Proceedings of the 7th Annual World Conference
of the Society for Industrial and Systems Engineering,
Binghamton, NY, USA
October 11-12, 2018

A Psychophysical Approach for Predicting Maximum Voluntary Contraction in Jordanian Cancer Patients at King Hussein Cancer Foundation Centre

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Abstract: Latest research shows that the handgrip strength is a significant factor in term of influencing an individual's performance in general. In this research, handgrip strength is linked with cancer-related fatigue (CRF) to be used as a subjective sense of tiredness and reduction of physical function. This research determines handgrip strength for cancer patients through measuring the Maximum Voluntary Contraction (MVC) for hand muscles, which is considered as a reliable tool for patient physical assessment. We chose a sample of 49 Jordanian cancer patients under treatment at King Hussein Cancer Center (KHCC) with ages range from 20 to 66 years old. A digital hand grip dynamometer was employed to measure the MVC data. Five different factors are involved as follows: Gender, Age, Cancer Type, Height, and Body Mass Index (BMI). The outputs (i.e., MVC values) were analyzed using Statistical Analysis methods, Mathematical Modeling and Neural Network Analysis, results were obtained in relation to the previously mentioned factors, independently. We found that the cancer type has major effects on MVC values, whereas Limited effects are found for BMI, Height, Age and Gender.

Keywords: Jordanian Cancer Patients, Isometric Hand Muscle Strength, Maximum Voluntary Contraction, Isometric Endurance Limit

Introduction

Although cancer is not a contagious disease, it is one of the most life-threatening diseases. Furthermore, it can badly affect the patient's lifestyle and the physiological state (Tolar & Neglia, 2003). Much research shows that environmental factors are responsible for around 95% of cancer cases, leaving only 5% due to genetics and other factors. Kravchenko et al. (2009) States that lifestyle factors such as smoking, stress, lack of physical activity and obesity increase the chance of developing cancer, besides other major cancer-causing factors, such as radiation, and pollution. Cancer types can be specified on tumor type (American Cancer Society, 2004). However, many other classifications can be found in the literature according to the effect and impact, such as extended cancer treatment periods, side-effects, patient's lifestyle and patient's special management.

Segen (2002) defines MVC as "the maximum force achieved in one single voluntary effort" and Tufts' University Nutrition Collaborative Center defines the same term as "power grip force resulted of forceful flexion of all finger joints" . Furthermore, Handgrip Strength test (HGS) is involved as an indicator of overall muscle strength (Mazzuoli et al., 2011).
In general, a person with strong hand has a strong body. Therefore, the MVC test is often used as an induction of general muscle strength (Al-Momani 2015).

Previous research on MVC shows the correlation with different diseases; for example, The American Academy of Neurology's (2014) proved that the people with lower MVC have a high risk of heart disease, especially if the age is over 65. Furthermore, Gerontology Department at Ain Shams University, Cairo (2013) proved that the lower MVC, the high chance of developing chronic kidney diseases. Nutritional status, composition of bone, and mental illness conditions affect the MVC as per Sirajudeen et al. (2012), Sanderson et al. (2014) and The American Academy of Neurology (2014). Mazzuoli et al. (2011) states that HGS is strongly correlated with postoperative complications and the length of hospital stay. They states that "cachexia seems to be a predominant cause of decreased muscle strength in patients, as most cachectic patients lose muscle mass, and strength" and "Muscle mass can be lost at 1% per month and strength at 2-4% per month in older advanced cancer patients" (Edgar et al. 2012). Granger, et al. (2013) defines Physical activity as any bodily movement produced by skeletal muscles, and result in energy consumptions, and explains that non-small cell lung cancer (NSCLC) is associated with impaired physical status and diminished physical activity, mainly due to the disease's treatment, whether it was surgery, chemotherapy, or radiotherapy. Varied physiological and psychological effects are prevalent in NSCLC, such as "exercise intolerance, weakness, and impaired gas exchange, and commonly a cycle of declined functionality ensues".

Kerri et al. (2012) implies that cancer survivors can safely engage in resistance exercises to improve lower and upper body strength, reducing the risk of falls, or future disability. Kerri et al. (2012) assures that "it can reverse muscle weakness, restore balance, and reduce falls and declined functionality in elders, even without cancer". Strategies to promote resistance training improve muscle strength greatly. Many researchers got the result that patients with lymphedema have lower and upper extremity muscle strength and greater activity limitation than normal people, in fact, it has been shown that resistance-strengthening exercises do not aggravate lymphedema, but cause additional swelling, and significantly reduced proximal arm volume and improved quality of life. Cancer patients have symptoms associated with reduced physical function, quality of life and subjective sense of tiredness. Evans, and Koichi T. et al, (2016) state the need to improve the quality of life for patients, and to address the issues surrounding cachexia. ANCOLI et al, (2001) states that in general, the relationship between cancer type and fatigue measured by MVC remains largely unknown and also affected by psychosocial factors (depression, anxiety insomnia, chronic pain, and nausea), beside treatment side-effects (surgery, radiotherapy, and chemotherapy).

Handgrip dynamometry, per Barata et al. (2016) is used to evaluate skeletal muscle function, it is a none costly measurement used to assess the functional capacity in patients. They explain that it is noninvasive, economic, portable, user friendly and sensitive to the short-term changes in the muscular function preceding disease-related malnutrition. Hand dominancy, studied by Kilgour et al, (2010, 2013) found predicted a variance of (3.2%) in right-sided HGS and of (2.7%) in left-sided HGS. Height effect: Alex et al, (2013) stated that there is strong relationship between height and dominant Maximum voluntary contraction (hand grip strength), For BMI effect: Montes (2001); Minnal (2014); Al Meanazel (2013), Hesham, 2015, Montes (2001) and Stulen and De Luca (1981) mentioned that MVC have strong relation with BMI, muscle diameter and also depends on muscle strength, some of above researchers mentioned that MVC depends on brain-related factors.

For Age effect: many researchers stated that no effect of age on isometric muscle strength (Chatterjee and Chowdhury (1991) and Yassierli et al, (2003) found same result at certain fraction of 40% of MVC, also mentioned is independent on gender in contrast with Bohannon et al, (2006) who stated that there is strong relationship between MVC and both (gender and age).For isometric endurance limit, on Chatterjee and Chowdhuri (1991) and Caldwell (1963) stated that there is no relationship between height effect and IE but there is strong relationship between. BMI and IEL according to Crosby and Wehbe (1994), Hesham, (2015), Fraser et al, (1999), Montes (2001), Sheriff et al,, (2012), Al Meanazel (2013), and Minnal (2014).

Research Methodology

This research experiment was done for [49] Jordanian Cancer patients at King Hussein Cancer Foundation (KHCC). Subjects did not have any physical hand injuries. Anthropometric measurements have been collected, and descriptive statistics can be summarized as follows: Age (20-62years), Weight (54-90Kg), Height (146-191cm), and BMI (19.133-34.716) for Males. Age (22-66years), Weight (56-90Kg), Height (147-181cm), and BMI (21.3-41.65) for Females. The dependent variables are: (MVC], and the independent variables are: Age (6 levels), Cancer Type (10 levels), BMI (3 levels), Height (3 levels), Gender (2 Levels) as shown in Table 1-1 below:

Table 1. Dependent and Independent Variables with their Levels

Dependent Variables	Independent Variables	Treatment Levels
MVC	Age (years)	1) A0: (20 – 25), A1: (25-30), A2: (30-35), A3: (35-40), A4: (40-45), A5: (> 45)
Fixed Factors	Cancer type	1) Colorectal Cancer(CC), Liver cancer(LC), Prostate gland(PG), Lymphoma(L), Thyroid Cancer(TC), Leukemia(LY), Non-small cell lung cancer(NSCLC), Head and neck cancer(HANC), breast cancer(BC), bone cancer(BNC)
1- Jordanian 2- Digital Dynamometer	Body Mass Index (BMI)	Small: S (19 – 25), Medium: M (25 – 30), Large: L (> 30)
	Height	Short: S (<= 170), Medium: M (170 – 181), Tall: T (> 181)
	Gender	Male , Female

Measuring tape was used to measure heights in (cm) and the Handgrip Circumference, a digital stopwatch was used to record the Endurance Limit (to the nearest .01sec) and a digital scale to measure weights in (kg). The objective of the research is to find and verify the major factors that affect static and dynamic grip forces in exertion and obtain the measurements for MVC. Subjects participate in the experiment at different times and under the same conditions. The overall research methodology and procedure to conduct MVC test is shown in Table (1-2) attached with this document.

Table 2. Overall Research Methodology for cancer patients

Start
Participants 49 cancer patients (Males and Females)
Gather Anthropometric Data (Independent Variables) 1. Age , 2. Weight, 3. Height , 4- Cancer Type, 5- Calculated BMI , 6- Gender
Maximum Grip Strength Test 1. Sitting with 180-degree hand to elbow 2. Hand grip Dynamometer adjusted to fit the GC 3. Each subject to exert maximum force on the Dynamometer 4. Do three Maximum Grip strength tests (for MVC) for 5 seconds , and 5-minute rest

The analysis included an Analysis of Variance (ANOVA), using Minitab 17, followed by the use of different modeling techniques to build models to predict MVC, also using Minitab 17. The detailed Analysis is attached in document, as Table 1-3. Below:

Table 3. Data Analysis and Modeling Methodology

Analysis and Modeling Methodology
MVC Data
Descriptive statistics (Model Adequacy Checks)
Perform ANOVA for Dependent Variables (MVC)
Develop Linear Regression (LR) Models
Develop Non-Linear Regression (NLR) Models
Develop Neural Network Model

Results And Discussion

(Maximum voluntary contraction (MVC) test: MVC (in Kg))

The experiments were performed on 49 subjects (20 to 66 years old), experiment results were analyzed in the following manner. First, descriptive statistics were provided. Then, correlation analysis, normality test, and outlier analysis were conducted. Since several dependent variables were considered in this study, ANOVA, using Minitab 17. In addition, linear and non-linear regression models were developed and compared, linear and non-linear regression models were developed and compared in addition to development Neural Network Model.

For maximum voluntary contraction analysis and discussion, the descriptive statistics were provided above, full factorial design of experiment for the following factors, level and values, (Age, 6 Levels, (A0, A1,A2, A3, A4, A5), (Height, 3 Levels,(S, M,T), (BMI, 3 Levels, (S, M,L) and (Cancer type,10 Levels,(BC, BNC, CC, HANC, L, LC, LY, NSCLC, PG, TC), tables 1-4 and 1-5 shows the ANOVA results for males and females, Model adequacy checks were tested for MVC data and found that assumptions are met for constant variance normality and independency, ANOVA with 85% confidence level was used to test the effects of the independent factors considered the overall situation of cancer patients status. Hypothesis is presented as none of the experiment independent variables have any effect on the output dependent variable, residual plots consist of normal probability plot, uniform distribution vs fits, uniform distribution vs order, and normal histogram shape distribution are developed and residual plots support normality assumption, table 1- 4 below show ANOVA results

Table 4. Analysis of Variance for General Factorial Design Males and Females

Source	DF (M)	Adj SS	Adj MS	F-value	P-value	DF (F)	Adj SS (F)	Adj MS (F)	F-value (F)	P-value (F)
Model	15	357.27	23.818	1.88	0.122	15	149.216	10.658	1.04	0.539
Linear	15	357.27	23.818	1.88	0.122	15	149.216	10.658	1.04	0.539
Age(cat)	5	60.33	12.066	0.95	0.477	5	38.823	7.765	0.76	0.621
Height(cat)	2	10.71	5.356	0.42	0.663	1	3.199	3.199	0.31	0.605
BMI(cat)	2	19.56	9.778	0.77	0.480	2	7.66	3.830	0.38	0.709
Cancer Type (cat)	6	234.22	39.036	3.09	0.038	6	96.728	16.121	1.58	0.0343
Error	14	176.97	12.641			4	40.814	10.203		
Total	29					20				

Major significant factor found is the cancer type, non-significant factors are BMI, Height, Age and Gender, this design concern R-sq = 78.25% For Males , and for females with R-sq = 80.75%, the patients bad psychological state might affect the experiment results. to get rid of multicollinearity issue, all significant factors are considered. MVC linear and non-linear regression equations were extracted using Minitab -17

Linear Model (Female), MAX MVC = 43.2 - 0.1136 Age - 0.048 Height - 0.179 BMI, (1)

Linear Model (Male), MAX MVC = 1.3 - 0.0872 Age + 0.0946 Height 0.478 BMI (2)

Non Linear Models, Males) MAX MVC = Age * Height / (-21.2207 + 8.64093 * Age + 0.00951782 * Age * Height - 0.122441 * Age * BMI) (3)

Non Linear Models, Female) MAX MVC = Age * Height / (-20.3595 - 4.17447 * Age + 0.0573285 * Age * Height + 0.0619121 * Age * BMI) (4)

For age effect results, there were a limited number of studies that covered the age groups of 20-25 and 40-50 years old. Most researchers do not agree on the most significant age group, possibly as a result of different experimental conditions. This dissertation includes age groups with 5-year age intervals, experiment result shows that for males, Highest MVC Value was for A1(25-<30): 32.8 kg, and Lowest MVC Value (Kg) for A5 (Above 45): 18.9 kg and for females Highest MVC Value was for A2 (20-<25): 31.4 kg, and Lowest MVC Value (Kg) for A5(Above 45): 20.1kg, Table 1- 5 linear equations for Max MVC with age effect.

Table 5. linear equations for Max MVC with age effect (Males & Females)

	Males	Females
A0	MVC = 3.2 - 0.295 Age + 0.0998 Height + 0.505 BMI	MVC = 50.7 - 0.340 Age - 0.075 Height - 0.278 BMI
A	MVC = 5.6 - 0.295 Age + 0.0998 Height	MVC = 59.5 - 0.340 Age - 0.075 Height -

1	+ 0.505 BMI	0.278 BMI
A 2	MVC = 4.5 - 0.295 Age + 0.0998 Height + 0.505 BMI	MVC = 56.3 - 0.340 Age - 0.075 Height - 0.278 BMI
A 3	MVC = 9.3 - 0.295 Age + 0.0998 Height + 0.505 BMI	MVC = 57.5 - 0.340 Age - 0.075 Height - 0.278 BMI
A 4	MVC = 6.8 - 0.295 Age + 0.0998 Height + 0.505 BMI	MVC = 61.0 - 0.340 Age - 0.075 Height - 0.278 BMI
A 5	MVC = 11.2 - 0.295 Age + 0.0998 Height + 0.505 BMI	MVC = 61.8 - 0.340 Age - 0.075 Height - 0.278 BMI

Height effect research found that height has a major effect on MVC where taller people exerted more MVC with additional 9.1% than medium, and 12.21% than short subjects. The Height Effect on MVC found the following, MVC (Kg, male) T (27.3), M (25.66), S(25.26) and MVC (Kg, female) T (27.327), M (24.83), S (25.294), Table s1- 6 through 1-7 show the general linear equations for MVC with different independent factors and effect for males and females).

Table 6. The general linear equations for MVC with height effect for males and females)

	Males	Females
M	MVC = -42.2 - 0.0771 Age + 0.307 Height + 0.676 BMI	MVC = 109.8 - 0.208 Age - 0.364 Height - 0.415 BMI
S	MVC =-37.8 - 0.0771 Age + 0.307 Height + 0.676 BMI	MVC = 103.3 - 0.208 Age - 0.364 Height - 0.415 BMI
T	MVC = -42.7 - 0.0771 Age + 0.307 Height + 0.676 BMI	There was no tall females found in the sample

BMI effect research shows that greater MVC is exerted by subjects with medium BMI, The BMI Effect on MVC found the following MVC (Kg, male) L(24.33), M(26.57), S(24.81) and MVC (Kg, female) L(24.56), M (25.53), S (25.39).

Table 7. The general linear equations for MVC with BMI effect for males and females

	Males	Females
L	MVC = -5.4 - 0.0920 Age + 0.1151 Height + 0.611 BMI	MVC =42.2 - 0.1295 Age - 0.091 Height + 0.027 BMI
M	MVC =-6.4 - 0.0920 Age + 0.1151 Height + 0.611 BMI	MVC = 46.3 - 0.1295 Age - 0.091 Height + 0.027 BMI
S	MVC = -4.7 - 0.0920 Age + 0.1151 Height + 0.611 BMI	MVC =46.3 - 0.1295 Age - 0.091 Height + 0.027 BMI

Cancer Type Effect researches shows that the most type of cancer affect human body efficiency but the most likely worst of them is bone cancer and Non-small cell lung cancer , figure 1-2 show the relation between cancer types and MVC , the Cancer Type Effect on MVC found the following the following:

MVC Male (Kg) : BNC(20.2),CC (27.82),HANC(25.73),L(20.4),LC(26.15),NSCLC(21.05),PG(28.94) (5)

MVC Female (Kg) BC(24.04),CC(24.34),HANC(20.1),LC(24.7),LY(22.1),NSCLC(21.55) (6)

Table 8. The general linear equations for MVC with Cancer type effect for males and females

	Males	Females
BNC	MVC = 6.4 - 0.0305 Age + 0.0614 Height + 0.206 BMI	MVC =42.2 - 0.1295 Age - 0.091 Height + 0.027 BMI
CC	MVC =13.2 - 0.0305 Age + 0.0614 Height	MVC = 4.3 + 0.0069 Age + 0.0900 Height

	+ 0.206 BMI	+ 0.187 BMI.
HANC	MVC = 11.1 - 0.0305 Age + 0.0614 Height + 0.206 BMI	MVC = -0.3 + 0.0069 Age + 0.0900 Height + 0.187 BMI
L	MVC = 6.8 - 0.0305 Age + 0.0614 Height + 0.206 BMI	
LC	MVC = 11.3 - 0.0305 Age + 0.0614 Height + 0.206 BMI	MVC = 12.5 + 0.0069 Age + 0.0900 Height + 0.187 BMI.
NSCL C	MVC = 7.0 - 0.0305 Age + 0.0614 Height + 0.206 BMI	MVC = 1.2 + 0.0069 Age + 0.0900 Height + 0.187 BMI
PG	MVC = 14.0 - 0.0305 Age + 0.0614 Height + 0.206 BMI	----------
BC	----------	MVC = 6.6 + 0.0069 Age + 0.0900 Height + 0.187 BMI
LY	----------	MVC = 2.9 + 0.0069 Age + 0.0900 Height + 0.187 BMI
TC	----------	MVC = 6.2 + 0.0069 Age + 0.0900 Height + 0.187 BMI

Conclusion and Future Work

Experimental studies were conducted with a psychophysical approach to examine the effect of static/dynamic forces, on the maximum voluntary contraction (MVC), fatigue limits for subjects in the cancer patients. In this comprehensive research, five independent factors were considered which are most likely to represent all possible factors, including new apparatus (digital dynamometer), cancer type and wide range of patients age (20 to 66 years old) subjects, the uniqueness and significance of the research was done on Jordanian cancer patients and illustrated in reliance of hand grip strength as a biological sign in medical (especially in cancer treatment), the results from this research add valuable information to researchers' work, it also proposes comprehensive models considering five different factors. Results were analyzed by many statistical test, mathematical modeling and machine learning techniques. General, detailed were developed to predict MVC, maximum isometric endurance limit of submaximal (20%, 40% and 60%).

The experimental calculated the maximum voluntary contraction (MVC) values. It is very important to consider all variables and conditions of experiments in comparing different models since there is no standardized procedure for all experiments, in contrast to many studies in the literature, this experiment considers all factors which might have a significant or limited effect, since it's a human social experiment, and non-significant factors found in this experiment were found significant in many other studies, during the last periods, all independent factors had correlation effects as expected, since most of them are related to subjects' physical factors (of the human body) such as height, weight, and body mass index.

ANOVA was conducted with full factorial experimental design, ANOVA tests verify cancer type as major significant factor, again we consider all factors since we know from literature that they are significant beside considering the experiment environmental condition and the status of cancer patient, residual plots, histogram of the residuals, residuals versus order of data normality assumption holds, main effects resulted that the model fit in ANOVA, regardless it is forming a straight line with few points that depart from the straight line, the general linear and nonlinear models for MVC Test and isometric endurance limit were shown in discussion for significant factors.

For The MVC part, the Age Effect on MVC concluded the following: Highest MVC Value was for A1(25-<30): 32.8 kg, and Lowest MVC Value (Kg) for A5 (Above 45): 18.9 kg and for females Highest MVC Value was for A2 (20-<25): 31.4 kg, and Lowest MVC Value (Kg) for A5(Above 45): 20.1kg, for height effect on MVC concluded the following :(Height has a major effect on MVC, Taller people exerted more MVC than medium (6.007%) and shorter (7.56%). For BMI Effect on MVC concluded the following: (BMI has a minor effect on MVC, Medium BMI subjects exerted higher MVC than large BMI subjects (by 3.79%) and small BMI subjects (by 0.054 %) and Highest MVC exerted in MVC (Kg, male, large BMI). For cancer Type Effect on MVC concluded the following:(Cancer type has a Major effect on MVC (NOT All types mostly exerted the same MVC), Highest MVC exerted by Prostate gland patients for males and Liver Cancer for Females. And lowest MVC exerted by bone cancer and lymphoma for males and leukemia and non-small cell lung cancer patients for females.

As for future work, researcher should conduct more future studies, increasing the sample size where more parameters could be included in the experiments since the literature showed great mean differences in MVC regarding

different parameters. to draw a more definitive conclusion. One could also study the relationship between subjects' MVC and survival rates from AIDS, heart diseases, high blood pressure diseases etc. Finally, an artificial neural network (ANN) model was developed using neural network toolbox in MATLAB 15, obtained the lowest RMSE and provided the better fit for the data than the mathematical models, Results show that the machine learning models (neural network) has learned and fitted the experiment data well. The neural network model outputs accurately resemble the experiment targets for the three datasets (training, testing, and validation).

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