World J. Surg. 20, 401–405, 1996

WORLD
Journal of
SURGERY

Severity Stratification and Outcome Prediction for Multisystem Organ Failure and Dysfunction

Jack E. Zimmerman, M.D., William A. Knaus, M.D., Xiaolu Sun, M.D., Douglas P. Wagner, Ph.D.

ICU Research Unit, Department of Anesthesiology, The George Washington University Medical Center, 2300 K Street N.W., Washington, D.C. 20037, U.S.A.

Abstract. Multiple organ system failure or dysfunction (MOSF/MODS) remains a major cause of morbidity and mortality in hospitalized adults. Among intensive care unit (ICU) patients the extent of physiologic derangement, the type of associated disease or injury, increasing age, and life-threatening comorbid conditions are the major determinants of risk for developing MOSF and for survival during the 1980s. Hospital mortality for patients with a single organ system failure (OSF) lasting more than 1 day approached 40%; and for those with two OSFs hospital mortality increased to 60%. These outcomes did not change over the decade. For patients with three or more OSFs persisting after 3 days of OSF, however, data suggest that between 1982 and 1990 the mortality has been reduced from 98% to 84% ($p = 0.0003$). Because of variations in the types and combinations of OSFs, associated disease, and extent of physiologic derangement, it is difficult to interpret variations in mortality among patients with one or more OSFs defined using categorical criteria. For this and other reasons, outcome prediction based on a comprehensive assessment of patient risk factors is a more sensitive, specific, useful approach to quantifying MODS than a simple count of the number and duration of OSFs. Because repeated assessment of risk factors during subsequent ICU days reflects complications and response to therapy, daily outcome predictions are even more precise than estimates at ICU admission. The ability to more accurately predict survival from MODS/MOSF can improve our ability to test new therapies, evaluate how outcome has changed over time, and assess the efficacy of supportive therapy for individuals.

The syndrome of multiple organ system dysfunction and failure (MODS/MOSF) is characterized by progressive or sequential development of otherwise unexplained dysfunction of multiple organs, most commonly in association with sepsis, injury, ischemia, or inflammation [1, 2]. Common to all these insults is a systemic inflammatory response and hypermetabolism that may or may not be associated with shock. Patients with MODS/MOSF have mortality rates that exceed 50%, and the syndrome accounts for a large proportion of hospital deaths among intensive care unit (ICU) patients [2, 3]. The objectives of this review are to: (1) define multiple organ system dysfunction and failure; (2) describe the patient characteristics that determine risk for developing MODS; (3) review the determinants of hospital mortality; and (4) describe recent progress in predicting outcome for individual patients with MODS/MOSF.

Correspondence to: J.E. Zimmerman, M.D.

Definitions

The term multiple organ system failure (MOSF) implies an all-or-nothing event that is either present or absent. As a result, most definitions of organ system failure (OSF) employ physiologic criteria to determine cutoff points indicating the presence or absence of OSF. In 1985 we developed this type of definition for five of the most common organ system failures (Table 1). These OSF definitions are precise, objective, and based on reproducible physiologic measurements [2]. With one exception—the definition of respiratory failure for patients who remain on a ventilator after 3 days—the definitions are independent of specific therapy and assume that each patient is receiving maximum support. Unfortunately, these and other definitions of OSF [4–6] ignore diagnosis and the typical continuum of dynamically changing organ function. Thus OSF probably represents only the most extreme point, or end-stage, of a dynamic, continuous process.

Recognizing these shortcomings, a consensus conference of the American College of Chest Physicians (ACCP) and Society of Critical Care Medicine (SCCM) recommended the term multiple organ dysfunction syndrome (MODS) to define the continuum of physiologic changes during which function is not capable of maintaining homeostasis [1]. Thus MODS might describe moderate renal or neurologic compromise [e.g., elevated serum creatinine or a Glasgow Coma Score (GCS) of 9–12] or total organ failure (e.g., oliguric renal failure or a GCS score of 3). Although not specifically described, MODS was intended to identify a continuum of physiologic change over time and to reflect patient prognosis.

Some authors have defined MODS using methods similar to those used to define OSF [7] (i.e., the use of physiologic cutoff points to define the presence or absence of organ dysfunction). Unfortunately, these categoric definitions of organ system dysfunction have limitations similar to those for OSF; that is, they ignore diagnosis, fail to reflect the dynamic aspects of the syndrome, and do not account for the marked variations in physiologic derangement and risks associated with different types and combinations of organ dysfunction. Despite these shortcomings, a prospective comparison of two systems, based on a limited sample, one defining MOSF and the other MODS, suggested that the two scales assess the same events and that a graded organ

Table 1. Definitions of organ system failure.

If the patient had one or more of the following during a 24-hour period (regardless of other values), OSF existed on that day.
Cardiovascular failure (presence of one or more of the following)
Heart rate $\leq$ 54/min
Mean arterial blood pressure $\leq$ 49 mmHg
Occurrence of ventricular tachycardia, ventricular fibrillation, or both
Serum pH $\leq$ 7.24 with $PaCO_2$ of $\leq$ 49 mmHg
Respiratory failure (presence of one or more of the following)
Respiratory rate $\leq$ 5/min or $\geq$ 49/min
$PaCO_2 \geq 50$ mmHg
$AaDO_2 \geq 350$ mmHg; $AaDO_2 = 713\ FIO_2 - PaCO_2 - PaO_2$
Dependent on ventilator on the fourth day of OSF (i.e., not applicable for the initial 72 hours of OSF)
Renal failure (presence of one or more of the following)[a]
Urine output $\leq$ 479 ml/24 hr or $\leq$ 159 ml/8 hr
Serum BUN $\geq$ 100 mg/dl
Serum creatinine $\geq$ 3.5 mg/dl
Hematologic failure (presence of one or more of the following)
WBC $\leq 1000\ mm^3$
Platelets $\leq 20{,}000\ mm^3$
Hematocrit $\leq$ 20%
Neurologic failure
Glasgow Coma Score $\leq$ 6 (in the absence of sedation at any one point of the day)

Reprinted from [2], with permission of the publisher.
[a]Excludes patients on chronic dialysis before hospital admission.

dysfunction (MODS) score adds no benefit for prediction of mortality [8].

Diseases Associated with MODS/MOSF

Infection, injury, inflammation, poor perfusion, and hypermetabolism are common features in most patients with MODS/MOSF. This situation has led to suggestions that an uncontrolled systemic inflammatory response and the effects of multiple mediators might be a potential cause for both the systemic inflammatory response syndrome (SIRS) and MODS [9]. Although useful for exploring pathogenesis and therapy, terms such as SIRS and MODS describe a combination of clinical findings rather than a well defined disease entity. We recently examined a more specific disease descriptor, the primary reason for ICU admission (admission diagnosis), among patients with multiple (two or more) OSFs defined using the methods listed in Table 1 [3].

In a survey of 2475 patients with MOSF, nonoperative diagnoses accounted for most (76%) of the admissions [3]. Six primary reasons for ICU admission (admission diagnoses) accounted for almost half (47%) of the nonoperative MOSF admissions: cardiac arrest, sepsis, pneumonia, congestive heart failure, and upper gastrointestinal (GI) bleeding due to ulcer or varices. Among 605 postoperative admissions, MOSF was most prevalent after operations for head trauma, elective abdominal aortic aneurysm repair, aortic dissection or rupture, GI perforation, GI inflammatory diseases, GI carcinoma, and valvular heart surgery. These seven diagnoses accounted for 43% of the postoperative MOSF cases. Trauma accounted for 176 (7%) of the 2475 MOSF cases, head trauma for 78%, and multiple trauma for 22%. Thermal injury is frequently associated with MOSF [5], but patients with burn injury were not included in the APACHE III database.

Risk Factors for Developing MODS/MOSF

Each of the injuries and diseases discussed above are associated with an increased probability of the patient developing MODS/MOSF. Other factors that increase the risk for developing MODS include one or more of the following: (1) delayed or inadequate resuscitation; (2) a persistent infectious or inflammatory focus; (3) a surgical "misadventure"; (4) the presence of a hematoma; (5) age $\geq$ 65 years; (6) prior organ dysfunction; (7) steroid therapy; (8) chronic health problems such as alcoholism, malnutrition, diabetes, or cancer; and (9) a serious physiologic abnormality at ICU admission [2–4, 9–11].

Physicians frequently confuse the role of severity systems for predicting hospital mortality from diseases associated with MOSF with its use for predicting the development of MOSF. Because severity scoring systems reflect many of the physiologic variables associated with the development of MOSF, severity scores are reasonable indicators of risk for MOSF [12, 13]. The APACHE III prognostic system also provides accurate estimates of hospital survival within many of the disease categories associated with MOSF [13, 14].

Outcome

Hospital survival after MOSF and its relation to the number and duration of OSF has been the focus of three large multicenter studies performed in the United States and France over the past decade [2, 3, 15]. Together these studies included 80 hospitals and 25,522 ICU admissions, among whom 12,423 (49%) had one or more OSFs. Each of these studies used the OSF definitions listed in Table 1.

The first analysis included 5677 ICU admissions at 13 U.S. hospitals between 1979 and 1982 [2]. Among these admissions 2724 (48%) of the patients developed one or more OSFs, and 795 (14%) had multiple (two or more) OSFs. For both nonoperative and postoperative patients, a single OSF lasting more than 1 day resulted in a hospital mortality approaching 40%; and for those with two OSFs for more than 1 day the hospital mortality rose to 60%. Mortality for 99 patients with three or more OSFs on day 4 of OSF or later was 98%. This 1979–1982 U.S. OSF study was

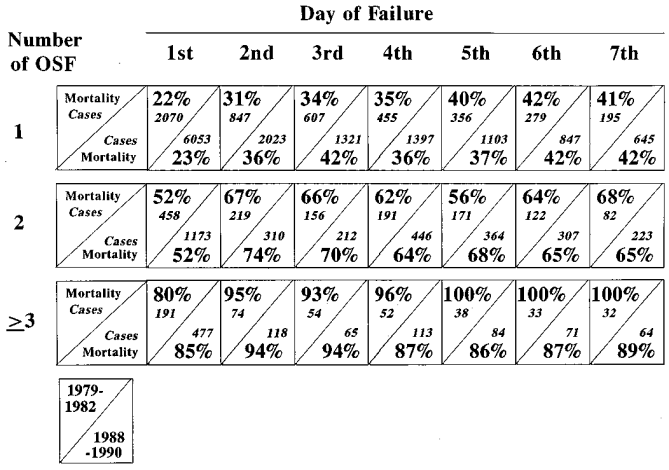

Fig. 1. Hospital mortality (U.S.) according to the number and duration of organ system failure for 2405 ICU admissions during 1979–1982 compared to 7703 ICU admissions during 1988–1990.

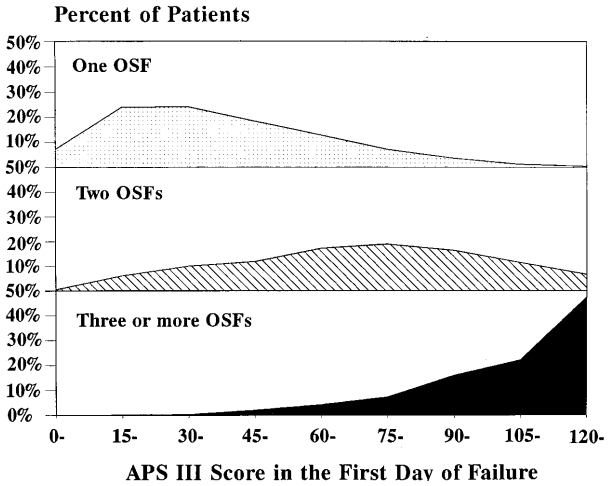

Fig. 2. Distribution of the acute physiology score (APS) of APACHE III measured on the first day of organ system failure (OSF) for 7703 patients. *Top:* 6053 patients with one OSF. *Middle:* 1173 patients with two OSFs. *Bottom:* 477 patients with three or more OSFs.

replicated among 2405 ICU admissions at 27 French hospitals during 1984 [15]. In contrast to the U.S. patients 1996 (83%) of the French patients had one or more OSFs on ICU day 1. Survival at hospital discharge was also related to the number and duration of the OSFs and was virtually identical to that reported in the 1979–1982 U.S. study. Mortality for 85 French patients with three or more OSFs (98%) was identical to that in the U.S. study.

The 1988–1990 APACHE III study of 17,440 admissions to 42 ICUs at 40 U.S. hospitals included 7703 patients with one or more OSFs (44%); multiple (two or more) OSFs occurred in 2364 (14%) of the admitted patients [3]. Figure 1 compares hospital survival, according to the number and duration of OSFs, of U.S. patients treated during 1988–1990 to those treated during 1979–1982. Hospital mortality for patients treated during 1988–1990 with one OSF (23–42%) and two OSFs (52–65%) was not significantly different for patients treated in the United States during 1979–1982 and France during 1984. Among 192 patients with three or more OSFs treated during 1988–1990, however, 30 patients survived (84% hospital mortality), a significant improvement ($p = 0.0003$) in outcome over that during the early 1980s (98% mortality).

Determinants of Outcome

Studies of the 10,427 patients admitted to the ICU who developed OSF and were treated in 60 ICUs at 53 U.S. hospitals over the past decade have defined the patient factors associated with hospital survival [2, 3]. Because OSF is such an important cause of death among ICU patients, many of the patient characteristics associated with hospital mortality also determine risk for developing OSF.

The number and duration of OSFs is closely related to hospital mortality (Fig. 1). The combination of OSFs also has an important impact on survival [3, 6, 7]. In the APACHE III study, for example, hospital mortality for patients with two OSFs varied from 20% to 76%: Mortality was 34% for 210 patients with renal and cardiovascular failure, 49% for 169 patients with respiratory and renal failure, and 76% for 148 patients with neurologic and cardiovascular failure [3].

As demonstrated in Figure 2, there are marked differences in the severity of the physiologic abnormalities on the first day of OSF. These differences explain, at least in part, the variations in risk for patients with different types and combinations of OSF.

The extent of physiologic abnormality, as measured by the acute physiology score (APS) of APACHE III, is the most important risk factor for the development of OSF and for hospital mortality due to OSF [3]. Although the severity of physiologic abnormality at ICU admission is associated with the subsequent risk for OSF, the APS measured on the first day of OSF is a more precise outcome predictor than APS measured at ICU admission. This improved accuracy is probably because outcome estimates on later ICU days summarize the physiologic consequences of evolving organ system dysfunction as well as the response to therapy.

The patient's ICU admission diagnosis also influences the prognosis for those with MOSF [2, 3, 5]. Hospital mortality is generally worse for MOSF patients with nonoperative diagnoses and those who have undergone emergency surgery. Mortality, for example, is lower among patients admitted after multiple trauma than for sepsis or cardiac arrest and lower for patients with OSF following elective repair of an abdominal aortic aneurysm in contrast to emergency repair after aneurysm rupture [3].

Increasing age and specific life-threatening comorbid conditions also increase the risk of death due to OSF. Because age reduces physiologic reserve, we believe patients who are 65 years or older are less able to tolerate the impact of acute injury or disease. In addition, when we studied 34 comorbid conditions among patients with OSF we found that seven—acquired immune deficiency syndrome (AIDS), hepatic failure, lymphoma, metastatic cancer, leukemia/multiple myeloma, immunosuppression with steroids of other drugs, and cirrhosis—had an impact on hospital mortality. We believe these comorbid conditions affect survival because they predispose to infection, an important cause of hospital deaths of patients with OSF. Although chronic cardiac, respiratory, and renal diseases also influence survival, we believe

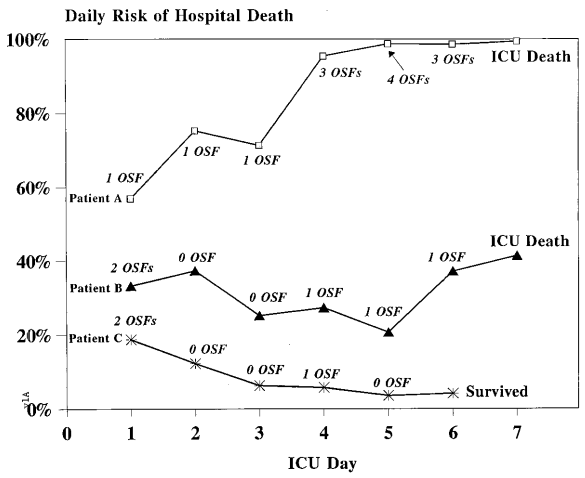

Fig. 3. Daily APACHE III risk of hospital death for three postoperative patients admitted to the ICU with gastrointestinal perforation who developed MOSF. Outcomes and the number of organ system failures (OSFs) on each ICU day are indicated for patients A, B, and C (see text for details).

their prognostic impact is probably captured by measuring physiologic abnormalities.

Outcome Prediction

Prognostic estimates that use the number and duration of organ system dysfunction or failure that are categorically defined using specific cutoff points [2, 5–7] are attractive because of their simplicity. Unfortunately, there are marked variations in the risk of hospital mortality for different types and combinations of OSF [3]. As emphasized previously, these risk variations are due to differences in patient characteristics, such as age, prior health status, ICU admission diagnosis, and extent of physiologic abnormalities.

We found that the APACHE III predictive model [13] provides better discrimination than prognostic estimates based on the number of OSFs [3]. These APACHE III mortality predictions were also more accurate when applied on the first day of OSF than were the predictions at ICU admission. Although the predictions on the first day of OSF or ICU admission are useful for group risk stratification, clinical trials, and quality assurance, they are insufficient for supporting decisions to limit life-supporting therapy for individual patients: Accurate prognostication requires an assessment of the dynamic aspects of critical illnesses, particularly the development of complications and response to therapy. Just as measurements of temperature and the white blood cell count help assess the effectiveness of drainage and antibiotics for an infection, so repeated measurement of physiologic changes during life-supporting ICU therapy can help assess an individual patient's daily risk for hospital death [14].

Figure 3 displays daily APACHE III prognostic estimates for three patients admitted to the ICU with MODS/MOSF following surgery for a gastrointestinal perforation. For each individual (patients A, B, C) Figure 3 displays the daily probability of hospital death and the number of OSFs as defined in Table 1 during ICU days 1 to 7. Patient A, a 67-year-old man, was admitted to the ICU after surgery for a perforated duodenal ulcer. The first-day APS of APACHE III was 76; most (72%) of the APS was accounted for by oliguria, elevated blood urea nitrogen (BUN) and creatinine, and a high mean arterial pressure and respiratory rate. The risk of hospital death was 57% on ICU day 1, and there was one OSF (acute renal failure). Despite maximal support with antibiotics, drainage, mechanical ventilation, and hemodialysis, there was persistent oliguria, fever, and leukocytosis. On ICU day 4 the patient developed hypotension (mean arterial pressure 54 mmHg) and a diminished level of consciousness (GCS 6) due to bacteremia and cerebral infarction. The day 4 risk of hospital death was 95%, and there were three OSFs (renal, respiratory, neurologic). Patient A died on ICU day 7.

Patients C and B in Figure 3 had courses different from that of patient A. Patient C, a 57-year-old man, was admitted after closure of a small bowel perforation and splenic disruption due to penetrating trauma. The first-day APS was 53, with most (74%) of the score accounted for by a widened $AaDO_2$ (448 mmHg), acidosis (pH_a 7.22), hypertension, tachycardia, and hypoalbuminemia. The ICU day 1 probability of hospital death was 19%, and there were two OSFs (respiratory and cardiovascular). By ICU day 5 patient C was removed from the ventilator, and the APS fell to 11. Patient C left the ICU on day 6 and survived hospitalization. In contrast, patient B, a 73-year-old woman, had a perforated colonic diverticulum. The first-day APS was 57, and there were two OSFs (respiratory and cardiovascular); the ICU day 1 probability of hospital death was 33%. On ICU day 7 there was one OSF (respiratory), the APS was 37, and the probability of hospital death was 41%. Patient B died on ICU day 36.

The daily risk predictions displayed in Figure 3 illustrate several points. First, because daily risk predictions reflect the individual's physiologic response to therapy it is possible to distinguish the prognosis for patients who on ICU day 1 are in the middle of the risk spectrum. These patients pose the greatest prognostic difficulty; but as demonstrated by patients A and C, it is possible to define an increasing probability of survival and nonsurvival using these methods. Second, except for extreme cases (three or more OSFs), the number of OSFs provides little information about the day-to-day probability of survival. Third, the most useful, reliable aspects of these estimates are the relative trends. For patient B the 41% ICU day 7 probability of hospital death, for example, summarizes this patient's current condition and indicates that the applied therapy has not reduced her 33% ICU day 1 risk. Finally, these probabilities are an accurate measure of the patient's likelihood of survival, but they do not predict whether an individual will live or die. Thus patient A's 95% risk of death on day 4 indicates marked deterioration since ICU day 1 (risk 57%). To some families or surgeons a 95% mortality risk might represent a reason to limit therapy, whereas for others it may signify a need for more aggressive therapy.

Objective prognostic estimates can help assess treatment effectiveness by distinguishing physiologic effect (e.g., changing laboratory findings) from patient benefit (i.e., reducing mortality risk). The resulting changes in risk can improve communication among specialists regarding their importance. Providing family members with objective information about mortality risk can also improve communication. Similar to providing patients with information about operative risk, pointing out daily prognostic trends can also improve decisions about continued therapy. These objective probabilities, however, should be viewed as a supplement to, not a replacement for, clinical judgment. Objective prognostic estimates

can assist decision-making, but additional medical facts together with the patient's preferences and values are required for sound clinical decisions.

Résumé

Le syndrome de défaillance ou de dysfonctionnement polyviscérale (multiple organ system failure = MOSF, multiple organ system dysfunction = MOSD) est une cause majeure de morbidité et de mortalité chez le patient hospitalisé. A la fin des années 80, parmi les patients en soins intensifs, pour déterminer le risque de la survenue d'un MOSF/MOSD ainsi que les chances de survie, ont été pris en compte le degré de dérèglement physiologique, le type de maladie ou de lésions associées, l'âge et les co-morbidités menaçant le pronostic vital. La mortalité des patients à l'hôpital avec un organe défaillant était de 40% et celle des patients avec deux organes défaillants, de 60%; ces chiffres n'ont pas beaucoup évolué depuis. Pour le patient ayant une atteinte de trois organes ou plus, persistant au-delà de trois jours, cependant, les données récentes suggèrent que la mortalité entre 1982 et 1990 a baissé de 98% à 84% (p = 0.0003). En raison des variations du type et des combinaisons d'organes défaillants, des maladies associées et du degré de défaillance viscérale, il est difficile d'évaluer et d'interpréter les variation de mortalité des patients ayant un ou deux organes défaillants définis selon des critères catégoriels. Pour ces raisons, ainsi que pour d'autres, la prédiction de l'évolution selon l'évaluation de facteurs de risque plutôt que sur le nombre et la durée des organes atteints est une méthode plus sensible, plus spécifique et utile. Parce que la répétition de l'évaluation de ces facteurs de risque pendant les jours suivants en soins intensifs est le reflet des complications et de la réponse à la thérapeutique, la mesure quotidienne de ces paramètres est encore plus précise que les données à l'admission. La possibilité de mieux prédire la survie à partir de ces données doit améliorer notre façon d'évaluer les nouvelles thérapies, l'évolution avec le temps et tester l'efficacité des moyens adjuvants pour chaque patient.

Resumen

La falla orgànica multisistèmica o disfunciòn orgànica mùltiple (FOMS/DOM) sigue siendo una causa principal de morbilidad y mortalidad en adultos hospitalizados. Entre los pacientes de la unidad de cuidado intensivo, la magnitud de la alteraciòn fisiològi ca, el tipo de enfermedad o de lesiòn asociada, el avance de la edad y las comorbilidades potencialmente letales, fueron los factores determinantes principales de riesgo de desarrollar FOM y de sobrevida en los años 1980's. La mortalidad operatoria con un a falla orgànica ùnica de màs de 1 dìa de duraciòn se acercò al 40%, y en aquellos pacientes con dos fallas orgànicas, la mortalidad operatoria se incrementò al 60%; estos resultados no cambiaron en el curso del decenio. Sin embargo, en pacientes con tres o màs fallas orgànicas persistentes despuès de 3 dìas, la informaciòn reciente sugiere que entre 1982 y 1990 la mortalidad se redujo de 98% a 84% (p =3D .0003). Debido a la variaciòn en los tipos y combinaciones de las fallas orgànicas en la enfermedad aso ciada y a la magnitud de la alteraciòn fisiològica, es dificil interpretar las variaciones en mortalidad en los pacientes con una o màs fallas orgànicas definidas mediante criterios de categorizaciòn. Por esta y otras razones, la predicciòn del resultado hecho con base en una evaluaciòn comprensiva de los factores de riesgo, representa un enfoque màs sensible, màs especìfico y màs ùtil en cuanto a la cuantificaciòn y a la disfunciòn orgànica que el simple conteo del nùmero y de la variaciòn de las fallas orgànicas. Por cuanto la evaluaciòn repetida de los factores de riesgo en el curso de los dìas subsiguientes en la unidad de cuidado intensivo refleja las complicaciones y la respuesta a la terapia, las predicciones diarias de resultado final son aun màs preciases que las estimaciones hechas en el momento de la admisiòn a la unidad de cuidado intensivo. La habilidad para predecir màs certeramente la sobrevida en el FOMS/DOM puede mejorar nuestra capacidad para probar nuevas terapias, evaluar còmo los resu ltados finales han cambiado en el curso del tiempo y determinar la eficacia de la terapia de soporte.

Acknowledgments

This study was supported by The Agency for Health Care Policy and Research (HSO 7137), The Department of Anesthesiology, George Washington University Medical Center, and APACHE Medical Systems, Inc.

References

1. ACCP/SCCM Consensus Conference Committee: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest *101*:1644, 1992
2. Knaus, W.A., Draper, E.A., Wagner, D.P., Zimmerman, J.E.: Prognosis in acute organ-system failure. Ann. Surg. *202*:685, 1985
3. Knaus, W.A., Zimmerman, J.E., Wagner, D.P., Sun, X., Hakim, R.B., Nystrom, P.O.: A comparison of risks and outcomes for patients with organ system failure 1982–1990. Crit. Care Med. (in press)
4. Tran, D.D., Cuesta, M.A., van Leeuwen, P.A.M., Nauta, J.J.P., Wesdorp, R.I.C.: Risk factors for multiple organ system failure and death in critically injured patients. Surgery *114*:21, 1993
5. Saffle, J.R., Sullivan, J.J., Tuohig, G.M., Larson, C.M.: Multiple organ failure in patients with thermal injury. Crit. Care Med. *21*:1673, 1993
6. Hebert, P.C., Drummond, A.J., Singer, J., Bernard, G.R., Russell, J.A.: A simple multiple system organ failure scoring system predicts mortality of patients who have sepsis syndrome. Chest *104*:230, 1993
7. Fagon, J.Y., Chastre, J., Novara, A., Medioni, P., Gilbert, C.: Characterization of intensive care unit patients using a model based on the presence or absence of organ dysfunctions and/or infection: the ODIN model. Intensive Care Med. *19*:137, 1993
8. Barie, P.S., Hydo, L.J., Fischer, E.: A prospective comparison of two multiple organ dysfunction/failure scoring systems for prediction of mortality in critical surgical illness. J. Trauma *37*:660, 1994
9. Beal, A.L., Cerra, F.B.: Multiple organ failure syndrome in the 1990s: systemic inflammatory response and organ dysfunction. J.A.M.A. *271*:226, 1994
10. Henao, F.J., Daes, J.E., Dennis, R.J.: Risk factors for multiorgan failure: a case control study. J. Trauma *31*:74, 1991
11. Sauaia, A., Moore, F.A., Moore, E.E., Haenel, J.B., Read, R.A., Lezotte, D.C.: Early predictors of postinjury multiple organ failure. Arch. Surg. *129*:39, 1994
12. Knaus, W.A., Draper, E.A., Wagner, D.P., Zimmerman, J.E.: APACHE II: a severity of disease classification system. Crit. Care Med. *13*:818, 1985
13. Knaus, W.A., Wagner, D.P., Draper, E.A., et al.: The APACHE III prognostic system: risk prediction of hospital mortality for critically ill hospitalized adults. Chest *100*:1619, 1991
14. Wagner, D.P., Knaus, W.A., Harrell, F.E., Zimmerman, J.E., Watts, C.: Daily prognostic estimates for critically ill adults in intensive care units: results from a prospective, multicenter, inception cohort analysis. Crit. Care Med. *22*:1359, 1994
15. Knaus, W.A., Rauss, A., Alperovitch, A., et al.: Do objective estimates of chances for survival influence decisions to withhold or withdraw treatment? Med. Decis. Making *10*:163, 1990