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Local application of gentamicin-containing collagen implant in the prophylaxis and treatment of surgical site infection following cardiac surgery

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ABSTRACT

Background: For the cardiac surgeon and patient the development of sternal wound infection is a serious post-operative complication associated with increased risk of death and also considerable morbidity.
Methods: Nine publications were identified using the PubMed online database and search terms 'gentamicin-containing collagen implant' plus 'surgical site infection', 'wound infection' and 'cardiac surgery'.
Results: Six out of eight studies demonstrated that prophylactic use of gentamicin-containing collagen implants (GCCI) significantly reduce the wound infection rate following cardiac surgery (via sternotomy) compared to standard treatment alone. The adjunctive use of GCCI is particularly beneficial in high-risk subjects e.g. diabetes and obese patients. GCCI significantly improve the morbidity associated with SSI following cardiac surgery by shortening the recovery phase and length of hospital stay; reducing the need for surgical revision and use of antibiotics. GCCI have been shown to be cost saving across a wide spectrum of patients. A further study has shown that GCCI may also have a therapeutic role to play in patients with deep sternal wounds.
Conclusion: This review demonstrates that when used dry prior to insertion GCCI can be effective in reducing the rate of SSI following cardiac surgery. GCCI have also been shown to be cost saving as they reduce the substantial morbidity associated with deep SSI. The adjunctive use of GCCI is particularly beneficial in high-risk patients. GCCI may also have a role to play in the treatment of deep sternal wound infection.
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1. Introduction

For the cardiac surgeon and patient the development of sternal wound infection is a serious post-operative complication associated with increased risk of death and also considerable morbidity, which in turn may substantially increase the length of hospital stay and associated cost of care. Sternal wound infection has a reported overall incidence between 0.5% and 6%.[1] However, in high-risk patients the incidence has been estimated at between 12 and 20% with an associated mortality rate between 14% and 47%.[1]

Independent risk factors associated with the development of surgical site infection (SSI) following cardiac surgery have been established by a number of authors.[2–4] In a study published in 2009 of 1359 cardiac surgery patients the presence of diabetes mellitus, chronic obstructive pulmonary disease (COPD) or a higher body mass index (BMI) increased the risk of patients developing deep sternal wound infection.[3] The length of time the patients were on cardiopulmonary bypass was also established as an independent risk factor for sternal wound infection.[3]

SSI is also an important cause of morbidity for patients undergoing cardiac surgery, which is reflected in the increased length of hospital stay (LOS) and associated costs.[5,6] For patients with deep sternal wound infections the LOS may increase from a mean of 10.7 days in infection-free patients to 35 days in patients with an SSI ($p < 0.001$).[5] Coello and colleagues estimated that the cost associated with the increased LOS for coronary artery bypass graft (CABG) patients who developed an SSI to be in the region of €4400.[6] The mean total cost associated with an SSI (i.e. including surgical revision, days in ICU etc) following cardiac surgery has been estimated to be €14,500 by Friberg and colleagues.[7]

Another challenge that the cardiac surgeon faces in trying to prevent SSI is that coagulase-negative staphylococci (CoNS) have become the most common causative organisms of sternal wound infections.[8] With CoNS infections the onset of SSI may be delayed and more insidious and may eventually require radical surgical revision to eradicte the infection.[9]

The mainstay of SSI prevention in cardiac surgery relies on aseptic surgery, an optimal wiring technique and the use of antibiotic prophylaxis administered systemically peri-operatively.[4,10] Long-term administration of systemic antibiotics may in turn lead to a greater risk of antibiotic resistance.[11–14]

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The emergence of local antibiotic-eluting products such as resorbable gentamicin-containing collagen implant (GCCI), deliver high local concentrations of gentamicin with corresponding low serum levels. This technology therefore offers a means of lowering the risk of antibiotic resistance by reducing the need for long-term administration of systemic antibiotics and also may avoid the toxicity of these regimens.[3] The use of collagen as a carrier also has a positive effect on wound healing.[15]

The objective of this article is to review the published clinical data for prophylactic application of resorbable GCCI following cardiac surgery in order to provide an overview of the efficacy and safety of GCCI in this indication with particular focus on high-risk patient groups.

2. Methods

Candidate publications were identified using the National Institute of Health PubMed database for articles published between January 1990 and July 2011. Articles were identified using the search terms 'gentamicin-containing collagen implant' plus 'surgical site infection', 'wound infection' and 'cardiac surgery'. Reference lists of recent review articles were also scanned for additional citations. The literature search was further supplemented by abstracts from international cardiac surgery congresses, which took place between January 2009 and July 2011. Review publications were excluded from the analysis. The search identified nine potential publications of which eight focused specifically on the prophylaxis of SSI in cardiac surgery. These studies concerned the use of two GCCI i.e. Collatamp® (EUSA Pharma [Europe], Oxford, United Kingdom) and GENTA-COLL® resorb (RESORBA Wundversorgung GmbH & Co. KG, Nuremberg, Germany). Collatamp contains gentamicin sulphate at a rate of 2 mg/cm.[2] The collagen in Collatamp is present at 2.8 mg/cm^2 and is type I collagen from a renatured bovine or equine source. One Genta-Coll collagen-gentamicin sponge of 2.5 × 2.5 × 0.5 cm contains 35 mg native equine collagen fibrils and 25 mg gentamicin sulphate, equivalent to 13.82–17.88 mg gentamicin.

The outcome measures of primary interest were the rate of SSI, need for surgical revision and re-hospitalisation as well as level of antibiotic usage. The level of evidence for each study was graded according to the criteria developed by Carruthers et al.[16]

3. Clinical experience

To date there have been nine clinical studies which have focused on the local application of gentamicin-containing collagen implants (GCCI) in the prophylaxis and treatment of SSI following cardiac surgery (Table 1). Four of the studies were of randomised, controlled design; four studies focused on a patient series with historical or contemporary controls and one study included a consecutive patient series without a control group. Three of the studies were graded as level 1.[16] In total these studies represent experience in $n = 5026$ patients treated prophylactically with GCCI ($n = 4673$ with Collatamp and $n = 353$ with Genta-Coll) following cardiac surgery. In 42 patients GCCI were used on a therapeutic basis.

3.1. Prophylaxis

The first randomised controlled study (and also the largest study to date) focusing on the prophylactic use of GCCI following cardiac surgery was published in 2005 (Table 1).[17] The majority of the subjects (73%) required a CABG via median sternotomy. At baseline the mean age of patients was 68 years; 76 were male and 18% had diabetes.

This large-scale study demonstrated a relative risk reduction in SSI of 47% in the GCCI-treated patients compared to those who received IV antibiotics alone. The incidence of sternal wound infection was 4.3% in the GCCI group and 9.0% in the control group (RR 0.47; 95% CI 0.33–0.0.68; $p < 0.001$). The use of GCCI as adjunctive treatment also significantly reduced the need for surgical revision by 54% (2.3% vs 4.0%, $p = 0.03$) and antibiotic usage by 64% (11.6% vs 18.0%, $p < 0.001$). In a sub-set analysis the use of GCCI was shown to be even more beneficial in preventing both superficial and deep SSI in high-risk patients. In either obese patients or in those with diabetes the relative risk of developing deep SSI was reduced by 56% (2.4% vs 4.4%; RR 0.56; 95% CI 0.31–1.00; $p = 0.047$) with use of GCCI in conjunction with standard treatment. In a separate analysis the authors demonstrated that the adjuvant use of GCCI with IV antibiotics was cost saving. This was due to fewer wound infections and lower costs despite the cost of the implants in all patients and especially in high-risk patients e.g. those with diabetes or BMI > 25 kg/m^2.[7]

Early operation for bleeding was more common in the GCCI group (4% vs 2.3%, $p = 0.03$). The study authors suggested that the incidence of early operation for bleeding in the GCCI group was similar to that seen in routine practice, and that the re-operation rate in the control group was lower than expected. There was no significant difference between the groups for all other general outcome measures e.g. hospital mortality, post-operative renal function etc. In a separate analysis of the microbiological findings from this study[23] the authors showed that GCCI reduced the incidence of SSI caused by all major clinically important bacterial species apart from *Propionibacterium acnes*. There was also no indication of any increase in the occurrence of gentamicin-resistant isolates.

In 2009 the same authors published the results of a consecutive series of 1359 patients in which GCCI had been used as routine clinical practice (Table 1).[3] The baseline characteristics of the patients were similar to those followed in the earlier study. The results were compared with those from the control group in the previous study. The analysis demonstrated similar benefit of using GCCI (+standard treatment) in significantly reducing the rate of SSI (overall, deep and superficial) and also need for surgical revision compared to standard treatment alone. Furthermore by comparing the microbiological results against those from the 2005 study the authors were also able to show that there had been no change in types of causative bacteria and no absolute increase in SSIs caused by aminoglycoside resistant microbes over time.

Four further studies have been published which support the positive results from the Friberg studies (Table 1).[4,10,20,21] Schersten and colleagues were motivated to study the use of GCCI after detecting an increase in the rate of deep sternal wound infection following cardiac surgery at their centre.[10] In 2005 the SSI had risen to 1.9% of cases compared to 1.0–1.3% between 2001 and 2004. The authors attributed this to an increase in the number of high-risk patients undergoing surgery and also an increase in the number of emergency operations where the patients were not adequately prepared for surgery. Following the addition of GCCI to their standard treatment protocol in a consecutive and unselected series of 1091 patients operated on in 2006 the rate of mediastinitis dropped to 0.75% (95% CI 0.22–2.18; $p < 0.05$) compared to the rate in the previous year.

A recently published randomised, controlled study which compared GCCI (+IV antibiotics) to a control group in which the surgeons inserted a collagen only implant (+IV antibiotics) also supports the positive outcome of the previously mentioned analyses (Table 1).[4] The patient population was similar to that of the Friberg studies (i.e. 74% male; 30% patients with diabetes and 53% undergoing CABG). The incidence of deep sternal wound infections was 3.52% in the control group compared to 0.56% in the GCCI group (Adjusted odds ratio, 0.15; 95% CI, 0.02–0.69; $p = 0.014$). The numbers needed to treat (NNT) for all sternal wound infections and deep sternal wound infections were 26 and 33, respectively. The study did not demonstrate any significant differences in any of the secondary outcome measures (e.g. post-operative bleeding) between the two groups.

Table 1
Overview of GCCI clinical publications in cardiac surgery.

Author & evidence grading	Product	Study design and population	Number of subjects and treatment groups	Results
Prophylaxis				
Friberg (2005)[17] Level 1	Collatamp®*	Randomised, controlled, two-centre study Patients undergoing cardiac surgery through median sternotomy – including operations in the ascending aorta	$n = 1950$ total patients Group I: $n = 983$ gentamicin-collagen implant + IV isoxazolyl-penicillin Group II: $n = 967$ IV isoxazolyl-penicillin alone (control)	**Wound infection (<2 mths post-operatively)**: Group I: 4.3% (42/983) vs Group II: 9.0% (87/967)(RR 0.47; 95% CI 0.33–0.68; $p < 0.001$) **Early reoperation for bleeding**: Group I: 2.3% (22/983) vs Group II: 4.0% (39/967) (RR 1.74; 95% CI 1.04–2.91; $p = 0.021$) **Antibiotic treatment**: Group I: 11.6% (114/983) vs Group II: 18.0% (174/967) (RR 0.64: 95% CI 0.52–0.80; $p < 0.001$)
Eklund (2005)[18] Level 3	Collatamp®	Randomised, controlled, single-centre study Patients undergoing elective CABG surgery via a median sternotomy, with cardiopulmonary bypass	$n = 542$ total patients Group I: $n = 272$ gentamicin-collagen implant + IV antibiotics Group II: $n = 270$ IV antibiotics alone (control)	**Wound infection (<3 mths post-operatively)**: Group I: 4.0% (11/272) vs Group II: 5.9% (16/270) (n.s.)
Schersten (2007)[10] Level 4	Collatamp®	A prospective patient series with historical controls Patients undergoing cardiac surgery	$n = 2026$ total patients Group I: $n = 1091$ gentamicin-collagen implant + IV isoxazolyl-penicillin Group II: $n = 935$ IV isoxazolyl-penicillin alone (historical controls)	**Wound infection (mediastinitis)**: Group I: 0.75% (8/1091) vs Group II: 1.9% (18/935) (95% CI 0.22–2.18; $p < 0.05$)
Friberg (2009)[3] Level 4	Collatamp®	A prospective patient series with historical controls Patients undergoing cardiac surgery, including surgery of the thoracic aorta operated via full median sternotomy	$n = 2326$ total patients Group I: $n = 1359$ gentamicin-collagen implant + IV isoxazolyl-penicillin, Group II: $n = 967$ IV isoxazolyl-penicillin alone (control)	**Wound infection (<60 days post-operatively)**: Group I: 3.7% (50/1359) vs Group II: 9.0% (87/967) $p < 0.001$ **Surgical revision**: Group I: 1.8% (24/1359) vs Group II: 3.9% (38/967)($p < 0.001$)
Bennett-Guerrero (2010)[19] Level 1	Collatamp®	Randomised, controlled, single-blind, multicentre study Patients undergoing cardiac surgery and at high-risk for sternal wound infection (diabetes, BMI > 30 or both)	$n = 1502$ total patients ($n =$ 1006 with diabetes [67%] and $n =$ 1137 BMI > 30 [76%]) Group I: $n = 753$ gentamicin-collagen implant + IV antibiotics Group II: $n = 749$ IV antibiotics alone (control)	**Wound infection (<90 days post-operatively)**: Incidence of all types of wound infection – Group I: 8.4% (63/753) vs Group II: 8.7% (65/749) (n.s.) Incidence deep wound infection – Group I: 1.9% (14/753) vs Group II: 2.5% (19/749) (n.s.) Incidence superficial wound infection – Group I: 6.5% (49/753) vs Group II: 6.1% (46/749) (n.s.) **Re-hospitalisation for sternal wound infection (<90 days post-operatively)**: Group I: 3.1% (23/753) vs Group II: 3.2% (24/749) (n.s.)
Cohen (2010)[20] Level 4	Collatamp®	Patient case series Patients undergoing cardiac surgery via sternotomy	$n = 216$ total patients Group I: $n = 108$ gentamicin-collagen implant + standard treatment Group II: $n = 108$ standard treatment alone (control)	**Wound infection**: Group I: 0.0% vs Group II: 9.0% ($p = 0.0220$).
Raja (2011)[21] Level 4	Collatamp®	Patient case series Patients undergoing cardiac surgery via sternotomy	$n = 194$ total patients Group I: $n = 97$ gentamicin-collagen implant + standard treatment Group II: $n = 97$ standard treatment alone (control)	**Wound infection**: Incidence of superficial wound infection – Group I: 2.1% (2/97) vs Group II: 6.2% (6/97) ($p = 0.01$). Incidence of deep wound infection – Group I: 2.1% (2/97) vs Group II: 3.1% (3/97)(n.s). **Post-operative complications**: Need for intra-aortic balloon pump – Group I: 2.1% (2/97) vs Group II: 5.2% (5/97) ($p = 0.04$). Need for haemofiltration – Group I: 3.1% (3/97) vs Group II: 7.2% (7/97)($p = 0.02$).
Schimmer (2011)[4] Level 1	GENTA-COLL®	Randomised, controlled, single-centre study Patients undergoing median sternotomy	$n = 720$ total patients Group I: $n = 353$ gentamicin-collagen implant + IV antibiotics Group II: $n = 367$ collagen implant + IV antibiotics (control)	**Wound infection (<30 days)**: Incidence of deep wound infection – Group I: 0.56% (2/353) vs Group II: 3.52% (13/367) (Adjusted odds ratio, 0.15; 95% CI, 0.02–0.69; $p = 0.014$). Incidence of superficial wound infection – Group I: 1.98% (7/353) vs Group II: 2.98% (11/367) (n.s). NNT – all sternal wound infections and deep sternal wound infections were 26 and 33 respectively.
Treatment				
Leyh (1999)[22] Level 5	Collatamp®	Patient case series Patients with deep sternal wound infection following cardiac surgery	$n = 42$ patients treated with gentamicin-collagen implant	Drainage samples were clear of infection for all 42 patients prior to removal and no re-infection occurred within 6 months of surgical debridement

* Collatamp® EG, Collatamp® G Cronocol®, Duracoll® Implant, Garacol®, Garacoll®, Garacoll® Implant, Garamacin® Pads, Garamycin®, Garamycin® Schwamm, Gentacoll®, Gentacoll® Implant, Gentalyn®, Gentimplant®, Sulmycin®, Sulmycin® Implant E Schwamm, Sulmycin® Implant Schwamm.

The analysis of two recently presented patient series also demonstrates the positive impact of GCCI in conjunction with standard antibiotic prophylaxis (Table 1).[20,21] In a retrospective review Cohen and colleagues compared a group of 108 patients who had received GCCI plus standard treatment to a group of matched contemporary controls on a 1:1 basis.[20] Seventy six per cent of patients in both groups underwent isolated coronary bypass surgery and 22% had diabetes. There was a significant difference in

the incidence of post-operative SSI between the two groups (0% GCCI vs 9% standard treatment; $p = 0.022$). In a similar study Raja and colleagues compared the adjunctive use of GCCI in a series of 97 patients deemed at high risk of developing SSI to a group of matched controls who received standard treatment alone (Table 1).[21] This study demonstrated a significant benefit of GCCI, which reduced the rate of superficial wound infection by 66% compared to standard treatment alone (2.1% GCCI vs 6.2% standard treatment; $p = 0.01$). Although the patients in the GCCI group also had a lower rate of deep wound infection compared to the control group, this difference did not reach statistical significance. Patients in the GCCI group also had significantly less requirement for intra-aortic balloon pump and haemofiltration. No side effects attributable to GCCI were reported.

In a study, which focused on a similar patient population but specifically in patients undergoing CABG the rate of SSI was numerically lower in the GCCI group (4.0%, 11/272) compared to the standard treatment group (5.9%, 16/270) (Table 1).[18] However, this difference did not reach statistical significance. There were three cases of mediastinitis (1.1%) in the GCCI group and five (1.9%) in the control group (n.s.). Bennett-Guererro and colleagues also reported equivocal results in 2010 in 1502 US patients at high-risk of developing SSI (i.e. diabetes and or BMI $>$ 30) (Table 1).[19] No significant difference could be detected between the GCCI + standard treatment group and those patients receiving standard treatment alone for any of the primary or secondary outcome measures. For example the incidence of all types of wound infection was 8.4% in the GCCI group vs 8.7% in the standard treatment group (n.s.) and for deep wound infection the corresponding figures were 1.9% and 2.5% respectively (n.s.). The re-hospitalisation rate for sternal wound infection (<90 days post-operatively) was 3.1% in the GCCI group vs 3.2% in the standard treatment group (n.s.).

3.2. Treatment

The therapeutic use of GCCI has been studied in a series of 42 patients with deep sternal wounds following elective cardiac surgery (Table 1).[22] A third of patients were suffering from diabetes and nearly half of the population were classified as obese. Patients underwent radical wound debridement with sternal fixation, placement of retrosternal suction drainage and utilising bilateral pectoralis major muscle flaps. Two GCCI (10 cm $\times$ 10 cm) were placed underneath, above and between the sternal edges and patients were also given IV antibiotics for up to 3 weeks. Susceptibility testing revealed that 8 out of the 52 infections were caused by organisms that were resistant to gentamicin. Eight of the 42 patients underwent prolonged ventilation and three out of 42 had multiple organ failure following surgical debridement, which complicated the post-operative course.

Out of 19 patients tested high gentamicin levels (>300 mg/mL) were detected in the mediastinal effusions for 36 h post-operatively, whereas the plasma levels were below 2 mg/mL. Drainage samples were clear of infection for all 42 patients prior to removal and no re-infection occurred within 6 months of the surgical debridement. No deaths occurred and no adverse events associated with GCCI were detected.

4. Discussion

The majority of the studies published to date have demonstrated that prophylactic use of GCCI can significantly reduce the wound infection rate following cardiac surgery (via sternotomy) compared to standard treatment alone. The adjunctive use of GCCI is particularly beneficial in high-risk patients such as those with diabetes and in obese patients. GCCI have also been shown to significantly improve the morbidity associated with SSI following cardiac surgery by shortening the recovery phase and length of hospital stay; reducing the need for surgical revision and use of antibiotics. As a result of reducing the SSI rate and subsequent complications GCCI have been shown to be cost saving across a wide spectrum of patients. GCCI may also have a therapeutic role to play in patients with deep sternal wounds.

Of the eight 'prophylactic' studies reviewed two did not show any significant benefit of local application of GCCI. In contrast to the six positive publications in cardiac surgery the study by Bennett-Guerrero and colleagues did not demonstrate any benefit of use of GCCI over standard treatment. The authors have put forward a combination of factors that they think may go some way to explaining the lack of benefit seen in the GCCI group including differences in design and ethnic differences between this study and the other positive cardiac studies. One important difference which the authors do not highlight is the fact that the protocol for the Bennett-Guerrero study required that the implants be wetted in saline prior to implantation.[24] The effect of the wetting of the implants has been researched by Lovering and colleagues and they have shown that pre-soaking may impact on the gentamicin release profile of the GCCI to cause premature depletion of the active compound in addition to that lost during the pre-soaking period.[25] The manufacturer's recommendation is that GCCI should be used dry prior to implantation.[26] Friberg points out that in contrast to the other published studies a large proportion of the sternal wound infections in the Bennett-Guerrero study were caused by gram-negative rods which are not normally found on the skin on the chest (and should not be present in the air in operating rooms) and this might suggest that contamination may have occurred later in the post-operative phase.[27]

Eklund et al. also showed no additional benefit of GCCI in reducing wound infection rate following cardiac surgery. The authors themselves concluded that the study population might have been too small to draw conclusions.[18]

5. Conclusion

This review demonstrates that when used dry prior to insertion GCCI can be effective in reducing the rate of SSI following cardiac surgery. GCCI have also been shown to be cost saving as they reduce the substantial morbidity associated with deep SSI. The adjunctive use of GCCI is particularly beneficial in high-risk patients. GCCI may also have a role to play in the treatment of deep sternal wound infection.

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Ethical approval

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Author contribution

Shahzad G Raja critically reviewed the manuscript for important intellectual content and approved the final version of the manuscript to be submitted.

Conflict of interest

Shahzad G Raja has received an honorarium and speaker fees from EUSA Pharma.

References

1. Franco S, Herra AM, Atehortúa M, Vélez L, Botero J, Jaramillo JS, et al. Use of steel bands in sternotomy closure: implications in high-risk cardiac surgical population. *Interact Cardiovasc Thorac Surg* 2009;**8**:200–5.
2. El Oakley RM, Wright JE. Postoperative mediastinitis: classification and management. *Ann Thorac Surg* 1996;**61**:1030–6.
3. Friberg Ö, Dahlin L-G, Källman J, Kihlström E, Söderquist B, Svedjeholm R. Collagen-gentamicin implant for prevention of sternal wound infection; long-term follow-up of effectiveness. *Interact Cardio Vasc Thorac Surg* 2009;**9**:454–8.
4. Schimmer C, Özkur M, Sinha B, Hain J, Gorski A, Hager B, et al. Gentamicin-collagen sponge reduces sternal wound complications after heart surgery: a controlled, prospectively randomozed, double-blind study. *J Thorac Cardiovasc Surg* 2012;**143**:194–200.
5. 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.
6. 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.
7. Friberg Ö, Dahlin L-G, Levin L-A, Magnusson A, Granfeldt H, Källman J, et al. Cost-effectiveness of local collagen-gentamicin as prophylaxis for sternal wound infections in different risk groups. *Scand Cardiovasc J* 2006;**40**:117–25.
8. Tegnell A, Arén C, Ohman L. Coagulase-negative staphylococci and sternal infections after cardiac operation. *Ann Thorac Surg* 2000;**69**:1104–9.
9. Mossad SB, Serkey JM, Longworth DL, Cosgrove 3rd DM, Gordon SM. Coagulase-negative staphylococcal sternal wound infections after open heart operations. *Ann Thorac Surg* 1997;**63**:395–401.
10. Schersten H. Modified prophylaxis for preventing deep sternal wound infection after cardiac surgery. *APMIS* 2007;**115**:1025–8.
11. Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. *Br J Surg* 1998;**85**:1232–41.
12. Morita S, Nishisho I, Nomura T, Fukushima Y, Morimoto T, Hiraoka N, et al. The significance of the intraoperative repeated dosing of antimicrobials for preventing surgical wound infection in colorectal surgery. *Surg Today* 2005;**35**:732–8.
13. Fujita S, Saito N, Yamada T, Takii Y, Kondo K, Ohue M, et al. Randomized, multicenter trial of antibiotic prophylaxis in elective colorectal surgery: single-dose vs 3 doses of a second-generation cephalosporin without metronidazole and oral antibiotics. *Arch Surg* 2007;**142**:657–61.
14. Suehiro T, Hirashita T, Araki S, Matsumata T, Tsutsumi S, Mochiki E, et al. Prolonged antibiotic prophylaxis longer than 24 hours does not decrease surgical site infection after elective gastric and colorectal surgery. *Hepatogastroenterology* 2008;**55**:1636–9.
15. Stemberger A, Grimm H, Bader F, Rahn HD, Ascherl R. Local treatment of bone and soft tissue infections with the collagen-gentamicin sponge. *Eur J Surg* 1997;**S578**:17–26.
16. Carruthers SG, Larochelle P, Haynes RB, Petrasovits A, Schiffrin EL. Report of the Canadian hypertension society consensus conference. I. Introduction. *CMAJ* 1993;**149**:289–93.
17. Friberg Ö, 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**:153–62.
18. Eklund AM, Valtonen M, Werkkala KA. Prophylaxis of sternal wound infections with gentamicin-collagen implant: randomized controlled study in cardiac surgery. *J Hosp Infect* 2005;**59**:108–12.
19. Bennett-Guerrero E, Ferguson Jr TB, Lin M, Garg J, Mark DB, Scavo Jr VA, et al. Effect of an implantable gentamicin-collagen sponge on sternal wound infections following cardiac surgery: a randomized trial. *JAMA* 2010;**304**:755–62.
20. Cohen G, Fremes S, Sever J, Moussa GT, Christakis GT, Goldman BS. Mitigation of sternal wound infection by application of a gentamicin impregnated collagen sponge at the time of sternal closure. In: presented at the Canadian cardiovascular congress; 2010. [Abstract 495].
21. Raja SG, Salhiyyah K, Rafiq MU, Felderhof J, Amrani M. Impact of gentamicin-collagen sponge on incidence of sternal wound infection in high-risk cardiac surgery patients: a propensity score analysis. In: presented at the World society of cardio-thoracic surgeons congress. Berlin: June 2011. [Abstract SOP55].
22. Leyh RG, Bartels C, Sievers HH. Adjuvant treatment of deep sternal wound infection with collagenous gentamicin. *Ann Thorac Surg* 1999;**68**:1648–51.
23. Friberg Ö, Svedjeholm R, Kallman J, Söderquist B. Incidence, microbiological findings, and clinical presentation of sternal wound infections after cardiac surgery with and without local gentamicin prophylaxis. *Eur J Clin Microbiol Infect Dis* 2007;**26**:91–7.
24. Corn T. Treating sternal wound infections after cardiac surgery with an implantable gentamicin-collagen sponge. *JAMA* 2010;**304**:2123.
25. Lovering AM, Sunderland J. Impact of soaking gentamicin-containing collagen implants on potential antimicrobial efficacy. *Int J Surg* 2012;**10**(Suppl. 1):S2–4.
26. Collatamp® summary of product characteristics. Revised February 2008.
27. Friberg Ö. Treating sternal wound infections after cardiac surgery with an implantable gentamicin-collagen sponge. *JAMA* 2010;**304**:2123.