Proceedings

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October 2nd, 2015
CYTOSORB - THERAPY

REGAIN CONTROL
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2nd International CytoSorb users meeting shows improved clinical evidence

The CytoSorb therapy is safe, easy to handle and able to stabilize the overshooting immune system. These are some of the main results of the second international CytoSorb users meeting, which took place in the first days of October 2015. We thank all 110 participants from 18 countries having joined this platform that enabled users, partners and distributors to exchange their experiences with CytoSorb. Case reports, case series and interim results from several controlled pilot studies were presented and discussed. This was a clear step in CytoSorbents’ continuous strategy to reach a high level of clinical evidence.

Key findings of the symposium include:

Safety & Ease of use
- Treatment has been safe in both critical illnesses and cardiac surgery in more than 8,000 human treatments to date
- CytoSorb is easy to use without technical complications in a wide range of blood pump systems, including dialysis, continuous renal replacement therapy (CRRT with citrate or heparin anticoagulation) and cardiopulmonary bypass

Efficiency
- CytoSorb therapy has contributed to patients’ clinical stability in many ways including:
  - Improving hemodynamic stability
  - Less need for vasopressors
  - Improving metabolic parameters
- Treatments in liver failure patients have confirmed previous reports of equivalent or superior removal of hepatic toxins from blood, compared with existing liver dialysis therapies. This might be a major new potential in the treatment of viral hepatitis, alcoholic liver disease and others.

Early use
- Several CytoSorb users showed that the therapy is being used in real-world situations much earlier as an adjunctive therapy to control deadly inflammation and to treat life-threatening illnesses, rather than as a last resort therapy.
Broad indication range

- CytoSorb has already been applied successfully in a broad range of serious conditions such as severe sepsis, SIRS, septic shock, trauma, rhabdomyolysis, pancreatitis, lung injury, liver and kidney transplantation, liver failure, influenza, cardiac surgery, post-operative inflammation, toxic shock syndrome and many others (e.g. tropical diseases such as Dengue Fever and Scrub Typhus)

- Preliminary results from two completed cardiac surgery randomized controlled pilot studies from University of Hamburg-Eppendorf and Medical University of Vienna, where CytoSorb was used intra-operatively in a heart-lung machine bypass circuit, as well as data from 142 cardiac surgery patients at University of Cologne, demonstrate:
  - Therapy was well-tolerated and safe without device-related issues, including no heparin removal, no bleeding or coagulation issues, no device set-up concerns
  - Preliminary initial cytokine data show that some cytokines were removed in CytoSorb treated patients compared to control, but overall inflammation in these shorter, lower risk surgeries, was not very high
  - Now that safety has been determined, all three trial sites are interested in extending their treatment experience to complex cardiac surgery, where the risk of inflammation and related complications is much higher
  - These clinical data on safety, ease of use, and feasibility are expected to increase the confidence of the cardiac surgery community to treat a wide range of open heart surgery patients in need with CytoSorb

On the following pages, you will have the opportunity to go through all the important information of a large part of the presentations at a glance. Enjoy your reading.

Please note, that summaries are not available for all presentations given at the meeting due to ongoing publication process.
Setting the stage, Prof Gerlach gave a comprehensive overview on the mechanisms of the body’s host response, current concepts of the SIRS-MARS-CARS continuum and potential therapeutic avenues.

**Host response:**
- Mechanisms of the host response after stimulation including cytokine generation pathways and cellular activation
- Interaction of macrophages with endothelium
- Interaction of macrophages with neutrophils
- Activation of coagulation
- Leukocyte adhesion
- Vasodilation, increased permeability and capillary leakage
- Neutrophils following chemotactic gradients from intravascular space into tissues

**Inflammation vs. anti-inflammation:**
- Interaction of macrophages with lymphocytes
- SIRS-MARS-CARS continuum

**Therapeutic trials:**
- Anti-TNF antibody
  - Mortality after TNF-MAb (800 patients) in patients with septic shock improved, however patients in the absence of shock died more often with the antibody therapy
  - TNFα is vital for local host response such as formation of local abscesses via fibrin (Echternacher 1992)
- NO inhibition
  - In the study from Lopez et al (2004), the nonselective nitric oxide synthase inhibitor 546C88 increased mortality in patients with septic shock
The impact of Cytosorb on the immune response

John Kellum, Pittsburgh, USA

In his presentation Prof Kellum reviewed the most recent evidence on the association between different patterns of cytokines and outcome as well as the CytoSorb technology itself, the underlying operating principle and future perspectives.

Cytokine Patterns and Survival

- Association of different IL-6 and IL-10 levels with mortality in pneumonia and sepsis

Hemoadsorption and CytoSorb technology

- Efficient in vitro elimination of key cytokines (TNFa, IL-6, IL-10) with CytoSorb
- Efficient removal of key cytokines (TNFa, IL-6, IL-10) and improved survival with CytoSorb in rat models of sepsis

Underlying operating principle

- Basics on the regulation of neutrophil recruitment via chemokine concentrations and their modulation via hemoadsorption using CytoSorb
- Retargeting and trafficking of neutrophils with enhanced neutrophil activity and bacterial clearance at the “true” site of infection

In summary, preclinical results with CytoSorb indicate:

- Broad spectrum removal of inflammatory mediators
- Reduced circulating concentration of inflammatory mediators in patients with ‘cytokine storm’
- Reprogramming of the innate immune response through modulation of chemokine gradients
- Protection of the epithelium in the kidney and liver (presumably related to removal of DAMPs/PAMPs)
- Significant improvement in survival in high-lethality animal models
Early application of CytoSorb in septic shock - A 10 vs 10 pilot study

Zsolt Molnar, Szeged, Hungary

Prof Molnar presented interim analysis results of the first 10 patients included into the ACESS trial (Adsorption of Cytokines Early in Septic Shock)

**Inclusion criteria comprised**

- Suspected sepsis of medical etiology
- IPPV
- PCT >3 ng/ml
- Norepinephrine ≥ 10 µg/min
- PICCO confirmed normovolemia and normal Cardiac Output
- Signs of hypoperfusion: ScvO₂, lactate, dCO₂, oligo-anuria, metabolic acidosis
- Patients in the treatment group received standard of care + additional CytoSorb treatment for 24 h while the control group received standard of care only

**Endpoints were defined as follows:**

**Primary:**
- Cytokine response at different time points (interleukins, TNFa)
- PCT, CRP
- Organ dysfunction (SOFA-score) at 48 hours

**Secondary:**
- Leukocyte heterogeneity, T-cell activation/apoptosis, adhesion marker expression
- Microcirculatory changes (OPS), tonometry

**Tertiary:**
- Outcomes (LOS, mortality)

**Interim results include:**

- CytoSorb treatment resulted in a marked decline in vasopressor need and serum procalcitonin levels and was associated with a steady decrease in SOFA score during the 24 hours of treatment and the 24 hour post treatment period compared to controls
- Predicted mortality by SOFA score improved under CytoSorb treatment as did PaO₂/FiO₂ ratio and extravascular lung water
- Obviously the cardiovascular organ system profits most

**CONCLUSIONS**

- Application of CytoSorb treatment as adjuvant therapy is safe and easy to apply, improves organ function and potentially attenuates the cytokine storm
- To get the most out of CytoSorb further knowledge is needed regarding:
  - In whom to treat and on which indications?
  - For how long to treat?
  - On what basis could treatment be individualised?
CytoSorb in cardiac surgery with cardiopulmonary bypass (CPB) - A 300 patient three-arm-study

Carolyn Weber, Cologne, Germany

Dr Weber reported on the preliminary results of their large prospective pilot study in patients undergoing elective coronary artery bypass grafting (CABG).

**Inclusion criteria comprised**
- Elective, isolated CABG surgery
- Age > 18 years
- Written informed consent

**Patients were 1:1:1 allocated to 3 groups:**
- CPB with Cytosorb - termed the Cytosorb group
- CPB without Cytosorb - termed the CPB group
- CABG without CPB - termed the OPCAB group

**Endpoints were defined as follows:**
- **Primary outcome measures:**
  - Perioperative cytokine release of IL-6, IL-8 and TNF-α
- **Secondary outcome measures:**
  - Standard post-CABG outcome measures
  - Length of ventilation, ICU stay
- **Interim analysis results** show a reduction of IL-6 in the CytoSorb group while levels of TNF-α and IL-8 are comparable in patients with CPB with and without CytoSorb.
- **Hormone levels** indicate a T3 slightly lower in the CytoSorb group, T4 and cortisol levels are comparable between the groups. Therefore, Dr Weber and colleagues suggest that decreased hormone levels of cortisol, T3 and T4 should be monitored postoperatively.

**CONCLUSIONS**
- The intraoperative use of Cytosorb is safe and easy to apply
- Preliminary study results and positive first experiences with the intraoperative application of cytokine adsorption show that Cytosorb is not inferior compared to standard therapy
- These first positive trends in clinical outcome measures have to be confirmed in a larger patients’ cohort

**Fig 1: Course of IL-6 between patient groups**

**Fig 2: Course of Cortisol between patient groups**
The International CytoSorb Registry - Current status

Frank Brunkhorst, Jena, Germany

Prof Brunkhorst gave an overview on the objectives, methods and status of the currently implemented international CytoSorb registry.

**Aim of the registry**...

... is to record the use of CytoSorb under real life conditions in as many cases as possible. For this, all CytoSorb applications in different clinical settings and in all patients who are treated with this technology are planned to be included. The gathered information will be used to augment the knowledge on the clinical efficacy of the technology, to optimize the quality of its therapeutic application, and to identify and promptly handle possible complications related to the use of CytoSorb.

**Study website:**
- www.cytosorb-registry.org

**Indications include:**
- Severe sepsis / septic shock
- Cardiac surgery with CPB (cardio-pulmonary bypass)
  - Preemptive CytoSorb use in OR
  - Postoperative CytoSorb use in ICU
- Other possible indications
  - Liver failure
  - Acute pancreatitis
- Trauma
- Burns
- ARDS with ECMO
- Other indications with ECLS

**Inclusion Criteria**
- Use of CytoSorb
- Age ≥ 18 years
- Signed informed consent

**Collected data comprise**
- Baseline data
  - Demographics
  - Indication
  - Comorbidities
- Scores
  - APACHE II, SAPS II, SOFA, Euro Score (cardiac patients)

**CytoSorb Treatment:**
- Number of adsorbers and treatment duration of each adsorber
- Concomitant therapies (RRT, vasopressors, glucocorticoids)

**Outcome**
- Mortality
- Length of ICU and hospital stay

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**CLINICAL STUDIES**

APACHE II/SAPS II-predicted in-hospital mortality

- Comparison with logistic regression model
- Observed in-hospital mortality

SOFA pre

- Comparison with t-test linear/quadratic modelling
- SOFA post

 Comparison with registry data

24 h pre

... CytoSorb application(s) ...

24 h post discharge

**Fig 1: Statistical analysis of registry data**
Levels of immunosuppressive drugs during CytoSorb treatment - In-vitro Study

Steffen Mitzner, Rostock, Germany

Prof Mitzner presented experimental protocol details and first preliminary results on the planned in-vitro study investigating the drug-adsorbing capacity of miniaturized CytoSorb hemoadsorption units

- The aim of this project is to obtain data, which allow further characterization of CytoSorb interactions with clinically relevant drugs in the blood stream
- The authors will use a two compartment in-vitro hemoperfusion circuit in which the test medium will be recirculated and blood sampled pre and post cartridge at determined time points
- Retention kinetics of the following clinical relevant drugs will be investigated: Cyclosporine A, Tacrolimus, Sirolimus, Methotrexate, Voriconazol, Meropenem, Piperacillin/Tazobactam, Moxifloxacin, Ceftazidim, Cefotaxim, Cefuroxim
- Current preliminary tests to validate the set-up proved that the in-vitro hemoperfusion circulation system caused no significant additional hemolysis and that CytoSorb performed well with respect to hemocompatibility. Further tests investigated the influence of the used test medium and a potential unspecific adsorption of substances
- Tests on the impact of the test medium (fresh frozen plasma + erythrocyte concentrate vs. whole blood) on retention kinetics of meropenem clearly showed different results of plasma concentration in dependence of the test medium. Adsorption of the drug was significantly lower in whole blood when compared to the reconstituted blood analogue. This is in line with the described case report by Zoller et al. in a patient on CytoSorb therapy in whom levels of meropenem and linezolid remained well above the lower therapeutic range with no negative impact on the effectiveness of antibiotic therapy

CONCLUSIONS

- Multiple sources of error exist when performing in-vitro experiments
- Data point towards a possible overestimation of removal rates of in-vitro generated data compared to in-vivo data
Case series of CytoSorb treatments in patients with severe sepsis

Tommaso Laddomada, Zingonia, Italy

Dr Laddomada reported on his experience in 9 patients with severe sepsis, septic shock, acute liver failure and rhabdomyolysis, all treated with CytoSorb + CVVHDF

**Severe sepsis (n=2)**

In patients with severe sepsis, procalcitonin levels could be reduced markedly during and after treatment with CytoSorb, while hemodynamics represented by mean arterial pressure could be kept stable.

**Septic shock (n=5)**

In patients with septic shock, CytoSorb treatment was associated with a clear reduction of norepinephrine and dopamine dosages, stabilized hemodynamics represented by mean arterial pressure as well as reduced procalcitonin plasma levels. Of note, in later non-survivors norepinephrine dosages even increased while mean arterial pressure was hard to stabilize at a level above 65 mmHg and procalcitonin levels tended to decrease much slower.

**Liver failure (n=1)**

Experience using CytoSorb in one patient with acute drug-induced liver failure shows a marked reduction of total bilirubin (55.76 % in 48 hours) and creatinine during and after treatment.

**Rhabdomyolysis (n=1)**

Usage of CytoSorb in one patient with rhabdomyolysis associated with acute renal failure and septic syndrome showed significant reduction of serum myoglobin (-83.3%) and creatine phosphokinase levels (-52.9%) as well as clear reductions in circulating creatinine, urea nitrogen and procalcitonin concentrations going along with a substantially improved kidney function.

### Table: Patients' Information

<table>
<thead>
<tr>
<th>Patients</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Severe Sepsis</td>
<td>Severe Sepsis + Acute Pancreatitis</td>
<td>Septic Shock</td>
<td>Septic Shock</td>
<td>Septic Shock</td>
<td>Septic Shock</td>
<td>Severe Sepsis + Acute Pancreatitis</td>
<td>Acute Liver Failure</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Surgery</td>
<td>Sleeve Gastrectomy</td>
<td>Bowel Obstruction</td>
<td>Bowel Resection</td>
<td>Sleeve Gastrectomy</td>
<td>Abdominal LPS</td>
<td>Coronary PTCA</td>
<td>Abdominal LPS</td>
<td>Sleeve Gastrectomy</td>
<td></td>
</tr>
<tr>
<td>Sex/Age</td>
<td>F/78</td>
<td>F/53</td>
<td>M/65</td>
<td>M/68</td>
<td>F/30</td>
<td>M/67</td>
<td>M/66</td>
<td>M/78</td>
<td>M/43</td>
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<tr>
<td>CRRT</td>
<td>CVVHDF (Heparin)</td>
<td>CVVHDF (Heparin)</td>
<td>CVVHDF (Heparin)</td>
<td>CVVHDF (Heparin)</td>
<td>CVVHDF (Ca-CI)</td>
<td>CVVHDF (Ca-CI)</td>
<td>CVVHDF (Ca-CI)</td>
<td>CVVHDF (Heparin)</td>
<td></td>
</tr>
<tr>
<td>CytoSorb treatments</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>ICU stay (d)</td>
<td>48</td>
<td>23</td>
<td>8</td>
<td>8</td>
<td>14</td>
<td>10</td>
<td>41</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>28 d Mortality</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>D</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>ICU Mortality</td>
<td>D</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>D</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
</tbody>
</table>

A = alive, D = died

### Conclusions

- CytoSorb therapy in combination with standard antibiotic therapy can have a clinical impact on:
  - Reduction of vasopressor need
  - Hemodynamic stabilization
  - Improvement in overall patient’s condition
  - Reduction of inflammatory markers (e.g. procalcitonin)
  - Reduction of leucocytes and temperature

- The combination of CytoSorb with CRRT treatment can improve renal function and the patient’s condition earlier.
Case series in post-operative cardiac surgery patients

Karl Träger, Ulm, Germany

In this case series Prof Träger reported on 16 patients after prolonged cardiopulmonary bypass (CPB) who developed post CPB SIRS and consecutive acute kidney injury necessitating continuous renal replacement therapy (CRRT) plus additional application of CytoSorb hemoadsorption

- CytoSorb treatment was associated with a decrease in cytokine levels during the treatment course (IL-6, IL-8)
- This decrease was paralleled by an ongoing stabilization of hemodynamic parameters as demonstrated in reduction of catecholamine demand despite maintained hemodynamic targets (e.g. cardiac index, MAP, SVR, ScvO2)
- Deranged metabolic parameters (i.e. lactate, base excess) could be effectively controlled during and after the treatment period
- Treatment with the CytoSorb device was safe and well-tolerated with no device related adverse events, and easy to implement as part of the CRRT circuit
- Prof Träger further reported on other therapeutic effects of CytoSorb treatment observed during his clinical routine such as the effective removal of bilirubin, myoglobin and free hemoglobin

CONCLUSIONS

- Treatment of patients presenting severe post CPB SIRS with CytoSorb resulted in sufficient control of elevated cytokine levels and clear stabilization of deranged hemodynamic, metabolic and organ function parameters
- CytoSorb therapy seems to be a promising new treatment approach in situations with uncontrolled cytokine release resulting in hemodynamic instability
- Future application of CytoSorb treatment in cardiac surgery might be twofold:
  - Therapeutic approach in SIRS post CPB, septic shock, severe reperfusion injury, severe hemolysis
  - Preemptive approach like in acute endocarditis, local infections, complex and long lasting surgery, long CPB and X-clamp time and Re-Do procedures
CytoSorb use in a case of liver failure

Christian Siebers, Munich, Germany

In his presentation Dr Siebers outlined his experience with CytoSorb use in a case of sepsis-associated liver dysfunction

- 36 year-old male with ulcerative colitis treated with prednisolone and azathioprine
- Patient developed septic shock with multiple organ failure (ARDS, AKI, liver dysfunction) due to opportunistic infections (Pneumocystis jirovecii, Cytomegalovirus)
- Very prominent acute liver dysfunction most likely due to viral hepatitis (Cytomegalovirus) with massive hyperbilirubinemia (conjugated bilirubin > 80%), decreased synthesis parameters and reduced hepatic detoxification capacity as indication for an extracorporeal liver support system
- Patient was treated with 6 cycles of albumin-dialysis (MARS/OPAL) followed by two cycles of CytoSorb
- Treatment with MARS and OPAL did not result in a reduction of serum bilirubin
- Subsequent treatment with CytoSorb resulted in a significant reduction of serum bilirubin levels with 48% reduction during the first and 36% during the second treatment

CONCLUSIONS

- CytoSorb is able to purge bilirubin from the bloodstream
- Bilirubin removal using CytoSorb is superior as compared to albumin dialysis
- No negative side effects were observed during or after the treatment
- More data are needed to show clear cut indications, timing, intervals and dosing as well as effects on survival
Use of CytoSorb in patients with myoglobinemia

Claus Krenn, Vienna, Austria

Prof Krenn reported his experiences with the application of the Cytosorb system in 2 patients with myoglobinemia

Case 1:

- 44-year-old man with ARDS and proven infection from legionella pneumophilia developing multiple organ failure with drastically increasing creatine kinase and myoglobin sera levels in combination with reduced urine excretion
- Two sessions with CytoSorb resulted in a significant removal of myoglobin and parameters of renal and liver function improved during and after treatment
- After commencement of CytoSorb therapy, the patient’s condition improved subsequently and renal function completely recovered
- No adverse or any device-related side effects were documented during or after the treatment sessions

Case 2:

- 72-year-old female patient collapsed at home and was immobile for about 6 hours exhibiting anuria, K⁺ increase, myoglobin serum levels of 200,000 ng/ml
- Patient received 3 treatments with CytoSorb in combination with citrate dialysis
- Combined treatment could be stopped on day 3 due to adequate urine output

CONCLUSIONS

- Rhabdomyolysis represents a severe syndrome with ICU admission rates of >80% and complications like disseminated intravascular coagulopathy (DIC), hypotension/shock, and renal failure
- It seems as if CytoSorb might be a therapeutic option in RRT due to rhabdomyolysis because of its excellent myoglobin binding properties
Role of CytoSorb in optimization of vasopressors and reduction of sepsis scores: A case series

Reshma Tewari, New Delhi, India

Dr Tewari reported on a retrospective evaluation where CytoSorb was successfully used in 10 patients with septic shock.

Aim of this investigation was to analyze:
- Number of vasopressors before and after therapy
- Dosing of each vasopressor before and after therapy
- Sepsis scores (APACHE II and SOFA) before and after therapy
- Survival to discharge
- Heart rate, blood pressure, respiratory rate, temperature

Patients:
- 10 patients were included in the study (5 men, 5 women)
- All patients had APACHE II > 15, SOFA score > 12
- Treatment with standard of care (SOC) and CytoSorb as adjunctive treatment
- Antibiotics included: meropenem, teicoplanin, clarithromycin, doripenem, fluconazole, metronidazole
- IV fluids included: saline, Ringer lactate, dextrose and sodium chloride, dextrose 25% and sepsis dosed steroids (hydrocortisone)
- Vasopressors included: norepinephrine, epinephrine, vasopressin, dobutamine, dopamine

CytoSorb treatment
- Duration was 6-24 hours
- Number of CytoSorb treatments: 1 - 5

Outcome:
- 6 patients survived
- Overall decrease in APACHE II and SOFA scores after CytoSorb treatment
- Urine output increased considerably after treatment
- Normalization of lactate levels in survivors
- Reduction of vasopressors during CytoSorb therapy
  - All 10 patients initially on high-dose epinephrine:
    - 7 patients required low dose after treatment
    - 2 were completely weaned off
    - Only 1 patient continued on high dose
  - Of 9 patients on vasopressin
    - 6 were completely weaned off
    - 2 patients required low dose after treatment
    - Only 2 patients continued on high dose
  - Of 2 patients on adrenaline, both were completely weaned off
  - Of 2 patients on dobutamine, no change in dose
  - Of 3 patients on dopamine, 2 were completely weaned off and 1 required low dose after treatment

CONCLUSIONS
- CytoSorb treatment was associated with a reduction of vasopressor dosages and might help in optimization of vasopressor therapy
- CytoSorb treatment was associated with an improvement in APACHE II and SOFA score
- Hemoadsorption with CytoSorb might be beneficial in patients with septic shock and/or multiple organ failure and help reduce mortality
### Table 1: Characteristics of Patients Treated with CytoSorb Therapy

<table>
<thead>
<tr>
<th>Pt No</th>
<th>Age, Sex</th>
<th>Diagnosis</th>
<th>No. of ECAI Used</th>
<th>APACHE 2 Before Therapy</th>
<th>APACHE 2 After Therapy</th>
<th>SOFA Before Therapy</th>
<th>SOFA After Therapy</th>
<th>Serum Lactate Before Therapy</th>
<th>Serum Lactate After Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35, M</td>
<td>Empysematous pyelonephritis with horseshoe kidney + septic shock and MODS</td>
<td>3</td>
<td>23</td>
<td>13</td>
<td>16</td>
<td>11</td>
<td>2.2</td>
<td>2.4</td>
<td>Survived</td>
</tr>
<tr>
<td>2</td>
<td>53, F</td>
<td>Acute pyelonephritis with septic shock and MODS</td>
<td>2</td>
<td>24</td>
<td>11</td>
<td>17</td>
<td>10</td>
<td>2.7</td>
<td>1.7</td>
<td>Survived</td>
</tr>
<tr>
<td>3</td>
<td>69, M</td>
<td>Infected diabetic foot, MRSA septicemia, septic shock with MODS</td>
<td>5</td>
<td>29</td>
<td>29</td>
<td>17</td>
<td>15</td>
<td>3.3</td>
<td>1.4</td>
<td>Death</td>
</tr>
<tr>
<td>4</td>
<td>46, M</td>
<td>Acute intestinal obstruction with perforation peritonitis (operated) with septic shock and MODS</td>
<td>3</td>
<td>26</td>
<td>12</td>
<td>12</td>
<td>9</td>
<td>4.2</td>
<td>1.5</td>
<td>Survived</td>
</tr>
<tr>
<td>5</td>
<td>75, F</td>
<td>Bronchial asthma with hospital acquired pneumonia, primary ARDS and septic shock</td>
<td>3</td>
<td>17</td>
<td>11</td>
<td>16</td>
<td>9</td>
<td>6.0</td>
<td>1.6</td>
<td>Survived</td>
</tr>
<tr>
<td>6</td>
<td>23, F</td>
<td>Fever with thrombocytopenia (croup typhus) with septic shock and MODS in post partum patient</td>
<td>3</td>
<td>15</td>
<td>10</td>
<td>10</td>
<td>7</td>
<td>1.8</td>
<td>1.4</td>
<td>Survived</td>
</tr>
<tr>
<td>7</td>
<td>34, F</td>
<td>Ca tongue (treated) with pneumonia septic shock and MODS</td>
<td>3</td>
<td>28</td>
<td>28</td>
<td>16</td>
<td>12</td>
<td>5.2</td>
<td>2.4</td>
<td>Death</td>
</tr>
<tr>
<td>8</td>
<td>51, M</td>
<td>Burst appendix with perforation with septic shock and MODS</td>
<td>1</td>
<td>30</td>
<td>24</td>
<td>16</td>
<td>12</td>
<td>2.3</td>
<td>2.2</td>
<td>Death</td>
</tr>
<tr>
<td>9</td>
<td>42, M</td>
<td>Acute necrotising pancreatitis with MODS</td>
<td>5</td>
<td>23</td>
<td>10</td>
<td>15</td>
<td>14</td>
<td>4.2</td>
<td>2.2</td>
<td>Death</td>
</tr>
<tr>
<td>10</td>
<td>38, F</td>
<td>Urosepsis with septic shock and MODS, morbid obesity, hypothyroidism, diabetes mellitus</td>
<td>3</td>
<td>30</td>
<td>7</td>
<td>15</td>
<td>4</td>
<td>4.4</td>
<td>0.7</td>
<td>Survived</td>
</tr>
</tbody>
</table>

#### Figure 1a: APACHE 2 Scores

![APACHE 2 Scores](image1a)

#### Figure 1b: SOFA Scores

![SOFA Scores](image1b)

#### Figure 2: Norepinephrine Dose in Patients Before and After Therapy

![Norepinephrine Dose](image2)
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SIRS and Sepsis

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