The Therapeutic Efficacy of Adjunct Therapeutic Plasma Exchange for Septic Shock with Multiple Organ Failure: A Single Center Retrospective Review

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**Background:** Sepsis remains a common condition with high mortality when multiple organ failure develops. The evidence behind therapeutic plasma exchange in this setting is promising but inconclusive. Our study aims to evaluate the efficacy of adjunct therapeutic plasma exchange for septic shock with multiple organ failure compared to standard therapy alone.

**Methods:** A retrospective, observational chart review was performed, evaluating outcomes of patients with catecholamine resistant septic shock and multiple organ failure in Intensive care units at a tertiary care hospital in Winston Salem, North Carolina from August 2015- March 2019. Adult patients with catecholamine resistant septic shock (≥ 2 vasopressors) and evidence of multiple organ failure (lactic acid >2, platelets < 200, and pH < 7.3) were included. Patients who received adjunct TPE were identified and compared to patients who received standard care alone. A propensity score using APACHE II score, SOFA score, and age was used to match patients, resulting in 40 patients in each arm.

**Results:** Mean baseline APACHE II and SOFA scores were 32.5 and 14.3 in TPE patients versus 32.7 and 13.8 in control patients. The 28-day mortality rate was 40% in the TPE group versus 62.5% in the standard care group (p=0.07). The subgroup of patients with pneumonia as the primary diagnosis had a 28-day mortality rate of 47.8% with adjunct TPE compared 81.3% with standard care alone (p = 0.05). Improvements in baseline SOFA scores at 48 hours were greater in the TPE group compared to standard care alone (p= 0.001). Patients receiving adjunct TPE had longer ICU and hospital lengths of stay.

**Conclusions:** Our retrospective, observational study in adult patients with septic shock and multiple organ failure showed the most improvement with adjunct TPE in patients with pneumonia as the primary source of sepsis. Hemodynamics and organ dysfunction improved with TPE regardless of source. A prospective, randomized clinical trial is needed to investigate TPE in adult sepsis and to identify subgroups that are most likely to benefit.

**Key words for indexing**
Septic shock, sepsis, multiple organ failure, MODS, plasma exchange, plasmapheresis
Background

Sepsis remains a common condition accounting for nearly 1.3 million U.S. hospitalizations including 25% of ICU admissions annually (1). Despite an overall improvement with early goal directed therapy, septic shock remains the most common cause of death in non-coronary intensive care units with mortality rates approaching 70% when multiple organ failure develops (2).

Investigators have gained an understanding of sepsis as a complex interaction of cytokine storm, systemic inflammation, endothelial dysfunction, capillary leak, and pathologic hemostasis similar to TTP (3, 4, 5, 6, 7). When fulminant, the end result is disseminated microcirculatory thrombosis resulting in tissue hypoxia, multiple organ failure, and death (8). Many innovative therapies have targeted specific components of this pathway but have largely failed to improve outcomes in clinical trials. Steroids, activated protein C, plasma filtration, ascorbic acid, polymyxin B hemoperfusion, and thrombomodulin have all been investigated without success (9, 10, 11, 12, 13, 14, 15). While each of these therapies may benefit individual patients with sepsis, the heterogeneity of sepsis syndrome makes it unlikely that any intervention targeting a single component of the pathway would be successful when utilized universally.

Therapeutic plasma exchange (TPE) is unique in that it offers a non-selective treatment. By filtering inflammatory cytokines, stabilizing endothelial wall membranes, and re-setting the hemostatic milieu, TPE may help restore normal physiologic pathways and potentially improve tissue perfusion, organ recovery, and survival (3, 7, 16, 17, 18).

Case reports, case series, meta-analyses, and a single adult prospective, randomized clinical trial over the past 40 years have yielded inconsistent results on the efficacy of TPE for sepsis (16, 19, 20, 21, 22). Based on the available data, the American Society for Apheresis (ASFA) offers a Category III, 2B recommendation for the use of TPE for sepsis with multiple organ failure, allowing for individualized use on a case to case basis (2, 23).
Using this recommendation as a guide, our institution has utilized TPE in select cases of catecholamine refractory septic shock with multiple organ failure. By incorporating markers of poor outcome (24, 25, 26, 27, 28, 29, 30, 31) as guidelines for consideration for TPE, we have sought to identify those patients with the clinical phenotype unlikely to survive with standard therapy alone (Table 1). In our retrospective, observational study we analyzed data from the electronic medical record and compared outcomes in patients meeting these criteria who received adjunct TPE to propensity matched patients meeting the same criteria who received standard therapy alone.

**METHODS**

**Study Design**

This retrospective, observational study on the effect of TPE as adjunct therapy for septic shock with multiple organ failure was conducted by reviewing the electronic medical records of adult patients, 18 years old and older, treated for septic shock at Novant Health Forsyth Medical Center from August 2015 to March 2019. The study was approved by the Institutional Review Board at Novant Health Forsyth Medical Center. Informed consent was not required as the study reports observational, retrospective data obtained from chart review.

**Study Subjects**

The “intervention group” patients were identified via the electronic medical record to include patients with the primary diagnosis of septic shock and a procedure code for apheresis during the specified time frame. Forty patients were identified who received at least one TPE treatment and met the criteria in Table 1.

The “control group” patients were identified using report filters meeting our institutional criteria for consideration of TPE in patients with sepsis within the same time frame as the intervention group. Patients with the primary diagnosis of shock plus each of the following flags were screened: 2 or more vasopressors, lactic acid > 2 mmol/L, platelet nadir < 200 x 10³/uL, and pH < 7.3. A total of 160 patients were identified. Two study researchers independently screened each patient for the criteria in Table 1, excluding 117 patients. Data was collected on the remaining 43 patients and propensity matching was performed as discussed below.
**Intervention**

All patients in both groups were treated for sepsis at the discretion of the attending intensivist. While a sepsis treatment protocol was available, individualized treatment occurred in both groups based on physician preferences (e.g., adjunct steroids, ascorbic acid, thiamine).

All patients receiving adjunct TPE underwent treatment with 1:1 plasma replacement for 120% of the patient’s plasma volume. The number of treatments was not standardized and varied by case, determined by the attending physician, and supported by ASFA recommendations. Treatments were prescribed daily until the treatment team felt that the patient had maximized benefit or demonstrated a lack of clinical response. While each provider may have used an objective measure to guide length of treatment, no standardized or universal guidelines were utilized. Forty two percent of patients received a single treatment and 92.5% had 5 or less treatments.

**Definition of Variables**

The primary study outcome was all cause 28-day mortality. Secondary outcomes included hospital mortality, new need for renal replacement therapy (RRT) during admission and at discharge, mortality associated with new need for renal replacement therapy, ICU length of stay, hospital length of stay, and change in SOFA and Cardiac SOFA scores 48 hours after identification in patients surviving at least 48 hours. "Time zero" for the intervention group was defined as the documented date and time of completion of the first plasma exchange treatment. "Time zero" for controls was defined as the first recorded vital signs in the Intensive Care Unit. Patients were propensity matched using APACHE II and SOFA scores on ICU admission while all primary and secondary outcomes were measured and calculated based on “time zero” defined above.

Patient charts were reviewed through hospital discharge or death. For patients discharged prior to day 28, mortality was assessed by searching subsequent admissions and online obituaries. Values used for calculation of the 48 hour SOFA scores were the most recent vital signs and labs to the exact hour of inclusion. Patients who expired prior to 48 hours were excluded from the SOFA analyses.

**Computation and Matching of propensity score**
Patients in the intervention and control groups were propensity score matched using age and ICU admission APACHE II and SOFA scores.

**Patient Characteristics**

The study included 80 patients with 40 in each arm. Baseline patient demographics are summarized in Table 2. Patients in both arms had a high mortality risk with similar baseline APACHE II and SOFA scores. While baseline SOFA scores were similar, patients in the intervention arm had higher SOFA scores at “time zero.” All patients presented with septic shock requiring at least two vasopressors and a majority required new start of renal replacement therapy. Patients in the two arms differed by ventilator requirement at inclusion with patients in the intervention group requiring ventilator support more frequently than those in the control group (p< 0.001). We noted no other differences in baseline characteristics though mean age was numerically higher in the control group (p=.08).

**Statistical Analyses**

Statistical analysis was performed by an independent researcher, using XLSTAT by Addinsoft (Windows version) and Xrealstats from [http://www.real-statistics.com/](http://www.real-statistics.com/) (Windows version) add-ins for Microsoft Excel. Univariate comparisons of baseline characteristics were made by unpaired t-test for continuous variables and Fisher's exact test for categorical variables. Chi-square test was used to test differences in infectious origin between the two groups. Changes in APACHE 2 and SOFA from baseline within a group were assessed by paired t-test. Fisher’s exact test was used to test differences in survival between groups. Multiple logistic regression was used to assess the effect of the treatment variable and SOFA scores. Data is presented as mean +/- standard deviation.

**Results**

Outcomes are summarized in Figure 1 and Table 3. The overall 28-day mortality rate was 40% in the intervention group versus 62.5% in the control group (p=0.07) (Figure 1). Hospital mortality was 42.5% with TPE compared to 65% with standard care alone (p=0.07). Table 4 reports mortality by primary site of infection and isolated pathogen(s). The subgroup of patients with pneumonia as the primary site who received adjunct TPE demonstrated improvement in 28-day
mortality compared to patients with pneumonia who received standard care alone (47.8% vs. 81.3%, p = 0.05). Additionally, changes in SOFA scores at 48 hours showed improvement from baseline in the TPE group compared to standard care alone (p=0.001). The mortality associated with new need for RRT was 48% in those receiving TPE compared to 78% in those receiving standard of care alone (p=0.06). There was no difference in need for RRT at discharge in survivors. Both ICU and hospital lengths of stay were longer in patients receiving TPE.

**DISCUSSION**

The efficacy of TPE in the treatment of sepsis is proposed to be due to its action at multiple levels of a complex pathway of multiple defense systems. An initial “cytokine storm” leads to global inflammation and disruption of the endothelium leading to vasodilation, capillary leak, and activation of the coagulation cascade (3, 4, 7, 16, 32). Attempts to slow this response have been an elusive target of therapy. Steroids and other anti-inflammatory agents have been investigated but have failed to show consistent benefit. While plasma filtration has been demonstrated to lower circulating levels of many of these mediators in both experimental and clinical studies (21, 32, 33, 34, 35), trials investigating survival with various forms of hemofiltration and cytokine binding have yielded inconsistent results (20, 21, 33, 35). Outcomes with adjunct steroids in sepsis remain inconsistent, and controversial. Targeted treatment for sepsis appears to require more than rebalancing inflammatory mediators.

TPE may offer further benefit by offsetting the effects of endothelial activation. Far from a passive conduit, the endothelium plays a major role in the sepsis pathway and has become a common target for therapy. Hypotension results not only from inflammatory vasodilation, but also from increased vascular permeability resulting from endothelial glycocalyx injury (3, 4, 5, 6, 32). Studies in septic and hemorrhagic shock have identified circulating markers of glycocalyx injury which have been associated with electron microscopic changes and increased mortality (5, 32, 36). Resuscitation with FFP has shown restoration of endothelial integrity as assessed by circulating levels of glycocalyx injury and microscopic appearance (32, 36). In cases of massive hemorrhage, mortality has improved with a transfusion strategy including FFP, (36) and we hypothesize that the hemodynamic
improvement as evidenced by improvement in cardiac SOFA scores in our patients using plasma as the replacement fluid is partially explained by this.

Another major clinical implication of endothelial activation is pathologic activation of the clotting cascade leading to a hyper-coagulable microcirculatory state. Decreased ADAMTS-13 activity and increased ADAMTS-13 inhibitors are prevalent leading to increased thrombogenic ultra-large von Willebrand factor (UL vWF) multimers resulting in diffuse microcirculatory platelet thrombosis. Increased plasminogen activator inhibitor (PAI-1) activity leads to decreased fibrinolysis and disseminated fibrin rich microcirculatory clotting. The net result is a non-consumptive, platelet and fibrin rich microcirculatory thrombotic state with non-specific coagulation findings, often distinct from DIC, TTP, and HUS (3, 7, 16, 37, 38). Activated Protein C and thrombomodulin are among therapies that have been investigated to reverse this process, without success (9, 10, 15). Plasma exchange is unique in that it addresses both the pathologic coagulation cascade and platelet dysfunction by removing the UL vWF multimers, ADAMTS-13 inhibitors, and PAI-1 while restoring ADAMTS-13 activity (7). Stegmayr and colleagues reported improved survival in patients receiving rescue plasma exchange in cases of shock with progressive acute DIC and multiple organ dysfunction syndrome. Patients in this retrospective review demonstrated an 82% survival compared to historically observed survival of < 20% in similar patient population (38). By restoring the hemostatic pathway, oxygen delivery and utilization appear to be restored, resulting in lactate clearance, improved organ function, and overall clinical improvement. It is this theory that is the basis of some providers in our practice to continue daily TPE through lactic acid clearance. While no specific laboratory values exist to reflect the microcirculation and tissue perfusion, lactate clearance with hemodynamic improvement serve as surrogates. Importantly, while the pathology of this process involves platelet dysfunction, it is unlikely that any absolute platelet value is associated with poor outcome or predictive of responsiveness to TPE. Furthermore, we believe that the pathophysiologic process is often well underway before absolute thrombocytopenia develops. As with any treatment for sepsis, early treatment is necessary for improved outcomes, and delaying treatment while awaiting an absolute value is likely to lead to worse response. Similarly, it is likely that no absolute platelet value is reflective of clinical response to treatment (with TPE or any other
intervention). For this reason, we did not require an absolute platelet count as criteria for treatment with TPE and did not monitor platelet values as a determinant of clinical responsiveness.

Our study has limitations beyond those common to retrospective, single center studies. First, the difference in “time zero” in the two arms potentially introduces bias. In a retrospective study, the intervention is easily defined, but since the control group did not receive treatment, we had to define an arbitrary “time zero.” ”Time zero” for the intervention group was defined as the time of documentation of the initial TPE completion (regardless of ICU admission date and time). For control patients, ”time zero” was defined as the time of the first recorded ICU vital signs. To limit bias, patients were propensity matched based on age, APACHE II score, and SOFA score on ICU admission. If anything, we believe this bias may favor the control group since patients who received TPE were potentially in the ICU longer before “time zero” as compared to the control group.

Furthermore, SOFA scores calculated at “time zero” were higher in the intervention group compared to the control group, predicting a higher mortality in this group (Table 2), (p = 0.001).

Second, while our institution does have a sepsis protocol, individual variation exists among providers. This variability may be unlikely to influence outcomes, as multiple trials have demonstrated no difference in mortality using various resuscitation strategies (39, 40). In addition, since both the control group and intervention group were cared for by the same providers during the same time frame, variation between groups should be similar.

The decision to utilize TPE was provider dependent and involved an interdisciplinary approach between the attending intensivist and nephrologist. Guidelines were developed and agreed upon (Table 1), but screening did not occur and TPE was not considered unless the attending physician felt that it might be beneficial. Therefore, some patients that may have been candidates for TPE were likely not considered for treatment and likely fell into our control group. Additionally, meeting the suggested criteria did not guarantee that TPE would be provided if the intensivist and nephrologist did not agree that the treatment was indicated. A large majority of TPE for sepsis was prescribed by a small number of providers within both groups. This bias cannot be eliminated from a retrospective trial where providing the intervention is not randomized, but using clearly defined, objective inclusion and exclusion requirements allows for matching and statistical comparison.
Another limitation of our trial was the lack of uniformity in duration of treatment in the intervention group. While most patients received between one and five treatments (92.5%), no objective guidelines were established at our facility to standardize the duration of TPE. Efficacy and duration were most often guided by hemodynamic response and lactate clearance. Many providers stopped TPE after vasopressor needs resolved, while others preferred a standing order for 3 or 5 treatments. Of the three patients receiving more than 5 treatments, two had prolonged admissions and received two separate courses of TPE, with different inciting infections. The third received treatment until normalization of platelets based on provider preference. The lack of consistent duration of treatment within the intervention arm raises the question of whether the number of treatments is impactful on clinical outcome. Further investigations are needed to identify objective measures to guide treatment.

The small sample size further limits interpretation of the results. The observed 22.5% absolute reduction in mortality did not reach statistical significance but strongly suggests clinical benefit. In addition, patients receiving TPE in our trial had improved SOFA and cardiac SOFA scores at 48 hours. While historically predicted mortality based on admission SOFA scores is likely overstated, trial data supports that trends in SOFA scores may be useful predictors of outcomes (41, 42, 43). Fortenberry and colleagues recently reported improvement in organ dysfunction (as reflected by changes in PELOD scores from baseline) and 28-day mortality in septic pediatric patients meeting similar criteria who received TPE (37). The information gained from these trials may help with development and design of a randomized trial, adequately powered to prospectively evaluate the clinical efficacy of TPE for sepsis.

In our trial the subgroup of patients with pneumonia showed the greatest benefit with adjunct TPE and multiple theories may help explain these results. The improvement in endothelial function may decrease capillary leak and decrease the likelihood of worsening non-cardiogenic pulmonary edema/acute respiratory distress syndrome (ARDS). The observed improvement in hemodynamics (as reflected by improved cardiac SOFA scores) may lead to improved volume status which has been associated with improved mortality in critical illness, particularly in respiratory failure (44, 45, 46, 47). Our study design did not allow for accurate fluid balance assessment due to
the retrospective nature of the study and the inability to confirm accurate inputs and outputs. A prospective trial could be designed to track daily volume status. Inclusion criteria incorporating lung injury scores may also help to identify patients most likely to benefit from TPE.

ICU and hospital lengths of stay were longer in the intervention arm but may not be reflective of true morbidity or cost as the standard care group had more early deaths. A larger sample size and longer follow-up interval are needed to assess the true impact on length of stay. More patients receiving TPE required new start renal replacement therapy, but the mortality associated with this treatment was clinically less in the TPE group (48% vs 78%, p = 0.06). There was no difference in new need for RRT at discharge in survivors in our trial. A larger sample size and long-term follow-up are also necessary to truly assess the effect of TPE on this important secondary outcome.

Lastly, the retrospective design of the trial was not optimal for detecting adverse events associated with TPE. All patients in our study were hemodynamically unstable. It is impossible to attribute hemodynamic instability to TPE or to exclude TPE as a contributing factor based on our review of documentation. There were no recorded complications attributed to temporary dialysis catheter placement (which was required for TPE). There may have been other potential adverse events that were unable to be tracked or identified. Knaup and colleagues recently performed a feasibility and safety trial in a similar patient population and reported no adverse events (32). The potential adverse effects of TPE are well documented (48), but a prospective, randomized trial would help identify potential adverse events associated with TPE specifically in the adult sepsis population.

The results of our trial are limited by design and the results cannot be used to change existing standards for the treatment of sepsis. Nevertheless, the results are very encouraging, and information gained from our experience should be used to assist with design of a multicenter, randomized, controlled trial to better assess this potentially useful intervention.

CONCLUSIONS

TPE has been proposed as a therapeutic option for sepsis but inadequate trial data exists to support or refute its efficacy in this patient population. Our results add to the body of evidence that support TPE in a subset of adult patients with sepsis but cannot be used to change practice.
standards. A multicenter, prospective, randomized controlled trial is needed to investigate the efficacy of TPE in septic shock with multiple organ failure.

**List of abbreviations**

ADAMTS-13: von Willebrand factor-cleaving protease; APACHE: Acute Physiology and Chronic Health Evaluation; ARDS: Acute Respiratory Distress Syndrome; ASFA: American Society for Apheresis; DIC: Disseminated Intravascular Coagulation; FFP: Fresh Frozen Plasma; HUS: Hemolytic Uremic Syndrome; ICU: Intensive Care Unit; PA-1: Plasminogen Activator Inhibitor-1; RCT: Randomized Controlled Trial; RRT: Renal Replacement Therapy; SOFA: Sequential Organ Failure Assessment; TPE: Therapeutic Plasma Exchange; TTP: Thrombotic Thrombocytopenic Purpura; ULvWf: Ultra-large von Willebrand Factor.

**Declarations**

**Ethics approval and consent to participate**

The Institutional Review Board and Novant Health Forsyth Medical Center approved the study (ID: 18-1041). Written informed consent was not required as the study reports observational, retrospective data obtained from chart review. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

**Consent for publication**

Not applicable

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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Author’s contributions

PK, JH, and AA collected clinical data from the EMR. PK, JH, AW, and LS interpreted data and wrote the manuscript. AA proofread the manuscript. SF calculated statistics and proofread the manuscript.

All authors read and approved the final manuscript.

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| **Table 1.** Study Population |
|-----------------------------|
| **Inclusion Criteria:** 1, 2, 3, and 4 plus A, B, OR C |
| 1. New known or suspected infection (with chance for source control if applicable) | A. Lactic acidosis and/or failure of lactic acid clearance |
| 2. Multiorgan failure (≥2 organs failing) | B. Worsening acidosis despite adequate fluid resuscitation and/or dialysis |
| 3. Two or more pressors, rapidly rising pressor needs, and/or inability to wean pressors⁰ | C. Mottling skin appearance despite appropriate resuscitation |
| 4. Acute drop in platelet count (+/- thrombocytopenia) | |
| **Exclusion Criteria:** |
| Cardiogenic shock | Active metastatic malignancy |
| Hemorrhagic shock | Limitations to aggressive care |
| Ischemic colitis without surgery | Planned withdrawal of care |
| Cardiac arrest at presentation | |

⁰Hypotension must be due to sepsis
### Table 2. Baseline characteristics of 80 matched patients

| Variable                        | TPE (n=40) | Standard Care (n=40) | p   |
|---------------------------------|------------|----------------------|-----|
| Gender M/F                      | 24/16      | 19/21                | 0.37|
| Mean age (years)                | 57.6 +/-13.4 | 63.6 +/- 16.2       | 0.08|
| Septic shock<sup>a</sup>        | 40 (100%)  | 40 (100%)            | 1   |
| Ventilator requirement          | 40 (100%)  | 29 (72.5%)           | <0.001|
| ESRD                            | 3 (7.5%)   | 3 (7.5%)             | 1   |
| Mean APACHE II                  | 32.5+/-6.0 | 32.7+/-7.0           | 0.89|
| Mean SOFA on admission          | 14.3+/-3.6 | 13.8+/-2.3           | 0.48|
| Mean SOFA at “time zero”<sup>b</sup> | 15.8+/-2.9 | 13.8+/-2.3           | 0.001|

#### Primary Site of Infection

| Site               | TPE | Standard Care | p   |
|--------------------|-----|---------------|-----|
| Pneumonia          | 23  | 16            | 0.22|
| GU                 | 6   | 8             |     |
| GI/biliary         | 6   | 6             |     |
| Skin/soft tissue   | 1   | 4             |     |
| Endocarditis       | 3   | 1             |     |
| Primary bacteremia | 1   | 5             |     |

<sup>a</sup>all patients included were on at least two vasopressors per selection criteria

<sup>b</sup>TPE “time zero” is time of first TPE completion; Standard Care “time zero” is hour of first recorded vital signs in ICU
### Table 3. Primary and secondary outcomes

| Outcome                                      | TPE (n=40)          | Standard Care (n=40) | p    |
|----------------------------------------------|---------------------|----------------------|------|
| **28 day mortality**                        |                     |                      |      |
| Total study population                       | 16 (40%)            | 25 (62.5%)           | 0.07 |
| Pneumonia group                              | 11/23 (47.8%)       | 13/16 (81.3%)        | 0.05 |
| Other groups                                 | 5/17 (29.4%)        | 12/24 (50%)          | 0.22 |
| Hospital mortality                           | 17 (42.5%)          | 26 (65%)             | 0.07 |
| Baseline SOFA in 48h survivors<sup>a</sup>   | 15.7 +/- 3.0        | 13.2 +/- 1.9         | <0.001|
| SOFA at 48 hours<sup>a</sup>                 | 12.6 +/- 4.5        | 12.6 +/- 3.6         | 0.96 |
| Change in SOFA<sup>a</sup>                   | 3.1 +/- 2.6         | 0.5 +/- 3.4          | 0.001|
| Baseline Cardiac SOFA in 48h survivors<sup>a</sup> | 4.0 +/- 0.17       | 3.7 +/- 0.9          | 0.17 |
| Cardiac Sofa at 48 hours<sup>a</sup>         | 1.5 +/- 1.54        | 2.7 +/- 1.6          | 0.003|
| Change in Cards SOFA<sup>a</sup>             | 2.47 +/- 1.52       | 1.0 +/- 1.5          | <0.001|
| New need for RRT during admission<sup>b</sup> | 25 (67.6%)          | 18 (48.6%)           | 0.16 |
| Mortality associated with new RRT            | 12 (48%)            | 14 (78%)             | 0.06 |
| New need for RRT at d/c in survivors         | 4 (30.8%)           | 1 (25%)              | 1    |
| ICU Length of stay<sup>c</sup>               | 16.6 +/- 15.8       | 9.1 +/- 9.1          | n/a  |
| Hospital Length of stay<sup>c</sup>          | 24.6 +/- 22.4       | 14.1 +/- 13.9        | n/a  |

<sup>a</sup>For patients who survived at least 48 hours. (n=34 for TPE arm and n=31 for standard arm)

<sup>b</sup>3 ESRD in each group

<sup>c</sup>Note that the standard care arm experienced more 28-day mortality
### Table 4. Mortality associated with infection site and pathogen

| Site of Infection        | Overall   | TPE        | No TPE     | p        |
|--------------------------|-----------|------------|------------|----------|
|                          | 24/39 (61.5%) | 11/23 (47.8%) | 13/16 (81.3%) | 0.05     |
| Pneumonia                | 2/14 (14.3%)  | 0/6 (0%)   | 2/8 (25%)  |          |
| GU/biliary               | 6/12 (50%)   | 2/6 (33.3%) | 4/6 (66.7%) |          |
| Skin/soft tissue         | 1/5 (20%)    | 1/1 (100%) | 0/4 (0%)   |          |
| Endocarditis             | 2/4 (50%)    | 1/3 (33.3%) | 1/1 (100%) |          |
| Primary bacteremia       | 6/6 (100%)   | 1/1 (100%) | 5/5 (100%) |          |

| Organism Cultured        | Overall   | TPE        | No TPE     | p        |
|--------------------------|-----------|------------|------------|----------|
| MRSA                     | 2/5 (40%)  | 1/3 (33.3%) | 1/2 (50%)  |          |
| Streptococcus            | 3/5 (60%)  | 1/2 (50%)  | 2/3 (66.7%) |          |
| Ecoli                    | 6/11 (54.5%) | 2/5 (40%) | 4/6 (66.7%) |          |
| Pseudomonas               | 2/2 (100%) | 1/1 (100%) | 1/1 (100%) |          |
| Enterococcus             | 1/2 (50%)  | 0/1 (0%)  | 1/1 (100%) |          |
| Enterobacter             | 3/8 (37.5%) | 2/3 (66.7%) | 1/5 (20%) |          |
| Klebsiella               | 2/6 (33.3%) | 0/4 (0%)  | 2/2 (100%) |          |
| Influenza                | 2/3 (66.7%) | 0/1 (0%)  | 2/2 (100%) |          |
| Serratia                 | 1/1 (100%) | 1/1 (100%) | n/a        |          |
| Candida                  | 1/1 (100%) | n/a        | 1/1 (100%) |          |
| Cdiff                    | 1/2 (50%)  | n/a        | 1/2 (50%)  |          |
| Salmonella               | 0/1 (0%)   | n/a        | 0/1 (0%)   |          |
| Culture negative         | 3/15 (20%) | 1/10 (10%) | 2/5 (40%)  |          |
| Polymicrobial\(^a\)      | 14/18 (77.8%) | 7/9 (77.8%) | 7/9 (77.8%) |          |

\(^a\)Note: pathogens in polymicrobial infections are not specified
**Figure 1.** 28-day survival in patients with septic shock and multiple organ failure receiving TPE in addition to standard therapy (*solid line*) or standard therapy alone (*dotted line*).