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Blood pressure in head injured patients

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Abstract

Objective
To determine the statistical characteristics of blood pressure readings from a large number of head injured patients.

Methods
The BrainIT group have collected high time resolution physiological and clinical data from head injured patients who require intracranial pressure (ICP) monitoring. We have examined the statistical features of this data set of blood pressure (BP) measurements with time resolution of up to 1 minute from 200 patients. The distributions of blood pressure measurements and their relationship with simultaneous ICP measurements are described.

Results
The distributions of mean, systolic and diastolic readings are close to normal with modest skewing towards higher values. There is a trend towards an increase in blood pressure with advancing age but this is not significant. Simultaneous blood pressure and ICP values suggest a triphasic relationship with a BP rising at 0.28mmHg / mmHg of ICP for ICP up to 32mmHg, 0.9mmHg / mmHg of ICP for ICP from 33 to 55mmHg and falling sharply with rising ICP for ICP over 55mmHg.

Conclusions
Patients with head injury appear to have a near normal distribution of blood pressure readings that are skewed towards higher values. The relationship between BP and ICP may be triphasic.
**Introduction**

Since its introduction in the 1960s\(^1\), invasive blood pressure (BP) monitoring has become an important part of patient management in high dependency and intensive care units. Despite widespread use of the modality\(^2\), few large data sets are available indicating its statistical features. Here we present the results of invasive blood pressure measurements made in 200 patients who were being treated for head injury.

These data have become available as a result of the BrainIT project that was conceived in 1997 and has grown into an international collaboration\(^3\) with the purpose of gathering data on the physiological parameters and treatments associated with significant head injuries with high time resolution. Over the period between 1998 and 2006 data capture systems were deployed in high dependency and intensive care units in participating neuroscience centres.

The relationship between ICP and BP has been recognised since first described by Cushing in 1901\(^4\). Several reports since then confirm a positive correlation particularly with higher ICPs\(^5\) during tracheal suction\(^6\) and simultaneous with ICP “B waves” in patients being investigated for normal pressure hydrocephalus\(^7\). Similar data to these from 80 patients having computerised monitoring of ICH following head injuries showed a positive correlation for ICPs over 25 but not for lower values\(^8\).

The difference between mean arterial and mean intracranial pressure (cerebral perfusion pressure or CPP) has assumed great importance as it is seen as a parameter for therapeutic optimisation in the care of head injured patients. Studies have demonstrated that the relationship between IPC or CPP and outcome both in adults\(^9\) and children\(^10\) alongside the development of guidelines for the management of severe head injury but any influence on improving outcome has yet to be demonstrated.

We describe the distributions of BP measurements, their relationship with simultaneously taken ICP measurements and the characteristics of the patients in whom the measurements were made.

**Patients and methods**

The primary goal of the EU funded BrainIT project was to collect detailed physiological, clinical and management data from head injured patients who required ICP and intra-arterial BP monitoring as part of their routine care. Twenty four participating centres were initially involved in the study. For each centre electronic equipment was provided for minute-by-minute collection of physiological data and also for the input of details of the clinical condition of the patients and management measures used. All data were anonymised prior to transfer to Glasgow, converted into a standard format and then entered into a database.

Approval for the study was obtained from the relevant local Ethical Committees and the first patient was recruited in July 2003. Data analyses were performed using Matlab version 6.5.

At the time of analysis a total of 200 patients had been recruited over a period of 24 months from 21 centres. Their age ranged from 4 to 83 years, with a mean and median of 37 and 33 years respectively, 162 were male and 38 female. The causes of injury were: assault = 17, fall = 56, pedestrian = 16, sport = 6, traffic = 85, work = 5 and 15 were unknown.

Presenting Glasgow coma scores were available for 184 of the 200 cases and served as an index of injury severity; they ranged from 3 to 15 with a distribution as shown in figure 1. The number of blood
pressure measurements per patient varied widely from 52 to 28,584 with the distribution shown in figure 2. Mean BP measurements were available for all patients. Of these a breakdown into systolic and diastolic BP was available in 171 patients.

The procedures for managing ICP varied between units but all used some treatment in response to adverse changes in measured pressures. Maintenance of ICP under a threshold value or CPP over a threshold value were both used as therapeutic targets in different patients. ICP thresholds ranged from none to 30mmHg and CPP from none to 70mmHg. There was also variation in the duration of pressure excursions beyond these thresholds that were seen as significant. This variation reflects the ongoing debate about the best way to manage raised ICP after head injury.

Some artifactual measurements are to be expected in a data set at this type. In order to minimise the inclusion of these readings measurements outside the credible physiological ranges were excluded. The distribution of measurements was observed and compared with the expected smooth distribution of natural phenomena. The data contains what appears to be a substantial overrepresentation of values of ICP of between 0 and -20mmHg. And of BP below 20mmHg. These values were excluded because it was assumed that a majority, though not all, were artefactual.

The statistical methods used are mainly descriptive. The points plotted in the figures represent mean values of BP. Confidence limits were calculated using Poisson distributions. The closeness of the distribution of BP data overall to a normal distribution was assessed using quantile v quantile (Q-Q) plots where the quantiles of the data set were plotted on the x axis against quantiles of a theoretical normal distribution with the same mean and variance on the y axis. (figure 4). Standardised third moments were calculated to give a quantitative measure of the amount of skew in the distributions. Least squares linear regression was used on the dataset presented in figure 5 to express BP as a function of ICP over two regions that were identified by visual inspection of the graph.

**Results**

**Blood-pressure distributions**

The dataset included 1.6, 1.6 and 1.8 million observations of diastolic, systolic, and mean blood pressures respectively. The distributions of these measurements are shown graphically in figure 3 and summary statistics are given in table 1. All three distributions are close to normal as can be seen in figure 3. Further analysis with Q-Q plots (figure 4) shows that none of the distributions are quite normal, all being skewed towards higher values.

**Table 1:** Means and Standard Deviations of invasive blood pressure data (mmHg)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Standardised third moment</th>
<th>No of obs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>140.41</td>
<td>23.10</td>
<td>0.36</td>
<td>1557767</td>
</tr>
<tr>
<td>Diastolic</td>
<td>66.21</td>
<td>13.78</td>
<td>2.10</td>
<td>1556760</td>
</tr>
<tr>
<td>Mean</td>
<td>89.43</td>
<td>16.23</td>
<td>1.74</td>
<td>1814850</td>
</tr>
</tbody>
</table>

**Relationship between BP and ICP**
Blood pressures may be higher on average in head injured patients than in others. The association between head injury and raised intracranial pressure may produce a reflex hypertension and in some cases therapeutic hypertension is used as a treatment for raised intracranial pressure. Simultaneous data on BP and ICP is available in the BrainIT dataset from 195 patients and shows the relationship between mean intracranial pressure and mean blood pressure (figure 5). There is wide variation in the number of measurements made at different values of ICP which reflects the relative rarity of readings above 35mmHg. The distribution of the number of simultaneous BP and ICP measurements as a function of both BP and ICP is shown in the contour plot of figure 6. This shows a two directional Normal distribution with slight skewing towards high ICP and BP values.

**Relationship between BP and age**

It is well recognised that BP rises with advancing age. A scatter plot of BP versus age for the patients in this series is shown in figure 7. The slight trend towards an increase in blood pressure with advancing age did not reach significance. 95% limits of the linear relationship between agent BP and of the individual values are also shown on the figure.

**Artefacts**

Certain features of the dataset suggest artefactual overrepresentation of particular values. The distribution of mean BP observations in the range of -100 to 30 mmHg shows peaks of numbers of observations at -91, -40, -19, and -4 mmHg. These clearly do not represent true physiological measurements. There is a large peak of 9784 data points at the BP of zero which is suspected to be an artefact. These artefactual measurements are excluded from the data presented in figures 3 to 7 and table 1. In the case of ICP measurements there is a peak at zero mmHg of ICP which is believed to be an artefact. It is suspected that the values of 1, 2, 3, and 4 mmHg ICP are also overrepresented in the dataset. This is indicated by distortion of the distribution of ICP values and also by the first four points on the graph of ICP versus BP (figure 5).

**Discussion**

The BrainIT dataset is one of the largest of high time-resolution invasive blood pressure in head injury. It was collected in a large number of units from different European countries. Certain features of data distribution analyses such as small deviation from a normal distribution can only be determined from large data sets.

The measurements made in head injured patients should be applied to other patients with caution. The relationship between mean ICP and mean blood pressure shown in figure 6 extends over the range of ICP that would normally be regarded as "normal" of between zero and 15 mmHg\(^{11,12}\). Even a population of patients with head injuries and relatively normal ICP may have a slightly raised blood pressure consequent upon changes in ICP within the normal range\(^{13}\). Furthermore the effects of the post traumatic stress response and sedation may have influenced the results.

The graph of figure 5 appears to naturally fall into four zones:

for ICP values between 4 and 32mmHg, blood pressure is related by the equation

\[
\text{Blood pressure} = 0.28 \times \text{ICP} + 84.4
\]

for ICP between 33 and 55mmHg this changes to

\[
\text{Blood pressure} = 0.28 \times \text{ICP} + 84.4
\]
Blood pressure = 0.90 * ICP + 61.6.

The upswing in the blood pressure values at ICPs of 0, 1, 2 and 3 mmHg may be an artefact as ICP measurements with these low values are overrepresented in the data set as can be seen in figure 7. The over-representation is believed to be quasi-randomly distributed in the data set. This means that the greater the proportion of artifactual readings at a specific value, the nearer the average BP at the value will be to the overall average. This may explain the initial down slope. If this were the full explanation the mean BP with ICP=0 would be expected to be just under the overall average of 89.29 mmHg but is 92.04 mmHg. It is interesting to note that the same down slope in BP for the range of ICP from 0 to 3 can be seen in the data reported by Czosnyka et al. The decline in blood pressure over ICP of 55 mmHg is probably real and reflects the fact that most cases under these circumstances are suffering from agonal coning.

The relationship between ICP and BP in figure 5 shows a tendency to maintain CPP at or above about 60 mmHg. There may be an iatrogenic component to this as maintenance of ICP or CPP were used as therapeutic targets. Physiological effects cannot be distinguished from the effects of treatment aimed at optimising ICP, BP or CPP because patients were selected to receive such treatment on the grounds of changes in the same parameters. It is not possible to separate treatment effects from selection effects in a dataset of this type but it is likely that for ICPs below 20 mmHg the effect seen is physiological because there is little reason to pharmacologically increase BP in response to ICP in this region. Of note is that contrary to the findings of Czosnyka et al we have observed a positive correlation between ICP and BP over this region.

Conclusions
Based on invasive blood pressure measurements in 200 head injured adult patients the distribution of blood pressure is not normal but skewed towards high values. The means (and standard deviations) of diastolic, systolic and mean measurements were 66 (13.8), 140 (23.2) and 89 (16.5) mmHg respectively.

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Authors contributions
P Mitchell, BA Gregson AD Mendelow and IR Chambers conceived analysis. P Mitchell, BA Gregson and IR Chambers performed the analysis. P Mitchell, BA Gregson, I Piper, G Citterio, AD Mendelow and IR Chambers helped draft the manuscript. I Piper, BA Gregson, G Citterio and IR Chambers are on the Steering Committee of BrainIT. All authors have had access to the all the data in the study and they held final responsibility for the decision to submit for publication.
Figure Legends

Figure 1
Histogram showing the distribution of pre-neurosurgical hospital Glasgow Coma Score.

Figure 2
Histogram showing the distribution of observations per patient. The distinction between mean blood pressure measurements and systolic/diastolic measurements is a consequence of different types of data collection system. All systems that collect systolic/diastolic measurements also calculate means but some only given means and not a systolic/diastolic breakdown.

Figure 3
Line plots showing the distributions of diastolic, systolic, and mean invasive blood pressures measurements.

Figure 4
Q-Q plots of the distributions of systolic (a), diastolic (b) and mean (c) blood pressures. In a Q-Q plot the quantiles measured from the dataset are plotted against the theoretical quantiles of a normal distribution that has the same mean and standard deviation as the dataset. A perfectly normally distributed dataset will have a Q-Q plot along the straight line plotted. The sigmoid deviation from the straight line seen in the three plots, most prominently in the mean plot, indicates skewing towards higher blood pressures.

Figure 5
The relationship between intracranial pressure and blood pressure. Ninety nine percent limits were chosen because 95% limits are too narrow to be resolved over most of the graph. The confidence limits are of the means and are based on Poisson distributions.

Figure 6
Contour plot of the distribution of the number of measurements with both mean BP and mean ICP rounded to the nearest whole number mmHg. Blood pressure is on the vertical axis and ICP on the horizontal axis. For example there were 707 measurements made with a mean ICP off 4 and simultaneous mean BP of 73.

Figure 7
Scatter plot of patient age v mean BP for individual patients. The 95% limits of the mean and values are shown. The slight positive relationship does not reach significance.
References

Figure 1

Presenting GCS, n=184
Figure 2
Distribution of number of measurements per patient, n=200

- Mean BP measurements
- Systolic & Diastolic measurements

Number of patients

Number of measurements per patient

0 15000 5001-10000 10001-15000 15001-20000 20001-25000 25001-30000
Figure 3
Distributions of BP measurements

- Systolic - 171 patients
- Diastolic - 171 patients
- Mean - 200 patients

Number of Measurements

BP value, mmHg
Figure 4

n=200

a
Systolic V Normal Q-Q

b
Diastolic V Normal Q-Q

c
Mean BP V Normal Q-Q
Figure 5
Average BP v ICP
195 patients

Mean BP
99% confidence limits