Alvaro Koenig[1], Paulo Dorneles Picon[2], Janaína Feijó[3], Eliezer Silva[4], Glauco Adrieno Westphal[5]

Estimate of the economic impact of implementing an in hospital protocol for the early detection and treatment of severe sepsis in public and private hospitals in southern Brazil

Estimativa do impacto econômico da implantação de um protocolo hospitalar para detecção e tratamento precoce de sepse grave em hospitais púbicos e privados do sul do Brasil

1. Master, Professor at Universidade da Região de Joinville – Univille; Phycisian from Comissão de Controle Hospitalar of Centro Hospitalar Unimed - Joinville (SC), Brazil.
2. PhD, Physician of Clinical Research Unit of Hospital das Clinicas de Porto Alegre - HCPA – Porto Alegre (RS), Brazil.
3. Physician from Hospital Municipal São José - Joinville (SC), Brazil.
4. Full Professor, Physician from Hospital Israelita Albert Einstein - HIAE, São Paulo (SP), Brazil.
5. PhD, Professor at Universidade da Região de Joinville – Univille; Physician from Centro Hospitalar Unimed and from Hospital Municipal São José - Joinville (SC), Brazil.

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Author for correspondence:
Alvaro Koenig
Infection Control Program Unimed
Joinville Hospital Center
Rua Orestes Guimaraes, 905
Zip Code: 89204-060 - Joinville (SC), Brazil.
E-mail: koenig@netvision.com.br

ABSTRACT

Objective: To analyze the economic impact of an early sepsis detection protocol in two general hospitals.

Methods: We analyzed data collected from a prospective study of septic patients before and after the implementation of a protocol for early diagnosis of severe sepsis. We conducted a cost-effectiveness analysis comparing: mortality rate, cost of sepsis treatment and indirect costs attributed to years of productive life lost to premature death in both phases.

Results: Two hundred seventeen patients were included, 102 in phase I and 115 in phase II. After protocol implementation, in private and public hospital, mortality rates decreased from 50% to 32.2% and from 67.6% to 41% ($p < 0.05$). The mean years of productive life lost due to sepsis decreased from 3.18 to 0.80 and 9.81 to 4.65 ($p < 0.05$), with a mean gain of 2.38 and 5.16 years of productive life, for each septic patient. Considering Brazilian gross domestic product per capita, estimated productivity loss due to sepsis decreased between 3.2 and 9.7 billion US dollars, varying based on the incidence of sepsis. Hospital costs were similar in both phases.

Conclusion: A protocol for early detection and treatment of in-hospital septic patients is highly cost-effective from a societal perspective.

Keywords: Sepsis/economics; Sepsis/diagnosis; Cost-benefit analysis; Brazil

INTRODUCTION

Sepsis manifests in distinct spectra of severity, depending on the time elapsed since the first manifestations. When sepsis evolves to dysfunction of one or more organs, it is called severe sepsis, and septic shock if there is hypotension that fails to respond to aggressive fluid resuscitation.[1]

The incidence of severe sepsis has increased 91.3% over the last 10 years. It occurs in 1 to 3 individuals per 1000 population in different regions of the world and is associated with high mortality rates, which have remained unchanged in this period.[1-3] In Brazil, approximately 25% of patients hospitalized in intensive care units (ICUs) meet the diagnostic criteria for severe sepsis or septic shock, with progressively increasing mortality rates due to sepsis (34.7%), severe sepsis (47.3%) and septic shock (52.2%).[4,5]

The grades of severity of septic syndrome in sepsis, severe sepsis and septic shock represent the temporal evolution of the same disease. Early identification of sepsis is therefore the most important step to increase the positive effects of the optimized treatment. Therefore, it is necessary to adopt hospital-

wide screening strategies that allow the in-hospital identification of septic patients in the initial phase of the disease. As occurs in acute myocardial infarction, delayed treatment of sepsis can severely impair prognosis.[6]

From an economic standpoint, sepsis represents huge expenses for the health system, as well as a significant loss of productivity stemming from long hospital stays and the accompanying high rates of mortality.[7,8] Estimates indicate that the direct cost of sepsis in the United States is approximately $US17 billion per year, which represents only 30% of the total cost of the disease if the social costs are also considered.[2]

Preventive measures, as well as the implementation of protocols for early detection and optimized treatment, are steps that aim to decrease morbidity and mortality rates and the costs associated with sepsis.[8]

The assessment of cost-effectiveness and cost-benefit ratios related to programs for the early detection and treatment of severe sepsis, from the perspective of the society and the payment source, is essential for deciding whether or not to implement such programs in the health care network in Brazil.

The aim of this study was to assess the impact of an early sepsis detection protocol on direct and indirect costs in two general hospitals.

METHODS

Data from a prospective before-after study[9] were used for the economic analysis, in which we evaluated outcomes prior to and after the implementation of a protocol for the early detection and treatment of sepsis. The present study was conducted in two hospitals in the city of Joinville, located in the state of Santa Catarina, Brazil: one public (fully funded by the Brazilian Unified Health Care System); and the other private. Both hospitals presented average to advanced levels of medical treatment. At both hospitals, patients were included and evaluated during two distinct phases:

Phase I (August of 2005 to October of 2006) – In this phase, in both hospitals, patients with sepsis were diagnosed by the attending physician or intensivist and managed in accordance with the Surviving Sepsis Campaign (SSC) protocol.[10] For each patient diagnosed with sepsis a research nurse calculated the time elapsed between the first clinical signs of sepsis and the definite diagnosis and treatment (delta T).

The institutional policies of both hospitals precluded the use of drotrecogin alpha in the sepsis protocol.

Phase II (November of 2006 to November of 2007) – Patients with severe sepsis diagnosed during phase II were treated in accordance with the same SSC protocol adopted in phase I, and the following clues for sepsis detection were added (protocol for the early detection of sepsis):

– Nurses became responsible for recording patients with any sign suggestive of infection, such as chills, oliguria, changes in the level of consciousness, changes in the most recent leukocyte count and a need for oxygen supplementation

– Vital signs were recorded by a single professional in a vital sign form for the whole ward and this form was analyzed by the ward nurse in each shift.

– Patients with any sign suggestive of infection or with two or more altered vital signs, as identified by the nursing staff evaluation, were evaluated by the attending intensivist.

After the diagnosis of severe sepsis had been confirmed, the treatment recommended in the SSC protocol was initiated.

The time elapsed between the first clinical signs of sepsis and the definite diagnosis and treatment (delta T) was calculated in the same way as in phase I. Exclusion criteria were shock due to noninfectious causes and end-stage disease with no prospect of cure.

The following clinical variables were evaluated in both phases:

– time to detection of sepsis (interval between the first recorded manifestation of sepsis risk and sepsis diagnosis)

– adherence to the 6-hour and 24-hour segments of the protocol

– length of hospital stay

– mortality

The following economic variables were assessed:

– primary: years of productive life lost due to sepsis; and the indirect costs to society resulting from the loss of productivity

– secondary: hospital costs for the treatment of sepsis, from the perspective of the payment source

In both phases, the direct costs were calculated only for the private hospital and included all expenditures for medication, daily rates (in the ICU and infirmary), diagnostic procedures, surgical procedures and medical fees. Costs were expressed in US dollars based on the mean value of the US$ in 2006. The following was calculated: the overall cost of hospital stays, the cost of ICU stays and the mean cost per day. Costs of doctor fees, diagnostic procedures and surgical procedures were calculated based on the Brazilian Hierarchical Classification

of Medical Procedures,[11] whereas the medication costs were calculated based on the Brazilian national pharmaceutical manual known as the BRASÍNDICE.[12]

Indirect costs were estimated using the human capital approach.[13] The hospital stay (in days) was computed as loss of productivity, and, in the event of death at an age lower than that of retirement,[14] the years of productive life lost due to sepsis were calculated using the following formulae:

Years of Productive Life Lost = 65 – *Age at death* (for males)

Years of Productive Life Lost = 60 – *Age at death* (for females)

The means of productive life years lost due to sepsis was calculated in both hospitals in both phases. Their differences between the two phases in each hospital were the mean number of years of productive life saved after the implementation of the protocol. This reduction in productive life years lost was used in the indirect cost estimate, taking the following factors into account: the incidence of sepsis of 1 to 3 cases per 1000 population;[15] the fact that, in 2006, Brazil had an adult population of 124 million individuals, of which 28 million had supplementary health plans; and the fact that the per capita income in the same year was $US5775.[16,17]

Total indirect cost = mean reduction in productive life years lost x sepsis incidence x adult population (insured and uninsured) x per capita income.

Intangible costs were not computed.

Statistical analysis

Categorical variables were expressed as proportions, and continuous variables were expressed as means and standard deviations. A 95% significance level was applied to all comparisons.

Length of hospital stay and the years of life lost due to sepsis were compared through Student's t-tests for independent samples. The hospital costs for survivors and nonsurvivors were analyzed separately. Differences in mortality rates between the phases and between the two hospitals were analyzed using the chi-square test.

Differences in direct cost in the private hospital between the phases were analyzed by the two-sample Wilcoxon rank-sum test. In order to identify variables associated with higher sepsis treatment costs, multiple regression analysis was performed using the following variables: age; Acute Physiology and Chronic Health Evaluation (APACHE) II score; length of ICU stay; and length of hospital stay($p > 0.2$ was considered for exclusion of the variable).

An Excel® database was created, and the statistical analysis was performed using the program Statistical Package for the Social Sciences, version 15.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

We evaluated data related to 217 patients diagnosed with severe sepsis: 102 in phase I (34 in the private hospital and 68 in the public hospital); and 115 in phase II (59 in the private hospital and 56 in the public hospital).

Costs related to development and implementation of the protocol for the early detection of sepsis comprised the following: the time required for the team of intensivists to review the medical literature and prepare the protocol; the duration of training of nurses for registering the signs suggestive of sepsis and identifying patients at risk; and the time required for active surveillance by infection control nurses in order to verify adherence to the protocol. The mean total cost per hospital was $US1382.

In both phases and in both hospitals, there was a predominance of males among the patients analyzed. Patients treated at the private hospital presented a higher mean age (63 vs 49 years), as well as having a higher mean APACHE II score in phases I and II 26.6 vs 21.5 and 25.2 vs 21.9, respectively, $p < 0.001$). The time to detection of sepsis decreased significantly from phase I to phase II: from 34.4 hours to 13.8 hours in the private hospital ($p < 0.003$); and from 33.8 hours to 6.8 hours in the public hospital ($p < 0.009$). The two hospitals were comparable in terms of the percentage reduction in the time to detection. The mortality rate also decreased significantly between the two phases ($p < 0.001$), and the percentage reduction was similar: 17.8% in the public hospital and 18.4% in the private hospital. The length of stay in the ICU and the length of hospital stay both varied greatly, but presented no significant differences between the two phases (Table 1).

Direct costs were comparable between the two phases, although there was great variability among patients. There was a tendency toward an increase in the total costs from phase I to phase II ($p = 0.07$), whereas the inverse was observed for the mean cost per day of hospitalization (Table 2). The multivariate analysis showed that only the length of stay in the ICU ($p < 0.001$) and the length of hospital stay ($p < 0.001$) had a direct influence on the hospital costs. Age and the APACHE II score were not significant determinants of the direct costs.

Mean overall hospital costs were significantly higher for nonsurvivors than for survivors (US$ 27,308 ±

Table 1 - Principal characteristics and outcomes

Characteristic	Private hospital		Public hospital	
	Phase I	Phase II	Phase I	Phase II
Male gender	19 (60)	30 (51)	49 (72)	36 (61)
Mean age (years)	63.2 ± 18.5[a]	63.2 ± 17.8[a]	51.1 ± 19.7[a]	47.0 ± 20.2[a]
APACHE II score at admission	26.62 ± 9.0[a]	25.15 ± 8.0[a]	21.5 ± 7.0[a]	21.9 ± 8.0[a]
Time to detection of sepsis (hours)	34.37 ± 41.0	13.80 ± 21.0[b]	33.8 ± 44.0	6.9 ± 8.4[b]
Mortality rate	50.0	32.2	67.6	41.0[b]
ICU stay (days)	13.4 ± 17.8	16.4 ± 15.3	14.3 ± 13.1	11.3 ± 9.4
Hospital stay (days)	28.8 ± 35.9	38.6 ± 31.3	32.20 ± 32.8	42.3 ± 35.7

APACHE II - Acute Physiology and Chronic Health Evaluation II; ICU – intensive care unit.
Results are expressed in number (%) or mean ± standard deviation. a → $p < 0.05$ between hospitals; b → $p < 0.05$ between phases.

Table 2 - Overall direct costs in each phase in the private hospital

Breakdown	Phase I	Phase II	p value
ICU cost	9.695 ± 12.387	13.644 ± 12.818	0.15
Total cost	17.726 ± 20.574	25.975 ± 21.513	0.07
Cost per day	960 ± 1.290	808 ± 585	0.44

ICU - intensive care unit. Values expressed in US dollars. Results expressed in mean ± standard deviation.

Table 3 - Years of productive life lost per patient in each phase

Type of hospital	Phase I	Phase II	Reduction[a]
Public	9.81 ± 15.0	4.65 ± 12.0 [b]	5.16 ± 13.0
Private	3.18 ± 4.0	0.80 ± 2.5 [b]	2.38 ± 3.0

a → Years of productive life per patient; b → $p < 0.05$ between phases.

25,985 *versus* US$ 20,021 ± 17,312, $p < 0.03$).

After the implementation of the protocol, there was a significant reduction in the number of years of productive life lost per patient in both hospitals. In the private and public hospitals, there was a gain of 2.38 and 5.16 years of productive life, respectively, per severe sepsis patient (Table 3).

If we consider the incidence of sepsis in the adult Brazilian population to be at the lower end of the range (1/1000 population), the estimated number of years of productive life saved after the implementation of the protocol for the early detection and treatment of severe sepsis would be 66,640 for the population with health plans and 495,360 for the beneficiaries of the Brazilian Unified Health Care System. If we consider the incidence to be at the upper end of the range (3/1000 population), we would save 199,920 and 1486,080 years of productive life, respectively. By multiplying the number of years of productive life saved by the per capita income in 2006, we can estimate annual economic savings to society, due to the reduction in loss of productivity of approximately US$ 3.2 billion (incidence of sepsis = 1/1000) and US$ 9.7 billion (incidence of sepsis = 3/1000).

DISCUSSION

In this analysis, we demonstrated that early detection and optimized treatment of septic patients through the use of clearly defined protocols enabled a reduction in the absolute mortality rate of approximately 18% in both hospitals. As a direct consequence, there was a decrease in the number of premature deaths and in the number of years of productive life lost.

Some economic analyses available show that standardization of treatment regimens reduces mortality and hospital costs. However, these analyses only address the direct costs of in-hospital treatment of septic patients.[2,7,8,18]

Comparisons between the findings of the present study and those of previous studies should be made with caution, taking into account the fact that we evaluated a specific protocol for the early detection and initiation of treatment of septic patients in hospital wards, emergency rooms and ICUs in a small sample of patients of only two hospitals.

Schorr et al.[8] demonstrated a significant reduction in the direct costs related to the treatment of patients with severe sepsis immediately after the implemen-

tation of treatment protocols recommended by the SSC.[10] Our study also evaluated a later phase (after the SSC protocols had been in place for one year), during which the mortality rates remained high, probably due to delayed diagnosis and delays in the initiation of the proper treatment. Attempts were made to reduce diagnostic delays and to evaluate the effect that such delays have on mortality.

In contrast to Schorr et al.,[8] we found that the direct costs to private health insurance plans did not decrease. Instead, there was a tendency toward an increase in such costs after the implementation of the protocol. The reasons for this are unclear, since the patient was diagnosed and treated during a shorter period and should be at lower risk for life-threatening organ dysfunction, as well as generating fewer expenses related to the subsequent treatment. Although the duration of ICU and hospital stays did not change significantly after the implementation of the protocol, these variables presented a positive correlation with the direct costs. In the comparison between survivors and nonsurvivors, the mean ICU costs and the total cost of hospitalization were significantly higher for the nonsurvivors ($p = 0.03$). The finding that the direct cost was higher for nonsurvivors suggests that there was a greater investment of diagnostic and therapeutic resources prior to death, which is probably attributable to the fact that, after the implementation of the protocol, diagnoses were made earlier. Another possibly explanation for the non-decrease in direct costs is that these data derive from an observational before-after study with a small sample and that direct costs were recorded only in one hospital.

In analyzing the direct costs of treatment of sepsis in Brazilian hospitals, a multicenter, prospective study[18] also demonstrated that fewer resources had been allocated to the survivors than to the nonsurvivors, the latter group presenting longer ICU stays, as well as being submitted to a greater number of diagnostic and therapeutic procedures over the course of hospitalization.

The costs to society deriving from the loss of productivity due to early mortality of patients with sepsis decreased significantly after the implementation of the protocol for the early detection and treatment of severe sepsis.

The estimate of years of productive life saved indicates that the protocol for the early detection and treatment of patients with severe sepsis can be highly effective. However, this data are limited and cannot be taken as definitive. First, patients who survive severe sepsis present a greater risk of death over the subsequent months and years. Quartin et al.[3] calculated that, on average, the life of a patient who survives sepsis is reduced by 2.6 years. Second, patients with severe sepsis can present comorbidities, such as heart failure and neoplasias, increasing the short-term risk of death. One limitation of the present study is that we did not have access to the comorbidity diagnoses of the septic patients, which could explain the greater expenditure with the latter.

In terms of monetary value, a gain of years of productive life provides considerable benefit to society, ranging from $US3 billion to $US9 billion, depending on the estimated incidence of sepsis in the adult population (1/1000 to 3/1000). Taking into account the fact that the incidence of sepsis in Brazil is likely similar to that observed in the United States,[4] as well as the fact that indirect costs account for 70% of the costs of sepsis[2,17] and that the mean direct costs per septic patient in the present study were similar to those previously reported for Brazil,[17] the estimates for the reduction of indirect costs found in this study seem to be realistic. However, these data should be interpreted with caution. Since the country faces high unemployment rates, the years of productive life gained do not necessarily translate to increased productivity from a societal perspective. Nevertheless, the years of productive life-annual per capita income product might be a limiting factor, negatively affecting the benefits generated by the implementation of the protocol.

Finally, a limiting factor about our results is that we studied a small sample of patients in only two median-sized hospitals in the south of Brazil. The observational before-after study design limits our certainty about the continuum of these observed mortality reductions and it is therefore not possible to extrapolate this results for the entire brazilian healthcare system. Continuous monitoring of the protocol is necessary to provide reliable data about the validity of our cost estimates and data mortality, before they can be considered for decision making at a public or private health level.

CONCLUSION

In conclusion, we can state that the implementation of a protocol for the early detection and treatment of severe sepsis in hospitalized patients is a low cost measure, is easily adopted and may be highly effective in reducing the number of years of productive life lost, thereby providing substantial benefits to society. Studies evaluating a greater number of variables that might influence the cost-benefit ratio, such as income, level of education and

comorbidities, are needed in order to generate economic information that is more precise.

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RESUMO

Objetivo: Analisar o impacto econômico de um protocolo de detecção precoce de sepse em dois hospitais gerais.

Métodos: Analisamos os dados colhidos em um estudo prospectivo em pacientes sépticos antes e após a implantação do protocolo de detecção precoce de sepse grave. Realizamos uma análise de custo-efetividade comparando: taxa de mortalidade, custo do tratamento da sepse e custos indiretos atribuídos a anos de vida produtiva perdidos por óbito prematuro em ambas as fases.

Resultados: Foram incluídos 217 pacientes, 102 na Fase I e 115 na Fase II. Após a implantação do protocolo, em hospital privado e em hospital público, as taxas de mortalidade caíram de 50% para 32,2%, e de 68,6% para 41% (p<0,05). A média de anos de vida produtiva perdida devida a sepse caiu de 3,18 para 0,80 e de 9,81 para 4,65 (p<0,05) com um ganho médio de 2,38 e 5,16 anos de vida produtiva para cada paciente séptico. Considerando o produto interno bruto per capita do Brasil, a estimativa de produtividade perdida devida a sepse caiu entre 3,2 e 9,7 bilhões de dólares americanos, variando com base na incidência de sepse. Os custos hospitalares foram similares em ambas as fases.

Conclusão: Um protocolo para detecção e tratamento precoce em pacientes hospitalizados com sepse é altamente custo-efetiva do ponto de vista social.

Descritores: Sepse/economia; Sepse/diagnóstico; Análise custo-benefício; Brasil

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