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Hospital discharge diagnoses in patients with positive blood cultures in an Italian academic hospital

Francesca Valent[1], Laura Deroma[2], Roberto Cocconi[2], Alessia Picierno[3] and Assunta Sartor[3]

[1]*SOC Istituto di Igiene ed Epidemiologia Clinica, Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy*
[2]*SOC Direzione Medica di Presidio, Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy*
[3]*SOC Microbiologia, Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy*

Abstract

Objective. To assess the sensitivity of hospital discharge diagnoses for identifying sepsis in patients with blood culture confirmation.

Methods. A cross-sectional study was conducted at the Italian 1000-bed University Hospital of Udine. The administrative databases of the Hospital were used as the source of information. Laboratory data were linked with hospital discharge data. We estimated the proportion of hospitalizations with at least 2 positive blood culture tests in which at least one discharge diagnosis indicated bloodstream infection.

Results. From 2011 to 2017, 3571 hospitalizations (1.2%) had positive blood culture tests. Of them, only 49.5% had at least one ICD-9-CM discharge diagnosis code of sepsis, with lower proportions in surgical than in medical wards.

Conclusions. The sensitivity of ICD-9-CM discharge codes for sepsis is low as compared with the blood culture gold standard. Using discharge codes for epidemiological estimates of sepsis, health planning and risk management may yield biased results. Audits and ICD coding training are needed.

Key words

- χ^2 test
- hospital discharge records
- discharge diagnosis
- sepsis
- blood culture
- sensitivity

INTRODUCTION

Sepsis is a severe and costly condition, whose incidence has been shown to be increasing by several studies in the USA [1] and in Europe [2].

However, the epidemiology of sepsis has often been studied using discharge diagnosis codes [1, 2], whose accuracy is controversial. In fact, sepsis definitions based on clinical data have been shown to have greater sensitivity for identifying hospitalizations with severe sepsis than methods based on claims data [3]. In addition, the use of "explicit" sepsis coding (i.e., ICD-9-CM codes 995.92 for severe sepsis or 785.52 for septic shock) seems to be more common in cases characterized by greater severity, care intensity and in-hospital mortality [4].

Some studies have validated discharge diagnoses against laboratory findings, estimating the positive predictive value (PPV) of selected discharge diagnosis codes. For example, in Denmark, hospital discharge records reporting ICD-10 codes for Gram-negative septicemia/sepsis and urosepsis were compared with Gram-negative bacteremia according to blood culture results obtained from the laboratory information system: the ICD-10 code A41.5 was quite accurate, whereas the A41.9B was not [5]. In the USA, the PPV of ICD-9 codes against laboratory values from medical records varied between 66 and 100% depending on the discharge diagnosis [6]. Those studies, however, did not estimate the sensitivity of discharge diagnoses to identify patients with a laboratory-confirmed blood infection. Another study estimated both sensitivity and PPV of Methicillin-resistant Staphylococcus aureus (MRSA)-specific hospital discharge codes using laboratory-confirmed infection as the gold standard in an American children's hospital and found low sensitivity and low PPV, concluding that pediatric MRSA bloodstream infections will be underestimated if only those discharge codes are used to identify cases [7]. Another study validated ICD administrative data for sepsis identification in Canada using medical charts and clinical diagnostic criteria as the gold standard; the authors could identify ICD-10-CA codes that optimized the performance of coded information both among intensive care unit (ICU) patients and among non-ICU patients, increasing sensitivity while slightly decreasing specificity and PPV. Nonetheless, sepsis still resulted undercoded [8].

Address for correspondence: Francesca Valent, SOC Istituto di Igiene ed Epidemiologia Clinica, Azienda Sanitaria Universitaria Integrata di Udine Pad. 16, Via Colugna 50, 33100 Udine, Italy. E- mail: francesca.valent@asuiud.sanita.fvg.it.

In Italy, the validity of hospital discharge diagnosis codes for identifying cases of sepsis has never been assessed. In the University Hospital of Udine, North-East of Italy, a health information system including both hospital discharge records and laboratory values is available.

The main objective of this study was to assess the sensitivity of hospital discharge diagnoses to identify sepsis in patients with blood culture confirmation, analyzing the administrative data of the health information system of the University Hospital of Udine. Secondary objectives were to describe characteristics of cases where discharge diagnoses failed to identify blood-culture-confirmed sepsis and to assess the frequency of sepsis-related discharge diagnoses in hospitalizations with no blood culture confirmation.

MATERIALS AND METHODS

This cross-sectional study was conducted at the University Hospital of Udine, a 1000-bed academic hospital located in the North-East of Italy and serving a population of more than 250 000 inhabitants. The administrative databases of the Hospital health information system were used as the source of information. All databases included in the health information system are completely anonymous; however, they can be linked with each other at the individual patient level through an anonymous stochastic key which is univocal for each subject across databases.

In particular, we analyzed data on all the blood culture tests processed by the Hospital Microbiology Laboratory from 2011 (the first year with complete laboratory data on blood culture tests) to 2017. The detail on the pathogens isolated from the blood and antibiograms, however, have only been available in the Hospital health information system since 2014.

A blood culture test was considered certainly positive if at least 2 aerobic or anaerobic bottles of blood drawn on the same occasion turned out positive. Tests with only one positive bottle might depend on contaminations. For each patient with blood cultures, we linked positive tests with data regarding the hospitalization during which the blood cultures were collected. Laboratory data were linked with hospital discharge data at the individual patient level through the anonymous stochastic key and through the date of blood collection, which had to be between the hospital admission and discharge dates.

We then analyzed the discharge diagnoses of all hospitalizations during which patients had positive culture tests. In Italy, up to 6 discharge diagnoses could be recorded. They are coded according to the ICD-9-CM. All 6 diagnoses were considered to assess whether sepsis had been recorded in the hospital discharge data. We considered as suggestive of sepsis any of the following ICD-9-CM codes, also used by Bouza *et al*. [2, 4] for bacterial or candida sepsis: 790.7 (bacteremia), 038.xx (septicemia), 995.91 (sepsis), 995.92 (severe sepsis), 785.52 (septic shock), 771.81 (septicemia [sepsis] of newborn), 421 (acute and subacute endocarditis), 003.1 (salmonella septicemia), 020.2 (septicemic plague), 036.2 (meningococcemia), 098.89 (gonococcemia), 112.5 (systemic candidiasis), 112.81 (candida endocarditis).

We assessed the proportion of hospitalizations with positive blood culture tests in which at least one discharge diagnosis corresponded to one of the above-listed codes, overall and stratified by calendar year, by discharge hospital unit (surgical *vs* medical ward), by hospitalization outcome (in-hospital death vs other), and by intensive care unit (ICU) stay during the hospitalization (yes *vs* no). The statistical significance of trends was assessed through the Cochran-Armitage test. The statistical significance of differences among years or units was assessed through the $\chi 2$ test. P-values < 0.05 were considered statistically significant.

We also investigated whether patient's demographic characteristics (age and sex) affected the likelihood of having sepsis coded among the discharge diagnoses through multivariate logistic regression analyses mutually adjusting for sex, age category (0-14, 15-64, 65-79, ≥ 80 years), type of ward of discharge (surgical *vs* medical) and calendar year. Odds Ratios (OR) and 95% Confidence Intervals were calculated.

For hospitalizations with positive blood culture tests but no discharge diagnoses suggestive for sepsis, we described the number of diagnoses that were recorded in the hospital discharge record and the main discharge diagnoses.

Then, we assessed the frequency of sepsis discharge diagnosis codes in cases with no laboratory-confirmed sepsis (i.e. no blood cultures, negative tests, or tests with only one positive bottle). Sensitivity, specificity, PPV and negative predictive value (NPV) of ICD-9 codes were estimated, using either laboratory-confirmed bloodstream infections (≥ 2 positive aerobic or anaerobic bottles) or tests with only 1 positive bottle as the gold standard.

Finally, to assess whether the sensitivity of hospital discharge diagnoses differed according to the pathogens isolated from the blood, we assessed the frequency of sepsis discharge diagnosis codes stratified by genera of the pathogens, for all patients with positive blood culture tests hospitalized from 2014 to 2017. In addition, to assess whether the sensitivity of hospital discharge diagnoses could be affected by antibiograms showing antimicrobial resistance, we analyzed the case of Klebsiella pneumonia and compared the sensitivity in case of isolation of Carbapenem-resistant strains (CRKP) with the sensitivity in case of Carbapenem-sensitive strains from 2014 to 2017, when antibiograms were available for analysis.

All the analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC, USA).

This article does not contain any studies with human or animal subjects performed by any of the authors. Since this analysis was based on anonymous administrative data, patient informed consent and Ethical Committee approval were not required in Italy.

RESULTS

From 2011 to 2017, blood cultures were obtained in 27 919 patients hospitalized at the University Hospital of Udine (9.3% of all hospitalizations), totaling 44 533

Table 1
Number and proportion of hospitalizations with positive blood culture test (≥ 2 positive aerobic or 2 anaerobic bottles), University Hospital of Udine, North-Eastern Italy, 2011-2017

Year	Total hospitalizations	Hospitalizations with positive blood culture tests	Hospitalizations with discharge diagnosis suggestive of sepsis
2011	45 224	428 (0.9%)	196 (45.8%)
2012	44 568	453 (1.0%)	218 (48.1%)
2013	43 526	459 (1.0%)	229 (49.9%)
2014	41 795	499 (1.2%)	253 (50.7%)
2015	41 440	549 (1.3%)	292 (53.4%)
2016	41 488	586 (1.4%)	301 (51.4%)
2017	41 671	597 (1.4%)	280 (46.9%)

blood culture tests. In 74.9% of cases, at least 2 sets of blood bottles were withdrawn as recommended [9]. Of all the 299 712 hospitalizations during the 7-year period, 3571 (1.2%) were characterized by positive blood culture tests (i.e., microbial growth in ≥ 2 aerobic or anaerobic bottles). The proportion of hospitalizations with positive blood culture tests showed an increasing trend over the study period (*Table 1*, p-value of Cochran-Armitage trend test < 0.001).

Of all hospitalizations with positive blood culture tests, approximately half had at least o e ICD-9-CM discharge diagnosis code suggestive of sepsis (49.5%), with non-significant differences across years (*Table 1*, p-value of χ^2 test = 0.21). There was great variability in the proportion of hospitalizations with ICD-9-CM discharge diagnoses suggestive for sepsis across the hospital units, ranging from 0 to 81.9% (p-value of χ^2 test < 0.001), with proportions all < 50% in surgical wards. In particular, of 713 discharges from surgical wards with positive blood culture tests, only 102 (14.3%) had a discharge diagnosis consistent with sepsis, whereas among the 2858 hospitalizations in medical wards, 1667 (58.3%) had a sepsis-related diagnosis (p-value of χ^2 test< 0.001). The proportion of hospitalizations with sepsis-related diagnoses in surgical wards did not show any trend during the study period, showing a maximum of 17% and a minimum of 10% with an oscillating pattern.

Overall, 595 patients (16.7%) had an ICU stay during the hospitalization. In surgical wards, the proportion of hospitalizations with sepsis-related diagnoses was higher in case of ICU stay than otherwise, although the difference was not statistically significant (17.4% *vs* 13.5% respectively, p-value of χ^2 test = 0.22). On the other hand, in medical wards the proportion of cases with sepsis-related diagnoses was lower in case of ICU stay (51.1%) than otherwise (59.7%, p-value of χ^2 test < 0.001).

In-hospital mortality of patients with a positive blood culture test was 20.7% (n = 740). In medical wards, there was virtually no difference in the proportion of cases with sepsis among the discharge diagnoses for patients who died in the hospital and for the others (57.6% and 58.5% respectively, p-value of χ2 test = 0.67). On the contrary, in surgical wards the frequency of cases with sepsis indicated among the diagnoses was almost double when patients died in the hospital (24.1%) than otherwise (13.4%, p-value of χ2 test 0.02).

Compared with patients ≥ 80 years of age, adults and younger elderly subjects with positive blood culture tests had lower likelihood to have sepsis recorded among the hospital discharge diagnoses *(Table 2)*. On the other hand, no association was observed with patient's sex. After adjusting for patient's demographics and calendar year, being discharged from a medical ward was significantly associated with having sepsis recorded, whereas in-hospital death was not associated with the likelihood of recording sepsis.

Table 2
Association of patient's demographic characteristics, calendar year, hospital discharge ward type, with discharge diagnosis of sepsis among hospitalized patients with positive blood culture tests (≥ 2 positive aerobic or 2 anaerobic bottles), University Hospital of Udine, North-Eastern Italy, 2011-2017

	OR[1]	95%CI
Sex		
Male	1.00	-
Female	0.97	0.84-1.12
Age category		
0-14	0.94	0.31-2.92
15-64	0.84	0.70-1.01
65-79	0.79	0.66-0.94
≥ 80	1.00	-
Type of discharge ward		
Surgical	1.00	-
Medical	8.22	6.56-10.29
Calendar year		
2011	0.87	0.67-1.14
2012	1.00	0.77-1.30
2013	1.08	0.83-1.41
2014	1.08	0.84-1,39
2015	1.22	0.95-1.56
2016	1.12	0.88-1.43
2017	1.00	-

[1]Adjusted for all factors in the table.

Of hospital discharge records not including sepsis among the 6 discharge diagnoses, 354 (19.6%) had all 6 diagnoses filled out; 225 (12.5%) had 5, 310 (17.2%) had 4, 350 (19.4%) had 3, 295 (16.3% had 2, and 272 (15.1%) had only 1 diagnosis recorded. Among those records, the main discharge diagnosis belonged to the infectious and parasitic diseases group in 63 cases (3.5%), to the neoplasms group in 376 cases (20.8%), to the circulatory diseases group in 311 cases (17.2%), to the respiratory diseases group in 159 cases (8.8%), to the digestive diseases group in 243 cases (13.4%), to the genitourinary diseases group in 158 cases (8.7%), to the injury group in 158 cases (8.7%), to the supplemental classification of factors influencing health status and contact with health services in 112 cases (6.2%, almost all V42.7, person with transplanted liver, and V58.11, encounter for antineoplastic chemotherapy). The remaining 226 had other main diagnoses.

In the study period, there were 3491 hospitalizations with at least one discharge code among those considered as suggestive for sepsis, without a laboratory confirmation. Only 213 (6.1%) were discharged from surgical wards. As shown in *Table 3*, sepsis was included among the discharge diagnoses more frequently when a blood culture test was done than otherwise, and more frequently when at least one bottle turned out positive than in case of no growth in any bottle.

Of 2231 patients with positive blood culture tests from 2014 to 2017, we found information on the pathogens that were isolated in 2184 cases. In 594 of them, more than one microorganism was isolated. There was very little difference in the frequency of sepsis discharge diagnoses among patients with only one isolated microorganism (784 cases/1560, 49.3%) and those with more than one microorganism (311/594, 52.4%; p-value of χ^2 test 0.20). *Table 4* shows the frequency of pathogen genera that were isolated from the blood and, for each genus, the proportion of hospitalizations with a sepsis discharge diagnosis. For the most frequently isolated pathogen genera, the percentage of hospitalizations with a sepsis discharge diagnosis was always < 60%. From 2014 to 2017, there were 41 hospitalizations with isolation of CRKP: a sepsis diagnosis was found in 63.4% of those hospitalizations. The frequency of sepsis diagnoses in 159 hospitalizations with isolation of non-resistant Klebsiella pneumoniae was lower (47.2%; p-value of χ^2 test 0.06). However, in the 11 cases of CRKP discharged from surgical wards, only 2 (18.2%) had a discharge diagnosis of sepsis, whereas sepsis was coded in 24 out of 30 cases discharged from medical wards (80.0%).

DISCUSSION

Accurate coding of hospital discharge diagnoses is crucial not only for reimbursement issues, but also for health management and, last but not least, for allowing valid epidemiological estimates. In fact, hospital discharge codes from administrative data are extensively used for studying the epidemiology of a plethora of diseases and conditions and have substantial impact on epidemiological estimates [10]. For this reason, much research is being conducted to assess their accuracy [11-16].

Sepsis is one condition whose epidemiology has also been studied through hospital discharge summaries [1, 4, 17] and diagnosis coding has been shown to have impact on epidemiological estimates [4]. Various measures of validity of discharge diagnosis codes for sepsis have been investigated, showing variable results depending on the particular diagnosis of interest, calendar year, setting [5-7, 18] and attempts to develop optimized ICD-based case definitions have been done to increase validity [8].

In Italy, a study conducted in the Veneto Region described the burden of sepsis-related mortality based on death certificates [19], whereas hospital discharge data have never been used for epidemiological estimates and their validity on sepsis had never been assessed so far.

Through a comparison of hospital discharge diagnoses ICD-9-CM codes with laboratory results, we found that only half patients with laboratory-confirmed bloodstream infections were discharged from the Italian University Hospital of Udine with a diagnosis suggestive of sepsis. Despite the proportion of hospitaliza-

Table 3
Distributions of hospitalizations in the University Hospital of Udine, North-Eastern Italy, 2011-2017, according to blood culture tests and sepsis discharge diagnoses

		Blood culture test with ≥ 2 positive bottles			Blood culture test with 1 positive bottle			Negative blood culture test			No blood culture test		
Year	Hospitalizations	N	n with sepsis diagnosis	%	N	n with sepsis diagnosis	%	N	n with sepsis diagnosis	%	N	n with sepsis diagnosis	%
2011	45 224	428	196	45.8	409	113	27.6	2726	134	4.9	41 661	182	0.4
2012	44 568	453	218	48.1	421	139	33.0	2670	136	5.1	41 024	176	0.4
2013	43 526	459	229	49.8	453	144	31.8	2916	155	5.3	39 698	212	0.5
2014	41 795	499	253	50.7	438	143	32.6	2924	162	5.5	37 934	165	0.4
2015	41 440	549	292	53.1	452	142	31.4	3128	165	5.3	37 311	201	0.5
2016	41 488	586	301	51.3	420	135	32.1	3256	187	5.7	37 226	203	0.5
2017	41 671	597	280	46.9	495	160	32.3	3640	226	6.2	36 939	211	0.6
Total	299 712	3571	1769	49.5	3088	976	31.6	21 260	1165	5.5	271 793	1350	0.5

Table 4
Proportion of sepsis discharge diagnoses in hospitalized patients with ≥ 2 positive aerobic or 2 anaerobic bottles, by genera of the isolated pathogens, University Hospital of Udine, North-Eastern Italy, 2014-2017

Genus	Total pathogen isolations[1]	% with sepsis diagnosis
Acinetobacter	9	33.3%
Actinomyces	1	0.0%
Aerococcus	1	100.0%
Aeromonas	6	83.3%
Alcaligenes	4	25.0%
Bacillus	3	66.7%
Bacteroides	28	50.0%
Brevibacterium	4	50.0%
Candida	150	58.7%
Chryseobacterium	2	50.0%
Citrobacter	26	26.9%
Clostridium	16	31.3%
Corynebacterium	14	50.0%
Cryptococcus	1	0.0%
Enterobacter	82	47.6%
Enterococcus	270	51.5%
Escherichia	717	54.4%
Fusobacterium	2	50.0%
Gemella	3	66.7%
Haemophilus	4	50.0%
Hafnia	1	0.0%
Klebsiella	256	46.5%
Kocuria	2	100.0%
Leuconostoc	1	0.0%
Listeria	11	36.4%
Morganella	7	57.1%
Neisseria	1	100.0%
Ochrobactrum	2	100.0%
Pantoea	2	50.0%
Peptostreptococcus	1	100.0%
Prevotella	2	50.0%
Propionibacterium	12	50.0%
Proteus	49	51.0%
Providencia	5	40.0%
Pseudomonas	140	52.9%
Raoultella	7	28.6%
Salmonella	13	69.2%
Serratia	35	37.1%
Shewanella	1	100.0%
Sphingomonas	3	0.0%
Staphylococcus	995	50.6%
Stenotrophomonas	18	38.9%
Streptococcus	175	55.4%
Torulopsis	18	50.0%
Yersinia	1	0.0%

[1]The sum of total isolations is greater than the number of hospitalizations with positive blood culture tests because of the isolation of multiple pathogens in 594 hospitalizations.

tions with laboratory-confirmed bloodstream infection had increased monotonically from 2011 to 2017, no analogous increase was evident in the sensitivity of discharge diagnoses. In our hospital, sensitivity of any of the ICD-9-CM codes we considered suggestive of sepsis was slightly lower than 50%, similar to that observed in Canada using an ICD algorithm from the Canadian Institute for Health Information [8].

In the late 1980s, Romano and Mark, in California, observed that acute conditions with quick resolution, such as mild sepsis, could be missed in the hospital discharge records if other complications, determining prolonged hospital stay, affected the patient [20]. This seems not to be the case in our hospital. Competing high-severity or high-impact diagnoses were unlikely explanations for the omission of sepsis-related codes from list of 6 discharge diagnoses in Udine, since in more than 80% of cases of omitted sepsis codes, less than 6 diagnosis codes were compiled. Among patients with positive blood culture test but no sepsis diagnosis, one fifth had a main discharge diagnosis of cancer. Not even an ICU stay was sufficient to increase the likelihood that a laboratory-confirmed sepsis is reported among the discharge diagnoses.

The undercoding of sepsis was much more common in surgical wards than in medical wards and, in surgical wards, was more likely in case of in-hospital death. Type of hospital ward seemed to be strongly associated with discharge diagnoses sensitivity even in the analysis controlling for patient's characteristics. Higher sensitivity was observed in the 2014-2017 sub-analysis when particular pathogens were isolated from the blood cultures: for example, sensitivity was greater than 60% in case of CRKP and less than 50% in case of Carbapenem-sensitive Klebsiella pneumoniae. Again, however, sensitivity was high only when patients were discharged from medical wards and very low in surgical wards. Audits are certainly worth being conducted in the wards where the undercoding is more evident, and periodical ICD coding training should be provided in our hospital.

In this study, we also observed that diagnoses of sepsis were assigned to patients with a single positive blood bottle, to patients with no positivity, and even to patients with no blood culture tests. The proportion of hospitalizations with a diagnosis of sepsis decreased steeply from cases with double positive blood test, to single positive cases, to negative cases, to no-blood-culture-test hospitalizations. Nonetheless, the absolute frequency of patients with a diagnosis of sepsis with no laboratory confirmation was twice the number of patients with correctly coded laboratory-confirmed sepsis. Of course, not all those cases were necessarily misclassified. A blood culture can turn out negative if a patient has already started antibiotic therapy, or the physician may be aware that the patient is septic because of his/her clinical history, without the need of a concurrent laboratory confirmation. In some cases, though, miscoding or even misdiagnosis can be an issue. A number of clinical conditions, in fact, can mimic sepsis (e.g., non-infectious causes of systemic inflammatory response syndrome, myocardial infarction, pericarditis, myocarditis, massive pulmonary embolism, etc.) [21] and differentiation may be challenging especially in the absence of a microbiological identification of the underlying cause.

The availability of administrative health data including laboratory results allowed a relatively quick assessment of the sensitivity of ICD-9 codes from hospital discharge records on sepsis in the University Hospital of Udine, using blood culture test double-positive results as a strict gold standard. On the other hand, we could not assess the extent of false positive ICD-9 codes, since we could not exclude sepsis in cases lacking two positive blood culture bottles.

CONCLUSIONS

Using ICD-9 discharge codes for epidemiological estimates of sepsis may yield biased results in the Hospital of Udine. We believe that, although this result is only based on data from a single hospital, it can be generalized to other Italian hospitals, since the frequency of errors and the characteristics of hospital discharge records are quite similar across the various Italian Regions [22]. Audits and ICD coding training are worth being implemented since the quality of diagnosis registration and coding is important for scientific research, health planning and risk management.

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Conflict of interest statement

None.

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