International Journal of Surgery (2008) 6, 238–245

INTERNATIONAL JOURNAL OF SURGERY

www.theijs.com

REVIEW

Staphylococcus aureus, the major pathogen in orthopaedic and cardiac surgical site infections: A literature review

Mitra Saadatian-Elahi [a,*], Remy Teyssou [b], Philippe Vanhems [a]

[a] *Laboratoire d'Epidémiologie et de Santé Publique, INSERM 271, Université Claude Bernard Lyon 1, 8 Avenue Rockefeller, 69373 Lyon Cedex 08, France*
[b] *Sanofi Pasteur, La division vaccins du groupe Sanofi-aventis, Lyon, France*

Available online 8 May 2007

KEYWORDS
Staphylococcus aureus;
Orthopaedic;
Cardiac;
Surgical site infection;
Surveillance

Abstract Due to the increasing number of orthopaedic and cardiac procedures, these units are considered as high-risk areas because of the potentially serious consequences of surgical site infections (SSI), primarily caused by *Staphylococcus aureus*. The goal of this review was to evaluate the impact of *S. aureus* on the incidence of SSI in these high risk wards. Studies were identified by a search on the MEDLINE literature using the following mesh terms: *S. aureus*, cardiac, orthopaedic, surgery, SSI. Beside, data from different surveillance systems were also included. Overall, biological investigation was performed only on a small proportion of identified SSIs. Of those identified, *S. aureus* represented the most common pathogen accounting for approximately 20% of all SSIs. Of the 59,274 hip prostheses reported from the HELICS surveillance network, *S. aureus* formed 48.6% of the pathogens (416 bacteria isolated). Similarly, it represented 43.7% of pathogens after coronary artery bypass grafting. Although *S. aureus* turned out to be the major pathogen, this work identifies the relative lack of knowledge on the overall incidence of *S. aureus* infections and on the impact of this pathogenic agent when taking into consideration the degree of wound contamination and category of SSI. There is a need for more detailed information on the role of *S. aureus* in the burden of surgical site infections and consequently how to establish multiple approach prevention programs.

Introduction

The number of surgical procedures being performed has increased during the last 30 years due to advances in surgical techniques, the increasing importance given to

* Corresponding author. Tel.: +33 4 78 77 70 31; fax: +33 4 78 00 93 86.
E-mail address: mitrasaadatian@yahoo.fr (M. Saadatian-Elahi).

1743-9191/$ - see front matter © 2007 Published by Elsevier Ltd on behalf of Surgical Associates Ltd.
doi:10.1016/j.ijsu.2007.05.001

healthcare priorities by the general public and longer lifetime expectancy. According to the latest available data from USA, more than 4 million surgical procedures were performed in 1999.[1]

Given that the overall number of surgical procedures is increasing, the burden of surgical site infection (SSI) could be more significant and should merit further attention. The situation could be further aggravated due to the related problems of antimicrobial resistance. SSIs comprise the third most frequently reported nosocomial infection (NI), representing 14–16% of all hospital nosocomial infections.[2,3] It has been reported that about 2–5% of patients undergoing surgery will develop SSI.[4–6] In addition to the increase of postoperative morbidity and mortality in surgical patients, SSIs are also the cause of increased hospitalization costs by lengthening the mean postoperative hospitalization stay (LOS).[7,8] Attributable mortality, morbidity and costs due to SSIs is of particular importance in the elderly because of their general, often fragile, health status, and the increasing number of operations performed in this population.[9]

Surgical site infections are primarily caused by bacteria, *Staphylococcus aureus* representing by far the most common pathogen found in surgical wounds.[3] This pathogenic agent is a Gram-positive spherical bacteria belonging to the Staphylococci group. It can cause suppurative infections ranging from superficial skin lesions to deep-seated infections. In orthopaedic and cardiac surgery, infections by this agent cause severe life-threatening complications. The purpose of the present work was to give an overview of the existing epidemiological data on the incidence of SSIs caused by *S. aureus* in orthopaedic and cardiac surgery.

Determinants of SSIs

The occurrence of SSI depends on several factors which might be classified into the following subgroups: (i) host derived factors such as advanced age,[10–12] diabetes mellitus[13–15] and malnutrition;[13,16–18] (ii) the duration of the surgical procedure;[19,20] (iii) factors related to the preparation of the patient and operative sites.[21]

In addition to common risk factors mentioned above, there are specific factors according to the type of surgery. In orthopaedic surgery, rheumatoid arthritis,[22,23] psoriasis, immunosuppression or prior surgery at the site of prosthesis[24,25] are associated with an increased risk of infection. In cardiac surgery, the most significant risk factors are BMI $> 40\ kg/m^2$ (OR: 2.95, 95%CI = 2.75–3.17), haemodialysis (OR: 2.12, 95% CI = 1.91–2.35), cardiogenic shock (OR: 2.11, 95%CI = 1.93–2.31), immunosuppressive treatment (OR: 1.51, 95% CI = 1.36–1.66), perfusion time 200 to 300 min (OR: 2.08, 95% CI = 1.89–2.29), perfusion time >300 min (OR: 1.96, 95% CI = 1.65–2.34), placement of an intra-aortic balloon pump (OR: 1.53, 95% CI = 1.44–1.63) and the presence of three or more anastomoses (OR: 1.28, 95% CI = 1.19–1.39).[26]

Risk factors for SSIs due to *S. aureus*

Between 10% and 35% of healthy subjects are considered as persistent nasal carriers of *S. aureus*,[27] preoperative nasal carriage of *S. aureus* being one of the major risk factors for developing *S. aureus* wound infection. In orthopaedic surgery, nasal carriage of *S. aureus* was the most important risk factor for developing SSI with an RR of 8.9 (95% CI = 1.7–45.5).[28] Similar results have been reported in cardiac surgery.[29–31] Compared to healthy subjects, some clinical conditions may increase nasal carriage and consequently lead to a higher risk of *S. aureus* SSI. In a study of 140 patients, 77% of diabetic subjects had nasal carriage of *S. aureus* compared to 33% in non-diabetic patients.[32] Likewise, patients treated by haemodialysis or peritoneal dialysis were found to carry nasal *S. aureus* more frequently than healthy subjects with rates ranging from 32% to 82% in haemodialysis patients and from 23% to 67% in those with peritoneal dialysis.[33] Infection with human deficiency virus (VIH) has also been associated with increased incidence of *S. aureus* nasal carriage with an OR of 2.5 (95% CI = 1.1–5.6).[34] The nasal carriage of *S. aureus* by the patient undergoing surgery is not the only source of infection. The association of its carriage by surgical personnel and the subsequent SSI has also been recognized.[35,36]

S. aureus bacteraemia has also been associated with higher risk of underlying SSI occurrence in several studies which suggested blood culture is an accurate test for the early diagnosis of post-operative SSIs in febrile patients.[37–39] In a study of patients undergoing coronary artery bypass grafting (CABG), mediastinitis occurred in 46 of 60 (76.7%) patients with positive blood cultures for *S. aureus*. The likelihood ratio of developing mediastinitis in subjects with *S. aureus* bacteraemia was 25 (95% CI: 14.7–44.4) as compared to those with negative blood culture for *S. aureus*.[40]

Importance of SSI in orthopaedic surgery

In the USA, orthopaedic surgical procedures are the fourth most common type of operation after obstetrical, cardiovascular and digestive procedures respectively.[41] In orthopaedic wards, SSIs represent approximately 20% of the overall nosocomial infections,[42] incidence rates differing according to the type of surgery. Orthopaedic units are classed as high-risk areas because of the potentially serious consequences of infection particularly in patients with prosthetics joints. One to five percent of prostheses become infected, leading to significant morbidity and severe functional impairment.

The extra cost attributable to SSIs has been estimated to almost US$40,000/infected case.[43] The mean length of additional postoperative hospitalization stay ranged from 12 to over 20 days.[43–45]

Main SSIs following orthopaedic surgery

Prosthetic joint infections

Over the past few decades orthopaedic implant surgery has become one of the most common types of orthopaedic surgery. Total arthroplasty in itself is a relatively safe procedure with incidence rates below 3%.[46] Nevertheless, it might lead to infections of the prosthetic material which are related to high morbidity and often lead to severe functional impairment. Prosthetic joint infections of the hip or the knee are the major surgical complications after total arthroplasty. Infection might occur within 6 months after the surgical procedure (acute); within 2 years of the

surgical procedure (sub-acute); or after 2 years of pain-free mobility (chronic).[47]

Staphylococci (coagulase-negative staphylococci and *S. aureus*) are the main causative agents in prosthetic joint sepsis, representing more than 40% of all concerned micro-organisms. Table 1 gives a summary of epidemiological data on the incidence and mortality rates of SSIs occurring after orthopaedic implant surgery.

Osteomyelitis

Vertebral osteomyelitis is the major type of infection observed after vertebral arthrodesis. Although it represents

Table 1 Incidence, morbidity and mortality rates of surgical site infections after orthopaedic surgery

Authors	Country	Type of surgery (no. of operations)	Incidence rate (%)	Mortality rate (%)	SSI due to *S. aureus*
Coello et al.[8]	UK	HPRO (24,002)	3.1	1.8	Not stated
		KPRO (11,785)	1.9	1.5	
Thomas et al.[48]	Australia	THR (1476)	4.9	0.0	Unknown
		TKR (1875)	5.15		
NNIS[49]	USA	HPRO (44,454)	RIC 0: 0.86 RIC 1: 1.65 RIC 2, 3: 2.52	Not stated	Not stated
		KPRO (66,360)	RIC 0: 0.88 RIC 1: 1.28 RIC 2, 3: 2.26		
		LAM (73,846)	RIC 0: 0.88 RIC 1: 1.35 RIC 2, 3: 2.46		
NINSS[50]	UK	HPRO (16,809)	1.24	Not stated	49%
		KPRO (15,792)	0.65		
		Hip (5364)	4.05		
		Hemiarthroplasty (3277)	2.01		
CCLIN Sud-est[51]	France	Orthopaedic overall (10,159)	0.9	Not stated	43%
		HPRO (1479)	2.5		
		KPRO (570)	0.5		
HELICS[52]	Europe	HPRO (59,274)	RIC 0: 2.0 RIC 1: 3.8 RIC 2,3: 5.6	Not stated	48.6%
		LAM (3142)	RIC 0: 0.8 RIC 1: 1.7 RIC 2, 3: 1.9	Not stated	Not stated
PREZIES[53]	The Netherlands	Elective HPRO and KPRO	1994: 17.0 1995: 10.0 1996: 5.0 1997: 3.0 1998: 1.0 1999: 2.0	Not stated	22.2 0.0 16.7 25.0 Unknown Unknown
INCISO (1997—1999)	France	Bone with osteosynthesis	1.2	0.9	Not stated
		Joint with prosthesis	1.1	0.1	
		HPRO or KPRO	1.9	1.5	
		Osteosynthesis removal	1.0	0.4	
		Overall	1.4	0.9	

SSI, surgical site infection; HPRO, hip prosthesis; LAM, laminectomy; KPRO, knee prosthesis, RIC, risk index category; SAB, *Staphylococcus aureus* bacteraemia.

HELICS (Hospital in Europe, Link for Infection Control through Surveillance) is a European network which includes over 600 hospitals in 10 countries: Belgium, Finland, France, Germany, Greece, Lithuania, the Netherlands, Poland, Spain, UK, Northern Ireland, Scotland and Wales.

only 2—4% of bone infections,[54] the consequences are serious and related to high morbidity and mortality. In studies with microbiological data, *S. aureus* represented between 40% and 75% of the identified microorganisms.[54—56]

SSIs related to arthroscopic surgery

The use of arthroscopy in the diagnosis and treatment of joint injuries is rising mainly because of the benefits of faster recovery and lower costs for both the patient and the healthcare system. The puncture wounds are small and the recovery is easier compared to ''open'' surgery. Arthroscopy is perceived as having low risk of SSI (0.01—0.48%), even if infections do occur occasionally. Following two incidents of arthroscopic infectious outbreaks in 1995 and 1998—1999, two case—control studies were carried out at a 100-bed private hospital in the USA.[57] Of the 27 cases identified (10 for the first period and 17 for the second period), the authors reported that *S. aureus* was the major pathogenic agent (44%), followed by Coagulase-negative *Staphylococcus* (30%). The major risk factors associated with an increased risk of SSI were intra-articular corticosteroid joint injection (OR: 9.3; 95% CI = 1.6—64.9) and preoperative razor shaving ($p = 0.03$).

Importance of SSI in cardiac surgery

Cardiovascular operations represent the second most frequent surgical procedures with more than 6 million operations carried out in the USA in 1999.[1] SSI in cardiac surgery patients is a serious complication leading to higher morbidity, mortality and prolonged hospital stay. In addition, the financial burden of such infections on the healthcare system can be colossal, adding an extra cost of almost US$40,000 per SSI.[58]

Main types of cardiac surgery involve cardiovascular implants, cardiac transplantation, and the increasingly common high-tech procedure of coronary artery bypass grafting (CABG). Patients undergoing such surgery have an increased risk of developing SSI because of the presence of multiple wounds (chest and lower extremity incision) and the use of post-operative invasive devices (i.e. pulmonary catheter).

S. aureus is the most common pathogen involved in the epidemiology of SSI after cardiac surgery (Table 2). Other major pathogens include *S. epidermidis*, *Enterococcus* spp. and Gram-negative organisms.[30]

Main SSIs following cardiac surgery

Mediastinitis

Mediastinitis or deep sternal wound infection (DSWI) is a rare but major complication after median sternotomy procedure, with incidence rates of 1—3%, but a mortality rate of almost 15%. The adjusted hazard ratio of long-term mortality for patients with DSWI was reported to be 2.44 (95% CI = 1.51—392).[69] Tracheostomy has been shown to be associated with an increased risk of DWSA after median sternotomy. In a recent retrospective review of 16,277 sternotomies, the rate of DWSA was 3.4% in patients with tracheostomy compared to 0.8% in patients without tracheostomy. The OR of developing DWSA after tracheostomy was 5.78 (95% CI = 4.29—7.80).[70] Similar results have already been reported by Curtis and collaborators who reviewed more than 6000 CABG.[71]

Emergency CABG was associated with a 10-fold increase (OR: 10.9; 95% CI = 2.7—44.7) in DSWI in a retrospective analysis of 863 patients.[72]

Endocarditis

Endocarditis is defined as an infection of the endocardial surface of the heart, which may include one or more heart valves, the mural endocardium, or a septal defect. The heart valves affected by the infection are primarily the mitral (28—45%) and aortic valves (5—36%). The incidence of infective endocarditis is low (less than 2%). However, surgical advances that permit more patients to undergo heart valve replacement will increase the extent of this problem. The mortality rate increases with increased age,

Table 2 Summary of incidence of SSI after cardiac surgery

Authors	Country	Type of surgery	No. of. operations	No. of. SSI (%)	SSI due to S.A or MRSA
Lepelletier et al.[59]	France	All	1268	38 (3)	Major pathogen
Immer et al.[60]	Switzerland	Sternotomy	5690	55 (0.97)	41.8% S.A
Upton et al.[61]	New Zealand	Median sternotomy	5176	70 (1.35)	82% S.A 16% MRSA
Tang et al.[62]	Canada	CABG	30102	232 (0.77)	
Crabtree et al.[63]	USA	CABG	4004	73 (1.8)	
Sharma et al.[64]	USA	CABG	3443	55(1.5)	49% S.A
Harrington et al.[65]	Australia	CABG	4474	349 (7.8)	32% MRSA
C-CLIN sud-est[51]	France	Overall cardiac surgery	1050	24 (2.3)	38.9% S.A
NNIS[49]	USA	CABG	15473	663 (4.3)	Not stated
HELICS[52]	Europe	CABG	28453	768 (2.7)	43.7%
Gummert et al.[66]	Switzerland	Sternotomy	9303	134 (1.44) DSWI	
Baskett et al.[67]	Canada	Sternotomy	9771	24 (0.25)	Not stated
Borger et al.[68]	Canada	CABG	8050	67 (0.83) DSWI	42%

S.A, *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; CABG, coronary artery bypass grafting; DSWI, deep sternal wound infection.

infection involving the aortic valve, development of congestive heart failure, central nervous system complications, and underlying disease. The morbidity, mortality and costs of these infections are higher than other NI, the case-fatality rate ranging from 10% to 30%.[73]

Infective endocarditis can occur after valve replacement or pacemaker implant. Infective endocarditis on pacemaker leads has been the subject of a synthetic review by Meune and collaborators[73] who selected 294 (183 men and 108 women) cases from the literature using the Duke criteria.[74] The main risk factors for developing endocarditis on pacemaker leads have been found to be diabetes, neoplasia, and corticoid treatments. Acute (<2 months after the surgery), sub-acute (>2 and <12 months) and chronic infective endocarditis (>12 months) represented 28%, 40% and 32% of all infections respectively. Microbiological analysis showed that *S. aureus* was the most abundant microorganism isolated in acute infections (40%) while *Staphylococcus epidermidis* was the main aetiological germ in sub-acute and chronic endocarditis (48.5%).

Prosthetic valve endocarditis (PVE) is also a rare but serious complication after cardiac surgery. The microbial aetiology is dominated by *S. epidermidis* followed by *S. aureus* accounting for about 30% and 20% of cases, respectively[75], but *S. aureus* is associated with higher mortality rates. In a recent study carried out using the International Collaboration on Endocarditis merged database (ICE-MD), the overall mortality among 61 patients with PVE due to *S. aureus* was 47.5%.[76]

Discussion

Studies with microbiological data have shown that *S. aureus* is the major pathological agent involved in the aetiology of surgical site infections in orthopaedic and cardiac surgery. Infection by *S. aureus* can lead to more serious complications in orthopaedic and cardiac procedures which use implanted biomaterials. *S. aureus* has the capacity to produce biofilms or slime layers of glycocalyx which form large microcolonies and adhere to the prosthetic material. These biofilms are less affected by antibiotics and ingestion by neutrophils.[77,78] They might consequently cause chronic infections associated with significant morbidity, pain, loss of function and death. Infection by *S. aureus* might also be influenced by host genetic factors. Recognition of microbial antigens during infection is mediated by Toll-like receptors (TLRs), which are transmembrane proteins that initiate the innate immune response to infection. Several TLRs share a common intracellular domain with cytokine receptors IL-1RI and IL-18R. IL-1RI deficient mice have been shown to be highly susceptible to *S. aureus* infection.[79,80] MyD88, the cytoplasmic adaptor molecule for the signalling of cellular response, as well as the interleukin-1 receptor-associated kinase-1 (IRAK-1) are also essential for protection against *S. aureus* infection.[80,81]

Integration of determinants of infection in prevention programs is important for the control of SSI, of which nasal carriage of *S. aureus* is one of the major risk factors. A diagnostic test to detect nasal carriage followed by elimination of nasal *S. aureus* seems therefore to be an efficient scheme to adopt. Mupirocin is the most common compound used in studies of nasal prophylaxis. In a recent randomized placebo-controlled clinical trial study of 3864 patients undergoing general, gynaecologic, neurologic or cardiothoracic surgery, the OR of *S. aureus* infection in patients treated with intranasal mupirocin compared to placebo was 0.45 (95% CI = 0.25–0.92).[82] Other authors have also reported significantly lower incidences in subjects undergoing cardiac surgery with perioperative mupirocin nasal ointment than in controls.[83,84] The use of mupirocin in orthopaedic surgery was associated with a non-significant decrease of *S. aureus* infection (RR: 0.19, 95% CI = 0.02–1.62)[85] indicating that mupirocin has no effect on the incidence of SSI by *S. aureus*, but other authors have provided conflicting results.[86] *S. aureus* bacteraemia has also been associated with an increased risk of infection.[37–40] Prevention programmes should therefore include systematic detection of such infections and consider postponement of the surgical procedure if necessary and feasible. Transient bacteraemia due to dental treatment has been associated with late prosthetic valve endocarditis and late prosthetic joint infection. Appropriate antibiotic prophylaxis during dental intervention might be of importance in reducing chronic infections in a high-risk population with prosthetic materials.[87]

The treatment of *S. aureus* SSIs is further complicated by the emerging problem of multidrug-resistant strains and in particular methicillin-resistant *S. aureus* (MRSA), which represent the dominant cause of *S. aureus* hospital-acquired infections. The problem of MRSA SSI is of particular importance in orthopaedic and cardiac surgery because of the potentially serious consequences of such infections. In a cohort study of subjects undergoing cardiac, orthopaedic and neurological surgery, 165 patients developed SSI methicillin-sensitive *S. aureus* SSI (MSSA SSI) and 121 had MRSA SSI. The adjusted odds ratio of 90-day mortality rate was 3.4 (95% CI = 1.5–7.2) in MRSA SSI patients as compared to patients with MSSA SSI.[88] The extensive use of antibiotics is the primary cause of *S. aureus* resistance. Improvements in the timing of initial administration, the appropriate choice of antibiotic agents, and shorter duration of antibiotic administration can therefore be considered as key points in reducing such resistance.

Routine surveillance is the basic element for successful identification of infections that cause high morbidity and mortality and for reducing SSIs rates.[53,89] Regular feedback of the data to surgeons and infection control activities carried out in parallel to surveillance has been shown to have an additional effect in lowering SSI rates.[90,91] The results of surveillance can be further completed by inter-hospital comparisons using benchmarking methods. Such comparison is currently facilitated by standardized nationwide surveillance networks which have recently been set up in several countries. Post-discharge surveillance is an important issue particularly in surgical wards. With the increasing trend for ambulatory surgery over the past decade, more SSIs are occurring after the patient has left hospital.[3,92–95] Developing post-discharge surveillance is therefore essential for the achievement of reliable SSI rates and for a better validity of inter-hospital comparisons. Telephone surveys or patient-completed questionnaires have been used for out-patient surveillance.[96,97] However, the validity of the data obtained needs to be proved by prospective studies comparing different methods of post-discharge surveillance.

In summary, *S. aureus* is the major pathological agent of surgical site infection. Numerous studies have investigated and identified the risk factors which might contribute to higher incidence of SSI related *S. aureus*. However, there is still relatively little information in the literature on the impact of this pathogenic agent when taking into consideration the degree of the wound contamination (clean, clean-contaminated, contaminated, and dirty) and the category of SSI (superficial, deep, and organ-space). Further prospective biochemical epidemiologic studies are warranted for a better understanding of the role of *S. aureus* in the burden of surgical site infections and consequently in the establishment of multiple-approach prevention programs.

Conflict of interest
None.

Funding
This work was supported by Sanofi-Pasteur.

Ethical approval
Not required.

References

1. Popovic JR, Hall MJ. 1999 National Hospital Discharge Survey. *CDC Advance Data* 2001:319.
2. Delgado-Rodriguez M, Gomez-Ortega A, Sillero-Arenas M, Llorca. Epidemiology of surgical-site infections diagnosed after hospital discharge: a prospective cohort study. *Infect Control Hosp Epidemiol* 2001;**22**:24—30.
3. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999;**20**:250—78.
4. Astagneau P, Rioux C, Golliot F, Brucker G, INCISO Network Study Group. Morbidity and mortality associated with surgical site infections: results from the 1997-1999 INCISO surveillance. *J Hosp Infect* 2001;**48**:267—74.
5. Geubbels EL, Mintjes-de Groot AJ, van den Berg JM, de Boer AS. An operating surveillance system of surgical-site infections in The Netherlands: results of the PREZIES national surveillance network. Preventie van Ziekenhuisinfecties door Surveillance. *Infect Control Hosp Epidemiol* 2000;**21**:311—8.
6. Mertens R, Jans B, Kurz X. A computerized nationwide network for nosocomial infection surveillance in Belgium. *Infect Control Hosp Epidemiol* 1994;**15**:171—9.
7. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999;**20**:725—30.
8. Coello R, Charlett A, Wilson J, Ward V, Pearson A, Borriello P. Adverse impact of surgical site infections in English hospitals. *J Hosp Infect* 2005;**60**:93—103.
9. McGarry SA, Engemann JJ, Schmader K, Sexton DJ, Kaye KS. Surgical-site infection due to *Staphylococcus aureus* among elderly patients: mortality, duration of hospitalization, and cost. *Infect Control Hosp Epidemiol* 2004;**25**:461—7.
10. Kaye KS, Schmit K, Pieper C, Sloane R, Kaughlan KF, Sexton DJ, et al. The effect of increasing age on the risk of surgical site infection. *J Infect Dis* 2005;**191**:1056—62.
11. Raymond DP, Pelletier SJ, Crabtree TD, Schulman AM, Pruett TL, Sawyer RG. Surgical infection and the aging population. *Am Surg* 2001;**67**:827—32.
12. de Boer AS, Mintjes-de Groot AJ, Severijnen AJ, van den Berg JM, van Pelt W. Risk assessment for surgical-site infections in orthopedic patients. *Infect Control Hosp Epidemiol* 1999;**20**:402—7.
13. Malone DL, Genuit T, Tracy JK, Gannon C, Napolitano LM. Surgical site infections: reanalysis of risk factors. *J Surg Res* 2002;**103**:89—95.
14. Vuorisalo S, Haukipuro K, Pokela R, Syrjala H. Risk features for surgical-site infections in coronary artery bypass surgery. *Infect Control Hosp Epidemiol* 1998;**19**:240—7.
15. Espehaug B, Havelin LI, Engesaeter LB, Langeland N, Vollset SE. Patient-related risk factors for early revision of total hip replacements. A population register-based case-control study of 674 revised hips. *Acta Orthop Scand* 1997;**68**:207—15.
16. Rapp-Kesek D, Stahle E, Karlsson TT. Body mass index and albumin in the preoperative evaluation of cardiac surgery patients. *Clin Nutr* 2004;**23**:1398—404.
17. Engelman DT, Adams DH, Byrne JG, Aranki SF, Collins Jr JJ, Couper GS, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. *J Thorac Cardiovasc Surg* 1999;**118**:866—73.
18. Pratt WB, Veitch JM, McRoberts RL. Nutritional status of orthopedic patients with surgical complications. *Clin Orthop Relat Res* 1981;**155**:81—4.
19. Ridgeway S, Wilson J, Charlet A, Kafatos G, Pearson A, Coello R. Infection of the surgical site after arthroplasty of the hip. *J Bone Joint Surg Br* 2005;**87**:844—50.
20. Ku CH, Ku SL, Yin JC, Lee AJ. Risk factors for sternal and leg surgical site infections after cardiac surgery in Taiwan. *Am J Epidemiol* 2005;**161**:661—71.
21. Barie PS, Eachempati SR. Surgical site infections. *Surg Clin North Am* 2005;**85**:1115—35.
22. Luessenhop CP, Higgins LD, Brause BD, Ranawat CS. Multiple prosthetic infections after total joint arthroplasty. Risk factor analysis. *J Arthroplasty* 1996;**11**:862—8.
23. Wilson MG, Kelley K, Thornhill TS. Infection as a complication of total knee-replacement arthroplasty. Risk factors and treatment in sixty-seven cases. *J Bone Joint Surg Am* 1990;**72**:878—83.
24. Brause Barry D. *Infection with prostheses in bones and joint*. In: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. 5th ed., vol. 1. New York: Churchill Livingstone; 2000. p. 1196—200.
25. Menon TJ, Wroblewski BM. Charnley low-friction arthroplasty in patients with psoriasis. *Clin Orthop Relat Res* 1983;**176**:127—8.
26. Fowler Jr VG, O'Brien SM, Muhlbaier LH, Corey GR, Ferguson TB, Peterson ED. Clinical predictors of major infections after cardiac surgery. *Circulation* 2005;**112**:I358—65.
27. Kluytmans JA, Wertheim HF. Nasal carriage of *Staphylococcus aureus* and prevention of nosocomial infections. *Infection* 2005;**33**:3—8.
28. Kalmeijer MD, van Nieuwland-Bollen E, Bogaers-Hofman D, de Baere GA. Nasal carriage of *Staphylococcus aureus* is a major risk factor for surgical-site infections in orthopedic surgery. *Infect Control Hosp Epidemiol* 2000;**21**:319—23.
29. Haas JP, Evans AM, Preston KE, Larson EL. Risk factors for surgical site infection after cardiac surgery: the role of endogenous flora. *Heart Lung* 2005;**34**:108—14.
30. Herwaldt LA. *Staphylococcus aureus* nasal carriage and surgical-site infections. *Surgery* 2003;**134**:S2—9.
31. Kluytmans JA, Mouton JW, Ijzerman EP, Vandenbroucke-Grauls CM, Maat AW. Nasal carriage of *Staphylococcus aureus* as a major risk factor for wound infections after cardiac surgery. *J Infect Dis* 1995;**171**:216—9.
32. Luzar MA, Coles GA, Faller B, et al. *Staphylococcus aureus* nasal carriage and infection in patients on continuous ambulatory peritoneal dialysis. *N Engl J Med* 1990;**322**:505—9.

33. Herwaldt LA. Reduction of *Staphylococcus aureus* nasal carriage and infection in dialysis patients. *J Hosp Infect* 1998; **40**:S13—23.
34. Sissolak D, Geusau A, Heinze G, Witte W, Rotter ML. Risk factors for nasal carriage of *Staphylococcus aureus* in infectious disease patients, including patients infected with HIV, and molecular typing of colonizing strains. *Eur J Clin Microbiol Infect Dis* 2002;**21**:88—96.
35. Weber S, Herwaldt LA, Mcnutt LA, Rhomberg P, Vaudaux P, Pfaller M. An outbreak of *Staphylococcus aureus* in a pediatric cardiothoracic surgery unit. *Infect Control Hosp Epidemiol* 2002;**23**:77—81.
36. Wang JT, Chang SC, Ko WJ, Chang YY, Chen ML, Pan HJ, et al. A hospital-acquired outbreak of methicillin-resistant *Staphylococcus aureus* infection initiated by a surgeon carrier. *J Hosp Infect* 2001;**47**:104—9.
37. San Juan R, Aguado JM, Lopez MJ, Lumbreras S, Enriquez F, Sanz F, et al. Accuracy of blood culture for early diagnosis of mediastinitis in febrile patients after cardiac surgery. *Eur J Clin Microbiol Infect Dis* 2005;**24**:182—9.
38. Lesens O, Hansmann Y, Brannigan E, Remy V, Hopkins S, Martinot M, et al. Positive surveillance blood culture is a predictive factor for secondary metastatic infection in patients with *Staphylococcus aureus* bacteraemia. *J Infect* 2004;**48**:245—52.
39. Gottlieb GS, Fowler Jr VG, Kong LK, McClelland RS, Gopal AK, Marr K, et al. *Staphylococcus aureus* bacteremia in the surgical patient: a prospective analysis of 73 postoperative patients who developed *Staphylococcus aureus* bacteremia at a tertiary care facility. *J Am Coll Surg* 2000;**190**:50—7.
40. Fowler Jr VG, Kaye KS, Simel DL, Cabell CH, McClachlan D, Smith PK, et al. *Staphylococcus aureus* bacteremia after median sternotomy: clinical utility of blood culture results in the identification of postoperative mediastinitis. *Circulation* 2003;**108**:73—8.
41. Mayhall CG. Staphylococcus aureus, *Hospital epidemiology and infection control*. 3rd ed. Baltimore: Lippincott Williams & Wilkins; 2004.
42. Janin B, Chevalley F, Raselli P, Livio JJ, Francioli P. Prospective surveillance of nosocomial infections in a traumatology and orthopedics service. *Helv Chir Acta* 1993;**60**:211—8.
43. Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ. The impact of surgical-site infections following orthopedic surgery at a community hospital and a university hospital: adverse quality of life, excess length of stay, and extra cost. *Infect Control Hosp Epidemiol* 2002;**23**:183—9.
44. Hebert CK, Williams RE, Levy RS, Barrack RL. Cost of treating an infected total knee replacement. *Clin Orthop Relat Res* 1996;**331**:140—5.
45. O'Donoghue MA, Allen KD. Costs of an outbreak of wound infections in an orthopaedic ward. *J Hosp Infect* 1992;**22**:73—9.
46. Migaud H, Sennevill E, Amzallag M, Laffarague P. Risque infectieux en chirurgie orthopédique. *EMC-Rhumatologie Orthopédie* 2005;**2**:151—72.
47. Lew P, Waldvogel FA. Infections of skeletal prostheses. In: Bennett JV, Brachman PS, editors. *Hospital infection*. 4th ed. Philadelphia: Lippincott Raven; 1998. p. 613—20.
48. Thomas C, Cadwallader HL, Riley TV. Surgical-site infections after orthopaedic surgery: statewide surveillance using linked administrative databases. *J Hosp Infect* 2004;**57**:25—30.
49. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004;**32**:470—85.
50. Health Protection Agency, Mandatory surveillance of SSI in orthopaedic surgery, England 2004—2005.
51. Caillet-vallet E, Bernet C, Hajjar J, Ayzac L, Fabry J. Réseau de surveillance des infections du site opératoire. *Iso Sud-est, Rapport général*, http://cclin-sudest.chu-lyon.fr; 2003.
52. HELICS. Hospital in Europe Link for Infection Control though Surveillance, http://helics.univ-lyon1.fr.
53. Schneeberger PM, Smits MH, Zick RE, Wille JC. Surveillance as a starting point to reduce surgical-site infection rates in elective orthopaedic surgery. *J Hosp Infect* 2002;**51**:179—84.
54. Stefanovski N, Van Voris LP. Pyogenic vertebral osteomyelitis: report of a series of 23 patients. *Contemp Orthop* 1995;**31**: 159—64.
55. McHenry MC, Easley KA, Locker GA. Vertebral osteomyelitis: long-term outcome for 253 patients from 7 Cleveland-area hospitals. *Clin Infect Dis* 2002;**34**:1342—50.
56. Dimar JR, Carreon LY, Glassman SD, Campbell MJ, Hartman MJ, Johnson JR. Treatment of pyogenic vertebral osteomyelitis with anterior debridement and fusion followed by delayed posterior spinal fusion. *Spine* 2004;**29**:326—32.
57. Babcock HM, Carroll C, Matava M, L'ecuyer P, Fraser V. Surgical site infections after arthroscopy: Outbreak investigation and case control study. *Arthroscopy* 2003;**19**:172—81.
58. Fry DE. The economic costs of surgical site infection. *Surg Infect* 2002;**3**:S37—43.
59. Lepelletier D, Perron S, Bizouarn P, Caillon J, Drugeon H, Michaud JL, et al. Surgical-site infection after cardiac surgery: incidence, microbiology, and risk factors. *Infect Control Hosp Epidemiol* 2005;**26**:466—72.
60. Immer FF, Durrer M, Muhlemann KS, Erni D, Gahl B, Carrel TP. Deep sternal wound infection after cardiac surgery: modality of treatment and outcome. *Ann Thorac Surg* 2005;**80**: 957—61.
61. Upton A, Roberts SA, Milsom P, Morris AJ. Staphylococcal poststernotomy mediastinitis: five year audit. *Aust NZ J Surg* 2005; **75**:198—203.
62. Tang GH, Maganti M, Weisel RD, Borger MA. Prevention and management of deep sternal wound infection. *Semin Thorac Cardiovasc Surg* 2004;**16**:62—9.
63. Crabtree TD, Codd JE, Fraser VJ, Bailey MS, Olsen MA, Damiano Jr RJ. Multivariate analysis of risk factors for deep and superficial sternal infection after coronary artery bypass grafting at a tertiary care medical center. *Semin Thorac Cardiovasc Surg* 2004;**16**:53—61.
64. Sharma M, Berriel-Cass D, Baran Jr J. Sternal surgical-site infection following coronary artery bypass graft: prevalence, microbiology, and complications during a 42-month period. *Infect Control Hosp Epidemiol* 2004;**25**:468—71.
65. Harrington G, Russo P, Spelman D, Borrell S, Watson K, Barr W, et al. Surgical-site infection rates and risk factor analysis in coronary artery bypass graft surgery. *Infect Control Hosp Epidemiol* 2004;**25**:472—6.
66. Gummert JF, Barten MJ, Hans C, Kluge M, Doll N, Walther T, et al. Mediastinitis and cardiac surgery—an updated risk factor analysis in 10,373 consecutive adult patients. *Thorac Cardiovasc Surg* 2002;**50**:87—91.
67. Baskett RJ, MacDougall CE, Ross DB. Is mediastinitis a preventable complication? A 10-year review. *Ann Thorac Surg* 1999;**67**: 462—5.
68. Borger MA, Rao V, Weisel RD, Ivanov J, Cohen G, Scully HE, et al. Deep sternal wound infection: risk factors and outcomes. *Ann Thorac Surg* 1998;**65**:1050—6.
69. Toumpoulis IK, Anagnostopoulos CE, Derose Jr JJ, Swistel DG. The impact of deep sternal wound infection on long-term survival after coronary artery bypass grafting. *Chest* 2005;**127**: 464—71.
70. Force SD, Miller DL, Petersen R, Mansour KA, Craver J, Guyton RA, et al. Incidence of deep sternal wound infections after tracheostomy in cardiac surgery patients. *Ann Thorac Surg* 2005;**80**:618—21.
71. Curtis JJ, Clark NC, McKenney CA, Walls JT, Schmaltz RA, Demmy TL, et al. Tracheostomy: a risk factor for mediastinitis after cardiac operation. *Ann Thorac Surg* 2001;**72**:731—4.

72. Sakamoto H, Fukuda I, Oosaka M, Nakata H. Risk factors and treatment of deep sternal wound infection after cardiac operation. *Ann Thorac Cardiovasc Surg* 2003;**9**:226—32.
73. Meune C, Arnal C, Hermand C, Cocheton JJ. Infective endocarditis related to pacemaker leads. A review. *Ann Med Interne (Paris)* 2000;**151**:456—64.
74. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. *Duke Endocarditis Service*. *Am J Med* 1994; **96**:200—9.
75. Chastre J, Trouillet JL. Early infective endocarditis on prosthetic valves. *Eur Heart J* 1995;**16**(Suppl. B):32—8.
76. Chirouze C, Cabell CH, Fowler Jr VG, Khayat N, Olaison L, Miro JM, et al. Prognostic factors in 61 cases of *Staphylococcus aureus* prosthetic valve infective endocarditis from the International Collaboration on Endocarditis merged database. *Clin Infect Dis* 2004;**38**:1323—7.
77. Hudson MC, Ramp WK, Frankenburg KP. *Staphylococcus aureus* adhesion to bone matrix and bone-associated biomaterials. *FEMS Microbiol Lett* 1999;**173**:279—84.
78. Gracia E, Fernandez A, Conchello P, Lacleriga A, Paniagua L, Seral F, et al. Adherence of *Staphylococcus aureus* slime-producing strain variants to biomaterials used in orthopaedic surgery. *Int Orthop* 1997;**21**:46—51.
79. Miller LS, O'Connell RM, Gutierrez MA, Pietras EM, Shahangian A, Gross CE, et al. MyD88 mediates neutrophil recruitment initiated by IL-1R but not TLR2 activation in immunity against *Staphylococcus aureus*. *Immunity* 2006;**24**:79—91.
80. Verdrengh M, Thomas JA, Hultgren OH. IL-1 receptor-associated kinase 1 mediates protection against *Staphylococcus aureus* infection. *Microbes Infect* 2004;**6**:1268—72.
81. Takeuchi O, Hoshino K, Akira S. Cutting edge: TLR2-deficient and MyD88-deficient mice are highly susceptible to *Staphylococcus aureus* infection. *J Immunol* 2000;**165**: 5392—6.
82. Perl TM, Cullen JJ, Wenzel RP, Zimmerman MB, Pfaller MA, Sheppard D, et al. Mupirocin And The Risk Of *Staphylococcus aureus* Study Team. Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections. *N Engl J Med* 2002; **346**:1871—7.
83. Martorell C, Engelman R, Corl A, Brown RB. Surgical site infections in cardiac surgery: an 11-year perspective. *Am J Infect Control* 2004;**32**:63—8.
84. VandenBergh MF, Kluytmans JA, van Hout BA, Maat AP, Seerden RJ, McDonnel J, et al. Cost-effectiveness of perioperative mupirocin nasal ointment in cardiothoracic surgery. *Infect Control Hosp Epidemiol* 1996;**17**:786—92.
85. Kalmeijer MD, Coertjens H, van Nieuwland-Bollen PM, Bogaers-Hofman D, de Baere GA, Stuurman A, et al. Surgical site infections in orthopedic surgery: the effect of mupirocin nasal ointment in a double-blind, randomized, placebo-controlled study. *Clin Infect Dis* 2002;**35**:353—8.
86. Davey P. Eradication of nasal carriage of *Staphylococcus aureus*—is it cost-effective? *J Hosp Infect* 1998;**40**:S31—7.
87. American Dental Association; American Academy of Orthopedic Surgeons. Antibiotic prophylaxis for dental patients with total joint replacements. *J Am Dent Assoc* 2003;**134**:895—9.
88. Engemann JJ, Carmeli Y, Cosgrove SE, Fowler VG, Bronstein MZ, Trivette SL, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis* 2003;**36**:592—8.
89. Douglas P, Asimus M, Swan J, Spigelman A. Prevention of orthopaedic wound infections: a quality improvement project. *J Qual Clin Pract* 2001;**21**:149—53.
90. van Kasteren ME, Mannien J, Kullberg BJ, de Boer AS, Nagelkerke NJ, Ridderhof M, et al. Quality improvement of surgical prophylaxis in Dutch hospitals: evaluation of a multi-site intervention by time series analysis. *J Antimicrob Chemother* 2005;**56**:1094—102.
91. Gastmeier P, Sohr D, Brandt C, Eckmanns T, Behnke M, Ruden H. Reduction of orthopaedic wound infections in 21 hospitals. *Arch Orthop Trauma Surg* 2005;**125**:526—30.
92. Surveillance des infections du site opératoire en France en 2003, Réseau Alerte Investigation Surveillance des Infections. *Rapport Iso-Raisin*, http://www.fc-sante.atrium.rss.fr/cclin-est/surveil_ISO.shtml; 2003.
93. Medina-Cuadros M, Sillero-Arenas M, Martinez-Gallego G, Delgado-Rodriguez M. Surgical wound infections diagnosed after discharge from hospital: epidemiologic differences with in-hospital infections. *Am J Infect Control* 1996;**24**:421—8.
94. Fields CL. Outcomes of a postdischarge surveillance system for surgical site infections at a Midwestern regional referral center hospital. *Am J Infect Control* 1999;**27**:158—64.
95. Mitchell DH, Swift G, Gilbert GL. Surgical wound infection surveillance: the importance of infections that develop after hospital discharge. *Aust NZ J Surg* 1999;**69**:117—20.
96. Fanning C, Johnston BL, MacDonald S, LeFort-Jost S, Dockerty E. Postdischarge surgical site infection surveillance. *Can J Infect Control* 1995;**10**:75—9.
97. Manian FA, Meyer L. Comparison of patient telephone survey with traditional surveillance and monthly physician questionnaires in monitoring surgical wound infections. *Infect Control Hosp Epidemiol* 1993;**14**:216—8.