



# Significant Reduction of Sternal Wound Infection in Cardiac Surgical Patients

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## Abstract

**Objective:** Sternal wound infections continue to be a major source of morbidity and mortality after cardiac surgery being associated with markedly increased hospital costs. Prophylactic antibiotics and glycaemic control have decreased but not eradicated this life-threatening complication. This multinational study was undertaken to determine whether a detailed infection prevention protocol using specific pre-, intra- and postoperative measures including topical application of antibiotics (Group B; novel closure group) would further reduce the incidence of sternal infections compared to established standard treatment (Group A; standard group).

**Patients and Methods:** 8,168 consecutive patients underwent cardiac surgery from February 2006 to June 2015: 4,615 patients in the novel closure Group B (prospectively included) and 3,553 patients in the standard Group A (retrospectively studied). Patients were matched using propensity score adjusted analysis. In both groups, a prophylactic second-generation cephalosporin was given prior to surgery and repeated once surgery exceeded six hours. Group A, but not Group B patients, received additional three doses of antibiotics after surgery. Patients were followed for one year to include external wound infection presenting after discharge from the hospital. Data are presented as the means and standard deviations for continuing variables and as occurrences and percentages for categorical variables. Welch's t-tests and  $\chi^2$  analyses were used to test statistical significance. Additionally, logistic regression analyses were applied separated into Group A and B in order to examine potential differential effects of established risk factors for sternal wound infections.

**Results:** The results are summarized in the Tables 1 to 4. Preoperative patient characteristics and risk factors such as diabetes, gender or age did not differ between groups while others significantly differed but with merely very small or small differences. There was a significant difference of major outcome factors in favour of the novel closure protocol (Group B) versus the standard treatment (Group A): incidence of superficial wound infection: 0.4% vs. 2.9%; deep sternal wound infection: 0.6% vs. 2.2%; number of infection related reoperations: 81 vs. 241 and number of muscle flap plasty in patients with sternal destruction: 0.2% vs. 1.1%. Admittedly, there was a significant increase of duration of stay on ICU related to Group B patients in Russia but not in the total sample. More important, use of the novel closure protocol revealed that mammary artery harvesting and body mass index were not significant risk factors anymore. Furthermore, the use of vancomycin was not associated with increased incidence of postoperative renal insufficiency. No patient developed vancomycin resistant infection. Occurrence of multi-resistant bacteria has not been observed.

**Conclusion:** This infection prevention protocol as presented here markedly reduces postoperative sternal wound infections, saves lives, reduces infection-related reoperations, muscle flap plasty surgeries, limits the use of postoperative antibiotics and is highly cost-effective. The use of topical antibiotics did not provoke the occurrence of multi-resistant nosocomial infections. This concept markedly reduces the risk of postoperative wound infections, and, hence, represents a major step with regard to the safety for patients undergoing cardiac surgery through a median sternotomy.

## Introduction

Despite various minimally invasive incisions, median sternotomy remains the most frequently

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**Table 1:** Preoperative patient characteristics (continuous variables).

Level of analysis		Age (SD) years	Height (SD) cm <sup>1</sup>	Weight (SD) kg <sup>1</sup>	Body mass index (SD) kg/m <sup>2</sup>
All sites	Control	61.46 (11.32)	171.88 (8.78)	79.69 (14.95)	27.64 (4.33)
	Novel closure	61.31 (10.94)	172.07 (9.07)	80.03 (15.08)	28.02 (4.54)
	p-value	0.565	0.544	0.525	< 0.001
	effect size	0.01	-0.01	-0.01	-0.09
Russia	Control	57.72 (8.94)	-	-	28.15 (4.14)
	Novel closure	58.3 (9.28)	-	-	28.68 (4.51)
	p-value	0.026	-	-	< 0.001
	effect size	-0.06	-	-	-0.12
Austria	Control	66.02 (12.98)	172.33 (9.11)	81 (15.39%)	27.25 (4.7)
	Novel closure	65.22 (12.87)	172.59 (9.95)	81.84 (16.54)	27.39 (4.63)
	p-value	0.182	0.547	0.259	0.534
	effect size	0.06	-0.03	-0.05	-0.03
Switzerland	Control	67.73 (10.75)	171.15 (8.16)	77.55 (13.94)	26.42 (4.11)
	Novel closure	67.48 (9.95)	171.47 (7.9)	77.94 (12.91)	26.45 (4.05)
	p-value	0.655	0.471	0.595	0.897
	effect size	0.02	-0.04	-0.03	-0.01

**Note:** <sup>1</sup>Data only available for Switzerland and Austria (Control: n=1,483, Novel closure protocol: n=1,744 for all sites).

Effect size: Cohen's  $\delta$

used incision in cardiac surgery, particularly in complex patients undergoing combined procedures. Postoperative sternal wound infections occur in up to 9% of patients [1]. Vacuum-assisted suction systems [2], omental grafts, breast flaps, allogenic bone grafts and reconstruction of the chest wall with various muscle flaps have been used to reduce the mortality and morbidity of sternal wound infections [3]. Nevertheless, even in modern era post-sternotomy mediastinitis is associated with a marked increase in acute and long-term mortality rates [4,5]. In addition, despite markedly improved results with muscle flap reconstruction [6], two thirds of patients complain about chest instability, loss of skeletal continuity and dominant right arm weakness even in strictly left-sided procedures, all causing sustained disability in up to 30% of patients which suffered from deep sternal wound infection [7].

Hence, prevention of infection is the most important measure. Prophylactic antibiotics and glycaemic control have decreased but not eradicated this life-threatening complication [8]. This multinational study was undertaken to determine whether a more detailed, multimodality infection prevention protocol using specific pre-, intra- and postoperative measures (novel closure Group B) would further reduce the incidence of sternal infections compared to standard treatment (Group A).

## Methods

### Study design

An observational cohort analysis with two sequential patient groups was performed at four different sites. The study started at the Hirslanden Klinik Im Park in Zurich, Switzerland and was subsequently extended to the Military Medical Academy St. Petersburg, the State Cardiovascular Surgery Center Penza, both in Russia, as well as the Medical University of Vienna, Austria.

### Study population

All consecutive patients undergoing cardiac surgery via full sternotomy either received the standard (Group A) or the novel closure protocol (Group B) (n=8,168). In the Hirslanden Klinik im

Park in Zurich Group A patients were operated on between May 2006 and September 2009 (n=564) and Group B patients between October 2009 and October 2014 (n=812), respectively. In the Military Medical Academy St. Petersburg, Group A patients operated between February 2006 and September 2009 (n=263) and Group B patients operated between October 2009 and June 2013 (n=220) have been included. In the State Cardiovascular Surgery Center Penza Group A patients operated between January 2011 and May 2012 (n=1,807) have been compared with Group B patients operated between June 2012 and April 2014 (n=2,651). Finally, in the Medical University of Vienna Group A patients have operated between March 2013 and February 2014 (n=919) and Group B patients between July 2014 and June 2015 (n=932).

### Novel closing protocol

This infection prevention protocol consists of several defined measures applied before, during and after surgery.

#### Preoperatively:

1. Reduction of the bacterial load in the nasal mucosa through application of mupirocin (Bactroban<sup>®</sup>) nasal ointment starting the day before surgery and continuing for four days after the operation.
2. Men shave the face; those with a beard shave the neck.
3. At the day of surgery, patients take a total body shower with chlorhexidine gluconate 4% (Hibiscrub<sup>®</sup>) or octenidin-dihydrochlorid 0.1% prior to transfer to the operating room.
4. Insertion of central venous catheters follows a strict, aseptic protocol: (a) cleaning of the site of the catheter insertion with chlorhexidine 2% in alcohol three times, paying strict attention to the rules of sterility; (b) after disinfection, the skin must be allowed to completely dry on its own; (c) to avoid injection into the central venous catheter too close to the skin, a 40 cm distance of central venous catheter stopcocks to the skin of the patient is used during and after surgery; stopcocks lying inside the patients bed are not allowed.

**Table 2:** Preoperative and perioperative patient characteristics (categorical variables).

Level of analysis		Gender (m/f)	Diabetes (yes/no)	Type of surgery Bypass surgery/ Valve surgery/Bypass and Valve/other surgeries)
All sites	Control	2,665 (75%)/888 (25%)	585 (16.5%)/2968 (83.5%)	1863 (53.8%)/870 (25.1%)/523 (15.1%)/204 (5.9%)
	Novel closure	3,462 (75%)/1153 (25%)	790 (17.1%)/3825 (82.9%)	2,227 (49.3%) /935 (20.7%)/853 (18.9%)/499 (11.1%)
	p-value	0.992	0.434	<0.001
	effect size	0.0001	0.01	0.11
Russia	Control	1,617 (78.1%)/453 (21.9%)	219 (10.6%)/1851 (89.4%)	1,309 (63.2%)/441 (21.3%)/286 (13.8%)/34 (1.6%)
	Novel closure	2,200 (76.6%)/671 (23.4%)	426 (14.8%)/2445 (85.2%)	1625 (56.6%)/455 (15.9%)/590 (20.1%)/201 (7%)
	p-value	0.218	<0.001	<0.001
	effect size	0.02	0.06	0.16
Austria	Control	631 (68.7%)/288 (31.3%)	289 (31.5%)/630 (68.5%)	325 (39.4%)/239 (28.9%)/142 (17.2%)/120 (14.5%)
	Novel closure	673 (72.2%)/259 (27.8%)	283 (30.4%)/649 (69.6%)	312 (37.6%)/199 (24 %)/160 (19.3%)/160 (19.3%)
	p-value	0.093	0.614	0.014
	effect size	0.04	0.01	0.08
Switzerland	Control	417 (73.9%)/147 (26.1%)	77 (13.7%)/487 (86.3%)	229 (41.6%)/190 (33.7%)/95 (16.8%)/50 (8.9%)
	Novel closure	589 (72.5%)/223 (27.5%)	81 (10%)/731 (90%)	290 (35.7%)/281 (34.6%)/103 (12.7%)/138 (17%)
	p-value	0.565	0.035	<0.001
	effect size	0.02	0.06	0.13

Note: effect size: Cramer's  $\omega$

5. Surgical site disinfection twice with Isopropyl alcohol 70% - chlorhexidine gluconate 2% in alcohol instead of iodine-povidone solution; again, the skin has been allowed to completely dry spontaneously before the patient is covered.

6. Systemic intravenous antibiotic prophylaxis with a second-generation cephalosporin at least 30 mins before starting surgery.

7. Second intravenous antibiotic prophylaxis if surgery takes more than six hours.

#### Intraoperatively:

8. Surgical technique: (1) No use of electrocautery in subcutaneous tissue; (2) In coronary revascularisation, preservation of the caudal bifurcation of the left and right mammary artery at the level of the epigastrium; (3) Sternal wound closure: mix of 3 gr. vancomycin with 4 ml NaCl which will result in a bone wax like material being brought into the sternal spongiosa; (4) Use of 6 to 8 figure-of-eight sternal wires particularly including reinforcement of the lower sternum; (5) After refixation of the bone, 80 mg of gentamycin is given directly on the sternum and the wires; (6) Closure of the fascia over the wires with Vicryl<sup>®</sup> rapide which will be resorbed within a few days; closure of the epigastric fascia with regular vicryl or Maxon<sup>™</sup>; (7) The subcutaneous fat layer is not sewn, even in obese patients; (8) 80 mg of gentamycin directly given on the subcutaneous fat; (9) Intracutaneous skin suture; (10) No episternal drainage tubes or drains. All other perioperative measures correspond to standard treatment: routine change of gloves after sternotomy and insertion of the sternal retractor, after two hours and before sternal wire fixation.

#### Postoperatively:

No special precautions were used after surgery. According to the previous standard treatment, patients in Group A received three dosages of the second-generation antibiotic after surgery, whereas Group B patients did not receive any antibiotics after surgery. Dressings over the median sternotomy wound are changed after 48 hrs only, or if the wound is wet. External thoracic stabilisation with

chest jackets is not used.

#### Data management

Informed patient consent was waived as the novel closure protocol was introduced as standard of care and applied in all suitable patients since introduction. Patient's characteristics and risk factors were documented prospectively in the electronic data capture systems of the individual hospitals. Risk scores (additive and logistic EuroSCORE I as well as the EuroSCORE II) were calculated and stored. Every wound infection was prospectively recorded in a wound-infection monitoring database. Furthermore, all patients in the defined time period were screened for sternal wound infections. Every infection was classified according to the El Oakley classification schema [9]. For practical purposes wound infection has been defined as superficial (without sternal reopening), or deep (with sternal reopening).

#### Statistical analysis

Descriptive statistics were used in order to describe the sample regarding preoperative patient characteristics. Continuous variables are presented as mean and Standard Deviation (SD) and categorical variables as total numbers and percentages. Preoperative patient characteristics were compared between the two cohorts by conducting Welch's t-tests (continuous variables) or  $\chi^2$  tests (categorical variables). Regarding the number of infections related reoperations a  $\chi^2$  Goodness-of-Fit test was applied assuming a uniform distribution. If necessary, Fisher's exact test was used to compute the p-value related to the  $\chi^2$  tests. Furthermore, Cohen's  $\delta$  and Cramer's  $\omega$  were calculated as effect sizes, respectively. Subsequently, two binary regressions were applied in order to assess an independent effect of the novel closure protocol including established risk factors as control variables. If no sternal wound infection occurred after the surgery these patients were coded as 0 and if a (superficial or deep) sternal wound infection occurred a 1 was assigned.

All descriptive as well as inferential statistics were conducted using patients from all four sites as well as at the national level (Russia,

**Table 3:** Wound infection related indicators.

Level of analysis		Number of infection related reoperations	Wound infection (yes/no)	Muscle flap plasty surgery (yes/no)	Duration of hospitalisation (days)	Duration of stay on ICU (days)
All sites	Control	241	182 (5.1%)/3365 (95.9%)	40 (1.1%)/3516 (98.9%)	13.11 (13.21)	3.86(8.59)
	Novel closure	81	48 (1%)/4565 (99%)	10 (0.2%)/4602 (99.8%)	12.85 (13.5)	4.04(9.74)
	p-value	<0.001	<0.001	<0.001	0.415	0.369
	effect size	0.5	0.12	0.06	0.02	-0.02
Russia	Control	64	75 (3.6%)/1995 (96.4%)	16 (0.8%)/2054 (99.2%)	10.62 (7.59)	2.35 (3.77)
	Novel closure	30	20 (0.7%)/2851 (99.3%)	4 (0.1%)/2867 (99.9%)	10.46 (6.74)	2.63 (4.36)
	p-value	<0.001	<0.001	<0.001	0.485	0.017
	effect size	0.36	0.11	0.05	0.02	-0.07
Austria	Control	309	47 (5.2%)/866 (95.8%)	15 (1.6%)/904 (98.4%)	17 (19.32)	7.12 (14.63)
	Novel closure	123	17 (1.8%)/913 (98.2%)	5 (0.5%)/927 (99.5%)	17.82 (22.11)	7.95 (18.41)
	p-value	<0.001	<0.001	0.023	0.391	0.277
	effect size	0.43	0.09	0.05	-0.04	-0.05
Switzerland	Control	54	60 (10.6%)/504 (89.4%)	9 (1.6%)/558 (98.4%)	13.84 (11.68)	4.1 (5.99)
	Novel closure	22	11 (1.4%)/801 (98.6%)	1 (0.1%)/808 (99.9%)	14.22 (13.62)	4.59 (7.54)
	p-value	<0.001	<0.001	0.002	0.594	0.193
	effect size	0.42	0.21	0.08	-0.03	-0.07

**Note:** Effect sizes: Cramer's  $\omega$  for number of infection related reoperations, wound infection and muscle flap plasty surgery. Cohen's  $\delta$  for duration of hospitalisation and stay on ICU

Austria and Switzerland) in order to enable national comparisons. All analyses were conducted by STATWORX using RStudio (Version 1.1.338) a p-value less than 0.05 was considered as significant.

## Results

Of the 8,168 patients operated in one of the four sites, 3,553 (43.5%) received the standard and 4,615 (56.5%) received the novel closure protocol, respectively. The allocation of patients in Russia was: Group A2070 (41.9%), Group B2871 (58.1%) patients; in Austria Group A919 (49.6%) and Group B932 (50.4%) patients; finally, in Switzerland Group A 564 (41%), Group B 812 (59%) patients.

Regarding the total sample, Group A and B were comparable in terms of preoperative and perioperative patient characteristics (Tables 1 and 2). Although there was a significant difference regarding body mass index and type of surgery, the difference was merely small. Patients operated in Russia differed significantly in all preoperative and perioperative patient characteristics except gender ( $p=0.218$ ), but the differences between the cohorts were also very small to small [1]. Patients from Austria differed solely in type of surgery and patients from Zurich differed in diabetes and type of surgery but again it was only a very small [1] difference.

<sup>1</sup>Cohen's  $\delta$  rules of thumb:  $|\delta| \approx 0.2$  small difference;  $|\delta| \approx 0.5$  medium difference;  $|\delta| \approx 0.8$  large difference.

Cramer's  $\omega$  rules of thumb:  $\omega \approx 0.1$  small difference;  $\omega \approx 0.3$  medium difference;  $\omega \approx 0.5$  large difference.

In order to assess potential benefits and risks associated with the novel closure protocol, groups were compared concerning wound infection related indicators (Table 3). Both in the total sample and at the national level the occurrences of wound infections and infection related reoperations were significantly reduced in the novel closure group ( $p<0.001$ , respectively). The reductions were medium to large and small to medium, respectively. Further analyses regarding wound infections that differentiated between no infection, superficial wound

infection and deep sternal wound infection revealed a significant effect of the novel closure protocol, too (both in the total sample and at the national levels,  $p<0.001$  respectively). The effect was largest in Switzerland (Cramer's  $\omega=0.21$ ) and somewhat smaller in all sites (Cramer's  $\omega=0.12$ ), Russia (Cramer's  $\omega=0.11$ ) and Austria (Cramer's  $\omega=0.09$ ). Consequentially, adjusted standardized residuals showed there were significantly less no infections (3,365 [94.9%]) and more superficial (104 [2.9%]) as well as deep sternal wound infections (78 [2.2%]) in Group A patients than there should be if the novel closure protocol would have had no impact. Complementary, there was an increased number of no infections (4,565 [99%]) and less superficial (19 [0.4%]) and deep wound infections (29 [0.6%]) in Group B patients. Hence, the novel closure protocol is both effective against deep and superficial sternal wound infections. The same pattern was also found at all national levels.

Furthermore, in Group B patients, the number of muscle flap plasty was significantly reduced at every level of the analysis ( $p<0.024$ , respectively). The duration of hospitalisation did not differ between groups at any level ( $p>0.39$ ) and the duration of stay on ICU was merely significantly increased in Russia related to the novel closure protocol ( $p<0.018$ ). Though there was a significant increase in Russia, however its size was merely small (Cramer's  $\omega= -0.07$ ).

Finally, two binary regression analyses (one for each group) were performed including established risk factors for sternal wound infections (Table 4). The use of the novel closure protocol eliminated uni- or bilateral mammary artery harvesting and body mass index as independent risk factors for postoperative sternal wound infection.

The incidence of central venous line associated blood stream infections decreased from 4.3/1,000 in Group A to 1/1,000 day in Group B. In Group A patients, the costs to treat a 5.5% incidence of postoperative sternal wound infection was calculated based on the individual hospital bills to be 860'000 USD per 100 patients undergoing cardiac surgery through a median sternotomy. Central venous line associated blood stream infections and costs of managing

**Table 4:** Binary regression analyses including the novel closure protocol and known risk factors for sternal wound infection.

Level of analysis		Factor	Beta	Odds ratio	95% CI	P-value	
All sites	Control (n = 2611)	Length of stay in hospital	0.05	1.054	1.043-1.065	< 0.001	
		<b>Mammary artery harvesting</b>					
		One IMA	0.48	1.62	1.037-2.593	0.039	
		BIMA	0.46	1.591	0.951-2.69	0.079	
		Diabetes	0.67	1.959	1.322-2.867	< 0.001	
		Body mass index	0.07	1.069	1.029-1.111	< 0.001	
		Nagelkerkes R <sup>2</sup>	0.15				
	Novel closure (n = 3659)	Length of stay in hospital	0.06	1.058	1.046-1.07	< 0.001	
		<b>Mammary artery harvesting</b>					
		One IMA	0.36	1.432	0.639-3.386	0.394	
		BIMA	0.14	1.145	0.435-3.058	0.783	
		Diabetes	0.79	2.195	1.058-4.402	0.03	
		Body mass index	0.03	1.029		0.414	
		Nagelkerkes R <sup>2</sup>	0.21				

**Note.** IMA: Internal Mammary Artery; BIMA: Bilateral IMA

sternal wound infection have only been investigated in Switzerland.

## Discussion

Surgical wound infection represents the most frequent and most expensive complication after routine cardiac surgical procedures using median sternotomy as standard incision. Sternal wound infection is associated with an increased early and late mortality, morbidity and reoperation rate [10]. Even in the current era, hospital mortality for deep sternal wound infection with or without mediastinitis is as high as 14% to 49% [11,12].

This novel sternal wound closure protocol reduced postoperative wound infections in patients undergoing cardiac surgery through a full median sternotomy. The present bundle of measures proved to be effective in a large, multicentre, international group of patients, independent of the local hygiene culture as well as the educational status of the participating experts. The elimination of sternal wound infections has not been achieved by using expensive infrastructural measures, but by the consequent incorporation of several individual measures into a stable, multimodality protocol.

The crucial point of the actual concept lies within the consequent and cost-saving adaptation of simple surgical rules in conjunction with a more extended topical use of antibiotics brought directly into the sternal wound before completing the operation. Hence, it is the treatment of the surgical wound, which decides if a postoperative wound infection will be facilitated or avoided. Endogenous as well as exogenous infection sources, virulence of microorganisms, infection risk scores, duration of operation as well as architectural and technical structure of the operating theatre including e.g. laminar flow systems, proved to be of secondary importance, yet almost insignificant. Even very sick patients with complex co-morbidities suffering from major and long-lasting surgery and spending several days on the intensive care station, e.g. with open sternum, remained mostly without postoperative sternal wound infection when using this protocol.

The overall risk of deep sternal wound infection prior to the introduction of the novel protocol was 5.1%, which is in the range of previous reports [1,13-16]. Up to 58% of postoperative wound infections are diagnosed after hospital discharge [17]. This explains, that the highest overall surgical site infection rate comprising

superficial as well as deep sternal wound infections in the standard group has been observed in Switzerland (10.6%), which is due to the complete follow-up of a dedicated hygiene team including all patients suffering from surgical site infection up to one year after surgery. Hence, due to the huge distances, the incidence of surgical site infection in the control group was probably higher in Russia and a more complete follow-up of these patients still would improve the results of this study. The current study represents a real-world setting at tertiary care centers, including high-risk patients with multiple combined procedures, heart transplant cases receiving immunosuppressive therapy and patients in whom the sternum was left open due to bleeding or hemodynamic instability.

The topical application of vancomycin or gentamycin for the prevention of sternal wound infection or as infection prevention in open fractures was previously described [18-21], but results have been mixed [6,22-23] for both. However, despite adequate disinfection of the surgical sternal wound, bacteria set free from the deep roots of the hairy follicles will always be found in the subcutaneous layer after skin incision because they cannot be reached by disinfection. Hence, the subcutaneous layer, traumatized and ischemic by electrocautery and running suture may represent the starting point for low-grade infection evolving into full sternal wound infection with or without deep mediastinitis. Accordingly, local measures inside of the sternal wound itself seems to be more important than systemic antibiotic prophylaxis as topical application achieves higher local antibiotic concentrations compared to the systemic application [24]. Therefore, we hypothesized that a combined protocol including the abandonment of electrocautery in the subcutaneous layer, the use of vancomycin and gentamicin as well as an increased number of sternal wires could have an additive effect together with the other pre- and postoperative measures such as the use of the nasal ointment mupirocin or chlorhexidine, known to reduce surgical site infection [25-28].

Topical application of antibiotics was not associated with negative events. Vancomycin blood levels measured during the first three days after surgery revealed vancomycin blood concentrations far below any clinically relevant levels, which have been confirmed by others, despite demonstrating serum concentrations up to six days after surgery [29]. Infections caused by gram-negative or fungal pathogens

did not increase in our experience, which has been closely monitored by our infection surveillance and hygiene team (Switzerland). In addition, topical vancomycin and gentamycin application did not influence perioperative renal function, which has also been confirmed by others [24].

The recommendations for the use of sternal wires were not uniformly followed. Although the overall increase of sternal wires was significant, the effect differed between the centers (e.g. a mean increase of 0.7 wires only per patient in Austria). This may explain the non-significant effect of the number of sternal wires in the multiple regression analysis. Nevertheless, a higher number of sternal wires and the reinforcement of the lower part of the sternum reduce the forces acting during a cough, which may exceed the strengths of the bone [28,30]. According to our protocol, six to eight simple figure-of-eight wires have found to be sufficient and cost effective omitting the need for more expensive sternal closure systems such as plates, Kryptonite bone cement or other complex and costly techniques [31-32].

A stronger adherence to this protocol may further reduce the wound-infection rate by eliminating cases of mere dehiscence leading to secondary wound infection. The most important reduction of surgical site infections has been observed in Switzerland, where all pre-, intra- and postoperative measures proposed have been strictly applied in every patient stressing the use of a multimodality approach instead of one single measure. Hence, the infection-related mortality rate in Switzerland was zero since the introduction of this sternal wound infection prevention protocol. The incidence of postoperative sternal wound infection decreased 7.6 times and the use of muscle flap plasty to reconstruct the anterior chest decreased 16 times. In most patients, the postoperative localized, superficial infection was treated by conservative measures such as removal of skin clips or parts of the intra-cutaneous sutures in conjunction with oral antibiotic treatment.

Diabetes, peripheral arterial occlusive and cerebrovascular disease as well as obesity are direct or surrogate markers for impaired wound healing and are well known to significantly contributing to wound infection. The use of the novel closure protocol eliminated body mass index as well as the use of uni- or bilateral mammary artery as risk factors for postoperative sternal wound infection.

Neither the presence of COPD, the smoking status, cortisone therapy, open-chest treatment after complex surgery and obesity, nor the combination of these risk factors did influence the incidence of sternal wound infection in the group treated by the novel closure protocol. Only insulin-dependent diabetes was found to be a stable risk factor for sternal wound infection in both groups: it was strong risk factor with standard treatment but only marginally significant with the use of the novel closure protocol. Incidentally, a significant decrease of the central venous line associated blood stream infections has been found in the protocol, but not in the standard group patients indicating the relationship between the surgical site and central venous catheter-related infection in cardiac surgery, known as “cross-talk” [33].

Our infection prevention protocol significantly reduces postoperative superficial and deep sternal wound infections and infection-related reoperations and limits the use of peri- and postoperative antibiotics. The occurrence of multi-resistant nosocomial bacterial and gram-negative infections has not been provoked. The use of expensive chest stabilizing jackets after surgery

has found to be unnecessary. Hence, this concept represents a major improvement with regard to the safety for patients undergoing cardiac surgery through a median sternotomy. In addition, the novel closure protocol proves to be highly cost saving: in patients treated with the standard protocol, 860,000 USD had to be invested for every 100 patients undergoing cardiac surgery to treat the consequences of a 5% incidence of sternal wound infection (Switzerland) – costs which have been saved by the highly significant reduction of surgical site infection after full median sternotomy. By eliminating sternal wound infection after cardiac surgery in Switzerland, an estimated 60,000,000 USD could be saved.

Adjusted standardized residuals follow a z-distribution and values greater than 2 reveal a significant deviation of the absolute frequency for this category from the expected frequency.

## Limitations

This is not a prospectively randomized study. The control group undergoing standard sternal closure has been analyzed retrospectively and has been compared with the prospectively included patients in whom the new infection prevention protocol had been used. The retrospective analysis of the patients in the control group has some limitations particularly in Russia with its wide distances and incomplete follow-up concerning minor infections. However, a more complete follow-up of these patients would have only increased the incidence of surgical site infection in the retrospectively analyzed control group, favoring the use of the novel closure protocol even more. The results collected from different sites match those observed in Switzerland where data have been collected by a team particularly dedicated to infection prevention and hygiene. In addition, the large number of patients studied compensates these drawbacks of the current study. Despite a prolonged study period, the use of the new infection prevention protocol was not associated by significant changes with regard to operating theatre organization, architectural changes or significant improvement of basic surgical techniques assumed to significantly influence the incidence of postoperative sternal wound infection. However, the widespread use of topical antibiotics in every patient may be excessive. Future prospectively randomized studies could limit the use of topical antibiotics to those patients individually identified to be at high risk for a sternal wound infection following cardiac surgery.

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