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ARTICLE

Hourly Rounding and Fall Prevention among the Elderly in Long Term Care: A change Process

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ABSTRACT

Long term care facilities have a rising rate of falls and fall related injuries with increasing cost and more hospitalization. Hourly rounding® is an evidenced based intervention that is proactive for nursing staff to be able to identify patient's needs. This helps with positive fall prevention outcome. This project focused on process improvement efforts for 10 weeks and examining the education and implementation of an evidenced-based hourly rounding program that assisted in reducing the number of falls in the pilot unit. The implementation of the intervention took place in a long-term care facility located in Dallas, Georgia. The hourly rounding tools used in this project were the Studer Group hourly rounding log and competency checklist with permission. Twenty staff members were included in the sample, age 18 years and 60 years. The unit has 41 residents who were included in the pilot case study design. Staff members were first educated regarding hourly rounding and documentation on the hourly rounding log was done two days before implementation and the pre and post fall rate was retrieved from the facilities fall database. Competency checklist was completed prior to implementation and post implementation to evaluate staff understanding of the main tenets of the 4 P's (potty, pain, possession, and position). For this project, descriptive statistics was used to help determine fall rates. Minitab was used to analyzed data and to determine if it was clinically significant. In the ten weeks following the hourly rounding implementation, participants performed hourly rounding by incorporating it to each resident's daily routine and documented their rounds on the log sheet. The results indicated that it is statistically significant and with a P-values = -<0.0001 and t-value = -5.81.

1. Introduction

Long term care (LTC) staff face a difficult task of keeping residents from falls and falls- related injuries daily. Residents in these facilities are 65 years and older. They have had longer stay in the facility, multiple comorbidities, cognitive and functional decline capabilities that put them at risks for falls. According to the CDC (2016). [1], older adults residing in long term care facilities account for about 30% of deaths from falls. With increasing frequency, patient fall account for the number one cause of injury and deaths from the entire older adult population. In these LTC facilities, yearly reported falls are over 100 among the older adult group. Twenty percent of fatal falls happen at long-term care facilities and these injuries can be detrimental with long term effect on the overall health of this group of adults with the average cost of hospitalization to treat an injury of $30,000 (CDC, 2016). [1]

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There is the need for organizations to develop and continue to enhance a culture of safety because patient safety is the cornerstone of high-quality healthcare (Mitchell, 2008). [2] The safety of the residents in these facilities must be guarded by nursing staff to prevent falls and fall- related injury. It is very important for fall prevention strategies to be multifactorial to help address the physical, psychological, functional, and educational components of the problem at hand. Nursing staff must be engaged in a collaborative and interdisciplinary manner in addressing ways to reduce falls and injuries related to falls (Wexler & D'Amico, 2015). [3]

1.1 Purpose

The purpose of this project was to improve resident's safety by decreasing the total number of falls as well as evaluate the effectiveness of education post implementation of hourly rounding® with the pilot unit's fall rate. The implementation of this quality improvement and evidence-based hourly rounding program allowed nursing staff to be more proactive resident's needs. One of the main objectives was to assess staff's compliance with performing the 4 P's as the main tenets of hourly rounding and documenting on the rounding log. During the pandemic, inconsistencies with documentation and floating of staff was taken into consideration. This project considered alternative outcomes from expected goals using clinical reasoning and changes were made accordingly. According to Simmons (2010), [4] clinical reasoning involves a complex process of utilizing formal and informal thinking methods intended to evaluate summed up patient information to determine whether alternative actions were valuable.

1.2 Local Knowledge of the Problem

According to the Georgia Department of Health (2016), from 1999 through 2014, an average of 1166 Georgians died from fall- related injuries which accounted for about 389 per year. Persons 65 years and older accounted for 75% of fall related deaths. (Georgia Department of Health, 2016). [5] The unit fall and fall with injuries is higher than the state and the national average of 3.8%. Based on monthly fall audits and data from facility's quality manager, the average number of monthly falls was 15 falls with injuries ranging from minor skin tears to fractures.

1.3 Significance of the Problem to Nursing and Healthcare

In implementing hourly rounding program in the Nursing center, the significance would include the involvement of creating a healthcare arena allowing for a reduction of falls and fall-related injuries. In the pilot unit there is a lack of a structured and multifactorial fall prevention program has led to an increase in falls thus residents' safety needs are not being met. Using the 4 P's during hourly rounding, is one of the common outcome measures.

1.4 Benefits of the Project to Practice

It is important that staff feel empowered and included in the decision-making process, as well as being educated on the importance of hourly rounding and fall reduction. Reducing the rates of falls in LTC has become a significant patient safety and quality initiative. Nurses can value the use of evidenced based intervention of hourly rounding for positive outcomes, thus decreasing falls and fall with injuries and costs. Implementing a structured hourly rounding protocol will allow the staff to be proactive in attending to resident's needs while addressing the 4 P's.

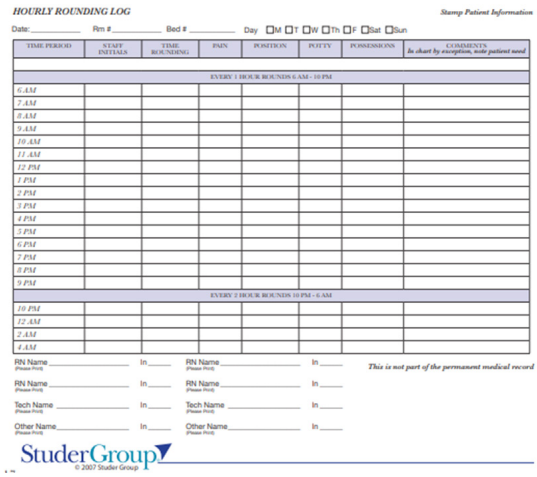
1.5 PICOT

The following is the PICOT question developed for this project:

For adult residents in LTC units aged 65 years and older (P) does education on hourly rounding provided to nursing staff (I) compared to no education on hourly rounding (C) reduce the number of falls among resident in the LTC units (O) over a ten-week period (T)?

2. Methodology

This project evaluated whether education and the implementation of an hourly rounding program impacted the number of resident falls in the pilot unit. The hourly rounding tools were the Studer Group hourly rounding log (see Figure A) and hourly rounding competency checklist (see Figure B). These tools were used to determine whether education and the implementation of hourly rounding interventions will affect the number of falls.


HOURLY ROUNDING LOG

Stamp Patient Information

Date:_____ Rm #_____ Bed #_____ Day ☐M ☐T ☐W ☐Th ☐F ☐Sat ☐Sun

TIME PERIOD	STAFF INITIALS	TIME ROUNDING	PAIN	POSITION	POTTY	POSSESSIONS	COMMENTS *In chart by exception, note patient need*
EVERY 1 HOUR ROUNDS 6 AM - 10 PM							
6 AM							
7 AM							
8 AM							
9 AM							
10 AM							
11 AM							
12 PM							
1 PM							
2 PM							
3 PM							
4 PM							
5 PM							
6 PM							
7 PM							
8 PM							
9 PM							
EVERY 2 HOUR ROUNDS 10 PM - 6 AM							
10 PM							
12 AM							
2 AM							
4 AM							

RN Name_____ In____ RN Name_____ In____

RN Name_____ In____ RN Name_____ In____

Tech Name_____ In____ Tech Name_____ In____

Other Name_____ In____ Other Name_____ In____

This is not part of the permanent medical record

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Figure A. Hourly Rounding Log (Studer Group, 2007)

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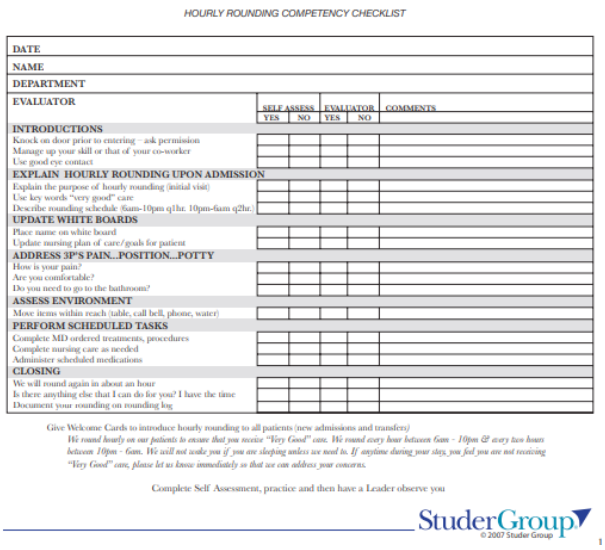

HOURLY ROUNDING COMPETENCY CHECKLIST

DATE					
NAME					
DEPARTMENT					
EVALUATOR	SELF ASSESS YES	SELF ASSESS NO	EVALUATOR YES	EVALUATOR NO	COMMENTS
INTRODUCTIONS					
Knock on door prior to entering – ask permission					
Manage up your skill or that of your co-worker					
Use good eye contact					
EXPLAIN HOURLY ROUNDING UPON ADMISSION					
Explain the purpose of hourly rounding (initial visit)					
Use key words "very good" care					
Describe rounding schedule (6am-10pm q1hr. 10pm-6am q2hr.)					
UPDATE WHITE BOARDS					
Place name on white board					
Update nursing plan of care/goals for patient					
ADDRESS 3P'S PAIN...POSITION...POTTY					
How is your pain?					
Are you comfortable?					
Do you need to go to the bathroom?					
ASSESS ENVIRONMENT					
Move items within reach (table, call bell, phone, water)					
PERFORM SCHEDULED TASKS					
Complete MD ordered treatments, procedures					
Complete nursing care as needed					
Administer scheduled medications					
CLOSING					
We will round again in about an hour					
Is there anything else that I can do for you? I have the time					
Document your rounding on rounding log					

Give Welcome Cards to introduce hourly rounding to all patients (new admissions and transfers)

We round hourly on our patients to ensure that you receive "Very Good" care. We round every hour between 6am - 10pm & every two hours between 10pm - 6am. We will not wake you if you are sleeping unless we need to. If anytime during your stay, you feel you are not receiving "Very Good" care, please let us know immediately so that we can address your concerns.

Complete Self Assessment, practice and then have a Leader observe you

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Figure B. Hourly Rounding Competency Checklist. (Studer Group, 2007)

2.1 Overview of the Design

The study design for this project is a case study design. This was achieved by observing effects of education and the implementation of hourly rounding in conjunction with addressing safety in terms of fall interventions measures of the residents in this unit. Education was provided to staff in the unit on hourly rounding and how to complete hourly rounding log sheets.

2.2 Sample/Setting

The residents in the selected unit are age 65 years and older male and female and are included in the population sample. The inclusion criteria for this project are resident's medical condition, age, assistive device usage. The project evaluated a unit in the facility, a 41 bed LTC unit that is experiencing an increase in the number of falls and explored how education and implementation of an evidence-based hourly rounding process combined with other multifactorial fall prevention strategies impacted the nursing-sensitive indicator of falls. There are 20 staff in this unit, Nurses (LPNs, RN,s) and Certified Nurse Assistance (CNAs).With education and implementation of evidenced-based proactive hourly rounding, this project aims at reducing falls in this unit to improve quality of life.

2.3 Methods

The hourly rounding tools used in this project was the Studer Group hourly rounding competency checklist and hourly rounding log. All 20-nursing staff in the unit attended a briefing session, capstone topic was presented including the implementation of hourly rounding. A day of education/teaching lasting two hours was provided to staff prior to implementing hourly rounding using the 4 "Ps" interventions. (Potty, Positioning, Pain and Possession). Education to staff included defining of the 4 "Ps" in hourly rounding, use of the Studer Group hourly rounding tools [6] and how to document in the hourly rounding log. Staff used the hourly rounding tool on a 24-hour basis for all residents in accordance with the 4 "Ps" and facility policy. After staff documentation, the hourly rounding logs were reviewed following a ten-week implementation period. Data collected from the hourly rounding log and fall audit log were analyzed.

2.4 Data Collection Procedures

Hard copies of the hourly rounding log spreadsheet were used to evaluate staff compliance and the impact of each hourly rounding component. Data for this study were collected from hard copy hourly rounding log sheets. On the 5th and 10th week period, hourly rounding competency checklist was completed to assess staff knowledge of hourly rounding. The hourly rounding log was used by trained/educated staff who were assigned unique identification code, P1 to P20 on a 24-hour basis for all residents. Each staff was educated to use their unique identification code to document on the hourly log indicating tasks completed based on the 4 Ps.

2.5 Data Analysis

Data was analyzed using Minitab statistical software. The paired t-test was used for this study. For this project, descriptive statistics were used to determine pre- and post- intervention, evaluate staff's understanding of the intervention and to determine staff readiness to change. Data reported included the shift when the fall occurred, location of fall and total number of falls for a 10-weeks period. No resident identifiers were included in the fall audit reports. For data analysis, descriptive analysis was performed to compare pre- and post-fall data before and after the education and implementation of hourly rounding. Post competency evaluation was done by observation of all twenty participants and compiling of data done. A percentage score was given to each participant based on observed tasks completed.

3. Results

In the ten weeks following the hourly rounding implementation, participants performed hourly rounding by incorporating it to each resident's daily routine. Table 1

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shows the pre-intervention fall rate data for the months March, April, and May. The post-intervention fall rates for the months June, July, and August are listed in Table 2. The number of falls were reduced in the months following post-intervention (see Table 3). The three months pre-fall data totaled 41falls and three months post fall data totaled 15 falls, hence a gross decrease of 36% (15/41) for the reviewed months. Minitab statistical software was used for analysis and a paired t-test was used to compare effectiveness of education pre- and post- implementation. A paired t-test of the 20 participants was performed and the results indicated that there was a statistically significant improvement in the number of falls post-intervention (t--5.81, p.-<0.0001) (see Table 4). A paired t-test indicated that there was a statistically significant improvement in participant knowledge on hourly rounding post-implementation. (t-18.76, p.-<0.0001) (See Table 5). Based on the results, the null hypothesis is rejected. The results are statistically significant and with a P-values below the significant level, this indicated change and improved knowledge with the participants.

Table 1. Pre-hourly rounding fall rate for March, April, and May

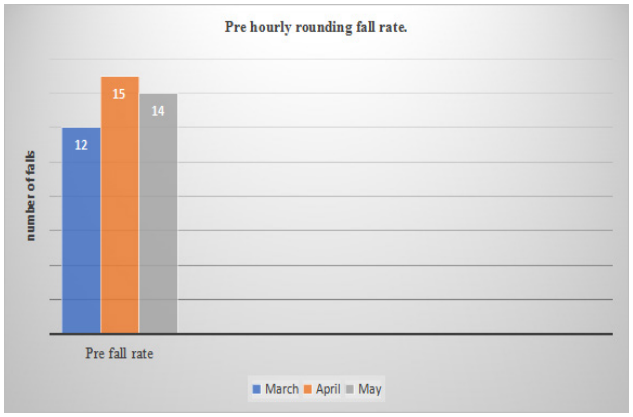

Table 2. Post-hourly rounding fall rate for June, July, and August, showing significant decrease in fall

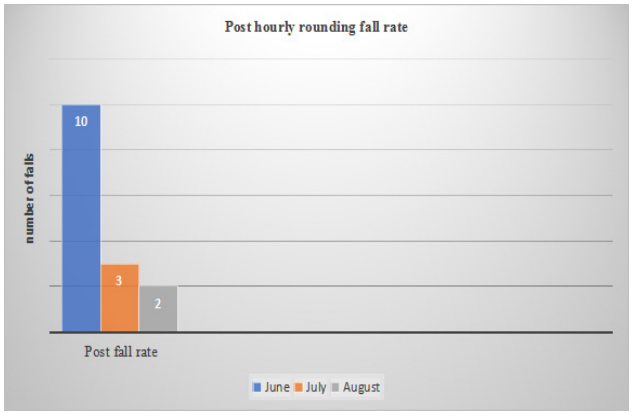

Table 3. Fall rates pre and post hourly rounding (Comparison Table)

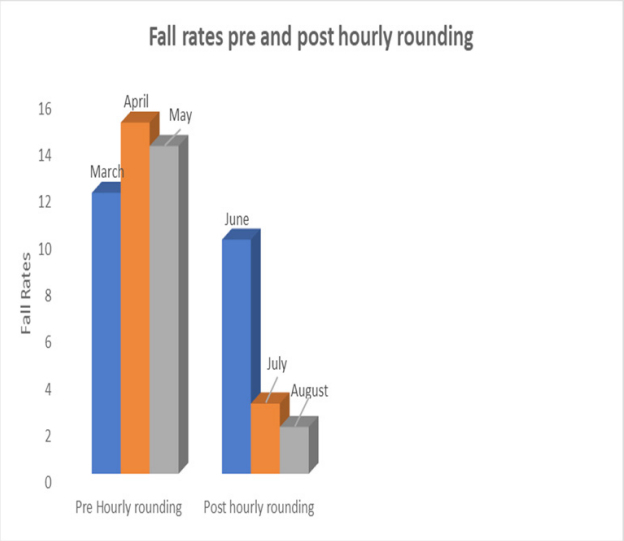

Table 4. Paired t-test Fall rate

Paired t: pre, post

Descriptive Statistics

Sample	N	Mean	StDev	SE Mean
pre	20	72.800	7.252	1.622
post	20	85.050	6.716	1.502

Estimation for Paired Difference

Mean	StDev	SE Mean	95% CI for μ_d
-12.250	9.425	2.107	(-16.661, -7.839)

μ_d: mean of (pre - post)

Test

Null hypothesis H_0: $\mu_d = 0$

Alternative hypothesis H_1: $\mu_d \neq 0$

T-Value	P-Value
-5.81	<0.0001

Table 5. T-test rounding Competency Checklist

Paired t: Pre, Post

Descriptive Statistics

Sample	N	Mean	StDev	SE Mean
Pre	20	41.700	10.423	2.331
Post	20	80.250	7.390	1.653

Estimation for Paired Difference

Mean	StDev	SE Mean	95% CI for μ_d
-38.550	9.191	2.055	(-42.851, -34.249)

μ_d: mean of (Pre - Post)

T-Value	P-Value
-18.76	<0.0001

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4. Discussion

The main purpose for this project was to determine if education and the implementation of hourly rounding would decrease the number of falls. According to Rapp et al., (2010), [7] in LTC falls are a major health concern among the elderly. Hourly rounding serves as a monitoring tool for the nursing staff to proactively meet the needs of the residents thereby maintaining safety and comfort. There was an improvement in staff performance involving change in behavior and practice. During data analysis it was noted that the first month showed inconsistencies with documentation in the log as well as appropriate use of unique assigned codes. Staff initials were occasionally noted on the log. Re-education was done on completing the hourly rounding log with the use of assigned codes. During the data collection phase, the CDC guidelines implemented during the pandemic played a role in changes with documentation. However, though there were many changes during this period, it was noted that staffing needs in the unit were consistent with little or no floating of staff.

5. Conclusions

This performance improvement project was successful in applying evidenced based practice with great outcome to decrease falls in the pilot unit of the nursing home. Based on the results, the number of falls were reduced in the months following post intervention. The three months pre-fall data totaled 41falls and three months post fall data totaled 15 falls, hence a gross decrease of 36% (15/41) for the reviewed months. Though, the implementation of hourly rounding is mostly instituted in the hospital, the outcome of this project indicated a positive outcome. Performing hourly rounding gave staff an understanding of being proactive rather than being reactive to the needs of the residents. Staff awareness was one of the changes noted in documenting of the actions in the hourly rounding log sheet and in attending to the resident's needs. The morale of the staff in implementing hourly rounding was heightened, and thus indicated a receptive attitude. Education provided before implementation created awareness, and therefore highlighted the importance of a fall prevention protocol that changed staff behavior when providing direct care.

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Glossary

4 P's = Potty, Pain, Possession, and Position
LTC = Long Term-Care
CDC = Center for Disease Control
PICOT = Population, Intervention, Comparison, Outcome, Time
CNA = Certified Nursing Assistant
RN = Registered Nurse
LPN = Licensed Practical Nurse

Funding

It is worth noting that this project received Institutional review board (IRB) approval number IRB00009705, and this manuscript is not presently under consideration for publication. There are no co-authors for this project.

There is no conflict of interest and no grant was received for this project. A written consent was received from participants prior to the project.

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ARTICLE

Postoperative Delirium in Elderly Patients May be Associated with Perioperative Blood Pressure Fluctuations

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ABSTRACT

Postoperative delirium (PD) is a common complication of surgery in elderly patients, but its pathophysiological mechanism remains unclear. In order to clarify the role of intraoperative hypotension and fluctuation of blood pressure in the development of PD, we conducted a follow-up study in elderly patients with intraoperative hypotension and fluctuation of blood pressure. A total of 237 patients underwent hip surgery between July 2018 and September 2019, and 158 patients who were eligible for inclusion were enrolled in the study. One day before the operation, the mentality of patients was evaluated by Mini-mental State Examination (MMSE), and the sex, age, height, and weight of the patients were recorded. Radial artery puncture was performed in all patients before anesthesia, intraoperative SBP, MAP and DBP were recorded, and the surgical events of the patients was recorded. The markers associated with PD (TNF-α, IL-6 and S-100β) were determined before and after surgery. Perioperative delirium (PD) was assessed by the prevailing standard of assessment, Confusion of Consciousness Assessment (CAM). Cognitive assessment was evaluated using the Mini-mental State Examination (MMSE). In addition, the timing and type of delirium were recorded. There were 158 patients which were accorded with the inclusion criteria came into the study. The results of our data showed that delirium occurred in 41 patients (25.9%) during the first week after surgery. In the comparison between the PD group and the non-PD group, it was found that the patients with postoperative delirium were older, lower body mass index and higher MMSE score before operation. Intraoperative blood pressure is low, usually more than 30% lower than preoperative blood pressure. The levels of TNF- α, IL-6 and Smur100 β were higher after operation. The increased incidence of postoperative delirium may be related to intraoperative hypotension and intraoperative blood pressure fluctuation. The pathophysiological mechanism may be that hypotension causes low cerebral perfusion, which in turn causes local inflammation in the brain. In addition, postoperative delirium is also more likely to occur in older patients with lower body mass index.

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1. Introduction

Elderly patients who receive surgical treatment are usually characterized by weakness, more underlying diseases, high surgical risk, and significantly increased risk of death. A variety of adverse consequences can occur after operation, including postoperative delirium, pulmonary infection, myocardial infarction, and cerebrovascular accident [1].

Delirium is a common neurological syndrome. Delirium is defined as an attention, consciousness, and cognitive disorder in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). The onset of the disease is usually urgent, and the condition fluctuates obviously. The syndrome is common in elderly patients. The cognitive function of the patients decreased, the degree of awakening changed, the perception was abnormal, and the night and day were reversed [2]. Among the elderly patients who received surgical treatment, the incidence of postoperative delirium (PD) was very high, and some studies showed that it was 8-73% [3]. Postoperative delirium, a clinical syndrome that can lead to serious complications, has a high incidence, and is associated with prolonged hospitalization, a gradual decline in cognitive ability and learning, a decline in postoperative self-care ability, and an increase in mortality [4]. The causes of delirium are considered to be multiple factors, and there is a correlation between preoperative health and predisposing factors [5]. At present, many studies have confirmed that the causes of postoperative delirium may be related to age, basic basis, type of operation, intraoperative hypotension, intraoperative blood transfusion, prolonged operation time, use of anesthetics and other risk factors, but the pathophysiology of its occurrence is still little known [6]. Some scholars have proposed that insufficient cerebral perfusion caused by intraoperative hypotension is one of the mechanisms of postoperative delirium. A large observational study shows that the risk of hypotension in the elderly during surgery is very high, and 66-85% of patients with hip fractures develop hypotension during surgery [7]. A recent clinical trial suggests that in order to reduce the incidence of postoperative delirium, avoiding intraoperative hypotension should be part of the intervention strategy [8]. However, when looking at other literatures, it is found that some research results are contradictory to those on this subject: some studies have suggested that intraoperative hypotension does not play a role in the development of postoperative insanity [8]. In addition, other studies have shown that intraoperative hypertension and vasopressor use can also lead to postoperative delirium. Therefore, the relationship between intraoperative blood pressure and postoperative delirium is controversial [9]. Whether intraoperative blood pressure management should be performed to avoid postoperative delirium is still controversial. In order to prove the role of blood pressure in the occurrence of delirium during operation, the blood pressure of elderly patients who needed surgical treatment was selected for an observational study.

2. Methods

2.1 Patient Recruitment

The study was approved by the Medical Research Ethics Committee, Affiliated Hospital of North China University of Science and Technology. Written informed consent was obtained preoperatively from each study patient. Inclusion criteria: Age≥65,ASA 2~3, Non-cardiac surgery, Operation time was less than three hours, All patients had no preoperative mental illness, normal cognitive ability, no long-term use of neuropsychiatric drugs or alcohol abuse, no serious illness (such as sepsis, renal or liver failure, severe respiratory failure), and no history of brain injury or stroke [10]. Exclusion criteria: Patients refused the study, unable to communicate verbally, had severe cognitive impairment preoperatively, and had advanced malignant tumors, patients with COPD, patients received intraoperative blood transfusion treatment. A total of 237 patients underwent hip surgery between July 2018 and September 2019, and 158 patients who were eligible for inclusion were enrolled in the study (M: 56, F: 102, mean age: 72 years, range: 65-98 years, mean body weight 60.9 kg, mean Body Mass Index (BMI) 23.1).

2.2 Preoperative Assessment

The mini-mental state examination scale (MMSE) can comprehensively, accurately, and quickly reflect the participants' mental state and the degree of cognitive impairment [11]. The scale includes the following seven aspects: time orientation, place orientation, immediate memory, attention and calculation, delayed memory, language, visual space. A total of 30 questions, the correct answer to each score of 1, wrong answer or do not know the score of 0, the total score of the scale ranges from 0 to 30. The score was 27-30: normal score < 27: cognitive impairment 21-26, mild 10-20, moderate 0-9, severe. Delirium was assessed by confusion assessment method (CAM), to screen participants for delirium before operation and 7 days after operation. Delirium has four characteristics: 1) rapid occurrence of disturbance of consciousness after operation, which changes greatly day and night, 2) lack of attention, 3) disturbance of perception, and 4) decline of cognitive ability. Typical patients with delirium may have characteristics (1) and (2) or (3) or (4),

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which can be defined as delirium when the criteria are met. According to the situation when delirium occurs, there are motor manifestations of hyperactivity or inactivity, and the type of delirium can be judged. Patients with low activity delirium may have decreased movement, confusion, lethargy, or coma, while patients with hyperactive delirium show restlessness, sleep disorders, irritability, and irritability. Data about the basic characteristics of the patient (such as age, sex, basal blood pressure, body mass index [BMI], underlying disease and type of operation) were obtained from the patient's medical records before operation. The preoperative physical condition was evaluated using the classification system of the American Association of Anesthesiologists (ASA). Blood samples were taken before operation, on the first day (24 h) and the third day (72 h) after operation, and the concentrations of serum tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and protein S-100 β (S- 100 β) were measured.

2.3 Surgical and Anesthetic Techniques

The selected patients were all patients undergoing hip surgery. ASA physical status class was 2~3. The choice of type of anesthesia is spinal anesthesia or general anesthesia, depending on the general condition of the patient, the type of surgery and the need for the depth of anesthesia. During general anesthesia, tracheal intubation was performed with etomidate (0.15~0.3 mg/kg), fentanyl (2~5 μg/kg) and cisatracurium besylate (0.1~0.2 mg/kg). Sevoflurane or combined propofol was used to maintain anesthesia during operation. Intermittent injection of fentanyl and cisatracurium besylate were used to maintain analgesia and muscle relaxation. Combined spinal-epidural anesthesia (CSEA) was used in regional anesthesia, and 0.5% ropivacaine was used in spinal anesthesia for 12~18 mg.

2.4 Measurement of Intraoperative Blood Pressure

During the operation, each patient received standard monitoring of blood pressure, electrocardiogram, blood oxygen saturation, pulse, end-respiratory carbon dioxide and body temperature. The heart rate and blood pressure of each patient were measured before operation in order to compare with intraoperative blood pressure. The preoperative basal blood pressure of each patient was calculated as a 3-day average. Before the beginning of anesthesia, the blood pressure of patients with continuous monitoring of invasive artery was established by means of local anesthesia. Items that need to be closely monitored include systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). The highest MAP(Max) and the lowest MAP (Min), were measured during the operation, and the difference between them was defined as blood pressure fluctuation (ΔMAP). The definition of intraoperative hypotension: (1) intraoperative relative hypotension, defined as SBP or MAP 30% or more than 30% lower than the patient's baseline, and (2) blood pressure below MAP 50 mmHg.

2.5 Statistical Analysis

Statistical analyses were performed using SPSS version 23.0 statistical software with intention to treat, measurement data was presented by mean ± standard deviation (x±S), comparison in the group used analysis of variance of repeated measurement, comparison between groups used *t*- test, count data were compared using the x^2 test. A *p*-value < 0.05 was considered statistically significant.

3. Results

3.1 Incidence of Delirium

On postoperative delirium was present in 41/158 patients (25.9%). The results showed that the onset of delirium was related to age, body mass index, and MMSE score. (Table 1)

Table 1. Baseline characteristics

Characteristics	NO n=117	Delirium	Yes n=41	*p*
Age, χ±*sd*	73.67±7.81		81.95±9.12	0.001
BMI,n(%)				0.001
<20	3(2.5)		6(14.9)	
20-25	71(60.5)		23(56.1)	
26-30	35(30.2)		10(24.3)	
>30	8(6.8)		2(4.7)	
MMSE, χ±*sd*	28.53±0.64		18.86±0.98	0.001
Type of Anesthesia,n(%)				
General anaesthesia	46(39.5)		19(47.3)	0.194
Regional (CSEA)	71(60.5)		22(52.7)	
Anaesthetic Drugs				
Etomidate(mg)	12.6 ±2.01		13.2±1.22	0.43
Fentanyl(mg)	0.65±0.11		0.67±0.12	0.79
Cisatracurium besylate(mg)	13.5±2.41		13.9±2.09	0.69
Sevoflurane(min)	82.77±10.62		80.55±8.23	0.62
Propofol(mg)	390.88±22.27		383±29.66	0.53
Ropivacaine(mg)	13.23±1.16		13.92±1.84	0.26
Coronary disease				
Hypertension, n (%)	26(22.2)		18(43.9)	0.16
Diabetes, n (%)	5(4.2)		3(7.5)	0.45
Atrial fibrillation n (%)	12(10.2)		6(14.6)	0.33
Duration of hypotension	9.78±12.2		8.98±9.5	0.84

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3.2 Intraoperative Hemodynamic

The statistical results of intraoperative blood pressure of patients showed that postoperative delirium was easy to occur when intraoperative hypotension and blood pressure fluctuation occurred. (Table 2)

Table 2. Intraoperative blood pressure in patients with and without delirium

Characteristics	NO n=117	Delirium	Yes n=41	*p*
SBP max	151.54±18.65		152.01±16.25	0.4980
DBP max	91.43±12.16		89±8.74	0.821
SBP min	129.22±14.24		104.66±13.84	0.001
DBP min	75.65±7.86		55.46±6.76	0.001
MAP max	109.18±16.40		108.38±7.89	0.712
MAP min	95.35±7.41		81.68±9.76	0.001
ΔMAP, med (min-max)	12.9 (-5.87-96.87)		17.23 (-2.58-55.46)	0.006

3.3 The TNF-α, IL-6 and S-100β Levels of Patients with PD

Patients with delirium had higher levels of TNF-α, IL-6 and S-100β than those without delirium. (Table 3, 4, 5)

Table 3. The levels of TNF-α in patients with and without delirium

Characteristics	NO n=117	Delirium	Yes n=41	*p*
TNF-α				
preoperative	63.95±7.21		62.84±10.98	0.863
Day1	69.73±9.92		81.68±12.35	0.001
Day2	75.17±16.79		92.13±10.30	0.001
Day3	68.26±6.55		95.17±11.18	0.001

Table 4. The levels of IL-6 in patients with and without delirium

Characteristics	NO n=117	Delirium	Yes n=41	*p*
IL-6				
preoperative	335.95±11.18		333.21±34.69	0.695
Day1	337.49±18.74		377.79±28.37	0.001
Day2	341.95±15.23		384.95±22.34	0.001
Day3	338.95±13.45		379.65±16.46	0.001

Table 5. The levels of S-100β in patients with and without delirium

Characteristics	NO n=117	Delirium	Yes n=41	*p*
S-100β				
preoperative	0.18±0.03		0.22±0.05	0.512
Day1	0.30±0.02		0.51±0.05	0.001
Day2	0.27±0.04		0.49±0.03	0.001
Day3	0.23±0.08		0.38±0.05	0.001

3.4 Multivariate Analysis of Postoperative Delirium

In the multivariate analysis, postoperative delirium was taken as the dependent variable (0 = no, 1 = yes), and the significant variable in the univariate analysis (Age, BMI, MMSE, SBP, DBP, MAP, postoperative TNF-α, IL-6 and S-100β) was used as the independent variable for logistic regression analysis. The results showed that ΔMAP, TNF-α, IL-6, Age, BMI was a high-risk factor for postoperative delirium. (Table 6)

Table 6. Multivariate logistic regression analysis

	β	*p*	OR	*95%CI*
Age	2.365	0.010	7.963	4.148~10.652
BMI	3.764	0.007	8.749	6.473~10.886
MMSE	1.496	0.021	4.252	2.019~6.748
SBP min	1.435	0.024	4.085	2.352~6.649
DBP min	2.063	0.012	5.123	3.748~7.191
MAP min	2.718	0.011	5.492	3.965~7.024
ΔMAP	4.742	0.000	16.452	10.81~22.248
TNF-α	4.012	0.001	13.742	7.285~20.360
IL-6	3.891	0.005	10.257	8.876~12.541
S-100β	2.573	0.010	6.652	3.358~8.872

4. Discussion

There were 158 patients which were accorded with the inclusion criteria came into the study. And our results showed that delirium occurred in 41 patients (25.9%) after surgery. The high intraoperative ΔMAP, elevated postoperative inflammatory factors (TNF-α, IL-6, S-100β), advanced age and low body mass index (BMI) were the main risk factors of postoperative delirium. Low systolic blood pressure, diastolic blood pressure and low MAP are also associated with postoperative delirium (PD). Other

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factors such as anesthetic methods, anesthetic drugs, and mild underlying diseases did not cause postoperative delirium. In addition, we also found that the preoperative and postoperative MAP values were also very significant between the non-delusional group and the delusional group. During surgery, even transient episodes of hypotension can lead to early or late postoperative delirium. Therefore, the occurrence of perioperative PD is related to blood pressure fluctuation, which can be used as a danger signal.

With the improvement of social economy and medical level, the global elderly population is increasing year by year. The increase of the elderly population leads to the problem of aging population. Among the patients receiving surgical treatment, the proportion of the elderly population is getting higher and higher. According to statistical analysis, a considerable proportion of elderly patients have temporary postoperative delusions of (PD), after surgery. Some patients have left behind long-term postoperative cognitive dysfunction (POCD) [12]. This phenomenon has aroused widespread concern among surgeons and anesthesiologists. At present, the pathophysiological mechanism of postoperative delirium is not completely clear. Several studies have shown that intraoperative hypotension and blood pressure fluctuations play a role in the development of delirium. But at the same time, studies have shown that the occurrence of delirium is not related to intraoperative hypotension and blood pressure fluctuations. Therefore, we established this study to verify the relationship between intraoperative hypotension and delirium by studying intraoperative hypotension and blood pressure fluctuations.

The results of this study showed that by comparing the PD group and the non-PD group, the larger the range of intraoperative blood pressure fluctuation, the higher the ΔMAP value, the higher the probability of postoperative PD. When there is a drop in blood pressure, we usually give corrective treatment, so that low blood pressure will not exist for a long time. Even though our anesthesiologist dealt with hypotension in time, delirium was inevitable after surgery. This suggests that even a short-term drop in blood pressure may lead to postoperative delirium. From this, we can conclude that maintaining the stability of blood pressure is good for elderly surgical patients. In the analysis of the risk factors of delirium, we found that the older the age, the lower the body mass index, the higher the risk of delirium. This may be related to the brain dysfunction caused by cerebrovascular self-regulation and insufficient glycogen supply in elderly patients. High preoperative MMSE scores suggest that patients may have cognitive impairment, and these patients also have a higher risk of postoperative delirium.

Another hypothesis of the pathophysiological mechanism of postoperative delirium is that insufficient cerebral perfusion during hypotension leads to local ischemia, which leads to brain dysfunction. Low cerebral perfusion can cause an increase in the production of reactive oxygen species. Increased production of reactive oxygen species in the brain can lead to increased excitatory transmitters, apoptosis, and local inflammation [13]. In this study, it was found that the serum levels of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and S-100 β in patients with postoperative delirium were significantly higher than those without postoperative delirium. It is estimated that intraoperative hypotension and blood pressure fluctuations lead to insufficient cerebral perfusion and local inflammation caused by cerebral ischemia. The invasion of inflammatory factors into the hippocampus may be the cause of postoperative insanity.

5. Conclusions

To sum up, we concluded that perioperative blood pressure decrease and blood pressure fluctuation are associated with postoperative delirium. Cerebral ischemia and local inflammation caused by intracranial hypoperfusion may be the pathological mechanism of delirium. The best treatment for postoperative delirium is prevention. Early identification and treatment of potential perioperative risk factors can prevent the occurrence of postoperative delirium.

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ARTICLE

Alzheimer's Disease among American Minority Populations: An Ecological Exploratory Study

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ABSTRACT

A significant public health concern with regards to increasing rates of Alzheimer's is that it disproportionately affects minority groups in the United States. The present ecological exploratory study uses secondary aggregate data from the fifty United States in the year of 2019. The purpose of this study was to address the disparities in Alzheimer's in minority populations in the US and explore associated factors. The "minority" populations considered were African American and Hispanic populations, and the "majority" population was referred to as "white". The data were extracted from the United States Census Bureau, the CDC National Center for Health Statistics, and the Behavioral Risk Factor Surveillance System (BRFSS) Dataset. The prevalence rates of Alzheimer's disease are greatest in both older Hispanic (12.2%) and African Americans (13.8%), compared to older whites (10.3%) in the investigated time period. Our results showed that being over 65 years old (p=.009), with a below-average ($62,843) median household income (p=.024), history of stroke (p=.029), and being a part of the Hispanic population (p=.036), were significantly associated with Alzheimer's mortality rates in the United States. By identifying disparities in access to Alzheimer's healthcare and at-risk communities, more comprehensive intervention strategies can be developed to promote change and advocate for more Alzheimer's education and resource allocation for minority populations.

1. Introduction

Alzheimer's disease is defined as a brain disorder that progressively gets worse over time [1]. According to the National Institute on Aging, Alzheimer's is "irreversible" and slowly inhibits an individual's ability to carry out basic bodily tasks that are necessary for survival [1]. Generally, individuals will begin to display symptoms of Alzheimer's around the age of 65 [1]. Though quite rare, those who display symptoms between the ages of thirty to early sixties, are classified as "early-onset" [1]. According to Healthy People 2020, "Alzheimer's disease is the most common form of dementia" [2]. In general, "Dementia" inhibits an individual's ability to function independently, maintain good health, and optimal well-being; symptoms typically

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include memory loss and problems understanding language and communicating [2].

Alzheimer's develops from a variety of factors that include genetics, lifestyle choices, environment, with the greatest risk factor being over the age of 65 [3]. Though some factors are impossible to prevent, it is important for individuals to protect the brain from substantial head injury, maintain a healthy heart, healthy diet, exercise, socialization, and avoid alcohol or tobacco in order to age in the healthiest way [3]. Brain health is strongly associated with heart health; so, conditions like heart disease, diabetes, and stroke are associated with higher risk of developing Alzheimer's [3]. Alzheimer's does not only affect the individual receiving the diagnosis but impacts the family members and caregivers that the individual must rely on [4]. To explain, the total cost of care for Americans with Alzheimer's in 2017 has been estimated to be 232 billion dollars and about 18.4 billion hours of care [4]. Such extensive amounts of time and money that come with caring for an individual with Alzheimer's underscore the importance of knowing the associated factors in order to receive the earliest diagnosis so that symptoms do not become more severe.

The prevalence of Alzheimer's is increasing globally but varies by country due to cultural and socioeconomic differences [5]. Generally, prevalence is greater in more developed countries and lower in underdeveloped countries [5]. It is most prevalent in the Americas and is least prevalent in less developed countries, such as Africa and the Middle East [5]. The proportion of individuals from developed countries with Alzheimer's is expected to be 71.2% by 2040; an increase from 60.1% in 2001 [5]. The disparity in prevalence of Alzheimer's in developed countries versus underdeveloped countries can be supported by differences in average life expectancy. Typically, individuals living in developed countries will have a longer lifespan as compared to individuals in underdeveloped countries [6]. Older age is highly associated with developing Alzheimer's [6]. It is predicted that the number of individuals over 65 living in developed countries is expected to hit 1 billion by 2030, which will affect future incidence rates of Alzheimer's [6].

Currently, 5.8 million Americans aged 65 and older are living with Alzheimer's disease (1 in ten Americans) [7]. It is the sixth leading cause of death in the United States overall, and the fifth-leading cause of death in individuals over 65 years old [7]. Individuals with Alzheimer's experience a high level of morbidity caused by years of poor health and disability, which gradually becomes more severe. Mortality generally results from complications related to years of living with poor health [6]. Reported deaths from Alzheimer's has increased 146.2% from 2000 to 2018 in the US [8]. According to the CDC, age-adjusted death rates by state range from 13.9 to 46.5 in New York and Georgia, respectively [9]. Death rates are generally the lowest for states in the North-East, and the highest for states in the South-East United States [9]. Trends indicate that incidence/prevalence of Alzheimer's will continue to increase as people continue to live longer and longer [1].

According to the Alzheimer's Association, "older Hispanics are about one-and-a-half times as likely as older whites to have Alzheimer's and other dementias, while older African-Americans are about twice as likely to have the disease as older whites" [3]. This disparity served as the basis for this present study. Currently, there is a gap in Alzheimer's research amongst minority populations in the United States as compared to the majority population [8]. The "minority" populations for this study refer to African Americans and Hispanic populations, while the "majority" refers to mostly whites. The purpose of this study is to address the disparities in Alzheimer's in minority populations and explore influencing factors.

The overall research goal is to analyze the recent trends of Alzheimer's mortality in the United States in minority populations compared to the majority and address possible explanations. Our hypotheses are first, Hispanic & African American populations had the highest prevalence of Alzheimer's in 2019. Second, Ethnic groups in the US that fall within the minority will show higher rates of Alzheimer's onset. The null hypothesis is the distribution of Alzheimer's mortality in the investigated period is not associated with being a part of a minority population in the United States.

2. Methods

The goal of our study was to test a potential association between Alzheimer's mortality rates with being a part of a minority population in the United States. We designed an analytical ecological exploratory study using secondary aggregate data. Each individual state in the United States represented a single unit of analysis.

The major outcome of our study was mortality due to Alzheimer's disease, which served as our dependent variable. To reiterate, Alzheimer's is defined as a brain disease that progressively worsens over time and eventually makes it impossible for individuals to carry out basic bodily functions [1]. Mortality due to Alzheimer's is increasing in the United States, as death results from

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years of living with health complications that progressively worsen [8]. Our research specifically focused on disparities in mortality rates among minority populations versus majority. This is because we wanted to recognize the gaps that currently exist in Alzheimer's research in minority populations. In sum, we explored an association between being a part of a minority population in the United States with Alzheimer's mortality, along with several other explanatory variables.

The dependent variable was Alzheimer's mortality rates [number of people that died due to Alzheimer's disease in the year of 2019 divided by the total population of the same year]. The independent variables in our study consist of each state's general population, and the percentage of each state's population of individuals over 65 years old. The main exposure we are investigating is being a part of a minority race population. So, we included the percentages of people that belong to "White alone", "African-American", and "Hispanic" populations. Other variables included; percentage of the population that has a bachelor's degree or higher, percentages of the population without health insurance, median household income [total income divided by the number of people living the household], adult obesity rates [people with BMI => 30 divided by total population size], prevalence of stroke [number of Americans who have had a stroke divided by total U.S. population], and prevalence of diabetes [number of Americans diagnosed with type II diabetes divided by total U.S. population].

The secondary data used in this study were extracted from the United States Census Bureau, the CDC National Center for Health Statistics, and the Behavioral Risk Factor Surveillance System (BRFSS) Dataset. We chose these sources of data because they are reliable, widely recognized open-access databases that include expansive information on each of the 50 states. We completed statistical testing using SPSS statistical software. The statistical tests we applied were bivariate analysis, followed by multivariate analysis and linear regression.

First, we tested our main outcome and every single variable first to determine if there was any association with our dependent variable, Alzheimer's mortality. All variables that had a level of significance equal to or below 0.2 were included in the regression analysis. Next, we took the associated independent variables and performed a linear regression using the "Enter" method. As a result, we were able to determine which variables remained associated with our dependent variable when influenced by our other independent variables.

3. Results

The main objective of our study was to explore any possible association with Alzheimer's mortality and being a part of a minority race in the United States. So, we considered data belonging to the African American population and the Hispanic population as representing "minorities", while White alone represents the "majority". We also tested for possible association with other independent variables on Alzheimer's mortality as well. The results of our statistical testing are explained in the following paragraphs.

3.1 Descriptive Analysis

Descriptive analysis shows that of the total United States (N = 50), the mean of the population aged over 65 years old is roughly 17%, 8% are uninsured, and 32% have achieved a bachelor's degree or higher. In terms of race distribution in the United States population, 79% are White alone, 11% are African American, 12% are Hispanic. These percentages are rounded up or down by 1% by looking at the closest decimal point. Descriptive analysis also showed high rates of other comorbidities, obesity, stroke, and diabetes. The mean rates of obesity, stroke and diabetes in the United States are 32%, 37%, and 22%, respectively (Table 1).

Table 1. Descriptive statistics according to investigated variables. USA, 2019.

Variables	Minimum	Maximum	Mean	Std. Deviation
Total Population	578,759.00	39512223.00	6550855.4800	7389409.68284
People aged 65+	11.40	21.20	16.9680	1.92359
Race/Ethnicity White alone	25.50	94.40	78.7100	12.31678
Race/Ethnicity African American	.60	37.80	11.1900	9.62656
Race/Ethnicity Hispanic	1.70	49.30	12.2660	10.45349
Median Income	43567.00	81868.00	60172.0000	9920.06437
Obesity Prevalence	23.80	40.80	32.1020	3.86763
History of Stroke	24.40	51.80	36.8080	6.10807
Uninsured	2.80	17.70	8.1940	3.04305
Education Bachelor's Degree or Higher	20.30	79.30	31.6502	8.58020
Diabetes Prevalence	14.60	36.20	21.9500	4.39147

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Table 2. Bivariate analysis among Alzheimer's mortality rates and investigated independent variables.

Variables	Significance Level
Total Population	.846
People aged 65+	.053
Race/Ethnicity White alone	.713
Race/Ethnicity African American	.114
Race/Ethnicity Hispanic	.086
Median Income	.001
Obesity Prevalence	.002
History of Stroke	.000
Uninsured	.008
EducationBachelor's Degree or Higher	.181
Diabetes Prevalence	.002

Median income (.001), obesity (.002), history stroke (.000), being uninsured (.008), prevalence of diabetes (.002), being over 65 years old (.053), education level (.181), being African American (.114), and being Hispanic (.086) were inserted in the linear regression Model (Table 3). After controlling by the above-mentioned variables, being over 65 years old (p=0.009), median income (p=0.024), history of stroke (p=0.029), and being Hispanic (p=0.036) were strongly associated with Alzheimer's mortality in the United States.

Table 3. Final model regression analysis.

Variables	B*	Std. Error*	Beta**	t	Sig.
(Constant)	77.032	29.097		2.647	.012
People aged 65+	-1.712	.623	-.384	-2.749	.009
Race/Ethnicity African American	-.117	.137	-.131	-.851	.400
Race/ Ethnicity Hispanic	-.252	.116	-.308	-2.174	.036
Median Income	.000	.000	-.480	-2.355	.024
Obesity Prevalence	-.550	.471	-.248	-1.169	.249
History of Stroke	.595	.262	.424	2.269	.029
Uninsured	.020	.446	.007	.045	.964
Education-Bachelor's Degree or Higher	.119	.143	.119	.829	.412
Diabetes Prevalence	.229	.384	.117	.596	.554

Dependent Variable: Alzheimer's Mortality; * Unstandardized Coefficients; ** Standardized Coefficients

4. Discussion

Associations between being a part of a minority group with an increased incidence of certain diseases in the United States have been discussed in existing literature. According to the National Institute of Allergy and Infectious Diseases, it has been widely "recognized that racial and ethnic differences affect susceptibility to infection and disease" [9]. Examples of these disparities include African Americans "represent almost half of new AIDS diagnoses", asthma disproportionately affects African American and Hispanic children in the inner-city, African Americans account for some of the "highest rates of chronic Hepatitis C and Hepatitis C-related deaths", and systemic lupus erythematosus can be up to three times more common among African American and Hispanic women [9].

It is also important to recognize other significant Alzheimer's disease patterns throughout the United States. Existing data from the CDC show that age-adjusted death rates due to Alzheimer's are highest in the southeastern region of the U.S., with the exception of Florida [10]. States with death rates ranging from 44.9 – 46.5 include: Alabama, Tennessee, Washington, Mississippi, and Georgia, respectively [10]. On the other hand, states with the lowest death rates due to Alzheimer's are generally located in the northeastern region of the United States [10]. States with death rates ranging from 13.9 – 19.5 include: New York, Maryland, Connecticut and Massachusetts [10]. Florida and Hawaii also have some of the lowest death rates due to Alzheimer's nationally, but are not a part of the northeastern region [10]. Recognizing differences in the disease patterns of Alzheimer's in the U.S. is important for determining if states with higher death rates also have higher populations of minority groups.

The Centers for Disease Control and Prevention (CDC) have concluded that Hispanic and African American populations will experience the largest increase in Alzheimer's disease and related dementias [7]. In the United States minority populations will be affected the most by Alzheimer's disease by the year 2060, when it is predicted that cases will rise to about 1 million people [7]. Our results showed significant associations among being Hispanic (p=.036), being over 65 years old (p=.009), median income (p=.024), and history of stroke (p=.029) with onset of Alzheimer's in the United States. According to the CDC, within the next 40 years Alzheimer's cases among Hispanic populations will increase seven times over today's estimates, and four times over today's estimates among African Americans [7]. This underscores why the main objective of our study was to investigate the association between being a part of either the Hispanic popula-

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tion or African American population in the United States with Alzheimer's disease. The significant association we found with being Hispanic and Alzheimer's disease in the United States corroborates with existing literature from the Alzheimer's Association [7].

The significant association we found between being over 65 years old and the onset of Alzheimer's has also been discussed in existing literature [1]. The National Institute of Aging points out that age-related changes in the brain may harm neurons and affect other types of brain cells to contribute to Alzheimer's damage [8]. It is imperative to recognize that the general population of the United States is not only aging, but also living longer. This aging population impacts not only the morbidity rates of Alzheimer's in the United States, but also contributes to large increases in the costs of Alzheimer's treatment.

We understand that it was important to take into account other social determinants of health that minorities in the United States face that may account for increased risk for developing Alzheimer's. Instead of considering only two specific ethnic populations, we also analyzed social determinants of health that may affect these minority populations. The National Institute on Aging informs that a variety of health, environmental, and lifestyle factors beyond genetics and natural aging can play a role in the onset of Alzheimer's [8]. This served as the basis for what other explanatory factors we chose as independent variables in our study.

Disparities in education, income, and access to health care/insurance that minorities experience can impact Alzheimer's onset [7]. For example, we found that income is a significant predictor of developing Alzheimer's. This association relates to how minority populations tend to have lower median income levels compared to majority populations in the U.S. low socioeconomic status among minority populations exacerbates the social determinants of health that may contribute to Alzheimer's onset. To explain, lower household income is associated with a lack of health insurance coverage, access to health screenings, adequate health education and consistent healthcare. All of which increase the risk for developing Alzheimer's disease. Moreover, the relationship between income level and being a part of a minority in the U.S. can largely account for the increased prevalence of Alzheimer's rates in minority populations.

Additional research suggests that vascular conditions such as stroke, diabetes, and obesity contribute to developing Alzheimer's [8]. Our results show that stroke is associated with the onset of Alzheimer's. According to the National Heart, Lung, and Blood Institute there are a variety of risk factors that increase the probability of having a stroke [9]. These factors include an unhealthy diet, lack of exercise, and an excessive use of alcohol and/or tobacco [9]. We understand that it is not justifiable to generalize the overall health habits of an entire ethnic population. However, we do acknowledge that minority populations are typically but not always, more susceptible to the environmental/lifestyle factors and social determinants of health that can increase risk for stroke. The association we found between stroke and Alzheimer's could account for disparities in rates of Alzheimer's in American minority populations.

It is also imperative to address the current chronic disease epidemic. Incidence of obesity, Type 2 diabetes, non-alcoholic fatty liver disease (NAFLD) and neurodegenerative diseases are increasing globally [11]. Obesity and type 2 diabetes prevalence is predicted to rise to 30% of the global population, and prevalence of NAFLD in Western countries is currently at 30% [11]. Unhealthy diets and sedentary lifestyles are the major contributors to developing the aforementioned chronic diseases [11]. To reiterate, we understand that it is not justifiable to make generalizations, but we do recognize that minority populations may be more highly susceptible to the lifestyle factors that may contribute to such chronic diseases that ultimately impact Alzheimer's development. For example, the Hispanic population in the United States has the highest rates of diabetes in adults and children, compared to any other race group [12]. Prevalence and incidence of type 2 diabetes is higher than the national average, despite Hispanics being the largest minority population in the United States [12]. Because additional research suggests that diabetes and obesity contribute to developing Alzheimer's, we cannot ignore that Hispanics are affected by the diabetes epidemic and are therefore at higher risk for developing Alzheimer's [8].

Nutritional and environmental factors impact the repression of certain anti-aging genes. To explain the anti-aging gene Sirtuin 1 is calorie sensitive, and therefore inactivated by unhealthy diets [13]. Research suggests that Sirtuin 1 (Sirt 1) is linked to the chronic disease epidemic discussed in the paragraph above [13]. There is an association between Sirt 1 being repressed early in the aging process due to chronic and neurogenerative diseases (including Alzheimer's disease) and programmed cell death [14]. According to the *Journal of Diabetes & Metabolic Disorders*, "Unhealthy western diets and lifestyles lead to circadian rhythm disorders with defective nutrient and caffeine metabolism associated with NAFLD, cardiovascular disease and T3D diabetes in the developed world" [15]. Implementing nutritional interventions in the United States would be an effective way to confront the chronic

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disease epidemic because overeating is directly associated with increased risk for the chronic diseases that are associated with a defective Sirt 1 gene [15]. Moreover, Sirtuin 1 is an anti-aging gene proven to become defective in the presence of unhealthy diets and is exacerbated by the chronic disease epidemic disproportionally affecting minority populations in the United States [13].

5. Study Limitations & Strengths

The first limitation of this study that should be considered is the ecological fallacy. The present study used secondary data to gather information from all of the 50 United States. We used secondary data from the Census.gov for each state's general population, including the percentage of that entire state population that is either Hispanic or African American. By considering the entire United States population, we recognize that there is a limitation with how many individuals actually contribute personal data to the Census. Thereby possibly skewing the accuracy of our generalized population data due to those who chose not to participate.

A second limitation relates to our method. We decided to focus on Hispanic and African American populations because they are the two largest minority populations in the United States, considering Census data. But we recognize that there are various other minority populations in the United States that we did not consider, and that various other minorities should be considered in future studies and research on the same topic. It should be noted that our analysis did not confirm that African Americans were associated with and faced equal disparities to Hispanic populations, however other studies pointed out the contrary. This can be due to reverse causation and or due to the fact that this data could be under reported.

Other limitations include not being able to follow up on participants of a study to understand if their health conditions have improved and how it impacts their current overall health in regard to having Alzheimer's. Also, this study is the first ecological study using secondary data that both of the researchers had completed. So, we recognize that there may be limitations with regards to our prior knowledge and experience.

Some strengths in this study are that the collection and interpretation of data help to fill in gaps in the literature published in regard to research conducted to analyze minority populations such as Hispanics and African American communities. Filling in this gap in current literature will promote future research on this topic to identify which factors are impacting minority populations the most. Which can possibly result in the identification of key components that lead to increased rates of Alzheimer's mortality. It will shed light on the importance of minority populations and their health in relation to Alzheimer's disease which evidence clearly shows that disparities exist. Furthermore, the probability of having a stroke and disparities regarding education, income, and access to health care/insurance that minorities experience can impact Alzheimer's onset.

6. Conclusions

Our results showed that being a part of the Hispanic population, being over 65 years old, history of stroke, and income are significantly associated with mortality due to Alzheimer's disease. We rejected our null hypothesis, which was that being a part of a minority group in the United States is not associated with increased risk for dying of Alzheimer's.

We hope that our study promotes minority research and recognizing gaps in healthcare by majority and minority. In addition, by pointing out disparities in access to healthcare and identifying at risk communities who suffer the most because of Alzheimer's, a comprehensive intervention strategy can be developed to promote change and advocate for more resources. We can infer that minority populations are much more likely to experience social determinants of health that negatively impact health outcomes, and thereby increase risk of dying from Alzheimer's disease.

Our findings explain how an association exists between Alzheimer's mortality rates with being a part of a minority population in the United States. Furthermore, the study found that mortality due to Alzheimer's is indeed increasing in the United States, and death results from years of living with progressive negative health conditions. We found that specific factors such as access to healthcare could possibly impact Alzheimer's mortality in the United States and minority populations face disparities in comparison to other populations.

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CASE REPORT

Parkinson Disease Patient with Wheezing Manifestations: A Case Report

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ABSTRACT

The dosing of anti-Parkinson drugs is considered as the optimal control of the symptoms of PD, and increasing the dose of drugs is a common method to treat the aggravate state of PD. However, this is a case of PD elderly patient who had nephritic syndrome, with an increase in the dose, the symptoms did not get improved, but a series of other adverse effects appeared.

1. Introduction

This is a case of Parkinson disease occurred in a 80-year-old male who had nephritic syndrome. With an increase in the dose of anti-Parkinson drugs (Madopar® 3/4 tablet, four times per day; SinemetCR® 1/2 tablet, one time per night; Entacapone 1/2 tablet, four times per day) due to the degression in efficacy, "Dopamine receptor excitement"—wheezing symptoms happened, which was relieved by the down-regulation in the dose of relevant drugs (Madopar® 3/4tablet, three times per day; DC SinemetCR® and Entacapone) to confirm the speculation of overdose. It reminds us that the seniors with PD is more sensitive to anti-Parkinson drugs on the basis of chronic kidney disease, and the highly personalized medications (such as Madopar®) are needed to relieve the relevant symptoms on their renal function.

2. Case Report

A 80-year-old male with 6-year history of Parkinson's disease, the patient had previously received Madopar® therapy, but he experienced wearing-off time over. Based on both the physician's and the patient' s assessment, the treatment was switched to 3/4 Madopar® (levodopa/ benserazide 200/50 mg) tablet four times per day, 1/2 Sinemet CR® (CR-carbidopa/ levodopa 50/200 mg) tablet one time per night, and entacapone 100 mg four times per day, with the aim of improving the curative effect. However, the patient has suffered from wheezing at rest for the last two years, the wheezing occurred 3 times a day, and each lasted for 30-60 minutes. No one knew why did the phenomenon happen so often? The omnibus symptoms

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consisted of wheezing, high blood pressure, elevated heart rate, sweating with facies dolorasa, but he knew what was happening the whole time.

Meanwhile, the patient has suffered from nephritic syndrome, a recent test of renal function showed that the creatinine clearance rate decreased (70.8 ml /min), and the urine microalbumin increased (79.4mg/L). Elevated urine β_2 microglobulin (1571μg/L), suggesting poor renal function. The other examinations showed that coronary CTA and UCG were generally normal. Therefore, it was considered that the excretion of the drugs he took before was remarkably reduced, leading to the accumulation of the anti-Parkinson drugs in his brain, so this dose causes the omnibus symptoms mentioned above. As a result, the doctor in charge gradually reduced the patient's anti-Parkinson medication to only 3/4 Madopar® tablet three times per day, and the omnibus symptoms described previously (wheezing, high blood pressure, elevated heart rate, sweating) were subsequently relieved.

3. Discussion

Generally speaking, the efficacy of anti-Parkinson drugs on a Parkinson individual, such as Madopar®, would wear off with the progress of Parkinson disease, and the agreement between physicians and patients might be easily reached to compensate the "loss", by means of increasing one-single dose or adding other kinds of anti-Parkinson drugs to it, to restore the previous effectiveness. Being worth mentioning, the renal function involving drug excretion in senile patients with Parkinson disease is also declined stepwise over the course due to aging [1]. In this case, the intention of elevation in dose to cover the "gap" somehow evolved into "overaction" of anti-Parkinson drugs in his brain, as a result, the omnibus symptoms of Dopamine-Receptor excitement (wheezing symptoms) occurred. The speculation mentioned above was confirmed by down-regulating the daily dose of relevant drugs (such as Madopar®) to relieve the wheezing symptoms, suggesting that we should pay more attention to this phenomenon of overdose from anti-Parkinson drugs in a senile PD patient with renal insufficiency. Levodopa-induced dyskinesias (LID) are abnormal involuntary movements that develop progressively with repeated dopamine replacement therapy in Parkinson's disease [2]. The pathophysiology of LID comprises many functionally-related abnormalities in neurotransmission which lead to abnormalities in the rate, pattern of breathing abnormality within and outside the basal ganglia [3]. Restrictive breathing abnormalities have been reported in 28% to 94% of people living with Parkinson's disease. The underlying mechanisms of this pattern of breathing abnormality in PD are not fully understood so far [4], which kept asking us to remember that the correlation between the patient's own personal condition and the appropriate amount of the drug couldn't be ignored.

4. Conclusions

Our speculation mentioned above was a bit different from those reviewed here, that is, the seniors with PD is more sensitive to anti-Parkinson drugs on the basis of renal degeneration and the highly personalized medications (such as Madopar®) are needed to relieve the relevant symptoms on their renal function; suggesting that geriatrician should pay more attention to the overaction of anti-Parkinson drugs in a senile PD patient with renal insufficiency.

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ARTICLE

A Study on the Prevalence of Musculoskeletal Disorders among Ageing Workforce of Indian Construction Industry

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ABSTRACT

Ageing work force is one of the leading causes behind the depletion in the growth rate of the labor force in construction industries. Construction industry is a paramount source of employment worldwide after agricultural industry explicitly in urban areas. Manual material handling in construction industries causes musculoskeletal disorders affecting both upper and lower extremities of the body. Studies on lower limb problems due to dynamic work like handling of heavy loads in construction industries are scanty. To analyze the level of exertion, ergonomics risk factors and the prevalence of work-related lower limb disorders among the young and elderly construction workforce. 20 male construction workers in the age group of i) 20 to 30 years (golden age group); ii) 50 years and above were selected from a local construction site in Mumbai. Demographic data like age, height, weight, BMI, body fat, waist hip ratio and risk assessment by questionnaires study comprising QEC, NMQ, VAS, and LEFS were collected. Compared to the golden age group, the elderly subjects were found to feel more discomfort in their lower back, knee and calf regions of lower limb due to immoderate forces and motions tolerated by their lower limbs during their daily work. Muscle pliability and proper coordination diminishes with age and it is appearing to be the most probable reason behind the pain experienced in their lower limbs might be due to improper techniques and postures. For elderly workers, age related limitations become an additional factor to maintain their normal work-life.

1. Introduction

Age and occupation are the intertwined factors that can lead to work related musculoskeletal disorders (WRMSD). Ageing being a vital disquiet among the workforce, so to assign the kind of aligned job to the worker as per their demographic details, requisite changes in the workplace has to be made. Age is not the sole risk factor for WRMSD, if precautions can be taken beforehand [1]. Recently, ageing population has become a considerable apprehension in developed countries. The ripening industrial labor force under present industrial structure and in the absence of appreciable increase in productivity and proper policy measures, creating a dearth in the labor force, leading to economic deceleration [2]. Ageing workforce set bigger pressure on the requirement of higher labor productivity, but education and skills of experienced workers will become a still more important means of complementing the declining growth in the numbers of work force. Labor hungry growth industries like constructions, retail,

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cafes, restaurants etc. are mostly affected [3]. Older workers are greatly valued due to their immense work and life experiences and skills that they had built up over a number of years but many factors which affect them to continue their work life in this industry such as incapability to do the strenuous physical jobs, age related health issues and proneness to injury which needs to be overcome, as the inflow of younger workforce is declining due to lack of job uncertainty and security [4] The most appropriate way to deal with this situation will depend on the pre-selection process of recruiting workers for a particular work on the basis of age and gender, and other physiological & psychological characteristics of the workers of the industry concerned as age affects the mobility, flexibility and strength of a person i.e. human kinetics and kinematics that hinders them to perform the normal work. Various industrial jobs involve various types of heavy labor work or manual material handling and many industrial workers might be in a high-risk category depending on the type of Musculo skeletal problems they were prone to.

In developing countries like India, among all the industries, construction industries provide much needed work opportunities for some of the poorest and most marginalized sections of society (WIEGO). To find the relationships between the level of exertion, ergonomics risk factors and the prevalence of work-related musculoskeletal disorders among the young and elderly construction workforce, this experimental study had been carried out.

2. Methodology

A cross sectional study was conducted among 20 construction workers from a local construction site in Mumbai. The study was commented after permission from the relevant authorities. A written consent was taken from the authority and the details of the study were explained. Information about the study was given at their workplaces. Selections of the subjects were based on non-probability convenient sampling. Selection of the construction site has been a mix of convenience and chance. Data was collected with the help of questionnaire, observation, photography and video recording technique.

There will be following groups:

(1) Elderly male workers of age 50 years and above

(2) Young male workers of age 20-30 years of same occupation

This part of the study was carried out with the help of questionnaire which comprised of demographic data and risk assessment data by Quick Exposure Checklist (QEC), Lower Extremity Functional Scale (LEFS), Nordic Musculoskeletal Questionnaire (NMQ), Visual Analogue Scale (VAS).

2.1 Data Analysis

All unconditional rejoinders for each subject were entered into an excel database and encrypted with numeric values before being analyzed. All collected data were encapsulated using descriptive statistics of mean, standard deviations (±SD) and percentages. Means and standard deviations (±SD) were used to describe the demographic details such as age height, weight, years of experience in that particular job. MSD prevalence rates by body site are calculated as a percentage of all the respondents. Preva-

Table 1. Basic descriptive characteristics of subject groups (N=10)

Variables	Elderly Men (n=10)			Young Men (n=10)			df	t
	Mean	SD	Range	Mean	SD	Range		
Age (years)	58.58	5.68	50.0-69.0	25.50	3.73	20.0-30.0		
Height(cm)	165.63	3.86	155.0-180.0	165.68	9.46	157.5-175.5	8	-0.05
Body Mass(kg)	65.5	11.1	56.9-73.1	63.43	8.20	51.8-74.9	8	0.72
Body Fat (%)	19.08	4.80	15.4-28.7	14.01	3.31	11.01-33.0	8	5.94*
BMI	20.23	6.54	17.6-26.58	23.18	5.47	19.4-32.3	8	3.720*

*p<0.01

Table 2. Occupation History

Variables	Elderly Men (n=10)		Young Men (n=10)	
	Mean	SD	Mean	SD
Working days/week	6.8	0.44	6.8	0.44
Daily Working Hours (%)	8.4	0.81	10.5	1.02
Overtime work (%)	3.2	1.77	4.0	3.99

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lence of all ciphered categorical data were tabulated and charts were plotted for reported symptoms. Statistical associations between independent variables and symptoms in any body site are evaluated using Pearson's Chi square and paired t-test was used to see the work exposure among the technicians experiencing the strain using to see the exposure among the technicians experiencing the strain using Statistical Package for the Social Sciences (SPSS 16).

3. Results and Discussions

Means and standard deviations for physical characteristics of the workers participating in this study are discussed in Table 1. In Table 2, the working schedules were quite hectic for the workers. They used to work almost daily 8 to 10 hours if they had a project in hand and most of the times due to heavy workload, they had to do overtime.

3.1 Characteristics of Work-related Musculoskeletal Disorders

Construction workers reported high prevalence of work-related musculoskeletal symptoms. Percentage of workers reported having discomfort associated with work tasks. The 12 month and 7- days prevalence rated of work-related musculoskeletal disorders reported by the workers were collected. Most of the respondents had reported low back problem in last 12 months as well as last 7 days, followed by knees (30.56%), ankles/feet (18.12% and 15.12%) and upper back (18.36% and 8.16%), the neck (8% and 4%), shoulder (4% and 4.08%), and wrists (3% and 3 %). It shows that the low back, knees, ankles/feet, upper back, neck and shoulders are the most commonly affected body parts among the workers. The result of the present study is very much similar to the study done by Wadell [5] who reported that the number of work-related MSD complaints, suffered during the past 12 months, caused or made worse by work and maximum reported problem were low back pain and lower extremity functional disorders that may be characterized as ephemeral diseases because the pain often subsides and disappears for a while and recurs a few months or years later. A large number of MSDs that recurs weekly were temporary in that the pain (or other symptoms) disappears with rest or when an activity is changed.

The majority (70%) of the respondents had reported work as the cause for their musculoskeletal symptoms while few (25%) reported accident as the casual factor for their musculoskeletal symptoms. Boschman et al [6] concluded a similar result where majority of the workers in construction sites reported their working activity as the most general cause of their proneness to musculoskeletal problems followed by accidents [7].

The subjects were also asked about their intensity of pain or discomfort. It showed that almost more than half of the respondents reported that the pain intensity was mild (60% in young respondents and 40% in elderly respondents), with 25% severity in young respondents and 40% severity in elderly respondents, but very few as extremely severe (15% in young respondents and 20% in elderly respondents). This result is in accordance with the study conducted by the Health and Safety Executive [8] which showed similar reported pain intensity among the older and younger workers. The study said that mild pain starts within a few months of work among the younger age group which turns into severity with age, as they ignore the pain because of their withstanding capacity. But with age this pain turns into chronic severity, so older population suffers from chronic pain rather than mild symptoms.

The frequency of musculoskeletal symptoms showed that nearly 35% young and 45% elderly respondents experience musculoskeletal discomfort in one or more times a week while 35% young and 20% elderly respondents experience musculoskeletal discomfort in one or more times a month whereas 20% young and 30% elderly respondents reported that they suffer daily and few of them (10% young and 5% elderly respondents) had reported the musculoskeletal discomfort one or more times a year. It was observed that majority of the workers experienced pain one or more times a week, so it can be said that the frequency of pain is quiet high among the respondents. Further it was found that the rated absenteeism from the work due to musculoskeletal symptoms. Most of them used to continue to work irrespective of their body discomforts.

Table 3. Relationships of work-related musculoskeletal disorders and the personal characteristics which are related to the work-related musculoskeletal disorders

Variables		Frequency of WMSDs	WMSDs (%)	Chi-square	p-value
Age	21-30 years	3 out of 10	15	5.208	0.023*
	50 years and above	9 out of 10	45		
Work Experience	>5 years	4	20	2.649	0.481
	>10years	9	45		
	>20 years	7	35		

significant* at df=1

There were some variables in the personal characteristics which were related to the work-related musculoskeletal disorders. Table 3 showed that the association of WMSDs were significantly associated with increasing age

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(χ^2=5.208; p=0.023) but no significant association were found with gender and work experiences. The prevalence rate of work-related musculoskeletal disorders was highest (45%) among the respondents who were at age group of 50 years and above. Further it was observed that the females (40%) were more prone to work related musculoskeletal disorders. Highest percentage of respondents (45%) experienced their first episode of WMSDs in their 10 years and above work experiences. Almost all of the respondents were doing overtime irrespective of age and gender and thus most of them found to be more prone to work related musculoskeletal disorders. Similar conclusion was drawn by Bodhare et al. [9] which said that globally, MSD is the largest single cause of work-related health issues, accounting for over 33% of all newly reported occupational illnesses in the general population and 77% in construction workers. Most of the elderly workers experienced discomforts more than one times a week and this was more frequent among the older workers compared to younger group both in case of males and females. Kuorinka et al. [10] observed similar relationship between personal characteristics and WRMSDs.

3.2 Musculoskeletal Symptoms among the Workers

Construction workers perform specially loading and unloading tasks were all analyzed using Nordic Questionnaire. The analysis showed that in different body parts the symptoms were maximum in knees and lower back (90% and 80% in elders; 65% and 65% in young respectively), followed by ankle/feet (60% in elders and 20% in young) and shoulder (45% in elders and 30% in young). For all the body parts the exertion level was high in the lower extremities than upper extremities while load carriage. This result is in accordance with the study conducted by the Health and Safety Executive [8] and Boschman et al [6] which showed maximum both elder and young workers had been suffering from low back pain followed by knees and ankles. Again, in their study it was revealed that elder workers were the most vulnerable age category.

3.3 Magnitude of the Musculoskeletal Discomfort among the Workers

Visual analogue scale (VAS) was used to measure the magnitude of the musculoskeletal discomfort experienced by the workers after their work. It was used to analyze the musculoskeletal strain in different body parts perceived by them. They rated the strain after their work exposure that is represented in Table 5.

The analysis of above table shows that there is a significant difference between the means of young and elderly workers scores of lower backs (t=-2.881, p=0.009); knees (t=2.598, p=0.017); calf (t=-2.331, p=0.030); thighs (t=-2.661, p=0.015). The negative t value shows that the intensity of pain has increased in the respective regions with age. Health and Safety executive [8] reported significant differences between the elderly and younger workers while assessing the pain intensity during the work of the construction workers.

Table 5. Reported intensity of pain after work exposure

Body Regions	Young	Elderly	T test	P value
Neck	0.0204	0.1222	-1.000	0.329
Shoulder	0.0346	0.2245	-1.429	0.169
Upper Back	0.7372	1.9837	-1.000	0.329
Lower Back	0.6531	1.5102	-2.881	0.009
Wrist	0.0612	0.1324	-1.385	0.182
Hips	0.0001	0.2657	-0.275	0.217
Thighs	0.0650	0.6335	-2.661	0.015
Buttocks	0.0000	0.2020	-1.000	0.329
Knees	0.1837	0.8776	-2.598	0.017
Calf	0.2178	0.9225	-2.331	0.030
Ankles	0.1783	0.4060	-1.000	0.329
Feet	0.1632	0.3645	-1.385	0.182

3.4 Lower Extremity Exertion

Functional assessment of the lower extremities is an essential aspect of the evaluation of both young and elderly people. To evaluate whether objective physical function tests can predict subsequent impairment in older people, we conducted this research. Objective tests of lower-extremity function were highly predictive of subsequent impairment among non-disabled older people living in the group. Measures of physical performance may identify older persons with a preclinical stage of disability who may benefit from interventions to prevent the development of frank disability. Extreme exertion was found maximum among elderly (40%) and moderate exertion (40%) was maximum among young respondents. Health and Safety Executive research [8] has also shown that in many workplaces where constant static standing or repetitive walking activity are involved, especially knee conditions are a concern and appear to be similar to conditions in other areas of the body, such as the lower back and ankles. Staff can suffer acute as well as overuse injuries, although overuse injuries appear to be more common. Elderly people showed extreme exertion in lower extremity in physical demanding work compared to younger group due to loss of flexibility and proper coordination of muscular activity

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and therefore lack of balance tends to make the exertion level higher in that case. The findings of the above study have shown similar trend like ways.

4. Conclusions

In the present study of 20 construction workers, it is found that the prevalence of musculoskeletal symptoms was high among the elderly workers compared to that of younger workers. The body parts that are mostly affected apart from upper limbs are lower back and lower extremities as this are the regular affected body sites for the construction workers but mostly got ignored until immobility ceased their work-life. It was found that the highest prevalence of MSD is observed in lower back causing severe back pain, followed by pain at knee, feet/ankle and pain at upper back regions as well. Most of the elderly workers claimed to perceive discomfit in their lower back region and knees when they are back to home. The workers claimed that this pain was due to the excessive force and motions used during their daily manual material handling work and the impact is felt to be the cumulative effect of ignored activity i.e., continuous walking activity during manual material handling. It was presumed that the back pain the workers were experiencing might be a result of their ignorance in the correct and ergonomic techniques in the mode of handling load. Musculoskeletal injuries, such as lower back pain, knee pain, slips and falls due to age related changes were very common in older workers, therefore, maintaining musculoskeletal health was important. Work stations and job tasks needed to be matched to the capacity of each worker. The workplace can be designed and redesigned as per the requirement of all the workers in order to accommodate both younger and older workers with the ability and desire to adapt themselves with the positive changes in the industry. This study will also help the employers to keep their aging employees healthier and working longer. Ergonomics programs and workplace design strategies will help the older employees perform their jobs productively and safely by reducing the 'performance gap'.

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ARTICLE

Effects of Free Time on Quality of Life in Elderly Caregivers

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ABSTRACT

Caregivers who contribute to health care of their patients are significantly more likely to experience emotional difficulty, physical difficulty, and financial difficulty, than caregivers who do not contribute. This study aimed to examine the effects of free time on health-related quality of life among elderly caregivers of dementia patients. In the intervention group, caregivers set aside free time every 30 minutes three times a week, while continuing to care for patients. During the free time, caregivers were free to spend time at home and do whatever they wanted. The control group received only usual care. The intervention period was six months. The Vitality subscale score of the SF-36 decreased significantly in the intervention group, despite more than half (57.1%) of participants showing improvements or no change in the rank of this subscale relative to baseline, as assessed by the Wilcoxon signed-rank test (not significant). Caregivers indicated that daily caregiving resulted in an accumulation of physical fatigue, and they continued to have little mental leeway. Caregivers also had difficulty securing free time, which may have hindered improvements to their vitality. There is a need to develop a home-based program that can alleviate caregiver stress and improve their quality of life.

1. Introduction

Family caregivers of dementia patients experience considerable burden [1]. Almost half of dementia patient caregivers reportedly experience stress at levels in moderate to very severe ranges [2]. Moreover, caregiving for dementia patients is associated with depression [3,4], and older caregivers are especially at increased risk of severe depressive symptoms [5].

Caregivers who contribute to health care of their patients are significantly more likely to experience emotional difficulty, physical difficulty, and financial difficulty, than caregivers who do not contribute. Compared to caregivers who do not contribute to health care activities, those who provide substantial contributions were more than five times as likely to experience participation restrictions in

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valued activities, and more than three times as likely to experience work productivity loss [6].

Intervention studies targeting caregivers of dementia patients found that psychoeducational intervention by telecommunication or face-to-face interviews improved quality of life (QOL) relative to a control group [7,8,9]. These methods hold promise in terms of providing remote support when people are restricted from going outside, for example, to care. Support via telemedicine using video conferencing has been shown to improve the resilience and well-being of both patients and caregivers compared to telephonic support [10].

Internet interventions for informal dementia caregivers can improve various aspects of caregiver well-being, for example, confidence, depression, and self-efficacy, provided that they comprise multiple components and are tailored to the individual [11]. Similarly, web-based interventions have the potential to reduce depressive symptoms, anxiety, stress, and distress among informal caregivers of chronically ill adults in the community [12]. However, fewer elderly individuals use computers and the Internet compared to younger people [13]. Therefore, other methods are needed to improve the health of the elderly at home.

Decision support for the selection of respite services by caregivers of patients with dementia was reported to be less burdensome [14]. In addition, intervention trials with relaxation techniques in caregivers of dementia patients were shown to improve stress, depression, and negative bias scores [15]. Previous studies have reported on relationships between free time and QOL among caregivers, as well as interventions aimed at ensuring free time for caregivers. These studies suggest that incorporating free time into the lives of caregivers may improve their QOL.

The purpose of this study was to examine the effects of free time on the QOL of elderly caregivers of dementia patients.

2. Methods

2.1 Research Design

This study was a randomized controlled trial. After consent was obtained from caregivers, they were randomly assigned to the intervention group or control group. In the intervention group, free time was set aside every 30 minutes three times a week while caregivers continued to provide routine care. During the free time, caregivers were free to spend time at home and do whatever they wanted. Caregivers of the control group received only usual care. The intervention period was six months.

2.2 Participants

The target population was elderly caregivers living with dementia patients.

2.3 Caregiver Assessments

The main outcome for caregivers was QOL after six months of intervention, as assessed by the SF-36, a measurement tool widely used to assess health-related QOL [16]. QOL was compared between the intervention and control groups at baseline and six months after initiation of the intervention.

2.4 Statistical Analysis

The Mann-Whitney U test was used to analyze data of the intervention and control groups at baseline. The Wilcoxon signed-rank test was used to analyze post-intervention data from the two groups. All statistical tests were two-tailed, with the significance level set at 5%.

2.5 Ethical Considerations

This study was approved by the ethics committee of Nagoya University Graduate School of Medicine. Caregivers who provided informed consent were included in the study and were informed that participation was voluntary.

3. Results

Table 1 summarizes the characteristics of caregivers of dementia patients. In the intervention group, 11 participants were female and the median care time was 6.0 hours. In the control group, 14 participants were female. In the intervention and control groups, the median number of family members living together (including the dementia patient) was 2.0, and relatives helping with care lived separately. In the intervention group, Physical Functioning, Bodily Pain, and Social Functioning subscale scores of the SF-36 were above the national norm, while Role Physical, General Health, Vitality, Role Emotional, and Mental Health subscale scores were below the national norm. In the control group, total SF-36 scores were generally lower than the national norm, and Role Physical and Mental Health subscale scores were much lower than the national norm.

Post-intervention changes in the intervention group are shown in Table 2. The Vitality subscale score was significantly decreased post-intervention relative to baseline, while other subscale scores did not significantly differ between baseline and post-intervention. Table 3 compares ranks in the intervention group after the intervention using

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the Wilcoxon signed-rank test. The Vitality subscale had a positive rank of 3, a tied rank of 9, and a negative rank of 9, which did not significantly differ from baseline, but the subjects improved (N=3). Positive and tied (positive/tied) ranks comprised 57.1% of the total. Physical Functioning and General Health subscales had positive/tied ranks in 61.9% of participants, and Social Functioning and Role Emotional subscales had positive/tied ranks in 71.4% of participants. Subscale and summary scores with more positive/tied ranks than negative ranks were observed for the following: Physical Functioning, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, Mental Health, and Mental component summary. The following had more negative ranks than positive/tied ranks: Role Physical (61.9%), Physical component summary (57.1%), and Role/Social component summary (57.1%).

Changes relative to baseline after the intervention in the control group are shown in Table 4. The Physical component summary (66.7%) had more negative ranks, while other subscale and summary scores had more positive/tied ranks.

Table 1. Baseline characteristics of caregivers

	Intervention		Control		
	Median	IQR	Median	IQR	P
Age	75.0	72.0-78.0	77.0	73.0-80.0	0.073
Gender Male/Female (N/%)	10 / 11		7 / 14		0.351
Care hours per day (hours)	6.0	2.5-14.5	8.0	2.0-16.0	0.561
Number of family members living together	2.0	2.0-2.5	2.0	2.0-2.0	0.499
SF-36 subscales					
Physical Functioning	50.6	43.4-54.2	47.0	29.0-54.2	0.221
Role Physical	45.8	34.2-55.7	39.1	22.5-55.7	0.378
Bodily Pain	50.1	40.3-54.6	44.7	35.4-49.7	0.075
General Health	44.2	39.2-52.2	41.5	37.8-50.9	0.503
Vitality	49.8	45.0-54.7	43.4	35.4-49.8	0.030
Social Functioning	50.6	34.5-57.0	44.1	31.2-53.8	0.236
Role Emotional	43.6	35.3-54.0	43.6	29.0-56.1	0.600
Mental Health	43.8	41.1-50.5	38.4	37.1-45.2	0.059
SF-36 summary scores					
Physical component summary	47.8	42.6-56.3	48.9	33.1-56.4	0.563
Mental component summary	49.2	40.2-57.1	44.1	36.4-51.2	0.242
Role/Social component summary	45.1	33.8-57.3	41.9	28.3-52.0	0.428

Notes: The SF-36 score represents the national norm. Data are presented as median. The number of family members living with the patient includes the dementia patient. IQR, interquartile range.

Table 2. Changes in the intervention group after intervention relative to baseline

Change after intervention (Δ)		N	Average rank	Rank sum	Z	P
SF-36 subscales						
Physical Functioning	Negative ranks	8	10.0	80.0	-.639	0.523
	Positive ranks	8	7.0	56.0		
	Tied ranks	5				
Role Physical	Negative ranks	13	8.8	114.0	-.766	0.444
	Positive ranks	6	12.7	76.0		
	Tied ranks	2				
Bodily Pain	Negative ranks	9	6.7	60.0	-.414	0.679
	Positive ranks	7	10.9	76.0		
	Tied ranks	5				
General Health	Negative ranks	8	8.4	67.5	-.785	0.432
	Positive ranks	10	10.4	103.5		
	Tied ranks	3				
Vitality	Negative ranks	9	7.1	64.0	-1.970	0.049
	Positive ranks	3	4.7	14.0		
	Tied ranks	9				
Social Functioning	Negative ranks	6	6.0	36.0	-.672	0.501
	Positive ranks	7	7.9	55.0		
	Tied ranks	8				
Role Emotional	Negative ranks	6	7.3	43.5	-.140	0.889
	Positive ranks	7	6.8	47.5		
	Tied ranks	8				
Mental Health	Negative ranks	10	10.1	100.5	-.524	0.600
	Positive ranks	11	11.9	130.5		
	Tied ranks	0				
SF-36 summary scores						
Physical component summary	Negative ranks	12	11.0	132.0	-.574	0.566
	Positive ranks	9	11.0	99.0		
	Tied ranks	0				
Mental component summary	Negative ranks	10	11.0	110.0	-.191	0.848
	Positive ranks	11	11.0	121.0		
	Tied ranks	0				
Role/Social component summary	Negative ranks	12	10.8	129.5	-.487	0.627
	Positive ranks	9	11.3	101.5		
	Tied ranks	0				

Change after intervention (Δ) = post-intervention value – baseline value.

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Table 3. Comparison of ranks in the intervention group after intervention

Ranks	SF-36 scale	Positive/tied ranks (N / %)	Negative ranks (N / %)
More positive/ tied ranks than negative ranks	Physical Functioning	13 / 61.9%	8 / 38.1%
	Bodily Pain	12 / 57.1%	9 / 42.9%
	General Health	13 / 61.9%	8 / 38.1%
	Vitality	12 / 57.1%	9 / 42.9%
	Social Functioning	15 / 71.4%	6 / 28.6%
	Role Emotional	15 / 71.4%	6 / 28.6%
	Mental Health	11 / 52.4%	10 / 47.6%
	Mental component summary	11 / 52.4%	10 / 47.6%
More negative ranks than positive/tied ranks	Role Physical	8 / 38.1%	13 / 61.9%
	Physical component summary	9 / 42.9%	12 / 57.1%
	Role/Social component summary	9 / 42.9%	12 / 57.1%

Table 4. Changes in the control group after intervention relative to baseline

Change after intervention (Δ)		N	Average rank	Rank sum	Z	P
SF-36 subscales						
Physical Functioning	Negative ranks	10	8.00	80.00	-.633	0.527
	Positive ranks	6	9.33	56.00		
	Tied ranks	5				
Role Physical	Negative ranks	9	5.94	53.50	-1.092	0.275
	Positive ranks	8	12.44	99.50		
	Tied ranks	4				
Bodily Pain	Negative ranks	9	9.17	82.50	-.504	0.614
	Positive ranks	10	10.75	107.50		
	Tied ranks	2				
General Health	Negative ranks	8	8.75	70.00	-.308	0.758
	Positive ranks	9	9.22	83.00		
	Tied ranks	4				
Vitality	Negative ranks	4	11.25	45.00	-.855	0.393
	Positive ranks	11	6.82	75.00		
	Tied ranks	6				
Social Functioning	Negative ranks	8	9.19	73.50	-.525	0.600
	Positive ranks	10	9.75	97.50		
	Tied ranks	3				
Role Emotional	Negative ranks	7	6.86	48.00	-.683	0.495
	Positive ranks	8	9.00	72.00		
	Tied ranks	6				
Mental Health	Negative ranks	7	5.86	41.00	-1.683	0.092
	Positive ranks	10	11.20	112.00		
	Tied ranks	4				
SF-36 summary scores						
Physical component summary	Negative ranks	14	9.25	129.50	-.487	0.627
	Positive ranks	7	14.50	101.50		
	Tied ranks	0				
Mental component summary	Negative ranks	8	11.81	94.50	-.730	0.465
	Positive ranks	13	10.50	136.50		
	Tied ranks	0				
Role/Social component summary	Negative ranks	8	12.00	96.00	-.678	0.498
	Positive ranks	13	10.38	135.00		
	Tied ranks	0				

Change after intervention (Δ) = post-intervention value – baseline value.

4. Discussion

This study examined the effects of free time on the QOL of elderly caregivers of dementia patients. Overall, setting aside free time did not improve QOL in home-based caregivers. In terms of post-intervention changes, the intervention group had a significant decrease in the Vitality subscale score of the SF-36, despite 57.1% of participants showing an improvement or no change in the score. Other subscale scores did not significantly differ between baseline and post-intervention.

In a previous intervention study, a program to support family caregivers suffering from above-average levels of depression and anxiety in the home management of dementia was implemented. After the six-month intervention period, neither the experimental group nor the control group showed improvements in these areas. However, the experimental group showed a clinically important improvement in QOL, experienced a slightly longer mean time to long-term institutionalization, found the caregiver role less problematic, and had greater satisfaction with nursing care than the control group [17]. Caregivers in the present study had QOL scores after intervention that were lower than baseline scores, indicating that caregivers were accumulating physical fatigue from daily caregiving and that they continued to have little mental leeway. These caregivers had difficulty securing free time, making it difficult for them to balance caregiving with their current situation, and this may have prevented them from improving their vitality. Through the intervention, caregivers hoped their vitality would improve and that they would become more energetic and motivated. The change in scores in the intervention group showed that some caregivers were able to improve or maintain their QOL, suggesting that the intervention may have had some effect. However, as a whole, the QOL of these caregivers decreased. These findings highlight the difficulty of developing a program to improve QOL without altering the care situation itself.

Home-based programs for caregivers of dementia patients have been reported to be important for QOL changes [18]. In this regard, developing programs that can maintain and improve the vitality of caregivers and enable them to lead their daily lives while caring for others in a lively and positive manner will be important. Home support has been reported to deepen the connection of caregivers to support [19]. Thus, exploring home-based intervention methods to improve caregiver QOL is meaningful. According to a previous study, respite care had no impact on care burden or mental health of caregivers, although there was a very high level of satisfaction [20]. This suggests the potential advantage of incorporating respite care into support pro-

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grams and providing time away from caregiving so that the caregivers can rest and conserve energy.

Some caregivers in the control group showed improvements (albeit non-significant) in health-related QOL scores. The increased number of caregivers with an improved Vitality subscale score might be attributed to the Hawthorne effect. For instance, caregiver QOL may have improved due to the psychological support provided by act of participating in the study itself, rather than having free time. It was suggested that there is an urgent need to improve the program according to the health status of dementia caregivers in the future.

5. Conclusions

The results of the present study suggest the need to develop a home-based program that can alleviate caregiver stress and improve QOL. A long-term follow-up study with a larger sample size will be needed to plan further intervention studies according to the QOL status of caregivers.

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Disclosure Statement

The authors declare no conflict of interest.

Author's Contributions

Akemi Hirano conceived the idea and designed the study, carried out the data analysis and interpretation, wrote the first draft of the manuscript, and contributed to the overall supervision of the study. Yusuke Suzuki, Koichiro Ina, and Toshio Hayashi recruited the participants. Yusuke Suzuki, Koichiro Ina, and Joji Onishi critically discussed all versions of the manuscript.

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ARTICLE

Factors Affecting Catecholamines in Caregivers of Patients with Dementia

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ABSTRACT

Background: Caregivers of dementia patients have significantly higher levels of serum IL-6 and CRP compared to non-caregivers, and the accumulation of everyday stressors reportedly promotes the induction of inflammatory markers. However, few studies have identified factors that affect catecholamine levels in caregivers who experience a combination of physical and mental stress from caregiving.
Purpose: This study aimed to identify physical factors that impact catecholamine levels in caregivers of dementia patients. **Methods:** Participants were elderly caregivers living together with elderly Alzheimer's-type dementia patients. We performed logistic regression analysis, with levels of adrenaline, noradrenaline, and dopamine (indicators of catecholamine) as dependent variables. **Results:** Caregiver BMI had a significant impact on adrenaline levels (OR: 0.792; 95%CI: 0.654-0.960) and noradrenaline levels (OR: 1.210; 95%CI: 1.009-1.451), whereas age had a significant impact on dopamine levels (OR: 1.162; 95%CI: 1.019-1.324). **Discussion:** While caregiver BMI significantly impacted adrenaline and noradrenaline levels, the mechanism underlying these relationships is unclear. One possibility is that obesity (BMI) and a rise in sympathetic nerve activity contributed to hypertension. Our findings suggest that chronic stress in elderly caregivers may potentially impair the dopaminergic activation system in the brain. **Conclusion:** There is a need to identify factors which increase BMI in caregivers. Future studies aimed at gaining a better understanding of the lifestyle habits of caregivers and intervention studies aimed at reducing their BMI are warranted.

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1. Introduction

The mortality risk of caregivers has been reported to be 63% higher than that of non-caregivers [1]. The chronic stress experienced by caregivers of dementia patients is thought to cause physiological changes in the body. Levels of D-dimer, a marker of fibrin formation and degradation, are reported to be significantly higher in caregivers than in non-caregivers [2]. Similarly, caregivers of dementia patients have higher serum IL-6 and CRP levels relative to non-caregivers, and the accumulation of everyday stressors promotes an increase in inflammatory markers [3].

Patients with probable Alzheimer's type dementia have a median survival period of 11.3 years from onset and 5.7 years from diagnosis [4]. Caregivers of dementia patients are reported to experience a greater level of physical burden and mental distress than caregivers of patients with other disorders [5]. One in three caregivers experiences depression, with depression occurring more frequently in caregivers of dementia patients compared to caregivers of patients with other chronic diseases [6].

Aging and chronic stress can have a devastating impact on the vulnerable brain [7]. The various emotions resulting from stress are caused by neurotransmitters such as noradrenaline and dopamine. Pathways triggered by these neurotransmitters have been studied in detail and are known to be closely related to emotions [8]. Activation of sympathetic nerves results in the secretion of catecholamines (adrenaline, noradrenaline, and dopamine), leading to vasoconstriction, increased heart rate, and increased blood pressure, which can result in the onset of circulatory disorders. Moreover, mental stress is known to excite sympathetic nerves [9]. Many organs are innervated by autonomic nerves. For instance, autonomic nerves innervate endocrine grands and regulate hormone secretion.

Only a few studies have examined factors which impact catecholamine levels when caregivers of dementia patients suffer from a combination of physical and mental stress due to caregiving. Therefore, the present study aimed to identify health-related factors which impact catecholamine levels in caregivers of dementia patients.

2. Methods

2.1 Participants

Participants were elderly caregivers living together with Alzheimer's-type dementia patients, and included caregivers who had good control of chronic diseases such as hypertension, diabetes, and dyslipidemia. Those with severe heart diseases and stroke were excluded.

2.2 Research Design

This was a cross-sectional study conducted to analyze factors which influence catecholamines in caregivers.

2.3 Caregiver Scales and Assessed Factors

To evaluate catecholamines, we assessed the levels of adrenaline, noradrenaline, and dopamine. Adrenaline has a heart-stimulating effect and is also involved in sugar and fat metabolism, noradrenaline has a hypertensive effect, and dopamine (a precursor of noradrenaline) has a specific effect on the central nervous system, renal system, circulatory system, and digestive system. The higher the levels of these catecholamines, the stronger their impact on the cardiovascular system.

The Japanese version of the Zarit Burden Interview (ZBI) was used to assess caregiver burden [10]. We also assessed BMI by caregivers.

2.4 Ethical Considerations

This study was approved by the ethics committee of Nagoya University Graduate School of Medicine. Participants provided informed consent after they received a clear explanation that participation in the present study was voluntary.

2.5 Statistical Analysis

For logistic regression analysis, dichotomized (high or low) levels of adrenaline, noradrenaline, or dopamine based on median levels were entered into the models as dependent variables. Statistical analyses were performed using SPSS25. $P<0.05$ was considered statistically significant.

3. Results

Of the participants, 23 were male and 29 were female. Levels of noradrenaline and dopamine were slightly higher than reference levels. Median systolic blood pressure values were 143.0 and 134.8 for males and females, respectively, with no significant difference between the two ($P=0.574$; Table 1).

Table 2 shows the results of the bivariate correlation matrix. Noradrenaline levels were significantly correlated with dopamine levels ($r=0.456$, $p<0.05$), but no significant correlation was observed between adrenaline and noradrenaline levels.

Table 3 shows the results of the bivariate correlation matrix for hormone secretion and caregiver factors. Adrenaline levels showed a significant negative correlation with BMI ($r=-0.345$, $P<0.05$), while noradrenaline

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levels showed a significant positive correlation with BMI (r=0.297, P<0.05). Dopamine levels showed a significant positive correlation with age (r=0.354, P<0.05).

Table 4 shows the results of a binomial logistic regression model with caregiver age, sex, total sense of care burden, BMI, and number of oral medications as independent variables. The high and low levels of each hormone were entered as dependent variables using the stepwise method. Hormone levels were dichotomized based on whether they were below or above the respective median level (0, 1) in order to extract factors that impact each hormone.

Caregiver BMI was extracted as a factor that significantly impacted adrenaline levels (OR: 0.792, 95%CI: 0.654-0.960) and noradrenaline levels (OR: 1.210, 95%CI: 1.009-1.451). Age was extracted as a factor that significantly impacted dopamine levels (OR: 1.162, 95%CI: 1.019-1.324). Binomial logistic regression analysis revealed that caregiver BMI significantly impacted.

4. Discussion

The present study identified age and BMI as health-related factors which impact catecholamine levels in caregivers of dementia patients.

Noradrenaline levels were found to be significantly correlated with dopamine levels. Stress is known to stimulate the hypothalamo-pituitary-adrenal system, as well as the sympathoadrenal system [11-13]. Adrenaline is secreted into the blood from the adrenal medulla, noradrenaline is secreted from sympathetic nerve endings, and cortisol is secreted into the blood from the adrenal cortex [14-16]. Both noradrenaline and dopamine are secreted from the adrenal medulla. Noradrenaline and adrenaline have been reported to inhibit the production of inflammatory cytokines by dendritic cells via β receptors [17-18]. However, little is known about their other effects. In the present study, noradrenaline and dopamine levels were correlated with each other, suggesting that both catecholamines may be an objective indicator of stress response, which we surmise reflects stress from caregiving.

Mental stress tests markedly induce epinephrine release [19]. Epinephrine (adrenaline) responses are negatively correlated with changes in BMI and waist circumference [20]. Moreover, noradrenaline levels at rest have been shown to be a positive predictor of BMI [21]. Although we identified caregiver BMI as a significant factor which impacts adrenaline and noradrenaline levels, how they are related mechanistically remains unknown. Some of the impairments in plasma glucose-insulin homeostasis noted in visceral obesity may be related to an abnormal metabolic response to an adrenaline challenge [22]. According to one study, only plasma norepinephrine and BMI were significant independent predictors of blood pressure, suggesting that obesity and heightened sympathetic nervous system activity contribute to blood pressure elevation [23].

Age was identified as a factor which significantly impacts dopamine levels. Dopamine levels and dopamine transporter density have been reported to decrease with age[24-25]. However, our results are inconsistent with the report that dopamine transporter density declines with age. Dopamine levels were heightened in our participants, despite them being elderly with a median age of 76 years. In fact, we found that dopamine levels tended to increase with age, with dopamine and age showing a positive correlation. This suggests that dopamine levels are increased in the elderly caregivers of the present study. One reason for this observation might be that caregiving activities stimulated the brain, which in turn led to the activation of dopamine receptors.

Our findings suggest that neurotransmission is likely to be highly active in elderly caregivers. Furthermore, given that dopaminergic neurons are reportedly more susceptible to neuroinflammation from chronic stress than other types of brain cells[26-27], chronic stress in elderly caregivers might impair the dopaminergic activation system in the brain.

5. Conclusion

The present study identified factors which impact catecholamine secretion due to stress in caregivers of dementia patients. Specifically, age and BMI were found to impact catecholamine levels. In view of this finding, identifying factors which contribute to increased BMI will be important. Future studies aimed at gaining a better understanding of the lifestyle habits of caregivers and interventional studies aimed at reducing BMI are needed. Furthermore, the small sample size was another limitation of this study. Accordingly, future studies should follow and observe these blood biochemical factors in the long term.

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Disclosure statement

The authors declare no conflict of interest.

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Table 1. Participant characteristics

	Median	IQR (25-75%)
Caregiver Age	76	72-79
Adrenaline (Ref: ≤100) (pg/mL)	39.5	22.3-56
Noradrenaline (Ref: 100-450) (pg/mL)	610	471-718.3
Dopamine (Ref: ≤20) (pg/mL)	21.0	14-31.3
BMI	23.4	20.7-25.2
SBP	142	125.5-147.8
DBP	78	72.8-87.5

BMI: Body mass Index, SBP: systolic blood pressure, DBP: diastolic blood pressure

Table 2. Associations of outcome measures

		1	2	3
1. Adrenaline	r	1.000		
	p (two-tailed)			
2. Noradrenaline	r	.137	1.000	
	p (two-tailed)	.333		
3. Dopamine	r	.188	.456*	1.000
	p (two-tailed)	.183	.001	

*r: Spearman's correlation coefficient; p: significance level, *p < 0.05*

Table 3. Correlations between catecholamines and caregiver factors

		Age	SBP	BMI
Adrenaline	r	.099	-.002	-.345*
	P	.487	.988	.012
Noradrenaline	r	.002	.030	.297*
	P	.991	.832	.032
Dopamine	r	.354*	-.066	-.069
	P	.010	.640	.625

*r: Spearman's correlation coefficient; p: significance level, p < 0.1, *p < 0.05, **p < 0.01*

Table 4. Logistic regression analysis with catecholamines as the dependent variable

					95% CI	
Dependent variable	Variable (covariate)	B	P	OR	Lower limit	Upper limit
Adrenaline	BMI	-.233	.017	.792	.654	.960
Noradrenaline	BMI	.191	.040	1.210	1.009	1.451
Dopamine	Caregiver age	.150	.025	1.162	1.019	1.324

Two groups for each catecholamines based on median values were created, as follows: adrenaline (<39.5=0; ≥39.5=1), noradrenaline (<610=0; ≥610=1), dopamine (<21=0; ≥21=1). B: partial regression coefficient, P: level of significance, 95%CI: 95% confidence interval, BMI: Body Mass Index.

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Author's contributions

Akemi Hirano conceived the idea and designed the study. Akemi Hirano carried out the data analysis and interpretation. Akemi Hirano wrote the first draft of the manuscript and Yusuke Suzuki, Koichiro Ina, Joji Onishi critically discussed all versions of the manuscript. Yusuke Suzuki, Koichiro Ina, and Toshio Hayashi recruited the participants, and Akemi Hirano contributed to the overall supervision of the study.

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