Incidence and mortality of post-operative sepsis in New South Wales, Australia, 2002–2009

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ABSTRACT

Objective: To describe the incidence and mortality of post-operative sepsis in New South Wales, Australia.

Design, setting and participants: A retrospective study of adult elective surgical admissions (n = 229 918) in 82 public acute care hospitals in NSW, 2002–2009.

Main outcome measures: Changes in the incidence rate of post-operative sepsis and sepsis-related mortality.

Results: Although the mortality rate among patients with sepsis decreased from 26.9% in 2002 to 20.2% in 2009 (P = 0.006 for adjusted trend), the incidence rate of sepsis increased from 12.7 to 15.8 per 1000 admissions (adjusted rate ratio [RR], 1.23; 95% CI, 1.06–1.42). Thus, the incidence rate of sepsis-related deaths remained unchanged (3.4 v 3.2 per 1000 admissions; adjusted RR, 0.90; 95% CI, 0.67–1.22), as did deaths from sepsis as a proportion of all elective surgical deaths (P = 0.96 for adjusted trend). The incidence rate of infections without a specified organism identified increased; was twice the rate of gram-positive infections (8.5 v 4.1 per 1000 admissions, P < 0.001); and was three times the rate of gram-negative infections (8.5 v 2.7 per 1000 admissions, P < 0.001). Also, compared with patients with gram-positive infections, patients with an unspecified infection were more likely to die (adjusted RR, 1.33; 95% CI, 1.13–1.57), but patients with gram-negative infections and mixed infections had a similar likelihood of death from their infection.

Conclusion: Over 8 years, the mortality from post-operative sepsis decreased, but its incidence rate increased, resulting in a lack of improvement in the incidence rate of sepsis-related deaths. The increasing incidence of post-operative sepsis and the poor record of identification of causative organisms remain a significant public health challenge.

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Sepsis is a common post-operative complication, which may account for one-third of all cases of sepsis.[1] Patients who develop sepsis during or after surgery can progress to multiple organ dysfunction, and have a significantly greater mortality rate during their hospital stay.[2-4] The cost of treating such patients was estimated as three times higher than treating surgical patients without post-operative sepsis.[5] Sepsis complicated by organ failure is also responsible for 10%–12% of admissions to intensive care units.[6,7] Finally, sepsis-related morbidity appears to have an adverse impact on long-term outcomes after hospital discharge.[8]

The American Agency for Healthcare Research and Quality (AHRQ) has developed a set of patient safety indicators (PSIs), including for post-operative sepsis (PSI 13), with the aim of detecting preventable hospital complications and adverse events after surgery.[9] These indicators are evidence-based measures of patient safety designed for use in administrative databases.[10] Over the past decade, this definition of post-operative sepsis has been widely used in the United States to measure aspects of patient safety and quality and to monitor the impact of quality improvement initiatives.[4,10-13] Based on the AHRQ methodology, the Organisation for Economic Cooperation and Development (OECD) Quality Indicator Project also included post-operative sepsis in its patient safety indicators.[14]

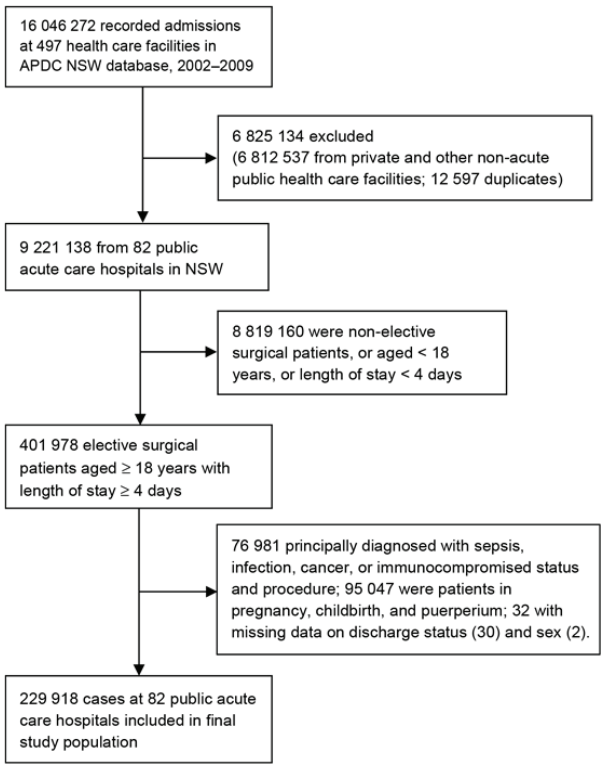
Despite such large data management initiatives, there are currently no large studies on measuring and reporting the epidemiology of post-operative sepsis in Australia. This is unfortunate because the issue is of major public health interest and because, given the unique aspects of the American health care system, there is uncertainty about the applicability of the US findings in Australia. Our aim was therefore to study the epidemiology of post-operative sepsis and sepsis-related mortality among adult elective surgical patients admitted in all public acute care hospitals between 2002 and 2009 in New South Wales, Australia, using AHRQ methodology.

Methods

Data source and study population

NSW is the most populous state in Australia, with a population of 7.3 million and 84 public acute care hospitals. We performed a retrospective study using NSW data from the Admitted Patient Data Collection (APDC), which includes demographic and diagnostic information on each public and private hospital admission episode. The medical records for each episode of care in the APDC were assigned codes based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM).[15] Each public hospital has certified, trained coders who use standardised procedures to generate these codes from information in

Figure 1. Derivation of the study sample



APDC = Admitted Patient Data Collection. NSW = New South Wales.

medical records (ICD-10-AM codes are listed in Appendix 1 and Appendix 2). Our study was approved by the NSW Population and Health Services Research Ethics Committee (LNR/11/CIPHS/64).

We included all elective surgical patients admitted to 82 of 84 NSW public acute care hospitals (excluding two children's hospitals) between 1 January 2002 and 31 December 2009. We identified our study population based on the selection criteria developed by the AHRQ for post-operative sepsis (PSI 13),[16] which targeted elective surgical patients aged ≥ 18 years with a length of stay of more than 3 days. Elective surgical patients were identified as patients who had had any operating theatre procedure performed as a primary procedure, and were not admitted through the emergency department. We excluded patients who were principally diagnosed with sepsis, infection, cancer or an immunocompromised state who needed immunocompromised state-related procedures at admission, because these patients had potential specific confounding factors. We excluded those who were assigned major diagnostic category 14 (pregnancy, childbirth and puerperium). Finally, we excluded patients with missing data on discharge status, sex, age, year or principal diagnosis (Figure 1). Patient demographic information included age, sex, country of birth, marital status, and advantage and disadvantage index scores of the Socio-Economic Indexes for Areas (SEIFA).[17] Hospital characteristics included location and peer groups (detailed descriptions are in Appendix 3).

Case definition and classification

Cases of sepsis were identified according to the AHRQ-defined diagnosis codes (ICD, Ninth Revision, Clinical Modification [ICD-9-CM]).[16] Because of the difference between coding systems in the US (ICD-9-CM) and Australia (ICD-10-AM), all diagnosis and procedure codes in the AHRQ definitions were translated to ICD-10-AM codes by referring to the OECD technical manual for PSIs.[18] We derived outcome variables using 54 non-principal diagnostic fields in the medical record by ICD-10-AM codes matched from the OECD manual (Appendix 1). We also categorised infectious organisms into gram-positive, gram-negative, mixed (gram-positive and gram-negative together) and unspecified organisms (Appendix 1).

Study outcomes

We studied the following outcomes from 2002 to 2009:

- incidence rate of post-operative sepsis: defined as the number of sepsis cases divided by the total study population, expressed per 1000 admissions
- sepsis case fatality rate: defined as the number of deaths among patients with sepsis divided by the number of sepsis cases, reported as a percentage
- incidence rate of sepsis-related deaths: defined as the number of deaths among patients with sepsis divided by the total study population, expressed per 1000 admissions
- proportion of sepsis-related deaths among all deaths in the study population, reported as a percentage
- incidence rates of sepsis cases involving specific infectious organisms: defined as the number of patients with specific infectious organisms divided by the study population, expressed per 1000 admissions.

Statistical analysis

We used the Rao–Scott χ^2 test to measure the association between categorical variables while adjusting for the hospital cluster effect. We derived adjusted rate ratios (RRs) for outcome variables using Poisson mixed models, which take into account the hospital cluster effect. We assessed crude and adjusted linear trend for the outcome variables after excluding a possible quadratic effect, using the study year as a continuous variable. We also derived an adjusted trend for each outcome variable, including calendar year, as a set of indicator variables (with 2002 as the baseline reference year).

Table 1. Distribution of study population and sepsis, by patient and hospital characteristics (pooled 2002–2009 data, *N* = 229 918)

Characteristic	Total (%)	Post-operative sepsis, *n* = 3563			Sepsis-related deaths, *n* = 875		
		n (%)	Incidence rate†	*P*	*n* (%)	Case fatality (%)	*P*‡
Age, years							
18–35	6.9%	218 (6.1%)	13.7	< 0.001**	29 (3.3%)	13.3	< 0.001**
35–55	20.9%	584 (16.4%)	12.1		67 (7.7%)	11.5	
55–75	44.4%	1531 (43.0%)	15.0		361 (41.3%)	23.6	
≥ 75	27.8%	1230 (34.5%)	19.2		418 (47.8%)	34.0	
Sex							
Male	46.3%	2159 (60.6%)	20.3	< 0.001**	497 (56.8%)	23.0	0.008*
Female	53.7%	1404 (39.4%)	11.4		378 (43.2%)	26.9	
Country of birth							
Australia or New Zealand	68.2%	2444 (68.6%)	15.6	< 0.001**	595 (68.0%)	24.3	0.214
UK, US or Canada	7.6%	218 (6.1%)	12.4		61 (7.0%)	28.0	
Non-English-speaking Europe	11.2%	387 (10.9%)	15.0		105 (12.0%)	27.1	
North Africa	2.0%	61 (1.7%)	13.5		16 (1.8%)	26.2	
Asia	2.6%	91 (2.6%)	15.0		26 (3.0%)	28.6	
Other	7.2%	260(7.3%)	15.8		54 (6.2%)	20.8	
Unknown	1.2%	102 (2.9%)	37.6		18 (2.1%)	17.6	
Marital status							
Married	56.2%	1920 (54.0%)	14.9	< 0.001**	469 (53.7%)	24.4	0.952
Single	41.6%	1476 (41.5%)	15.5		364 (41.6%)	24.7	
Unknown	2.2%	161 (4.5%)	31.6		41 (4.7%)	25.5	
SEIFA quartile							
1st (most disadvantaged)	25.5%	947 (27.0%)	16.1	< 0.001**	232 (26.5%)	24.5	0.518
2nd	24.4%	839 (23.6%)	14.9		191 (21.8%)	22.8	
3rd	24.9%	868 (23.4%)	15.1		219 (25.0%)	25.2	
4th (most advantaged)	24.4%	841 (23.6%)	15.0		219 (25.0%)	26.0	
Unknown	0.7%	68 (1.9%)	40.6		14 (1.6%)	20.6	
Local health district of facility							
Metropolitan	67.7%	2579 (72.4%)	16.6	< 0.001**	624 (71.3%)	24.2	0.416
Rural and regional NSW	32.3%	984 (27.6%)	13.3		251 (28.7%)	25.5	
Peer hospital group							
Principal referral group	62.0%	2658 (74.3%)	18.7	< 0.001**	671 (76.7%)	25.2	0.024*
Ungrouped acute care	2.3%	29 (0.9%)	5.4		7 (0.8%)	24.1	
Major metropolitan and non-metropolitan	28.3%	798 (22.6%)	12.3		190 (21.7%)	23.8	
District group 1	6.1%	62 (1.7%)	4.4		6 (0.7%)	9.7	
District group 2	1.3%	16 (0.4%)	5.4		1 (0.1%)	6.3	

SEIFA = Socio-Economic Indexes for Areas. UK = United Kingdom. US = United States. NSW = New South Wales. † Per 1000 admissions. ‡ Using Rao–Scott χ^2 test. * $P < 0.05$. ** $P < 0.01$.

We adjusted for patient demographic variables (age, sex, country of birth, marital status and SEIFA score) and hospital characteristics (location and peer groups).

To ensure the robustness of our findings, we conducted a sensitivity analysis by removing codes R57.8 and T81.8 from sepsis coding (results are shown in Appendix 4). As a preliminary step, we examined the Elixhauser and Charlson comorbidity indices, based on the ICD-10 coding scheme,[19] but did not include them in the adjusted model because of recent reports of potential biases introduced in using these indices for risk adjustment in epidemiological studies.[20-22]

We have considered $P < 0.05$ to be statistically significant, and we show 95% confidence intervals. We performed all analyses using Stata version 13 (StataCorp).

Results

Patient characteristics

Of 229 918 selected elective surgical admissions between 2002 and 2009, 72.2% were patients who were 55 years or older, almost half were men, most were born in Australia or New Zealand (68.2%) and most were married

Table 2. Observed trends, incidence rate and adjusted rate ratio of post-operative sepsis and sepsis-related deaths (*N* = 229 918)

Group	Total	2002	2003	2004	2005	2006	2007	2008	2009	Trend *P*
All admissions										
Patients, *n*	229 918	28 352	28 701	28 696	29 630	30 422	29 952	28 193	25 972	–
Deaths, *n*	3304	409	438	450	386	441	451	397	332	–
Incidence rate†	14.4	14.4	15.3	15.7	13.0	14.5	15.1	14.1	12.8	0.018*
Adjusted RR (95% CI)	–	1.00	1.03 (0.90–1.18)	1.03 (0.90–1.18)	0.84* (0.73–0.97)	0.94 (0.82–1.07)	0.95 (0.83–1.08)	0.86* (0.74–0.99)	0.82* (0.71–0.95)	–
Post-operative sepsis										
Patients, *n*	3563	360	409	481	445	487	501	470	410	–
Incidence rate†	15.5	12.7	14.3	16.8	15.0	16.0	16.7	16.7	15.8	Quad†
Adjusted RR (95% CI)	–	1.00	1.13 (0.98–1.30)	1.33** (1.15–1.52)	1.14 (0.99–1.32)	1.23** (1.07–1.41)	1.27** (1.10–1.45)	1.27** (1.10–1.46)	1.23** (1.06–1.42)	–
Sepsis-related deaths										
Patients, *n*	875	97	131	124	87	122	120	111	83	–
Case fatality (%)	24.6	26.9	32.0	25.8	19.6	25.1	24.0	23.6	20.2	0.006**
Adjusted RR (95% CI)	–	1.00	1.17 (0.90–1.53)	0.95 (0.72–1.24)	0.74* (0.55–0.99)	0.91 (0.69–1.19)	0.89 (0.68–1.17)	0.84 (0.64–1.12)	0.73* (0.54–0.98)	–
Incidence rate†	3.8	3.4	4.6	4.3	2.9	4.0	4.0	3.9	3.2	0.28
Adjusted RR (95% CI)	–	1.00	1.35* (1.03–1.76)	1.28 (0.98–1.67)	0.84 (0.63–1.13)	1.14 (0.87–1.49)	1.13 (0.86–1.48)	1.07 (0.81–1.42)	0.90 (0.67–1.22)	–
Proportion of all surgical deaths (%)	26.5	23.7	29.9	27.6	22.5	27.7	26.6	28.0	25.0	0.96
Adjusted RR (95% CI)	–	1.00	1.29 (0.99–1.68)	1.20 (0.91–1.57)	0.99 (0.73–1.32)	1.19 (0.91–1.57)	1.12 (0.85–1.47)	1.25 (0.95–1.66)	1.12 (0.83–1.50)	–

RR = rate ratio. Quad = quadratic. † Quadratic (linear = 0.004; quadratic = 0.022). * $P \leq 0.05$, ** $P < 0.01$.

(56.2%) (Table 1). Most patients were admitted to facilities in the metropolitan area (67.7%), and more than half the admissions were patients who had had surgery in principal referral hospitals (62.0%).

Of 3563 cases of post-operative sepsis (1.6%), 77.5% of patients were 55 years or older, and 2159 were men (60.6%) (Table 1). The incidence rate of post-operative sepsis in men was nearly twice the rate in women (20.3 v 11.4 per 1000 admissions, $P < 0.001$). Patients born in the United Kingdom, US, Canada and North Africa had a lower incidence rate than other country groups ($P < 0.001$). Patients who were single or lived in the most disadvantaged areas had higher incidence rates of post-operative sepsis (all $P < 0.001$). Hospitals in metropolitan areas or classed as principal referral hospitals reported greater incidence rates of post-operative sepsis compared with hospitals in rural and regional NSW or their peers ($P < 0.001$). Among patients who developed post-operative sepsis, 875 (24.6%) died during hospitalisation. Of these, higher rates of case fatality were observed among those 55 years or older ($P < 0.001$), women (26.9% v 23.0%, $P = 0.008$) and patients admitted to principal referral hospitals ($P = 0.024$).

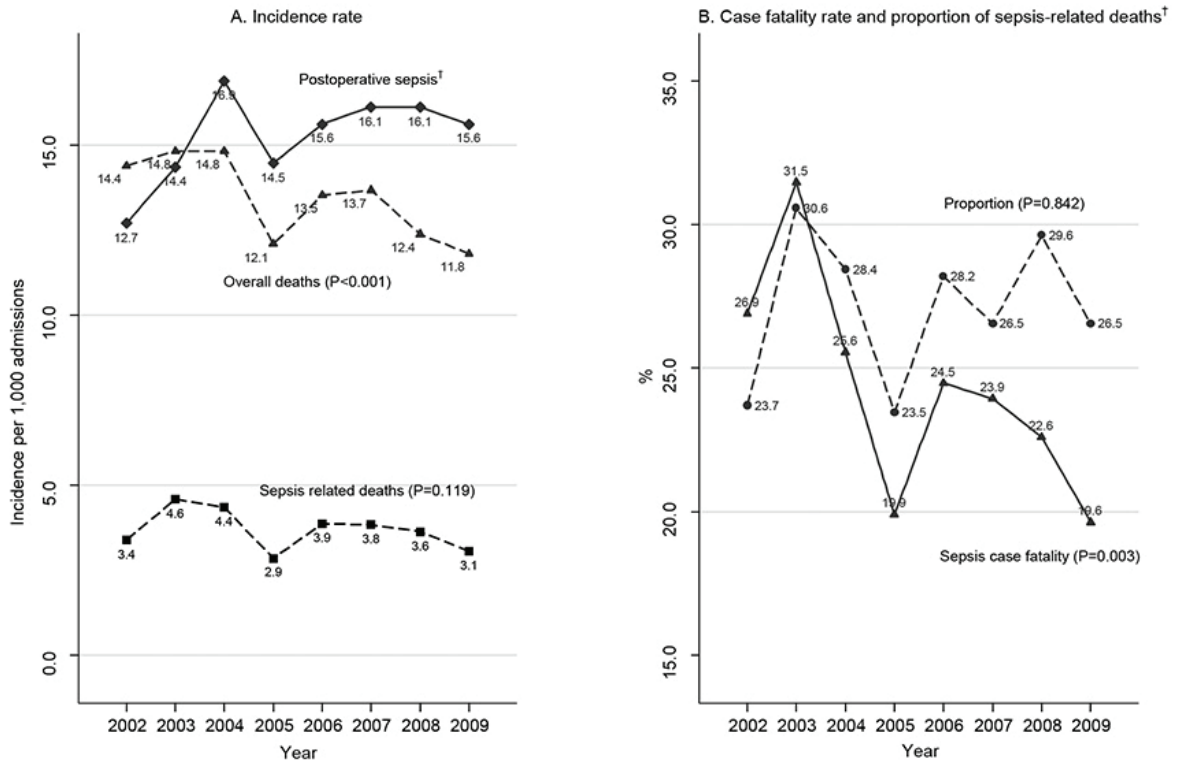
Trends in post-operative sepsis rates and related outcomes

Among the whole study population, 3304 patients (1.4%) died in hospital (Table 2). The overall surgical mortality rate decreased from 1.4% in 2002 to 1.3% in 2009 ($P = 0.018$). There was a significant increase in the incidence rate of post-operative sepsis, from 12.7 per 1000 admissions in 2002 to 15.8 per 1000 admissions in 2009 (adjusted RR, 1.23; 95% CI, 1.06–1.42), and a significant decrease in the case fatality of sepsis (from 26.9% in 2002 to 20.2% in 2009; $P = 0.006$ for adjusted trend). The incidence rate of sepsis-related deaths was not significantly different in 2009 (3.2 per 1000 admissions) compared with 2002 (3.4 per 1000 admissions; adjusted RR, 0.90; 95% CI, 0.67–1.22). There was no significant change in the proportion of sepsis-related deaths among overall deaths during the same study period ($P = 0.96$ for adjusted trend) (Table 2 and Figure 2).

Types of infectious organisms

There was no significant change in the incidence rate of gram-positive infections between 2002 and 2009 ($P = 0.742$ for trend) (Figure 3). The incidence rates of gram-negative and mixed infections showed quadratic trends during the

Figure 2. A. Risk-adjusted incidence rates of post-operative sepsis and overall surgical deaths
B. Sepsis-related case fatality rate and proportion of sepsis-related deaths among overall surgical deaths

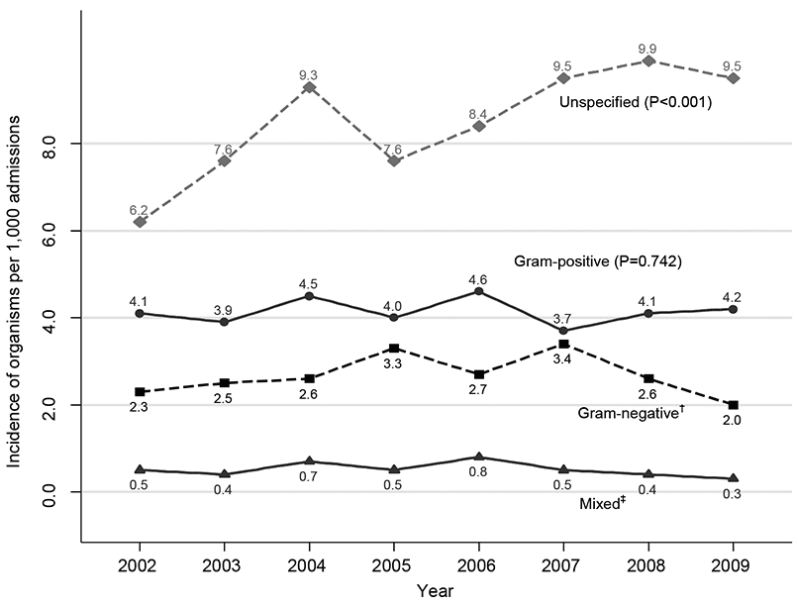


† Proportion of post-operative sepsis-related deaths among overall surgical deaths.

same period (initially increasing then decreasing), but there was a significantly increasing trend in the incidence rate of unspecified infections (from 6.2 per 1000 admissions in 2002 to 9.5 per 1000 admissions in 2009; P = 0.001 for trend).

Among all patients with sepsis, 26.7% contracted gram-positive infections, 17.4% were infected with gram-negative bacteria, 3.3% had mixed infections of gram-positive and gram-negative bacteria, and 52.6% were diagnosed with unspecified infections (Table 3). The incidence rate of unspecified infections was twice the rate of gram-positive infections (8.5 v 4.1 per 1000 admissions, P < 0.001) and three times the rate of gram-negative infections (8.5 v 2.7 per 1000 admissions, P < 0.001).

Figure 3. Observed trends in incidence rate of infecting organisms in post-operative sepsis



† P: linear = 0.002, quadratic = 0.002. ‡ P: linear = 0.064, quadratic = 0.031.

Table 3. Observed post-operative sepsis-related mortality and adjusted rate ratio, by type of infectious organism (pooled data 2002–2009; *N* = 229 918)

	Cases of sepsis (*n* = 3563)		Sepsis-related deaths (*n* = 875)		
Infectious organism	*n* (%)	IR*	*n* (%)	Mortality rate (%)†	Adjusted RR (95% CI)
Gram +ve	952 (26.7%)	4.1‡	194 (22.1%)	20.4	1.00
Gram –ve	620 (17.4%)	2.7§	104 (11.9%)	16.8	0.79 (0.62–1.01)
Mixed	117 (3.3%)	0.5¶	30 (3.4%)	25.6	1.29 (0.87–1.93)
Unspecified	1874 (52.6%)	8.5	547 (62.5%)	29.2	1.33** (1.13–1.57)

IR = incidence rate. RR = rate ratio. * Per 1000 admissions. † $P < 0.001$. ‡ Unspecified v gram +ve ($P < 0.001$; 95% CI, 3.9–4.8). § Unspecified v gram –ve ($P < 0.001$; 95% CI, 5.4–6.2). ¶ Unspecified v mixed ($P < 0.001$; 95% CI, 7.6–8.4). ** $P < 0.01$.

Compared with patients with gram-positive infections, patients with unspecified infections were more likely to die (29.2% v 20.4%; adjusted RR, 1.33; 95% CI, 1.13–1.57). Patients with gram-negative infections (16.8% v 20.4%; adjusted RR, 0.79; 95% CI, 0.62–1.01) and mixed infections (25.6% v 20.4%; adjusted RR, 1.29; 95% CI, 0.87–1.93) were similar to those with gram-positive infections.

Discussion

We conducted a large retrospective cohort study of the epidemiology of post-operative sepsis in adult patients having elective surgery in NSW, Australia, from 2002 to 2009. We found that post-operative sepsis was more common in men; that patients who were single or lived in disadvantaged areas had the highest incidence rate among social groups; that metropolitan or principal referral hospitals reported the greatest incidence among health care facilities; and that a higher case fatality rate was observed among older people, women and principal referral hospital patients. Importantly, we found that the incidence rate of post-operative sepsis increased in 2009 compared with 2002, while the sepsis case fatality rate decreased by a quarter. As a result, the overall population incidence rate of sepsis-related deaths did not change significantly, and the proportion of sepsis-related deaths among all elective surgical deaths remained unchanged. Finally, we found that infections in which no organism was specified accounted for more than half of overall cases of sepsis and that such patients had almost double the risk of death.

Based on the same AHRQ definition of post-operative sepsis as we used, and using US state-wide administrative data, Vogel and colleagues[10] found an increasing trend in the incidence rate of post-operative sepsis after elective surgery (from 0.67% to 1.74%), with an average rate of 1.1%, which was slightly lower than the rate in our study (1.6% in 2006). They also found a decreasing sepsis case fatality rate (from 27.1% to 23.9%), and we found a decrease from 26.9% to 20.2%. Another study by Bateman and colleagues[11] also focused on elective surgical patients and was based on a nationally representative sample in the US. Using a similar definition to the AHRQ one, Bateman and colleagues reported an increasing post-operative sepsis incidence rate, from 0.7 per 1000 admissions in 1997 to 1.3 per 1000 admissions in 2006, with a lower overall average rate than the rate in NSW (0.9 v 1.6 per 1000 admissions). Other studies have also reported that post-operative sepsis is more common in men,[10,11] and in people from more disadvantaged social groups[10,11] or institutions dealing with more complex surgery.[11] No comparable data exist for non-English-speaking Europeans as an at-risk ethnic group. The higher case fatality rate among older people and women and among people in centres that perform more complex surgery has also been previously reported.[11]

Previous studies have reported changes in the predominant organisms that cause sepsis. Before 1987, gram-negative bacteria were the most common cause, after which gram-positive bacteria became dominant, accounting for 52.1% of all sepsis infections, with an annual rate of increase of 26.3%.[23] Another study in the US found that sepsis caused by gram-positive bacteria was more likely to lead to acute organ dysfunction than sepsis caused by gram-negative bacteria (31% v 25%, $P < 0.01$).[24] None of these studies focused on elective surgical patients. Our study is the first to suggest that gram-positive bacteria are the most frequently specified infectious organism in post-operative septic patients in NSW adult public acute care hospitals; that the majority of infectious organisms causing post-operative sepsis were unspecified; and that unspecified organisms are increasing as a proportion of causative agents. The most common situation now is therefore that the infectious organism is not isolated, and such patients have the highest mortality.

Strengths and limitations

This is the first large epidemiological study in Australia and outside the US to provide evidence of a steady increase in the incidence rate of post-operative sepsis, with a simultaneous reduction in its case fatality leading to an unchanged incidence rate of sepsis-related deaths. It is also the first to show a persistently high incidence of failed microbiological identification and its associated higher mortality. These findings imply that there has been significant progress in the treatment of sepsis, but that this progress has not been matched by similar progress in the

prevention of post-operative sepsis or in the diagnosis of the responsible infectious agent.

We used the internationally adopted definition of sepsis[25] and highlight the unresolved challenges of preventing the development of sepsis. Our inclusion of only elective surgical patients reduced the possibility of community-acquired sepsis being a confounding factor, and made our results more specific and relevant for clinicians and policymakers. Our finding that a specific microbiological diagnosis is not achieved for more than 50% of patients implies that there is a need to develop better microbiological identification techniques. Finally, the higher mortality in patients with unspecified infectious organisms provides a specific focus for future investigations and interventions.

Our study also has limitations. First, the results were based on NSW acute care hospital surgical patient data and may not be generalisable to other settings, but it seems unlikely that such findings would materially differ from other states in Australia. Second, we studied the period 2002–2009 specifically because it provided important evidence to understand the background to and impact of a designated "Sepsis Kills" program, introduced in 2010 by the Clinical Excellence Commission of NSW. This program aimed to achieve better prevention, earlier identification and timely treatment of sepsis. Third, despite the use of professional and certified coders to extract chart data, the absolute accuracy of such data extraction cannot be guaranteed. Finally, because post-operative sepsis can occur after hospital discharge, the true incidence of post-operative sepsis in our study may have been underestimated.

Conclusion

Post-operative sepsis remains a major health care problem contributing to a significant proportion of deaths after elective surgery. Despite a reduced case fatality rate, and due to an increased incidence rate of sepsis, the overall population incidence rate of post-operative sepsis-related deaths has not decreased. It is important to note that, in patients with post-operative sepsis, the rate of non-diagnosis of a specific microbiological causative agent remains high and associated with greater mortality. Improved prevention and microbiological diagnosis should together be the focus of future research and interventional strategies to decrease post-operative sepsis-related deaths.

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