Multi-centre prospective internal and external evaluation of the Brompton Harefield Infection Score (BHIS)

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Abstract

Background: Previously, we reported that the Brompton Harefield Infection Score (BHIS) accurately predicts surgical site infection (SSI) after coronary artery bypass grafting (CABG). The BHIS was developed using two-centre data and stratifies SSI risk into three groups based on female gender, diabetes or HbA1c > 7.5%, body mass index ≥ 35 , left ventricular ejection fraction < 45% and emergency surgery. The purpose of this study was to prospectively evaluate BHIS internally as well as externally.

Methods: Multi-centre prospective evaluation involving three tertiary centres took place between October 2012 and November 2015. SSI was classified using the Public Health England protocol. Receiver operating characteristic (ROC) curves assessed predictive accuracy.

Results: Across the four hospital sites, 168 of 4308 (3.9%) CABG patients had a SSI. Categorising the hospitals by BHIS score revealed that 65% of all patients were low risk (BHIS 0–1), 26% were medium risk (BHIS 2–3) and 8% were high risk (BHIS ≥ 4). The area under the ROC curve was in the range of 0.702–0.785. Overall area under the ROC curve was 0.709.

Conclusions: BHIS provides a novel, internally and externally evaluated score for a patient's risk of SSI after CABG. It enables clinicians to focus on strategies to prospectively identify high-risk patients and improve outcomes.

Keywords

Surgical site infection, surveillance, statistics

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Background

Since the 1970s, coronary artery bypass grafting (CABG) has evolved to become one of the commonest and most successful of all operative procedures. The symptomatic and survival benefit of this surgery is well recognised (Wheatley, 2002). Surgical site infection (SSI) following CABG surgery is universally acknowledged as a serious complication (Sharma et al., 2004). Although the incidence of SSI after CABG remains low, the effects on the periprocedural outcome are enormous (Lenz et al., 2016). The latest Public Health England (PHE) data show the inpatient and readmission CABG SSI incidence is 3.7% based on five-year data to

March 2016 (PHE, 2016). The impact of SSI on morbidity and mortality as well as its cost implications are significant and widely reported (Graf et al., 2010).

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Figure 1. Brompton Harefield Infection Score (BHIS). A predictive model for SSI risk in CABG patients.

Diabetes, Glycated Hb <7.5% = 1 or Diabetes, Glycated Hb ≥7.5% = 3 BMI ≥35 = 2 Female = 2 Emergency = 2 LVEF <45% = 1		
Group	Total Score	% Patient Distribution
Low risk	0-1	66%
Med risk	2-3	26%
High risk	≥4	8%

Stratifying patients' risk of SSI after CABG is a strategy to aid patient selection, counselling, risk modification and surgical management. Recognising the need for a specific prognostic scoring system for predicting the likelihood of SSI after CABG, incorporating both a patient's intrinsic risk of infection preoperatively and a weighting of risk factors, we developed and validated the Brompton Harefield Infection Score (BHIS) index (Raja et al., 2015) (Figure 1). The BHIS was developed using two-centre data and stratifies SSI risk into three groups based on female gender, diabetes or HbA1c > 7.5%, body mass index (BMI) ≥ 35, poor left ventricular ejection fraction (LVEF) and emergency surgery. The purpose of this study was to prospectively evaluate BHIS as an SSI predictive tool internally as well as externally.

Methods

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local ethical committees approved the study and the requirement for individual patient consent was waived. The authors adhered to STROBE guidelines (Vandenbroucke et al., 2014) for reporting observational studies. Continuous, prospective surveillance data on SSI were collected and validated via external audit bodies. Public Health England 2013 protocol was used to confirm SSI following CABG (PHE, 2013). Subsequent multi-centre prospective validation involving two additional tertiary centres took place between October 2012 and November 2015, with a final total of 4308 CABG patients and 168 instances of SSI. All SSIs were identified prospectively by trained surveillance specialist nurses and confirmed by a senior clinician.

Differences between the two groups (those who developed SSI and those who did not) were compared using the Pearson χ^2 or Fisher's exact test. Continuous data were analysed using the two-tailed t-test or Mann-Whitney U test for parametric and non-parametric data, respectively. Comparisons between the results at different institutions were accomplished using analysis of variance and the Pearson χ^2 test. Goodness of fit and Hosmer-Lemeshow test results were assessed. For the Hosmer-Lemeshow test,

a *P* value that was not statistically significant (i.e. *P* > 0.05) was considered to indicate reasonable model fit. Receiver operating characteristic (ROC) curves were used to assess predictive accuracy. Somers' *Dxy* rank correlation coefficient was used as measure of discrimination. *Dxy* corresponds to $2*(C-0.5)$ where *C* is the area of ROC (aROC) curve (concordance probability). R version 2.15.2 (<http://www.R-project.org>) and rms package (R package version 4.0-0. <http://CRAN.R-project.org/package=rms>) statistical software packages were used for statistical analysis.

Results

The multi-centre validation analysis was undertaken based on 4308 cases pooled from four hospital sites, each contributing varying numbers of cases across varying time periods (Hospital 1 – 1688 cases, 1 January 2013 – September 2015; Hospital 2 – 970 cases, 1 October 2013 – September 2015; Hospital 3 – 1195 cases, 1 November 2012 – April 2015; Hospital 4 – 455 cases, 1 October 2012 – November 2013). The separate analysis and cohort of patients for validation ensured there was no statistical overfitting of the initial model.

Across the four hospital sites, 168 of 4308 (3.9%) CABG patients had a SSI. Categorising the hospitals by BHIS score revealed that 65% of all patients were low risk (BHIS 0–1), 26% were medium risk (BHIS 2–3) and 8% were high risk (BHIS ≥ 4). The SSI incidence was lowest in the BHIS group 0–1 at 2%, 6% in BHIS group 2–3 and highest in BHIS group ≥ 4 at 13%. The validated variables are presented in Table 1. Area under the curve (aROC) for the four hospitals is presented in Figure 2. These demonstrate the sensitivity of the model appears to be in trade-off against its specificity. The overall observed BHIS score distribution vs. predicted and SSI risk for each of the four hospital sites are presented in Table 2. Hospital 2 appears to perform less well despite being significantly different from Area = 0.5, noting that a generally well-fitting model does not necessarily mean good discrimination for some hospitals as this depends on the strength of the explanatory variables. The overall area under the ROC curve was 0.709 for the BHIS.

Table 1. BHIS variables tested for dataset (n = 4308), four hospital sites.

BHIS variable	Value	Frequency count (n)	Total (%)
			Frequency (%)
BMI	< 35	3833	89.0
	≥ 35	375	8.7
	Missing	100	2.3
Diabetes management	Not diabetic	2674	62.1
	Oral therapy	865	20.1
	Insulin	312	7.2
	Diet controlled	90	2.1
	Missing	367	8.5
HbA1C	Not diabetic	2674	62.1
	≤ 7.5	481	11.2
	> 7.5	324	7.5
	Missing	829	19.2
Ejection fraction estimation	Good (LVEF ≥ 50%)	3315	76.9
	Moderate (LVEF 30–49%)	796	18.5
	Poor (LVEF < 30%)	152	3.5
	Missing	45	1.0
Gender	Male	3538	82.1
	Female	770	17.9
Operative urgency	Elective/Urgent	4200	97.5
	Emergency	98	2.3
	Salvage	10	0.2

Discussion

In this study, we prospectively tested, both internally and externally, the BHIS and its predictive capacity for all types SSI after CABG at four tertiary centres with a large volume of operations. The five predictors in the BHIS—female gender, diabetes or HbA1c > 7.5%, BMI ≥ 35, LVEF < 45% and emergency surgery (Figure 1)—all have strong biologic plausibility to be associated with SSI after CABG (Fowler et al., 2005; Harrington et al., 2004; Lu et al., 2003; Olsen et al., 2003; Vuorisalo et al., 1998).

Female gender has been strongly associated with SSI after CABG (Lemaignen et al., 2015; Rochon et al., 2017). The differences in fat distribution, impaired peripheral circulation (Friedman et al., 2007) and tension of the breast upon the sternotomy skin wound (Lemaignen et al., 2015) are some of the pathophysiologic mechanisms for delayed wound healing and wound leakage, leading to SSI particularly sternal wound infection in women.

The mechanisms underlying the susceptibility to infectious diseases in diabetics are not completely understood, but the evidence suggests that hyperglycaemia results in the formation of advanced glycation end products, which can affect host

cell function by impairing humoral response, complement activation, chemotaxis, adhesion and phagocytosis as well as intracellular and extracellular killing (Casqueiro et al., 2012; Koh et al. 2012; Freidman et al., 2007; Gan, 2013; Gatti et al., 2016). As a consequence, diabetic patients are at increased risk of SSI, and such a risk seems to be highest in patients undergoing cardiac surgery (Martin et al., 2016).

Obese patients suffer a higher incidence of postoperative superficial or deep wound infections (Wigfield et al., 2006). Birkmeyer et al. (1998) reported that in obese patients the rate of wound infections was as up to three times higher after adjustment of other predictors of this outcome. Moulton et al. (1996) found increased superficial sternotomy wound infections and conduit harvest site infections in patients with a BMI > 30. Similarly, Tolpin et al. (2009) established an odds ratio of 2.9 associated with obesity for sternal wound complications in a multivariate analysis of 6504 patients. Obesity and its associated insulin resistance, endothelial dysfunction and systemic pro-inflammatory and thrombotic states predispose to SSI after CABG (Loop et al., 1990).

Patients with impaired LVEF are also more likely to develop SSI after CABG (Abuzaid et al., 2015; Sakamoto

Figure 2. BHIS area under receiver operating characteristic (aROC), by hospital site. **Table 2.** Hospital-specific data.

BHIS: Distribution by group; actual patients observed (%) (predicted patients (%))	Overall group total (n) SSI risk (%) (95% CI) modified Wald method	Hospital 1 SSI risk (%) (95% CI)	Hospital 2 SSI risk (%) (95% CI)	Hospital 3 SSI risk (%) (95% CI)	Hospital 4 SSI risk (%) (95% CI)
Low risk (BHIS 0–1); 66 (65)	55/2809 2 (1.5–2.5)	0.5 (0.2–1.1)	1.7 (0.9–3.1)	9.5 (6.6–13.5)	4.2 (2.3–7.2)
Medium risk (BHIS 2–3); 26 (27)	70/1163 6 (4.8–7.5)	3.2 (1.9–5.2)	3.2 (1.5–6.3)	7.7 (5.1–11.3)	17.6 (12.1–25.0)
High risk (BHIS ≥ 4); 8 (8)	43/336 13 (9.6–16.8)	6.6 (3.5–12.0)	13.3 (7.4–22.4)	20.0 (12.2–30.9)	25.8 (13.5–43.5)
CI, confidence interval.					

et al., 2003). Poor perfusion state coupled with inotropic and vasoconstrictor support are the pathophysiologic mechanisms for SSI in the presence of impaired left ventricular function (Abuzaid et al., 2015; Sakamoto et al., 2003).

Emergency surgery is a well-recognised independent risk factor for all types of complications after coronary artery surgery (Heilmann et al., 2013). Emergency surgery implies that there is not enough time for several recommended procedures, such as optimising blood glucose levels, implementing antiseptic measures, screening for methicillin-resistant *Staphylococcus aureus* (MRSA) or the timely application of prophylactic antibiotics. Patients are likely to be in poor general condition and immunologically compromised (Heilman et al., 2013; Wetzel et al., 2006). These conditions all potentiate the risk of SSI.

Some components of the BHIS, such as diabetes and obesity, are modifiable patient factors. Our scoring system may help identify patients who could benefit from a targeted approach using interventions aimed at reducing the risk of SSI in those highest at risk (Cannoletta et al., 2015), including negative pressure therapy for clean closed surgery wounds in high-risk patients (World Health Organization, 2016).

This study has several potential limitations. First, the total number of SSI events was relatively small ($n = 168$), limiting the ability to identify associations with a large number of variables. There was a small number of centres and limited number of risk factor data collection other than BHIS data. Another limitation of our study was a significant proportion (19.2%) of HbA1C (Glycated Hb) levels missing from our dataset across the four hospitals. This was due to its absence on the nationally collected cardiothoracic dataset. One potential improvement based on this study would be its inclusion as an additional variable in the national dataset. An additional limitation is that it was not possible to consider additional risk factors to allow us to compare against a range of candidate models. Finally, a model fit does not necessarily mean better discrimination as discrimination depends on better explanatory variables.

Our internal and external evaluation of the predictive SSI score suggest that patients from a small number of different hospitals, who might be expected to have somewhat different risk profiles, have an area under ROC curve similar to the original derivation cohort. This implies that the original level of sensitivity/specificity found for the scoring system, described by the area under its ROC curve, was not the result of a chance finding in the first study by Raja et al. (2015), nor a result of characteristics specific to the derivation cohort of patients, which might not be present in other cohorts.

Conclusions

We present a prospectively evaluated a score for predicting (all type) SSI risk in patients undergoing CABG. BHIS is a

reproducible risk stratification model for CABG surgery where, on average, there is a 71% probability of correctly classifying a patient with SSI, which represents a fair but not excellent degree of discrimination. This risk index can also be used to optimise co-morbidities of patients included in this model and to target interventions accordingly.

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