liver function tests. Patients with central line placement and hepa- 
inrin exposure were associated strongly with mild thrombocytopenia (p<0.0001). Drug therapies that were correlated with 
thrombocytopenia included Heparin, Protonix, Lasix, Ativan and 
Zoferon and antibiotics such as Vancomycin, Cephalospinors and 
Levaquin.

Conclusion Drug regimens should be evaluated daily for minimi- 
zation of adverse drug events including thrombocytopenia. Once 
the diagnosis is suspected, clinicians should identify the medication 
and/or risk factors causing secondary thrombocytopenia to assess 
the timeline of development. Co morbidity associated with thromb- 
ocytopenia was sepsis syndrome, liver disorder, alcoholism and 
atrial fibrillation. Medications commonly associated with drug- 
duced thrombocytopenia include glycoprotein IIb/IIIa inhibitors, 
cinchona alkaloids, antibiotics, anti-convulsants, and heparin. 
Thrombocytopenia generally resolved in most patients with critical 
management of the disease and discontinuation of the offending 
medication.

S75 HIGH DOSE VITAMIN D SUPPLEMENTATION IMPROVES 
EXTRAVASCULAR LUNG WATER INDEX AND IN-VIVO TREG 
AND LL37 RESPONSES POST-OESOPHAGECTOMY

doi:10.1136/thoraxjnl-2012-202678.081

1RCA Dancer, 1D Parekh, 1AR Martineau, 1GD Perkins, 1DR Thickett. University of 
Birmingham, Birmingham, UK; 2Barts the London School of Medicine and Dentistry, 
London, UK; 3Warwick Medical School, Coventry, UK

Acute Lung Injury occurs in around 25% of patients post 2 stage 
oesophagectomy. We have previously shown that levels of 25-OH 
vitamin D are low in these patients and that those patients with the 
lowest levels of vitamin D are more likely to develop Acute Lung 
Injury post-operatively. In vitro, vitamin D has been shown to pro- 
mote the differentiation of regulatory T cells (Treg) and the expres- 
sion of LL37 (cathelicidin), an antimicrobial peptide.

We have given 13 patients a one-off high dose vitamin D supple- 
ment 3–14 days prior to oesophagectomy. Numbers of circulating 
regulatory T cells were analysed both pre- and post-supplementation. 
Plasma levels of LL37 were measured by ELISA. Extravascular Lung 
Water Index (EVLWi) was measured pre-operatively, post-op- 
eratively and on the day following surgery. Changes in LL37 and EVLWi 
were compared with results from a cohort of patients (n=50) who had 
not been supplemented.

Pre-operative vitamin D levels between the two groups were sig- 
nificantly different. The proportion of CD3+CD4+ T cells which were 
CD25+CD127loFoxP3+ increased post vitamin D supple- 
mentation (median pre vitamin D=5.8, median post vitamin 
D=7.3, p=0.028). Whilst levels of LL37 decreased post-operatively 
in the cohort who had not received vitamin D, levels were main- 
tained in supplemented patients. Post-operative EVLWi measured 
lower than pre-operative values in patients receiving vitamin D 
supplementation. This contrasts with patients who did not receive 
vitamin D supplementation in whom an increase in EVLWi was seen. 
This difference persists on post-operative day 1, with a net 
increase being seen in patients who did not receive vitamin D and a 
net decrease in those who did (see table).

Conclusions A stat high dose vitamin D supplement restored vita- 
mim D levels in the week before oesophagectomy. This was associ- 
ated with elevated circulating Treg levels in vivo and an increase in 
post-operative plasma LL37 expression suggesting the vitamin D 
supplementation was biologically active.

Patients receiving vitamin D had no perioperative increase in 
extravascular lung water compared to our historical cohort suggest- 
ing that vitamin D protects against alveolar epithelial damage per- 
haps in part due to effects on circulating Treg cells and anti-microbial 
peptide production.

Abstract S75 Table 1 Effects of Vitamin D supplementation on median 
values of Vitamin D, EVLWi and LL37

<table>
<thead>
<tr>
<th>Vitamin D supplementation</th>
<th>No Vitamin D supplementation</th>
<th>p value (Mann-Whitney U test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-OH Vitamin D level</td>
<td>76 nmol/L</td>
<td>25 nmol/L</td>
</tr>
<tr>
<td>Change in EVLWi 00 post-op</td>
<td>−1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Change in EVLWi 01 post-op</td>
<td>−1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>% change in plasma LL37</td>
<td>10.9</td>
<td>−17.8</td>
</tr>
</tbody>
</table>

S76 PROTEOLYTIC CLEAVAGE OF ELAFIN BY 20S PROTEASOME 
MAY CONTRIBUTE TO INFLAMMATION IN ACUTE LUNG 
INJURY

doi:10.1136/thoraxjnl-2012-202678.082

1A Kerrin, 1S Weldon, 1A Chang, 1T Craig, 1AJ Simpson, 1C O’Kane, 1DF McAuley, 
1C Tiggart. Queen’s. 1University Belfast, Belfast, United Kingdom; 2National Institutes 
of Health, Bethesda, USA; 3University of Newcastle, Newcastle, United Kingdom

The Aim of this study was to characterise temporal changes in 
elafin concentration in patients with acute lung injury (ALI) and to 
evaluate whether a decrease in elafin levels is due to elevated prote- 
ase activity. Previous work has shown that unregulated protease 
activity can cause proteolytic cleavage of elafin, impairing the 
inmate immune function of the protein. Bronchoalveolar lavage 
fluid (BALF) was obtained from patients with ALI within 48 hours 
of onset of ALI (day 0), at day 3 and at day 7. Elafin levels were 
quantified by ELISA. Elafin susceptibility to proteolytic cleavage by 
ALI BALF was assessed by Western blot and by HPLC-Mass Spec- 
trometry. Elafin levels were found to be significantly increased at 
the onset of ALI compared to healthy volunteers and fell significa- 
tly by day 7 compared to day 0. In contrast, levels of secretory 
leukocyte protease inhibitor (SLPI) did not decrease over time. This 

decrease in elafin was due to cleavage by the 20s proteasome which 
was significantly increased in ALI BALF. Incubation of ALI BALF 
with the proteasome inhibitor epoxomicin confirmed that 20s pro- 
teasome protease activity was responsible for proteolytic cleavage of 
elafin resulting in diminished anti-elastase activity. In addition, 
free neutrophil elastase (NE) activity significantly increased in ALI 
BALF from day 0 to day 7. In conclusion, elafin concentrations 
decrease within the pulmonary compartment over the course of ALI 
as a result of proteolytic degradation. This loss of elafin may predis- 
pose, in part, to excessive inflammation in ALI.
S76 Proteolytic Cleavage of Elafin by 20S Proteasome May Contribute to Inflammation in Acute Lung Injury

A Kerrin, S Weldon, A Chang, T Craig, AJ Simpson, C O’Kane, DF McAuley and C Taggart

Thorax 2012 67: A38
doi: 10.1136/thoraxjnl-2012-202678.082