ARTICLE

Long-term Health Status in Childhood Survivors of Meningococcal Septic Shock

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Objective: To assess long-term health status in patients who survived meningococcal septic shock in childhood.

Design: Medical and psychological follow-up of a cross-sectional cohort.

Setting: Pediatric intensive care unit (PICU) of a tertiary care university hospital.

Participants: All consecutive patients with septic shock and purpura who required intensive care between 1988 and 2001.

Intervention: Patients and their parents were invited to our follow-up clinic 4 to 16 years after PICU discharge.

Outcome Measures: Health status was assessed with a standard medical interview, physical examination, renal function test, and the Health Utilities Index Mark 2 (HUI2) and 3 (HUI3).

Results: One hundred twenty patients (response rate 71%) participated in the follow-up (median age at PICU admission, 3.1 years; median follow-up interval, 9.8 years; median age at follow-up, 14.5 years). Thirty-five percent of patients had 1 or more of the following neurological impairments: severe mental retardation with epilepsy (3%), hearing loss (2%), chronic headache (28%), and focal neurological signs (6%), like paresis of 1 arm. One of the 16 patients with septic shock–associated acute renal failure at PICU admission showed signs of mild chronic renal failure (glomerular filtration rate, 62 mL/min/1.73m^2; proteinuria; and hypertension). Scores were significantly lower on nearly all HUI2 and HUI3 attributes compared with Dutch population data, indicating poorer health in these patients.

Conclusions: In patients who survived meningococcal septic shock in childhood, one-third showed long-term neurological impairments, ranging from mild to severe and irreversible. Patients reported poorer general health as measured by HUI2 and HUI3.

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SEPTIC SHOCK WITH A PETECHIAL and/or purpuric rash is a life-threatening clinical syndrome that is predominantly caused by *Neisseria meningitidis*. It is characterized by a sudden onset and rapid progression in previously healthy children. Younger children (<3 years) are known to have more severe disease and higher risk of case fatality.[1] Despite better understanding of the pathogenesis of meningococcal septic shock (MSS) and advances in therapeutic interventions, this syndrome had a high morbidity and mortality in the Netherlands until the implementation of a national vaccination campaign against serogroup C *N meningitidis*.[2]

Few studies have reported long-term incidences of adverse physical health consequences in patients who survived MSS.[3-5] However, these studies did not differentiate outcomes by the severity of the disease; the study populations included patients with sepsis, septic shock, or meningitis. In addition, major risk factors for developing adverse consequences have not been well identified.

We hypothesized that patients who survived MSS in childhood are at a higher risk for adverse physical health outcomes because of the permanent organ damage caused by shock and thrombosis (disseminated intravascular coagulation). More insight into these matters could enable clinicians to provide anticipatory guidance and support to patients after discharge from the pediatric intensive care unit (PICU). The aim of this study was to investigate the long-term physical health consequences in patients who survived MSS in childhood. We also assessed various putative determinants of adverse health outcomes in patients.

METHODS

PATIENT SELECTION

This study was a medical and psychological follow-up of a cross-sectional cohort of all consecutive surviving patients with septic shock and purpura who required intensive care treatment at least 4 years ago (1988-2001) and their

parents. Patients were recruited from the PICU at the Erasmus MC–Sophia Children's Hospital, a tertiary care university hospital. All consecutive surviving patients aged 1 month to 18 years with a clinical picture of MSS and their parents were eligible for this study. Meningococcal septic shock was defined as septic shock with petechiae and/or purpura.[6] The Erasmus MC medical ethical review board approved the study protocol. Written informed consent was obtained from parents and patients by sending a standard letter requesting their participation in our study. Those with an insufficient command of the Dutch language were excluded. Parents and patients who agreed to participate were invited by mail to visit the clinic. The follow-up visits took place in 2005-2006.

DATA ANALYSIS AT PICU ADMISSION

During the study period, patients consecutively admitted with MSS were included in several sepsis studies.[7-11] In these studies, medical data were collected prospectively at various points in the course of the disease. These data, with demographic and clinical data, were pooled into 1 database and analyzed. Severity of illness was determined by using the Pediatric Risk of Mortality Score, vasopressor score ([dopamine dose × 1] + [dobutamine dose × 1] + [epinephrine dose × 100] + [norepinephrine dose × 100] + [phenylephrine dose × 100], all doses given in μg/kg/min), and the disseminated intravascular coagulation score (**Table 1**).[12-14]

Table 1. Disseminated Intravascular Coagulation Score

Measure	Score[a]
Platelet count, $\times 10^3/\mu L$	
>100	0
≤100 and >50	1
≤50	2
Fibrin dimers, μg/mL	
<0.25	0
≥0.25 and <5	2
≥5	3
Prothrombin time, s	
<15	0
≥15 and <19	1
≥19	2
Fibrinogen, mg/dL	
>10 000	0
≤10 000	1

SI conversion factors: To convert fibrin dimers to milligrams per liter, multiply by 1.0; fibrinogen to micromoles per liter, multiply by 0.0294; platelet count to $\times 10^9$ per liter, multiply by 1.0.

[a] A score of 5 or greater indicates the presence of disseminated intravascular coagulation.

ASSESSMENT AT FOLLOW-UP

Medical Interview and Physical Examination

Parents and patients were invited to the follow-up 4 to 16 years after PICU discharge. They were interviewed by 1 pediatrician (C.M.P.B.) in a semistructured format using a standard questionnaire with regard to health consequences and medical care since having MSS. Complaints were defined as chronic if they occurred after MSS and if they were still present at the follow-up visit. One pediatrician performed (C.M.P.B.) a general physical examination of the patient. Skin scarring and orthopedic sequelae due to MSS are described elsewhere.[15]

Briefly, 48% of the patients had skin scarring due to purpura (ranging from barely visible to extremely mutilating scars); 8% had amputation(s) of extremities (ranging from 1 toe to both legs and 1 arm); and 6% had leg-length discrepancies.

Measurements of body weight, height, head circumference, and mid-upper arm circumference were performed.[16] All measurements were performed by 1 observer in whom intraobserver variability for mid-upper arm circumference was tested before the study.

Assessment of Renal Function

Patients who had developed septic shock–associated acute renal failure (ARF) during PICU admission, defined as serum creatinine concentration more than twice the upper level of normal range for age (including patients who received renal replacement therapy [RRT]), were identified. In these patients, persisting renal damage was assessed at the time of follow-up with the following measurements: serum creatinine, from which a glomerular filtration rate (GFR) per 1.73 m^2 of body surface area was estimated using the modified Schwartz or Cockroft formula (according to age); the average of 3 measurements of blood pressure by automated sphygmomanometry; and protein and creatinine excretion averaged from 3 first morning urine samples.[17]

Significant proteinuria was defined as a protein to creatinine ratio in urine of above 20 mg/mmol (0.2 mg/mg).[18] Blood pressure standard deviation (SD) scores were used from a study by Jackson et al.[19]

Health Status Questionnaires

General health status was assessed using the Health Utilities Index Mark 2 (HUI2) and 3 (HUI3), based on the 15-item HUI questionnaire.[20,21] The HUI2 and HUI3 are validated health status classification systems consisting of 6 and 8 attributes, respectively. Each HUI attribute is assigned on the basis of respondents' answers to 1 or more items on the 15-item HUI questionnaire. Scores range from 1 (no functional limitations) to 4, 5, and 6 (severe functional limitations). Single-attribute utility scores were calculated and ranged from 0 (worst health status) to 1 (best health status).[21]

A HUI2 and HUI3 multi-attribute utility score, indicating overall health, was calculated based on single-attribute utility scores.[22,23] Normal scores for HUI2 and HUI3 came from a representative sample of 1435 Dutch school children aged 5 to 13 years.[20,21] Parents of patients aged 4 to 17 years completed the 15-item HUI questionnaire, whereas patients aged 18 years and older completed it themselves. We also used a visual analog scale to rate overall health, with a score ranging from 0 (worst health) to 100 (best health).[24] If the patient was younger than 18 years, his or her parent completed the scale. The 15-item HUI questionnaires were sent by mail with the request that they be completed at home. Parents themselves could decide who (mother or father) would complete the HUI questionnaire.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS, version 12.0 (SPSS Inc, Chicago, Illinois). Comparisons between participating patients and nonparticipants were made using the Mann-Whitney *U* test for age at time of PICU admission, length of PICU stay, and severity of illness. The χ^2 test was used to compare sex between the 2 groups. To compare patients with and patients without adverse neurological outcomes for age at time of PICU admission, severity of illness scores, and serum glucose level (lowest and highest), we used the Mann-Whitney *U* test; we used the χ^2 test for the presence of meningitis (*N meningitidis* cultured in liquor or pleocytosis) and convulsions during PICU admission.

Table 2. Survivors of Meningococcal Septic Shock by Participation in Follow-up

Characteristics	Median (Range)		P Value[a]
	Patients With Follow-up (n=120)	Patients Without Follow-up (n=59)	
Sex, M/F, No.	63/57	27/32	.43
Age at time of PICU stay, y	3.1 (0.1-17.9)	5.4 (0.2-14.3)	.12
Length of PICU stay, d	3 (1-51)	3 (1-36)	.55
Mechanical ventilation, No.	46	23	.93
PRISM	15 (1-37)	15 (0-41)	.64
Presence of DIC, No.	99	41	.1
DIC score[b]	6 (3-8)	6 (2-8)	.72
Administration of inotropic drugs, No.	86	47	.25
Vasopressor score	15 (0-403)	11 (0-145)	.71

Abbreviations: DIC, disseminated intravascular coagulation; PICU, pediatric intensive care unit; PRISM, Pediatric Risk of Mortality Score.

[a] The Mann-Whitney *U* test was used to compare age at time of PICU admission, length of PICU stay, and severity of illness in the 2 groups; the χ^2 test was used to compare sex.

[b] Score of 5 or greater indicates presence of DIC.

All patient anthropometric data were compared with published average values from a Dutch population study performed in 1997 and transformed into SD scores using a software program (Growth Analyzer 3; Nederlandse Groeistichting, Rotterdam, the Netherlands).[25] We tested the association between putative predictor variables (age at time of PICU admission, severity of illness scores, and follow-up interval) and anthropometric SD scores by using the Spearman correlation. The Mann-Whitney *U* test was used to compare anthropometric SD scores between patients with and without orthopedic sequelae. The Mann-Whitney *U* test was used to compare our patients' HUI2 and HUI3 scores with individual normative data from a general population survey.[20] $P \leq .05$ (2-sided) was considered significant.

RESULTS

PATIENT SAMPLE

The target population consisted of 179 patients. Of these patients, 9 were lost to follow-up: 1 patient had severe adverse outcomes (mental retardation with epilepsy) and died several years after the MSS; 7 patients lived abroad at the time of follow-up; and 1 was untraceable. Of the remaining 170 eligible patients, 145 agreed to participate, 120 of whom visited the follow-up clinic. The median follow-up interval was 9.8 years (range, 3.7-17.4 years). The median age of patients at the follow-up visit was 14.5 years (range, 5.3-31.1 years). Twenty-five patients and/or parents did not want to visit the follow-up clinic on practical (eg, no time because of a busy job) or emotional (too emotional to go to a hospital) grounds and preferred to fill out the questionnaires at home. Another 25 patients or parents did not respond to the invitation or refused to participate at all for practical or emotional reasons. The overall response rate, excluding patients lost to follow-up, was 71% (120 of 170 patients). To check for possible selection bias, we compared characteristics between participating patients and nonparticipants (**Table 2**). Patients did not differ with respect to age at time of PICU admission or severity of illness.

At PICU admission, a causative organism was isolated in 100 of the 120 patients (83%) who visited the follow-up clinic. In 99 patients (82.5%), *N meningitidis* was cultured in blood. Of these patients, 78 (79%) had serogroup B *N meningitidis* and 13 (13%) had serogroup C *N meningitidis*; in 8 patients (8%), the serogroup was not determined. A lumbar puncture was also performed in 67 patients (56%): *N meningitidis* was cultured in liquor in 45 patients (67%) and pleocytosis was found in 11 patients (16%) with negative cultures.

HEALTH CONSEQUENCES

Of the 120 patients, 3 (3%) developed severe mental retardation (total IQ < 70) with epilepsy (2 with spastic quadriplegia) for which they needed multispecialty medical care on a regular base. One of these 3 patients died a few months after his follow-up visit (cause of death related to severe retardation with epilepsy and spastic quadriplegia). Before the MSS, all 3 patients had normal motor, cognitive, and emotional development. All 4 patients with severe mental retardation (including the patient who died before our follow-up study) differed significantly with respect to age at time of PICU admission (median, 0.7 years; $P < .01$), severity of septic shock (median Pediatric Risk of Mortality Score, 32, $P < .01$; median vasopressor score, 140, $P < .05$), median lowest serum glucose level (32.4 mg/dL [to convert to millimoles per liter, multiply by 0.0555]; $P < .01$), and the presence of convulsions ($P < .01$) compared with patients without severe retardation. Neuroimaging performed in the weeks after PICU discharge showed diffuse atrophy due to ischemia and necrosis (n=2) and bilateral occipital hypodensities due to venous brain infarcts (n=1).

Of the remaining 117 patients, 39 (33%) had 1 or more of the following neurological impairments: hearing loss (n=2), chronic headache (n=34), and focal neurological signs (n=7). In the 2 patients (2%) with sensorineural hearing loss after MSS, one patient had 80-db bilateral hearing loss that required a hearing device and the other had 30-db perception loss at 250 Hz (55 db at 2000 Hz). These 2 patients were already undergoing audiologic treatment. Thirty-four patients (28%) reported chronic headaches, ranging from mild to severe. Seven patients (6%) had 1 or more of the following chronic focal neurological signs: sensory loss in 1 arm, paresis of 1 arm, paresthesia of the foot and/or hand, and resting and intention tremor of both hands. Some of these patients already had these focal neurological signs at the time of PICU discharge. In only 1 patient with focal neurological signs (sensory loss and paresis of 1 arm), neuroimaging and electroencephalography performed in the months following PICU discharge showed left cerebral hemisphere atrophy with a slow electroencephalography pattern. Statistically significant differences regarding severity of illness scores or presence of meningitis were not found between patients with and patients without hearing loss, chronic headache, or focal neurological signs.

GROWTH

Growth data of 113 patients (95%) were collected at follow-up. In 7 patients (including 5 of the 16 patients with orthopedic sequelae), anthropometric measurements were not

Table 3. Long-term Renal Function Assessment in Survivors of Meningococcal Septic Shock

	At PICU Admission			At Follow-up Visit					
								Blood Pressure, mm Hg	
Patient/Sex	Age, y	Max Creatinine, μmol/L	RRT	Age, y	Creatinine, μmol/L	GFR	Protein to Creatinine Ratio in Urine	Systolic	Diastolic
1/F[a]	13	684	Yes	25.5	61	105			
2/M	0.8	118	Yes	17	60	117	6.51	<95	<90
3/M	9	880	Yes	15	112	62	22.67	>95	>95
4/M[b]	0.7	189	Yes	10.5	28		17.18	<90	<90
5/M	4	124	No	10	52	111	11.32	<90	<90
6/M[a]	8.5	137	No	17	72	105		<90	<90
7/F	10.5	155	No	24	71	96		>95	>95
8/F	0.7	157	No	13	60	115	8.06	<90	<90
9/F	2	159	No	15.5	60	108	6.21	<90	<95
10/M	0.7	159	No	10	33	143			
11/F[a]	12.5	174	No	24.5	92	100			
12/M	1	177	No	9	39	139	13.64	<90	<95
13/F	6	189	No	21.5	69	124	54.02	<90	>95
14/F	4.5	202	No	8.5	45	124	22.22	<90	<90
15/M	13.5	243	No	26	79	158	5.52	<90	<90
16/M	3.5	267	No	8	40	130	13.27	<90	<90

Abbreviations: GFR, glomerular filtration rate; Max, maximum; PICU, pediatric intensive care unit; RRT, renal replacement therapy.
[a] Renal function assessments were performed by patient's general practitioner. Urine protein to creatinine ratio and/or blood pressure were not measured (reason unknown).
[b] The GFR could not be calculated because measurement of height was impossible owing to severe spastic quadriplegia with contractures of lower limbs.

performed for different reasons (spastic quadriplegia with contractures, extensive amputations, and severe lower-limb discrepancy). Anthropometric SD scores were similar to those found in the general population. One of the 113 patients (0.9%) had a weight-for-age SD score of −2 SDs or less, whereas 3 patients (2.7%) had length-for-age SD scores of −2 SDs or less. Univariate analysis of anthropometric SD scores in relation to age at time of PICU admission, severity of illness scores, and follow-up interval resulted in 1 significant relationship: age at time of PICU admission was significantly associated with length-for-age SD scores ($P<.01$, Spearman $r=-0.26$), indicating lower length-for-age SD scores with older age at time of PICU admission. Patients with and without orthopedic sequelae did not differ with respect to anthropometric SD scores.

RENAL FUNCTION

Of the 120 patients, 19 (16%) had temporarily developed septic shock–associated ARF during PICU admission. Four (3%) received RRT (continuous venovenous hemofiltration [n=1] and continuous venovenous hemodiafiltration [n=3]). In all 4 cases, RRT was commenced because of the development of severe acute oliguric renal failure. In these 4 patients, renal function improved and RRT was discontinued.

At the time of follow-up, we referred the 19 patients who had septic shock–associated ARF (including the 4 who received RRT) to the outpatient nephrology clinic of our hospital. Twelve of them visited our clinic, while another 4 went to their general practitioner (for practical reasons) for investigation of their present renal function (**Table 3**). The remaining 3 did not show up at the outpatient nephrology clinic (reasons unknown) or refused further investigations.

One patient (patient 3) was already under the treatment of a pediatric nephrologist since his PICU discharge because of mild chronic renal failure (GFR of 60-90 mL/min/1.73 m^2 and proteinuria). This was the only patient with impaired renal function (GFR, 62 mL/min/1.73m^2) combined with hypertension and proteinuria at the time of the study for which he was being treated with an angiotensin-converting enzyme inhibitor. His renal failure was slowly progressive since discharge from the PICU. This patient had had fulminant MSS (Pediatric Risk of Mortality Score, 30; vasopressor score, 155; disseminated intravascular coagulation score, 7; and severe ARF requiring RRT). Two patients (patients 13 and 14) had isolated proteinuria with a normal GFR. One patient (patient 7) had isolated hypertension with a normal GFR. This patient was overweight, with a body mass index of 32 (calculated as weight in kilograms divided by height in meters squared). Statistical analysis to compare severity of illness between patients with and without impaired renal function was not performed as there was only 1 patient with impaired renal function.

GENERAL HEALTH STATUS

Table 4 presents HUI2, HUI3, and visual analog scale scores in patients and the reference group. Patients had significantly lower scores on nearly all HUI2 and HUI3 attributes.

COMMENT

In patients who survived MSS in childhood, one-third showed long-term neurological impairments, ranging from mild to severe and irreversible. Patients reported poorer general health as measured by HUI2, HUI3, and the visual analog scale.

Table 4. HUI2, HUI3, and Visual Analog Scale Scores of Patients Who Had Meningococcal Septic Shock

Test	Mean (SD)		*P* Value
	Patients (n=120)	Reference Group (n=1435)	
HUI3 single-attribute utility score			
Vision	0.98 (0.10)	0.99 (0.04)	.01
Hearing	1.00 (0.0)	1.00 (0.04)	.55
Speech	0.93 (0.16)	0.97 (0.08)	.01
Ambulation	0.97 (0.15)	0.99 (0.04)	<.01
Dexterity	0.98 (0.13)	1.00 (0.02)	<.01
Emotion	0.96 (0.07)	0.98 (0.07)	<.01
Cognition	0.90 (0.21)	0.97 (0.09)	<.01
Pain	0.94 (0.13)	0.98 (0.08)	<.01
HUI3 multi-attribute utility score	0.82 (0.25)	0.93 (0.12)	<.01
HUI2 single-attribute utility score			
Sensation	0.90 (0.18)	0.95 (0.12)	<.01
Mobility	0.97 (0.15)	1.00 (0.03)	<.01
Emotion	0.95 (0.10)	0.97 (0.08)	<.05
Cognitive	0.93 (0.16)	0.98 (0.06)	<.01
Self-care	0.97 (0.16)	0.99 (0.06)	.41
Pain	0.96 (0.09)	0.99 (0.05)	<.01
HUI2 multi-attribute utility score	0.88 (0.16)	0.94 (0.09)	<.01
Visual analog scale, overall health	85.4 (15.3)	92.7 (9.2)	<.01

Abbreviations: HUI2, Health Utilities Index Mark 2; HUI3, Health Utilities Index Mark 3.

HEALTH CONSEQUENCES

Four patients developed severe and irreversible neurological damage (2 died several years after MSS). This was probably due to the severity of the shock (as expressed by their young age, high severity of illness scores, and hypoglycemia), leading to brain ischemia or infarcts. Another cause could have been prolonged convulsions, probably caused by brain ischemia and/or hypoglycemia.

The incidence of hearing loss was low (2%) and this is comparable with findings from the study by Koomen et al,[26] who found that the incidence of hearing loss after meningococcal meningitis was 4%. Although our study focused on patients with MSS, most of our patients (83%) were also found to have meningitis (*N meningitidis* cultured in liquor and/or pleocytosis) when a lumbar puncture was performed. It should, however, be noted that in nearly half of the patients, especially patients admitted more recently, a lumbar puncture was not performed because of the possible adverse effects (further compromise of the hemodynamics, bleeding, or cerebral edema with herniation). Although both patients with hearing loss had meningitis, significant differences regarding presence of meningitis were not found between patients with and patients without hearing loss.

A notable result was that nearly one-third of the patients reported chronic headache. Causes of chronic headache in patients after MSS could be tension-type headache (eg, in patients with cognitive dysfunction) or chronic hydrocephalus due to meningitis. The focal neurological signs in the extremities, reported by few patients (6%), could be due to venous cortical brain infarcts or brain atrophy.

Headache and focal neurological deficits have previously been described in survivors of bacterial meningitis.[27,28] In our study, however, significant differences regarding presence of meningitis were not found between patients with and patients without chronic headache or focal neurological signs.

GROWTH

In MSS survivors, growth did not seem impaired since the percentages of SD scores of –2 SDs or less were in line with the normal population (2.5%). Although older age at time of PICU admission was significantly associated with lower length-for-age SD score, we do not think that this finding is clinically significant. Interestingly, we did not find growth abnormalities in patients with orthopedic sequelae. It should be noted, however, that in patients with the greatest disabilities, we were not able to perform anthropometric measurements.

RENAL FUNCTION

One of the 16 examined patients (6%) with septic shock–associated ARF (1 of 4 patients [25%] necessitating RRT) showed signs of persistent kidney damage, manifested as mild chronic renal failure, proteinuria, and hypertension. His renal failure may progress further with age, possibly necessitating long-term dialysis or renal transplantation in the future. The incidence of long-term impaired renal function in our patients, as measured by estimated GFR, is in line with findings from the study by Slack et al.[3] They reported mild to moderate reduction of estimated GFR in 25% of patients 4 years after meningococcal sepsis–associated ARF that necessitated RRT.

Proteinuria after MSS may reflect the loss of a considerable amount of glomeruli owing to septic shock–associated acute tubular necrosis. Though the GFR may, by hyperfiltration of the remaining glomeruli, be normal at the time of measurement, it could decline over time if the proteinuria is left untreated. Therefore, patients with proteinuria and normal GFRs should have periodic checkups of their GFR, proteinuria, and blood pressure.

GENERAL HEALTH STATUS

Patients showed lower health statuses in all HUI2 and HUI3 attributes (except HUI3 hearing and HUI2 self-care) and the visual analog scale, indicating that their present general health statuses were perceived as relatively poor. In our previous study, we found significantly poorer health-related quality of life scores, mainly on physical domains (like general health perception), in MSS survivors compared with normative data.[29] This could indicate that the patients' episodes with MSS and present health status had a negative effect on their present physical health–related quality of life. Furthermore, the lower scores in HUI2 and HUI3 cognition attributes and in the HUI3 speech attribute were in line with earlier findings, in which poorer outcomes on intellectual functioning were found in children who survived invasive meningococcal disease.[30] Surprisingly, lower scores were reported on the HUI3 vision attribute (indicating that patients could not see well enough to read ordinary print or recognize people from a distance), though patients did not report this problem during the medical interview.

STUDY STRENGTHS AND LIMITATIONS

A unique feature of this study is its homogeneous patient sample and long-term investigation. Standardized assessment procedures were used.

Several limitations of our study should be acknowledged. This is an observational study (no controls) from 1 center. The response rate was satisfactory, though not high (71%). However, we think that this may not have influenced the results because participating patients and nonparticipants did not differ with respect to age at time of PICU admission or severity of illness.

Assessments of health status and HUI2, HUI3, and visual analog scale scores before MSS were not available. The HUI2, HUI3, and visual analog scale scores were elicited by parental report if the patient was aged younger than 18 years and in patients aged 18 years or older by self-report; they were compared with normative data derived from parental reports in a general Dutch population sample (aged 5-13 years). Dutch normative self-report data are not yet available. It could be interesting to compare our group with patients, matched on age and timing of follow-up interval, who were admitted to the hospital or PICU because of another disease.

CONCLUSIONS

If the incidence of chronic headache, assessed with a validated headache questionnaire, remains high, predictors should be identified. Some careful recommendations can be made regarding long-term renal function assessment. In our opinion, MSS survivors with septic shock–associated ARF, especially those necessitating RRT, should undergo periodic measurements of blood pressure, serum creatinine with calculation of estimated GFR, and urine protein to creatinine ratio. In light of the relatively poor scores found on HUI2 and HUI3 attributes, standard assessment of vision, emotional distress, and neuropsychological and cognitive functioning is warranted in MSS survivors to intervene in an early phase after the MSS.

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