An update review on risk factors and scales for prediction of deep sternal wound infections

Alessandra Buja, Alessandra Zampieron, Sara Cavalet, Daniele Chiffi, Paolo Sandonà, Angela Vinelli, Tatjana Baldovin, Vincenzo Baldo

Buja A, Zampieron A, Cavalet S, Chiffi D, Sandonà P, Vinelli A, Baldovin T, Baldo V. An update review on risk factors and scales for prediction of deep sternal wound infections. Int Wound J 2012; 9:372–386

ABSTRACT

Surgical site infections are the most common nosocomial infections in surgical patients. The preventable and the unmodifiable risk factors for deep sternal wound infections (DSWI) have been amply assessed in the literature. The aim of this review was to describe the results of the numerous published studies to describe all the DSWI risk factors and the scales devised to predict SWI, with a view to providing an update on this issue. A comprehensive search of the Medline and Embase databases was performed (considering studies from January 1995 to April 2011); and a manual search was also conducted using references cited in original publications and relevant review articles. There are several risk factors associated with DSWI, which could be classified in four categories as demographic (e.g. sex and age), behavioural (e.g. smoking and obesity), baseline clinical conditions (e.g. diabetes, hypertension and COPD) and surgical operative risk factors (e.g. duration of operation and emergency operation). Six scales for predicting the risk of DSWI are described in the literature: they vary not only in accuracy but also in ease of application and they are applied at different times (some only preoperatively and others also postoperatively). This study provides a broad update on our knowledge of the risk factors for DSWI and the scales for prediction with a view to improving the management of infections at cardiosurgery units.

Key words: Infection control • wound infection

Key Points

- surgical site infections (SSIs) are the most common nosocomial infection in surgical patients and wound site infections are a major cause of postoperative illness, accounting for approximately one in four of all nosocomial infections
- an estimated 40–60% of these infections are thought to be preventable

Authors: A Buja, MD, PhD, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy; A Zampieron, BSN, MSN, Azienda Ospedaliera di Padova, Padova, Italy; S Cavalet, BSN, Azienda Ospedaliera di Padova, Padova, Italy; D Chiffi, DPhil, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy; P Sandonà, MD, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy; A Vinelli, MD, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy; T Baldovin, BS, PhD, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy; V Baldo, MD, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy

Address for correspondence: A Buja, MD, PhD, Department of Environmental Medicine and Public Health, University of Padua, Padua 35127, Italy

E-mail: alessandra.buja@unipd.it

INTRODUCTION

Surgical site infections (SSIs) are the most common nosocomial infection in surgical patients and wound site infections are a major cause of postoperative illness, accounting for approximately one in four of all nosocomial infections (1). SSIs can be considered the most common preventable adverse outcome after major surgical procedures and the second most common adverse event occurring in hospitalised patients. An estimated 40–60% of these infections are thought to be preventable (2). The Center for Disease Control and Prevention defines deep sternal wound infections (DSWI) as infection involving incisional deep soft tissue within 30 days of the operation (3). The reported incidence of DSWI ranges from

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0·7% (4,5) to 2·3% (6). This is a potentially life-threatening complication and is associated with a higher morbidity, including a higher incidence of postoperative myocardial infarction, stroke and low output syndrome (7) and a higher early mortality (8,9), while its influence on long-term mortality is debated in the literature (8,10). These detrimental health outcomes are a primary concern and make it essential to consider all removable or containable risk factors for DSWI. The consequences of such infections also entail an increase in health care costs because of a greater need for parenteral antibiotic therapy, longer hospital stays, postoperative resternotomies. Both the preventable and the unmodifiable risk factors for DSWI have been amply discussed in the literature to shed light on possible prevention strategies as well as to identify patients carrying the greatest intrinsic risk of DSWI (4,11–13). Several scales (14–20) for predicting the risk of SWI have been defined, in addition to the general National Nosocomial Infection Surveillance (NNIS) System risk index (21,22), which is thought to perform well across a broad range of surgical procedures, but has been judged inadequate in stratifying patients undergoing coronary artery bypass surgery in terms of their risk of acquiring a SSI (23).

The aim of this review was to describe the results of the numerous published studies to pinpoint all DSWI risk factors and the scales for predicting them with a view to providing an update on this issue.

METHODS

Search method

A comprehensive search of the Medline and Embase database was performed (considering studies from January 1995 to April 2011) and a manual search was also conducted using references cited in original publications and relevant review articles. The search process involved combining the MeSH terms 'deep wound infection', 'risk factors' and 'prediction scale'. These keywords were expanded in the search so as to include all articles investigating the same issue using different terms (i.e. 'sternal wound infection', 'prospective study' and 'epidemiology').

Study selection and variables

Each publication identified by this process was reviewed and included in this study if the following criteria were met: (i) observational, not experimental studies; (ii) studies published after 1995; (iii) studies not designed to validate scales and (iv) studies published in English. When the results of a study were published more than once, only the latest and most complete article was included in the analysis.

The data were tabulated by name of the article's first author, year, place, study design, demographic characteristics of the sample (mean age, gender as the percentage of males), pathological and therapeutical conditions, behavioural factors, preoperative-intra-post-surgical conditions. Finally, we tabulated any reported early mortality and mortality at 1 or more years.

The criteria for defining the accuracy of prediction scales were drawn from arbitrary guidelines (based on a suggestion by Swets 1988) (24), distinguishing between non informative (AUC$\hat{}$0·5), scarcely accurate (0·5 < AUC < 0·7), moderately accurate (0·7 < AUC < 0·9), highly accurate (0·9 < AUC < 1) and perfect tests (AUC$\hat{}$1). For the Goodman–Kruskal non parametric correlation coefficient, Haley suggests that a risk index with a *G* value of less than 0·3 has a poor predictive power, 0·3–0·5 has a moderate predictive power and more than 0·6 has a high predictive power (25).

RESULTS

The characteristics of the studies considered in the analysis are given in Table 1.

The risk factors associated with DSWI are shown in Tables 2 and 3.

The six SWI risk prediction scales found in literature are represented in Table 4.

DISCUSSION

Many studies described four categories of risk factors that raise the risk of DSWI, that is, patients' demographic features, clinical conditions, behavioural factors and preoperative–intra-post-surgical conditions.

Demographic features

Age

A correlation between the risk of DSWI and age emerged in many studies, older age being associated with a higher probability

Key Points

- the aim of this review was to pool the results of the numerous published studies to pinpoint all DSWI risk factors and the scales for predicting them with a view to providing an update on this issue
- a comprehensive search of the Medline and Embase database was performed (considering studies from January 1995 to April 2011) and a manual search was also conducted using references cited in original publications and relevant review articles

Key Points

- demographic features: age and sex
- baseline clinical variables: diabetes, immunosuppressive treatments, immunosuppressed conditions, heart failure and COPD

Table 1 Characteristics of the studies considered in the analysis

Author (year of publication)	Type of study	Period	Location	Number of patients	Control group	Mean age	Male (%)	Number of deep sternal wound infections (%)	Early mortality (30-day mortality)	Mortality at 1 year
Sofer (1999) (26)	Retrospective observational	1996/04 to 1997/08	Israel	545		65	79	9 (1·7)	11 (2%)	
Nakano (2008) (27)	Prospective cohort study	2000 to 2005	Japan	1500		67·8	72·7	12 (0·8)		
Olsen (2002) (11)	Retrospective	1996/01 to 1999/06	USA	1980		61	64·9	37 (1·9)		8 (21·6%)
Trick (2000) (13)	Case control	1995/01 to 1998/03	USA	1796	90		n.r.	30 (1·7)		
Toumpoulis (2005) (8)	Retrospective study	1992/01 to 2002/03	USA	3760		64·1	69·1	40 (1·1)	6 (15%)	
Zacharias (1996) (28)	Retrospective study	1991/01 to 1994/12	Canada	2317		63	n.r.	21 (0·9)		
Borger (1998) (4)	Retrospective study	1990/02 to 1995/12	Canada	12 267			72·1	92 (0·7)	1 (1%)	
Hollenbeak (2000) (29)	Case control/cost analysis	1996/04 to 1997/08	USA	1519	160	64·8	77·7	41 (2·7)		
Lu (2003) (5)	Retrospective study	1997/04 to 2001/03	UK	4228		63·5	82·4	28 (0·7)	7 (25%)	
Ridderstolpe (2001) (30)	Retrospective cohort study	1996/01 to 1999/12	Sweden	3008		65·4	72·5	47 (1·6)	1 (1%)	7 (7·2%)
Kohli (2003) (31)	Prospective cohort study	1990/04 to 1995/12	Canada	11 508		60	73	133 (1·2)	(1.8%)	(5.6%)
Filsoufi (2009) (9)	Retrospective cohort study	1998/01 to 2005/12	France	5798		64	62	106 (1·8)	15 (14·2%)	27·6%
Fakih (2007) (32)	Retropective + case control	2000/01 to 2004/09	USA	3578		67·2	65·1	70 (1·9)		
Steingrimsson (2004) (33)	Case control	1997/01 to 2004/12	Iceland	1650	163	66·2	72·4	41 (2·5)	4 (9·8%)	7 (17%)
Sakamoto (2003) (12)	Retrospective study	1987/01 to 1999/12	Japan	863		61·2	65·5	17 (2·0)		
Savage (2007) (34)	Retrospective cohort study	2002 to 2004	USA	120 793		64·6	67·7	2018 (1·7)		
Sachithanandan *et al*. (2008) (35)	Prospective cohort study	2001/01 to 2005/12	UK	4586		63·4	74	76 (1·7)	7 (9·2%)	
The Parisian Mediastinitis Study Group (1996) (6)	Prospective cohort study	1993/03 to 1993/04	France	1830			68·6	42 (2·3)		

Table 2 Demographic, baseline clinical condition and behavioural factors

Author (Year of publication)	Demographic			Baseline clinical conditions																						Behaviour	
	Sex	Race	Age	Diabetes (NIDDM or IDDM)	Hypertension	Corticosteroid use	Immunosuppresion	Hemodynamic instability	Congestive heart failure or poor ejection fraction	NYHA class ≥3	Ejection fraction (LVEF)	Renal failure pts on dialysis	Hepatic failure	Chronic Renal Failure	Previous cardiac surgery	Previous (or recent) myocardial infarction	Prior percutaneous coronary intervention	Angina	peripheral vascular disease	Aortic surgery	Extensive aortic calcification	Extension of coronary artery disease	History of stroke	COPD	Smoking	Obesity or BMI >30
Sofer (1999) (26)			B	B																				M		
Nakano (2008) (27)	M			M					M			B		M					B							
Olsen (2002) (11)	B	B		M											B	B										M
Trick (2000) (13)				M																						
Toumpoulis (2005) (8)				M				M				M				B					B					
Zacharias (1996) (28)	B			M																						M
Borger (1998) (4)	M			M															B	B				B	B	B
Hollenbeak (2000) (29)														M												M
Lu (2003) (5)				M						B	B															B
Ridderstolpe (2001) (30)				M						M								B	M					B	M	M
Kohli (2003) (31)			B	M							B			B					B							
Filsoufi (2009) (9)				M	B				B		B	B				M				M	M		B	M		M
Fakih (2007) (32)									B					B	B				B						B	M
Steingrimsson (2004) (33)			B	M		M				M	M								M				M	B	M	M
Sakamoto (2003) (12)																										
Savage (2007) (34) (only patients diabetic)	B		B	B	B		B			B		B		B		B	B	B	B					B	B	B
Sachithanandan *et al*. (2008) (35)			M	M										B											M	
The Parisian Mediastinitis Study Group (1996) (6)	B		M	M																						M

B = variable signifcative associate with DSWI only in bivariate analysis; M = variable significative associate with DSWI in multivariate analysis.

Table 3 Preoperative, intraoperative, and postoperative factors

Author (Year of publication)	Hospitalization before operation	Reoperation (previous sternotomy)	Cardiopulmonary bypass	Preoperative endocarditis	CABG ± valve	Emergency CABG Surgery	Urgency of operation (timing)	IABP	Residents surgeon	No. of diseased vessels	Bilateral ITA use	Number of grafts	Staples used for chest skin closure	AB prophylaxis >60 min before incision	Cefuroxime >2hs before incision	Clamp duration	Mechanical ventilation	Ventilation time	Duration of anesthesia	Respiratory failure	Operation time	Blood transfusions	Re-exploration (bleeding)	Prolonged po stoperative (or ICU)	Gastrointestinal complicance	Sepsis and/or endocarditis	Length of stay	Drainage >3 days
Sofer (1999) (26)						**M**																						
Nakano (2008) (27)											**M**											B					B	
Olsen (2002) (11)								B	**M**							B						B						
Trick (2000) (13)											B		**M**															
Toumpoulis (2005) (8)											**M**									B					B	**M**	B	
Zacharias (1996) (28)								B		B	**M**							B				**M**	**M**					
Borger (1998) (4)		B	B								**M**							B										
Hollenbeak (2000) (29)														**M**										B				
Lu (2003) (5)								B			B	B					**M**	B			B		B					
Ridderstolpe (2001) (30)					B						**M**							**M**				B						
Kohli (2003) (31)		**M**			B			B			B	B								B	B	B		B				
Filsoufi (2009 (9))	**M**				**M**															B			B		B	B		
Fakih (2007) (32)					B																**M**			B				
Steingrimsson (2004) (33)					B													**M**				B	**M**					
Sakamoto (2003) (12)					**M**	**M**		**M**																B			B	
Savage (2007) (34) (only patient diabetic)			B			B		B		B								B				B		B				
Sachithanandan *et al.* (2008) (35)	B																	**M**										
The Parisian Mediastinitis Study Group (1996) (6)		**M**			**M**		B				**M**								**M**					B				

B = variable significative associate with DSWI only in bivariate analysis; M = variable significative associate with DSWI in multivariate analysis.

Table 4 Scales for predicting the risk of SWI

Risk index	Risk factors	Scores	Scoring system	Estimated risk	Predictive infection
Toronto risk index (predicted SWI) (35)	Diabetes	Yes, score 2·5 No, score 0	Total score 0–5, risk group 1	1·9%	Area under the ROC curve was 0·64 (less accurate)
	Internal mammary artery harvested	Yes, score 3 No, score 0	Total score 5·5–9, risk group 2	6·5%	
	Reopening because of complications within 4 days	Yes, score 4 No, score 0	Total score 9·5–11·5, risk group 3	15·6%	
	4 or more postoperative days in the intensive care unit	Yes, score 5 No, score 0	Total score 12 or >, risk group 4	28·3%	
Preoperative score system (predicted SSI) (14)	Diabetes	If, yes, score 1 No score 0	Risk score is calculated by adding the score for each risk factor present: 0–3	Each point in the scoring system represents about a twofold risk of SSI	Area under the ROC curve was 0·64 (less accurate)
	BMI of 30 or > but <35	If, yes, score 1 No, score 0			
	BMI of 35 or greater	If, yes, score 2 No score 0			

Risk Index		Risk Factors	Scores		Scoring system	Estimated risk	Predicted infection
Sternal wound infection prediction scale-R (SWIPS and SWIPS-R) (predicted SWI) (15)			Yes, score between 1 and 9		Cut-off score: *25 for the SWIPS *28 for the SWIPS-R	Not reported	Correctly diagnosed 62·1% with SWIPS and 72·8% with SWIPS-R (moderately accurate)
			SWIPS	SWIPS-R			
	Preoperative	Smoking	NA	9			
		Diabetes mellitus IDDM	9	7			
		Diabetes mellitus NIDDM	7	5			
		COPD	6	8			
		Preoperative stay in intensive care unit	4	4			
		Obesity >30 (kg/m^2)	4	4			
		Advanced age (>70)	5	3			
		Sex (male)	1	1			
		Impaired immune response	8	8			

Table 4 (*Continued*)

Risk Index		Risk Factors	Scores	Scoring system	Estimated risk	Predicted infection
	Intraoperative	Bilateral internal mammary artery	8	6		
		Single internal mammary artery	3	3		
		Long operative time >4 hours	7	7		
		Re-exploration for bleeding	6	6		
		Long cardiopulmonary bypass time >2 hours	6	6		
	Postoperative	Hypoperfusion/hypotension	7	8		
		Ventilatory support >48 hours	5	6		
		Pharmacologic support	2	NA		
		Dopamine/Dobutamine alone	NA	2		
		All others	NA	6		
		Postoperative CPR	5	7		
		Hypoxaemia	4	5		
		Banked-blood transfusions	5	3		

Risk Index		Risk Factors	Scores	Scoring system	Estimated risk	Predicted infection
Euroscore emergency operation (predicted SWI and mortality) (16)			Yes, score between 1 and 4	Total score 0–3, low risk	0·7%	For Euroscore additive: area under the ROC curve was:
	Euroscore additive (17)	Age	1			0·72 predicted infection
		Sex: female	1			0·78 for 30 days mortality
		Serum creatinine >200	2			0·77 for long term (6-month mortality rates) (moderately accurate)
		Extracardiac arteriopathy	2			
		Pulmonary disease	1	Total score 4–6, intermediate risk	3%	
		Neurological dysfunction	2			
		Previous cardiac surgery	3			
		Recent myocardial infarct	2			
		Left ventricular ejection fraction 30–50%	1			

Table 4 (*Continued*)

Risk Index	Risk Factors	Scores	Scoring system	Estimated risk	Predicted infection
	Left ventricular ejection <30%	3	Total score >6, high risk	7·2%	
	Systolic pulmonary pressure >60 mmHg	2			
	Active endocarditis	3			
	Unstable angina	2			
	Emergency operation	2			
	Critical preoperative state	3			
	Ventricular septal rupture	4			
	Other than isolated coronary surgery	2			
	Thoracic aortic surgery	3			

Risk Index		Risk Factors	Scores		Scoring system	Estimated risk		Predicted infection
Society of thoracic surgeons risk Score (predicted SWI) (18)	Preoperative variables		Preop only	Combined	(1 point each risk factors)	Preop only	Combined	Preoperative: area under the ROC curve was: 0·72 (20) preoperative score 0·80 (20) for short term (30 days mortality rates) 0·81 (20) for long term (6-month mortality rates) (moderately accurate)
		Age (5–55 years)	1 point	1 point	0	0·9	0·8	
		BMI (30–40 kg/m^2)	4 points	3 points	1	1	0·9	
		BMI (40+ kg/m^2)	9 points	8 points	2	1·1	1	
		Diabetes	3 points	3 points	3	1·3	1·2	
		Renal failure	4 points	4 points	4	1·5	1·3	
		Congestive heart failure	3 points	3 points	5	1·6	1·5	
		Peripheral vascular disease	2 points	2 points	6	1·9	1·8	
					7	2·1	2	
		Female gender	2 points	2 points	8	2·4	2·3	
		Chronic lung disease	2 points	3 points	9	2·7	2·7	
		Cardiogenic shock	6 points	NA	10	3·1	3	
		Myocardial infarction	2 points	NA	11	3·5	3·5	
		Concomitant surgery	4 points	NA	12	4	4	

Table 4 (*Continued*)

Risk Index		Risk Factors		Scores	Scoring system	Estimated risk		Predicted infection
	Intraoperative variables	Perfusion time 100–200 minutes	NA	3 points	13	4·5	4·5	Intraoperative: area under the ROC curve was: 0·76 (20) intraoperative score 0·82 (20) for short term (30-day mortality rates) and for long term (6-month mortality rates) (moderately accurate)
					14	5·1	5·2	
		Perfusion time 200–300 minutes	NA	7 points	15	5·8	6	
					16	6·6	6·7	
		Intra-aortic balloon pump	NA	5 points	17	7·4	7·6	
					18	8·2	8·5	
					19	9·1	9·4	
					20	9·9	10·2	
					21	10·7	11·1	
					22	11·4	11·8	
					23	12·1	12·5	
					24	12·9	13·4	
					25	13·6	14	
					26+	16	16·2	

Risk Index	Risk Factors	Scores	Scoring system	Estimated risk	Predicted infection
Alfred Hospital risk index (predicted SSI) (19)	Obesity Peripheral or cerebrovascular disease Insulin-dependent diabetes mellitus	Risk index A only three factors, each of which is determined preoperatively	Risk score is calculated by adding a unit each present risk factor: 0–3	0 = 6·8% 1 = 11·8% 2 = 17·5% 3 = 40%	Risk index A: *G* Goodman–Kruskal correlation coefficient value 0·3299 (IC95:0·2039–0·4559) (moderate predictive power)

Table 4 (*Continued*)

Risk Index	Risk Factors	Scores	Scoring system	Estimated risk	Predicted infection
	Procedure exceeding 5 hours	Risk index B includes the same three risk factors, but the duration can only be determined postoperatively	Risk score is calculated by adding a unit each present risk factor: 0–4	0 = 6·3% 1 = 11% 2 = 15·4% 3 = 35·3% 4 = not reported	Risk index B: G Goodman–Kruskal correlation coefficient value 0·3405 (IC95:0·2245–0·4565) (moderate predictive power)
National Nosocomial Infection Surveillance risk index (predicted SSI for CABG surgery) (20–22)	Patient with an American Society of Anesthesiologists (ASA) preoperative assessment ASA > 2	If, yes, points 1 No, point 0	Risk score is calculated by adding a unit each present risk factor: 0–3	0 = 0	Area under the ROC curve was 0·64 (20) moderate discrimination for infection 0·65 (20) for short term (30-day mortality rates) 0·64 (20) for long term (6-month mortality rates) (less accurate)
	Operation classified as contaminated or dirty-infected	If, yes, points 1 No point 0		1 = 2%	
	Operation lasting over T hours, where T depends upon the operative procedure being performed	If, yes, points 1 No, point 0		2 = 5·8%	

BMI, body mass index; ROC, receiver operating characteristic; SSI, surgical site infection; SWI, sternal wound infections.

of preoperative comorbidities and postoperative complications (36). Many age-associated comorbidities increase a patient's sensitivity to infections, although malnutrition seems to be the main cause of a worse immune function in the elderly (37).

Sex

Males have more hair follicle, which can facilitate major microbial colonisation of the skin, while preoperative shaving can cause local skin irritation.

Baseline clinical variable and therapeutical conditions

Diabetes

Diabetes predisposes patients to DSWI by two main routes, first by delaying the healing of the surgical wound, and second by reducing the patient's immune response. Diabetes has a negative impact on the healing process through a number of mechanisms. During the inflammatory phase, diabetes-related vascular changes such as capillary basement membrane thickening, limited vasodilation and platelet dysfunction result in poor leukocyte infiltration, inadequate oxygenation and clotting dysfunction. In the proliferative phase, a decreased presence of fibroblasts, collagen and growth factors within the wound further delays the essential matrix formation needed to fill the wound (38). Delayed wound closure during the maturation phase is evident, with prolonged wound granulation and reduced myoblast contractility. Diabetes makes the tissues a more favourable environment for micro-organisms by damaging lymph, nerve and blood vessels.

Some research has also shown that diabetic patients have an impaired immune function: their neutrophil function is depressed, affecting adherence to the endothelium, chemotaxis and phagocytosis (39). The antioxidant system involved in bactericidal activity is weakened and cell-mediated immunity is depressed. These impairments are exacerbated by hyperglycaemia and acidaemia, but are substantially (if not entirely) reversed by normalising pH and blood glucose levels (40).

Diabetes control demands a contribution from more than one specialist. The anaesthetist needs to monitor patients' serum glucose before the surgical procedure and plan suitably adjusted intraoperative insulin therapy (41). Surgeons should ensure that proper glucose control is maintained after the procedure (for least 48 hours). Nurses should educate patients to maintain glycaemic control, especially patients whose hyperglycaemic is only discovered at the preoperative workup.

Immunosuppressive treatments or immunosuppressed conditions

It is common knowledge that the immune system plays a crucial part in controlling infection and its suppression for therapeutic purposes (e.g. in patients on chronic corticosteroid or cyclosporine treatment, or chemotherapy) seems to raise the risk of a SWI (33).

Heart failure and COPD

During wound healing, the damaged tissues' continuity and function are re-established, but this can only happen if the microcirculation is restored and the tissues are nourished (42). A continuous supply of oxygen to the tissues via the microcirculation is vital to the healing process and for resisting infection. A poor cardiac pump function (NYHA $\geq$3) and chronic obstructive pulmonary disease do not help proper tissue perfusion and oxygenation, they delay the process of wound healing. Oxygen delivery to wounds depends on blood oxygenation and perfusion and the diffusion distance from the blood to the tissue, which relates to the partial oxygen pressure (43,44). Oxygenation is fundamental to cell motility and activity, and involved in healing inflammation, proliferation, collagen synthesis and angiogenesis. In inflammatory processes, hypoxia leads to anaerobic metabolism and causes acidosis and an ATP production insufficient for maintaining normal cell function, especially because the site of a wound is metabolically so active (45). Neutrophils and macrophages produce enzymes that require oxygen to function properly, and hypoxia consequently blunts their oxidative killing activity (46). In proliferation phases, hypoxia stimulates the expression of type IV collagenase and reduces the expression of laminin-5, which inhibits keratin cell motility. It was also showed that low levels of ROS, produced when a cell is in hypoxia, as in hydrogen peroxide solution, inhibited the migration and proliferation of keratin cells (47).

Molecular oxygen is also essential during collagen synthesis. Hydroxylation of proline and lysine in procollagen is a crucial step in collagen maturation. Procollagen molecules cannot form stable triple helices without hydroxyproline. Hydroxylation requires high amounts of oxygen (48).

Behavioural factors

Smoking

Smokers tend to have a poor wound healing function caused by a reduction in both local flow and tissue oxygen tension, which can delay the healing process, as described earlier (49). Wound oxygenation is also reduced by microvascular obstructions caused by platelet aggregation. Some studies also found that smokers are often more prone to bacterial infections and inflammatory diseases than non smokers, because of the hundreds of toxic components contained in cigarettes (50) and their impairment of the immune system.

Obesity

Obesity is strongly associated with diabetes mellitus and can give rise to technical difficulties and prolonged operating times that can contribute to the onset of DSWI (51). Even in an analysis adjusted for diabetes and duration of surgery, it was found that obesity remained an independent risk factor for DSWI. In the obese, the abundant adipose tissues produce and release a variety of proinflammatory and anti-inflammatory factors (52). Differences in serum (and tissue) concentrations have been reported for various antibiotics in obesity. The underlying causes of these alterations are due to the physiologic changes that can alter both Vd and drug Cl. The changes observed in GFR are particularly difficult to predict with current methods. Obese patients may be incorrectly dosed with the use of fixed (underdosed) or TBW-based dosing (overdosed) when the contribution of pharmacokinetic alterations in obesity is unrecognised (53). There is also a greater risk of dehiscence because of straining of subcutaneous sutures. It has been reported that a personalised education and dietary measures before surgery could have positive long-term effects and reduce the obesity-related risk of infections (54).

Surgical operative risk factors

Internal thoracic artery. Patients needing a CABG using the internal thoracic artery (ITA) carry a higher risk of DSWI. The perforating branches of the ITA perfuse the sternal region so using the ITA reduces subsequent sternal perfusion, as showed in animal as well as human studies.

Prolonged operating times. A poor tissue oxygenation during a lengthy surgical procedure and ventilation treatment could be a cause of a higher postoperative risk of DSWI, as suggested in some studies (55). A prolonged duration of the procedure could in itself increase the risk of DSWI in cells damaged by drying on exposure to air and surgical retractors. It also predisposes patients to infections directly via the higher likelihood of contamination of the incision or tissue desiccation (56). Longer procedures are more likely to be associated with blood loss, contributing to tissue hypoxaemia and shock, and reducing the patient's general resistance.

Blood transfusions. A large meta-analysis showed that patients who receive a blood transfusion have a higher risk of postoperative infectious complications than patients who do not (57). Blood transfusions temporarily induce an acquired immune suppression and therefore also a potentially increased risk of postoperative infectious complications. In particular, four possible mechanisms have been proposed (58), including an immunomodulatory effect mediated by immunologically active white blood cells (WBCs) that downregulate the recipient's immune function; soluble biological response modifiers released from WBCs during the storage of blood; and soluble human leukocyte antigen peptides or other soluble mediators that circulate in allogeneic plasma. The fourth possible mechanism is not an immunomodulatory effect, but involves a mechanism by which blood transfusion leads to postoperative organ dysfunction, which in turn predisposes to infection.

Re-exploration. Re-exploration for bleeding after surgery and other reasons for an unplanned return to the operating room can increase the risk of infection because they expose patients to further wound attack from airborne microbial agents. Haematoma is also a good pabulum for microbial growth.

Key Points

- behavioral factors: smoking, obesity
- surgical operative risk factors: preoperative factors: internal thoracic artery, prolonged operating times
  postoperative factors: blood transfusions *re-exploration, postoperative hypoxaemia or ventilatory support, postoperative CPR, hypotension*

Key Points

- our literature review identified six scales for predicting the risk of SWI and another general tool for predicting nosocomial infections, which can also be applied to SWIs, that is, the NNIS risk index
- the value of these different tools was evaluated by means of the receiver operating characteristic (ROC) curve, which is a fundamental tool for assessing prognostic scales
- the only risk scale that enabled a straightforward preoperative assessment was found moderately accurate but a different statistical approach (not area under ROC curve) was used, preventing a direct comparison of its accuracy with other scales
- in conclusion, this study provides a broad update on what we know about the risk factors for SWI and the risk scales that can be used to manage infection control at cardiosurgery units. other scales

Postoperative hypoxaemia or ventilatory support. Low cardiac output syndrome or respiratory impairment after surgery could cause inadequate tissue oxygenation, interfering with the healing process as explained earlier.

Postoperative CPR. Cardiopulmonary resuscitation places the sternum at risk of fracture or dehiscence and the body only diverts the blood to the vital organs (59).

Prediction scales

Our literature review identified six scales for predicting the risk of SWI and another general tool for predicting nosocomial infections (Table 4), which can also be applied to SWIs, that is, the NNIS risk index. The value of these different tools was evaluated by means of the receiver operating characteristic (ROC) curve, which is a fundamental tool for assessing prognostic scales. In a ROC curve, the true positive rate (sensitivity) is plotted as a function of the false positive rate (100 specificity) for different cut-off points on a scale (60). The area under the ROC curve is a measure of how well a cut-off can distinguish between two diagnostic groups (SWI+/SWI−). Two of the risk indexes and the NNIS showed a limited accuracy, while the other four specific indexes proved moderately accurate. The latters are more complicated, however, and not very easy to apply. Two of the moderately accurate scales, one of the less accurate and the NNIS all need variables inherent in the surgical and/or postoperative phases, however, and so they can only assess patients after they have undergone surgery. Risk indexes that have to be used postoperatively can only enable a risk adjustment for the purposes of comparing the performance postoperatively, whereas scales for use preoperatively facilitate the preoperative design of prevention strategies (e.g. optimising diabetes control prior to surgery, or adopting a different prophylactic antibiotic regimen). In any case, the only risk scale that enabled a straightforward preoperative assessment was found moderately accurate, but a different statistical approach (not area under ROC curve) was used, preventing a direct comparison of its accuracy with other scales.

In conclusion, this study provides a broad update on what we know about the risk factors for SWI and the risk scales that can be used to manage infection control at cardiosurgery units.

REFERENCES

1 Nichols RL. Preventing surgical site infections: a surgeon's perspective. Emerg Infect Dis 2001;7:220–4.
2 Burke JP. Infection control - a problem for patient safety. N Engl J Med 2003;348:651–6.
3 Mangram AJ, Horan C, 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 Borger MA, Rao V, Weisel RD, Ivanov J, Cohen G, Scully HE, David TE. Deep sternal wound infection: risk factors and outcomes. Ann Thorac Surg 1998;65:1050–6.
5 Lua JCY, Graysonb DA, Jhaa P, Srinivasana AK, Fabria BM. Risk factors for sternal wound infection and mid-term survival followingcoronary artery bypass surgery. Eur J Cardiothorac Surg 2003;23:943–9.
6 The Parisian Mediastinitis Study Gruop. Risk factors for deep sternal wound infection after sternotomy: a prospective, multicenter study. J Thorac Cardiovasc Surg 1996;111:1200–7.
7 Tang GH, Maganti M, Weisel RD, Borger MA. Prevention and management of deep sternal wound infection. Semin Thorac Cardiovasc Surg 2004;16:62–9.
8 Toumpoulis IK, Anagnostopoulos CE, DeRose JJ. The impact of deep sternal wound infection on long term survival after coronary artery bypass grafting. Chest 2005;127:464–71.
9 Filsoufi F, Castillo JG, Rahmanian PB, Broumand SR, Silvay G, Carpentier A, Adams DH. Epidemiology of deep sternal wound infection in cardiac surgery. J Cardiothorac Vasc Anesth 2009;23:488–94.
10 Cayci C, Russo M, Faisal C, Timothy M, Vefa O, Michael A, Mehmet C, Jeffrey A. Risk analysis of deep sternal wound infections and their impact on long-term survival: a propensity analysis. Ann Plast Surg 2008;61:294–301.
11 Olsen MA, Hopkins PLBD, Polish B, Sundt TM, Fraser VJ. The risk factors for deep and superficial chest surgical-site infections after coronary artery bypass graft surgery are different. J Thorac Cardiovasc Surg 2002;124:136–45.
12 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.
13 Trick W, Scheckler WE, Tokars JI, Jones KC, Reppen ML, Smith EM, Jarvis WR. Modificable risk factors associated with deep sternal site infection after coronary artery bypass grafting. J Thorac Cardiovasc Surg 2000;119:108–14.
14 Friedman ND, Bull AL, Russo PL, Leder K, Reid C, Billah B, Marasco S, McBryde E, Richards MJ.

An alternative scoring system to predict risk for surgical site infection complicating coronary artery bypass graft surgery. Infect Control Hosp Epidemiol 2007;28:1162–8.
15 Hussey LC, Leeper B, Hynan LS. Development of the sternal wound infection prediction scale. Heart Lung 1998;27:326–36.
16 Roques F, Nashef SAM, Michel P, Gauducheau E, De Vincentiis C, Baudet E, Cortina J, David M, Faichney A, Gavrielle F, Gams E, Harjula A, Jones MT, Pinna Pintor P, Salamon R, Thulin L. Risk factors and outcome in European cardiac surgery: analysis of the Euroscore multinational database of 19030 patients. Eur J Cardiothorac Surg 1999;15:816–23.
17 Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. Eur J Heart 2003;24: 882–3.
18 Fowler VG, O'Brien SM, Muhlbaier LH, Corey GR, Ferguson TB, Peterson ED. Clinical predictors of major infections after cardiac surgery. Circulation 2005;112 Suppl 1:1358–65.
19 Russo PL, Spelman DW. A new surgical-site infection risk index using risk factors identified by multivariate analysis for patients undergoing coronary artery bypass graft surgery. Infect Control Hosp Epidemiol 2002;23:372–6.
20 Paul M, Raz A, Leibovici L, Madar H, Holinger R, Rubinovitch B. Sternal wound infection after coronary artery bypass graft surgery: validation of existing risk scores. J Thorac Cardiovasc Surg 2007;133:397–403.
21 National Nocosomial Infections Surveillance (NNIS) System Report. Data summary from January 1992 through June 2004. Am J Infect Control 2004;32:470–85.
22 Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG, Banerjee SN, Edwards JR, Tolson JS, Henderson TS, Hughes JM. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nocosomial Infections Surveillance System. Am J Med 1991;91 Suppl 3B:152S–7S.
23 Roy MC, Herwaldt LA, Embrey R, Kuhns K, Wenzel RP, Perl TM. Does the Centers for Disease Control's NNIS system risk index stratify patients undergoing cardiothoracic operations by their risk of surgical-site infection?. Infect Control Hosp Epidemiol 2000;21:186–90.
24 Swets JA. Measuring the accuracy of diagnostic systems. Science 1988;240:1285–93.
25 Haley R. Measuring the intrinsic risk of wound infection in surgical patients. Probl Gen Surg 1993;10:396–417.
26 Sofer D, Gurevitch J, Shapira I, Paz Y, Matsa M, Kramer A, Mohr R. Sternal wound infections in patients after coronary artery bypass grafting using bilateral skeletonized internal mammary arteries. Ann Surg 1999;229:585–90.
27 Nakano J, Okabayashi H, Hanyu M, Soga Y, Nomoto T, Arai Y, Matsuo T, Kai M, Kawatou M. Risk factors for wound infection after off-pump coronary artery bypass grafting: should bilateral internal thoracic artries be harvested in patients with diabetes? J Thorac Cardiovasc Surg 2008;135:540–5.
28 Zacharias A, Habib RH. Factors predisposing to median sterotomy complications. Chest 1996;110:1173–8.
29 Hollenbeak CS, Murphy DM, Koenig S, Woodward RS, Dunagan WC, Fraser VJ. The clinical and economic impact of deep chest surgical site infections following coronary artery bypass graft surgery. Chest 2000;118:397–402.
30 Ridderstolpe L, Gill H, Granfeldtb H, Ahlfeldt H, Rutbergb H. Superficial and deep sternal wound complications: incidence, risk factors and mortality. Eur J Cardiothorac Surg 2001;20:1168–75.
31 Kohli M, Yuan L, Escobar M, David T, Gillis G, Comm B, Garcia M, Conly J. A risk index for sternal surgical wound infection after cardiovascular surgery. Infect Control Hosp Epidemiol 2003;24:17–25.
32 Fakih MG, Sharma M, Khatib R, Berriel-Cass D, Meisner S, Harrington S, Saravolatz L. Increase in the rate of sternal surgical site infection after coronary artery bypass graft: a marker of higher severity of illness. Infect Control Hosp Epidemiol 2007;28:655–60.
33 Steingrimsson S, Gottfredsson M, Kristinsson KG, Gudbjartsson T. Deep sternal wound infections following open heart surgery in Iceland: a population-based study. Scand Cardiovasc J 2008;42:208–13.
34 Savage EB, Grab JD, O'Brien SM, Ali A, Oku EJ, Perez-Tamayo A, Eiferman DS, Peterson ED, Edwards FH, Higgins RS. Use of both internal thoracic arteries in diabetic patients increases deep sternal wound infection. Ann Thorac Surg 2007;83:1002–7.
35 Sachithanandan A, Nanjaiah P, Nightingale P, Wilson IC, Graham TR, Rooney SJ, Keogh BE, Pagano D. Deep sternal wound infection requiring revision surgery:impact on midterm survival following cardiac surgery. Eur J Cardiothorac Surg 2008;33:673–8.
36 Stamou SC, Dangas G, Dullum MK, Pfister AJ, Boyce SW, Bafi AS, Garcia JM, Corso PJ. Beating heart surgery in octogenarians: perioperative outcome and comparison with younger age groups. Ann Thorac Surg 2000;69:1140–5.
37 Lesourd B. Protein undernutrition as the major cause of decreased immune function in the elderly: clinical and functional implications. Nutr Rev 1995;53 4 pt 2:S86–91.
38 King L. Impaired wound healing in patients with diabetes. Nurs Stand 2001;15:39–45.
39 Gallacher SJ, Thomson G, Fraser WD, Fisher BM, Gemmell CG, MacCuish AC. Neutrophil bactericidal function in diabetes mellitus: evidence for association with blood glucose control. Diabet Med 1995;12:916–20.
40 Kramer R, Groom R, Weldner D, Gallant P, Heyl B, Knapp R, Arnold A. Glycemic control and reduction of deep sternal wound infection rates: a multidisciplinary approach. Arch Surg 2008;143:451–6.
41 Rassias AJ, Marrin CA, Arruda J, Whalen PK, Beach M, Yeager MP. Insulin infusion improves

neutrophil function in diabetic cardiac surgery patients. Anesth Analg 1999;88:1011–6.
42 Rodriguez PG, Felix FN, Woodley DT, Shim EK. The role of oxygen in wound healing: a review of the literature. Dermatol Surg 2008;34:1159–69.
43 Gottrup F. Oxygen in wound healing and infection. World J Surg 2004;28:312–5.
44 Jonsson K, Jensen JA, Goodson WH, West J, Hopf HW, Hunt TK. Tissue oxygenation, anemia, and perfusion in relation to wound healing in surgical patients. Ann Surg 1991;214:605–13.
45 Broussard CL. Hyperbaric oxygenation and wound healing. J Vasc Nurs 2004;22:42–8.
46 Allen DB, Maguire JJ, Mahdavian M, Wicke C, Marcocci L, Scheuenstuhl H, Chang M, Le AX, Hopf HW, Hunt TK. Wound hypoxia andacidosis limit neutrophil bacterial killing mechanisms. Arch Surg 1997;132:991–6.
47 O'Toole EA, Goel M, Woodley DT. Hydrogen peroxide inhibits human keratinocyte migration. Dermatol Surg 1996;22:525–9.
48 Hunt TK, Zederfeldt B, Goldstick TK. Oxygen and healing. Am J Surg 1969;118:521–5.
49 Jensen JA, Goodson WH, Hopf HW, Hunt TK. Cigarette smoking decreases tissue oxygen. Arch Surg 1991;126:1131–4.
50 Xu M, Scott JE, Liu KZ, Bishop HR, Renaud DE, Palmer RM, Soussi-Gounni A, Scott DA. The influence of nicotine on granulocytic differentiation - inhibition of the oxidative burst and bacterial killing and increased matrix metalloproteinase-9 release. BMC Cell Biol 2008; 9:19–33.
51 Eklund AM, Lyytikäinen O, Klemets P, Huotari K, Anttila VJ, Werkkala KA, Valtonen M. Mediastinitis after more than 10,000 cardiac surgical procedures. Ann Thorac Surg 2006;82:1784–9.
52 Lago F, Dieguez C, Gómez-Reino J, Gualillo O. The emerging role of adipokines as mediators of inflammation and immune responses. Cytokine Growth Factor Rev 2007;18:313–25.
53 Pai MP, Bearden DT. Antimicrobial dosing considerations in obese adult patients. Pharmacotherapy 2007;27:1081–91.
54 Blissmer B, Riebe D, Dye G, Ruggiero L, Greene G, Cadwell M. Health-related quality of life following a clinical weight loss intervention among overweight and obese adults: intervention and 24 month follow-up effects. Health Qual Life Outcomes 2006;4:43–51.
55 Friberg O, Svedjeholm R, Söderquist B, Granfeldt H, Vikerfors T, Källman J. Local gentamicin reduces sternal wound infections after cardiac surgery: a randomized controlled trial. Ann Thorac Surg 2005;79:153–61.
56 Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS. Surgical site infection (SSI) rates in the United States, 1992-1998: the National Nosocomial Infections Surveillance System basic SSI risk index. Clin Infect Dis 2001; 33 2 Suppl:S69–77.
57 Hill GE, Minei JP, Frawley WH, Griffith KE, Forestner JE. Allogeneic blood transfusion increases the risk of postoperative bacterial infection: a meta-analysis. J Trauma 2003;54:908–14.
58 Vamvakas EC. Possible mechanisms of allogeneic blood transfusion: associated postoperative infection. Trans Med Rev 2002;16:144–60.
59 Vaska PL. Sternal wound infections. AACN Clin Issues CritCare Nurs 1993;4:475–83.
60 Metz CE. Basic principles of ROC analysis. Semin Nucl Med 1978;8:283–98.