patients in whom **BIS** monitoring was used. Memory and executive functions were assessed before, one week, and three months after surgery. Two cognitive tests showed at least two standard deviation **(SD)** decrease from baseline in patients one week after surgery. After three months, six tests showed at least one SD decrease from baseline. BIS scores were significantly higher after **CPB** in patients with versus without **POCD** one week after surgery. The BIS scores during and after CPB and throughout the surgery were also higher in patients with versus without **POCD** three months after surgery. The results suggest that there may be a relationship between **POCD** and anesthetic depth in patients undergoing **CABG**.

Keywords : coronary artery surgery, cardiopulmonary bypass, postoperative cognitive dysfunction, bispectral index monitoring.

I. Introduction

Postoperative cognitive dysfunction (POCD) is an important cause of morbidity in patients undergoing cardiac surgery.(Newman et al., 2001) POCD is characterized by a reduced ability to concentrate, impaired understanding of language, memory deficits, and diminished social reintegration.(Moller et al., 1998; Rasmussen, Christiansen, Hansen, & Moller, 1999) Patients with POCD frequently have prolonged intensive care unit and hospital stays, may be less able to care for themselves, may not participate fully in rehabilitation efforts, and often require readmission to the hospital.(Marshall & Chung, 1999; Roach et al., 1996; Wilmore & Kehlet, 2001) Major risk factors for POCD include preexisting cognitive dysfunction, co-existing diseases, and age.(Ancelin et al., 2001; Moller, et al., 1998) Whether the type of anesthesia plays a role in the development of POCD remains somewhat controversial, although recent data suggest that incidence and severity of POCD are not likely influenced by anesthetic technique. (Rasmussen, 2006; Wu, Hsu, Richman, & Raja, 2004) However, Farag et al reported that cognitive processing speed was greater in patients who received deeper levels of general anesthesia, as measured using bispectral index (BIS) values, after noncardiac surgery.(Farag, Chelune, Schubert, & Mascha, 2006) These intriguing findings suggested the hypothesis that POCD and the depth of anesthesia may be related. However, the only study conducted to date that tested this hypothesis failed to demonstrate such relationship between anesthetic depth and short-term POCD in patients undergoing orthopedic, gynecologic, or plastic surgery.(Steinmetz, Funder, Dahl, & Rasmussen, 2010)

The relationship between anesthetic depth and POCD has not been examined in patients undergoing cardiac surgery. This patient population is particularly vulnerable to developing POCD because of exposure to potentially adverse consequences of cardiopulmonary bypass (CPB) and intraoperative manipulation of the heart and proximal great vessels.(Butler, Rocker, & Westaby, 1993; Slogoff, Girgis, & Keats, 1982) Our group has studied POCD in cardiac surgical patients for several years.(Hudetz, Gandhi, Iqbal, Patterson, & Pagel, 2011; Hudetz et al., 2009; Hudetz, Patterson, Byrne, Pagel, & Warltier, 2009; Hudetz, Patterson, Iqbal, Gandhi, & Pagel, 2010) As a result, our group has an established database of cardiac surgical patients in whom short- and medium-term POCD has been examined. We used this database to retrospectively examine the hypothesis that a relationship between intraoperative BIS values and POCD exists in patients undergoing coronary artery bypass graft (CABG) surgery using CPB.

II. Subjects and Methods

The protocol was approved by the Institutional Review Board of the Zablocki Veterans Administration Medical Center, Milwaukee, Wisconsin. All subjects provided written informed consent.

Eighty nine patients undergoing CABG were identified in our database in whom intraoperative BIS

Author [α] : Assistant Professor and Director of Clinical Research of Anesthesiology, Department of Anesthesiology, Clement J. Zablocki Veterans Administration Medical Center 5000 W. National Avenue Milwaukee, WI 53295 Tel: (414) 384-2000 Ext. 46856,
E-mail : jhudetz@mcw.edu

Author [Ω β ψ ¥] : Department of Anesthesiology, Medical College of Wisconsin, Clement J. Zablocki Veterans Administration Medical Center, Milwaukee, Wisconsin, USA.

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monitoring was used. Inclusion criteria included ≥55 years of age, providing written informed consent, and scheduled for elective coronary artery surgery with CPB. We used historical nonsurgical patients from our database to establish the diagnosis of POCD in CABG patients.(Hudetz, et al., 2011) These nonsurgical patients also had coronary artery disease; inclusion of this group was important to account for practice effects of repeated cognitive testing. Exclusion criteria included a history of a cerebrovascular accident in the last three years, permanent ventricular pacing, previously documented cognitive deficits, or vascular dementia (Hachinski score(Hachinski & Munoz, 2000) greater than four). Patients with hepatic impairment (aspartate aminotransferase or alanine aminotransferase more than twice the upper normal limit) and chronic renal insufficiency (creatinine >2 mg/dl) were also excluded.

a) Cognitive testing

Baseline cognitive functions were assessed with a standard neuropsychometric battery, including recent verbal and nonverbal memory and executive functions, within one week before surgery as previously described.(Hudetz, et al., 2011) Briefly, cognitive functions were reassessed one week or at hospital discharge (whichever occurred first) and three months after surgery. Three parallel forms of the tests were used except for Stroop and Digit Span; the latter tests are not vulnerable to practice effects. Story Memory(Wilson, Cockburn, Baddeley, & Hiorns, 1989) and Word List Memory(H. B. Benedict, Schretlen, Groninger, & Brandt, 1998) were used to test recent verbal memory. Recent nonverbal memory(R. H. Benedict, Schretlen, Groninger, Dobraski, & Shpritz, 1996) and executive functions (Backward Digit Span,(Wechsler, 1997) Semantic Fluency,(Randolph, 1998) Phonemic Fluency(Benton & Hamsher, 1989), and the Color-Word Stroop Test, third part(Bohnen, Twijnstra, & Jolles, 1992)) were also tested. Depression was assessed with the Geriatric Depression Scale 15-item version.(Yesavage et al., 1982)

b) BIS monitoring

BIS electrodes were applied according to the manufacturer's instructions (Aspect Medical Systems, Inc, Newton, MA). BIS monitoring started immediately after anesthesia induction and continued until the end of surgery. BIS values were recorded at five minute intervals throughout surgery.

c) Anesthetic technique and conduct of cardio-pulmonary bypass

Midazolam, fentanyl, and etomidate were used for anesthetic induction and isoflurane and fentanyl were used for maintenance. This is our standard anesthetic protocol for all of our patients undergoing cardiac surgery assigned for POCD testing.(Hudetz, et al., 2011) All CABG patients underwent a standard median sternotomy. Myocardial protection during CPB consisted of antegrade and retrograde cold blood cardioplegia administered at regular intervals, topical hypothermia, and systemic hypothermia. A dose of continuous warm blood cardioplegia was administered during rewarming before removal of the aortic cross clamp. CPB flows and mean arterial pressure were maintained between 2.4 and 2.5 L/min/m^2 and between 55 and 70 mmHg, respectively, during CPB.

d) Statistical analysis

Group comparisons were made using unpaired t tests for continuous variables, and chi-square or Fisher's exact test for dichotomous variables. Z-scores were used to assess cognitive change from baseline to one week or discharge and to three months after surgery.(Moller, et al., 1998) The z-score for the change in performance on each neuropsychological test was calculated by using the following formula: z-score = [(Change Score) - (Mean Change $Score_{control}$)] / (SD Change $Score_{control}$). An average z-score for each test was calculated. Cognitive dysfunction for each patient was defined as a deterioration of at least two standard deviations from baseline on at least two measures of the ten-test cognitive battery.(Moller, et al., 1998) Cognitive dysfunction was assessed for each patient at both one week and three month time-points. Patients were divided into groups with versus without POCD at both time points. BIS values between these patient groups were compared using the Wilcoxon rank-sum test. The null hypothesis was rejected when $p<0.05$. All errors were reported as standard deviations. Statistical calculations were performed using NCSS 2001 (NCSS, Kaysville, UT) software.

III. Results

Baseline medical and demographic data including age and education were similar between patients with or without POCD (Table 1). Baseline cognitive scores were also similar between groups (Table 2). Performance on two cognitive tests showed at least a two SD decrease from baseline (immediate word list recall and delayed word list recall) and performance on five additional tests demonstrated at least a one SD decrease (figure reconstruction, immediate story recall, delayed story recall, digit span, and Stroop) at one week after surgery in patients undergoing coronary artery surgery (Table 3). After three months, performance on six tests (figure reconstruction, immediate story recall, delayed story recall, immediate word list recall, delayed word list recall, and digit span) continued to show at least a one SD decrease from baseline (Table 3). Thus, cognitive function appeared to be somewhat improved three months compared with one week after surgery. Except for a significantly prolonged ICU stay in patients with POCD one week after CABG, surgical parameters were

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similar between groups (Table 4). The average values were significantly higher after in patients with versus without one week after surgery (Table 5). Average BIS values were also significantly ($p<0.01$) higher during and after in patients with versus without three months after surgery (Table 5). Notably, average BIS scores were also significantly ($p<0.0001$) higher during the entire surgical procedure in patients with three months after surgery (Table 5).

IV. Discussion

The results of this retrospective analysis suggest that there may be a relationship between the depth of anesthesia as evaluated using BIS and POCD in patients undergoing CABG using CPB. Patients who did not meet the diagnostic criteria for POCD one week and three months after surgery had modestly lower BIS values compared with those with POCD. Although the differences between groups were statistically significant (table 5), their clinical relevance remains unclear because BIS values are normally quite variable. Additionally, BIS monitoring does not necessarily provide a linear indicator of "anesthetic depth." Nevertheless, the current findings suggest the intriguing hypothesis that deeper planes of anesthesia may exert relatively greater degrees of neuroprotection in patients during cardiac surgery. The precise mechanisms responsible for these findings are unclear and were not examined here. However, the total amounts of isoflurane, fentanyl and midazolam used during surgery were similar between groups and most likely do not account for the observed results. Similarly, no differences in patient demographics or the duration of surgery, CPB, or aortic cross clamp time were observed between groups.

The current findings in patients undergoing CABG are supported by the results of two earlier studies. Farag et al(Farag, et al., 2006) randomized 74 patients to a lower (median 38.9) or higher (median 50.7) BIS regimen during spinal, abdominal, or pelvic surgery. Cognitive testing was performed before and 4-6 weeks after surgery. The processing speed index was significantly higher in patients in the low compared with the high BIS group. These results suggested that deeper levels of anesthesia may be associated with improved cognitive function after surgery. Our results also suggest that a lower BIS value (38 ± 3) was associated with preservation of cognitive performance compared with a modestly higher (but statistically different) BIS value (42 ± 3) in which POCD was more frequently observed. More recently, Steinmetz et al(Steinmetz, et al., 2010) examined the effects of anesthetic depth on short-term cognitive function in 70 patients undergoing orthopedic, gynecologic, or plastic surgery. Cognitive functions were assessed before and within one week after surgery. The authors reported that there did not appear to be an association between depth of anesthesia quantified using BIS and the presence of POCD one week after surgery. Our findings with CABG patients are also in general agreement with those Steinmetz et al,(Steinmetz, et al., 2010) as lower average BIS values throughout the entire procedure were not associated with improved cognitive functions one week after CABG surgery. Our findings further suggest, in agreement with the data of Farag et al,(Farag, et al., 2006) that lower BIS values during the entire surgery are associated with improved medium-term cognitive functions three months after surgery. It is highly likely that patients are less affected by immediate postoperative factors and pain medications when cognitive testing is performed at least one month after surgery, in contrast to the median of three to four days after surgery reported in the Steinmetz et al(Steinmetz, et al., 2010) study. The ability to examine BIS values before, during, and after CPB provided a framework by which we may subsequently examine specific periods of cardiac surgery with their potential relationship to subsequent cognitive function. Indeed, the data suggested that lower BIS values after bypass alone were associated with improved short-term cognitive performance, whereas lower BIS values both during and after CPB were predictive of less POCD three months after surgery. However, the current retrospective observational study was not designed to prospectively address this issue.

The current results should be interpreted within the constraints of several other potential limitations. Our study is small, as only 89 patients undergoing CABG were retrospectively examined. Whether the current results may be extrapolated to patients undergoing other types of cardiac surgery is unknown. BIS and other processed EEG monitors have well-known limitations because these devices analyze EEG signals from the frontal lobe alone(Azim & Wang, 2004; Dahaba, 2005; Merat et al., 2001) and the current results should be considered with these technical limitations in mind. Cognitive performance was reassessed three months after cardiac surgery, which may be considered as "medium-term" follow-up. Whether similar results would be obtained if patients were evaluated after a more prolonged period of time after surgery is unknown. The current investigation included only male veterans, and whether similar results occur in women undergoing CABG surgery is unknown. The current findings that lower BIS values may exert more profound neuroprotective effects against POCD are very preliminary, and will have to be confirmed by a larger randomized trial that includes both sexes before any change in anesthetic practice could be suggested.

In summary, the current results suggest that there may be a relationship between the incidence of short- and medium-term POCD and anesthetic depth assessed using BIS in patients undergoing coronary artery surgery using CPB. Further studies are warranted to examine this hypothesis.

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Table 1 : Demographics and medical data

	(+)POCD ***N=48***	**(-)POCD** ***N=41***	***p*(s)**
Age, yr	68±9	68±7	0.82
Education, yr	12±2	12±2	0.5
Caucasian (%)	41(85)	40(98)	0.06
Married (%)	27(56)	28(68)	0.24
Current smoker (%)	9(19)	11(27)	0.36
Hypertension (%)	44(92)	37(90)	0.82
Hypercholesterolemia (%)	43(90)	37(90)	0.92
Angina (%)	18(38)	18(44)	0.54
Arrhythmia (%)	7(15)	8(20)	0.54
Myocardial infarction (%)	8(17)	7(17)	0.96
Peripheral vascular disease (%)	7(15)	3(7)	0.33
Diabetes (%)	25(52)	24(59)	0.54
Congestive heart failure (%)	8(17)	4(10)	0.38
Stroke (%)	4(8)	1(2)	0.37
Sleep disorder (%)	16(33)	18(44)	0.31
Depression (%)	9(19)	8(20)	0.93
GDS-15	3±3	3±3	0.25
Antihypertensive drug (%)	39(81)	30(73)	0.36
Diuretic drug (%)	18(38)	16(39)	0.88
Lipid lowering drug (%)	43(90)	32(78)	0.13
Hachinski score >=4, baseline (%)	0(0)	0(0)	

Data are mean±SD or number (%), POCD: groups are separated to (+) and (-) POCD based on cognitive performance 1 week after surgery, GDS-15: geriatric depression score (fifteen items), the *p* values are from *t*-test for continuous variables and Chi-square or Fisher's exact test for dichotomous variables; p(s): p values between the two surgical groups

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Table 2 : Cognitive scores under baseline conditions

	(+) POCD *N=48*	(-) POCD *N=41*	*p*(s)
Figure Reconstruction	20±8	20±7	0.91
Delayed Figure Reproduction	8±3	7±3	0.79
Immediate Story Recall	18±5	18±5	0.60
Delayed Story Recall	10±3	9±3	0.20
Immediate Word List Recall	27±8	24±6	0.05
Delayed Word List Recall	6±3	5±3	0.10
Digit Span	9±2	8±2	0.10
Semantic Fluency	15±4	16±3	0.09
Phonemic Fluency	11±4	12±5	0.44
Stroop	39±13	38±12	0.90

Data are mean±SD, POCD: groups are separated to (+) and (-) POCD based on cognitive performance 1 week after surgery, *p*(s): p values between the two surgical groups

Table 3 : Z-scores at 1 week and 3 months after surgery in patients with or without POCD

	1 week		3 months	
	(+) POCD	(-) POCD	(+) POCD	(-) POCD
Figure Reconstruction	-2.7	-0.9	-2.9	0.0
Delayed Figure Reproduction	-1.1	0.1	-1.2	0.5
Immediate Story Recall	-2.0	-0.3	-3.6	0.0
Delayed Story Recall	-2.5	-0.4	-3.7	0.1
Immediate Word List Recall	-3.0	-1.1	-2.5	-0.9
Delayed Word List Recall	-3.4	-1.4	-2.8	-0.8
Digit Span	-1.8	-0.6	-2.3	-0.9
Semantic Fluency	-0.6	-0.3	-0.4	-0.1
Phonemic Fluency	-0.9	-0.3	-0.3	-0.2
Stroop	-1.6	-1.0	-1.3	-0.4

Data are mean±SD

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Table 4 : Surgical and postoperative parameters in patients with or without POCD

		1 week			3 months	
	p_{all}	(+) POCD 1w	(-) POCD 1w	p_{all}	(+) POCD 3m	(-) POCD 3m
Anesthesia, min	0.62	458±78	450±62	0.46	421±55	437±65
Surgery, min	0.94	355±79	356±65	0.14	309±51	338±54
ACC time, min	0.26	115±43	125±41	0.31	102±39	120±50
Before CPB, min	0.77	194±45	192±41	0.74	187±48	181±2
During CPB, min	0.62	147±53	152±47	0.24	127±45	148±54
After CPB, min	0.39	120±32	114±30	0.44	110±16	119±38
Isoflurane, %	0.21	0.81±0.23	0.75±0.19	0.23	0.74±0.18	0.82±0.17
Fentanyl, mcg	0.46	1131±349	1193±433	0.45	1227±644	1083±322
Midazolam, mg	0.31	6±3	5±3	0.03	7±3	5±2
ICU stay, day	0.008	4±2	3±1	0.45	3±2	3±1
Hospital stay, day	0.09	7±3	6±3	0.44	6±1	6±2

Data are mean±SD, ACC: aortic cross clamp, CPB: cardiopulmonary bypass, p_{all}: p values at 1 week and 3 months after surgery

Table 5 : Average BIS values in patients with and without POCD

	BIS value			
	Entire Surgery	Before CPB	During CPB	After CPB
POCD 1 week				
(+)	40±3	40±1	39±3	41±2
(-)	39±3	41±3	38±3	39±1
p value	0.08	0.69	0.55	<0.05
POCD 3 months				
(+)	42±3	41±2	41±3	43±1
(-)	38±3	40±2	36±3	38±1
p value	<0.0001	0.34	<0.01	<0.01

Data are mean±SD, *p* values are from *t*-tests

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Predictive value of fetal nuchal translucency in the screening of chromosomal aberrations

By Dragan Lončar
GOC, CC Kragujevac, Serbia

Abstract – In search for specific early ultrasound signs that could indicate an increased risk of hereditary or acquired disorders of the fetus, scientific research confirms the value of exceptional ultrasound findings nuchal translucency (NT). The aim of the study was to determine the predictive value of the diameter of fetal NT in the detection chromosomopathy. The investigation included 317 pregnant women with monofetal pregnancies gestational age of 11 to 14 weeks. The control group consisted of pregnant women in whom amniocentesis was recognized after a neat result of fetal karyotype. We determined the limit of physiological and pathological findings of the value of NT, but we used the diameter of NT that we get in pregnant women with pathological score of amniocentesis as a potentially pathological values. Mean value of NT in the control group was 1.92 ± 0.39 mm, and the group with pathological findings karyotype fetus was 2.49 ± 0.37 mm, which is a statistically significant difference ($p<0.05$). Mean value of distance issues coccyx in the control group was 64.83 ± 8.23 mm, and the group with pathological karyotype 60.12 ± 8.48 mm, gestational age in the control group was 7.10 ± 87.40 days, and pathologic 85.69 ± 3.98 days, which speaks of homogeneity of the investigated sample ($p> 0.05$).The probability that a patient with negative findings to be healthy is NT 1.0. NT sensitivity as a marker for chromosomopathy was 1.0. The rate of false positive findings of the 0.026. Specificity of NT as a marker for chromosomopathy is 0.97. The probability that a patient with positive findings NT really be sick is 0.5. Valid findings NT can be considered safe ultrasonographic markers in the assessment of absence chromosomopathy. Pathological finding, given the low positive predictive value of NT must be amended and other prenatal tests before pregnant invasive give advice on prenatal diagnosis.

Keywords : *nuchal translucency, ultrasonography, chromosomopathy, predictive statistics.*

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Abstract - In search for specific early ultrasound signs that could indicate an increased risk of hereditary or acquired disorders of the fetus, scientific research confirms the value of exceptional ultrasound findings nuchal translucency (NT). The aim of the study was to determine the predictive value of the diameter of fetal NT in the detection chromosomopathy. The investigation included 317 pregnant women with monofetal pregnancies gestational age of 11 to 14 weeks. The control group consisted of pregnant women in whom amniocentesis was recognized after a neat result of fetal karyotype. We determined the limit of physiological and pathological findings of the value of NT, but we used the diameter of NT that we get in pregnant women with pathological score of amniocentesis as a potentially pathological values. Mean value of NT in the control group was 1.92 ± 0.39 mm, and the group with pathological findings karyotype fetus was 2.49 ± 0.37 mm, which is a statistically significant difference ($p<0.05$). Mean value of distance issues coccyx in the control group was 64.83 ± 8.23 mm, and the group with pathological karyotype 60.12 ± 8.48 mm, gestational age in the control group was 7.10 ± 87.40 days, and pathologic 85.69 ± 3.98 days, which speaks of homogeneity of the investigated sample ($p> 0.05$).The probability that a patient with negative findings to be healthy is NT 1.0. NT sensitivity as a marker for chromosomopathy was 1.0. The rate of false positive findings of the 0.026. Specificity of NT as a marker for chromosomopathy is 0.97. The probability that a patient with positive findings NT really be sick is 0.5. Valid findings NT can be considered safe ultrasonographic markers in the assessment of absence chromosomopathy. Pathological finding, given the low positive predictive value of NT must be amended and other prenatal tests before pregnant invasive give advice on prenatal diagnosis.

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I. Introduction

In the antenatal protection - monitoring growth and development of the unborn child in most European countries, standard is recommended to do three ultrasound: between 9 - 12 week, and 19th - 22 and 29 weeks as - 32 weeks (1). In any irregularities or the occurrence of complications in pregnancy an additional ultrasound provides additional safety to pregnant women, and gynecologists to monitor pregnancy. In search for specific early ultrasound signs - markers that could indicate an increased risk of hereditary or acquired disorders - chromosomopathy fetus, scientific studies confirm the exceptional value of ultrasound findings nuchal fold (nuchal translucency, NT) (2).

Author : GOC, CC Kragujevac, Serbia

Nuchal crease ultrasound findings indicate fluid accumulation (lymph) between the skin and subcutaneous fascia in the neck or the back door and embryos, which reveals the ultrasound between the 11th - 14 week of pregnancy, or when the distance between threads coccyx (CRL- crown to rump length) between 45 to 84 mm (3).Usually tolerate less than the thickness of folds 99th percentile for CRL. Numerous studies show a connection between the findings of the ultrasound markers (nuchal crease > 3 mm) with specified chromosomal aberrations, especially with aneuploidy and Down syndrome. Correlation of findings with Down syndrome is the most important measure by which to study this phenomenon classified ultrasound findings vratnog folds in screening procedures for Down syndrome. In most of these studies (King's group) in over 96,000 pregnancies (22 perinatal center, 306 gynecologists) is the ultrasound findings revealed 82% of fetuses with Down syndrome (frequency of false positives: 8.3%). In addition to connections with chromosomal aberrations, there vratnog folds also a marker for other genetic syndromes, where usually a heart anomalies. Fetal NT increases with CRL and therefore is very important to take into account the gestational period when it is determined whether the measured NT increased or not (4). The study involving 96,127 pregnancies, the mean value and 95 percentile of the NT CRL of 45 mm were 1.2 and 2.1 mm, and the CRL of 84 mm 1.9 and 2.7 mm (5). In pregnancies with fetal NT below the 99th Percentile (3.5 mm), the decision of parents about whether the fetal karyotype to work will depend on individual risk, which is made from a combination of mother's age, ultrasound findings and free β-HCG and PAPP-A in the serum of mothers between 11-13 +6 weeks (6).

II. Aim

The aim of this study was to determine the predictive value of fetal diameter nuchal translucency in detecting chromosomopathy.

III. Methods

The study was conducted at the Clinic for Gynecology and Obstetrics, Clinical Center of Kragujevac monofetal intrauterine pregnancies in the first trimester of pregnancy in peroid 2007-2009. year. During the research we use clinical experimental model studies. Each patient in the planned inclusion in the

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study, we thoroughly explain the plan and purpose of the review, all tests included in the study gave their voluntary written consent for testing after the read information to the patient. The investigation included 317 pregnant women with monofetal pregnancies observiranih by the Commission genetic counseling GAK KC Kragujevac.

Conditions for the inclusion of pregnant women in the study were related to the pregnancy, the following parameters:

1. Distance CRL (crown to rump length) must range from 45 to 84 mm.
2. Gestational age pregnancy must be of 11-13 +6 weeks.

The measurement of fetal NT, we used high-resolution ultrasound Aloka Pro Sound 3500 with the option "make loop" for the return of images, which allow caliper measurements to one decimal. The image on the screen to what extent NT included only the head and upper chest. Magnification was maximum, so that little scroll caliper to measure changes only 0.1 mm. Nuchal translucency is measured when the fetus in a neutral position. We measured the maximum thickness of subcutaneous clearing up between the skin and soft tissue that is located above the cervical part of spine. Caliper were placed on the lines that define the crease so that it can hardly see the white border line clusters behind the door. During our review we made more measurements, and taking account of maximum thickness. If the navel cord located around the fetal neck (in about 8% of cases), we measured NT thickness above and below the umbilical cord and used the average of these two measures. For statistical processing were used and non-parametric and parametric tests for testing the significant difference t test, $\chi 2$ test, Fisherov exact probability test and contingency tables in the calculation of parameters predictive statistics.

IV. RESULTS

This chapter shows the results of our research:

Table 1 : Overview ultrasonography markers in a group of pregnant women with pathological karyotype result after early amniocentesis

Number evidencionog protocol-year	Nuchal translucency inn mm (NT)	Crown to rump length inn mm(CRL)	Gestational age in days (GS)	Score karyotype after early amniocentesis
3-2007	2.2	60	86	46,xy/47xyy
11-2007	3.0	62	88	46,xx/46,xx; del 7t(7;17)
47-2007	2.5	65	88	47,xy +21
151-2007	2.6	63	86	47xy+21
74-2008	1.8	73	90	47, xy+18
76-2008	2.4	72	89	Robertson translocation 45, xy,-14, -21 +t (14q;21q)
158-2008	2.5	56	82	47, xx+21
99-2008	2.6	65	87	Robertson translocation 45,xx,-14,-21+t (14q21q)
161-2008	2.7	48	81	47, xx+21
164-2008	2.0	50	81	46,xy/46, y del(x)t(7;x)q35;q22)
162-2008	1.9	48	78	46,xy/46,xy (-4q3)
167-2008	3.1	48	80	47,xy+21
231-2009	2.8	61	89	47,xx+21
267-2009	2.6	71	91	47,xx+21
237-2009	2.4	56	87	46,xx/47,xx t (9;6)(q31;q14)
271-2009	2.8	64	88	46, xy/47,xy+13

Table 2 : Overview mean values and standard deviations ultrasonography parameters in the total sample

Parameters	Pathological karyotype =16	Control group =311	P
Nuchal Translucency (mm)	2.49±0.37	1.92±0.39	<0.05
Crown to rump length fetus (mm)	60.12±8.48	64.83±8.23	p>0,05
Gestational age in days	85.69±3.98	87.40±7.10	p>0.05

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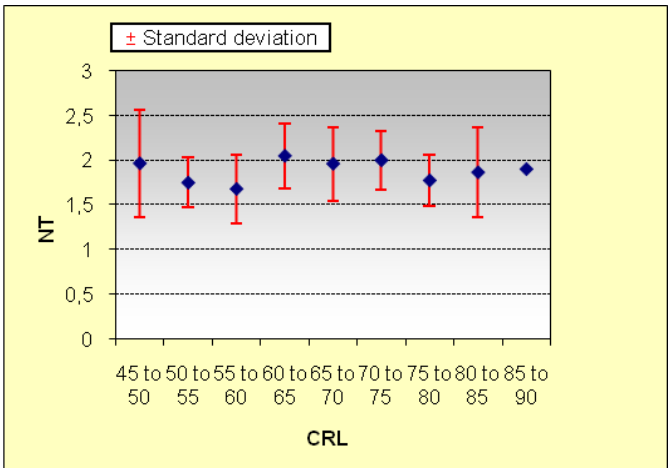
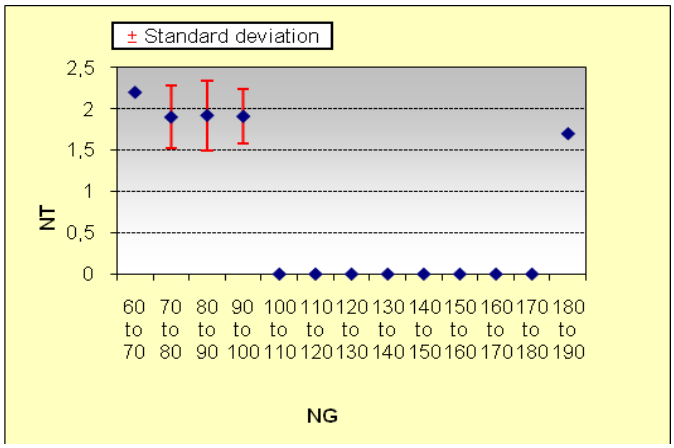
Diameter nuchal translucency is statistically significantly different in the examined groups of pregnant women ($p<0.05$).

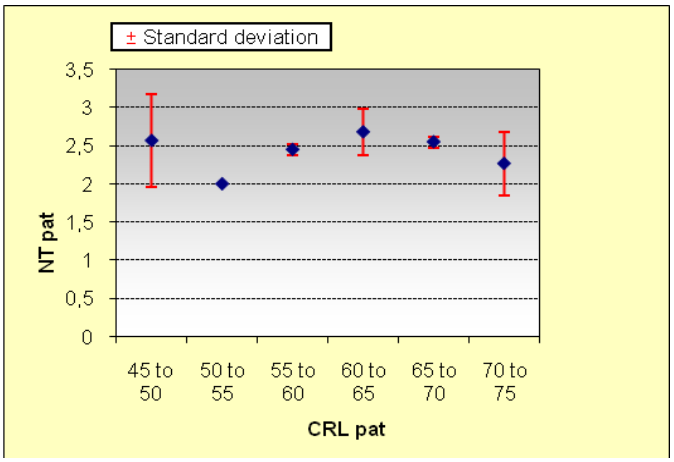
Histogram 1. Distribution of values nuchal translucency (NT) in relation to the distance between crown to rump length fetus (CRL) in the total sample



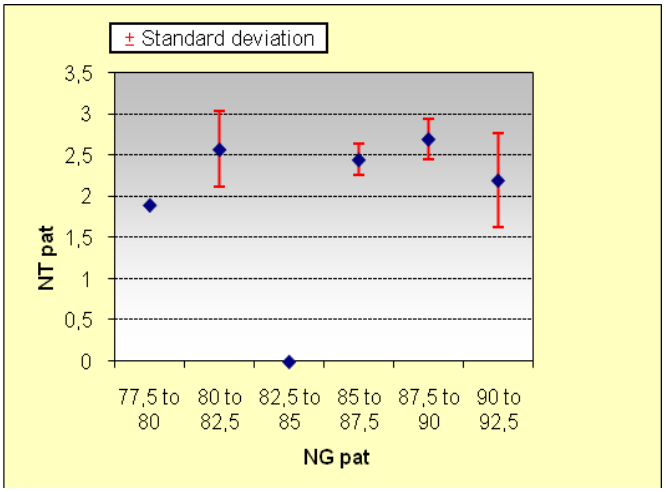
Histogram 2. Distribution values nuchal translucency (NT) in relation to gestational age of pregnancy (NG) in the total sample



Histogram 3. Distribution of values nuchal translucency (NT patology) with pathological karyotype compared to the distance between crown to rump length fetus (CRL patology)



Histogram 4. Distribution of values nuchal translucency (NT patology) with pathologic karyotype in relation to gestational age of pregnancy (NG patology)



Was done early amniocentesis karyotype results obtained are divided into two groups as follows: pregnant women with numerical aberrations (SP) and those that have structural disorders on the level of chromosomes (LP).

Using contingency tables oderđivali have predictive value nuchal translucency (NT) as a possible marker invasive prenatal screening of pregnant women in gestational age from 11 to 13 +6 weeks.

Table 3 : Contingency table

Test score	The disease is present	Disease absent	Total
Positive	SP	LP	SP+LP
Negative	LN	SN	LN+SN
Only	SP+LN	LP+SN	N

The disease is present

Table 4 : Numeric display of contingency tables in our sample of pregnant women investigated

Rezultat testa	The disease is present	Disease absent	Total
Positive	8	8	16
Negative	0	301	301
Only	8	309	317

The positive predictive value (SP/SP+LP)
Negative predictive value (SN/SN+LN)

Positive predictive value shows the number of people with positive findings that have the disease.

Negative predictive value shows the number of people with negative test findings that do not have the disease.

The probability that a patient with positive findings and NT stavrno be ill, or that have numeric aberrations is 0.5.

The probability that a patient with negative findings nuhalne translucence (NT) to be healthy is 1.0.

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Sensitivity measurements nuchal translucency (NT) as a marker for chromosomopathy we determined according to the formula:

$$SPP = SP/SP+LN = 1.0$$

False positive rate is determined by the following formula:

$$SLP = LP/LP+SN = 0.026$$

The specificity of measuring nuchal translucency (NT) as a marker for chromosomopathy we determined according to the formula:

$$SSN = SN/SN+LP = 0.97.$$

V. Discussion

More prospective intervention study was concerned with the implementation of NT screening in routine clinical work (7). In some tests, screening positive group was defined by the boundary value of fetal NT or combined risk derived from the mother's age and deviation from the normal median NT for CRL. Important results of these tests were: (1) NT was successfully measured in more than 99% of cases, (2) there is the inevitable variation in false positive rates and detection rates between different studies because of differences in the age of the studied women, age distribution examined population and used the limits NT or risk, and (3) in the combined data of more than 200, 000 pregnancies, including more than 900 fetuses with trisomy 21, screening by NT identified more than 75% of fetuses with trisomy 21 and other major chromosomopathy with rate of false positive findings of 5% and the rate of detection was about 60% of the rate of false positive findings than 1% (7) . The largest study, coordinated by the Foundation for fetal medicine, 306 adequately trained operator monofetal reviewed 100,311 pregnancies in 22 center in the United Kingdom (8). In all cases the measured CRL and NT were calculated and the individual risks based on age of mother, gestational age and fetal NT. Pregnancy outcomes were obtained in 96,127 cases, including 326 cases with trisomy 21 and 325 with other chromosomopathy. Mean gestation at the time of screening was 12 weeks, and the average age of mothers 31 years. Estimated risk for trisomy 21 was above the 1 in 300 or more in 8% of normal pregnancies, 82% trisomy 21 pregnancies and 78% with other chromosomopathy. For screening positive rate of 5%, detection rate was 77% (95% konfidens interval 72-82%). The issue of fetal case fatality has advantages over screening in the second trimester - prenatal diagnosis earlier and consequently less traumatic termination of pregnancy for those couples who opt for this option. Potential lack of earlier screening is that identifying those with pregnancy chromosomopathy to be abortively spontaneously. About 30% of all fetuses with trisomy 21 die between 12 weeks of pregnancy and term deliveries. The issue of spontaneous intrauterine fetal death in thec hromosomopathy, of course, a potential criticism of antenatal screening methods, including biochemical screening in the second trimester, because the fetal mortality rate between 16 weeks gestation and term deliveries about 20%. From prenatal screening studies is not possible to know how to pregnancies with fetuses with trisomy 21 are broken, actually completed live birth children, but it is still possible to assess the impact of prenatal screening on the prevalence of trisomy 21 in live-born children. This can be done by comparison the number of live births with trisomy 21 with the number estimated on the basis of prevalence of trisomy 21 live births by age of mother and age distribution of mothers examined population. In the screening study, the Foundation for fetal medicine, a combination of mother's age and fetal NT, limit the risk of 1 in 300 had a false positive rate of 8% and the detection rate of 82% (8) . It is estimated that prenatal screening followed by invasive diagnostic and selective termination of fetal trisomy 21 with a reduced prevalence of potential live births with trisomy 21 in about 78-82%. The ability to obtain reliable measure NT thickness depends on adequate training, using standard techniques and motivation operators. The importance of all three components can be seen in the example of the differences in results between the intervention and observational examination, during which operators measure the thickness of NT, but did not act in case of increased thickness (7). In intervention studies, over 99% of the NT thickness measurement was successful, unlike observational studies, where NT was successfully measured in only 75% of cases. In addition, the intervention studies, NT thickness was increased in 76% of trisomy 21 and 4.2% normal fetal chromosome, compared with 38% and 5.0% of cases in observational studies. In observational studies, ultrasound examinations were often made in inadequate gestation, and the operators or were not properly trained or were not motivated enough to measure the NT. In one of the studies, for example, where the operators told not to spend more time measuring NT than they need to measure the CRL, NT thickness was successfully measured in only 66% of cases (9). In another survey, CRL was less than 33 mm in 54% of the operators, which is said to measure NT within three minutes, it could not do in 42% cases (10) . These methodological problems are highlighted in the study performed monofetal to 47,053 pregnancies examined between 6 and 16 weeks (11). In 23% of the patients was not possible to obtain a valid NT measurement was performed because of inadequate gestation, the operators could not obtain the appropriate measures or any of the pictures was of acceptable quality. An example of the differences between observational and interventional studies and the testing Crosley and associates (12). In this observational survey, examined the 17,229 and fetal NT was successfully measured in 73% of cases. In the following examination of more than

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2000 pregnancies in which the results of the examination given to women, fetal NT was successfully measured in 99.8% of cases. The results of our study show that in the total sample 5.04% pathological karyotype, of which 50% of the numerical aberrations, which is in accordance with the above results from the literature. Predictive value of NT ultrasonography as markers for chromosomopathy if used in isolation is questionable, which is also confirmed in the literature. Results statistically significant difference in NT thickness in a group of pregnant women with pathological karyotype was expected ($p>0.05$) in the tested groups which speaks of homogeneity of the sample that we questioned.

VI. Conclusion

Valid findings nuchal translucency can be considered safe ultrasonographic markers in the assessment of absence chromosomopathy. Pathological finding, given the low positive predictive value must be amended and other prenatal tests before the pregnant woman give advice on the need to undergo prenatal diagnosis invasive.

List of Abbreviations
CRL - embryonic crown-rump length
NT - fetal nuchal translucency

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The Treatment of Stercoral Peritonitis Caused By Colorectal Carcinoma

By Ivana Djordjevic, Goran Stanojevic
University of Niš

Abstract – Introduction: Stercoral peritonitis (SP) caused by perforation of the colon due to colorectal carcinoma (CRC) represents one of the most difficult types of peritoneal inflammation with complex clinical presentation. Aim of the study was to establish frequency of CRC as a cause of stercoral peritonitis, type of treatment, postoperative complications, length of hospital stay and mortality among our patients.

Methods: Retrospectively we have analyzed two groups of patients. Group A: patients treated in period from 01.01.2001 to 31.12.2006, and group B consisted of patients treated from 01.01. 1995 to 31.12.2001. Surgical approach was different in those groups since we have accepted new strategies in the treatment of colonic perforations caused by CRC from the year 2000.

Results: In group A we have operated 56 patients, median age 62.9, in most of the cases (35.71%) SP was caused by carcinoma of the left colon. In group B, we operated 65 patients, median age 60.5, most of SP also cased by the cancer of the left colon (38.46%).

Keywords : *stercoral peritonitis (SP), colorectal carcinoma (CRC)*

GJMR-B Classification: *NLMC Code: WI 650, WI 600,*

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The Treatment of Stercoral Peritonitis Caused By Colorectal Carcinoma

Ivana Djordjevic [α], Goran Stanojevic [Ω]

Abstract - Introduction: Stercoral peritonitis (SP) caused by perforation of the colon due to colorectal carcinoma (CRC) represents one of the most difficult types of peritoneal inflammation with complex clinical presentation. Aim of the study was to establish frequency of CRC as a cause of stercoral peritonitis, type of treatment, postoperative complications, length of hospital stay and mortality among our patients.

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In both groups, there was similar number of minor complications (wound infection, peristomal abscess, personal irritation of the skin, stomal necrosis) 34 in group A and 39 in group B. This was not the case for major complication were in group A we recorded 30 different major complications (wound dehiscence, anastomotic leakage, intraabdominal abscess, fistula formation, and stomal retraction) opposed to 63 in group B. The higher percentage of complications in group B reflected to higher mortality rate (60%), opposed to mortality rate of 30% in group A.

Conclusion: Following new strategies in the treatment of stercoral peritonitis caused by CRC in recent years, we have managed to reduce rate of postoperative complications and mortality as well as hospital stay among these patients.

Keywords : stercoral peritonitis (SP), colorectal carcinoma (CRC)

Rezime - Sterkoralni peritonitis (SP) uzrokovan perforacijom debelog creva zbog kolorektanog karcinoma (CRC) jedan je od najtežih oblika zapaljenja peritoneuma, kompleksne kliničke slike. Cilj ispitivanja je da, retrospektivno-prospektivnom studijom naših bolesnika, utvrdimo učestalost (CRC) kao uzroka SP, način lečenja, postoperativne komplikacije, dužinu hospitalizacije i mortalitet bolesnika. Bolesnici su podeljeni u dve grupe: grupa A (od 01.01.2001-31.12.2006. god) i grupa B (od 01.01.1995 do 31.12.2000 god.). Podela je uradjena na osnovu uvodjenja i poštovanja novih stavova u lečenju CRC i SP (grupa A). U grupi A, operisano je 56 bolesnika, prosečne starosti 62,9 godina: najviše sa karcinomom levog kolona -20 (35,71%).. U B grupi operisano 65 bolesnika prosečne starosti 60,5 god., najviše sa karcinoma levog kolona -25 (38,46%)

Hirurčki postupci kod ovih boesnika su se razlikovali čto je rezultovalo vćom stopom komplikacija i smrtnosti. U A i B grupi lakčih komplikacija je bilo oko 60%, dok je težih komplikacija u A grupi bilo oko 53% , a u B grupi oko 96%. Visok procenat težih komplikacija u B grupi odrazio se i na stopu smrtnosti koja je u B grupi iznosila60%, dok je u A grupi bila duplo niža. Poštovanjem algoritama lečenja CRC i SP skraćuje se dužina hospitalizacije bolesnika, smanjuje nastanak komplikacija ii mortalitet.

Ključne reči : sterkoralni peritonitis, kolorektalni karcinom

I. Introduction

Stercoral peritonitis (SP) represents inflammation of visceral and parietal peritoneum caused by various bacterial species. This is a secondary peritonitis and it represents severe type of intraabdominal infection and abdominal related sepsis. Due to surgery and effective modalities of medical treatment, extremely high mortality rate of 90% from the beginning of the century has reduced to 15-40%.

The aim of our study is to establish colorectal carcinoma (CRC) as a cause of SP, type of surgery, postoperative complications, hospital stay and mortality during two periods. We'll analyze weather following new strategies in the treatment of stercoral peritonitis caused by CRC in recent years, we have managed to reduce rate of postoperative complications and mortality as well as hospital stay among these patients.

II. Material and Methods

This is retrospective-prospective study of our patients treated for stercoral peritonitis caused by CRC at Surgical Clinic, Clinical Center Nis. We have analyzed two groups of patients. Group A: patients treated in period from 01.01.2001 to 31.12.2006, and group B: patients treated from 01.01.1995 to 31.12.2001. We analyzed type of treatment, hospital stay, postoperative complications and mortality. Surgical approach was different in those groups since we have accepted new strategies in the treatment of colonic perforations caused by CRC from the year 2000.

III. Results

In group A we operated 435 patients for peritonitis, 56 of them had SP (12.87%) caused by CRC. Male gender predominated: 38(67.87%) men opposed

Author [α] : Surgical Clinic, Clinical Center Nis, Serbia Ivana Đorđević, Trg Učitelj Tase 3/4, tel. 062 511951, E-mail : ivanaz62@gmail.com
Author [Ω] : Goran Stanojevic, ul. Dusana Popovica 32, tel. 062 337877, E-mail : stgoran@medfak.ni.ac.rs

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to 18(32.14%) women, mean age 62.9 years (51-76). In group B we recorded 326 patients with peritonitis, 65(19.23%) of them had SP caused by CRC. There were 37(56.92%) men and 28(43.07%) women, mean age 60.5 years (37-84 years). In both groups most of patients had left-sided CRC: group A 20 pts (35.71%) and in group B 25 (38.46%) (Table 1). With further analysis of our results we established significant difference in type of surgery among those groups (Table 2a, 2b and 2c).

There is difference in rates of postoperative complications among groups. We recorded minor complications as: wound infection, peristomal abscess, stomal necrosis, parastomal skin irritation, and major complications as: wound dehiscence, anastomotic leakage, postoperative abscesses of abdomen, stercoral fistula formation and retraction of stoma (Table 3). Average hospital stay in group A was 16 days (10- 22 days), and in group B 21 day (11-31 day). Mortality in group A and group B according to type of surgery is described in Table 4.

IV. Discussion

Stercoral Peritonitis (SP) is a severe disease with an uncertain prognosis. Due to high concentration of aerobic, endotoxins of Gram-negative and especially egzotoxins of anaerobic bacteria, a quick penetration of these components occurs resolving in diffuse peritonitis, systemic infection and sepsis. Toxins primarily affect heart cells, endothelium, hepatocytes, kidney cells, and cells of immune system. Because of the ischemic, toxic and metabolic damage, cell necrosis occurs leading to septic shock and multiple organ failure in the end. Acute Physiology Score (APS) is commonly used to describe the intensity of pathophysiological disorder, while APACHE I I score helps in describing the incidence, morbidity and mortality rate. Patients with SP are placed in the third group with mortality rate of over 40% according to this score.

Treatment of SP caused by colonic carcinoma considers:

A. Permanent and successful elimination of septic source (respecting oncology principles)
B. Evacuation of necrotic and purulent content out of abdominal cavity

Removing the cause of infection is basically the most important step in surgical treatment of SP. CRC is the third most common form of cancer, equally distributed in both gender. Etiology of origin is unknown and risk factors are various (2). Complications aside, this cancer is followed by a high rate of mortality, and 5-year rate of survival correlates to the stage of carcinoma (Dukes A – about 90%: Dukes C – less then 60%) in case of elective surgery.

The very first principles of diagnosis and treatment of SP were noted during Hippocrates's era, while the first principles of surgical treatment were set by Martin Kirschner in 1926. SP is an acute condition, demanding an urgent surgical treatment. Reanimation and preoperative treatment consider besides the correction of hypovolemic and acidobase balance, a prophylactic use of antibiotics. The presence of CRC is often discovered during operation; therefore the surgeon is forced to decide about the type of operation according to the pathological finding and patient's condition.

The first colostomy used as a procedure to resolve intestine perforation caused by CRC, was created in 18th century. The basic principles of this treatment were set by Mikulicz (Vorlagerungs methods). This way of treatment was preformed for decades, until two stage procedure and the immediate anastomosis were introduced. If the SP is caused by perforation of the right colon affected by carcinoma, right hemicolectomy with Brook's unipolar ileostoma is the common treatment. Immediate anastomosis is acceptable only if protective ileostoma was made. Right hemicolectomy without anastomosis is preformed far more often. Performing immediate anastomosis is related to a high risk of postoperative complications.

Carcinoma of the left colon and rectum resulting in SP is a special problem. It is recommended not to perform coloanoanastomosis during first stage of procedure, but to create a colostomy. Nowadays, reconstructive surgeons support immediate anastomosis of left colon even with presence of diffuse peritonitis and perforation, in strictly selected cases, explaining that this maneuver do not effect mortality and morbidity in patients (5).

It is considered that the risk of immediate anastomosis of right and left colon is the same if the patients are hemodynamicly stable. Immediate anastomosis should not be considered only in hemodynamicly unstable patients, whether obstruction or perforation of colon is involved (6).

Localization of carcinoma do not affect postoperative mortality and 5-year rate of survival (7,8), but patient's general condition, severity of SP, the promptness of preformed procedure, surgeon's skill (9), and whether oncological principles are respected(total lymphadenectomy) (10). Regardless of the procedure extensiveness, a 5-year rate of survival is 20-30%.

According to many colorectal surgeons of GBA (Grate Britain Association) it is possible to determine the risky patients (RIX- risk-stratification index) which would help in survival prognosis (11,12,13). The methods of treatment of SP caused by colorectal origin are still a subject of discussion: one or two stage operation. High rate of mortality in these patients (over 40%) leaves the question:

A. Primary colostomy in patients in poor general condition. Postoperative occlusions of intestine after Loop ileostomy or Loop transversocolostomy are

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quite often. Loop transversocolostomy is recommended only as protective colostomy (14).

B. Intestine resection (along with tumor removal and lymphadenectomy) with immediate anastomosis and protective ileo or colostomy and finishing anastomosis during second stage. Postoperative mortality in this patients is 86%, while in those treated palliative is 39 % (15).
C. Subtotal colostomy, if radical operation is needed, in patients in good condition (16,17).

After removing the source of infection the treatment is continued with evacuation of necrotic and purulent content out of abdominal cavity: mechanical cleaning, debridment, intraoperative lavage with ceftriaxon, and drainage of abdominal cavity. Some recent studies show that intraoperative lavage with ceftriaxon or metronidasol completely exclude the possibility of postoperative abscess development. According to some other authors, performing lavage with 20 l of saline solution decreases development of postoperative complications, abscesses and the need for reintervention.

Special attention should be paid to severe forms of SP when it is recommendable to proceed with closed postoperative lavage, which actually represents the continuum of intraoperative lavage. Using this method, the risk of developing adhesive ileus is decreasing. The method of choice in treatment of highly severe forms of SP is staging lavage with temporary abdomen closure, which avoids the negative effect of increased abdominal pressure and the risk of intestine perforation.

According to many authors, there is no difference in postoperative mortality between planed and relaparotomy on demand (18,19). Second-look operations can be quite useful in case of severe SP followed by expressed organ necrosis, and in patients that developed septic shock with consecutive coagulopathy.

Knowing and respecting the principles of medical approach in stercoral peritonitis caused by colonic cancer perforation, patients in group A were treated with following surgical procedures:

- Solving SP, which was presented as a late diffuse peritonitis in majority of patients.
- Removal of tumor, which was often perforated (regarding the oncological principles)
- Performing immediate anastomosis only in selected cases. The majority of patients underwent ileo and colostoma creation as well as Hartmann's procedure.

In patients in group A suffering from right colon carcinoma, right hemicolectomy with Brook's unipolar ileostoma was preformed in 47.05%, while only 29.41% of patients underwent right hemicolectomy with immediate anastomosis. In patients with left colon carcinoma, the most preformed procedure was colon resection with unipolar colostoma (45%) and left hemicolectomy with bitubular colostoma (25%), while immediate anastomosis were not created. All patients suffering from rectal carcinoma underwent Hartmann's procedure (100%) (Table 2a).

Much more various procedures were preformed in patients in group B. In patients with right colon carcinoma, right hemicolectomy with immediate anastomosis was used more often (54,16%), while right hemicolectomy with Brook's ileostoma was preformed rarely (8,33). In patients with left colon carcinoma, colostomas were created the most (13,8%), while left hemicolectomy with immediate anastomosis was preformed rather often (9,23%). Rectal carcinoma was solved equally by colostoma creation and Hartmann's procedure (43,75%) (Table 2b).

During this study, special attention was paid to the number and type of complications after the first stage of procedure. The study showed that patients were in terminal phase of disease, with poor preoperative condition and signs of systemic infection. Very often, surgical procedures had to be preformed without adequate colon preparation, after brief and urgent preoperative reanimation. Postoperative complications (such as accretion of laparotomy "per secundam", laparotomy and anastomosis dehiscention, stercoral fistula) were rather the result of poor general condition in patients then inadequate operative technique (stoma complications, postoperative abscess, or other liquid collections in abdominal cavity, etc.).

According to results, about 60% of patients in Group A suffered from minor complications which were treated using conservative procedures, while 50% of patients suffered form serious complications treated both conservatively and operatively. The percentage of patients with minor complications were rather similar in Group B, while harder complications occurred far often – 96,92% of patients, among which 70% underwent reintervention (Table 4).

Cause of death was closely related to general condition of patients (azothemia, cardiovascular, renal or multiple organ dysfunction) and severity of primary disease. SP and CRC occurring separately are related to a high mortality rate, therefore this rate increases when they need to be treated at the same time. Mortality rate in group A was 32.14%, and 60% in group B. There is a significant difference between mortality rate in relation to the type of performed surgical procedure: in right hemicolectomy with unipolar ileostoma it was 37,5% in patients within group A, and 50% in group B; Hartmann' procedure, as a most frequently used procedure in rectal carcinoma, was related to a mortality rate of 42,1% in group A, towards 71,42% in patients in group B.

Prognosis, frequency of complications and mortality rate depend on various factors: Hinchey classification (Stage II-IV), APACHE II (> 19), SOFA

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(score 8), MOF (score 7), Mannheimer Peritonitis Index (MPI score 30), age of patients (over 65y.) – 26.9 % (20). According to results from 1994, mortality rate was 19.6 %(21), while in 2002, it was 16.9 %, although that's closely related to the type of procedure. When primary resection with anastomosis had been performed, mortality rate was 11.1%, though it was 22,2% when anastomosis was not included. Not one patient with MPI less then 25 passed away, while in patients with MPI from 26-36, mortality rate was 38.5 % (22). Localization of carcinoma also affects mortality rate. In left colon carcinoma it was 22.4 %, and if it had been associated to a high Peritonitis Severity Score (PSS) it was increased by 15.4 % (23). Mortality rate during the first 30 postoperative days, according to the results from 2001, was 14%, while one year survival was 55% and 5 year – 14%. Intestine perforation located proximal then carcinoma was related to a higher morbidity and mortality rate then perforation located on tumor itself (24). Intrahospital mortality during 30 days was 40.5 % in 2006, while during 2 years it was 64.3% (25). Further studies were performed trying to determine the difference between mortality and survival rate with perforative and non-perforative CRC. Mortality rate as well as metastasing in first 30 days was extremely high, while according to the results from 2008, 2 year survival was 47% in perforative and 54% in non-perforative carcinoma, and 5 year survival was 28% versus 33% (26).

Comparing these results to ours, which imply only for intrahospital mortality, results gained in group A were similar to the ones presented in literature, while results within group B were high above average.

V. Conclusion

SP caused by CRC is one of the most severe secondary peritonitis, and still is a great surgical issue. During examination period (group A) it was noticed in 12% of all peritonitis, while during control period (group B) it was rather often - 19%.

Surgical procedures used during treatment of patients in group A considered immediate anastomosis in 8.92%, while creation of unipolar ileostomy and colostomy were present in about 53%. In group B, immediate anastomoses were created in 30% of patients, and unipolar ileostomy and colostomy in nearly 60%. Total amount of minor complications in both groups was around 60%, while serious complications were presented with 53% in group A and 96% in group B. This significant difference between results referring to serious complications in our groups affected mortality rate, which was much higher in group B.

Considering that this were patients dealing with late stage of malignant disease, complicated with severe systemic disorders, shown results represent a fine success in treatment of this patients as well as the improvement of surgical and reanimation procedures comparing to earlier results.

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Table1 : Localization of CRC among our patients

	Group A		Group B		p
	n	%	n	%	
	17	30,35	24	36,92	0,57
	20	35,71	25	38,46	0,902
	19	33,92	16	24,61	0,355
	56	100	65	100	0,304

Table 2a : Type of surgery in group A (according to tumor localization)

	Total	Type of surgery	N	%
Right colon	17	RH with anastomosis	5	29,41
		RH with unipolar ileosomy Brook-u	8	47,05
		RH with ileostomy and transversecolostomy	2	11,76
		Cecostomy	2	11,76
Left colon	20	LH with unipolar colostomy	4	20
		LH with bipolar colostomy	5	25
		Cecostomy	2	10
		Resection with unipolar colostomy	9	45
Rectum	19	Hartmann' procedure	19	100
RH-right hemicolectomy; LH-left hemicolectomy				

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Table 2b : Type of surgery in group B (according to tumor localisation)

	Total	Type of surgery	N	%
Right colon	24	RH with anastomosis	13	54,16
		RH with unipolar ileosomy sec Brooke	2	8,33
		RH with ileostomy and transversecolostomy	4	16,66
		Colostomy	2	8,33
		Cecostomy	3	12,5
Left colon	25	LH with anastomosis	6	9,23
		Cecostomy	2	8
		Colostomy	9	13,84
		Resection with unipolar colostomy	8	12,3
Rectum	16	Exteorisation of transverse colon	2	12,5
		Colostomy	7	43,75
		Hartmann' procedure	7	43,75
RH-right hemicolectomy; LH-left hemicolectomy				

Table 2c : Comparative analysis

	Type of surgery	Group A	Group B	p
Right colon	RH with anastomosis	5	13	0,147
	RH with unipolar ileosomy Brook-u	8	2	0,043
	RH with ileostomy and transversecolostomy	2	4	0,685
	Colostomy	0	2	0,499
	Cecostomy	2	3	0,999
Left colon	LH with anastomosis	0	6	0,03
	LH with unipolar colostomy	4	0	0,043
	LH with bipolar colostomy	5	0	0,019
	Cecostomy	2	2	0,999
	Resection with unipolar colostomy	9	8	0,74
	Colostomy	0	9	0,004
Rectum	Exteorization of transverse colon	0	2	0,499
	Colostomy	0	7	0,015
	Hartmann' procedure	19	7	0,004
RH-right hemicolectomy; LH-left hemicolectomy				

Table 3 : Postoperative complications

Complication	Group A	Group B	Total group A	Total group B	p
Wound infection	10 (17,85%)	11 (16,92%)	34 (60,71%)	39 (60%)	0,085
Peristomal abscess	3 (5,35%)	3 (4,61%)			
Stomal necrosis	5 (8,92%)	6 (9,23%)			
Parastomal skin irritation	16 (28,57%)	19 (33,92%)			
Wound dehiscence	8 (14,28%)	13 (20%)	30 (53,57%)	63 (96,92%)	0,085
Anastomotic leakage	3 (5,35%)	10 (15,38%)			
Postoperative abscess	8 (14,28%)	14 (21,53%)			
Stercoral fistula	6 (10,71%)	15 (23,07%)			
Retraction of stoma	5 (8,92%)	11 (16,92%)			
Total	64	102			

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Table 4 : Mortality in group A and group B according to type of surgery

Type of surgery	Group A 56 patients		Group B 65 patients		p
	n	Mortality	n	Mortality	
RH and LH with anastomosis	5	4 (80%)	19	15 (78,94%)	0,01
RH with unipolar ileostomy	8	3 (37,5%)	2	1 (50%)	0,043
RH with ileostomy and transversocolostomy	2	0	4	3 (75%)	0,685
Cecostomy	4	1 (25%)	5	3 (60%)	0,999
Resection with unipolar colostomy	9	0	8	4 (50%)	0,144
LH with unipolar colostomy	4	1 (25%)	0	0	0,043
LH with bitublar colostomy	5	1 (20%)	0	0	0,019
Colostomy	0	0	18	6 (54,54%)	0,00006
Exteorization of transverse colon	0	0	2	2 (100%)	0,499
Hartmann' procedure	19	8 (42,1%)	7	5 (71,42%)	0,004
Total	56	18 (32,14%)	65	39 (60%)	0,304
RH-right hemicolectomy; LH-left hemicolectomy					

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Magnetic Resonance Presentation of Intracranial Meningiomas

By Jelena Stefanovic, Dragan Stojanov, Petar Bosnjakovic, Daniela Benedeto-Stojanov , Nebojsa Ignjatovic
University of Medicine Nis

Abstract – Magnetic resonance (MR) has become the most important imaging method in the diagnosis of intracranial meningeomas. The aim of this study was to present the characteristics of meningiomas. Thirty patients with histologically proven intracranial meningiomas were studied. There were 20 female and 10 male patients (median=53±15 years). All MR examinations were performed on the MR apparatus, the strength of which is 1.5T. All patients were scanned with T1, T2-weighted imaging (T1WI, T2WI), FLAIR and contrast-enhanced T1WI. Most of the tumors showed on T1WI the isointense signal (80%) and hypointense signals (20%). On T2WI, most of tumors showed isointense signal (80%) and hyperintense signal (20%). On FLAIR, the majority of tumors showed isointense signal (80%) and hyperintense signal (20%). After contrast administration, significantly intensive sign in contrast-enhanced T1WI was observed in 90% of the tumors, while 10% showed moderate enhancement. Supratentorial lesions were found in 83,34% of cases and infratentorial lesion were demonstrated in 16,66% of cases. MRI characteristics of intracranial meningiomas are various. Intracranial meningiomas usually show isointense and hypointense signals on T1WI; isointense and hyperintense ones on T2WI; isointense and hyperintense ones on FLAIR images, with intense enhancement after contrast administration. The most common is supratentorial localisation.

Keywords : *MR, meningioma*

GJMR-A Classification : *NLMC Code: WL 200, WL 141, WN 185,*

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Magnetic Resonance Presentation of Intracranial Meningiomas

Jelena Stefanovic[α], Dragan Stojanov[Ω], Petar Bosnjakovic[β], Daniela Benedeto-Stojanov[Ψ], Nebojsa Ignjatovic [¥]

Abstract - Magnetic resonance (MR) has become the most important imaging method in the diagnosis of intracranial meningeomas. The aim of this study was to present the characteristics of meningiomas. Thirty patients with histologically proven intracranial meningiomas were studied. There were 20 female and 10 male patients (median=53±15 years). All MR examinations were performed on the MR apparatus, the strength of which is 1.5T. All patients were scanned with T1, T2-weighted imaging (T1WI, T2WI), FLAIR and contrast-enhanced T1WI. Most of the tumors showed on T1WI the isointense signal (80%) and hypointense signals (20%). On T2WI, most of tumors showed isointense signal (80%) and hyperintense signal (20%). On FLAIR, the majority of tumors showed isointense signal (80%) and hyperintense signal (20%). After contrast administration, significantly intensive sign in contrast-enhanced T1WI was observed in 90% of the tumors, while 10% showed moderate enhancement. Supratentorial lesions were found in 83,34% of cases and infratentorial lesion were demonstrated in 16,66% of cases. MRI characteristics of intracranial meningiomas are various. Intracranial meningiomas usually show isointense and hypointense signals on T1WI; isointense and hyperintense ones on T2WI; isointense and hyperintense ones on FLAIR images, with intense enhancement after contrast administration. The most common is supratentorial localisation.

Key words : *MR, meningioma*

I. Introduction

Meningiomas are common intracranial tumors that arise from the cells covering the external arachnoid layer (1) compressing the brain (2). Meningiomas represent 20-26% of all primary intracranial neoplasms. They represent 20% of all intracranial tumors in men and 38% in women. 94% of meningiomas are benign, 4% are atypical and 1% is anaplastic. Benign meningiomas are more common in women, whereas atypical and anaplastic forms are frequent in men (3).

They also present as primary intracranial neoplasms, together with astrocytomas, that produce distant metastases in the lung and breast (4,5). They appear in the middle decades of life with a female predominance in incidence M:F=1:1.5 to 1:3. They show the geographic (includes 30% of intracranial tumors in Africa) and ethnic predominance (Caucuses, Spanish, African-Americans (6,4). Meningioma has estrogenic (0-94%) and progesterone receptors (40-100%).

Besides these receptors, the expression of androgen receptors can be found in meningiomas with approximately equal frequency, so that 69% present in males and 31% in women (6).

The beginning of magnetic resonance application (MR imaging - MRI) in the early 1980s radically changed the routine radiological diagnosis of primary and secondary brain tumors. Today, MRI is a key modality not only for diagnosis of lesions, but also for the assessment of type and grade of the tumor and degree of spreading into the surrounding tissue (7). On MR imaging, meningiomas are presented with various signals depending on the sequence. On T1WI, they show isointense signal and hypointense signal, and on T2WI they show hyperintense signal. After the application of gadolinium, on contrast-enhanced T1WI sequences, meningiomas show intense staining, which can be heterogeneous in some cases (7,8). We presented MR imaging findings of 30 patients with meningeoma.

II. Method

A prospective study involved a group of 30 patients with histologically proven intracranial meningiomas in the period 2004-2009. The study included 20 women (66.66%) and 10 men (44.44%), with mean age 53±15 years. All patients underwent surgical resection of the tumor; histological diagnosis of tumors was determined according to WHO classification.

DW MRI method was performed in the Center for Radiology Niš, on the Siemens Avanto MR device, whit magnetic fields of 1.5T. The examinations were performed in all patients, up to seven days before surgery, according to the standard protocol with the following sequence: T1WI, T 2WI, F LAIR and post contrast T1W.

Comparison of representation of certain findings by the level of T sequences between patients with different histological diagnoses was performed by Fisher exact probability test of the null hypothesis (Fisher's exact test).

III. Results

MR imaging was performed in 30 patients in the period 2004-2009 and intracranial meningiomas were diagnosed. The study included 20 (66.66%) women and

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10 (44.44%) men, with the female predominance in incidence M:F=1:2. The youngest patient was 29 years old and the oldest 73 years, with mean age 53±15 years.

Table 1 : Distribution of patients compared to histopathological diagnosis and sex

Histopathological diagnosis	Sex		Total
	Woman	Man	
Meningothelial meningiomas	10 (66,66%)	5 (33,34%)	15 (50%)
Fibroblastic meningiomas	7 (70%)	3 (30%)	10 (33,33%)
Cystic meningiomas	3 (60%)	2 (40%)	5 (16,67%)
Total number of meningiomas	20 (66,66%)	10 (44,44%)	30 (100%)

From the total number of patients (30), meningothelial meningiomas were diagnosed in 15 (50%) patients, 66.66% of women and 33.34% of men. Fibroblastic meningiomas were found in 10 (33.33%) patients, 70% of women and 30% of men. Cystic meningiomas were diagnosed in 5 (16.67%) patients, 60% of women and 40% of men.

According to the results obtained in our study, there is a female predominance in the incidence M:F=1:2.

Table 2 : Distribution of patients compared to histopathological diagnosis and age Histopathological diagnosis

Histopathological diagnosis	Parameter				
	Xsr	SD	Med	Min	Max
Meningothelial meningiomas	64,00	6,25	62,00	59,00	71,00
Fibroblastic meningiomas	48,67	17,05	48,00	26,00	72,00
Cystic meningiomas	46,00	.	46,00	46,00	46,00
Total number of meningiomas	53,00	15,11	54,00	26,00	72,00

According to the results obtained in our study, meningiomas occur in the middle decades of life, with mean age 53±15 years.

The anatomic distribution of tumors

Table 3 : The anatomic distribution of tumors

Supratentorial	Infratentorial
Convexity 13 (43,33%)	Cerebellopontine angle 3 (10%)
Parasagittal region 5 (16,66%)	Petrous apex 2 (6,66%)
Parafalcine 2 (6,66%)	
Occipital diploe 1 (3,33%)	
Anterior fossa 1 (3,33%)	
Middle fossa 1 (3,33%)	
Tentorium 2 (6,66%)	
25 (83,34%)	5 (16,66%)

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In our study, all patients had a solitary lesion before surgery. Supratentorial localization was reported in 25 (83.34%) patients. The tumor was localized in the cerebral convexity in 13 (43.33%) patients, parasagital region in 5 (16.66%)patients, parafalcine in 2 (6.66%) patients, occipital diploe in 1 (3.33%) patient, anterior fossa in 1 (3.33%) patient, middle fossa in 1 (3.33%) patient, tentorium in 2 (6.66%) patients.

Infratentorial localization was confirmed in 5 (16.66%) patients. The cerebellopontine angle in 3 (10%) patients, and petrous apex in 2 (6.66%) patients.

According to the results obtained in our study, taking into account the localization of tumors, meningiomas have statistically significantly more supratentorial localization - 83.34%, compared to infratentorial localization in 16.66%.

a) Radiologic Finding

The frequency of isointense findings on T1WI (80%) was significantly higher ($p<0,05$ 0,01) than the frequency hypointense finds 20%. Hyperintense and mixed findings were not recorded in patients examined.

The frequency of isointense findings on T2WI (80%) was significantly higher ($p<0,05$ 0,01) than the frequency hyperintense finds 20%. Hypointense and mixed findings were not recorded in patients examined.

The frequency of isointense findings on FLAIR (80%) was significantly higher ($p<0,05$ 0,01) than the frequency hyperintense finds 20%. Hypointense and mixed findings were not recorded in patients examined.

The frequency of intensive findings on post-contrast T1WI (90%) was significantly higher ($p<0,05$ 0,01) than the frequency of moderate discoloration (20%). All patients had negative findings on post-contrast T1WI sequences.

Table 4 : Representation tumor on T1WI sequences compared to histopathological diagnosis

Histopathological diagnosis	Results			
	Iso	Hypo	Hyper	Mixed
Meningothelial meningiomas	15 (100,0%)	-	-	-
Fibroblastic meningiomas	9 (90%)	1 (10%)	-	-
Cystic meningiomas	-	5 (100,0%)	-	-
Total number of meningiomas	24 (80,0%)	6 (20,0%)	-	-

Table 5 : Representation tumor on T2WI sequences compared to histopathological diagnosis

Histopathological diagnosis	Results			
	Iso	Hypo	Hyper	Mixed
Meningothelial meningiomas	15 (100,0%)	-	-	-
Fibroblastic meningiomas	9 (90%)	-	1 (10%)	-
Cystic meningiomas	-	-	5 (100,0%)	-
Total number of meningiomas	24 (80,0%)	-	6 (20,0%)	-

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Table 6 : Representation tumor on FLAIR sequences compared to histopathological diagnosis

Histopathological diagnosis	Results			
	Iso	Hypo	Hyper	Mixed
Meningothelial meningiomas	15 (100,0%)	-	-	-
Fibroblastic meningiomas	9 (90%)	-	1 (10%)	-
Cystic meningiomas	-	-	5 (100,0%)	-
Total number of meningiomas	24 (80,0%)	-	6 (20,0%)	-

Table 7 : Representation tumor on post-contrast T1WI sequences compared to histopathological diagnosis

Histopathological diagnosis	Results		
	None	Moderate	Intensive
Meningothelial meningiomas	-	1 (6,67%)	14 (93,33%)
Fibroblastic meningiomas	-	2 (20%)	8 (80%)
Cystic meningiomas	-	-	5 (100,0%)
Total number of meningiomas	-	3 (10%)	27 (90%)

Given the intensity of the signal, according to data obtained in our study, the majority of tumors on T1WI show isointense (80%) and hypointense signals (20%). On T2WI, the majority of tumors (80%) show isointense and the hyperintense signals (20%). On FLAIR sequence, the majority of tumors show isointense (80%) and hyperintense signals (20%). After contrast application, on post-contrast T1WI sequences, 90% of tumors showed extensive staining, and 10% of the tumors moderate staining, which is a statistically significant difference ($p<0.01$) (Table 6).

IV. Discussion

Meningiomas represent 20-26% of all primary intracranial neoplasms (3), i.e. 14-20% (9). They appear in the middle decades of life with a female predominance in incidence 2:1 (4,6,10-13), and 2.2:1 based on the data available in the reference literature (14), which is in agreement with the results obtained in our study, where the average age is 53±15 years, with a female predominance in incidence 2:1.

Meningiomas present as solitary lesions. Multiple meningiomas are rare lesions. Only 1-9% of intracranial meningiomas had multiple lesions (15), or 4.4% according to literature data (14). In our study, all lesions were solitary. Extracranial metastasis of malignant meningiomas are rare, occurring in less than 0.1% of all meningiomas (16). In our study, all patients with no extracranial metastases.

a) Anatomic distribution

Taking into account the tumor localization, De Monteand (13) on the basis of his researches and literature data show the distribution of meningioma: parasagittal and parafalcine 25%, convexity 19%, sphenoidal ridge 17%, supra sella (tuberculum) 9%, posterior pit 8%, olfactory groove 8%, middle fossa (Meckel's cave) 4%, tentorium 3%, peritorcular region 3%, 1-2% lateral ventricles, foramen magnum 1-2%, 1-2% optical path.

Based on the research by Monroe (17) et al., the convexity and parasagittal region are the most common localizations of meningioma in more than 50%. However, studies by other researchers provide data on 23.5% of para-sagittal, parafalcine and convex localizations, intraventricular (23.5%) in the Sylvian fissure (8.8%), petroclival (8.8%), CPA (5,9%), and foramen magnum, tuberculum sellae, cavernous sinus, sphenoidal ridge in 32.3% of cases (18). According to Huang et al. (19) the most common site of meningiomas

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is convexity, while Hadidy et al. (14) in their study reported the para-sagittal one in 23.3% of cases.

According to the results obtained in our study and taking into account the localization of tumors, meningiomas statistically significantly occupy supratentorial localization in 83.34% of cases, compared to infratentorial localization in 16.66% of cases.

b) Radiologic Findings

There are several studies that have considered the signal characteristics of meningioma on MR imaging. Signal intensity of the tumor mass is variable on T1WI, T 2WI and FLAIR sequences (20-22). On T1WI, most tumors are isointense in respect to gray matter (56-94%), while hypointense ones occur in 20-48% of cases and hyperintense are very rare. On T2WI, about 50% meningiomas are isointense, 4-18% hypointense, while 35-44% are hyperintense (20,21).

According to the results obtained in our study and taking into account the localization of tumors, meningiomas statistically significantly occupy supratentorial localization in 83.34% of cases, compared to infratentorial localization in 16.66%.

In our study, with respect to signal intensities, the majority of tumors on T1WI show isointense (80%) and hypointense (20%) signals. On T2WI, the majority of tumors show isointense (80%) and hyperintense (20%) signals. On FLAIR sequence, most of the tumors show isointense (80%) and hyperintense (20%) signals. Meningiomas show intense staining after contrast applications on post-contrast T1WI sequences (20,21,23). Tumor staining in patients with meningiomas can help to identify anatomical boundaries of larger lesions that can be isointense on T1WI.

In our study, after contrast application on the post-contrast T1WI sequences, 90% of the tumors show extensively staining, and 10% of tumors have moderate staining of tumor.

Hadidy et al. (14) reported that the majority of meningiomas presented with isointense signal on T1WI and T2WI, hyperintense signal on FLAIR and intense staining. Yao et al. (24) in their study reported that meningiomas on T1WI had predominantly hypointense signal on T2WI and hyperintense signal on FLAIR sequences. Huang et al. (14) in their study of 76 patients concluded that isointense or hyperintense signals on T2WI were reported in 70.6% of cases, while a study of 106 patients on post-contrast T1WI showed significant intense staining in 82.5% of patients.

V. Conclusion

MRI characteristics of intracranial meningiomas are different. With regard to signal intensities, intracranial meningiomas on T1WI show isointense and hypointense signals. On T2WI, isointense and hyperintense signals are shown. On FLAIR sequences, isointense and hyperintense signals are shown. After contrast application, on the post-contrast T1WI sequences meningiomas show intense staining. The most common are supratentorial localizations.

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Dilated Cardiomyopathy and Hypothyroidism with concomitant CAD - a debatable scenario

By Bilal Bin Abdullah ,Mehboob M Kalbur gi ,M d Zoheb , S atya srinivas
Al Ameen medical college,Karnataka, India.

Abstract – The concept of dilated cardiomyopathy with concomitant coronary artery disease and hypothyroidism is yet a matter of debate although many theories have been postulated with this regard. We report overt heart failure due to dilated cardiomyopathy in an elderly lady with significant coronary artery disease and hypothyroidism. Early suspicion, evaluation and judicious use of thyroxine with appropriate anti ischaemic measures proved beneficial with a better prognostic outcome in this patient.

Keywords : *heart failure, dilated cadiomyopathy,ischemic heart disease, hypothyroidism. CADcoronary artery disease.*

GJMR-B Classification: *NLMC Code:WG 370, WG 120, WG 142,*

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Dilated Cardiomyopathy and Hypothyroidism with concomitant CAD - a debatable scenario

Bilal Bin Abdullah [α] ,Mehboob M Kalburgi [Ω] , Md Zoheb , Satya srinivas [β]

Abstract - The concept of dilated cardiomyopathy with concomitant coronary artery disease and hypothyroidism is yet a matter of debate although many theories have been postulated with this regard. We report overt heart failure due to dilated cardiomyopathy in an elderly lady with significant coronary artery disease and hypothyroidism. Early suspicion, evaluation and judicious use of thyroxine with appropriate anti ischaemic measures proved beneficial with a better prognostic outcome in this patient.

Keywords : heart failure, dilated cadiomyopathy, ischemic heart disease, hypothyroidism. CAD- coronary artery disease.

I. Introduction

Thyroid hormone has many effects on the heart and vascular system.[1] The heart is very sensitive to alterations in serum thyroid levels. Many of the clinical manifestations of hyperthyroidism and hypothyroidism are due to the ability of thyroid hormone to alter cardiovascular hemodynamics.[2] Thyroid hormone metabolism is altered in many patients with acute or chronic cardiac disease, as it is in patients with other non-thyroidal illnesses. Cardiac manifestations of thyroid hormones are due to dyslipidemia, accelerated atherogenesis, reduced heart rate, contractile states of myocardium and pericardial effusion.

The prevalence and clinical importance of myocardial dysfunction in hypothyroidism are generally overlooked. Nonspecific histological abnormalities have been demonstrated repeatedly in the hearts of myxoedema patients since first reported in 1888 in report of a committee of the Chemical Society of London.[3] The structural changes together with haemodynamic changes in heart of a hypothyroid patient termed as hypothyroid cardiomyopathy [4-6] has shown a good response to thyroxine replacement.

Ischaemic cardiac events have also been implicated in causing transient thyroid dysfunction. But whether the cardiomyopathy associated with both ischemic heart disease and hypothyroidism are interrelated is still a matter of debate as significant improvement has been seen in patients treated concurrently for the two different conditions.

Author [α] : Professor and Head of the department, Department of medicine, Al Ameen medical college, Bijapur-586108 Karnataka, India. Email : drbilal28@yahoo.com

Author [Ω β] : Professor, Post graduate student, Al Ameen medical college and Hospital , Bijapur- 586108, Karnataka, India.

II. Case Report

A 61 year old lady presented to the emergency department of a tertiary institution with exertional dyspnoea since 1 week with no documented medical history. On examination the patient was mildly cyanosed, pulse rate 120 beats per minute; regular rhythm, blood pressure 110\90 mmHg, respiratory rate 32cycles/min, saturation of O2 85% with elevated JVP. Cardiovascular examination showed tachycardia with gallop rhythm and bilateral basal crepititions .A clinical diagnosis of heart failure was made. All preliminary investigations were within normal range except the lipid profile which was altered with total cholesterol- 320 mg /dl, LDL cholesterol - 180 mg/dl, HDL- 40 m/|dl, TG -380 mg \dl with normal values of CPK and Troponin-I. Electrocardiogram showed sinus tachycardia with no ST -T changes. Chest x-ray showed cardiomegaly (figure 3 a) with pruning of upper lobar veins and peri hilar congestion. 2D Echocardiography showed global hypokinesia with an inter ventricular septal thickness of 8.1 mm, mild mitral regurgitation, no regional wall motion abnormalities, minimal pericardial effusion and an left ventricular ejection fraction (LVEF) of 27%. She was decongested with diuretics and recovered symptomatically. An emergency coronary angiography was performed, which revealed a triple vessel disease with blocks of –left anterior descending (LAD) 60 %, left circumflex (LCX) 100%, mid right coronary artery (RCA) 100%. Respecting her LVEF of 27% she was subjected to conventional treatment. A true benefit of an interventional revascularization in this patient was a dilemma at this point, hence this patient was contemplated for radio nucleotide 99m technetium (Tc) –resting myocardial perfusion study (figure 1,2) which showed severe degree of resting myocardial perfusion defects in the anterior wall, inferior and lateral walls including the apex and septum, corresponding to LAD, RCA, LCX territories and minimal to moderate degree of viable myocardium, LV dilatation with evidence of systolic and diastolic dysfunction .Her above follow up pointed out to a ischemic cause of the underlying heart failure and she was promptly started on conventional oral anti ischemic measures(Aspirin 150mg, clopidogrel 75mg), ACE inhibitors(ramipril 1.25mg) ,statins (atorvastatin 40mg) , aldosterone antagonist (

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eplerenone 25mg) and low dose diuretics.(torsemide 20 mg). With this therapy her symptoms were brought under control. In the mean time her thyroid profile was awaited which pointed towards frank hypothyroidism. She was started cautiously with Levothyroxine 0.25 micro gram per day which was gradually built upto a dose 0.1 mg over 3 weeks duration. Following this treatment she showed significant improvement in her symptoms and was later discharged after fixing the dose of thyroxine at 0.1mg/ day.

During serial follow ups, 4 months after her discharge, she was asymptomatic, active and able to carry out her routine activities .She was reinvestigated to study her present status and therapeutic response. Her chest x-rays (figure 3 b, c) taken then showed significant reduction in cardiac size. Echocardiography showed improved LVEF to 55%. Her lipid profile and thyroid function test were also within normal ranges. She was continued on her medications and has been doing well till date.

III. Discussion

Thyroid hormone has many effects on the heart and vascular system.* Many of the clinical manifestations of hyperthyroidism and hypothyroidism are due to the ability of thyroid hormone to alter cardiovascular hemodynamics.The hemodynamic effects of hypothyroidism are opposite to those of hyperthyroidism, although the clinical manifestations are less obvious. Prompt evaluation here made the diagnosis of congestive cardiomyopathy. We believed this to be related to the underlying coronary pathology with respect to her altered lipids, low ejection fraction, poor LV systolic function and global hypokinesia supported with coronary angiogram. Radionuclide tech 99 resting myocardial perfusion scan revealed significant perfusion defects with viable myocardium. PET studies of O2 consumption in patients with hypothyroidism have revealed that myocardial work efficiency is lower than in normal subjects.[7]Significant dyslipidemia in a slim elderly patient (BMI-20) prompted us to investigate her thyroid status as such an accelerated coronary atherosclerosis due to hypercholesterolemia in hypothyroidism and post menopausal ladies has already been postulated*

Some theories have explained overt hypothyroidism to occur following an acute coronary event or acute myocardial infarction,*but the phenomena is a sub clinical state of hypothyroidism and in heart failure, patients have low serum T3 concentration and the degree is proportional to severity of heart failure as per NYHA functional classification.[8] We were in a dilemma as to whether the heart failure has depressed the thyroid hormones or hypothyroidism per se is only the true cause for this cardiomyopathy. Here significant elevation of TSH more than 150 and significant reduction in T3 and T4 made the diagnosis of hypothyroid cardiomyopathy. We had initially thought of IV T3 as an immediate therapy to tide over this crisis but due to its non availability we treated this patient cautiously with thyroxine initiating with the lowest possible dose, gradually building up the dose to a maximum of 0.1 mg within 6 weeks. In fact risk versus benefits with thyroxine therapy in elderly patients with concomitant coronary artery disease were thought seriously as thyroxine is known to improve the cardiac contractility and reduce the peripheral vascular resistance and has no effect in improving the LVEF .Theories have explained maximum beneficial effects of thyroxine in patients who were diagnosed to have heart disease in long standing hypothyroidism*but in our case it was a risk as patient was tachycardic. Many of the patients with severe heart failure in hypothyroidism with significantly compromised LVEF, poor LV systolic function and a jeopardized myocardium are expected to have prolonged QT interval and abrupt initiation of thyroxine therapy in them may culminate with torse de pointes, ventricular arrhythmias and a premature sudden cardiac death.

Whether the thyroid condition in this case was a separate preexisting entity precipitating the underlying cardiac events or whether it was precipitated by the cardiac event was yet to be explained.

IV. Conclusion

Patients with thyroid diseases often have symptoms and signs indicating changes in cardiovascular hemodynamics. Indeed, symptoms and signs referable to the cardiovascular system may be the only manifestations of thyroid dysfunction, and thyroid function should therefore be assessed by the measurement of serum thyrotropin concentrations in patients with cardiovascular disease. Patients with cardiovascular disease, like patients with other nonthyroidal illnesses, have changes in thyroid hormone metabolism that may alter cardiac function. Although some data suggest that the thyroid replacement therapy may benefit some patients with cardiovascular disease, further studies are required to establish specific treatment recommendations.

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FIGURES

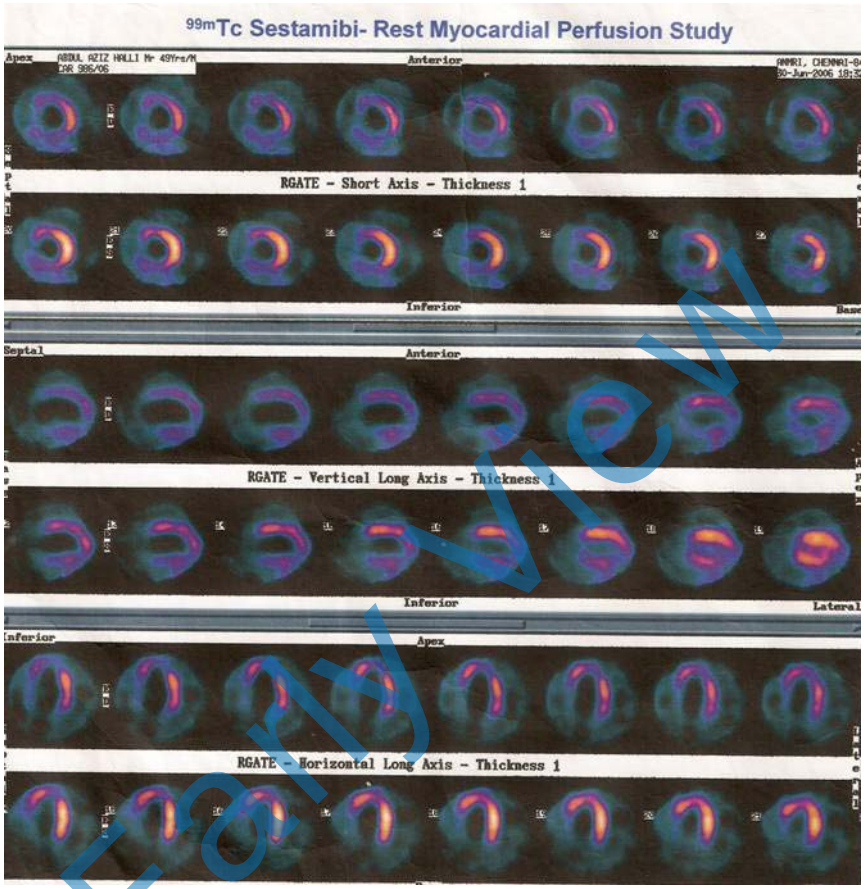

Figure 1

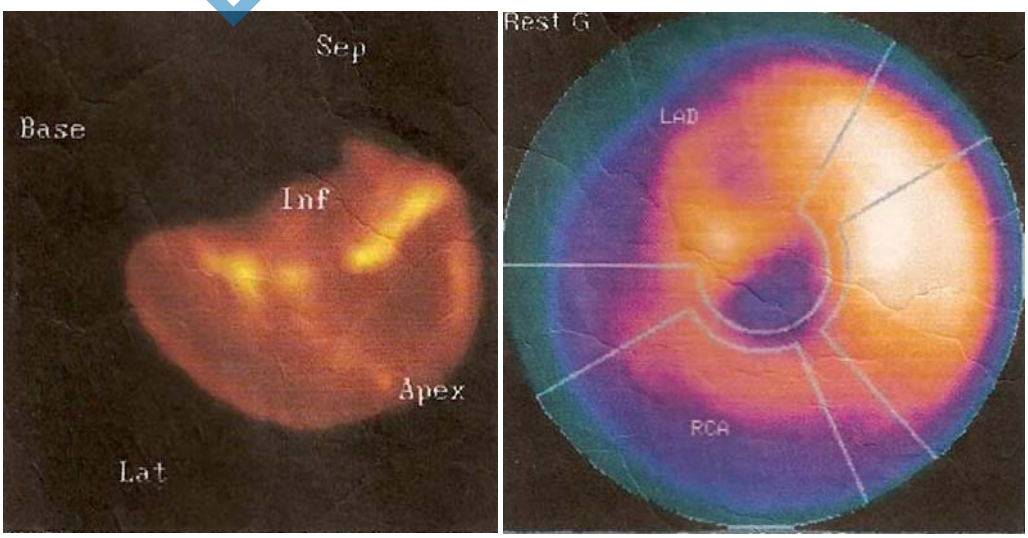

Figure 2

Early view

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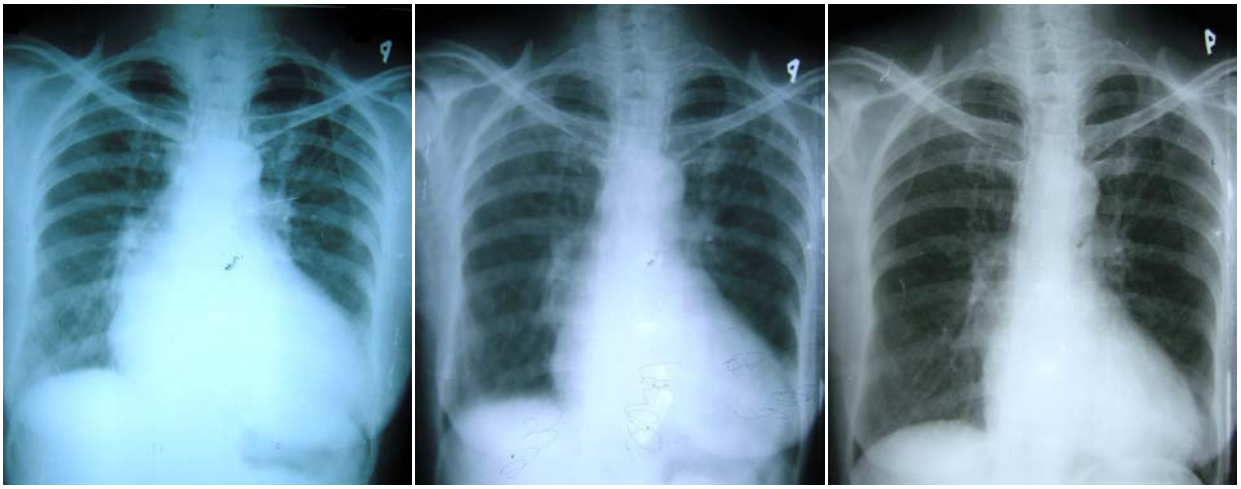

a b c

Figure 3 : Serial chest radiographs of the patient (a) at the time of presentation (b, c) during follow up following onset of therapy

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Clinical Significance of Perceived Occupational Stress Influencing Body Mass and Osteopenia: A Pilot Study

By Dr.T. Anil Kumar, Dr. Suresh.D.R
ESIC Medical College & PGIMSR, Rajajinagar , Bangalore.

Abstract – Introduction: Studies demonstrating perceived occupational stress, obesity & osteopenia among industrial workers are very limited. This pilot study was conducted to analyze the inter-relationships, if any, between stress, obesity and osteopenia among industrial workers. Materials and Methods: All patients who attended the health camps aging from 18 years to 70 years of either sex were the subjects of the study. They were subjected to General Physical Examination along with measurement of anthropometric parameters (Body Mass Index, Waist to hip ratio) Blood pressure and Systemic examination. Perceived Stress Scale (4 point) accepted worldwide for assessment of Stress was given in the form of Clinical Questionnaire to the subjects. Blood samples from the patients were subjected to random blood sugar and lipid profile. Bone Scan was done to assess the Bone Density as a marker of Osteoporosis. Comparison of the parameters obtained were done using appropriate statistical methods. Correlations were done using Pearson's correlation co-efficient. All statistical tests were conducted at 5% level of significance.

Keywords : *Perceived stress scale; Osteopenia; Obesity; Bone density; Waist to Hip ratio.*

GJMR-B Classification: *WM 172.5, WM 176, WB 112,*

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Clinical Significance of Perceived Occupational Stress Influencing Body Mass and Osteopenia: A Pilot Study

Dr.T. Anil Kumar[α], Dr. Suresh.D.R[Ω]

Abstract - Introduction: Studies demonstrating perceived occupational stress, obesity & osteopenia among industrial workers are very limited. This pilot study was conducted to analyze the inter-relationships, if any, between stress, obesity and osteopenia among industrial workers.

Materials and Methods: All patients who attended the health camps aging from 18 years to 70 years of either sex were the subjects of the study. They were subjected to General Physical Examination along with measurement of anthropometric parameters (Body Mass Index, Waist to hip ratio) Blood pressure and Systemic examination. Perceived Stress Scale (4 point) accepted worldwide for assessment of Stress was given in the form of Clinical Questionnaire to the subjects.

Blood samples from the patients were subjected to random blood sugar and lipid profile. Bone Scan was done to assess the Bone Density as a marker of Osteoporosis. Comparison of the parameters obtained were done using appropriate statistical methods. Correlations were done using Pearson's correlation co-efficient. All statistical tests were conducted at 5% level of significance.

Results: The Body Mass Index & Waist to Hip ratio correlated with osteopenia. The Obese persons had increasing osteopenia along with increased lipid profiles. Overweight persons had slight osteopenia along with normal lipid profile. Persons who were perceived to be under stress had poor control of Blood Sugar inspite of being treated with oral hypoglycaemic agents. Most of the subjects had high scores on perceived stress scale, high incidence of substance abuse, lack of knowledge regarding healthy diet & healthy lifestyle.

Conclusion: Identification of factors contributing to stress & effective counselling will have a greater impact on mental & physical health of persons covered under ESIC Health Scheme. Regular Health Education Programmes will ensure a good Quality of life (including Healthy lifestyle)& prevents morbidity. Prevention of osteoporosis & obesity by regular health check ups, good exercise & healthy diet should be a major concern.

Keywords : Perceived stress scale; Osteopenia; Obesity; Bone density; Waist to Hip ratio.

I. Introduction

Stress refers to a psycho physiological response of a living organism to a perspective challenge, change or threat. Occupational stress (job stress) is a psychosocial disorder which is an impact of the interaction between the worker and his work environment on the worker themselves. If left unidentified it can cause serious physical and physiological illness to the individual, which affects both the individual and the organization. Occupational stress may occur due to stress factors at the individual level, or at the organization level or at the interface of the two. Industrial workers with perceived psychological stress can have impaired job performance and increased risk of stress-related illness such as hypertension, risk factors of coronary heart disease, depression, sleep disorders etc. [1]

It is also likely that stress-induced elevations of cortisol may contribute to a tendency to overeat, which in turn contributes to obesity. Obesity itself is associated with disturbances in Hypothalamic-Pituitary-Adrenal axis (HPA) function, leading to cortisol dysregulation. Obesity is associated with a state of chronic low grade inflammation which is associated with various systemic diseases. The relationship between the obesity and bone density in industrial workers with occupational stress has not been well documented. [2]

Hence, this pilot study was conducted to observe the relationship, if any between the occupational stress, obesity and bone mass in industrial workers under Employees' State Insurance Scheme.

II. Materials and Methods

A cross-sectional study was conducted on all patients who attended the ESICMC & PGIMSR Model Hospital Health Camps (n = 105 out of total 300) aging from 18 years to 70 years of either sex. Patients with chronic diseases, infections, chronic medications, psychiatric disorders, cancers etc were excluded from the study. The data collection was done for around 8 hours so as to cover all those in the day shift. Perceived Stress Scale (4 point) accepted worldwide for assessment of Stress was given in the form of Clinical Questionnaire to the subjects which was formulated and adapted as suitable for the industrial workers. The questionnaires were constructed in English and later translated to the native language (Kannada) with the help of Expert. The researcher and the administration agreed prior that each participant would spend no more than ten minutes on the questionnaire. The time was considered critical as the absence of participant from work would mean production delay. The idea of research was clearly explained to the participants in a

Author α : Professor & Head, Department of General Medicine, ESIC Medical College & PGIMSR, Rajajinagar , Bangalore – 560010.
E-mail : buddhatozen@yahoo.co.in
Author Ω : Assistant Professor, Department of Biochemistry, Employees' State Insurance Corporation – Medical College & Postgraduate Institute Of Medical Sciences & Research, Rajajinagar, BANGALORE. E-mail : drsuri77@yahoo.com

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common gathering. The participants were allowed to interact with the researcher and clarify the concepts explained. Following this the participants who were willing to participate were asked to sign the informed consent forms. The subjects filled the questionnaire with the help of the researcher regarding understanding of questions. The 10-item scale assesses feelings and thoughts during the last month. The PSS measures the degree to which situations in one's life are perceived as stressful. It is more strongly related to life event impact scores as opposed to the number of stressful events, thereby representing one's appraisal of the events as being stressful. The participants were asked to rate their feelings on a scale of 0–4, with 0 indicating never and 4 indicating very often. The PSS scores range from 0 to 40, with higher scores indicating higher levels of stress.[3, 4]

General Physical Examination along with measurement of anthropometric parameters including Body Mass Index (BMI), Waist to hip (W/H) ratio, Blood pressure & Systemic examination (cardiovascular, respiratory, gastrointestinal, endocrine & neurological system) were carried out on all subjects Subjects stood barefoot during all anthropometric assessments. Waist circumference was measured by a tape measure at the midpoint between the upper iliac crest and lower costal margin in the midaxillary line. W/H ratio was correlated with Asian Standards. (Women 88-90, Men 100-102). BMI was categorized into three types: Normal (18.5-24.9), overweight (25-29.9) & Obese (30-39.9). [5, 6]

Blood samples from the patients were subjected to biochemical & Pathological investigations like blood sugar, lipid profile & Haemogram by the Laboratory Personnel under the supervision of the Faculty.

Dual Energy X-Ray Absorptiometry (DEXA) Bone Scan was done to assess the Bone Density. Bone Density was expressed as T-Score (T-score is a comparison of a person's bone density with that of a healthy 30-year-old of the same sex). A T-score of *-2.5 or lower* qualifies as osteoporosis. A T-score of *-1.0 to -2.5* signifies *osteopenia*, meaning below-normal bone density without full osteoporosis. [7]

Comparison of the parameters obtained were done using ONE WAY ANOVA test. Correlations between the anthropometric measurements, biochemical data, Perceived stress scale & the degree of osteopenia (based on bone density index) were done using Pearson's correlation co-efficient. All statistical tests were conducted at 5% level of significance using SPSS software & online statistical tools.

III. Results

Based on the BMI, the subjects were grouped into Normal, Overweight & Obese persons. Perceived stress was more in obese group compared to overweight & normal group. Although osteopenia was increasing with increasing BMI, the increments were insignificant. Mean Arterial Pressure was increased in overweight & obese persons. Overweight persons had slight osteopenia along with normal lipid profile. The Obese persons had increasing osteopenia along with increased lipid profiles. Persons who were perceived to be under stress as per the Perceived Stress Scale Questionnaire had poor control of Blood Sugar with increasing BMI, inspite of being treated with oral hypoglycaemic agents. (TABLE 1)

In Normal & overweight subjects, stress was correlating negatively with obesity & increasing osteopenia. In obese group, stress was correlating positively with increasing W/H ratio & osteopenia. Also, W/H ratio correlated positively with increasing osteopenia in obese persons. Most of these correlations were statistically insignificant. (TABLE 2)

Many subjects who had high scores on perceived stress scale had high incidence of substance abuse, lack of knowledge regarding healthy diet & healthy lifestyle.

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Table 1 : showing the comparison of measured parameters among the study group

	MEAN AGE(YRS)	PSS SCORE	BMI (Kg/m^2)	W/H	MAP (mm Hg)	Bone Density (T Score)	RBS (mg/dl)	TOTAL CHOL (mg/dl)	LDL – C(mg/dl)	TG (mg/dl)
NORMAL (n=59)	33.90± 7.8	14.86± 1.5	20.37± 3.3	0.91± 0.1	92.97± 8.9	1.66 ± 0.5	89 ± 9.2	145 ± 15	92 ± 7.5	168 ± 8
OVER WEIGHT (n=29)	36.55±7. 5	16.3± 0.9	27.4± 1.3	0.95± 0.1	99.21± 15.0	1.69 ± 0.5	106 ± 8.5	186 ± 18	118 ± 9.3	189 ± 12
OBESE (n=17)	42.06±6. 0	16.9± 1.3	33.58± 3.3	0.99± 0.1	93.65± 11.9	1.76 ± 0.4	114 ± 10.6	209 ± 16.7	124 ± 8.6	215 ± 11.3
P VALUE		<0.05*	<0.05 *	<0.05 *	>0.05	>0.05	<0.05*	<0.05*	<0.05*	<0.05*

(* - p<0.05 – significant)

Table 2 : showing the correlations of measured parameters among the study group

	NORMAL (n=59)		OVERWEIGHT(n=29)		OBESE(n=17)	
	R value	P value	R value	P value	R value	P value
PSS & W/H	-0.09	0.49	-0.03	0.87	0.53	0.028*
W/H & BMD	0.03	0.82	0.40	0.03*	0.48	0.051
PSS & BMD	-0.27	0.038*	-0.04	0.83	0.17	0.514

(* - p<0.05 – significant)

IV. Discussion

According to the WHO report, "Raising Awareness of Stress at Work in Developing Countries" in 2007, occupational stress is one of the most common forms of stress in developing countries as the socioeconomic status, social inequalities and overpopulation forces employees to work based on job availability without a choice. Occupational stress (job stress) is a psychosocial disorder which is an impact of the interaction between the worker and his work environment on the worker themselves. Studies have shown that blue collar workers are highly vulnerable to occupational stress, both in developed and developing world. Those predominantly affected belong to the labour class as in other developing countries. Work-related stress and mental fatigue are mainly blamed on expectations of better performance, deadlines and competition over the last few years. According to the increasing financial burden to support families; health disorders neglected due to job conditions and work conflicts. [8]

In our study, most of the subjects had increased score of perceived Job stress which correlated with increasing body mass. The hypothalamic-pituitary-adrenal (HPA) axis plays a central role in the regulation of energy metabolism through the actions of the glucocorticoids. Stress may contribute to HPA axis dysregulation, tendency to overeat, which in turn contributes to a cascade starting with obesity and ending with type 2 diabetes and CVD. [9] Dallman et al. proposed a mechanism by which food intake is rewarded during periods of stress because eating becomes associated, through negative feedback, with a reduction of central corticotropin-releasing factor (CRF) activation, a core component of the stress response. Dysregulation of the HPA axis has been documented in individuals exposed to chronic stress. The Whitehall II Study found a higher incidence of obesity in people reporting higher levels of job stress. The majority of studies examining stress- HPA axis relationships have either focused on job stress alone or treated body mass index (BMI) as a confounding variable and controlled for it rather than examining its independent relationship to stress and HPA axis function. In a review of the findings from several of their studies, Bjorntorp and Rosmond

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describe the neuroendocrine abnormalities associated with visceral obesity and report a decreased cortisol variability in relation to increased abdominal obesity. [10, 11]

Although we cannot establish causal pathways from this cross-sectional analysis, it is possible that higher stress levels caused altered HPA axis function, which in turn contributed to increases in BMI. But, the bidirectional nature of the relationship between BMI and stress, genetically mediated adaptations which might cause obesity and perceived stress as a consequence of social stigma associated with obesity cannot be ruled out. A key component of obesity is intra-abdominal accumulation of fat, which is responsible for a great portion of the increased CVD risk associated with obesity. [12]

Obese group in our study showed increasing osteopenia with increasing W/H ratio & BMI. In obesity, adipose tissue is infiltrated with an increased amount of macrophages, which are an important source of inflammatory cytokines. Obese humans express higher levels of TNF-a in adipose tissue than do lean individuals. Adipose tissue also produces other proinflammatory factors including interlukin-6 (IL-6) and C-reactive protein (CRP). Obesity has also been implicated in the development or progression of musculoskeletal diseases such as osteoarthritis, a common inflammatory bone disease. Obesity may decrease bone formation (osteoblastogenesis) while increasing adipogenesis because adipocyte and osteoblasts are derived from a common multi-potential mesenchymal stem cell. Obesity may increase bone resorption through upregulating proinflammatory cytokines such as IL-6 and TNF alpha. These proinflammatory cytokines are capable of stimulating osteoclast activity through the regulation of the RANKL/RANK/OPG pathway. Obesity is associated with significant increase in serum leptin and decrease in adiponectin. The action of leptin on bone appears to be complex and both positive and negative effects have been reported. [13, 14, 15]

V. Limitations of the Study

The results from this study might be limited to a localised region of Bangalore and cannot be directly compared with results from other parts of India considering the diversity in culture and other factors within the country. Another key limitation of this study is the number of study subjects. All statistical results are significant but certainly have a wide confidence interval. This clearly indicates a small sample size. Also, we have not measured any laboratory parameters indicative of stress like salivary cortisol, dehydro-epi-androsterone etc due to time constraints. To address these limitations, we are proposing a follow-up study of this sample to determine the prospective relationships among stress, obesity, and HPA axis dysfunction.

VI. Conclusion

Psychological stress appears to influence the body mass and osteopenia though the causal relationships among perceived stress, obesity, and HPA function remain to be elucidated. Identification of factors contributing to stress & effective counselling will have a greater impact on mental & physical health of industrial workers. Regular Health Education Programmes will ensure a good Quality of life (including Healthy lifestyle)& prevents morbidity. Prevention of osteoporosis & obesity by regular health check ups, good exercise & healthy diet should be a major concern.

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Automatic fall detection of elderly living alone at home environment

By Ivo T. Iliev , Serafim D. Tabakov , Ivan A. Dotsinsky
Technical University of Sofia, Bulgaria.

Abstract – Recently the problems connected with the ageing population all over the world have become more and more severe. Many projects have been developed to enable the people to live longer in home environment, thus keeping their independence together with reducing the expenses of the public health care. The results in this area have a quick public impact. Different sensor systems have been proposed for monitoring the functional abilities in elderly and for detecting their functional decline. The sensors are located in the bathroom, bedroom, closet, front door, kitchen, living room and shower. The statistic shows that 30% of the old people fall at least once a year and 75% of these events are responsible for accidental death. The feeling of fall increases the anxiety and the depression in the elderly. Therefore, the monitoring system must enable the caregiver to track remotely the user's walk around the rooms and to perceive immediately the falls without the need of confirmation request. We started to develop and implement a low-cost system directed to monitor the user walk, to detect the falls and to check the cardiac activity by analysing the photo-pletismographic signals. An interface for communication between the patient and health care expert is also provided. This paper is aimed to report the results obtained in reliable fall detection of solitary living elderly.

Keywords : *fall detection; elderly living alone; accelerometer signals.*

GJMR-N Classification: *NLMC Code: WA 300-39*

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Automatic fall detection of elderly living alone at home environment

Ivo T. Iliev[α], Serafim D. Tabakov[Ω], Ivan A. Dotsinsky[β]

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Keywords : fall detection; elderly living alone; accelerometer signals.

I. Introduction

Recently the problems connected with the ageing population all over the world have become more and more severe. In 2035 a third of the Europeans will be over 65 years old (Ambient Assisted Living Joint Programme, 2008; Communication from the Commission to the European Parliament 2010; COOP-005935-HEBE, 2006). People over age 65 in the United States are expected to hit 70 million by 2030. It has been reported (Qixin Wang et al., 2006) that the number of elderly people living alone in Korea has increased by 100% during the last ten years. According to data published by the Bulgarian National Institute of Statistics (2011), the relative part of the population older than 65 years has reached 23.5%. Nowadays, the average life expectancy is extended up to 80 years. At the same time the percentage of people with disabilities is dramatically growing (Giles et al, 2003). The need for health care and social assistance will lead to expense's growth by 4-8% of the Gross Domestic Product (De Ipiña et al, 2008). As a result, objectives about cost reduction in the public health services will arise simultaneously (COOP-005935-HEBE, 2006).

Ambient Assisted Living (AAL) is an initiative from the European Union (International newsletter on micro-nano integration, 2007), which is aimed to improve the life quality of adults by implementing new Information and Communication Technologies (ICT). The goal is to enable the people to live longer in home environment, thus keeping their independence together with reducing the expenses of the public health care. The results in this area have a quick public impact.

Aviles-Lopez et al (2010) tested in laboratory a platform intended to be implemented in nursing home. The concept of the AAL system is based on the appearance of new types of mobile and embedded computing devices. Data about blood pressure, sugar levels etc. should be acquired, derived and communicated in fast and reliable way. Other intelligent components of the care monitoring are the closed circuit camera system and the sensors with embedded accelerometer. The patients may also communicate the caregiver by depressing a button on their wearable tag or say another command. No details about the hardware and software implementation are given. The reported platform is planed to meet the needs of solitary living elderly by a sophisticated approach. However, the expected price of the instrumentation may be onerous for several users and nursing homes.

Alexander et al (2008) reported results of an expert review on sensor system used for monitoring the functional abilities in elderly and for detecting their functional decline. The sensors are located in the bathroom, bedroom, closet, front door, kitchen, living room and shower.

Healey and Logan (2005) presented a prototype wearable monitoring system capable of recording, transmitting and analyzing continuous ECG and accelerometer data. The system also provides an application for recording activities, events and potentially important medical symptoms. The authors conducted experiments using the system for activity monitoring, exercise monitoring and medical screening tests and reported good preliminary results. Sitting and walking activities were recorded in office environment by means of accelerometer. The RMS values of the signals or their variance were used for discriminating the

Author[α] : Assoc. Prof. PhD. Technical University of Sofia, Bulgaria. E-mail : izi@tu-sofia.bg
Author[Ω]: Assist. Prof. PhD. Technical University of Sofia, Bulgaria.
Author[β]: Prof. PhD. DSc. Bulgarian Academy of Sciences.

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epochs with lower and higher amplitudes, corresponding to sitting and walking movements.

Holtzinger et al (2010) evaluated the user acceptance of a wrist device, designed to monitor vital signs and to detect situations, such as falls, unconsciousness, etc., and aimed a further study to show the acceptance level of the elderly to the personal monitoring.

The statistic shows that 30% of the old people fall at least once a year and 75% of these events are responsible for accidental death (COOP-005935-HEBE, 2006). The feeling of fall increases the anxiety and the depression in the elderly. Therefore, the monitoring system must enable the caregiver to track remotely the user's walk around the rooms and to perceive immediately the falls without the need of confirmation request. Many technologies have been investigated for automatic fall detection: bed and chair pressure detection; vibration analysis; video monitoring; sensor devices like accelerometers, tilt sensors, gyroscopes; 'watch-type' and belt-worn' design. No descriptions of algorithms for fall detection are available.

We started to develop and implement a low-cost system directed to monitor the user walk, to detect the falls and to check the cardiac activity by analysing the photo-pletismographic signals. An interface for communication between the patient and health care expert is also provided. Some preliminary considerations were recently reported at the XX International Scientific Conference on Electronics'11, September 2011 in Sozopol, Bulgaria (Dimitrov et al; Sapundjiev et al). This paper is aimed to report the results obtained in reliable fall detection of solitary living elderly.

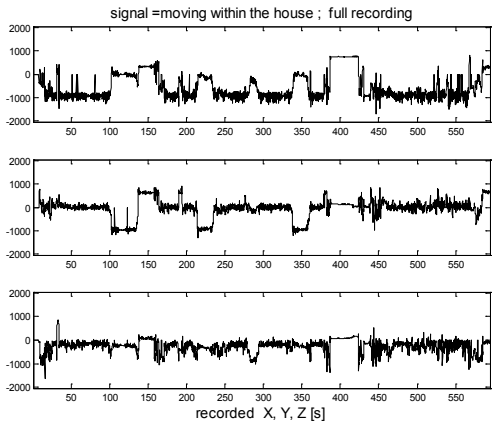
II. Materials

The selected and used sensor of motion activity is the 3D accelerometer LIS302DL, produced by Semiconductor Technology. Its parameters are: 3x5x0.9 mm size; power supply in the range of 2.16 V through 3.6 V; consuming power lower than 1 mW; 12C/SPI interfaces. The accelerometer signals are emitted according to the SimplisiTI protocol, using CC1110 and CC1111 (Texas Instruments) low-power sub-1 GHz system-on-chip (SoC) designed for low power wireless applications. The inherent sampling rate SR is near to 9 Hz; the digital code uses 8 bits but with irregular resolution.

Signals during different activities of a volunteer are stored in commonly used Laptop by an appropriately written program on Visual Basic. The recorded signals represent several epochs and episodes of movements within the house; falling on the floor; falling on the bed; sleeping; feeding; reading; and watching TV.

The acquired signals were further processed in MATLAB environment. They were studied in the time and the frequency domain to find the useful signal manipulation leading to reliable discrimination between fall detection and natural movements accompagnying other activities of the monitored subject.

Some of these signals are presented in Fig. 1 to Fig. 4, which show relatively long epochs of user's activities. The ordinate units are relative; the abscissas are scaled in *s*.



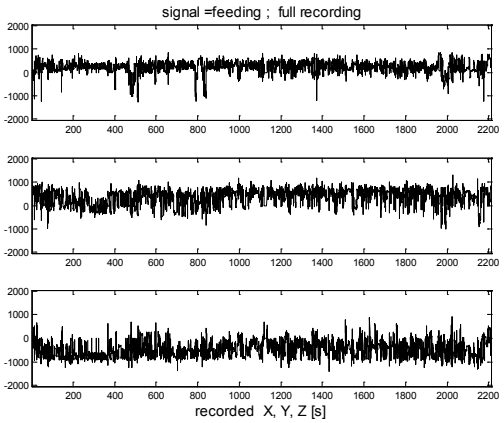
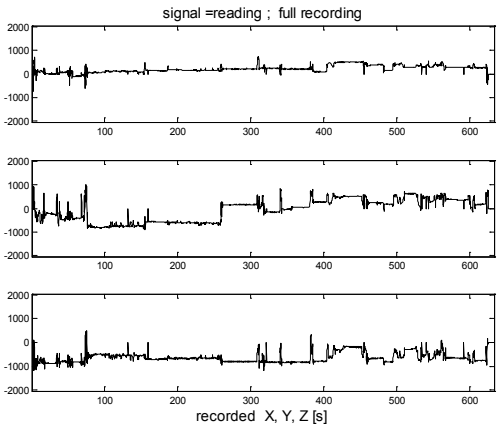


Fig. 1 : Moving within the house.
Fig. 2 : Feeding.



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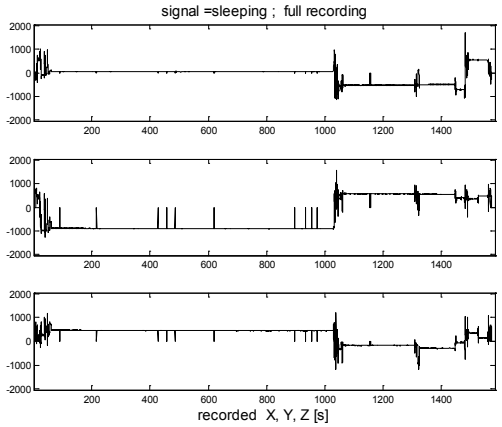

Fig. 3 : Reading.

Fig. 4 : Sleeping.

III. Algorithm

The signals generated by the accelerometer in the three space directions *X*, *Y* and *Z* are currently summed and a first derivative of the sum is calculated using its first differences. This derivative is then raised to second power but the result is divided by a coefficient of 32 to reduce the excessive amplification of the result. The value of 32, which is not crucial, is chosen because of the simple division. An appropriate threshold is finally introduced to detect user's falls among other normal movements.

Version of the algorithm, which calculates the first differences separately for each of the three signals before summing them, was tested without obtaining any advantages. Therefore, this version was abandoned since the computation time is slightly prolonged.

The first differences were taken first as signed and then as unsigned addends. No influence on the fall detection accuracy was observed. We speculate that on the one hand, the signed addends may give priority to the vertical signal component, which is practically unidirectional, while the other components collect bidirectional fluctuations. On the other hand, the unsigned non-vertical components may contribute to better discrimination between crucial fall on the floor and abrupt movement of elderly, which is going down to bed or armchair.

IV. Results and Discussion

The following Figures present selected episodes of different activities. The three signals *X*, *Y* and *Z*, shown in the first three subplots, are subjected to processing and analysis. The forth subplot depicts the differentiated sum of the signals, $V_1=\Delta V=\Delta (X+Y+Z)$; the fifth demonstrates the amplification of the high frequency components after raising to second power, $V_2= V_1^2/32$; and the last subplot may contain rectangular pulses that mark recognized falls in case they are simulated by the volunteer in the corresponding recording. The ordinate units are relative; the abscissas are scaled in *s*.

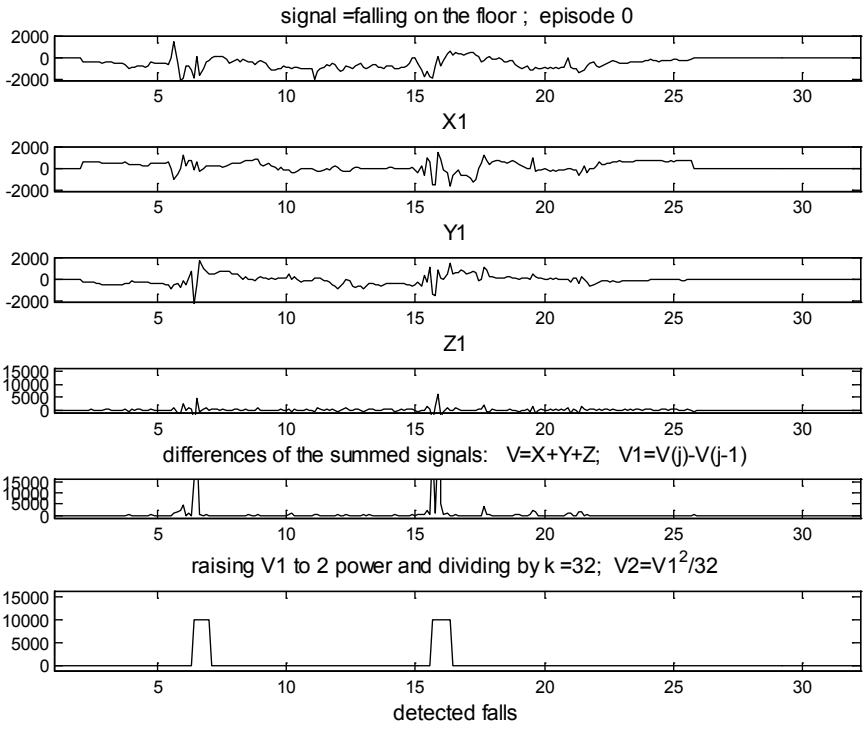

Fig. 5 : Correct fall detections on the floor.

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Fig. 5 shows two recorded falls, which are recognized. The parts of the signal corresponding to them are extremely emphasized compared to the movements before and after the falls. The fall patterns are going far beyond the vertical scale, which is reduced to be approximately near to the amplitude scaling of the other episodes thus allowing a correct assessment of the movement differentiation and detection.

Fig. 6 demonstrates the reliable suppression of user's normal movement, although the volunteer received instruction to try to introduce maximum amplitude of the extremities during the walk. No fall detections can be observed in the last subplot. This is normal since the processed signal (subplot 5) remains below 1000 relative units that are far from the 10000 units chosen as fall detection threshold.

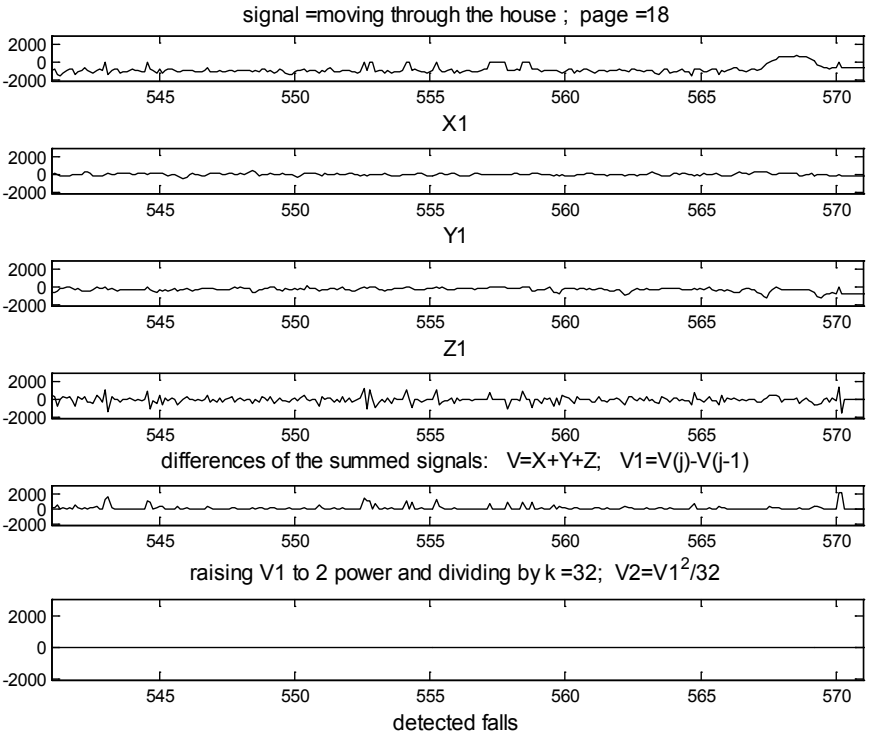

Fig. 6 : Neglected movements through the house.

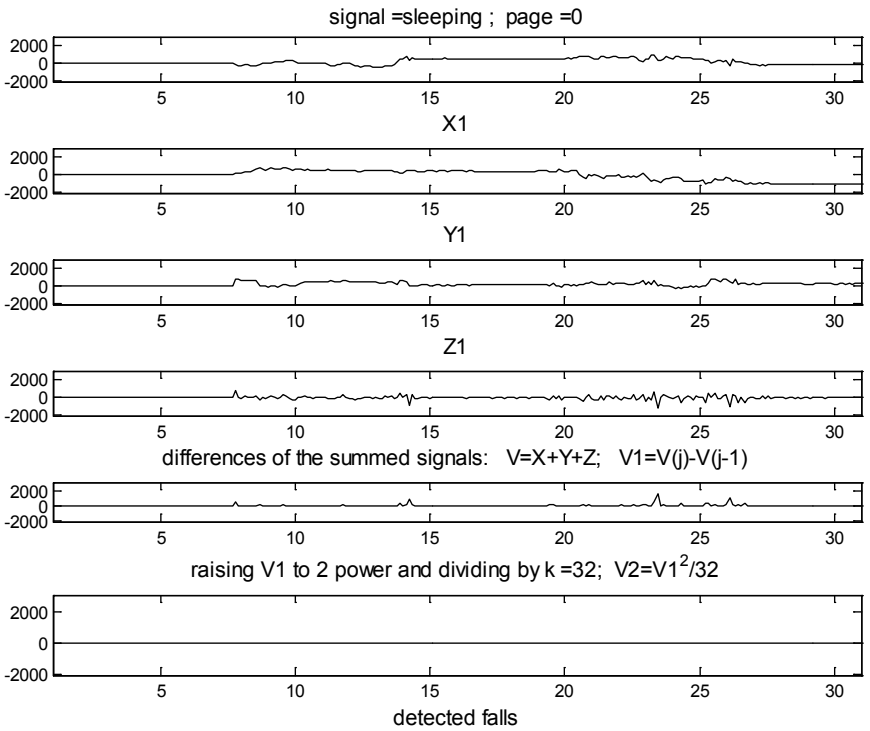

Fig. 7 : Neglected movements during sleeping.

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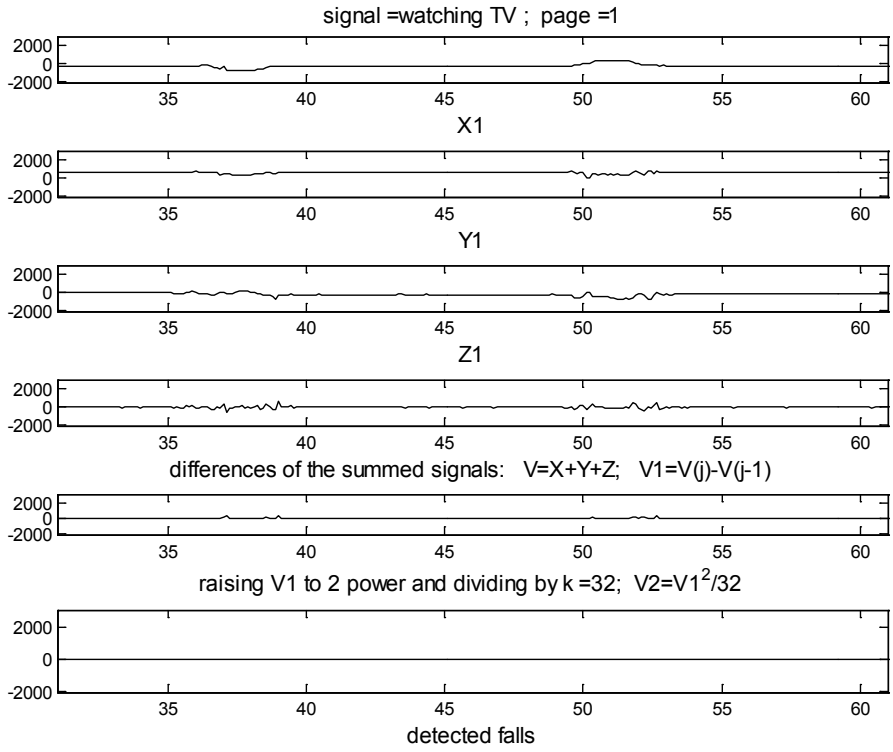

Fig. 8 : Neglected movements during TV watching.

The next Fig. 7 and Fig. 8 illustrate the accelerometer signals during sleeping and watching TV. The other not presented in the paper processed recordings do not differ from the shown episodes. Even the recommended to the volunteer jerky movements during several falls on the bed did not provoke false detections

V. Conclusion

The results obtained by processing numerous recordings of normal and abnormal movement of solitary living elderly prove that the developed algorithm for fall detection is extremely reliable. Besides, it is very simple and fast real time going.

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L-lysine Neuro-Dynamic Optimal Control

By Tatiana Ilkova , Mitko Petrov
Assist. Prof. PhD. Bulgarian Academy of Sciences.

Abstract – In this paper Neuro-dynamic programming (NDP) is proposed as an alternative to alleviate the "curse of dimensionality" of the Dynamic programming (DP) for optimal control of a fed-batch fermentation process in the L-lysine production. The most effective and cheapest method for the Llysine biosynthesis (in biological active form) is the microbiological method via a direct fermentation. In this paper an optimization method of the L-lysine production from strain Brevibacterium flavum 22LD is used and that is NDP. The results show that the quality of L-lysine enhances at the end of the process. The proposed method is particularly simple to implement and can be applied for on-line optimization.

Keywords : *dynamic programming, neural network, Llysine fermentation, optimal control.*

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L-lysine Neuro-Dynamic Optimal Control

Tatiana Ilkova [α], Mitko Petrov [Ω]

Abstract - In this paper Neuro-dynamic programming (NDP) is proposed as an alternative to alleviate the "curse of dimensionality" of the Dynamic programming (DP) for optimal control of a fed-batch fermentation process in the L-lysine production. The most effective and cheapest method for the L-lysine biosynthesis (in biological active form) is the microbiological method via a direct fermentation. In this paper an optimization method of the L-lysine production from strain Brevibacterium flavum 22LD is used and that is NDP. The results show that the quality of L-lysine enhances at the end of the process. The proposed method is particularly simple to implement and can be applied for on-line optimization.

Keywords : dynamic programming, neural network, L-lysine fermentation, optimal control.

I. Introduction

L-lysine is an essential amino acid, which means that it is essential to human health, but cannot be produced by the body. For this reason L-lysine must be obtained from food. Amino acids are the building blocks of the protein. Lysine is important for proper growth and it plays an essential role in the production of carnitine, which is a nutrient responsible for converting fatty acids into energy and helping to lower cholesterol.

The insufficient L-lysine quantity in the fodders reduces the biological value of the fodder doses, it also reduces the weight increase and the further productiveness of the agricultural animals, decreases the fodder quality, used for a kilogram growth and decreases the product quantity from animal origin. L-lysine is also used in the food industry for farming, in the medicine as a component of the infusion solution (blood substitutes) and as generally strengthening patent medicines. Lysine appears to help the body absorb and conserve calcium and it plays an important role in the formation of collagen, a substance which is important for the bones and connective tissues including skin, tendon, and cartilage (Anastassiadis, 2007).

Amino acids are the basic bioelements of proteins, which are the most important macromolecules for the functions of humans and animals. Out of the 20 L-amino acids, which are found worldwide in most of the living organisms, L-lysine is one of the nine essential amino acids for human and animal nutrition (Anastassiadis, 2007).

Author [α] : Assist. Prof. PhD. Bulgarian Academy of Sciences
E-mail : tanja@biomed.bas.bg
Author [Ω] : Assist. Prof. PhD. Bulgarian Academy of Sciences
E-mail : mpetrov@biomed.bas.bg

Neuro-dynamic programming (NDP) is proposed as an alternative to alleviate the "curse of dimensionality" of the Dynamic programming (DP). The term NDP expresses the reliance of the methods, described in this article with respect to both the DP and the neural network concepts. The term reinforcement learning is also used in the artificial intelligence community where the methods originated from. Using common artificial intelligence terms, the methods help the systems "learn how to make good decisions by observing their own behavior and use built-in mechanisms for improving their actions through a reinforcement mechanism" (Bertsekas & Tsitsiklis, 1996).

The key idea is to use a scoring function to select decisions in complex dynamic systems, arising from a broad variety of applications for engineering design, operations research, resource allocation, finance, etc. This is much similar to a computer chess, where positions are evaluated by means of a scoring function and the move that leads to the position with the best score is chosen. NDP provides a class of systematic methods for computing the appropriate scoring functions using approximation schemes and simulation/evaluation of the system's performance (Driessens & Dzeroski, 2004).

Using common artificial intelligence terms, the methods allow the systems to "learn how to make good decisions by observing their own behavior and use built-in mechanisms for improving their actions through a reinforcement mechanism". In more mathematical meaning "observing their own behavior" relates to simulation and "improving their actions through a reinforcement mechanism" relates to the iterative schemes for improving the quality of approximation of the optimal cost function, the Q-factors or the optimal policy. There has been a gradual realization that the reinforcement learning techniques can be fruitfully motivated and interpreted in terms of classical DP concepts such as the value and policy iteration (Barto et. all, 1995; Sutton, 1988).

NDP is a relatively new class of the dynamic programming methods for control and sequential decision making under uncertainty. These methods have the potential of dealing with some problems that were thought to be intractable for a long time due to either a large state space or the lack of an accurate model. They combine ideas from the fields of neural networks, artificial intelligence, cognitive science, simulation, and approximation theory. In recent years

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the method has been applied successfully for an optimal control of fermentation process (FP). The literature sources show that the calculating time is significantly reduced, while the desired products quantity is increased (Kaisare et. all, 2003; Ikova & Petrov, 2008).

The aim of this study is to develop optimal feed rate strategy of biotechnological process in L-lysine production using Neuro-dynamic control.

II. Process Specifics and L-Lysine Production Mathematical Model

The development of a multi-step bio-technological process requires three steps, comprising of:

- Identification and characterization of a suitable biological system (microorganism, biocatalyst).
- Increase of bioreactor productivity by systematic media optimization and adaptation of fermentation technology to a developing process.
- Downstream process (cell separation by centrifugation or ultrafiltration, separation, evaporation and drying) (Anastassiadis, 2007).

In addition to physical parameters like pH, agitation and aeration rate, air saturation, temperature, dissolved carbon dioxide and foaming, the medium composition is a very important factor highly influencing fermentation processes, which are often a subject of extensive process development and optimization studies. The culture medium has to satisfy the requirements of microbial growth and production in a suitable manner. L-lysine can be produced either using a chemical or a biochemical method, which is economic, even though relatively low yields are obtained during the extraction of L-lysine, requiring specific installations and the use of expensive products. The stereospecificity of amino acids and the steadily increasing L-lysine demand necessitates indispensably their fermentative production (the L isomer) over synthetic processes.

The experimental investigations are done in a 15 L bioreactor that is included in an Automatic Control System. The Automatic Control System is flexible and includes control of the following parameters of the process: rotation speed, oxygen partial pressure, temperature, pH, foam level, gas flow rate, flow rates of the main substance. The process is led in the next conditions:

- Temperature T=300C;
- pH pH=6.8-7.6;
- pO_2 pO_2=20-30%;
- Gas flow rate Q_G=60 L h-1;
- Rotation speed n=450 min-1;
- Maximum bioreactor volume 15 L.

For the L-lysine fermentation defined media is used which acquires nutrients that require pure growth and essential additives or alternatively undefined media containing natural organic substances such as soybeanhydrolyzate, corn steep liquor, yeast extract or peptone is used. Common fermentation media for L-lysine production contain various carbon and nitrogen sources, inorganic ions and trace elements (Fe++, Mn++), amino acids, vitamins (biotin, thiamine-HCl, Nicothin amide) and numerous complex organic compounds. An upper expression of genes is also achieved by optimizing the composition of the media and the culture technique in addition to the physiological and genetic parameters (Anastassiadis, 2007).

The model of the fed-batch processes includes the dependences between the concentrations of the basic variables of the process: cell mass concentration (bacteria Brevibacterium flavum), substrate concentration, L-lysine, Threonine concentration and oxygen concentration in the liquid phase. The general scheme of the L-lysine is shown in Figure 1.

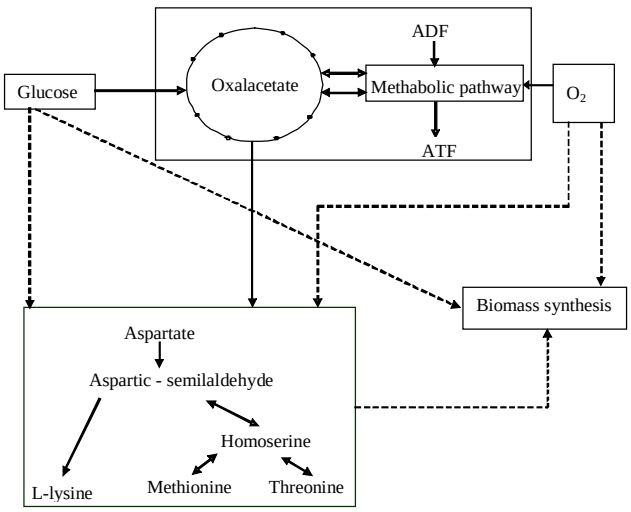

Fig.1 : A general metabolite pathway of the L-lysine biosynthesis.

The mathematical model of the process is based on the mass balance equations as a perfect mixing in the bioreactor is adopted. The model of the process has the following type (Anastassiadis, 2007):

$$\frac{dX}{dt} = \mu X - \frac{F}{V} X \quad (1)$$

$$\frac{dS}{dt} = \frac{F}{V}(S_{in} - S) - k_5 \mu X - k_6 X - k_7 \eta X \quad (2)$$

$$\frac{dTr}{dt} = \frac{F}{V}(Tr_{in} - Tr) - k_{13} \mu X - \frac{F}{V} Tr \quad (3)$$

$$\frac{dC_L}{dt} = k_l a(C^* - C_L) - k_{14} \mu X - k_{15} X - k_{16} \eta X - \frac{F}{V} C_L \quad (4)$$

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$$\frac{dL}{dt} = \eta X \quad (5)$$

$$\frac{dV}{dt} = F \quad (6)$$

The specific rate of L-lysine synthesis and specific consumption rate have the following form:

$$\mu = \frac{k_1 Tr\ C_L}{[(k_2 + Tr)(k_3 + S_0 - S)(k_4 + C_L)]} \quad (7)$$

$$\eta = \frac{k_8 S C_L}{[(k_9 + S)(k_{10} + S)(k_{11} + C_L)(k_{12} + C_L)]} \quad (8)$$

where: μ – specific rate of L-lysine synthesis, h^{-1}; η – specific consumption rate of L-lysine, h^{-1}; X – biomass concentration, g l^{-} ; L – L-lysine concentration, g l^{-1}; S – glucose concentration, g l^{-1}; V – working liquid volume, l; F – feed flow rate, l h^{-1}; Tr – Threonine concentration, mg l^{-1}; t – process time, h; C_L – dissolved oxygen concentration, g l^{-1}; C* – equilibrium dissolved oxygen concentration, g l^{-1}; S_{in} – input feed substrate concentration, g l^{-1}; Tr_{in} – input feed Threonine concentration, g l^{-1}; $k_l a$ – volumetric liquid mass transfer coefficient, h^{-1}.

The initial conditions in the model (1) - (8) have the follows values:

$X(0) = X_0 = 3.00$ g l^{-1}; $S(0) = S_0 = S_i = 100.00$ g l^{-1}; $Tr(0) = Tr_0 = Tr_{in} = 100.00$ mg l^{-1}; $L(0) = 0.00$ g l^{-1}; $C_L(0) = C^* = C_0 = 6.1 \times 10^{-3}$ g l^{-1}; $V(0) = V_0 = 10.00$ l.

The model coefficients in (1) - (8) have the following values:

$k_1 = 20.8$, $k_2 = 42.0$, $k_3 = 28.0$, $k_4 = 1.1$, $k_5 = 1.01$,
$k_6 = 0.07$, $k_7 = 0.51$, $k_8 = 62.0$, $k_9 = 28.0$,
$k_{10} = 37.0$, $k_{11} = 4.0$, $k_{12} = 0.12$, $k_{13} = 6.10$,
$k_{14} = 448.0$, $k_{15} = 22.0$, $k_{16} = 209.0$, $k_l a = 120$.

III. Neuro-Dynamic Optimal Control of the Process

The objective of this work is to find the optimal feed flow rate (F(t)) of a fed-batch process, such as the L-lysine production that will raise L-lysine at the end of the process, i.e.:

$$\max_u Q = \int_{t_0}^{t_f} L(t)V(t)\,dt \quad (9)$$

where: t_0 – initial time, t_f – final time of the fermentation. Therefore, the control objective is to drive the reactor from the low product steady state to the desirable high product rate. It may be considered as a step change in the set point at time t=0 from the low product concentration to the high product concentration steady state.

In the systems the decisions are made in stages. The outcome of each decision is not fully predictable but can be anticipated to some extent before the next decision is made. Each decision results in some immediate cost, but it also affects the context in which the future decisions are to be made and thus it affects the cost incurred in future stages. DP provides a mathematical formalization of the tradeoff between the immediate and future costs. Generally, in DP formulations there is a discrete-time dynamic system whose state evolves according to the given transition probabilities that depend on the decision/control u.

DP is an elegant way to solve the introduced optimization problem (9). It involves a stagewise calculation of the cost-to-go function to arrive at the solution not just for a specific initial state, but for a general initial state. Once obtained the cost-to-go function, represents a convenient vehicle to obtain the solution for a general state. In very few cases the stagewise optimization to obtain analytically a closed-form expression for the cost-to-go function has been solved. The conventional approach to the problem involves gridding the state space, calculating and storing the cost-to-go for each grid points as one marches backward from the first stage to the last. For an infinite horizon problem the number of iteration required for convergence can be very big. Such an approach is seldom practically feasible due to the exponential growth of the computation with respect to the state dimension. Unfortunately, from the very beginning it was apparent that an increase of the dimensionality of the problem, i.e. an addition of reservoirs, caused an exponential increase in the time required to find a solution. This is referred to as the "curse of dimensionality", which must be removed so that this approach can find a widespread use.

NDP aims to develop a methodological foundation for combining dynamic programming, compact representations, and simulation to provide the basis for a rational approach to complex stochastic decision problems (Bertsekas & Tsitsiklis, 1996; Kaisare et. all, 2003).

Two fundamental DP algorithms, policy iteration and value iteration, are the starting points for the NDP methodology. The most straightforward adaptation of the policy iteration method operates as follows: we start with a given policy (a rule for choosing a decision u at each possible state i), and we approximately evaluate the cost of that policy (as a function of the current state) by least-squares-fitting a scoring function to the results of many simulated system trajectories using that policy. A new policy is then defined by minimization in Bellman's equation where the optimal cost is replaced by the calculated scoring function and the process is repeated. This type of algorithm typically generates a

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sequence of policies that eventually oscillates in a surrounding of an optimal policy. The resulting deviation from optimality depends on a variety of factors, principal among which is the ability of the architecture of scoring function to accurately approximate the cost functions of the various policies.

NDP uses simulated process data received under suboptimal policies to fit an approximate cost-to-go function – generally by fitting artificial network. With the value iteration approach NDP the initial approximate cost-to-go function in the future was improved by an iteration procedure based on Bellman equation. In this way the simulation role has two points. First, by simulation the process under a reasonably chosen suboptimal policy and all possible operating parameters it provides set data points that define the relevant "working" region in the state space. Second, the simulation provides the cost-to-go value under the suboptimal policy for each state visited, which iteration of the Bellman equation can be initialed with (Kaisare et. all, 2003).

In this paper we will demonstrate NDP approach not only for reducing the computational demand, but also for improving the controller performance through the use of the cost-to-go approximator. A neural network is chosen as an approximator to obtain cost-to-go as a function of system states. While a properly trained neural network has good interpolation capabilities, one may not be used to extrapolate over the regions of state space that are not covered during its training. Extrapolation by neural network results in deteriorated performance of the controller.

The policy improvement theorem states that a new policy that is greedy (a greedy policy is one whose current cost is the least) with respect to the cost-to-go function of the original policy is as good as or better than the original policy.

When the new policy is as good as the original policy the above equation becomes the same as Bellman equation.

The relevant regions of the state space are identified by simulation of NDP control and the initial suboptimal cost-to-go function is calculated from the simulation data. In this survey a functional approximator is used to interpolate between this data. The improvement is obtained through the iteration of the Bellman equation. When the iteration converge this off-line computed cost-to-go function can be used for an on-line optimal control calculation for the bioreactor (Xiong & Zhang, 2005).

NDP uses neural network approximations for the approximation of cost-to-go function. The cost-to-go function was not used to generate an explicit control law; instead, it was used in an on-line optimization to reduce the large (or infinite) horizon problem to a relatively short horizon problem. The method was found to be robust to approximation errors. Both deterministic (step changes in kinetic parameters) and stochastic problems (random variations in kinetic parameters and feed composition) were explored Lee J.M., & Lee, J. H., 2009; Tosukhowong & Lee J. H., 2009).

a) NDP algorithm

The following notations are used for description of the algorithm:

The general simulation-approximation scheme involves computation of the converged cost-to-go approximation off-line. The architecture of the scheme is shown in Figure 2. Step 1, Step 2, Step 3 and Step 4 represent the "Simulation part", and 5 and 6 the "Cost Approximation Part".

The simulation-based approach involves computation of the converged profit-to-go approximation off-line. The following steps describe the general procedure of NDP algorithm:

1. Performing of simulations of the process with chosen suboptimal policies under all representative operating conditions. Starting with a given policy (a rule for choosing a decision u at each possible state i), and approximately evaluate the cost of that policy (as a function of the current state) by least-squares-fitting a scoring function to the results of the many simulated system trajectories using that policy.
2. Calculation of the ∞-horizon cost-to-go for each state visited during the simulation, using the simulation data. The solution of one-stage-ahead cost plus cost-to-go problem results in the improving of the cost values. Cost-to-go is the sum of the single state cost from the next point to the end of the horizon.
3. The deviation, which is a result of the optimality, depends on a variety of factors, principal among which is the ability of the architecture of Bellman function to approximate accurately the cost functions of the various policies.
4. A new policy is then defined by minimizing Bellman's equation where the optimal cost is replaced by the calculated scoring function and the process repeats. This type of algorithm typically generates a sequence of policies that eventually oscillate in a surrdounding of an optimal policy.
5. Fitting a neural network function approximator to the data to approximate the cost-to-go function as a smooth function of the states.
6. As described above the improved costs are again fitted to a neural network, to obtain subsequent iterations of Bellman functions, and so on ..., until convergence is accomplished.
7. Policy update may sometimes be necessary to increase the coverage of the state space. In this case more suboptimal simulations with the updated policy are used to increase the coverage or the number of the data points in certain region of the state space.

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The NDP algorithm block- scheme is shown in Fig. 2.

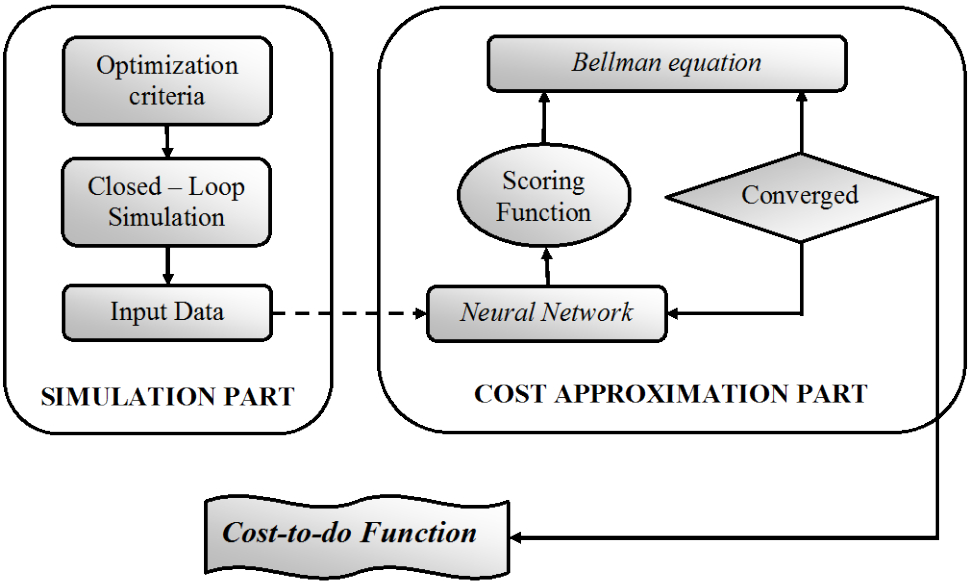

Fig.2 : NDP algorithm block-scheme.

Take into consideration that when starting with a fairly good approximation of the cost-to-go (which has to be a result of using a good suboptimal policy), the cost iteration has to converge fairly fast – faster than the conventional stagewise cost-to-go calculation.

The next values of F are examined 0.2, 0.4, 0.5, 0.7, that can cover the possible rang of variations. The bioreactor was started at three different W(0) values for each of the parameter values around the low product yield steady state.

A functional approximation relating cost-to-go with augmented state was obtained by the neural network – with five hidden nodes, six input nodes and two output nodes. The neural network presented a good fit with a mean error of 10-3 after training for 1000 epoch.

Improvement of the cost-to-go is obtained through the iterations of the Bellman equation. This method is known as a value iteration (or value iteration). The solution of the one-stage-ahead cost plus cost-to-go problem, results in the improvement of the cost values. The improved prices were again fitted to the neural network, described above to obtain subsequent iterations of Belman function and so on ..., until they are converged. Cost is said to be "converged" if the sum of the absolute error is less than 5% of the maximum cost. The cost is converged in 7 iterations for our system.

The converged cost-to-go function from above was used for solving the one-stage-ahead problem.

The optimal value of feed flow rate before and after optimization is shown in Fig.3. The L-lysine production before and after optimization is shown in Fig.4. Fig.4 shows the increase of the L-lysine after optimization by 39.41%.

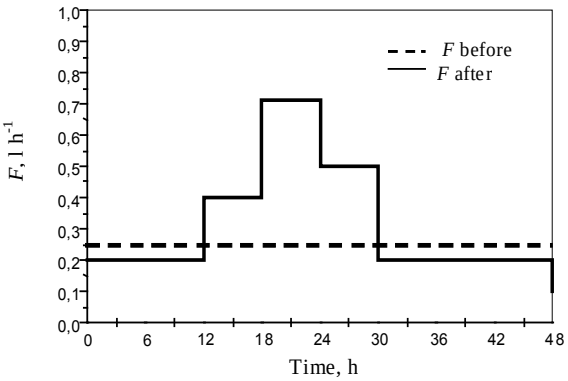

Fig.3 : Optimal feed flow rate before and after optimization.

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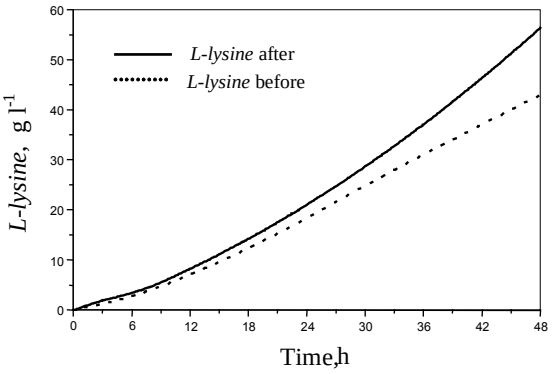

Fig.4 : L-lysine concentration before and after optimization

The process was stopped at the 48th hour because at this hour the fermentation was led. For proving of the choice of stopping of the optimization final hour the procedure was extended to the 54th hour. The results show that after 48th the process stands still and it continuing is economically disadvantageous. It becomes clear that after 48th the process goes into a steady state. Therefore, the fixed right end for 48 hours is appropriate.

In this optimization problem the time is discredited in six hours. It is assumed that this is a step of discretization of this process in terms of features and well-known computational difficulties.

IV. Conclusion

An approach for the optimal control of fermentation processes for a L-lysine fed-batch fermentation is developed for searching an optimal feed rate strategy using Neuro-dynamic control. It is proposed as a method for alleviation of the "curse of dimensionally" of DP.

The conventional approach to solving an optimization problem with DP method involves gridding of the state space, solving the optimization for each grid point and performing the stagewise optimization until convergence. Exhaustive sampling of state space can be avoided by identifying relevant regions of the state space by simulation under judiciously chosen suboptimal policies, which is presented using NDP methods with the help of a neural network for functional approximator.

The results show that the L-lysine quantity is highly raised at the end of the process which is the desired criterion for process quality. The result shows that NDP is a convenient and easy to use application method for optimal control. The approach is particularly simple to implement and it should be used for on-line implementation, after necessary additional training of the relevant neural network is obtained.

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the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

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7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

8. Use the Internet for help: An excellent start for your paper can be by using the Google. It is an excellent search engine, where you can have your doubts resolved. You may also read some answers for the frequent question how to write my research paper or find model research paper. From the internet library you can download books. If you have all required books make important reading selecting and analyzing the specified information. Then put together research paper sketch out.

9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

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15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

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16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. **Pick a good study spot:** To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. **Think technically:** Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be

sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page

- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

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Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to

shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.
- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic

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principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.

- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

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The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

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- The **major constraint** is that you must independently make all content, tables, graphs, and facts that are offered in the paper. You must write each part of the paper wholly on your own. The Peer-reviewers need to identify your own perceptive of the concepts in your own terms. NEVER extract straight from any foundation, and never rephrase someone else's analysis.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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