Prognostic Factors of Carcinoma Cervix

Hypoglycemia Symptoms

Troponin I in Emergency Department

Vacuum Assisted Closure in Non Healing Ulcers
AMRITA
GLOBALLY RANKED
No.1
PRIVATE UNIVERSITY
IN INDIA

Global Rankings

THE WORLD UNIVERSITY RANKINGS
No.1 Ranked Private University in India

THE WORLD UNIVERSITY RANKINGS
No.1 Ranked International Outlook in India

QS UNIVERSITY RANKINGS BRICS
No.1 Ranked International Faculty in India

www.amrita.edu
Editorial
2 The Future Looks Bright
H. Kumar

Spiritual Message
3 Protect Yourself

Original Article
4 How Valid are the Classical Prognostic Factors of Carcinoma Cervix in the Era of Concurrent Chemotherapy and Conformal Radiation
Vishnu Rajan Nambiar, Beena K, Dinesh M

10 Point Of Care Troponin I in Emergency Dept–More Than Just a Confirmation
Vishnu Manohar, Bharath Prasad S, Ajith V, Krupanidhi Karunanithi, Arun Kumar, Nande Mohan, Naveen Mohan, Sreekrishnan TP, Gireesh Kumar.

13 Sapheno-Femoral Junction Anatomy and Haemodynamics in Indian Patients
Riju R, Manikanta Prabhu, Vaidyanathan s

20 A Study of Vacuum Assisted Closure in Non-Healing Ulcers
Manoj V V, Faizal Ali AA

26 Hypoglycemia Symptoms & Its Management in Patients with Diabetes Mellitus

32 Correlation of Six Minute Walk Distance with Clinical & Spirometric Parameters in COPD
Libin Antony P F, Nithya Haridas, Sundaram K R, Arun Nair, Hari Lakshmanan P, Sumi Soman

Case Report
37 Adult Onset Still’s Disease with Facial Palsy – A Rare Presentation
Urs Vishnu Dev, Henry R A, Joseph J, Oomen A T, Rao G G

40 Residual Cyst: An Unusual Presentation of a Usual Scenario
Anju P David, Dhanya Mary Sam, Sreeja P Kumar, Jaeson Mohanan Painatt, Beena Varma, Renju Jose, Marina Lazar Chandy

43 Melioidosis: Presenting As Pyopneumothorax
Supriya Adiody, Lt Col V P Gopinathan, Lais Mohammed
The Future Looks Bright

H. Kumar

The last few decades have seen an explosive growth in research in various areas of Modern Medicine which has translated into better care for patients. On the surgical front - organ transplantation including multi-organ transplants have become more common and Robotic Surgery has made selected surgical procedures very precise, reducing morbidity and complications to a minimum, while laproscopic surgeries have dramatically cut down the incision size and reduced hospital stay. On the diagnostic front new and more detailed imaging modalities now provide us with three dimensional views of the human anatomy which were previously beyond imagination. New markers to aid diagnosis and also plan therapy have greatly enhanced our skill in selecting patients for a more personalised treatment approach. Research in the field of genetics and proteomics is re-defining our understanding of disease processes and may pave the way for new innovative treatment modalities. There have been a large number of new drugs particularly in the treatment of cancer, diabetes and heart diseases which have contributed to increased longevity of patients. The newer drugs are more precise and targeted therapy of diseased tissue alone is now a reality.

So overall it would be fair to state that the achievements and new inventions have significantly expanded the scope and precision of the practise of medicine. These benefits are visible in every field and specialization of Medicine. In India medical research has picked up speed in recent years and significant contributions can be expected in the coming days. Research in each and every aspect of medicine is ongoing all over the world, and this certainly augurs well for the continued development of the science in the coming years.

The challenge for us as physicians is to retain our compassion for the patient even as we embrace and utilise all the rapidly evolving new technologies for the benefit of our patients. If we use the technological developments and inventions without losing our human touch, then we will be able to deliver very high quality care to our patients in the future.
We tend to spend a lot of time finding faults in others and criticizing the world around us. The world appears to be full of flaws. The roads are full of pot holes, many people are hungry and poor, many others may be sick and in bed. Corruption is rampant and terrorism and destructive tendencies are on the increase. The list of problems and things that are wrong in this world are endless. What can one do in this situation? What would be the right approach in this flawed world? Shouldn’t we try to solve the numerous problems we see around us? These are some of the questions that plague many well meaning people.

In this context Amma once narrated the following parable. One day a king was going around to various parts of his kingdom on an inspection tour. During his journey a thorn pricked his foot. This upset the king greatly and he immediately summoned his minister. “A thorn has pricked my foot. To prevent such a situation from arising again, I want you to clear the whole country off thorns and also carpet the whole country so that my feet will not be pricked again,” he ordered the minister.

The minister trembled when he heard this. For he knew that both tasks were impossible. It was not possible to rid the entire country off thorns and it was impossible to carpet the entire country. But he didn’t dare to tell the king that his orders were impossible to carry out. So instead he made an alternative suggestion to the king, “Sire, instead of removing all the thorns and carpeting the whole country, why don’t we arrange for you to wear a strong comfortable pair of shoes which will protect your feet from the danger of thorn pricks?” The king lauded the minister for his simple but effective solution to the problem.

It is not feasible to remove and the pain and suffering and problems that we see around us. It is far more sensible to protect ourselves from these thorn pricks by developing the right attitude. It is more sensible to get immunised to protect yourself from a disease rather than trying to kill or eliminate all the disease causing organisms. Once we become aware the world around us and understand spiritual principles we will be in a position to protect ourselves from the sources of pain which are an integral part of our world. Think about it, the solution lies in changing our attitude and understanding the nature of the world, not in changing the world (which anyway is impossible).
How Valid are the Classical Prognostic Factors of Carcinoma Cervix in the Era of Concurrent Chemotherapy and Conformal Radiation

Beena K, Vishnu Rajan Nambiar, Dinesh M

ABSTRACT

Aim: To evaluate the significance of established prognostic factors of carcinoma cervix in the concurrent chemo radiation era.

Materials and methods: From January 2007 to December 2011, a total of 138 new cervical cancer patients received radical concurrent chemo radiotherapy from our centre and were retrospectively analyzed for the impact of prognostic factors on outcome.

Results and Conclusion: The patients in the study had a median follow up of 33 months (range 1-80 month’s). Majority of our patients (53.6%) were in the FIGO stage IIB and only 2.8% of the patients were staged IVA. Univariate and multivariate analysis were carried out for various patient, tumour and treatment related factors and their impact on survival. The factors that had emerged as statistically significant prognosticators for disease free survival (DFS) include an Hb level of less than 11g/dl at presentation, and presence of para-aortic node, while the presence of any associated comorbidity reduced the OS of these patients. On multivariate analysis, low initial haemoglobin level (Hb <11g/dl) was found to significantly lower the DFS (p = 0.006). The reported late grade 3 and 4 toxicities were 5.8%.

Keywords: Concurrent chemoradiotherapy, Carcinoma Cervix, Prognostic factors.

INTRODUCTION

Cervical cancer is the 3rd most common cancer among women worldwide1. International incidences vary widely, reflecting, in part, differences in cultural attitudes toward sexual promiscuity and the availability of programs to screen for, and treat pre-invasive disease. Every year 72,825 women die from this disease in India1. As per the ‘WHO-WHS India’ data, the cervical cancer screening coverage in the country is a meagre 2.6% [4.9% in urban women of 18-69 years, and 2.3% in rural women of 18-69 years]2.

There are various predictive and prognostic factors known to have an impact on carcinoma cervix. Many such factors have been studied or are under study to recognize an association with the outcome and these include patient-related factors like age and initial haemoglobin, treatment related factors, such as total treatment duration, and tumour related factors like, tumour size, histology and more recently, various molecular biomarkers.

Most of the studies of these prognostic variables were done in the pre-concurrent chemotherapy era and were based on surgical series or RT series, which did not use contemporary RT protocols. There is a renewed interest and need to re-evaluate the effects of common clinical and pathologic factors in today’s era of concurrent chemoradiotherapy. So this analysis is on a select group of patients who received radical chemo-radiation for carcinoma of the cervix at our centre during a 5 year period.

Aim of the study

Assessment of the prognostic factors associated with carcinoma cervix, with respect to overall survival (OS), and disease-free survival (DFS).

Materials and Methods

This is a retrospective study of biopsy proven cervical cancer patients treated with radical, concurrent chemoradiation at the Amrita Institute of Medical Sciences, Kochi, between 2007 – 2011. A total of 138 patients received radical concurrent chemo radiation and brachytherapy and were eligible to be analysed in our study. Data collection was done from hospital medical records.

All cases were investigated with routine hematological and biochemical examination, X-ray chest, and sonography of abdomen and pelvis before starting radiotherapy treatment. Computed Tomography /MRI data was available for a few patients. All patients were examined and staged clinically according to the FIGO 2009 staging system.

Patients with Stage Ib2-Stage III and a select group of stage IVA received radical concurrent chemoradiation. All patients treated with concurrent chemoradiation, received external beam radiation (EBRT) using 3D Conformal radiotherapy (3DCRT) and intra-cavitary High –Dose Rate (HDR) brachytherapy. As this study included patients from 2007-2011, the dose schedules used were 45-50 Gy in 20-25 fractions at 1.8-2 Gy per fraction, treated daily, for 5 days a week. Patients with para-aortic nodes at presentation received extended field RT with...
upper border above renal hilum (D12-L1). For routine 4 field box technique, the upper border was at L4/L5 junction. Portal imaging was done weekly for treatment verification.

Concurrent chemotherapy was given with weekly Cisplatin 40mg/m2, and patients who could not tolerate Cisplatin received Carboplatin.

All patients were assessed by the third week of external radiation and given HDR intracavitary brachytherapy, anytime after 3rd week depending on the central disease response, using Iridium-192 source (MicroSelectron) for 2-3 sittings, each one week apart. The most common dose schedule used was 700cGy x 3 sittings. Other schedules included 800cGy x 2 or 900cGy x 2 sittings.

All intracavitary applications were performed under spinal anaesthesia. CT based planning was done for each sitting. Dose prescription was initially done to Point A. The plans obtained were manually optimized to minimize bladder, rectal and sigmoid doses while ensuring adequate target coverage. Patients were followed up weekly, with blood counts and renal function tests, during the course of treatment. Post-treatment follow-up, with clinical examination, was done at 1 month post completion of treatment, and after that every 3 months for 2 years, every 6 months until the 5th year and then annually thereafter. Post treatment imaging was done only if clinically indicated. Toxicity assessment was done according to RTOG acute and late radiation morbidity criteria.

### Statistical Methods

Kaplan Meier estimate of survival rate was computed for the subgroups of all prognostic factors. To test the statistical significance of the difference in survival rate between various subgroups of each factor, log-rank test was applied and univariate and multivariate analyses done. Chi-square test was used to determine association.

### Ethical Issues

The study was approved by Institutional review board and no ethical issues were involved in this study since it is a retrospective review.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>50</td>
<td>36.2%</td>
</tr>
<tr>
<td>Absent</td>
<td>88</td>
<td>63.7%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50yrs</td>
<td>46</td>
<td>33.3%</td>
</tr>
<tr>
<td>51-65yrs</td>
<td>75</td>
<td>54.3%</td>
</tr>
<tr>
<td>&gt; 65 yrs</td>
<td>17</td>
<td>12.4%</td>
</tr>
<tr>
<td>NLR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 2.195</td>
<td>66</td>
<td>47.8%</td>
</tr>
<tr>
<td>≤ 2.195</td>
<td>67</td>
<td>52.2%</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 11g/dl</td>
<td>124</td>
<td>89.8%</td>
</tr>
<tr>
<td>&lt; 11g/dl</td>
<td>14</td>
<td>10.2%</td>
</tr>
<tr>
<td>Pelvic Node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>8</td>
<td>5.8%</td>
</tr>
<tr>
<td>Absent</td>
<td>130</td>
<td>94.2%</td>
</tr>
<tr>
<td>PA Node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>4</td>
<td>2.9%</td>
</tr>
<tr>
<td>Absent</td>
<td>134</td>
<td>97.1%</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (IIB IIA)</td>
<td>21</td>
<td>15.2%</td>
</tr>
<tr>
<td>Locally Advanced (IIB-IVA)</td>
<td>117</td>
<td>84.8%</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>4</td>
<td>2.9%</td>
</tr>
<tr>
<td>Absent</td>
<td>134</td>
<td>97.1%</td>
</tr>
<tr>
<td>Treatment Duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 8 weeks</td>
<td>11</td>
<td>8%</td>
</tr>
<tr>
<td>≤ 8 weeks</td>
<td>127</td>
<td>92%</td>
</tr>
<tr>
<td>EQD2 (T)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 74Gy</td>
<td>36</td>
<td>26.1%</td>
</tr>
<tr>
<td>&gt; 74Gy</td>
<td>102</td>
<td>73.9%</td>
</tr>
<tr>
<td>No. of Chemo Cycles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 cycle</td>
<td>3</td>
<td>2.2%</td>
</tr>
<tr>
<td>2 cycle</td>
<td>6</td>
<td>4.3%</td>
</tr>
<tr>
<td>3 cycle</td>
<td>17</td>
<td>12.8%</td>
</tr>
<tr>
<td>4 cycle</td>
<td>46</td>
<td>34.6%</td>
</tr>
<tr>
<td>5 cycle</td>
<td>61</td>
<td>45.9%</td>
</tr>
<tr>
<td>Uterine body extension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>6</td>
<td>4.3%</td>
</tr>
<tr>
<td>Absent</td>
<td>132</td>
<td>95.7%</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCC</td>
<td>123</td>
<td>89.1%</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>12</td>
<td>8.7%</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

Table 1: Patient Characteristics.
RESULTS

A total of 138 patients who received radical CTRT were eligible for analysis.

The patients in the study had a median follow up of 33 months (range 1-80 months).

Patient characteristics were as shown in Table:1.

The overall survival (with a range of 2 – 82 months) at 2 years and thereafter, was 93.2% (Graph:1) The DFS (with a range of 1 – 80 months) was 85.9% at 2 years, 81.1% at 3 years, and 78.2% at 4 years and thereafter (Graph:2).

On comparing the survival of patients with and without co-morbidities, those who had any form of co-morbidities had an OS of 97.3% at 3 years compared to 86.7% for those who had none (p = 0.026) (Graph:3).

Neutrophil-lymphocyte ratio (NLR) has been less studied as a prognostic factor in carcinoma cervix. In our study, the median NLR value was obtained (2.195) and the patients were divided into two groups based on this, and no significant correlation was found.

The patients were grouped into those with an initial Hemoglobin level of 11g/dl or more, and those with an initial Hb, less than11g/dl. The DFS for patients with low Hb levels were lower, with 69.6% vs 96.3%, 69.6% vs 93.7% and 44.8% vs 57.8% at 1, 2 and 3 years.

Prognostic factors

The patient related factors, which were studied included the age at diagnosis, presence of co-morbidities, neutrophil-lymphocyte ratio at presentation, and initial haemoglobin.

To assess the function of age, this study had subdivided the patients into 3 groups, based on the age – i) $\leq$ 50 years, ii) >50, $\leq$ 65 years, iii) > 65 years. With a p value of 0.582 for OS and 0.162 for DFS, there was no significant difference between the groups, though there was a trend towards better disease-free survival in the ‘above-65 years’ age group.
years respectively (p = 0.002). There was also a trend towards better overall survival in the group with higher initial hemoglobin levels (p = 0.134). (Graph: 4)

The tumour related factors that were analyzed included the presence of pelvic or para-aortic nodes at presentation, tumour histology, FIGO stage, presence of hydronephrosis or uterine body extension of tumour.

The presence of para-aortic nodes at presentation was found to be a significant prognostic factor, compared to those who were node negative, with a DFS of 75% vs 92.6%, 75% vs 86.2% and 0% vs 82.5% at 1, 2 and 3 years respectively (p = 0.048). A trend towards better overall survival was also seen, in the node-negative group (0.143) (Graph: 5).

The presence of pelvic nodal disease at presentation showed a trend towards poorer OS, (p = 0.103), and there was no association with DFS (p = 0.474).

The patients were grouped into those having a histology of squamous cell carcinoma, adenocarcinoma or others, and no statistically significant association

<table>
<thead>
<tr>
<th>Variable</th>
<th>p Value for OS</th>
<th>p Value for DFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes : 50</td>
<td>0.026</td>
<td>0.699</td>
</tr>
<tr>
<td>No : 88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes : 31</td>
<td>0.842</td>
<td>0.271</td>
</tr>
<tr>
<td>No : 107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 50 yrs : 46</td>
<td>0.162</td>
<td>0.582</td>
</tr>
<tr>
<td>51-65 yrs : 75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 65 yrs : 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophil-Lymphocyte Ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 2.195 : 66</td>
<td>0.810</td>
<td>0.367</td>
</tr>
<tr>
<td>&lt; 2.195 : 67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;/= 11 g/dl : 124</td>
<td>0.134</td>
<td>0.002</td>
</tr>
<tr>
<td>&lt; 11 g/dl : 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic Node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes : 8</td>
<td>0.474</td>
<td>0.103</td>
</tr>
<tr>
<td>No : 130</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Para-aortic Node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes : 4</td>
<td>0.143</td>
<td>0.048</td>
</tr>
<tr>
<td>No : 134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (IIB-IIA) : 21</td>
<td>0.584</td>
<td>0.097</td>
</tr>
<tr>
<td>Locally Advanced (IIB-IVA) : 21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes : 4</td>
<td>0.651</td>
<td>0.187</td>
</tr>
<tr>
<td>No : 134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 8 weeks : 11</td>
<td>0.419</td>
<td>0.727</td>
</tr>
<tr>
<td>&lt;/= 8 weeks : 127</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval Between EBRT &amp; Brachy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None : 60</td>
<td>0.568</td>
<td>0.858</td>
</tr>
<tr>
<td>&gt;/= 1 day : 30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQD2 (T)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;/= 74 Gy : 36</td>
<td>0.437</td>
<td>0.437</td>
</tr>
<tr>
<td>&gt; 74 Gy : 102</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of Chemo Cycles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 cycle : 3</td>
<td>0.462</td>
<td>0.516</td>
</tr>
<tr>
<td>≤ 3 cycles, &gt; 3 cycles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 cycles : 6</td>
<td>0.516</td>
<td>0.695</td>
</tr>
<tr>
<td>3 cycles : 17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterine body extension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes : 6</td>
<td>0.545</td>
<td>0.695</td>
</tr>
<tr>
<td>No : 132</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCC : 123</td>
<td>0.636</td>
<td>0.759</td>
</tr>
<tr>
<td>Adeno : 12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 : Summary of Results.
could be made with respect to DFS ($p=0.759$) or OS ($p=0.636$).

Uterine body extension was documented in only 6 patients, and no significant correlation with DFS ($p=0.695$) or OS ($p=0.545$) could be made.

The study population were grouped into early (IB-IIA) and locally advanced (IIB to IVA) cervical cancers, with 21 patients in the former group and 117 in the latter, respectively. A trend towards poorer disease-free survival (0.097) was observed in advanced stages, but no statistically significant correlation was seen with OS ($p=0.584$).

The treatment related factors studied were the overall treatment time, the dose delivered and number of chemotherapy cycles received.

The patients were divided into two groups – one with overall treatment time ≤ 8 weeks, and the other, with > 8 weeks. With only a small number (11 vs 126) of patients having a treatment duration more than 8 weeks, no association with OS ($p=0.419$) or DFS ($p=0.727$) could be established.

The 2 Gy equivalent dose (EQD2) for tumour control (with $\alpha/\beta=10$), was calculated and the patients were categorized as those who received ≤ 74Gy (36 patients) or >74Gy (102 patients). There was no difference between the two groups (receiving $\leq 74$Gy or $>74$Gy) in terms of OS ($p=0.437$) or DFS (0.700).

The effects of various prognostic factors were as given in table 2:

Multivariate analysis was done, by including all the factors which had a ‘p value’ of less than 0.2 on univariate analysis. For OS, these included age, comorbidities, haemoglobin and para-aortic nodes, while for DFS, this included hemoglobin, pelvic and para-aortic nodes, hydronephrosis and stage.

On multivariate analyses, the presence of any comorbidity ($p=0.027$) was found to significantly reduce the overall survival, while initial low hemoglobin level ($p=0.016$) was found to be a significant factor associated with lower DFS.

Follow-up

The patients in the study population had a period of follow-up ranging from 1 month to 80 months, with a median follow-up period of 33 months. The status at last follow up was as follows: Alive, NED (112 patients); Alive with disease (18 patients); Dead with disease (7 patients); dead due to other cause (1 patient).

DISCUSSION

Cervical cancer is a major health problem for women in rural India 1 and the systematic implementation of screening and preventive strategies to reduce the burden of disease have not been possible due to various factors.

The study of various prognostic and predictive factors, that may affect the outcome in cervical cancer patients, assume significance in this context, as these factors could play an important role in optimizing the currently available therapeutic regimes, to derive maximal results.

Over the years, various prognostic variables have been studied, mostly based on surgical series and in the pre-chemotherapy era. As recently the focus has shifted to the studies of various molecular markers as prognosticators, this analysis has attempted to re-evaluate many patient-related, tumour-related and treatment-related prognostic factors, in the present era of concurrent chemoradiation.

Besides prognostication at the outset, many of these factors, including pre-treatment hemoglobin, treatment duration, radiation dose delivered, chemotherapy cycles etc are modifiable factors, and which, if established as outcome altering variables, would help the oncologist to achieve more optimum results with the currently available treatment modalities.

Various patient-related, tumour related and treatment-related factors were analyzed in this retrospective study, to assess their prognostic significance.

Our study did not find any significant association between age and survival, though some published studies have shown a better prognosis for the older age groups, compared to younger patients 1,4.

In this study, the majority of patients were staged as FIGO IIB (74), followed by IIB (33), while there were only 4 patients staged IVA. Stage distribution matches with the prognostic factor analysis study of the two GOG protocols 120 and 165 by Monk et al3. But we could not establish a significant correlation between stage and survival, suggesting that the FIGO staging, currently in use, may not be an adequate predictor of survival.

Neutrophil- Lymphocyte ratio (NLR) has not been widely evaluated as a prognostic factor in cervical cancer. In the only study published in literature, a Korean study, 1061 patients were divided into those with an NLR value of above 1.9 or below 1.9, and those with higher NLR values were found to have a poorer prognosis9, but our study failed to demonstrate a significant correlation.

Pre-treatment haemoglobin has been evaluated as a prognostic factor in various studies, many of which have shown a correlation between lower pre-treatment haemoglobin {<12 vs $\geq 12g/dl$; <11 vs $\geq 11g/dl$, etc} values and poorer prognosis, with pre-treatment blood transfusions altering this scenario7,9,10,11.

In our analysis, patients with initial hemoglobin levels lower than 11g/dl, had a significantly worse outcome compared to patients with Hb ≥11g/dl, with DFS at 2 years 69.6% vs 93.7% and at 3 years 59.7% vs 87.8% ($p=0.002$).

The presence of pelvic or para-aortic nodes, at the time of initial presentation, was another factor that was analyzed to ascertain prognostic significance.

Several studies have demonstrated a poorer outcome in patients with pelvic or para-aortic nodal positivity at
presentation. Though our study could not demonstrate a correlation between pelvic nodes and survival (p =0.103 for OS, and p=0.474 for DFS), probably due to the low numbers, there was a significant reduction in the disease-free survival in patients who had para-aortic nodes at presentation, from 92.6% to 75% at 1 year and from 82.5% to 0% at 3 years (p=0.048).

Fifty of the 138 patients in our study had some form of comorbidity documented, and patients who had any comorbidity were found to have a lower OS than patients who did not have any (p =0.26). But no association between comorbidities and toxicity could be established (p =0.556).

Analyses of the toxicities in our study group, revealed a very low rate of grade 3 and 4 toxicity (5.8%), could be due to the careful 3DCRT planning and CT based brachytherapy.

Reviewing the results of our study, in univariate analysis, the factors that had emerged as statistically significant prognosticators of poor survival include an Hb level of less than 11g/dl at presentation and presence of para-aortic nodes, both of which reduced the disease-free survival, while the presence of any associated comorbidity reduced the overall survival of these patients. On multivariate analysis, low initial hemoglobin level (p=0.006) was found to predict a poor disease-free survival, and the presence of any comorbidity, was a significant variable in predicting poor overall survival.

Limitations of the Study

This being a retrospective analysis, it was subject to the limitations of the study design.

Data regarding all the prognostic factors were not available in the old records.

CONCLUSION

The FIGO clinical stage, though widely used does not correlate well with DFS or OS. FIGO staging alone, with its inherent fallacies, may not be a good predictor of survival in cervical cancer. Though it may be continued to be used for uniform reporting and comparison, a newer staging system incorporating adequate imaging investigations, may need to be introduced for widespread use, resources permitting.

Low initial haemoglobin levels (<11g/dl) at presentation, and presence of para-aortic nodes at the time of diagnosis, were prognostic variables which had a significant adverse effect on the disease-free survival, while the presence of any comorbidity, predicted a poor overall survival. Therefore, correction of anemia to maintain haemoglobin levels above 11g/dl, with blood transfusions, prior to initiation of treatment, should be integrated into every treatment protocol.

Five percent of our patients had isolated para-aortic failure, and this was not predicted by the prognostic factors analysed. Similarly, the need for factors which could predict the systemic recurrences, may also be stressed, to accommodate a more intensive systemic therapy in these patients at the outset.

The future of cervical cancer treatment demands optimization of currently available therapeutic strategies, to attempt to negate the effects of the adverse clinical factors, and pursue the identification of molecular markers, which, besides prognostication, could pave way for developing targeted therapies for clinical application.

REFERENCES

ABSTRACT

ACSM is a life threatening emergency, but with a timely diagnosis and a well-planned early intervention the outcome will be favourable. As the clue to the extend of myocardial damage lies in the cardiac markers, it is of prime importance to test for cardiac enzymes in all the patients who is presented to ED with symptoms suggestive of ACS.70 subjects were enrolled in to the study who presented to ED with symptoms suggestive of ACS. And the initial Point of care troponin I values were analysed under various perspectives like morbidity, PTCA in NSTEMI etc. And the results concluded with the importance of PoCT-cTn in ED, and it’s role other than in diagnosing ACS.

Keywords – Point of care troponin I , ACS , NSTEMI, PTCA.

INTRODUCTION

Acute coronary syndrome (ACS) is caused by athero-thrombotic lesions of the heart that are associated with a thrombus formation on a ruptured atherosclerotic plaque, leading to a reduction in the supply of oxygen and nutrients to the heart muscle and impairing cardiac functions, presenting acute myocardial infarction (AMI)³. ACS reflects the spectrum of coronary artery disease (CAD) resulting in acute myocardial ischemia and includes unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI)³,⁴.

Only two thirds of chest pain patients (66%) present to hospitals responsible for emergency hospital admissions; the main reason being the fear of acute myocardial infarction (AMI). Among the chest pain patients, half of presentations (46%) had chest pain with unlikely ischemic chest pain or ACS, but one third of them (33%) experienced MI, and one fifth (21%) of them had unstable angina or likely ischemic chest pain⁴.

To distinguish different spectra of ACSs and non-cardiac cases and to do appropriate risk stratification and triage, current guidelines of ACS require a cardiac Troponin I sample taken on arrival or at least 6 hours after the onset of chest pain⁵. But in practical aspects there are limitations for guidelines especially in developing countries; like delay in arriving at the ED, unavailability of Troponin I point of care tests in peripheral hospitals which hinder early diagnosis and shifting the patients to cardiac care centres and financial constraints of patients which serve as an obstacle in providing an optimal treatment to the patients.

Any elevation in Troponin I levels indicates some degree of myocardial necrosis. Therefore, Troponin I has become a gold standard cardiac marker (CM) of MI due to its high diagnostic specificity and prognostic value in the clinical setting⁶,⁷. However, Troponin I is time dependent and needs to be detected within a few hours of chest pain onset. Point-of-Care testing of Troponin (PoCT-cTn) is a rapid test and practical in clinical settings. Point-of-Care Testing (PoCT) is defined as testing conducted at or near the site of patient care, allowing blood samples to be processed immediately⁸. It can provide rapid results of point of care Troponin I with turnaround times as short as 15-30 minutes in comparison with laboratory testing needing 60-90 minutes⁹. Point of care Troponin I can significantly reduce the turnaround time from testing to results, allowing more immediate patient triage and effective management.

There are various studies done in establishing the importance of Cardiac Troponins as a powerful tool in the diagnosis, predictor of mortality and morbidity in acute coronary syndromes. But there are only very less information available regarding the importance of Point of care Troponin I other than its diagnostic value.

Our aims in this study were to
1. To identify whether any correlation exists between the initial Troponin I Point of care value and the morbidity.
2. Variation of initial Troponin I in STEMI and NSTEMI cases.
3. Association of Initial Troponin I and PTCA in NSTEMI cases.

Material and Methods

This retrospective study was conducted in Amrita Institute of Medical Science, Emergency Medicine Department.

Point of care blood analysis for Troponin I is done using a standard point of care analysing machine. It is a rapid immuno fluorescent quantitative assay.

Study Population and Study design

Details were collected of all patients presenting to the emergency department with symptoms which lay in the spectrum of acute coronary.
syndrome. All of them primarily came to our center and the onset of symptoms was within the past 24 hrs. For all these subjects a Troponin I Point of care test was done and recorded. The collected data included: Age, Sex, Diagnosis, Troponin I POC, Presenting symptom, Date of admission, Date of discharge, PTCA was done during the stay or not.

Morbidity of the patient was assessed by the number of days of hospital stay, and duration of more than 10 days was considered as an arbitrary cut off.

Documents found in the Amrita hospital information system was used to complete the data, and the patient’s information was recorded and kept confidential.

Exclusion criteria
1. History of acute coronary syndrome within the last 1 months.
2. Recent Cardio Thoracic Trauma or surgery, cardiac pulmonary resuscitation or Cardioversion in the past 4 weeks.
3. Patients who are known case of Renal Failure or admitted with sepsis.

Statistical Analysis
From the study done by Philip Haaf et al ; 2012 with 95 % confidence interval and 15% allowable error sample size comes to 70 in my study.

RESULTS
3.1: Trop I and STEMI / NSTEMI
The study conducted constituted a total of 43 % STEMI cases and 57 % NSTEMI cases. In the 43 STEMI cases, a total of 11 cases were Anterior wall MI and Lateral wall MI, and 32 cases were Inferior wall MI.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency of Initial Trop I (ng/dl)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>0.01-1 1-5 5-10</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>26      10 21</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27      32 41</td>
<td></td>
</tr>
</tbody>
</table>

Here we can see that the Troponin I value is being elevated in both NSTEMI and STEMI, but when the initial Troponin I is compared between STEMI and NSTEMI, In the STEMI patients the value of initial Troponin I is highly elevated than the NSTEMI patients, and is proved statistically significant.(p value < 0.01)

Troponin I and Duration of Hospital Stay
In our study there were a total of 57 % cases who had total duration stay more than 10 days.

<table>
<thead>
<tr>
<th>Correlation between Initial Trop I and duration of stay</th>
<th>Trop I (ng/dl)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.01</td>
<td>0.01, 5-10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-0, 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-16</td>
<td></td>
</tr>
<tr>
<td>Duration of stay</td>
<td>&lt;10 days 20</td>
<td>15 8</td>
</tr>
<tr>
<td></td>
<td>&gt;10 days 7</td>
<td>17 33</td>
</tr>
<tr>
<td>Total</td>
<td>27 32 41</td>
<td></td>
</tr>
</tbody>
</table>

When the initial Troponin I values were compared in determining the association of initial Troponin I and Duration of stay in the hospital, it was found that as the initial Troponin I value was high, the total duration of stay in the hospital was also longer. 80.49% of patients with Tro I POC more than 5ng/dl had hospital stay more than 10days in comparison to 25.9% of patients with Tro I POC less than 1ng/dl. This was found to be statistically significant. (P value < 0.01).

Correlation between PTCA and Trop I POC in NSTEMI Cases

<table>
<thead>
<tr>
<th>Correlation between PTCA and Trop I POC in NSTEMI Cases</th>
<th>Trop I (ng/dl)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-5 5-10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PTCA</td>
<td>NO</td>
<td>33 10</td>
</tr>
<tr>
<td></td>
<td>YES</td>
<td>3 11</td>
</tr>
<tr>
<td>Total way</td>
<td>36 21</td>
<td></td>
</tr>
</tbody>
</table>

The above table is the correlation between NSTEMI patients who underwent PTCA and initial Troponin I values. We can see that in the NSTEMI cases that have been taken for PTCA the value of Initial Trop I was higher than those who did not have PTCA; 78.5% of patients who underwent PTCA had high initial Troponin I in comparison to 23.2% of those who had PTCA with initial Troponin I less than 5ng/dl. It was statistically significant. (P value < 0.01).

DISCUSSION
The point of care Troponin I is a very useful tool for Emergency Physicians in arriving at the diagnosis of acute coronary syndrome in very limited time. But other than its role in helping with the diagnosis, does the initial troponin I convey anything more? With this perspective, we enrolled 100 subjects presented to the ED with symptoms lying in the spectrum of ACS and for those Troponin I point of care test was done.
Hence a point of care cardiac Troponin I testing should be done to estimate the myocardial injury at the earliest.

The role of troponin I in establishing the extent of myocardial injury has been extensively studied and proved. In our study we attained results of high elevation in Troponin I for STEMI cases when compared to the NSTEMI cases. [Fig 1] This result was comparable with the studies conducted by J.S. Noble et al. As the myocardial injury is more in STEMI cases the initial Troponin I was at a higher level. As the pathophysiology behind STEMI puts the heart into extensive myocardial damage than in the NSTEMI, the elevation in troponin I can be logically correlated.

We checked for the correlation between initial troponin I levels to morbidity of patients with respect to their hospital stay and found out that patients who had higher initial Troponin I of care had longer duration of hospital stay. [Fig 2]

As the extent of myocardial damage is more, the prognosis of the patient is poor. This result is compatible with the same outcome obtained in the study conducted by Marcello Galvanni et al.

With the advance of PTCA the mortality due to ACS and its complications has been decreased drastically and a near normal cure can be given to the patients with ACS. Hence, PTCA has been implemented in many centers as a primary modality in STEMI cases. In our study we have compared the relation between the initial troponin I and incidence of PTCA. In this, the chances of taking up the patients for PTCA were found to be high in cases where the initial Troponin I was also high. Primary angiography and stenting are the main treatment modalities in STEMI.

In our study an elective angiogram was done for all NSTEMI cases. But PTCA was done in only 24.5% of patients, of these 78.5% patients had high initial Troponin I values. A statistical significance was found between elevation in Troponin I and incidence of PTCA in this group of NSTEMI patients. [Fig 3] Despite, lack of evidence supporting our outcome, from our study we propose that NSTEMI patients with high initial Troponin I should be considered for PTCA at the earliest.

A very well performed, randomized controlled trial in a much larger population is required to substantiate our results.

CONCLUSION

ACS is a life threatening emergency, but with a timely diagnosis and a well-planned early intervention the outcome will be favourable. As the clue to the extent of myocardial damage lies in the cardiac markers, it is of prime importance to test for cardiac enzymes in all the patients who is presented to ED with symptoms suggestive of ACS.

In our study, high initial Troponin I was found in STEMI patients in comparison to NSTEMI, moreover it was associated with increased morbidity (p value < 0.01). A high initial troponin I in NSTEMI cases had an increased incidence for PTCA among them (p value < 0.01).

Hence the importance of Point of care Troponin I for an Emergency Physician other than in confirming the diagnosis of ACS, is that it can be taken as a nominant tool in taking up the patients for a definitive management and the planning and work up of the patient can be started from the ED.

Time is not only Brain, It can be Heart also!

REFERENCES

Sapheno-Femoral Junction Anatomy and Haemodynamics in Indian Patients

Riju R, Manikanta Prabhu, Vaidyanathan s

ABSTRACT
Varicose veins, a common disease in surgical practice, has vexed surgeons for ages, due to its various problems. We hereby present a pilot study of 80 consecutive patients who underwent anatomical and haemodynamic evaluation at the time of Trendelenburg procedure.

Aim
1. To study the location of the saphenofemoral junction (SFJ) in relation to the pubic tubercle.
2. To locate variations in the pattern of tributaries around the SFJ.
3. To analyse the haemodynamics of the SFJ.

Materials and methods
80 consecutive patients who underwent Trendelenburg procedure from August 2007 to August 2008 are presented. Radiological and clinical evaluation were done and patients were subjected to Trendelenburg procedure at which time position of the Sapheno-Femoral junction (SFJ) in relation to pubic tubercle was measured, also noting nature and number of tributaries. A demonstration of the severity of reflux was made and all the information was noted and computed.

Results
We found that in the Indian patient the position of the SFJ was higher and more medial than the Western counterpart. There were fewer tributaries in the Indian patient. The external pudendal artery was seen more commonly in the Indian patient and could act as a landmark for identification of the SFJ.

Conclusion
SFJ was seen at a much higher point contrary to the popular anatomy. High incision using the pubic tubercle as the reference point gives good exposure for flush ligation and identification of the tributaries at the SFJ thereby preventing inadequate primary surgery. In our study, there are between 4-5 tributaries at the SFJ and these need to be completely identified and disconnected. Deep external pudendal artery is seen as it goes laterally at the lower border of the cribiform facia and forms a good marker of the termination of GSV and presence of the SFJ.

INTRODUCTION
Varicose veins are a common disease with a prevalence of approximately 20% in the adult population. The standard treatment of this disease for over a century has been the Trendelenberg procedure. This has been a durable procedure and has stood the test of time. The problem with this procedure has been the high incidence of recurrence and failure, most often due to missed veins.

Aims
1. To study the location of the saphenofemoral junction (SFJ) in relation to the pubic tubercle.
2. To locate the variations in the pattern of tributaries around the SFJ.
3. To analyse the haemodynamics of the SFJ

Material and methods
This is the pilot part of an ongoing prospective study. All patients with primary varicose veins of the GSV system presenting to our department either with or without complications were included in the study. The study was started in August 2007.

There were a total of 80 patients who were enrolled in the initial part of the study. Patients with recurrent varicose veins, short segment varicosities, associated arterial disease and deep vein thrombosis were excluded.

A thorough clinical examination was done to assess the disease and to rule out deep venous insufficiency. A CEAP classification of the patients’ disease was done. A hand held Doppler was done using an 8 mHz probe to grade the reflux at the Sapheno Femoral junction (SFJ). Reflux lasting less than 5 seconds was classified as Grade I, 5-10 seconds was classified as grade II and > 10 seconds was classified as Grade III. A study of Ankle Brachial index using the hand-held Doppler was done to exclude patients with arterial system disorder. The patients were then subjected to a formal Duplex Doppler assessment to rule out associated deep vein disease.

Patients then underwent procedure under either spinal or general anaesthesia. All the patients were placed in a supine position with the index limb kept slightly flexed and externally rotated at the hip. A hockey stick shaped incision was taken about 1 finger breadth below the groin extending downwards as necessary. The position of the pubic tubercle was marked and two lines were drawn, one vertically downwards and another at right angles to the first so as to measure the distance of the SFJ from the
pubic tubercle in two planes – below and lateral to the pubic tubercle. A calliper was used to measure the exact distance.

The great saphenous vein (GSV) was dissected out and the termination and all the tributaries in the operative field were exposed. Femoral vein was identified for 1 cm above and below the SFJ. Number of tributaries, variations in the tributaries, distance of pubic tubercle from the SFJ, bifid termination of GSV, presence of Saphena varix and its distance from the SFJ, presence and location of the deep external pudendal artery were noted. All the tributaries were ligated and disconnected. At this point, the GSV was divided and on table demonstration of the SFJ reflux was done. Flush ligation of SFJ was done. Now the distance of the SFJ from the lines drawn medially and above it were measured at its closest distance. The measurements were recorded in the patients’ operative notes. Data for the last two years were taken and analysed.

RESULTS

Out of 80 patients included in the study, 50 were males and 30 were females. Mean average distance of SFJ 2.7 cm below and 3.0 cm lateral to pubic tubercle.

Female and Male comparison.

Although the graph shows that females have more medial and superiorly situated saphenofemoral junction in relation to pubic tubercle, this was not statistically significant. This change could be due to the anatomic characteristic of the male android pelvis.

Majority of the patients were C5 with healed ulcer

Majority of patients had a Grade 2 reflux with the reflux lasting 5-10 seconds as detected by a hand-held Doppler.

In 72 out of 80, i.e. 90% cases in our study, we were clearly able to demonstrate the superficial external pudendal artery between the LSV and the common femoral vein in the fossa ovalis. In two cases we found the artery crossing the GSV anteriorly at the SF junction. Saphena varix was seen in 20 patients (25%) with mean average distance of about 6.25 cm below the saphenofemoral junction. The closest varix was 1.8 cm from the SFJ and farthest was 8 cm from the SFJ. A Bifid GSV was found in 10 of the 80 patients (12.5%).

DISCUSSION

For this study, all the patients with primary varicose veins were evaluated with hand-held Doppler, Duplex scan and clinical examination preoperatively and then underwent Trendelenburg surgery. Preoperatively, pubic tubercle was marked and intraoperatively saphenofemoral junction was measured in relation to pubic tubercle and the number and pattern of tributaries were recorded.

Out of 80 patients included in the study, 50 patients were males and 30 were females. Patients included in the study were in the age range of 20-71 years. The maximum numbers of patients were in the range of 40-60 years of age. Average age of presentation was 47 years.

The commonest presenting symptom was pain and recurrent ulceration. Majority of our patients belonged to CEAP 5 classification. The duration of presentation...
ranged from 2 years to 40 years (mean: 12.8 years).

**Hand-held Doppler (HHD)**

Traditional clinical examination using Trendelenburg test and tourniquet testing is unreliable. Salaman et al. and Campbell et al. found 92 percent accuracy with the HHD probe at the SFJ. All the patients underwent preoperative hand-held Doppler and the reflux was graded accordingly. Grade 1- < 5 secs, grade 2 - 5-10 secs, grade 3 > 10 secs. Nicos Labropoulos et al. demonstrated the cut off value for reflux in the superficial veins to be greater than 500 ms and the reflux cut-off value for the femoropopliteal veins to be greater than 1000 ms. In our study, we have graded the reflux at the SF junction with hand-held Doppler and 65 percent of our patients had grade 2 reflux (5-10 secs) which is higher compared to previous studies. Mercer et al. observed that the most important aspect to be noted in doing HHD is there is always interobserver and intraobserver errors that cannot be avoided. Discrepancies in the operative planning and inadequate surgery based on the findings with HHD alone occurred quite frequently.

We compared the CEAP with HHD grading and were not able to demonstrate a significant relationship between the two; the p value was insignificant. In a climate of limited finances and expertise, patients with reflux in the LSV alone will, as a group, benefit the least from routine imaging. However, a policy of not imaging these patients will leave sites of reflux undetected and untreated. We have also used HHD for measuring the ankle brachial pressure index and excluded the arterial disease in the limbs. Hence there is no doubt that HHD is a very good screening tool and like ultrasound abdomen has become part of clinical examination, HHD has become the extended part of clinical examination in the venous and arterial disease.

**Anatomy**

Sapheno-femoral junction (SFJ):

Historically, the saphenofemoral junction has been described to be 3.5 - 4 cm below and lateral to pubic tubercle. In contrast to the historical description, in the present study, mean average distance of SFJ was 2.7 cm below the pubic tubercle with majority of the patients between 2.6-3cm, which is higher than that described. Ass Ndiaye et al described that on average, the top of the arch of the great saphenous vein projected out 10.88 cm (8.5–14) from the ventral cranial iliac spine; 3.83 cm (2–6) from the pubic tubercle;
and 4.19 cm (2.5–5.5) from the inguinal ligament. Perrin et al believed that the saphenous opening projects between 2.5 cm and 3.5 cm underneath and inside the pubic tubercle. In contrast to the above mentioned literature, a study conducted by Royle et al in 1981 showed 70% of the SF junction was at the level of pubic tubercle and few cases even high above the pubic tubercle.

Donnelly et al described that they carried out the procedure through an incision above and parallel to the groin crease. The textbook Vascular Surgery principles and Techniques Haimovici advises incision along the inguinal crease.

In view of the above mentioned variations supported by the literature, we recommend a high incision in the upper aspect of thigh 1 cm below the pubic tubercle which gives sufficient exposure for identification of SF junction and tributaries. The setting up of a fixed anatomical marker, the pubic tubercle, combined with the data on anatomical variations, allows meticulous surgery and prevents inadequate primary surgery.

**Tributaries:**

1) **Number of Tributaries**

Standard anatomy names four tributaries (superficial circumflex iliac, the superficial epigastric and the superficial and deep external pudendal veins) that typically enter the LSV in the femoral triangle. Two other veins, the posteromedial or accessory saphenous and anterolateral tributary, are described as entering the thigh, or occasionally at the level of the femoral triangle. However, Moore et al and Ellis et al, whilst alluding to the variable contribution of other tributaries, named only three typical tributaries (superficial epigastric, superficial circumflex iliac and superficial external pudendal) to the LSV in the groin.

In our study, the number of tributaries varied from 3 to 7 in number. McDonnelly et al demonstrated 1 to 10 in number tributaries.

<table>
<thead>
<tr>
<th>No of tributaries 3</th>
<th>No of tributaries 4 or 5</th>
<th>No of tributaries &gt; 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our study</td>
<td>8.75%</td>
<td>86.25%</td>
</tr>
<tr>
<td>Donnelly et al 14</td>
<td>57%</td>
<td>38%</td>
</tr>
<tr>
<td>Konrad Janowski et al (18)</td>
<td>63%</td>
<td>30.1%</td>
</tr>
<tr>
<td>Mansberger et al (19)</td>
<td>80%</td>
<td>16%</td>
</tr>
</tbody>
</table>

The study conducted in 1950 by Mansberger et al combined cadaveric and operative surgery of 61 dissections.

With the above mentioned data, it is clear that majority of patients in the present study had 4 or 5 tributaries in contrast to the literature were most patients had 4 tributaries or less.

2) **Percentage of incidence of tributaries**

We have also compared with a Korean cadaveric dissection study conducted by Myung-Hoon Chun et al and were able to demonstrate a similar percentage of tributaries in our live dissection study. This has been demonstrated in the Fig.

<table>
<thead>
<tr>
<th></th>
<th>Myung hoon chu cadavericdissection (n=249) J. Korean medicalsceince</th>
<th>Our study N=8</th>
</tr>
</thead>
<tbody>
<tr>
<td>External pudendal</td>
<td>95.2%</td>
<td>91.23%</td>
</tr>
<tr>
<td>Circumflex iliac</td>
<td>83%</td>
<td>81.26%</td>
</tr>
<tr>
<td>Superficial Epigastric</td>
<td>77%</td>
<td>70%</td>
</tr>
<tr>
<td>Posteromedial</td>
<td>82.3%</td>
<td>83.2%</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>67%</td>
<td>76.3%</td>
</tr>
</tbody>
</table>
3) Anatomical variants of the Long Saphenous vein and its proximal tributaries

Regarding the anatomical variations in the tributaries of the Saphenofemoral junction there has been many classifications starting with Glasser et al in 194321 and Konrad Janowski in 200418. It is important to identify the variations as there is more likelihood of leaving behind unligated tributaries or even the saphenofemoral junction. This is analogous to common bile duct injury during Cholecystectomy where the surgeon is unaware of the anatomical variants. Both will lead to devastating problems.

A “normal pattern” of tributaries present in the study was 51.25%, in contrast to other studies20,21 where it was described to be much less. The famous comment on hernia by Cooper22 who said: “No disease of the human body belonging to the province of surgeon requires in its treatment, a better combination of accurate anatomical knowledge with surgical skill than hernia in all its varieties” holds true for the Trendelenburg surgery also as 50% of the patients have some form of anatomical variant.

The noted anatomical variants in our study can be classified based on the Glasser21 classification, as follows:

- Prominent LSV joined by 4 or 5 separate tributaries in its terminal 4 cm, the normal situation (41 cases – 51.25%).
- More than five tributaries joining the LSV in the area of the fossa ovalis (6 cases – 7.5%).
- True double LSVs, joining right at the fossa ovalis after independently receiving an anterolateral tributary in one instance and a posteromedial tributary in the other, and then sharing drainage from the abdominal wall and pudendum. (10 cases – 12.5%).
- Dominant anterolateral tributary, receiving circumflex iliac and epigastric tributaries before joining a LSV (7 cases – 8.75%).
- Prominent postero medial tributary (the “accessory saphenous vein”) that merges with the external pudendal, (8 cases – 10%).
- Bifid LSV with prominent postero medial tributary forming a H shaped junction (1 case – 1.25%).
- Double saphena varix in the same line of LSV (1 case .125%).
- All tributaries entering into the saphena varix (1 case .125%).
- LSV dividing and reforming just before the SF junction (1case – 1.25%).
- Prominent postero medial or anterolateral tributary draining into the common femoral vein (4 – 5% cases).

4) Absence of tributary to LSV

Nabatoff et al23 described the major saphenous vein draining into the femoral vein separately without any tributaries in 2 cases. Donnelly et al also described a small number of dissections (8 out of 2089 i.e. 0.4%) showing no tributaries to the LSV, with only junctional tributaries identified. We have not encountered this type of anomaly in our study.

5) Junctional tributary

In our study, we have 8 cases (10%) documented to have one junctional tributary. Out of these, 6 cases (75%) were located laterally and 2 cases (25%) medially. Donnelly et al14 described a significantly higher incidence of junctional tributaries (33.4%), and that too, more than one. Of these, 76.2% are located medially, 13.1% were located laterally and 10.8% above the junction.

External pudendal artery (EPA)

The EPA crosses between the great saphenous vein and femoral vein in the fossa ovalis and is a good landmark for the saphenofemoral junction24.

Our study showed that in 72 out of 80, ie 90% cases, we were clearly able to demonstrate the EPA between the LSV and the common femoral vein in the fossa ovalis and it is a very good landmark of the saphenofemoral junction. We also identified two cases where the EPA was found to traverse anterior to the LSV exactly at the SF junction. Donnelly et al14 showed that reliance on the EPA to identify the SFJ was potentially misleading as it was identified in 22.5% of cases only and they concluded that presence of EPA is an indication of anatomical variants and not a landmark for SF junction.

Saphena Varix

Saphena varix was seen in 25% of our patients with a mean average distance of about 6.25 cm below the SFJ. The probable etiology described in literature why saphena varix occurs far from the SF junction and not at SF junction is that the pressure exerted by the reflux occurs more frequently in the anterior wall of the long saphenous vein.

Methods of preventing inadequate surgery

Prominent truncal tributaries and tributary pairing or splitting predispose to misidentification and missed tributaries, but incomplete circumferential dissection of the fossa ovalis is the necessary concomitant for these errors to actually occur. Failure to define the fossa’s less prominent infero-medial border is the usual fault, leading to mistaking the juncture of a prominent thigh tributary with the LSV for the true SFJ and, for this reason, overlooking proximal tributary veins. The dyes of venous surgery have repeatedly emphasized the importance of circumferential dissection of the fossa ovalis and inspection of the most cephalad 5 to 6 cm of the LSV9,23,26,27,28.
Stonebridge and coworkers\textsuperscript{20} Bergan and Ballard\textsuperscript{30}, and others, dismayed by the frequent finding of recurrent reflux from linkage of a persistent junctional tributary to varicose remnants in the thigh, advanced the concept of spatial separation a step further. They advocated doing an extended tributary resection, which is done by drawing each primary tributary into the wound until one of its own tributaries is exposed, then interrupting both, and the primary tributary’s junction with the LSV, and resecting the intervening segment. Doing an extended tributary resection probably has a secondary benefit in ensuring a thorough and inclusive dissection of all primary tributaries. Other surgeons have advocated opening the fossa ovalis, incising the femoral sheath, and exposing several centimeters of the femoral vein proximal and distal to the fossa to interrupt direct superficial-to-deep connecting veins that might otherwise be missed\textsuperscript{32,31,32}. The latter maneuver has not received wide acceptance because of concern about scar restriction of the femoral vein or the possibility of facilitating growth of new superficial-to-deep connecting veins. Neither femoral vein exposure nor the more widely applied extended ligation has prospective data in support of these surgical techniques.

**Methods of preventing inadequate surgery**

SFJ was seen at a much higher point contrary to the popular anatomy. High incision using the pubic tubercle as the reference point gives good exposure for flush ligation and identification of the tributaries at the SFJ thereby preventing inadequate primary surgery. In our study, there are between 4-5 tributaries at the SFJ and these need to be completely identified and disconnected. Deep external pudendal artery is seen as it goes laterally at the lower border of the cribriform fascia and exposing several centimeters of the femoral vein proximal and distal to the fossa to interrupt direct superficial-to-deep connecting veins that might otherwise be missed. The latter maneuver has not received wide acceptance because of concern about scar restriction of the femoral vein or the possibility of facilitating growth of new superficial-to-deep connecting veins. Neither femoral vein exposure nor the more widely applied extended ligation has prospective data in support of these surgical techniques.

**REFERENCES**


6. K. G. MERCER, D. J. A. SCOTT and D. C. BERRIDGE Preoperative duplex imaging is required before all operations for primary varicose veins.


32. K. G. Mercer, D. J. A. Scott and D. C. Berridge, Preoperative duplex imaging is required before all operations for primary varicose veins, British Journal of Surgery 1998, 85, 1495–7
A Study of Vacuum Assisted Closure in Non-Healing Ulcers
Manoj V V*, Faizal Ali AA**

ABSTRACT

Background
Non healing ulcers are worrisome to the physician and cause anxiety and financial burden to the patient. Vacuum assisted closure (VAC), a recent addition in the armamentarium of wound management offers a solution.

Aim
The aim of this study was to compare the treatment outcomes of VAC and standard wound therapy in non-healing ulcers of varied aetiology.

Materials and methods
A prospective randomized study was conducted in 50 patients admitted with non-healing ulcer and open musculoskeletal injuries. VAC and conventional group comprised of 25 patients each.

Results and conclusions: The VAC group of patients significantly fared better in terms of lesser hospital stay and quicker healing of the ulcer compared to the conventional group. The study confirmed that VAC was definitely superior to standard wound therapy.

key words
Vacuum assisted closure, ulcer, wound healing, negative pressure wound therapy, diabetic ulcer, traumatic ulcer.

INTRODUCTION

Acute and chronic wounds affect at least 1% of the population and are relatively inexpensive, readily available and easy to apply (McCallon)7. They represent a sizeable risk factor for hospitalization, amputation, sepsis, and even death. From the patient’s perspective, wound therapy is often uncomfortable, painful and financially draining. An acute wound is defined as any interruption in the continuity of the body’s surface (Kranke et al.), as in burns, crushing injuries and lacerations (MacLellan)2,3,4. A wound is deemed chronic when it requires a prolonged time to heal, does not heal, or recurs (Kranke et al.). Conventional wound therapy consists of initial surgical debridement (Bowler), then twice a day either wet to moist (WM) gauze dressings or Opsite dressings, to cover the wound (Joseph)5,6. They are relatively inexpensive, readily available and easy to apply (McCallon)7.

Vacuum assisted closure (VAC) is a universally accepted method for dressing. This was pioneered by Dr Louis Argenta and Dr Michael Morykwas in 19938. It has proved its efficacy for wound dressing with faster wound healing and shorter hospital stay. The purpose of this type of wound management is to decrease wound healing time and to facilitate wound care in situations considered difficult or non-healing. Its simplicity and efficacy have made it a favoured method for wound management. In addition, numerous other applications have been reported, ranging from treatment of orthopaedic wounds with exposed bone, tendon, or hardware in the management of acute burns or even as an adjunct to skin grafting and artificial dermis grafting.

The traditional application of cups containing heated air to wounds by the Chinese thousands of years ago may be a precursor of negative pressure wound therapy (NPWT)9. This was first used successfully in the early 1950s to manage exudate and accelerate wound healing. The technique has been shown in practice to remove excess interstitial fluid and transmit a mechanical force to the surrounding tissues producing deformation of the extracellular matrix and promoting a reduction in wound size10. In western medicine, the first use of a vacuum was in the form of suction bells popularized in the nineteenth century by Junod (9). For a wound to heal there should be a continuous flow to the site and drugs should be adjusted11. Given the large and increasing burden of diabetic and other wounds, the Indian patient will greatly benefit from advances in wound care12,13.

Still in our hospital, majority of dressings remain conventional. Clinical knowledge about the management of difficult to treat wounds is limited owing to the lack of high quality evidence. Aim of our study was to show the advantage of VAC over conventional dressing.

AIM OF STUDY

• To study the advantage of vacuum assisted closure over conventional dressing in the management of chronic non-healing ulcers.
• To study the difference in rate
of amputation, hospital stays in case and control groups.

MATERIALS AND METHODS

Study design and setting

It was a prospective randomized controlled study conducted at a tertiary care center for one year extending from June 2012 to May 2013. Patients were selected from general surgery and orthopaedic wards. Patients were categorized as 25 cases and 25 controls, randomized during admission. The study was cleared by the Institutional Ethics Committee.

Inclusion criteria

Patients included in study were classified according to the grade of the ulcer (Wagner classification) (14, 15, 16). All grades were included except grade 0 and 5. All cases of diabetic and traumatic ulcers in patients aged between 13 and 70 years were taken. Outcome variables studied included the difference in rate of healing, hospital stay and cultures before & after VAC.

Exclusion criteria

Patients with fistula, necrotic tissue in eschar, osteomyelitis (Untreated), exposed blood vessels, gangrenous foot, active bleeding and patients undergoing anticoagulant therapy and malignancy were excluded.

Methodology

The cases and controls were selected from the general surgery and orthopaedic wards randomized on an alternating basis. Informed consent was taken from the patients. Doppler study was performed to assess the vascularity of the limb before the procedure and x-ray taken to rule out osteomyelitis. After debridement of the wound, VAC dressing was applied after hemostasis (Figures 1-6). Pre VAC swab for C & S was taken. A piece of pre sterilized foam (open-pore foam of polyurethane of 35 ppi density and 33 mm thickness with 400–600 microns pore size) was cut to the size of the wound and is placed on it. Then a perforated drainage tube (Romovac suction drain tube) was placed. Now a second piece of foam was placed on the underlying foam and tube. The whole foam with tube was covered with a sterile transparent dressing (Opsite). The tube was connected to a suction apparatus with a negative pressure of 100 to 125 mm of Hg for 10 minutes hourly for 12 consecutive hours. Rest of the time this drainage tube was connected to the Romovac suction apparatus. Dressing changed after 72 hours and post VAC culture was taken. Three cycles of dressings and vacuum were applied.

Control groups were given conventional dressings. The wound was cleaned with hydrogen peroxide and Povidone Iodine and moist saline dressings given. Dressings were changed twice daily. Cultures were taken after 72 hours. The outcome variables were assessed in terms of hospital stay, presence of discharge, number of SSG, number of amputations and culture sterility. The two authors assessed the wounds separately. Neither the patients nor the assessors were blinded.
Statistical Analysis

Data were analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 10. To elucidate the comparison between controls and cases, Chi square test was used as nonparametric test. Student’s t test was used to compare mean values between two groups. For all statistical evaluations, a two-tailed probability of value, < 0.05 was considered significant.

Ethical issues

Though the proposed study included an invasive procedure, no major ethical issues were expected. The study was cleared by Ethics committee and written informed consent of the study participants was taken.

Conflict of interests if any

There was no additional burden imposed on the patient through this study. There was no financial support for the study from any external agencies. There was no conflict of interests in this study.

OBSERVATIONS AND RESULTS

Both case and control groups were matched in terms of age, gender and grade of ulcer. Duration of hospital stay in days was found to be statistically significant between the two groups. Control population stayed more days in hospital than cases. Majority (19 patients) among the case group left hospital within three weeks’ time, whereas 12 patients from the control population stayed for more than three weeks (Table- 1, Fig- 7).

### Table- 1

<table>
<thead>
<tr>
<th>Duration of Hospital Stay (Days)</th>
<th>Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Cases</td>
</tr>
<tr>
<td>7 - 14</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>4.00%</td>
<td>24.00%</td>
</tr>
<tr>
<td>14 - 21</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>8.00%</td>
<td>28.00%</td>
</tr>
<tr>
<td>21 - 28</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>40.00%</td>
<td>24.00%</td>
</tr>
<tr>
<td>28 - 35</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>24.00%</td>
<td>20.00%</td>
</tr>
<tr>
<td>&gt; 35 days</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>24.00%</td>
<td>4.00%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Chi Square: 11.012; P &lt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table- 1. Case group had a shorter hospital stay at any point of time which was statistically significant.
After 35 days, 6 patients from the control group were still hospitalized, whereas there was only one patient in the case group. The mean duration of stay between the groups was also significant (Table-2); 30.4 days compared to 22.2 days in the VAC group. This was significant since both groups were matched in terms of grading of ulcer.

VAC dressing had almost similar effects on ulcer with normal and abnormal Doppler study. It fared better in patients with normal Doppler study though it was not statistically significant (Table-3). Besides, though insignificant, 4 among the case group had osteomyelitis which was not a hindrance in healing since only one patient remained hospitalized after 35 days (Table-4).

At the end of 3 cycles of VAC, the patients were assessed in terms of presence or absence of discharge, culture positivity, rates of amputation and feasibility of split skin grafting (SSG). VAC dressing was better with less discharge, more SSG before discharge and less rate of amputation. Chi-square test showed that the study was significant as p-value was less than 0.001 (Table-5, Fig-7). Of the 25 cases, 12 patients were grafted with SSG and 2 underwent amputation. In the conventional group, none could be grafted in the stipulated time of 35 days and there were 6 amputations.

Chi-square test showed significant statistical association as cultures pre and post VAC remained sterile. Besides, 90% unsterile culture turned sterile after VAC (p-value < 0.001 (Table-6).

<table>
<thead>
<tr>
<th>Doppler Finding</th>
<th>Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Cases</td>
<td>Total</td>
</tr>
<tr>
<td>Normal</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>76.00%</td>
<td>72.00%</td>
<td>74.00%</td>
</tr>
<tr>
<td>Vascular Impairment</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>24.00%</td>
<td>28.00%</td>
<td>26.00%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Chi Square: 0.104; P &gt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table-3. Doppler findings in cases and controls.

<table>
<thead>
<tr>
<th>X Ray Finding Osteomyelitis</th>
<th>Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Cases</td>
<td>Total</td>
</tr>
<tr>
<td>Absent</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>84.00%</td>
<td>84.00%</td>
<td>84.00%</td>
</tr>
<tr>
<td>Present</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>16.00%</td>
<td>16.00%</td>
<td>16.00%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Chi Square: 0.000; P &gt; 0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table-4. Osteomyelitis had no significant correlation between the groups.

At the end of 3 cycles of VAC, the patients were assessed in terms of presence or absence of discharge, culture positivity, rates of amputation and feasibility of split skin grafting (SSG). VAC dressing was better with less discharge, more SSG before discharge and less rate of amputation. Chi-square test showed that the study was significant as p-value was less than 0.001 (Table-5, Fig-7). Of the 25 cases, 12 patients were grafted with SSG and 2 underwent amputation. In the conventional group, none could be grafted in the stipulated time of 35 days and there were 6 amputations.

Chi-square test showed significant statistical association as cultures pre and post VAC remained sterile. Besides, 90% unsterile culture turned sterile after VAC (p-value < 0.001 (Table-6).

<table>
<thead>
<tr>
<th>Outcome/Plan</th>
<th>Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Cases</td>
<td>Total</td>
</tr>
<tr>
<td>Discharge</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>76.00%</td>
<td>44.00%</td>
<td>60.00%</td>
</tr>
<tr>
<td>Split Skin Graft</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>48.00%</td>
<td>24.00%</td>
<td></td>
</tr>
<tr>
<td>Amputation</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>24.00%</td>
<td>8.00%</td>
<td>16.00%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Chi Square: 16.133; P &lt; 0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table-5. VAC group fared better with less discharge, more SSG and lesser amputation.

<table>
<thead>
<tr>
<th>Culture Sterility in Cases</th>
<th>Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre VAC</td>
<td>Post VAC</td>
<td></td>
</tr>
<tr>
<td>Sterile</td>
<td>5</td>
<td>23</td>
</tr>
<tr>
<td>20.00%</td>
<td>92.00%</td>
<td>56.00%</td>
</tr>
<tr>
<td>Non Sterile</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>80.00%</td>
<td>8.00%</td>
<td>44.00%</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Chi Square: 26.299; P &lt; 0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table-6. VAC was significantly superior with 92% of culture becoming sterile.
DISCUSSION

Our study confirmed the efficacy of VAC dressing over conventional dressing in terms of better outcome for the patient. It decreased hospital expenses, hospital manpower and the nursing care required. Our study is in accordance to observations available in literature1,7,18. At the end of 35 days of observation, 24% from the conventional group and 4% from the VAC remained hospitalized. This was in accordance to observation by McCallon and Nather average stay in the hospital for VAC group was approximately 22 days8,19. Significant reduction in bacterial growth in the VAC group corroborated with the observations of K Sinha et al20.

The foam-based technique, originally developed by Argenta and Morykwas (1997), used a sealed polyurethane foam dressing attached by a tube to a vacuum pump at a sub-atmospheric pressure of 125 mm Hg. More recently developed NPWT systems utilize flexible drains and gauze and are based on the Charikar-Jeter technique20,21,22. Polyurethane foam dressing showed newly formed granulation tissue trespassing into the polyurethane foam, making its removal painful during dressing changes23. Umut et al did a retrospective study using Charikar-Jeter therapy and has reported superior results in terms of lesser pain and cost than foam dressing24. He used decreasing pressures with each sessions starting with 125 mm Hg initially. They suggest that it is useful especially for SSG. Evidence for the optimum pressure is limited. Morykwas showed using laser Doppler needle flow probes that local tissue perfusion increased with increasing pressures up to 125 mm Hg.

We did not have any complications attributable to VAC per se, but there were two amputations. Cases of periwound maceration and infection reported however may not be VAC-related. There are reports of minor discomfort with the application of pressures greater than 100 mm Hg1.

Most studies currently consisted of small sample sizes or methodological limitations so that any results should be interpreted with caution1. Though our study was randomized, blinding was not done and hence bias could not be ruled out. The dimensions of ulcers were not taken as a measurement of ulcer healing as in studies by Wanner and Ford. In Fords study, for the initial reduction of ulcer volume by 50%, there was no difference between the groups. In the biopsy of granulations, he observed an increase in leucocytes in the conventional group and more capillaries in the VAC group25,26.

NPWT therapy is not the answer for all wounds; however it can make a significant difference in many cases. In much of the current literature on NPWT comparing it with more traditional dressings wound healing has been measured in “time to complete healing” or epithelialization. This may be an inappropriate measure of effectiveness as NPWT is most useful in difficult cavity or highly exudative wounds. NPWT is a useful tool in moving a wound to a point where more traditional dressings or more simple surgical reconstructive methods can be used.

conclusions

VAC dressing decreased hospital stay. It improved pus culture sterility.

There was an improvement in outcome by decreasing the number of amputations and increasing the number of patients undergoing skin grafting.

VAC dressing had better result in patients with Normal Doppler and also in non-active osteomyelitis

Though effective VAC calls for training to ensure appropriate and competent use.

REFERENCES


17. High-pressure suction drainage via a polyurethane foam in the management of poststernotomy mediastinitis by Pedro A. Catario.

18. A Blinded, Prospective, Randomized Controlled Trial of Topical Negative Pressure Wound Closure in India. Author : Gita N. Mody.


Hypoglycemia Symptoms & Its Management in Patients with Diabetes Mellitus

ABSTRACT
Introduction: Hypoglycemia is a common occurrence in people with diabetes and most commonly it is the result of pharmacologic intervention. Avoiding fear of hypoglycemia is often the major impediment for achieving optimal glycemic control. Moreover, hypoglycemia is sometimes associated with significant morbidity and even mortality.
Aim: To identify the common symptoms and find out how patients are managing their hypoglycemia in diabetes.
Methods: It is a prospective analysis of patients with diabetes, who came to Department of Endocrinology and Diabetes during a period of Feb 2016 to Dec 2016. Consecutive Type-1 and Type-2 diabetic patients were selected for this study. A total of 127 patients were selected and given questionnaire regarding hypoglycemia. The data was subsequently analyzed.
Results: In this study 64.4% were males, 34.6% females and most of them are Type-2 diabetic (95%). Most of the patients were under treatment for diabetes. Results revealed that most of the patients have awareness about hypoglycemia (84%) and the incidence of moderate and severe hypoglycemia varies from patient to patient. Only very few patients carried snacks for sudden episodes of hypoglycemia [never-15%, rarely-12%, sometimes 33%, always 29.9%]. Most of them carried candy for their treatment (48.5%). In this study none of the patients had a glucagon emergency kit. And the most common symptoms were sweating (83.5%), tremor (74%), fatigue (67.7%), anxiety (57.5%), and visual symptoms (68.5%).
Conclusion: Hypoglycemia awareness was high in our study subjects. But most common reason of hypoglycemia on our study subjects is due to delayed meals. Even though they know about hypoglycemia and its symptoms, most of them were not doing anything to prevent it. Hence greater attention should be given in order to prevent and minimize the risk of hypoglycemia.

INTRODUCTION
Diabetes mellitus, also known as diabetes, is a metabolic disease in which a person has high blood glucose, either because the body does not produce enough insulin, or their cells do not respond to the insulin produced. People with diabetes develop further health complications as inadequate blood sugar control, can lead to heart disease and stroke, as well as damage to kidneys, nerves and retina. It is a major health problem worldwide, which affects a significant percentage of the Indian population.

According to the International Diabetes Federation, in 2012, more than 371 million people worldwide have Diabetes. In India, 63 million people have diabetes as of 2012, and the number is estimated to increase to 101 million by 2030.

The goal of diabetes treatment is the maintenance of an adequate metabolic control to prevent or delay the development of complications. However, a therapeutic effort to keep the values of glycated hemoglobin within the recommended target in many cases leads to an increased risk of hypoglycemia.

Hypoglycemic episodes, especially the severe ones, have significant clinical, social and economic impact. From the clinical standpoint, physical morbidity of an episode of hypoglycemia ranges from unpleasant symptoms to seizure and coma; rarely, it causes sudden, presumably cardiac arrhythmic death or, if it is profound and prolonged, brain death.

To minimize the risk of hypoglycemia, careful education regarding the symptoms and treatment of hypoglycemia, with regular reinforcement, is extremely important because of the recognized gaps in the knowledge base of these individuals.

So we conducted a prospective study to find out the symptoms and management of hypoglycemia as reported by patient with Diabetes.

METHODS AND MATERIALS
This is a prospective study. The patients were recruited from Department of Endocrinology and Diabetes, Amrita Institute of Medical Science and Research Center. The Diabetic patients who attended the outpatient clinic were selected for this study. A validated questionnaire was administered to these patients to determine the hypoglycemia management and symptoms status. In the case of children and elderly patients, parental and bystander input was also taken into consideration in completing the questionnaire. The questionnaire include, personal data of the patient, current treatment of Diabetes, awareness about hypoglycemia, how they are treating their hypoglycemia and also symptoms of hypoglycemia.
After collecting the data, statistical analysis was done using SPSS software version 11.0 at Research Center, Amrita Institute of Medical Sciences Kochi.

RESULTS
In total eligible patients males are more in number than females. We got 95.3% Type 2 patients and 4.7% Type 1 diabetic patients. Of that majority of patients were taking insulin. In this about 85% patients are aware of their hypoglycemia. (Table : 1)

Our study showed that 42.5% patients gets hypoglycemia weekly, 19.7% gets hypoglycemia daily, 13.4% gets monthly once, 11% gets once in 2 months.(Fig -1)

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>PERCENTAGE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>64.4</td>
</tr>
<tr>
<td>Female</td>
<td>34.6</td>
</tr>
<tr>
<td>Type of DM</td>
<td></td>
</tr>
<tr>
<td>Type-1</td>
<td>4.7</td>
</tr>
<tr>
<td>Type-2</td>
<td>95.3</td>
</tr>
<tr>
<td>Current treatment of DM</td>
<td></td>
</tr>
<tr>
<td>Diet control</td>
<td>5.5</td>
</tr>
<tr>
<td>OHA</td>
<td>11</td>
</tr>
<tr>
<td>insulin</td>
<td>34.6</td>
</tr>
<tr>
<td>Diet + OHA</td>
<td>10.2</td>
</tr>
<tr>
<td>Diet + insulin</td>
<td>13.4</td>
</tr>
<tr>
<td>OHA + insulin</td>
<td>22.8</td>
</tr>
<tr>
<td>OHA + insulin + Diet</td>
<td>2.4</td>
</tr>
<tr>
<td>Awareness of hypoglycemia</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>84.3</td>
</tr>
<tr>
<td>No</td>
<td>15.7</td>
</tr>
</tbody>
</table>

Table : 1 Base line characteristics of the study subjects.
When asked about the cause of hypoglycemia, 30.7% got hypoglycemia due to less food, 21.3% got hypoglycemia due to insulin overdose, 11% got due to over exercise, 11.8% didn’t know the reason for hypoglycemia, and 25% patients have combined reasons for their hypoglycemia. (Fig-2)

It has been showed that 33.1% of patients sometimes carry snacks with them, 29.9% of them always carry snacks with them, 15% never carries snacks with them, and 12.6% rarely carries snacks with them. (Fig-3)

About 52% of the study population, treat their hypoglycemia when sugars below 70mg/dl, 30.7% patients don’t know when to treat hypoglycemia, 14.2% patients treat their hypoglycemia when sugars below 100mg/dl.

When asked how they self treated hypoglycemia 48.8% of patients use candy to treat their hypoglycemia, 25.2% uses glucose powder to treat, 17.3% took meals to treat their hypoglycemia.

The common symptoms of hypoglycemia were sweating (86%), visual symptoms (68%), fatigue (67%), tremor/shakiness (74%), and anxiety (57%) (Fig-4). Other symptoms such as nausea, dizziness, confusion, abnormal sleep were also assessed but they were not commonly seen. None of the study subjects carried glucagon emergency kit to treat their hypoglycemia.

---

**Figure 1:** Graph showing how often patients get hypoglycemia.

**Figure 2:** Graph showing the reason of hypoglycemia.

**Figure 3:** Graph showing how often they carry snacks.
DISCUSSION

In 2005, the America Diabetes Association work shop on hypoglycemia released a report entitled “De fining and reporting Hypoglycemia in Diabetes”\(^3\). In that report, recommendations were primarily made to advise the US food and Drug Administration (FDA) on how hypoglycemia should be used as an end point in studies of new treatments for diabetes. In 2009, the Endocrine Society released a clinical practice guideline entitled Evaluation and Management of Adult Hypogly cemia Disorders,” which summarized how clinicians should manage hypoglycemia in patients with diabe tes\(^4\). People with diabetes need not always self -treat at an estimated glucose concentration of < 70mg/dl. Options other than Carbohydrate ingestions include repeating the test in the short term, changing behavior [e.g: avoiding driving or elective exercise until the glucose level is higher], and adjusting the treatment regimen. Although the alert value has been debated \(^5\), a plasma concentration of < 70mg/dl can be used of hypoglycemia in diabetes. In this study we include several cut off values, that patients refers to treat their hypoglycemia and it shows about 52% of patients use 70mg/dl as their cut off value, 30.7% of my study population don’t know when to treat their hypoglycemia and some of the patients refers 100mg/dl and 150mg/ dl to treat their hypoglycemia.

Severe hypoglycemia is an event requiring assistance of another person to actively administer carbohydrate, glucagon or take other corrective actions. Plasma glucose concentrations may not be available during an event, but neurological recovery following the return of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration\(^6\). In our study we assessed about severe hypoglycemia experienced by our study population and it was noted that 3.1% of the study population experienced severe hypoglycemia once in 3 months, 2.4% of patients experienced severe hypoglycemia once in 6 months and 93.7% never experienced severe hypoglycemia in the last 6 months. Moderate symptomatic hypoglycemia is an

![Fig 4: Diagrams showing common symptoms of hypoglycemia.](image-url)
Hypoglycemia Symptoms & Its Management in Patients with Diabetes Mellitus

CONCLUSION

Hypoglycemia still represents a common acute complication for individuals with diabetes.

Our study on hypoglycemia suggested that, knowledge about hypoglycemia among patients with diabetes varies from patient to patient. We noticed that hypoglycemia awareness was high in our study subjects. But most common reason of hypoglycemia on our study subjects was due to delayed meals. Even though they know about hypoglycemia and its symptoms, most of them were not doing anything to prevent it.

None of the patients had ever heard about glucagon kit and hypo tab. Hence greater attention should be given to the choice of individualized targets and treatment schemes as well as better self-management education, in order to prevent and minimize the risk of hypoglycemia.

REFERENCES

8. Hypoglycemia and Diabetes: A report of a workgroup of the American Diabetes Association and The Endocrine Society ELIZABETH R,MD 1 JOHN ANDERSON,MD 2 BELINDA CHILDS.
10. BondsDE, MillerME, Bergenstal RM, et al. The association be-

Correlation of Six Minute Walk Distance with Clinical & Spirometric Parameters in COPD

Libin Antony P F*, Nithya Haridas**, Sundaram K R***, Arun Nair****, Hari Lakshmanan P****, Sumi Soman*

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a progressive condition associated with morbidity and mortality. Spirometry, the diagnostic test for COPD, is not widely available. Many a time it is effort dependent and hence, a poor indicator of the functional status. Six Minute walk test, an indicator of functional status, would be a better prognostic marker for follow up of patients.

Aim of study: To assess correlation of 6 minute walk distance with post bronchodilator FEV1 in patients with COPD

Methodology:

Patients diagnosed with COPD were subjected to spirometry and 6 Minute walk tests after collecting their baseline demographic and disease characteristics, including MMRC dyspnea scale, BMI, duration of illness, number of exacerbations in past year, medication intake, and home oxygen use. Correlation between 6MWD and clinical and spirometric variables estimated using SPSS software version 20.

Results:

Study included 51 patients. FEV1 (mean-53.45%) (r -0.293) FVC (mean-65.25%) (r-0.307) showed no correlation with 6MWD. MMRC scale of dyspnea (r-0.497) Borg dyspnea scale (r-0.505) showed positive correlation with 6MWD. Age (67.76 +/- 7.99yrs) (r-0.141) exacerbation frequency (mean-1.33) (r-0.149) duration of symptoms (6.94 +/- 9.22yrs) (r-0.283) showed no correlation.

Conclusion: Six Minute walk distance failed to show positive correlation with spirometric parameter and clinical parameters. 6MWD cannot replace spirometry in patients with COPD. It may be used for functional evaluation of patient who cannot perform spirometry.

Keywords: 6 minute walk distance, spirometry, COPD, functional evaluation.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive disease characterized by persistent airflow limitation leading to frequent exacerbations and hospitalizations. Functional capacity and thereby quality of life in COPD are affected by several factors. Spirometry is the gold standard for diagnosis and prognostication of COPD. At times it fails to reflect the functional level of the patient.

Measurement of daily activities like walking distance measurements would be a better predictor of the functional level of the patient.

Measurement of walking distance has been used to evaluate the functional capacity of patients with chronic respiratory & cardiac disease. In 1963, Balke introduced a method to look at the functional capacity by measuring the total distance walked by the patient during a certain period of time. In 2002, the American Thoracic Society (ATS) approved the Six Minute Walk Test as a standard test for clinical pulmonary function laboratories. The relationship between the walking distance in a certain period of time and the functional capacity of patients with COPD has been investigated in various studies.

This study aims to find the correlation of six minute walk distance (6MWD) with clinical & spirometric parameters in patients with COPD.

Objectives

Primary: To assess the correlation between 6 Minute walk distance (6MWD) and Post bronchodilator FEV1 in COPD patients.

Secondary: To find correlation between 6 Minute Walk Distance and other baseline patient variables namely MMRC dyspnea scale, BMI, duration of illness, number of exacerbations in past year.

Study Design

This cross-sectional observational study includes all patients who underwent treatment for COPD from a tertiary care centre pulmonary OPD over a 5 month period from November 2014 to March 2015.

Inclusion Criteria

1. Patients with clinical diagnosis of COPD (GOLD criteria).
2. Clinically stable during the preceding 1 month.
3. Patients who are on standard care for COPD for at least 1 month.

Exclusion Criteria

1. Other diseases including unstable coronary artery disease, severe LV dysfunction, uncontrolled hypertension, active neurological, rheumatological or peripheral vascular diseases, any other disease limiting patient’s movement.
All patients who were diagnosed to have COPD by a Pulmonologist based on clinical features and spirometry were interviewed using a questionnaire. Those who met the inclusion criteria and exclusion criteria were enrolled. Their baseline demographic and disease characteristics, including modified medical research council (MMRC) dyspnea scale, body mass index (BMI), duration of illness, number of exacerbations in past year, medication intake, home oxygen use were documented. Pulmonary function tests including spirometry and 6 Minute walk tests were done as per ATS guidelines. Spirometric indices including FEV1, FVC, FEV1/FVC, peak expiratory flow rate, FEF25-75, and 6MWT parameters namely 6MWD, percentage desaturation during walk test, were noted. Correlation between 6MWD and clinical and spirometric variables was estimated by appropriate statistical methods.

### Sample Size

Sample size was calculated based on the study conducted by Bavarsad et al \(^4\) \((r = 0.36, P < 0.05)\) and power = 80\% , Desired confidence interval = 95\% , Calculated minimum sample size was 50. This study included 51 cases.

### Statistical Analysis

All data were stored electronically. Data collected were checked for accuracy and completeness, coded and entered into the Statistical Package for Social Science (SPSS) software version 20.0.

The correlation between 6MWD and pulmonary function test measurements was evaluated using Pearson’s correlation coefficient. The correlation between 6MWD and Gold group was done using student’s t test. The criterion for statistical significance is a p value <0.05. This study was approved by the Institutional Ethics committee.

### RESULTS

A total of 51 COPD patients were included in the study within 50-83 yrs of age. The mean age of the group was 67.76±7.998 years. For the group the mean duration of symptom was 6.94±9.23 years and the median was 3.00. The mean Exacerbations was 4.00±0.99 times / year. The mean forced expiratory volume in 1 second was 53.46%± 21.25%. The mean forced vital capacity percentage was 65.25%±18.24% and the mean 6 minute walk distance was 391.37±124.55 mts. The mean baseline saturation at the beginning of 6 minute walk test was 93.75%±6.04\% . (table 1)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Median</th>
<th>Std. deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(n=51)</td>
<td>50.00</td>
<td>83.00</td>
<td>67.7647</td>
<td>69.00</td>
<td>7.9989</td>
</tr>
<tr>
<td>Duration of symptoms (yrs)(n=51)</td>
<td>1.00</td>
<td>48.00</td>
<td>6.9412</td>
<td>3.00</td>
<td>9.2291</td>
</tr>
<tr>
<td>Exacerbations (Last 1yr)(n=51)</td>
<td>.00</td>
<td>4.00</td>
<td>1.3333</td>
<td>1.00</td>
<td>0.9933</td>
</tr>
<tr>
<td>MMRC dyspnea grade(n=51)</td>
<td>.00</td>
<td>4.00</td>
<td>2.3529</td>
<td>2.00</td>
<td>9.2291</td>
</tr>
<tr>
<td>Borg dyspnea scale(51)</td>
<td>.00</td>
<td>7.00</td>
<td>1.8824</td>
<td>1.00</td>
<td>2.3949</td>
</tr>
<tr>
<td>FEV1(n=51)</td>
<td>17.50</td>
<td>105.50</td>
<td>53.4569</td>
<td>51.70</td>
<td>21.2461</td>
</tr>
<tr>
<td>FVC(n=51)</td>
<td>35.60</td>
<td>106.10</td>
<td>65.2549</td>
<td>65.70</td>
<td>18.2392</td>
</tr>
<tr>
<td>6MWWD(n=51)</td>
<td>80.00</td>
<td>640.00</td>
<td>391.3725</td>
<td>400.00</td>
<td>124.5475</td>
</tr>
<tr>
<td>duration of smoking(yrs) (n=47)</td>
<td>1.00</td>
<td>60.00</td>
<td>26.3404</td>
<td>25.00</td>
<td>13.6879</td>
</tr>
<tr>
<td>Smoking Score(n=47)</td>
<td>0.1</td>
<td>125.0</td>
<td>25.931</td>
<td>17.50</td>
<td>28.5</td>
</tr>
</tbody>
</table>

Table-1 Variables-Descriptive Statistics.

15. 7% of the patients belonged to GOLD A (mild), 19.6% GOLD B (moderate), 29.41% to GOLD C (severe) and 35.29% to GOLD D (very severe).

As shown in table 2 100% of the patients of GOLD A, 90.0% of GOLD B, 93.4% of GOLD C and 66.8% of GOLD D could walk more than 300m. Only 3 (5.8%) patients walked <100 m and 24 patients (47.58%) could walk >400 m. For statistical analysis, four GOLD groups were clubbed into 2 groups namely Group 1 which included GOLD A & GOLD B and group 2 which included GOLD C & GOLD D. The mean distance walked by group 1 which included the mild and moderate COPD cases was 428.89±69.10 mts, and for group 2 that includes the severe and very severe cases, the mean distance was 370.91±143.1mts. The difference was statistically not significant (p value- 0.196). The cases with mild to moderate dyspnea covered the longer distance during 6MWD (table -3).
Table 2 6 minute walk distance in GOLD groups.

<table>
<thead>
<tr>
<th>6MWD</th>
<th>Gold group</th>
<th>Number</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100m</td>
<td>1(A and B)</td>
<td>18</td>
<td>428.8889</td>
<td>69.102</td>
<td>0.196</td>
</tr>
<tr>
<td></td>
<td>2(C and D)</td>
<td>33</td>
<td>370.9091</td>
<td>143.098</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Mean hospital stay was higher for the control group.

VARIABLES                 | CORRELATION(r) | P-VALUE |
--------------------------|----------------|---------|
Age                       | -0.141         | 0.324   |
Duration of symptoms (yrs) | -0.305         | 0.029   |
Exacerbations (Last 1yr)  | -0.234         | 0.099   |
MMRC dyspnea grade        | -0.497         | <0.001  |
Borg dyspnea scale        | -0.505         | <0.001  |
FEV1                      | 0.186          | 0.191   |
FVC                       | 0.252          | 0.075   |
Duration of smoking(yrs)  | 0.242          | 0.087   |
Gold group                | -0.319         | 0.023   |
S Score                   | 0.231          | 0.134   |
BMI                       | 0.014          | 0.922   |

Table 4: Spearman Rank Correlation Of Variables With 6MWD.

Duration of symptoms: This study demonstrated negative correlation between duration symptom and six minute walk distance, i.e higher the duration of symptom, lower the distance walked (p<0.05). MMRC dyspnea grade: Statistically significant negative correlation was observed between mMMRC dyspnea grade and six minute walk distance, i.e higher the grade of dyspnea lower the distance walked. (p<0.001)(Fig1)

Borg dyspnea scale: Statistically significant negative correlation between borg dyspnea scale and six minute walk distance was observed. i.e higher the dyspnea lower the distance walked (p<0.001). (Figure 2)

FEV1%: study showed no correlation between FEV1% & 6MWD. (r value 0.186 p value 0.191) (Figure 3)

FVC%: Study showed no correlation between FVC & 6MWD. (r value 0.252 p value 0.075) (Figure 4)

GOLD group: Statistically significant negative correlation was also observed between gold classification group and 6 minute walk distance. i.e higher the GOLD classifications group lower the distance walked (p<0.05).
CONCLUSION

6 Minute Walk Test did not show significant correlation with the spirometric variables and clinical parameters like age or exacerbation frequency. It showed significant correlation with mMRC & Borg scale of dyspnea. 6MWT cannot substitute spirometry in patients with COPD. But it can be used for functional and spirometric parameters of chronic obstructive pulmonary disease.

The present study showed no correlation between 6MWD and FEV1 (r= +0.186 p value 0.191) with mean FEV1 =53.457+/21.246 (Table 2) which goes against the findings of the study done by Brasil Santos D et al. (r = 0.4 and p < 0.001) and Bavarsad et al (r = 0.36, P < 0.05). Results were similar to result of study by Kodevala et al. ( r value-0.280 p value 0.062)

The analytic findings of FVC showed that, it has no correlation with 6MWD (r = 0.252 p value 0.075) and mean was 65.255+/18.239 Results are against the finding of the study by Al Ameri HF et al in which FVC showed correlation with r= + 0.46.

Present study demonstrated negative correlation with mMrc grade of dyspnea (r=-0.497, p<0.001) i.e.; Higher the grade of dyspnea (mMRC), lower the distance. This result was similar to study by Khandelwal et.al (r=-0.42,p value <0.05)but in contrast with the findings of Chhabra et al in which MMRC dyspnea scale does not show any correlation with 6 MWD.

There was negative correlation between Borg dyspnea scale & 6 MWD. ( r=-0.505 p value <0.001)

This study demonstrated negative correlation between gold score and 6MWD which was statistically significant (r=-0.319, p<0.023) which is similar to the findings by Mănescu et al.

The study showed that the difference in 6MWD between patients in GOLD group A + B and GOLD group C + D was statistically not significant. However mean 6 MWD was higher in GOLD (A+B) group than GOLD (C+D) group.

Study failed to demonstrate correlation between 6MWD and age of patient, BMI, duration of smoking, smoking score, number of exacerbations in the previous year. This is different from the findings by Ramana than et al., in which 6MWD significantly correlated with age (r = -0.29), Duration of symptoms showed a slight negative correlation with 6 MWD ( r=-0.305 p value- 0.029). This reflects a decline in functional status of the patient with long standing disease and exacerbations.

There is no correlation between the 6MWD and Spirometric parameters in COPD patients. The 6MWD is a simple, convenient, and effective exercise test. But it lacks good correlation with the spirometric indices. in COPD patients.

DISCUSSION

COPD is a progressive disease characterized by persistent airflow limitation. According to GOLD international COPD guidelines, spirometry is the gold standard for accurate and repeatable measurement of lung function. However, it is only one of the means of interpreting COPD disease severity. Other measures, such as the MMRC dyspnea scale for measuring breathlessness, exacerbation frequency, body mass index, quality of life assessment, and exercise capacity all help to build a more complete picture. Quantitative assessment of symptoms like dyspnea, measurement of PEFR and exercise test like 6-minute walk test (6MWT), which are cheaper modes of investigation, can be considered to substitute the spirometry as a severity assessment tool at places where spirometry is not available. Traditionally follow up and titration of medications have been done with the help of repeat spirometric examinations. 6 minute walk test is a cheaper test which can be used for the functional evaluation of the patient.

Spirometry is a complex procedure that requires considerable effort from the individual and in late stage of the disease, the objective parameters like FVC, FEV1 and DLCO may not be sensitive enough to detect subtle changes in functional status improvement. In this cross sectional observation study, we tried to assess the correlation of six minute walk distance with clinical and spirometric parameters of chronic obstructive pulmonary disease.

The present study showed no correlation between 6MWD and FEV1 (r=-0.186 p value 0.191) with mean FEV1 =53.457+/21.246 (Table 2) which goes against the findings of the study done by Brasil Santos D et al. (r = 0.4 and p < 0.001) and Bavarsad et al (r = 0.36, P < 0.05). Results were similar to result of study by Kodevala et al. ( r value-0.280 p value 0.062)

The analytic findings of FVC showed that, it has no correlation with 6MWD (r = 0.252 p value 0.075) and mean was 65.255+/18.239 Results are against the finding of the study by Al Ameri HF et al in which FVC showed correlation with r= + 0.46.

Present study demonstrated negative correlation with mMrc grade of dyspnea (r=-0.497, p<0.001) i.e.; Higher the grade of dyspnea (mMRC), lower the distance. This result was similar to study by Khandelwal et.al (r=-0.42,p value <0.05)but in contrast with the findings of Chhabra et al in which MMRC dyspnea scale does not show any correlation with 6 MWD.

There was negative correlation between Borg dyspnea scale & 6 MWD. ( r=-0.505 p value <0.001)

This study demonstrated negative correlation between gold score and 6MWD which was statistically significant (r=-0.319, p<0.023) which is similar to the findings by Mănescu et al.

The study showed that the difference in 6MWD between patients in GOLD group A + B and GOLD group C + D was statistically not significant. However mean 6 MWD was higher in GOLD (A+B) group than GOLD (C+D) group.

Study failed to demonstrate correlation between 6MWD and age of patient, BMI, duration of smoking, smoking score, number of exacerbations in the previous year. This is different from the findings by Ramana than et al., in which 6MWD significantly correlated with age (r = -0.29), Duration of symptoms showed a slight negative correlation with 6 MWD ( r=-0.305 p value- 0.029). This reflects a decline in functional status of the patient with long standing disease and exacerbations.

There is no correlation between the 6MWD and Spirometric parameters in COPD patients. The 6MWD is a simple, convenient, and effective exercise test. But it lacks good correlation with the spirometric indices. in COPD patients.

CONCLUSION

6 Minute Walk Test did not show significant correlation with the spirometric variables and clinical parameters like age or exacerbation frequency. It showed significant correlation with mMRC & Borg scale of dyspnea. 6MWT cannot substitute spirometry in patients with COPD. But it can be used for functional
evaluation of patients who cannot perform spirometry. Further large scale studies are necessary to substantiate the findings in this study.

REFERENCES
5. GOLD COPD guidelines 2015.
Adult Onset Still’s Disease with Facial Palsy – A Rare Presentation

Urs Vishnu Dev, Henry R A, Joseph J, Oomen A T, Rao G G

ABSTRACT
Adult Onset Still’s disease is an inflammatory disorder characterized by quotidian (daily) fevers, arthritis, and an evanescent rash. Neurological manifestations in a patient with Still’s Disease are very rare and usually occur during the late stage of the disease. Only a few reports are available in literature. Neurological impairment in AOSD may lead to life-threatening complications, i.e., brain stem hemorrhage, fatal seizures, hemiplegia, meningo-encephalitis, cranial nerve palsy, or sensorineural hearing loss. Here we report a patient with AOSD and right facial nerve palsy.

Keywords: Adult Onset Still’s Disease, Neurological manifestations, Facial palsy

INTRODUCTION
Adult Onset Still’s disease (AOSD) is an inflammatory disorder characterized by quotidian (daily) fevers, arthritis, and an evanescent rash. The etiology of Adult Onset Still’s disease (AOSD) is unknown. The diagnosis of Adult Onset Still’s disease (AOSD) is, in part, a diagnosis of exclusion that can generally be made based upon the presence of the characteristic clinical and laboratory features in the absence of another condition that may cause similar symptoms and findings. The neurological manifestations in a patient with Still’s Disease are very rare and usually occur during the late stage of the disease. Equally rare is the incidence of cranial nerve involvement in Still’s Disease. In this patient, the diagnosis of AOSD and right seventh cranial nerve palsy could be made since the extensive search for both infectious and connective-tissue disorders, and malignancies were negative and all manifestations completely resolved with steroids and NSAIDs.

CASE REPORT
A 37 year old lady with no known co-morbidities, residing in the Middle East presented with complaints of fever and body ache since 2 weeks duration. About a week later, this was associated with the onset of erythematous rashes over the upper and lower limbs. Prior to coming to our hospital, she was admitted in a local hospital with low grade fever, myalgia, fatigue and joint pains. She was extensively evaluated and no possible cause for the fever was found. About a week after the onset of symptoms, she noticed deviation of the angle of the mouth to the left side. There was no history of other systemic complaints. She came here for further diagnostic evaluation and management.

On Clinical Examination, she was conscious and oriented. She had pallor, cervical lymphadenopathy and a right lower motor neuron facial palsy. Musculo skeletal examination revealed swollen and tender joints, mainly the wrists, elbows and the knees. Initial blood tests revealed Neutrophilic leukocytosis (TC-15,800/cu.mm, Neutrophils-91.5%), markedly elevated CRP (119.2 mg/L), ESR (60mm 1st hour) and Hepatic transaminases (SGPT-93 IU/L, SGOT-213 IU/L). Coagulation parameters were within normal limits. Peripheral Smear revealed normocytic normochromic anemia with no atypical cells or blasts. Considering the clinical picture, the possibility of an underlying malignancy, especially a lymphoma or leukemia was considered. Ultrasound abdomen revealed hepatosplenomegaly. Chest radiograph done was unremarkable. However, a normal bone marrow examination ruled out an underlying hematological malignancy along with Macrophage Activation Syndrome. Based on a strong clinical suspicion, serum ferritin levels were sent which were markedly elevated (112377 ng/ml). ANA profile and Anti ds DNA, along with Anti CCP were negative. With fulfillment of the Yamaguchi criteria, a diagnosis of Adult Onset Still’s Disease was made. Subsequently, she was started on steroids (1mg/kg in view of moderate disease activity) and NSAIDs. She showed good clinical response to treatment. The laboratory parameters also improved with serial reduction of ESR, CRP levels and normalization of hepatic transaminases within ten days. Serum ferritin levels returned to normal limits by 1 month. She was continued on tapering doses of steroids. The facial palsy also recovered by 1 month.

The occurrence of a neurological manifestation, especially facial nerve involvement is extremely rare and only a handful of cases are reported in the literature. The diagnosis was possible only after ruling out the possibility of an underlying malignancy or a connective tissue disease.

DISCUSSION
Adult Onset Still’s disease (AOSD) is an inflammatory disorder characterized by quotidian (daily) fevers, arthritis, and an evanescent rash. The etiology of Adult Onset Still’s disease (AOSD) is unknown; both

*Dept. of Internal Medicine, AIMS, Kochi.
The neurological manifestations in a patient with Still’s Disease are very rare and usually occurs during the late stage of the disease. Only a few reports are available in literature. Denault et al in 1990 reported sensori-motor peripheral neuropathy which resolved with steroid therapy. A case of Miller-Fisher variant of Guillan-Barre Syndrome has been reported in association with Still’s Disease. Regnato et al in 1987 reported a patient with AOSD and right sided LMN facial palsy and mentioned that only 7% of patients had neurological manifestations. Neurological impairment in AOSD may lead to life-threatening complications, i.e., brain stem hemorrhage, fatal seizures, hemiplegia, meningo-encephalitis, cranial nerve palsy, or sensorineural hearing loss. In this patient, the diagnosis of AOSD and right seventh cranial nerve palsy could be made since the extensive search for both infectious and connective-tissue disorders, and malignancies were negative and all manifestations completely resolved with steroids and NSAIDs. This case emphasizes the importance of recognizing neurological complications at an early stage in AOSD, resulting in both accurate management and decreased risk of severe sequelae. It also highlights the need to be aware of the possibility of neurological manifestations in a patient with AOSD.

The diagnosis of Adult Onset Still’s disease (AOSD) is, in part, a diagnosis of exclusion that can generally be made based upon the presence of the characteristic clinical and laboratory features in the absence of another condition that may cause similar symptoms and findings.

The most commonly used criteria, termed the Yamanouchi classification criteria requires the presence of five features, with at least two being major diagnostic criteria. In addition, the presence of any infection, malignancy, or other rheumatic disorder known to mimic AOSD in its clinical features precludes the diagnosis of AOSD, at least for the purpose of research.

<table>
<thead>
<tr>
<th>General</th>
<th>Cardiopulmonary</th>
<th>Gastrointestinal</th>
<th>Hematopoietic</th>
<th>Musculoskeletal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, Rashes</td>
<td>Pericarditis, pleural effusions, and transient pulmonary infiltrates, ARDS</td>
<td>Abdominal pain, peritonitis, hepato-megaly</td>
<td>Splenomegaly, lymphadenopathy, MAS and HLH</td>
<td>Arthritis, Arthralgia, Myalgia</td>
</tr>
</tbody>
</table>

Table 1 - The major clinical features of Adult Onset Still’s disease (AOSD)

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fever of at least 39°C (102.2°F) lasting at least one week.</td>
<td>• Sore throat</td>
</tr>
<tr>
<td>• Arthralgias or arthritis lasting two weeks or longer.</td>
<td>• Lymphadenopathy</td>
</tr>
<tr>
<td>• A nonpruritic macular or maculopapular skin rash that is salmon-colored in appearance and usually found over the trunk or extremities during febrile episodes.</td>
<td>• Hepatomegaly or splenomegaly</td>
</tr>
<tr>
<td>• Leukocytosis (10,000/microL or greater), with at least 80 percent granulocytes.</td>
<td>• Abnormal liver function studies, particularly elevations in aspartate and alanine aminotransferase and lactate dehydrogenase concentrations</td>
</tr>
<tr>
<td>• Negative tests for antinuclear antibody (ANA) and rheumatoid factor (RF)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 – Yamaguchi Criteria for diagnosis of Adult Onset Still’s Disease
REFERENCES

Residual Cyst: An Unusual Presentation of a Usual Scenario

Anju P David*, Dhanya Mary Sam*, Sreeja P Kumar*, Jaeson Mohanan Painatt**, Beena Varma*, Renju Jose*, Marina Lazar Chandy*

ABSTRACT
A residual cyst is a cyst that persists even after the extraction of the affected teeth. These cysts are generally found to be asymptomatic and are incidental findings during routine imaging procedure. But this is not the case when the cyst becomes infected. This is the case report of a female patient with a complaint of persistent watery discharge from the right side of upper jaw. On further evaluation, it turned out to be a residual cyst in the maxillary antrum, which is rare. Presentation, diagnosis and management of the cyst are discussed.

Key words: Edentulous, Maxillary Antrum, Odontogenic, Radiopaque mass, Residual cyst.

INTRODUCTION
A cyst is a pathological cavity filled with fluid, lined by epithelium and surrounded by a definite connective tissue wall. The cystic fluid is either secreted by the cells lining the cavity or derived from the surrounding tissue fluid. Cysts are more commonly seen in the jaw bones as most of the cysts originate from the rests of odontogenic epithelium1.

Cysts of the jaws are broadly classified into odontogenic and non-odontogenic. Residual cysts are inflammatory odontogenic cysts. The term residual cyst refers to the radicular cyst that has been left behind even after the extraction of the associated tooth. Residual cysts are seen in both the jaws, although slightly more in the mandible, with its epicenter being in the periapical region of the involved and missing tooth. In case of the mandible, the epicenter is always positioned above the inferior alveolar nerve canal. Residual cysts can cause displacement or resorption of the adjacent tooth. The cyst may invaginate into the maxillary sinus or down into the inferior alveolar canal1.

CASE REPORT
A 63 year old female patient reported to the Department of Oral Medicine and Radiology, Amrita School of Dentistry, Cochin, with a chief complaint of watery discharge from right upper back teeth region since 5 months. According to the patient, the present complaint started with toothache and pus discharge in relation to upper right back teeth, following which extraction of the upper right molars were done 2 months back. But her symptoms persisted. Pain was dull aching and intermittent in nature which aggravated while stooping forward. Extraction procedure was uneventful. The discharge was continuous; purulent initially and later, watery in nature. There was no difference in the amount and frequency of discharge before and after extraction. General examination of the patient was not contributory. On extra-oral examination, there was no facial asymmetry but deviated nasal septum and tenderness of right maxillary sinus region were present. Lymph nodes were not palpable. Intra oral examination revealed missing 16,17,18 with healed extraction socket. A mild erosion on the alveolar mucosa of 18 was the only significant pathological finding. There was no vestibular swelling (Fig 1).

On palpation, tenderness and pus discharge were present in relation to right maxillary buccal vestibular area. There was no expansion of cortical plates (Fig 2). As a part of chair-side investigations, air blow test and fine needle aspiration (FNA) were done. The former was negative. FNA revealed pus initially which was followed by blood. IOPAR of the affected edentulous site revealed a break in the floor of maxillary sinus. Haziness was present within the sinus. (Fig 3)
Panoramic radiograph revealed a well defined, smooth, dome shaped radio-opaque mass with corticated border in relation to the posterior aspect of maxillary sinus. The radio-opaque mass was of size $3 \times 2.5$ cm approximately. The lesion extended antero-posteriorly 1 cm away from the anterior border of maxillary sinus to 0.5 cm from the posterior border, supero-inferiorly, 1 cm above the right upper alveolar ridge, overlapping the infraorbital margin. Other findings include multiple missing and carious teeth. (Fig 4)

CT with contrast revealed a $2 \times 2 \times 2.6$ cm expansile lesion with peripherally enhancing soft tissue causing erosion of the lateral and superior wall of maxilla and bulging into the right maxillary sinus. The lesion shows an intra-oral opening with absent teeth (Fig 5).

A surgical enucleation (Caldwell Luc) (Fig 6) procedure was carried out under local anesthesia. Histopathology of the specimen (Fig 7) revealed a cystic lumen with a bit of stratified squamous lining epithelium and a fibrous capsule. Numerous cholesterol clefts along with few giant cells and haemosiderin pigmentation were seen in the deeper part of cyst wall.

Thus, on the basis of histopathological report, a final diagnosis of infected residual cyst was arrived at. The healing was uneventful without any swellings or other complications.
DISCUSSION

Majority of the Cyst in the body are odontogenic in origin. The presence of a tissue with potential for intrabony proliferation from around 42nd day of conception to almost 25th year of extra uterine life predisposes jaws to have maximum number of cysts. This is accentuated by the presence of inflammation around bone by way of gingivitis, periodontitis and of course dental causes related periapical lesions. These infections can have local extension, as in our case. Many a time distant invasion by way of anachoresis is also possible which underlines the necessity for maintaining oral health.

Radicular cysts are the most common of all jaw cysts, comprising about 52-68% of all cysts affecting human jaws. They most commonly involve adult males between the 3rd - 5th decade of life. This is not in agreement with the present case wherein the patient was a female in her 7th decade with lesion in maxillary antrum. Smaller lesions can be detected during routine dental radiography. Larger lesions are slow-growing with expansion of cortical plates and result in facial asymmetry. Secondary infections result in pain. Periapical inflammatory tissue that is not curetted at the time of extraction may give rise to an inflammatory cyst called residual periapical cyst. The histological and clinical features are similar to that of radicular cyst. With time, many of these cysts exhibit an overall reduction in size and spontaneous resolution can occur when there is a lack of continued inflammatory stimulus.

The residual cyst appears as a round to oval radio-lucency of variable size within the alveolar ridge at the site of previous tooth extraction. As the cyst ages, degeneration of the cellular contents within the lumen occasionally leads to dystrophic calcification and central luminal radiopacity. A detailed study of the clinical, histopathological and radiographic findings are important because there are multiple cysts that have similar presentations. The residual cyst seems to occur more often in the mandible. But, in the present case, it was seen within the maxillary antrum, which is rare.

The mandibular canal, teeth and the floor of maxillary sinus can be deviated due to the slow growing cyst which is correlating with the radiographic finding of the present case. The anatomy of the maxillary sinus, especially due to its proximity to the first molar, increases the possibility of post-extraction oro-antral communication (OAC). OAC can be caused by chronic dental infections also leading to subsequent radicular cyst formation. The development of cyst will interrupt the sinus mucosa resulting in faster propagation of infection within the sinus. This contributes to the reasoning for the patient not having any intraoral swelling.

Literature reveals rare instances of development of squamous cell carcinoma within the periapical cyst. Therefore, even in the absence of symptoms, treatment should be instituted for all persistent intra bony pathologies. Residual cyst can be treated by either marsupialization or enucleation depending on the size of the cyst. In the present case, due to its smaller size and intact cortical lining, enucleation was done. Usually complete bone repair occurs in lesions with intact cortex thus avoiding the need for bone grafting.

CONCLUSION

Residual cyst, being asymptomatic unless secondarily infected, has high chance of being undiagnosed. In this context, dentists should be vigilant enough at history taking, clinical examination along with adjuvant radiographs for the correct diagnosis.

References

CASE REPORT

A 47 year old male, diabetic & hypertensive on regular medications for 5 years & with past history of Tuberculosis was referred to our tertiary care centre with 2 weeks history of high grade fever with chills, cough with purulent expectoration & 5 days history of left sided catching type of chest pain & breathlessness. He was being treated as a case of pneumonia in a local hospital for a week before referring to us on worsening of symptoms. On admission to our hospital he was febrile, sick looking with PR 120/min & RR of 32/min. Clubbing was noted, Respiratory System: chest movements were decreased on left, with dull percussion note and bilateral coarse crepitations, P/A hepatomegaly. Other systems were unremarkable.

Investigations

Hb 11.5, TC-13400, DC-N89 L6 M5 ESR:56mm/hr, RBS – 221, Liver function tests - SGOT-84, SGPT-69, Alkaline Phosphatase-551, S albumin 2.4, A/G Reversal - 0.4, Bilirubin total 1.3 & Renal parameters were within normal range on admission. HIV ELISA & HBS Ag were negative.

Chest X-ray revealed left sided hydro-pneumothorax (fig 1).

In view of past history of tuberculosis & diabetic status, reactivation of tuberculosis was considered.

Intercostal tube for drainage was put on the day of admission and purulent fluid was drained suggesting pyopneumothorax & empirical antibiotics were started. Gramstain of the pleural fluid showed bipolar staining Gram negative bacilli, with typical closed safety pin appearance(fig 2). Burkholderia Pseudomallei, the causative organism was confirmed in culture. Pleural fluid & sputum for AFB were negative.

USG Abdomen showed chronic liver disease with portal hypertension & splenomegaly, no ascites. Both kidneys showed features of resolving pyelonephritis.

He was managed with intravenous doses of Cefazidime & oral chloramphenicol based on the sensitivity reports & continued on ICD drainage, insulin for controlling blood sugar and other supportive measures. ICD was later removed as the lungs expanded and there was no e/o persisting pleural collection(fig - 3). But he later developed hepato renal dysfunction & condition worsened necessitating ICU care and ventilation and finally he succumbed to the illness.

DISCUSSION

Melioidosis also known as Pseudoglanders or Whitmore’s disease is caused by Burkholderia Pseudomallei, a gram negative bacillus previously classified under the genus pseudomonas. The infection can be acquired by inoculation of environmental organisms through penetrating wounds, inhalation or the aspiration of contaminated water. The infection is more common in agricultural workers. Other predisposing factors are diabetes mellitus, alcoholism, renal disease, cirrhosis, chronic lung disease, chronic granulomatous disease,
malnutrition or immunosuppression\textsuperscript{3,4}. Melioidosis most frequently affects the lungs. Lung involvement may be the primary focus of infection or may be part of the multiorgan dissemination in patients with septicemia. Chest radiographic changes include air space consolidation, lung abscess, nodular densities often with cavitation mimicking TB and less commonly pleural effusion\textsuperscript{5}.

The diagnosis is by microscopic examination of aspirate which reveals bipolar or unevenly staining gram negative rods. It has a low specificity and sensitivity. Bacterial identification by culture is the only accepted gold standard. Resistance to aminoglycosides & older generation penicillins & cephalosporins is characteristic. Even with optimal treatment the mortality from acute severe Melioidosis is as high as 30-47\%\textsuperscript{5}. In patients who survive, there is often chronic morbidity resulting both from the disease itself and the underlying condition.

Documented reports of Melioidosis from India have been few and sporadic. Lack of awareness, low index of suspicion and inability of rural population to access health services probably contribute to the paucity of reports from Indian sub-continent.

To summarise, Melioidosis needs to be considered in any diabetic patient from endemic areas with acute fulminant septicemia or chronic granulomatous disease mimicking tuberculosis.

REFERENCES

INSTRUCTIONS TO AUTHORS

The Amrita Journal of Medicine publishes original manuscripts, meta-analyses and reviews, debates, interesting clinical cases, guidelines and consensus statements of clinical relevance and letters relating to all fields of medical and surgical specialties.

We reserve the right to copy or edit accepted manuscripts, reviews, letters and editorials. Correct proofs will be sent to the corresponding author for final approval. The editors and publishers are not responsible for the opinions expressed by contributors to the Amrita Journal of Medicine.

ABSTRACT: A Structured abstract of not more than 250 words should accompany each original article, systematic review or meta analysis. Abstracts for original contributions should be divided by individual headings into paragraph entitled: Objectives, Methods, Results and Conclusions.

Case reports should include a brief abstract describing the case history and literature review. Reviews must have an abstract included, which can be unstructured. Editorials need not include an abstract. Abbreviations or references to figures or tables should not be used in the abstract.

ORIGINAL ARTICLES: All original manuscripts should include the following:

Abstract: Structured abstract as described above.

Introduction: The specific aim(s) and a priori hypothesis need to be stated.

Methods: Must include sufficient information to judge the quality of the work, including statistical analysis and study power where appropriate.

Results: Please do not duplicate results present in the text and tables.

Discussion: Consider including a brief statement of the major findings, the meaning of the study including possible explanations and implications for clinicians, the findings in relation to other studies and consideration of important differences in results, the strengths and weaknesses of the present study, and what are the unanswered questions and future research needs.

Authors are required to include in addition to a structured abstract, a separate paragraph with 4-8 bullet points under the heading what is known on the subject and what this research adds. This information will be included as a table at the end of the article, and is to be aimed at simply explaining the study’s importance and knowledge gained from it to those who are non-experts in the particular fields.

RANDOMIZED CLINICAL TRIALS (RCTs): RCTs are encouraged and will be fast tracked in the review and publishing schedule. Randomized clinical trials must all report their data in accordance with CONSORT Consolidated Standards of Reporting Trials statement. This ensures that you provide enough information for editors, peer reviewers, and readers to see how the trial was performed and to judge whether the findings are likely to be reliable. Please provide the following, as described in the CONSORT statement:

Five extra sub headed section in the main text of the paper: Protocol, assignment, masking, participant flow and follow up analysis.

A completed checklist for editors and reviewers (not for publication) showing that you have described 21 key points in your report.

All RCTs must meet CONSORT guidelines, and include the CONSORT checklist with submission. We may choose not to use all of the sub headings in the published version of the paper for reasons of readability.

For further enquiries, please visit: https://www.consort-statement.org/

SYSTEMATIC AND CLINICAL REVIEWS: Reviews of systematic and clinical topics are encouraged for publication... Include a brief methods section on how the information was found. An abstract must be included. Inclusion of illustrations to illustrate teaching concepts is strongly encouraged. Review should be not longer than 2500 - 3000 words, excluding references, tables and illustrations.

CASE REPORTS: Selected case reports will be considered but should write to present new clinical observations, new method of treatment or interesting cases that carry a message to the reader for diagnosis or treatment of patients. Case reports must be short and focused, and consist of not more than 1500 words excluding references. An abstract should accompany the report.

EDITORIALS: Editorials must consist of not more than 1000 words excluding references.

DEBATES: They must be written by different authors for the pros and cons, and will be crisp and short in nature, consisting of not more than 1000 words excluding references.

LETTERS TO THE EDITOR: Letters to the editor will be considered if they are written on published articles or reviews. Letters must be submitted within three months of the original or review articles. Letters should be not more than 400 words. Should cite the previous article that appeared in the Amrita Journal that is being discussed, and should include not more than 5 other references.

REFERENCES: All the references should be numbered consecutively and be listed according to the order in which they are referred to in the text of the manuscript. The references should be typed doublespaced and abbreviations of journals must conform to those used in Index Medicus of the National Library of Medicine. The format should conform to the example listed below.

References to an article with 3 or less authors:


References to an article with more than 3 authors:


Reference to a book:


Reference to a chapter in a book:


TABLES: Each table should have an appropriate title, self-explanatory, and should not duplicate the text. The data should be logical and well organised so that it can be used to compare or classify related items. Table should be numbered consecutively in Arabic numerals beginning with 1.

ILLUSTRATIONS: Colour illustrations are allowed, and will not usually attract a cost to authors.

One set of original illustrations should be mailed. All the illustrations of graphs, artwork, and photographs should be numbered in consecutive Arabic numerals and submitted. A label should be affixed to the back of each illustration with the name of the senior author, manuscript title, figure number and an arrow indicating the top of the figure. The legend(s) of all figures should be typed double-spaced on a separate sheet of paper. When appropriate, arrows should be placed on photographs and drawings to indicate the portions to which reference is made. In the legends for photomicrographs, the magnification and stain utilized should be included.

RAPID COMMUNICATIONS: Rapid communications are welcomed and are guaranteed rapid decision and publication if accepted.

INVESTIGATION INVOLVING HUMAN SUBJECTS: All clinical research papers submitted which involves human or animal subjects must be accompanied by evidence of Institutional Review Board or Ethics Committee Review. The date the project was approved, when available, should be included.

MEASUREMENTS: All measurements should be in metric units.
Value Driven Leadership through

- Quality that is Infinite
- Service that Cares
- Hardwork that Endures

Making Positive Difference to lives across the globe

Alkem Laboratories Ltd.
Alkem House, Senapati Bapat Marg, Lower Parel, Mumbai - 400 013, Tel: 022 38829999