Gentamicin-collagen sponge reduces the risk of sternal wound infections after heart surgery: Meta-analysis

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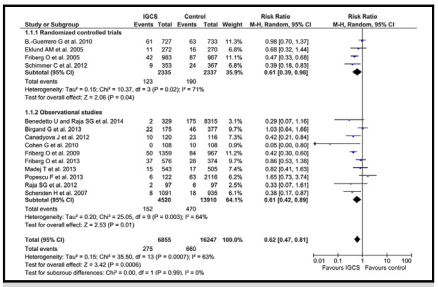
ABSTRACT

Objectives: Sternal wound infections are serious postoperative complications that increase the length of hospital stay and healthcare costs. The benefit of implantable gentamicin-collagen sponges in reducing sternal wound infections has been questioned in a recent multicenter trial. We aimed to perform a comprehensive meta-analysis of studies assessing the efficacy of implantable gentamicin-collagen sponges in sternal wound infection prevention.

Methods: Multiple databases were screened for studies assessing the efficacy of implantable gentamicin-collagen sponges after heart surgery. The primary end point was sternal wound infection, and secondary end points were the occurrence of deep sternal wound infection, superficial sternal wound infection, mediastinitis, and mortality. Randomized controlled trials and observational studies were analyzed separately. By means of meta-regression, we examined the correlation between sternal wound infection and extent to which the bilateral internal thoracic artery was harvested.

Results: A total of 14 studies (N = 22,135, among them 4 randomized controlled trials [N = 4672]) were included in the analysis. Implantable gentamicin-collagen sponges significantly reduced the risk of sternal wound infection by approximately 40% when compared with control (risk ratio [RR], 0.61; 95% confidence interval [CI], 0.39-0.98; $P = .04$ for randomized controlled trials and RR, 0.61; 95% CI, 0.42-0.89; $P = .01$ for observational studies). A similar, significant benefit was demonstrated for deep sternal wound infection (RR, 0.60; 95% CI, 0.42-0.88; $P = .008$) and superficial sternal wound infection (RR, 0.60; 95% CI, 0.43-0.83; $P = .002$). The overall analysis revealed a reduced risk of mediastinitis (RR, 0.64; 95% CI, 0.45-0.91; $P = .01$). The risk of death was unchanged. A significant positive linear correlation ($P = .05$) was found between the log RR of sternal wound infection and the percentage of patients receiving bilateral internal thoracic artery grafts.

Conclusions: Implantable gentamicin-collagen sponges significantly reduce the risk of sternal wound infection after cardiac surgery, with evidence consistent in randomized and observational-level data. However, the extent of this benefit might be attenuated in patients receiving bilateral internal thoracic artery grafts. (J Thorac Cardiovasc Surg 2015;149:1631-40)



Efficacy of implantable gentamicin-collagen sponge in preventing sternal wound infections.

Central Message

Implantable gentamicin-collagen sponge significantly reduces the risk of sternal wound infection after cardiac surgery by nearly 40% with evidence highly consistent in randomized- and observational-level data. However, the extent of this benefit might be attenuated in patients receiving bilateral internal thoracic artery grafts.

Perspective

Recent randomized study introduced substantial uncertainty regarding the efficacy of implantable gentamicin-collagen sponge in sternal wound infections prophylaxis. Present study confirms and corroborates in a systematic fashion the findings from the previous studies showing statistically significant reduction of sternal wound infections in patients in whom gentamicin sponge was implanted. Lower benefit conferred by the gentamicin sponge in patients receiving bilateral internal thoracic artery grafts should direct the surgeon's attention to these patients in particular because other potentially preventive measures must be undertaken in this population.

See Editorial Commentary page 1641.

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Received for publication Nov 22, 2014; revisions received Jan 13, 2015; accepted for publication Jan 20, 2015; available ahead of print Feb 19, 2015.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2015.01.034

Abbreviations and Acronyms

BITA = bilateral internal thoracic artery
BMI = body mass index
CI = confidence interval
DSWI = deep sternal wound infection
IGCS = implantable gentamicin-collagen sponge
logRR = log risk ratio
RCT = randomized controlled trial
RR = risk ratio
SSWI = superficial sternal wound infection
SWI = sternal wound infection

Supplemental material is available online.

Routine intravenous antibiotic prophylaxis initiated before cardiothoracic surgery has been consistently shown to reduce the postoperative rates of infections and in turn associated morbidity and mortality.[1] Sternal wound infections (SWIs) are serious postoperative complications increasing both length of hospital stay and healthcare costs. Several early randomized and observational studies demonstrated implantable gentamicin-collagen sponges (IGCSs) to further reduce (by 33%-62%) the infectious complications compared with intravenous (IV) prophylaxis alone when inserted between sternal halves immediately before closure of the mediastinum.[2-5] These implants deliver high concentrations of gentamicin locally within the wound, therefore preventing the systemic adverse effects of such high regimens and at the same time lowering the risk of acquired bacterial resistance to antibiotics.[6] On the other hand, the recent SWIPE-1[7] trial questioned those results, showing no extra benefit of IGCS among US patients at high baseline risk, including diabetes, body mass index (BMI) >30 kg/m^2, or both. The study showed no difference between IGCS and control groups for the outcomes of superficial SWI (SSWI), deep SWI (DSWI), and rehospitalization for wound infection at 90-day follow-up. Driven by the conflicting results and limited number of randomized studies, we aimed to perform an updated and comprehensive meta-analysis of randomized controlled trials (RCTs) with an addition of observational data to further corroborate the obtained results. In addition, for the first time, we try to explore the efficacy of the IGCS in the setting of bilateral internal thoracic artery (BITA) harvest.

MATERIALS AND METHODS

Data Sources and Search Strategy

Established methods were used in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement for reporting systematic reviews and meta-analyses in health care interventions.[8] PubMed, EMBASE, CINAHL, Scopus, the Web of Science, the Cochrane Register of Controlled Clinical Trials (CENTRAL), and Congress proceedings from major cardiothoracic and cardiothoracic societies meetings were screened for randomized and observational studies comparing the efficacy of the IGCS in prophylaxis of SWI after cardiac surgery with placebo or no intervention. Search terms were *gentamicin collagen sponge, gentamicin implant, gentamicin sponge, cardiac surgery, heart surgery, DSWI, SSWI,* and *mediastinitis*. No language, publication date, or publication status restriction was imposed. Both blinded and open-label trials were considered eligible. The most updated or inclusive data for each study were used for abstraction. References of original and review articles were cross-checked.

Selection Criteria and Quality Assessment

Citations were screened at title/abstract level and retrieved as full reports if they fulfilled the inclusion criteria: (1) human studies; (2) RCTs or observational studies with control group; and (3) prespecified outcome of SWI reported. Two independent reviewers (M.K. and W.P.) selected the studies for the inclusion and extracted studies and patient characteristics of interest and relevant outcomes; divergences were resolved by consensus after discussion with a third reviewer (L.A.). Three authors (M.K., W.P., and M.E.K.) independently assessed the trials' eligibility and risk of bias. The bias risk for randomized studies was assessed using the components recommended by the Cochrane Collaboration, that is, random sequence generation and random allocation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias.[9] The quality of observational studies was appraised with the Newcastle–Ottawa Scale, a tool used for assessing the bias (the selection of the study groups, the comparability of the groups, and the ascertainment of the exposure or outcome of interest) in case-control and cohort studies included in a systematic review or meta-analyses.[10]

Outcome Measures

The primary end point was the occurrence of SWI after cardiac surgery. Secondary end points were the occurrence of DSWI, SSWI, mediastinitis, and mortality. Definitions for the type, degree, and depth of the infection were applied as per study protocol.

Statistical Analysis

Data were analyzed according to the intention-to-treat principle. Randomized and observational studies were assessed separately. Risk ratios (RRs) and 95% confidence intervals (CIs) were used as summary statistics. Heterogeneity was assessed by the Cochran Q test.[11] The statistical inconsistency test was $I^2 = [(Q \_ df)/Q] \times 100\%$, where Q is the chi-square statistic and df is its degrees of freedom. Thresholds for the interpretation of I^2 for low, moderate, and considerable degree of heterogeneity were values of 25%, 50%, and 75%, respectively.[12] Pooled RRs were calculated using a fixed-effects model for a randomized trials subset in case of low heterogeneity. Pooled RRs from observational studies were calculated using random-effects model with the Mantel–Haenszel method as the most conservative approach. Potential publication bias was examined for the primary end point constructing a ''funnel plot'' in which the standard error of the log risk ratio (logRR) was plotted against the RR. The asymmetry of the plot was estimated both visually and by a linear regression approach. Random-effects meta-regression analyses accounting for within- and between-study variations were conducted to evaluate linear correlations between the occurrence of any surgical site infection and the percentage of patients in each study receiving BITA and single internal thoracic artery (SITA) grafts, with the sample size as weight.[13] Finally, we addressed the influence of each study and potential publication bias by testing whether deleting each study in turn would have significantly changed the pooled results of the meta-analysis for the