A Multivariate Regression Model Of Mortality Associated With Fungal Infections In Pediatric Burn Patients

F. Emdad, L. K. Branski, C. D. Djukom, CC. Finnerty, D.N. Herndon, and M.G. Jeschke

Department of Surgery, The University of Texas Medical Branch, Galveston, TX

1. INTRODUCTION

Burn patients are cited among the highest-risk groups for invasive fungal infections. Infectious complications are common cause of morbidity and mortality in burn patients. Severely burned patients are ideal immunosuppressed host, fungal infections in these persons are difficult to prevent or eradicate. Recent publications have shown the clinical importance of adequately managing fungal infection due to increased mortality. The premortem diagnosis of fungal infection to allow appropriate treatment occurs in only 15% to 40%, this low rate as well as the mortality rate for burn patients with fungal infection of more than 90% calls for a special attention to fungal infection. A recent multi-center study of fifteen burn units over two years showed a wide range of fungal infection rates (0.7 – 24%) and highest mortality for infections with Aspergillus. Candida was the most frequently cultured fungal organism, although associated with the lowest mortality rate (Ballard J et al. J Burn Care Res 2008;29(1):213-221 ). The purpose of our study is to determine the incidence of fungal infections and mortality associated with fungal infection in pediatric burn population for a ten-year study. We hypothesized that, when the number of fungus involved increase, the incidence of death increase.

2. OBJECTIVES

We wanted to predict in this study, the impact that each fungal infection and/or a concomitant fungal infection has on mortality. Therefore, we developed a prediction model for mortality in a pediatric burn population with fungal infections. We developed a model of multivariate analysis to predict the survival when one infection , 2 and 3 infections are present. We found that the predicted mortality rate varies, and depends more on the type of fungus than the number of fungus involved.

3. HYPOTHESIS

We hypothesized that infections with different fungal strains – separately or combined – influence patient mortality, and when the number of fungus involved increase, the incidence of death increase.

4. METHODS

This retrospective study was performed in a consecutive patient cohort of 10 years at a single specialized pediatric burn center. Of the 3,645 patients admitted between January 1998 and December 2008, three hundred six patients with a mean age of 7±5 years, a mean total body surface area (TBSA) burn of 55±22%, and a mean full-thickness burn size of 43±27% were included in the analysis. These patients were diagnosed with at least one of the following six fungal strains during their acute hospital stay: Candida albicans (CanA), other Candida species (Can), Aspergillus species (Asp), Curvularia species (Cur), Fusarium species (Fus), and/or Rhizomucor (Rhi). We investigated and modeled the mortality rate and applied logistic multiple regression assuming mortality as the dependent variable and the fungal infections and the total burn size (TBSA)
as the independent variables. We used the mortality model to calculate the probability to survive. We simulated 462 patients with different TBSA ranged from zero to a hundred and compared the mortality curves when patients have one infection (six cases), a combination of two infections (15 cases), and a combination of three infections (20 cases). We calculated the probability of survival based on the model which follows and provided the figures for each case (Figures 1-5). Statistics were performed using Number Cruncher Statistical Systems (NCSS) software to model the probability of mortality. Receiver Operating Characteristic (ROC) analysis was performed to test the model’s performance. The change in mortality versus the independent variables was calculated by Wald statistics. p<0.05 was accepted as significant.

5. RESULTS

The logistic multiple regression based on the above mentioned criteria resulted in the equation:

\[ \text{Logit}(p) = 4.96 -1.61*(\text{Asp}) + .33*(\text{CanA}) + .15*(\text{Can}) -.57*(\text{Cur}) -.61*(\text{Fus}) -.78*(\text{Rhi}) -.04*(\text{TBSA}). \]

ROC for this model was 0.81. As expected, an increased burn size results in higher mortality with a coefficient of -0.04. The coefficients for Asp, Cur, Fus, and Rhi were negative, indicating that with an increased total negative coefficient and the combination of more than one fungal infection, the probability to survive decreases. Surprisingly, the coefficients for CanA and Can were positive, indicating that infections with these strains separately do not cause higher morality in the selected population. Based on the Wald statistics, Asp and TBSA were the two separate variables that caused a significant increase in mortality (p<0.003 and p<0.001, respectively). The combination of CanA, Asp, and Rhi were associated with the highest mortality (Figures 1-5).

6. CONCLUSIONS

We were able to develop, based on logistic multiple regression, a model to predict survival in burn patients with fungal infections. Burn size and infection with Curvularia or Aspergillus are the most important variables that influence mortality, and when more than one fungal infection is present, the concomitant presence of Candida, Aspergillus and Fusarium proved to be the most deadly combination. These results will allow us to improve treatment schemes in burned patients at greater risk of dying. Interestingly, the combination of Rhizomucor and Candida, is predicted to do better than the combination of Aspergilus and Candida but the 3 fungus together had a poor outcome.
Figure 2: The probability of survival when one infection is present.

Figure 3: The probability of survival when a combination of two infections is present.
Figure 4: The probability of survival when a combination of three infections is present.

Figure 5: The probability of survival when a combination actually exist in our patient population.