"The Effect of Sitagliptin on Carotid Artery Atherosclerosis in Type 2 Diabetes"

Literature Review and Data Analysis

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"On my honor, I have not given, nor received, nor witnessed

any unauthorized assistance on this work"

Abstract

Statistical analysis was performed using the raw data from a study entitled, “The Effect of Sitagliptin on Carotid Artery Atherosclerosis in Type 2 Diabetes.” There were 442 men and women who participated in the primary analysis of the study. Statistical tests were performed to better understand whether or not sitagliptin treatment would have an effect on the progression of atherosclerosis while also successfully managing type 2 diabetes. Descriptive statistics, chi-square, t-tests, and linear regressions were performed to answer the following specific research questions. A chi-square test was used to determine if the population mean of the allocation of treatment was higher in the mean population of males over females. Two separate t-tests were run. The first t-test was performed to determine whether the population mean of intima-media thickness (IMT) was lower in patients receiving treatment than in patients not receiving treatment. The second t-test was performed to determine whether or not the population mean of systolic blood pressure (SBP) was lower in patients receiving treatment than in patients not receiving treatment. A linear regression model and correlation were used to determine if there was a statistically significant linear relationship between IMT and age.

"The Effect of Sitagliptin on Carotid Artery Atherosclerosis in Type 2 Diabetes"

Literature Review

A randomized study was performed on participants with type 2 diabetes mellitus (T2DM) to compare the effects of sitagliptin treatment to conventional treatments and therapies in the context of both diabetes and coronary artery disease (Oyama 2016). Previous studies that have been done suggest the dipeptidyl peptidase-4 inhibitors are conducive to providing cardiovascular protection, thus researchers wanted to use a medication in this class, sitagliptin, to test whether or not it would be effective in slowing the progression of the carotid IMT levels in patients who were participating in the study (Matsubara 2012). Conventional therapies include diet, exercise, and some non-incretin-related drug intervention for patients with type 2 diabetes, which essentially means that patients with type 2 diabetes were given a medication that was guaranteed to just regulate insulin levels without having any cardiovascular effects (Oyama 2016). The effects of the sitagliptin compared to the conventional methods were measured by evaluating intima-media thickness (IMT) of the carotid artery, HA1c levels, and systolic blood pressure. IMT of the carotid artery is an extremely effective marker that can be used to track atherosclerotic cardiovascular disease. Therefore, researchers were able to effectively monitor the effects of these various types of treatments on both coronary artery disease and type 2 diabetes mellitus. Endpoints in experimental data were determined by the percentage change in the mean IMT values in participants after a 12-month-period as well as a 24-month period of treatment (Oyama 2016).

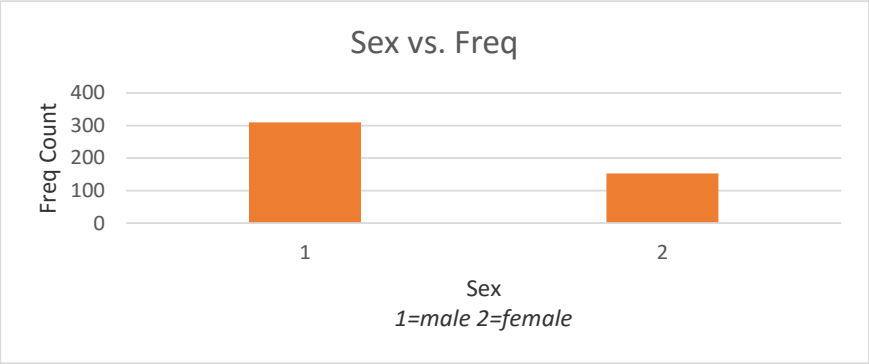
Individuals selected for the study were all 30 years of age or above and had been previously diagnosed with type 2 diabetes. Allocation of sitagliptin treatment versus conventional treatment was completely randomized for all 442 men and women participating in

the study. 222 participants were administered sitaglipin treatment, while 220 participants were in the conventional therapy group (Oyama 2016). This study was conducted at 48 different medical centers within Japan. Patients with type 1 diabetes, heart failure, prior cardiovascular or diabetes related complications were excluded from the study along with any patients who were already receiving DPP-4 inhibitors in other medications (Matsubara 2012).

At the end of 24-month study, researchers found that there was no evidence to support the alternative hypothesis that sitagliptin treatment would have a more positive effect on the rate of progression of the IMT than conventional treatments and therapies (Oyama 2016). Thus, researchers accepted their null hypothesis, which stated that there were not any significant differences found between the baseline characteristics of patients who were administered the sitagliptin treatment, and patients who received conventional treatment. While there have been other anti-T2DM drugs that have been found to lower the rate of atherosclerosis, this study did not provide this evidence (Matsubara 2012). However, the sitagliptin treatment may still have potential, so further research studies would be warranted.

Descriptive Statistics

Category Variables: Allocation of Treatment and Sex



There were more males than females that participated in the study. 66.8% of participants were males, while 33.2% of paticipants were females. 222 pariciapants were used to test the efffectiveness of the sitagliptin treatment, while the other 220 participants, the control group, were adminstered the conventional treatment.

Continuous Variables: SBP, IMT, and Age

5 Number summary	Min	Q1	Median	Q3	Max
IMT (mm)	0	0.94	1.24	1.81	12.9

When determining the thinkness of artery walls in participants, patients ranged from having no evidence of atherosclerosis at all to having arterial wall thicknesses of 12.9mm. The mean IMT reading for patients was 1.547mm, values above 3.115mm were reported as outliers, and the sample variance was 1.190mm.

5 Number summary	Min	Q1	Median	Q3	Max
SBP	80	118.5	132	138	190

Systolic blood pressures of patients participating in the study ranged from 80 to 190 mmHg over the course of the study. The mean SBP for participants was 128.272 mmHg, values under 89.25

and above 167.25 mmHg were outliers in the dataset, and the sample variance was 259.13 mmHg.

5 Number summary	Min	Q1	Median	Q3	Max
Age	38	64	70	76	91

There was a high frequency of participants from the ages of 70-80 who participated in the study. Ages of participants in the study ranged from 38 to 91 years of age. The mean age of participants was 69.5, ages under 47 were considered outliers, and the sample variance was 84.21 years of age.

Research Question: Is the population mean of the allocation of treatment higher in the mean population of males or females?

Null Hypothesis: The population mean of the allocation of treatment is the same for the population mean of males as it is for females participating in the study.

Alternative Hypothesis: The population mean of the allocation of treatment is the higher for males than it is for females participating in the study.

Statistic	DF	Value	Prob
Chi-Square	1	0.0044	0.9473

The p-value from the reported data ($p=0.9473$) is greater than the critical value ($\alpha=0.05$), so there is not enough statistical evidence to determine whether the allocation of treatment was based on the sex of the participants. Thus, events occurred as a result of chance and the researcher must fail to reject the null hypothesis.

Research question: Is the population mean IMT lower in patients receiving treatment than the population mean IMT in patients not receiving treatment?

Null Hypothesis: The population mean IMT of patients receiving treatment is the same as the population mean IMT of patients who are not receiving treatment.

Alternative Hypothesis: The population mean of IMT levels of patients receiving treatment is less than the population mean IMT of patients not receiving treatment.

T-Test: Two-Sample Assuming Equal Variances (IMT)

P(T<=t) two-tail	0.563215513

According to T-test results, the researcher must fail to reject null hypothesis. The p value ($p=0.56$) is much larger than the alpha ($\alpha=0.05$), which suggests that using sitagliptin treatment had no affect on the IMT of patients. There is not enough statistical evidence to prove that the sitagliptin treatment affected the IMT.

Research question: Is the population mean of SBP lower in patients receiving treatment than the population mean SBP of patients not receiving treatment?

Null Hypothesis: The population mean SBP of patients receiving treatment is the same as the population mean SBP of patients who are not receiving treatment.

Alternative Hypothesis: The population mean of SBP levels of patients receiving treatment is less than the population mean SBP of patients not receiving treatment.

T-Test: Two-Sample Assuming Equal Variances (Systolic Blood Pressure)

P(T<=t) two-tail	0.55312267

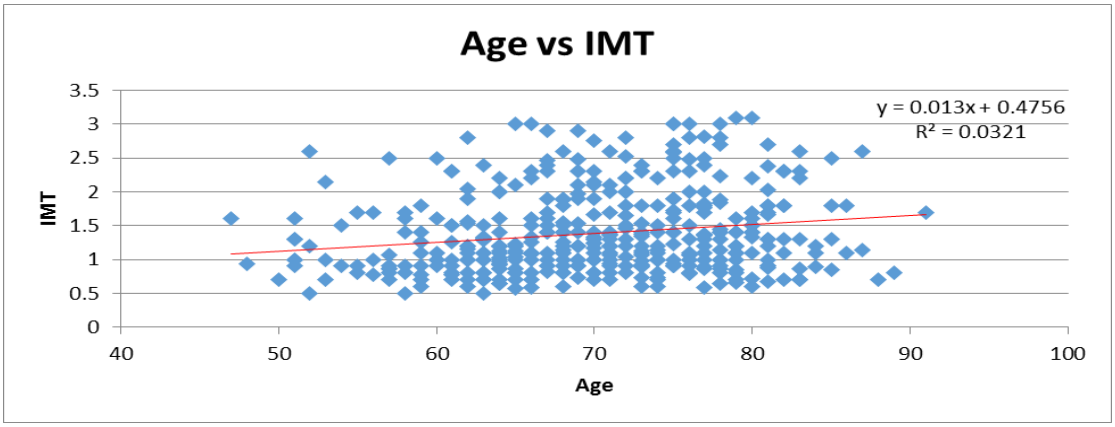
According to T-test results, the researcher must fail to reject null hypothesis. The p value ($p=0.55$) is larger than the alpha ($\alpha=0.05$), which suggests that the sitagliptin treatment had no affect on the SBP of the participants in the study. There is not enough statistical evidence to prove that the sitagliptin treatment affected the SBP.

Linear Regression *Analysis of IMT and Age*

Research Question: Is there a statistically significant linear relationship between IMT and age?

Null Hypothesis: There is not a statistically significant linear relationship between IMT and age.

Alternative Hypothesis: There is a statistically significant linear relationship between IMT and age.



In the output above, predictor variables of IMT and age are significant because the p-value (p=0.0186) is less than alpha (α=0.05), thus there is statistical evidence to reject the null hypothesis. Therefore, there is statistical evidence to support the alternative hypothesis that there is a linear relationship between age and IMT. The equation that represents this linear relationship is y=0.013x+0.4756. Every time there is a 1-year increase in age, there is a 0.013mm increase in the IMT.

Correlation - Age and IMT $r^2 = 0.0321$

When comparing age and IMT there was a very weak, positive correlation (r=0.1792). This correlation represents the data that can be explained by the linear regression, and in the case the regression comparing age and IMT, only 3.21% of the data can be explained by the linear regression. Thus, this is not a good model to use.

Conclusion

Results from statistical analysis indicate that there was not enough statistical evidence to support the alternative hypothesis, which stated that the sitagliptin treatment would lower the rate of atherosclerosis in patients participating in the study. Chi-square results indicate that there is not enough statistical evidence to determine whether the allocation of treatment was based on the sex of the participants, t-test results indicate that there is not enough statistical evidence to prove that the sitagliptin treatment affected neither the IMT nor the SBP. The linear regression model indicated that there was a significant linear relationship between the IMT and the age, but the R^2 value indicated that this regression was not a good model. These statistical results support the findings of the researchers who conducted the study, since there were not any significant differences found between the baseline characteristics of patients who were administered the sitagliptin treatment and patients who received conventional treatment. Thus, the null hypothesis was accepted.

Literature Cited:

Matsubara, Junichi, et al. "A dipeptidyl peptidase-4 inhibitor, des-fluoro-sitagliptin, improves endothelial function and reduces atherosclerotic lesion formation in apolipoprotein e–deficient mice." *Journal of the American College of Cardiology* 59.3 (2012): 265-276.

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