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Epidemiology, recognition and documentation of sepsis in the pre-hospital setting and associated clinical outcomes: a prospective multicenter study

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Abstract

Introduction: General practitioners (GPs) and the emergency medical services (EMS) personnel have a pivotal role as points of entry into the acute care chain. This study was conducted to investigate the recognition of sepsis by GPs and EMS personnel and to evaluate the associations between recognition of sepsis in the pre-hospital setting and patient outcomes.

Methods

Design: prospective, observational study during a 12 week period in the emergency department (ED) of two academic hospitals.

Study population: Patients >18 years presenting with sepsis at the ED. The information available in the ED discharge letter and the ED charts was used to make a definite diagnosis of sepsis, severe sepsis and septic shock

Outcome measures: primary: recognition/documentation of sepsis. Secondary: ED arrival time to antibiotic administration, in-hospital mortality, hospital length of stay (LOS) and intensive care unit (ICU) admission.

Results: A total of 301 patients were included in the study. GPs and EMS personnel correctly identified and documented 31.6% (n=114) and 41.4% of all sepsis patients (n=140) respectively. Recognition and documentation of sepsis improved with increasing severity. The mean time to administration of antibiotics (TTA) was nearly halved for the group of patients where sepsis was documented (GP: 66,4 minutes, EMS: 65,6 minutes) compared to the group in which sepsis was not documented (GP: 123,9 minutes, EMS: 101,5 minutes; p= 0.365 and p= 0.024 respectively).

Conclusions

There is room for improvement in the recognition of sepsis, severe sepsis and septic shock by practitioners working in the pre-hospital setting. Documentation of sepsis prior to arrival in hospital led to a reduced time delay in administration of antibiotics.

Keywords

sepsis, recognition, prehospital, general practitioner, emergency medical services

Key points

- Improved pre-hospital recognition and documentation of sepsis leads to shorter time to administration of antibiotics

Introduction**Background**

Sepsis is a medical emergency that poses a heavy burden on the health care system. The incidence of sepsis is rising worldwide, with an average of 56 to 91 cases per 100 000 individuals¹ and with reported mortality rates ranging from 15% to 80% depending on the severity of the illness.²⁻⁴ Until recently, sepsis was defined by signs of infection together with a generalized inflammatory reaction, the systemic inflammatory response syndrome (SIRS). Timely recognition of sepsis is of great importance as this contributes to a faster and targeted treatment, thereby preventing progression towards severe sepsis

or septic shock with multi-organ failure, which is associated with a high mortality and morbidity.^{5,6} Furthermore, providing timely treatment is associated with a shorter length of stay (LOS) in the hospital and a decrease in health care costs.^{6,7}

Importance

More than half of patients with sepsis are transported by emergency medical services (EMS) and many are primarily evaluated by general practitioners (GP).⁸ Early recognition and initiation of treatment by the EMS personnel can lead to a significant decrease in time of initiating targeted therapy at the emergency department (ED).^{5,6} Handover and collaboration between healthcare providers (pre-hospital to

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hospital) has been shown to improve patient safety.⁹⁻¹⁶ However, it is known that the recognition and documentation of sepsis by EMS personnel and hospital physicians is poor.^{3,8,17}

Goals of this investigation

This study aimed:

1. to investigate the ability of GPs and EMS personnel to recognize sepsis
2. to investigate if there is an association between recognition and documentation of sepsis and patient outcomes,

Methods

Study design and setting

A prospective observational study was performed during a 12 week period between 30th June 2014 and 21st September 2014 at the ED of two tertiary care hospitals in Amsterdam: VU University Medical Centre and Academic Medical Centre. Both of these centres receive approximately 30.000 ED visits per year. This study was approved by the medical ethical committee of both hospitals.

Selection of participants

Patients presenting at the ED during the 12 week study period were screened by assessing the initial diagnosis at ED presentation for eligibility. If infection was suspected at presentation, the ED chart and ED discharge letter were reviewed to confirm the diagnosis and assess eligibility. Eligible patients were adults (aged 18 years or older), presenting at the ED and meeting the international criteria for the definition of sepsis, severe sepsis or septic shock.¹⁸

Patients were included if the diagnosis sepsis was specifically documented in the ED discharge letter, or if the diagnosis sepsis could be made based on the documented patient history, physical examination and other relevant diagnostic tests in the ED charts. The research team consisting of two experienced acute physicians (each with more than 10 year experience in acute medicine) and two young doctors with experience in internal medicine made the final diagnosis based on the above mentioned documents. Patients were excluded if one of the following was applied: 1) no suspected infection present in ED letter and the ED charts 2) less than two positive SIRS criteria, 3) sterile inflammation (e.g. pancreatitis), or 4) presenting to the ED within 28 days with the same diagnosis.

Methods

Data were extracted from patient medical records being either 1) GP referral letters, 2) EMS forms, and 3) inpatient medical records (including ED

charts). A patient database was constructed and the following data was collected: demographic data, comorbidity, means of transportation and urgency of transportation (if applicable), triage level at ED presentation, National Early Warning Score (NEWS)¹⁹ at ED presentation, documentation of vital parameters (the SIRS criteria), laboratory values, diagnostic procedures, treatment data and microbiologic data.

The primary outcome was the correct recognition and thereafter documentation (see below for definition) of sepsis, severe sepsis and septic shock by the GP and EMS personnel compared to the diagnosis made in the ED. The secondary outcome parameters were: in-hospital mortality, hospital LOS, intensive care unit (ICU) admission and LOS, time to antibiotics (TTA) and the severity of sepsis.

Definitions

The following definitions were used in order to categorize recognition and documentation of sepsis in the handovers from the GPs and EMS personnel:

- Documentation:

- a. *Complete*: documentation of suspected infection and at least two or more SIRS criteria. The term sepsis did not necessarily have to be documented as a preliminary diagnosis.
- b. *Suboptimal*: documentation of suspected infection OR two or more SIRS criteria
- c. *Inaccurate*: no documentation of suspected infection, and no documentation of more than 2 SIRS criteria.

- Recognition (= same as complete documentation): documentation of suspected infection and at least two or more SIRS criteria. If there was complete documentation, sepsis was presumed to be recognized.

A complete documentation of the vital signs needed to diagnose a sepsis patient was defined as 'documented suspected infection together with all of the SIRS criteria': respiratory rate (RR), heart rate (HR) and temperature. This was a pragmatic approach as diagnostic instruments to measure white blood cell count are unavailable in the pre-hospital setting. We defined an incomplete documentation when two, or less than two SIRS criteria were documented.

Statistical analysis

For data collection and analysis SPSS (IBM SPSS Statistics 20.0) was used. Population characteristics were summarized into descriptive statistics (mean and standard deviation $\pm$ SD). To compare categorical data, Chi-square tests or Fisher's exact test were used. When differences in between groups were to

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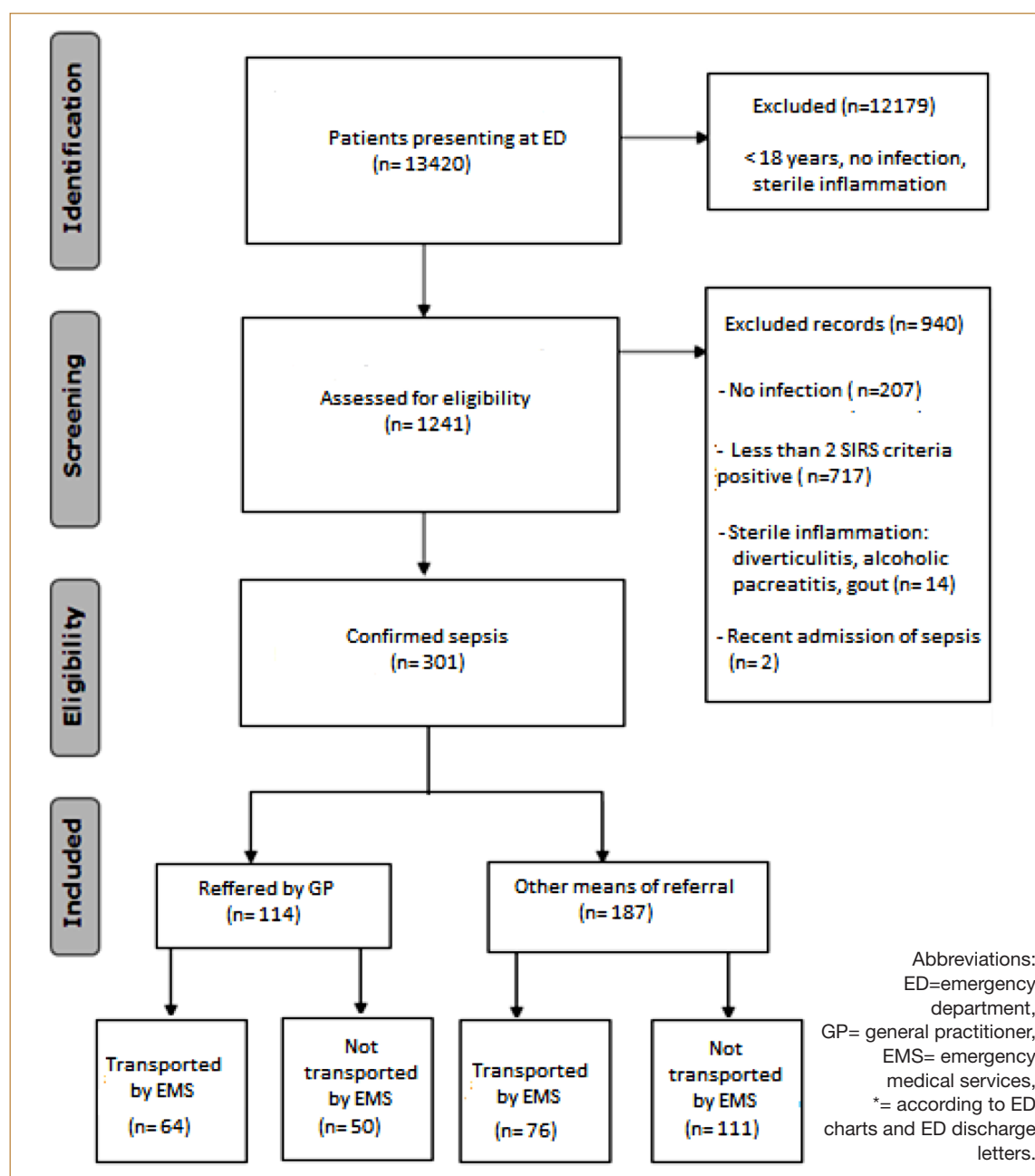


Figure 1. Flowchart of study population

be evaluated, one-way ANOVA tests were used; $p < 0.05$ was considered to be statistically significant.

Results

Characteristics of study subjects

Of the 13420 patients who presented at the ED during the study period, a total of 1241 patients were screened for eligibility (figure 1). A total of 301 patients fulfilled the inclusion criteria. The remaining 940 patients were excluded due to following reasons: 207 (22%) had no infection according to the ED charts and ED discharge letters,

717 (76.3%) did have an infection but with less than two positive SIRS criteria, 14 (1.5%) had a sterile inflammation and 2 (0.2%) patients were excluded due to recent admission with the same diagnosis. Patient characteristics are summarized in table 1.

Means of transport and urgency EMS transport

Patients who were transported by EMS after being referred by the GP, were transported with the highest urgency (A1- transport) of ambulance transportation in 56.8% ($n=29$). Triage was performed by the EMS personnel (Supplementary table 1a and 1b). The remaining patients (43.2%; $n=22$) were considered

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Table 1. Baseline characteristics of patients

n (%) ^a	All patients (n= 301)	Patients referred by GP (n= 114)	Other modes of referral (n= 187)
Age, mean (SD), y	59.6(18.9)	63.9 (19.3)	56.9 (18.2)
Gender (% male)	168 (55.8)	56 (49.1)	112 (59.9)
Any co-existing conditions (%)	248 (82.4)	94 (82.5)	154 (82.4)
History of cancer	104 (34.6)	35 (30.7)	69 (36.9)
Hypertension	88 (29.2)	36 (31.6)	52 (27.8)
Coronary heart disease	60 (19.9)	22 (19.3)	38 (20.3)
Chronic heart failure	46 (15.3)	17 (14.9)	29 (15.5)
Diabetes mellitus	42 (14.0)	16 (14)	26 (13.9)
Neurological diseases	50 (16.6)	25 (21.9)	25 (13.4)
Chronic renal disease	51 (16.9)	19 (16.7)	32 (17.1)
Chronic obstructive pulmonary disease	53 (17.6)	17 (14.9)	36 (19.3)
Liver disease	23 (7.6)	7 (6.1)	16 (8.6)
HIV/Aids	5 (1.7)	2 (1.8)	3 (1.6)
Use of immunosuppressant	11 (3.7)	4 (3.5)	7 (3.7)
Use of antibiotics	50 (16.6)	21 (18.4)	29 (15.5)
Absent or dysfunctional spleen	1 (0.3)	0 (0)	1 (0.5)
Morbid obesity	5 (1.7)	1 (0.9)	4 (2.1)
Other co-existing conditions than mentioned above	103 (34.2)	44 (38.6)	59 (31.6)
Urgency ambulance ride ^b			
A1	71 (23.6)	32 (28.1)	39 (20.9)
A2	30 (10.0)	16 (14.0)	14 (7.5)
B	15 (5.0)	6 (5.3)	9 (4.8)
Missing information or not with ambulance	185 (61.5)	60 (52.6)	125 (66.8)
ED triage ^c			
ESI- 1	11 (3.7)	3 (2.6)	8 (4.3)
ESI- 2	55 (18.3)	25 (21.9)	30 (16.2)
ESI- 3	206 (68.4)	74 (64.9)	132 (70.6)
ESI- 4	25 (8.3)	10 (8.8)	15 (8.0)
ESI- 5	0 (0.0)	0 (0.0)	0 (0.0)
Missing information	4 (1.3)	2 (1.8)	2 (1.1)

a =values are numbers (percentages), unless otherwise indicated; b=A1:highest urgency. A2 average urgency. B lowest urgency; c= Urgency to see a doctor at ED; “-” indicating unknown values. Abbreviations: GP=general practitioner, SD=standard deviation ED= emergency department

less urgent (A2- and B-transport), while 22.2 % (n=5) of these patients had septic shock. The percentages are similar for patients transported by ambulance, who were not referred by the GP: 63.3% (n=38) were transported with the highest urgency, while 36.7% (n=20) were considered less urgent, of which 30% (n=6) had septic shock.

Primary outcome:

documentation and recognition of sepsis

The documentation in the referral letter of the GP was complete in 31.6% (n=36), suboptimal in 28.1% (n= 32) and inaccurate in 10.5% (n=12) of the cases (table 2). For the EMS personnel this was 41.4% (n=58), 21.4 (n=30) and 8.6% (n=12). The GPs did

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Table 2. Primary Outcomes: documentation and recognition of sepsis

n (%) ^a	All patients (n=301)	Total patients referred by GP (n=114)	Total patients with ambulance (n=140)	GP with ambulance (n =64)	GP without ambulance (n= 50)	Other referral way with ambulance (n= 76)	Other referral way without ambulance (n= 111)
Accurateness of documentation and recognition							
Complete documentation	285 (94.7)	36 (31.6)	58 (41.4)	22 (34.4)	14 (28.0)	36 (47.4)	107 (96.4)
Suboptimal documentation	11 (3.7)	32 (28.1)	30 (21.4)	16 (25.0)	16 (32.0)	14 (18.4)	2 (1.8)
Inaccurate documentation	2 (0.7)	12 (10.5)	12 (8.6)	4 (6.3)	8 (16.0)	8 (10.5)	1 (0.9)
No referral letter present	3 (1.0)	34 (29.8)	40 (28.6)	22 (34.4)	12 (24.0)	18 (23.7)	1 (0.9)
Preliminary diagnosis sepsis documented ^b	67 (22.3)	14 (12.3)	29 (20.7)	13 (20.3)	1 (2.0)	16 (21.1)	15 (13.5)
Complete documentation of relevant vital parameters	184 (61.1)	22 (19.3%)	62 (44.3%)	16 (25.0)	6 (12.0)	46 (60.5)	58 (52.3)
Variables documented in primary survey							
Respiratory rate	194 (64.5)	27 (23.7)	79 (56.4)	20 (31.3)	7 (14.0)	43 (56.6)	58 (52.3)
Oxygen saturation	272 (90.4)	43 (37.7)	89 (63.6)	26 (40.6)	17 (34.0)	48 (63.2)	99 (89.2)
Blood pressure	290 (96.3)	113 (99.1)	93 (66.4)	34 (53.1)	22 (44.0)	57 (75.0)	107 (96.4)
Heart rate	291 (96.7)	58 (50.9)	99 (70.7)	35 (54.7)	22 (44.0)	55 (72.4)	110 (99.1)
Body temperature	295 (98.0)	65 (57.0)	139 (99.3)	39 (60.9)	28 (56.0)	44 (57.9)	110 (99.1)
Suspected infection	301 (100)	74 (64.9)	81 (57.9)	37 (57.8)	30 (60.0)	42 (55.3)	109 (98.2)

a =values are numbers (percentages). unless otherwise indicated; b =working diagnosis sepsis

not send a referral letter in 29.8 % (n=34) of the patients they referred and the EMS personnel did not provide an EMS form in 28.6% (n=40). However, when a referral letter was present, the GP or EMS personnel did document suspicion of infection in almost half of the cases (respectively 41.2% (n=47) and 43.6% (n=61)).

The diagnosis of sepsis, severe sepsis and septic shock were documented almost twice as often in the EMS forms (20.7%; n= 29) as compared to the GP referral letters (12.3%; n=14). Complete documentation was considered as correct recognition. An association of improved recognition of sepsis with increasing severity was seen at the GP (p-value=<0.0001) and the ambulance staff (p-value=0.034).

A complete documentation of the relevant vital parameters was present in 19.3% (n=22) of the GP

referral letters versus 44.3% (n=62) of the EMS forms. The least documented vital parameter by the GP and the EMS personnel was the respiratory rate, respectively in 23.7% (n=27) and 45% (n=63), followed by the oxygen saturation; 37.7% (n=43) at the GPs and 52.9% by the EMS.

Secondary patient related outcomes

The majority of all patients included in this study had sepsis (70.1%, n=211), followed by septic shock; (20.9%, n=63) and severe sepsis (4.3%, n=13). Of the remaining patients (5%, n= 15) there was either insufficient information to categorize the severity of sepsis (n=9) or the eventual diagnosis was not sepsis (n= 6) based on the hospital discharge letter. The in-hospital mortality was 5.0%, with a mean age at the time of death of 71.8 ± 15.0 years. The hospital admission rate was 78.4 % (n=236), with a mean

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Table 3. Secondary patient outcomes by mode of referral and means of transport

Mode of referral and means of transport n (%) ^a	All patients (n=301)	Total patients referred by GP (n=114)	Total patients with ambulance (n=140)	GP with ambulance (n =64)	GP without ambulance (n= 50)	Other referral way with ambulance (n= 76)	Other referral way without ambulance (n= 111)
Severity of sepsis							
Sepsis	211 (70.1)	82 (71.9)	78 (55.7)	40 (62.5)	42 (84.0)	38 (50.0)	90 (81.1.)
Severe sepsis	13 (4.3)	6 (5.3)	12 (8.6)	6 (9.4)	0 (0.0)	6 (7.9)	1 (0.9)
Septic shock	63 (20.9)	20 (17.5)	40 (28.6)	14 (21.9)	6.0 (12.0)	26 (34.2)	17 (15.3)
No sepsis	5 (1.7)	3 (2.6)	4 (2.9)	2 (3.1)	1 (2.0)	2 (2.6)	1 (0.9)
Insufficient information	9 (3)	3 (2.6)	6 (4.3)	2 (3.1)	1 (2.0)	4 (5.3)	2 (1.8)
NEWS score mean, (SD)	6 (3.1)	5.7 (3.1)	7.2 (3.1)	6.8 (2.9)	4.2 (2.9)	7.6 (3.42)	5.0 (2.3)
Number of hospital admissions	236 (78.4)	91 (79.8)	131 (93.6)	61 (95.3)	30 (60.0)	70 (92.1)	75 (67.6)
Length of hospital stay, days (SD) ^b	6.3 (9.1)	6.2 (8.5)	8.6 (10.7)	7.9 (8.6)	4.2 (8.0)	9.1 (12.2)	4.4 (6.3)
Number of ICU admissions	31 (10.3)	11 (9.6)	25 (17.9)	7 (10.9)	4 (8.0)	18 (23.7)	2 (1.8)
Length of stay at ICU. days (SD) ^b	6.9 (11.8)	5.8 (5.2)	7.4 (13.0)	5.5 (5.2)	6.3 (6.0)	8 (14.8)	2 (1.4)
Mortality	15 (5.0)	8 (7.0)	10 (7.1)	5 (7.8)	3 (6.0)	5 (6.6)	2 (1.8)
TTA, mean (SD)	117.4 (93.5)	115.9 (100.2)	103.7 (90.6)	97.1 (88.3) ^c	159 (114.8)	108.6 (92.8)	130.4 (85.8)

a=values are numbers (percentages). unless otherwise indicated; b=Days; c=n= 39/64 time to antibiotics was available. Abbreviations: GP=general practitioner, SD; Standard Deviation, NEWS=national early warning score, ICU=intensive care unit, TTA= time to antibiotics

length of hospital stay of 6.3 days (SD 9.09), (table 4). Whereas 31 patients (10.3%) were admitted to the ICU with a mean duration of ICU stay of 6.9 days.

The mean TTA was 117.4 ($\pm$ SD 93.51) minutes for all patients. Patients who were transferred by the EMS, with or without GP referral, had a shorter TTA than patients who came by other means of transport (table 3). The mean TTA was nearly half the time for the group of patients where sepsis was documented (GP: 66.4 minutes (n=14), EMS: 65.6 minutes (n=29)) compared to the group in which sepsis was not documented (GP: 123.9 minutes (n=100), EMS: 101.5 minutes (n=111)). The p-values were respectively: p= 0.365 and p= 0.024.

An association between TTA and length of hospital stay was present, although the association was not significant (p=0.453). In contrast, there was no association between TTA and mortality. Patients who died during admission did not have a significantly longer TTA (mean: 111.46 minutes $\pm$ 115.92) compared to patients that did not die (mean: 118.21 minutes $\pm$ 90.76).

Discussion

To the best of our knowledge, this study is also the first to evaluate the association between recognition and documentation of sepsis in pre-hospital setting and patient outcomes.

The results of this study have demonstrated that there is room for improvement in the recognition and documentation of sepsis amongst EMS personnel and GPs in the Amsterdam region of the Netherlands. In addition, the documentation of severity of sepsis, as well as the documentation of relevant vital signs to diagnose a septic patient was often incomplete. Some patients with septic shock were transported by the EMS to the ED with a low urgency, which may have contributed to delays in initiation of antibiotic treatment.

Time to administration of antibiotics after arrival in hospital almost halved for the group of patients where sepsis was documented by the GPs and EMS staff compared to the group where documentation was inaccurate. A non-significant trend towards improved patient outcomes was noted when documentation and recognition of sepsis were better.

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The levels of recognition and documentation of sepsis may have been influenced by lack of awareness of the importance of timely recognition of this syndrome and documentation of the primary survey. It was encouraging to note that recognition and documentation of sepsis by EMS personnel in our study was improved in comparison to previous studies (41.4% vs. 13.7%).^{8,20} The ongoing PHANTASi trial²¹ may have contributed to this improvement. This study is investigating the effects of training EMS personnel in recognizing and initiating treatment in the pre-hospital setting, together with early administration of antibiotics for patients suspected of (severe) sepsis and septic shock. This trial commenced a year prior to our present study and may have had a positive effect by increasing the awareness of sepsis amongst EMS personnel.

In our study, the documentation of sepsis was assessed by collecting information solely from medical records. This could have resulted in the exclusion of valuable information which may have been communicated verbally by GPs and EMS personnel to the ED, leading to an underestimation of the actual recognition of sepsis by the GP and EMS personnel.

Overall, vital parameters were better documented in the ED (results not shown) than by EMS personnel or the GP, which is in accordance with previous studies.^{8,22} Of all vital parameters, the respiratory rate was the least documented parameter in all three settings (GP, ambulance, ED), while this is one of the most informative, and therefore most important, vital parameter to measure. This is due to the fact that even subtle changes in the hemodynamic stability provide a change in respiratory rate and it is commensurately correlated with the mortality.²³

The observed reduction in the TTA, when the diagnosis sepsis was documented, is in concordance with previous studies.^{3,5,24} In addition, a shorter TTA was associated with a shorter hospital LOS. However, there was no association between TTA and in-hospital mortality.

The epidemiology and infection characteristics observed in this study correspond with those observed in various studies. Hospital LOS, as well as the length of ICU stay, was shorter in this study compared to several other studies performed in patients with sepsis, severe sepsis and septic shock.^{3,25-40} However, there has been trend towards shorter hospital LOS in all in hospital patients compared to previous years.⁴⁰ The percentage of ICU admissions and in-hospital mortality was lower than in other studies.^{27,33,39} This could be attributed to the smaller number of severely ill patients in this study, which was conducted at the ED, whilst most other studies were performed on ICUs with a larger proportion of severely ill patients.

Early recognition and rapid treatment of sepsis is important to achieve better patient outcomes, such as a reduced mortality rate, length of hospital admission and reduction in ICU admissions. It is known that better recognition and documentation in pre-hospital setting lead to faster and better treatment in the hospital. Recently, the Third International Consensus Definitions for Sepsis and Septic Shock recommended that an adapted for of the Sequential(sepsis-related) Organ Failure Assessment (SOFA) score, the so-called quickSOFA (qSOFA),⁴¹ can be used as a simple prompt to identify infected patients outside the intensive care who are likely to be septic. Although not validated in the pre-hospital setting, this is an easy to use score, which has the potential to improve the ability of healthcare providers to correctly recognize patients with sepsis or at risk of developing sepsis. Studies to validate q-SOFA in the pre-hospital setting are needed to determine whether this can be used to improve recognition and timely treatment of sepsis.

Conflict of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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