ABSTRACT

Hypertension and blood pressure are closely related, and hypertension is directly related with stroke. There are different type of blood pressures such as basal, diastolic, maximum, mean arterial, systolic, mean central venous. The present report examines the determinants of systolic blood pressure for two different groups of cardiac patients. One group of cardiac patients is those who underwent dobutamine stress echocardiography, and the other group is Worcester heart attack study. Many systolic blood pressure determinants, their effects, and correlations have been focused in the current report.

INTRODUCTION

Hypertension (HT) and blood pressure (BP) are directly related, and co-exist. Generally, 30% of the adult population are affected with HT, while HT is highly related with stroke for 54%, and with ischemic heart disease for 47% [1-4]. In practice, pharmacotherapy is used to manage HT. Even though there are many HT management drugs available in the market, the response rate to any specific drug is approximately 50%-55%. It is known that using HT drugs, only one out of three patients with HT have their BP controlled to specific level [3,5]. There are several risk factors such as lifestyle, age, sleep apnoea, biochemical parameters, genetic effects, which are considered as the casual factors for uncontrolled BP [6-8]. Recently, some articles have focused the BP determinants [5,8-10]. The European Society of Hypertension (ESH) [11] and also the American Heart Association [12], separately reported the self-monitoring guidelines of BP by patients at home (HBPM) in 2008. Some articles have verified the performance of HBPM in the diagnosis of HT phenotypes (white-coat, sustained, masked HT) in treated and untreated subjects, by using ambulatory BP monitoring (ABPM) [13-16].

The current article examines the systolic blood pressure (SBP) determinants for two groups of cardiac patients. The first group consists of cardiac patients with dobutamine stress echocardiography (DSE). The data set of the considered DSE cardiac patients (UCLA stress echocardiography data) in the current study consists of 31 factors/variables on 558 individuals, which is originally taken from a total of 1183 patients referred for DSE between March 1991 and March 1996 to the UCLA Adult Cardiac Imaging and Hemodynamics Laboratories. For every subject, 31 factors/variables have been examined and noted. The considered data set in the current analysis consists of 558 individuals with all non-missing information on 31 factors/variable. Note that the DSE is widely and successfully applied to identify an individual with or without known coronary artery disease has ischemia. The patient population, data collection method, and the DSE used are clearly described in [17,18]. The second group consists of cardiac patients of the Worcester heart attack study (WHAS) which was conducted by Dr. Robert J. Goldberg, Department of Cardiology at the University of Massachusetts Medical School. The WHAS data set contains 21 variables/factors on 500 subjects [19]. This data can be found at the following Wiley’s FTP site: ftp://ftp.wiley.com/public/sci_tech_med/survival. This data set has been collected to identify the variables/factors which are correlated with trends over time in the survival &
incidence rates, following hospital admission for acute myocardial infarction (AMI). This data set has been collected beginning in 1975 and extending through 2001 on all AMI patients admitted to hospitals in the Worcester, Massachusetts Standard Metropolitan Statistical Area.

Systolic blood pressure is the amount of pressure that blood exerts on vessels while the heart is beating. In a blood pressure reading (for example, 120/80), it is the number on the top. If the top and bottom blood pressures are both too high, a person is said to have high blood pressure. If only the top number is higher than 140, the person has a condition called isolated systolic hypertension. On the other hand, the diastolic blood pressure (DBP) is the amount of BP when the heart is relaxed. DBP is the bottom blood pressure in a BP reading. With high blood pressure, the average systolic blood pressure reading is higher than 140 and the average diastolic blood pressure reading is higher than 90 [11,12]. For high blood pressure individuals, the small blood vessels in the vital organs are most affected over time. These blood vessels become scarred, hardened, and less elastic, which means that they are more likely to get blocked or rupture (leading to organ damage or even organ failure). Therefore, maintaining a normal blood pressure is a vital part of reducing the risk of a heart attack, stroke, or organ damage. Best of our knowledge, there is a little study of the determinants of systolic blood pressure for DSE and WHAS data sets. So, the following issues are considered in the current report (for DSE and WHAS data sets) from our published articles [5,9,10,18]. The following hypotheses are considered in the current article. What are the determinants of systolic blood pressure (SBP) for two groups of cardiac patients such as DSE, and WHAS patients? How are the determinants associated with the SBP? How are the determinants influencing the SBP?

Statistical methodology

The present report is based on our previous published articles [5,9,10,18], where the data sets have been analyzed using both the joint generalized linear Log-normal and gamma models. Both the models are clearly described in these articles. Interested readers are requested to go through the articles [10,20-23] to understand the statistical methodology. In the following sections, we examine two data sets DSE and WHAS which are clearly described in Introduction, based on both the stated models.

Dobutamine stress echocardiography (DSE) data, analysis and interpretation

DSE data: The DSE data set is clearly described (patient population, data collection method, DSE method) in [17,18]. The origin of the DSE data set is UCLA Adult Cardiac Imaging and Hemodynamics Laboratories (for DSE between March 1991 and March 1996). The DSE data set contains 558 subjects along with 31 variables/ factors. For ready reference the factors/ variables are reproduced as follows. The DSE study attribute and variable characters are basal heart rate (HR) (BHR), basal blood pressure (BP) (BBP), double product (DP) of BBP & BHR (BDP), peak HR (PHR), systolic BP (SBP), DP of PHR & SBP (DPPHSB), gender (Sex) (male=0, female=1), age (Age), maximum HR (MRH), used dobutamine dose (Dose), maximum BP (MBP), percent maximum predicted HR (PMHR), DP of maximum Dose & MBp (DPMDDBP), ejection fraction on dobutamine (DoseEF), baseline cardiac ejection fraction (BEF), dobutamine dose at maximum double product (DobDose), chest pain (yes (y)=0, no (n)=1) (Cspain), resting wall motion abnormality on echocardiogram (Ecogm) (y=0, n=1) (Rwma), positive stress on echocardiogram (Ecogm) (y=0, n=1) (Pose), new myocardial infarction (MI) (y=0, n=1) (NEMI), recent angioplasty (y=0, n=1) (NePtca), recent bypass surgery (y=0, n=1) (NeCabg), death (y=0, n=1) (Death), history of hypertension (y=0, n=1) (HisHT), history of diabetes (y=0, n=1) (HisDM), history of MI (y=0, n=1) (HisMI), history of coronary artery bypass surgery (y=0, n=1) (HisCABG), history of smoking (no=0, medium=1, high=2) (HisCig), baseline electrocardiogram diagnosis (normal=0, equivocal =1, MI=2) (Ecg), history of angioplasty (y=0, n=1) (HisPtca), any event such as death or NeMI, or NePtca, or NeCABg (death=0, no=1) (Event).
Systolic blood pressure of DSE data analysis: The DSE data set contains systolic blood pressure (SBP) along with many other variables/ factors as stated above. The analysis of SBP is given in [18], using joint gamma generalized linear model analysis. In the analysis, SBP is considered as the response variable, and the remaining others are considered as the independent variables. A little accurate analysis of SBP (along in the same line of [18]) is reproduced in the present report (Table 1).

Interpretations of Systolic blood pressure (SBP) analysis of DSE data

The systolic BP mean model of DSE data set (Table 1) interprets the followings:

1) The mean systolic blood pressure (MSBP) of DSE cardiac patients is inversely correlated with the basal heart rate (BHR) (P=0.0001), indicating that the MSBP increases or decreases according as BHR decreases or increases.

2) The MSBP is directly correlated with the double product (DP) of basal BP (BBP) & BHR (BDP) (P=0.0016), implying that MSBP increases as the BDP increases, and vice versa.

3) The MSBP is inversely correlated with the peak heart rate (PHR) (P<0.0001), indicating that MSBP decreases as the PHR increases.

4) The MSBP is directly correlated with the DP of PHR & SBP (DPPHSB) (P<0.0001), implying that MSBP increases as DPPHSB increases. Note that SBP is a direct function of DPPHSB.

5) The MSBP is directly correlated with the used dobutamine dose (Dose) (P=0.0268), indicating that MSBP increases as the Dose increases. Therefore, care should be taken in applying the amount of dobutamine dose.

6) The MSBP is directly correlated with the maximum heart rate (MHR) (P<0.0001), implying that MSBP increases as the MHR increases.

Table 1: Joint mean & dispersion model results of systolic blood pressure for DSE data set from gamma fit.

| Covariate       | Estimate | Standard error | t-value | P-value |
|-----------------|----------|----------------|---------|---------|
| Constant        | 3.87061  | 0.05211        | 74.251  | <0.0001 |
| BHR             | -0.00101 | 0.00032        | -3.872  | 0.0001  |
| BDP             | 0.00012  | <0.0001        | 3.171   | 0.0016  |
| PHR             | -0.00891 | 0.00031        | -30.452 | <0.0001 |
| DPPHSB          | 0.00012  | <0.0001        | 52.283  | <0.0001 |
| Dose            | 0.00051  | 0.00021        | 2.222   | 0.0268  |
| MHR             | 0.01091  | 0.00052        | 20.141  | <0.0001 |
| PHR             | -0.00063 | 0.00031        | -2.162  | 0.0312  |
| MBP             | 0.00721  | 0.00033        | 22.501  | <0.0001 |
| DPMDOBP         | -0.00011 | <0.0001        | -23.981 | <0.0001 |
| Sex             | -0.00552 | 0.00391        | -1.442  | 0.1504  |
| Cstpain         | -0.00511 | 0.00372        | -1.382  | 0.1682  |
| Rwma            | 0.00531  | 0.00453        | 1.191   | 0.2343  |
| Pose            | 0.00233  | 0.00471        | 0.493   | 0.6243  |
| HisHT           | -0.00732 | 0.00381        | -1.932  | 0.0541  |
| HosCabg         | -0.00471 | 0.00582        | -0.822  | 0.4126  |
| Ecg 1           | 0.00171  | 0.00402        | 0.443   | 0.6601  |
| Ecg 2           | 0.00603  | 0.00603        | 1.012   | 0.3129  |
| Constant        | -0.02501 | 0.02703        | -9.711  | <0.0001 |
| BBP             | 0.03502  | 0.00602        | 5.751   | <0.0001 |
| PMHR            | -0.01901 | 0.00631        | -3.081  | 0.0022  |
| Age             | 0.00911  | 0.00662        | 1.412   | 0.1591  |
| Cstpain         | -0.31103 | 0.15981        | -1.963  | 0.0505  |
| Rwma            | -1.08201 | 0.15662        | -6.891  | <0.0001 |
| Pose            | -0.32031 | 0.17621        | -1.822  | 0.0693  |
| NeMI            | -1.94532 | 0.33072        | -5.883  | <0.0001 |
| HisHT           | 0.60141  | 0.16682        | 3.612   | 0.0003  |
7) The MSBP is inversely correlated with the percent maximum predicted heart rate (PMHR) \((P=0.0312)\), indicating that MSBP decreases as the PMHR increases.

8) The MSBP is directly correlated with the maximum blood pressure (MBP) \((P<0.0001)\), indicating that MSBP increases as the MBP increases, and vice versa.

9) The MSBP is inversely correlated with the DP of maximum Dose & MBP (DpDMDOBP) \((P<0.0001)\), indicating that MSBP decreases as the DpDMDOBP increases.

10) The MSBP is inversely partially correlated with the Sex (male=0, female=1) \((P=0.1504)\), indicating that MSBP of male DSE cardiac patients is higher than female.

11) The MSBP is inversely partially correlated with the chest pain (Cstpain) (yes=0, no=1) \((P=0.1682)\), indicating that MSBP of DSE cardiac patients with chest pain is higher than DSE patients with no chest pain.

12) The MSBP is inversely correlated with the history of hypertension (HisHT) (y=0, n=1) \((P=0.0541)\), indicating that MSBP of DSE cardiac patients with HisHT is higher than DSE patients with no HisHT.

The systolic BP variance model (Table 1) interprets the followings:

13) The SBP variance (SBPV) of DSE cardiac patients is directly correlated with BHR \((P<0.0001)\), indicating that SBPV increases as the BHR increases. Note that mean and variance of SBP is oppositely associated with BHR.

14) The SBPV is inversely correlated with the PMHR \((P=0.0022)\), indicating that SBPV decreases as the PMHR increases. Note that the both mean and variance of SBP are inversely correlated with PMHR.

15) The SBpV is inversely correlated with the Cstpain \((y=0, n=1) \((P=0.0505)\), indicating that SBPV of DSE cardiac patients with chest pain is higher than DSE patients with no chest pain. Note that the chest pain is similarly associated with both the mean and variance of SBP.

16) The SBPV is inversely correlated with the resting wall motion abnormality on echocardiogram (Rwma) \((y=0, n=1) \((P<0.0001)\), indicating that SBPV of DSE cardiac patients with Rwma is higher than DSE patients with no Rwma.

17) The SBPV is inversely correlated with the positive stress on echocardiogram (Pose), \((y=0, n=1) \((P<0.0001)\), indicating that SBPV of DSE cardiac patients with Pose is higher than DSE patients with no Pose.

18) The SBPV is directly partially correlated with the age \((P=0.1591)\), implying that SBPV of DSE cardiac patients increases at older ages.

19) The SBPV is inversely correlated with the new myocardial infarction (NeMI) \((y=0, n=1) \((P<0.0001)\), indicating that SBPV of DSE cardiac patients with NeMI is higher than DSE patients with no NeMI.

20) The SBPV is directly correlated with the history of hypertension \((y=0, n=1) \((HisHT) \((P=0.0003)\), implying that SBPV of DSE cardiac patients with HisHT is lower than DSE patients with no HisHT.

**Worcester heart attack study (WHAS) data, analysis and interpretation**

**WHAS data:** The WHAS data set is given in [19] and it is currently studied in
The data set is collected by Dr. Robert J. Goldberg, Cardiology Department, and University of Massachusetts Medical School. The data set can be observed at the site: ftp://ftp.wiley.com/public/sci_tech_med/survival. The present data set contains 500 subjects with 20 attribute characters/variables, which are: sex (0=male, 1=female), age (in hospital admission), systolic BP (SBP), heart rate (HR), diastolic BP (DBP), history of cardiovascular disease (0= no, 1=yes) (HisCVD), body mass index (BMI), cardiogenic shock (0=no, 1=yes) (CSO), atrial fibrillation (0=no, 1=yes) (AFB), congestive heart complications (0=no, 1=yes) (CHC), myocardial infraction (Mi) order (0=first, 1=recurrent) (MIOrder), complete heart block (0=no, 1=yes) (CAV3), MI type (0=non Q-wave, 1=Q-wave) (MIType), cohort year (1=1997, 2=1999, 3=2001) (CYear), admission date in hospital (AdTime), last follow up date (FoDate), discharge date from hospital (DisDate), hospital stay time in days (HSDays), status of discharge from hospital (0=alive, 1=dead) (SDHos), at last follow-up patient status (0=alive, 1=dead) (PSFu). Note that, Q wave denotes the normal left-to-right depolarisation of the interventricular septum.

Systolic blood pressure of WHAS data analysis: The WHAS data set contains systolic blood pressure (SBP) along with 19 other attribute characters/variables as stated above. The analysis of SBP is given in [10] using joint Log-normal generalized linear model analysis. In the analysis, SBP is considered as the response variable, and the remaining others are considered as the independent variables. A little accurate analysis of SBP (along in the same line of [10]) is reproduced in the present report (Table 2).

**Interpretations of Systolic blood pressure (SBP) analysis of WHAS data**

The systolic BP mean model of WHAS data set (Table 2) interprets the followings:

1) The mean SBP (MSBP) is directly correlated with age (P=0.0132), implying that MSBP decreases at younger ages, and vice versa. The minimum age of the subjects is 30 years, while the average age is 69.852 years.

2) The MSBP is directly correlated with sex (0=male, 1=female) (P=0.0021), implying that MSBP is lower for male than female acute MI (AMI) patients.

3) The MSBP is inversely correlated with HR (P<0.0001), implying that MSBP decreases as the HR increases, and vice versa.

4) The MSBP is positively related with diastolic BP (DBP) (P<0.0001), implying that MSBP decreases as the DBP decreases, and vice versa.

### Table 2: Joint mean & variance model results of systolic blood pressure from Log-normal fit for WHAS data set.

| Model             | Covariate                        | Estimate | Standard error | t-value | P-value |
|-------------------|----------------------------------|----------|----------------|---------|---------|
| **Mean Model**    | Constant                         | 4.32852  | 0.07441        | 58.172  | < 0.0001|
|                   | Age                              | 0.00151  | 0.00059        | 2.491   | 0.0132  |
|                   | Sex                              | 0.04742  | 0.01567        | 3.032   | 0.0021  |
|                   | heart rate (HR)                  | -0.00121 | 0.00032        | -3.681  | < 0.0001|
|                   | diastolic BP (DBP)               | 0.00712  | 0.00036        | 19.882  | < 0.0001|
|                   | body mass index (BMI)            | 0.00192  | 0.00150        | 1.261   | 0.2082  |
|                   | history of cardiovascular disease (HisCVD) | 0.04091  | 0.01611        | 2.541   | 0.0112  |
|                   | atrial fibrillation (AFB)        | -0.05291 | 0.02069        | -2.562  | 0.0113  |
|                   | cardiogenic shock (CSO)          | -0.17611 | 0.04565        | -3.861  | < 0.0001|
|                   | MI Type (MIType)                | -0.06121 | 0.01676        | -3.652  | < 0.0001|
|                   | cohort year (CYear)2            | -4.16612 | 0.16081        | -25.907 | < 0.0001|
|                   | history of cardiovascular disease (HisCVD) | 0.48221  | 0.15142        | 3.182   | 0.0021  |
|                   | cardiogenic shock (CSO)          | 0.46822  | 0.33282        | 1.407   | 0.1603  |
|                   | MI order (MIOrder)              | -0.20521 | 0.13941        | -1.470  | 0.1421  |
|                   | cohort year (CYear)3            | 0.25712  | 0.15841        | 0.798   | 0.4280  |
|                   | cohort year (CYear)2            | 0.52612  | 0.16752        | 3.139   | 0.0021  |

Systolic blood pressure of WHAS data analysis: The WHAS data set contains systolic blood pressure (SBP) along with 19 other attribute characters/variables as stated above. The analysis of SBP is given in [10] using joint Log-normal generalized linear model analysis. In the analysis, SBP is considered as the response variable, and the remaining others are considered as the independent variables. A little accurate analysis of SBP (along in the same line of [10]) is reproduced in the present report (Table 2).

**Interpretations of Systolic blood pressure (SBP) analysis of WHAS data**

The systolic BP mean model of WHAS data set (Table 2) interprets the followings:

1) The mean SBP (MSBP) is directly correlated with age (P=0.0132), implying that MSBP decreases at younger ages, and vice versa. The minimum age of the subjects is 30 years, while the average age is 69.852 years.

2) The MSBP is directly correlated with sex (0=male, 1=female) (P=0.0021), implying that MSBP is lower for male than female acute MI (AMI) patients.

3) The MSBP is inversely correlated with HR (P<0.0001), implying that MSBP decreases as the HR increases, and vice versa.

4) The MSBP is positively related with diastolic BP (DBP) (P<0.0001), implying that MSBP decreases as the DBP decreases, and vice versa.

### Table 2: Joint mean & variance model results of systolic blood pressure from Log-normal fit for WHAS data set.

| Model             | Covariate                        | Estimate | Standard error | t-value | P-value |
|-------------------|----------------------------------|----------|----------------|---------|---------|
| **Mean Model**    | Constant                         | 4.32852  | 0.07441        | 58.172  | < 0.0001|
|                   | Age                              | 0.00151  | 0.00059        | 2.491   | 0.0132  |
|                   | Sex                              | 0.04742  | 0.01567        | 3.032   | 0.0021  |
|                   | heart rate (HR)                  | -0.00121 | 0.00032        | -3.681  | < 0.0001|
|                   | diastolic BP (DBP)               | 0.00712  | 0.00036        | 19.882  | < 0.0001|
|                   | body mass index (BMI)            | 0.00192  | 0.00150        | 1.261   | 0.2082  |
|                   | history of cardiovascular disease (HisCVD) | 0.04091  | 0.01611        | 2.541   | 0.0112  |
|                   | atrial fibrillation (AFB)        | -0.05291 | 0.02069        | -2.562  | 0.0113  |
|                   | cardiogenic shock (CSO)          | -0.17611 | 0.04565        | -3.861  | < 0.0001|
|                   | MI Type (MIType)                | -0.06121 | 0.01676        | -3.652  | < 0.0001|
|                   | cohort year (CYear)2            | -4.16612 | 0.16081        | -25.907 | < 0.0001|
|                   | history of cardiovascular disease (HisCVD) | 0.48221  | 0.15142        | 3.182   | 0.0021  |
|                   | cardiogenic shock (CSO)          | 0.46822  | 0.33282        | 1.407   | 0.1603  |
|                   | MI order (MIOrder)              | -0.20521 | 0.13941        | -1.470  | 0.1421  |
|                   | cohort year (CYear)3            | 0.25712  | 0.15841        | 0.798   | 0.4280  |
|                   | cohort year (CYear)2            | 0.52612  | 0.16752        | 3.139   | 0.0021  |
5) The MSBP is directly partially correlated with body mass index (BMI) (P=0.2082), implying that MSBP increases or decreases according as the BMI increases or decreases.

6) The MSBP is directly correlated (for the AMI patients) with the cardiovascular disease history (0=no, 1=yes) (HisCVD) (P=0.0112), implying that MSBP is lower for AMI patients with no HisCVD.

7) The MSBP is inversely correlated with the atrial fibrillation (0=no, 1=yes) (AFB) (P=0.0113), implying that MSBP is lower for AMI patients with having AFB.

8) The MSBP is inversely correlated with the cardiogenic shock (0=no, 1=yes) (CSO) (P<0.0001), implying that MSBP is lower for AMI patients with having CSO.

9) The MSBP is inversely correlated with the MI type (0=non Q-wave, 1=Q-wave) (MIType) (P<0.0001), implying that MSBP is lower for AMI patients with having Q-wave MIType.

The systolic BP variance model of WHAS data set (in Table 2) interprets the followings:

10) The SBP variance (SBPV) is directly correlated with the HisCVD (0=no, 1=yes) (HisCVD) (P=0.0021), implying that SBPV is lower for AMI patients with no HisCVD.

11) The SBPV is partially directly correlated with CSO (0=no, 1=yes) (P=0.1603), implying that SBPV is higher for AMI patients with having CSO.

12) The SBPV is partially inversely correlated with myocardial infarction (MI) order (0=first, 1=recurrent) (MIOrder) (P=0.1421), indicating that SBPV is higher for AMI patients at first MIOrder.

13) The SBPV is directly partially correlated with cohort year (1=1997, 2=1999, 3=2001) (Year) at the year 2=1999 (P=0.1062) and 3=2001 (P=0.1602), implying that SBPV is higher for AMI patients at the year 2=1999 and 3=2001, than the year 1997.

CONCLUSIONS

The present research report considers the determinants of systolic BP based on two different data sets on cardiac patients. One data set is related with cardiac patients who under DSE, and the other data set is related with acute myocardial infarction (AMI) patients. In both the cases, most of the factors are different. For DSE data set, it is noted that mean SBP is directly related with maximum BP and basal BP, while for AMI data set, the mean SBP is directly related with diastolic BP. Therefore, systolic BP should be considered along with basal, diastolic, maximum, mean arterial, and mean central venous BPs. For DSE data set, basal and peak heart rate are inversely correlated, while maximum heart rate is directly correlated with the mean systolic BP. Note that basal heart rate is directly correlated with the variance of systolic BP. Also for AMI data set, heart rate is inversely correlated with the mean systolic BP. Therefore, heart rate is an important determinant of systolic BP. Dobutamine dose used is directly correlated with the mean systolic BP. Therefore, medical practitioners should care on applying the dobutamine dose. History of cardiovascular diseases are also important risk factors for systolic BP (for both the data sets). For AMI data set, cardiogenic shock is also a significant risk factor for mean systolic BP. The determinants of systolic BP may be different for diabetes, cardiac shock, and kidney disease patients. To identify the determinants of systolic BP, researchers should perform separate study for each type of patients. Medical doctors will be benefited with the present findings. All individuals should care on systolic BP at higher ages.
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