Triclosan-coated sutures and surgical site infection in abdominal surgery: the TRISTAN review, meta-analysis and trial sequential analysis

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Abstract

Introduction Surgical site infection (SSI) is a frequent complication of abdominal surgery causing increased morbidity. Triclosan-coated sutures are recommended to reduce SSI. The aim of this systematic review and meta-analysis was to evaluate the evidence from randomized controlled trials (RCT) comparing the rate of SSI in abdominal surgery when using triclosan-coated or uncoated sutures for fascial closure.

Methods A systematic literature search was conducted using Medline, EMBASE, the Cochrane library, CINAHL, Scopus and Web of Science including publications until August 2017. The quality of the RCTs was evaluated using critical appraisal checklists from SIGN. Meta-analyses and trial sequential analysis were performed with Review Manager v5.3 and TSA software, respectively.

Results Eight RCTs on abdominal wall closure were included in the meta-analysis. In an overall comparison including both triclosan-coated Vicryl and PDS sutures for fascial closure, triclosan-coated sutures were superior in reducing the rate of SSI (OR 0.67; 0.46–0.98). When evaluating PDS sutures separately, there was no effect of triclosan-coating on the rate of SSI (OR 0.85; 0.61–1.17). Trial sequential analysis showed that the required information size (RIS) of 797 patients for triclosan-coated Vicryl sutures was almost reached with an accrued information size (AIS) of 795 patients. For triclosan-coated PDS sutures an AIS of 2707 patients was obtained, but the RIS was estimated to be 18,693 patients.

Conclusion Triclosan-coated Vicryl sutures for abdominal fascial closure decrease the risk of SSI significantly and based on the trial sequential analysis further RCTs will not change that outcome. There was no effect on SSI rate with the use of triclosan-coated PDS sutures for abdominal fascial closure, and it is unknown whether additional RCTs will change that.

Keywords Incisional hernia · Laparotomy closure · Hernia prevention · Guidelines

Introduction

Surgical site infection (SSI) is a frequent complication of abdominal surgery with a reported incidence of 10–20% with the highest incidences in contaminated and dirty fields [1–3]. SSI is associated with increased length of hospital stay, reoperations and the development of incisional hernias [4]. Furthermore, SSI represents an economic burden to the healthcare system [5, 6]. Well-known patient-related risk factors for SSI are smoking, obesity and diabetes [7–9]. Furthermore, diffuse peritonitis, long-lasting open surgery and hypothermia during surgery is associated with SSI [10, 11]. Skin preparation with antiseptics and preoperative antibiotic
prophylaxis for clean-contaminated and contaminated surgery have proved efficient for decreasing SSI rate [10].

In the last decades, the agent triclosan has been introduced in toothpaste and soaps for its antifungal and antibacterial properties [12]. Triclosan affects the cytoplasmatic membrane of both Gram negative and positive bacteria, and even in small concentrations it has bacteriostatic effects. In surgery, sutures represent an implanted foreign material and therefore a risk for SSI. In in vitro studies, triclosan reduced bacterial colonization and biofilm formation on sutures [13]. Furthermore, small doses of triclosan seem safe to use [14]. Therefore, the use of triclosan-coated sutures seems promising in reducing the risk of SSI.

The Global Guidelines on the Prevention of SSI by WHO were recently published and the use of triclosan-coated sutures was recommended to reduce the risk of SSI, independent of the type of surgery [15]. The recommendation was conditional and based on moderate quality of evidence. Further, previous reviews and meta-analyses have concluded that the use of triclosan-coated sutures decrease the rate of SSI significantly and thereby lead to savings in all surgical specialties [16–21]. However, these meta-analyses included all types of surgical procedures i.e. orthopedic, cardiac, abdominal and breast surgery. Additionally, most randomized controlled trials (RCTs) evaluating triclosan-coated sutures used fast-absorbable sutures. Supposedly, abdominal surgery cannot be compared with i.e. orthopedic surgery when evaluating the risk of SSI. Due to the different properties of a fast-absorbable braided polyglactin 910 (Vicryl®) suture and a slowly absorbable monofilament polydioxanone (PDS®) suture, it is our hypothesis that the effect of triclosan-coated Vicryl (VICRYL® Plus) and PDS (PDS® Plus) sutures should be assessed separately. Accordingly, this systematic review, meta-analysis and trial sequential analysis (TSA) were conducted to evaluate RCTs that compared triclosan-coated Vicryl or PDS sutures for the closure of abdominal wall fascia with SSI as the primary outcome.

Materials and methods

A study protocol was written and registered on Prospero (CRD42016046054) before the initiation of the systematic review and meta-analysis. The data are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [22].

Inclusion criteria

The aim of the study was to evaluate published RCTs comparing triclosan-coated sutures and uncoated sutures for abdominal fascial closure. The primary outcome was SSI. All types of incisions, all indications for surgery and both emergency and elective laparotomies were included. All types of triclosan-coated sutures (fast-absorbable and slowly absorbable) were included. Only human studies on adults ≥ 18 years of age were included.

Search strategy

A systematic search was done independently by two authors (NAH, FM) in the following databases: Medline, EMBASE, Cochrane, SCOPUS, CINAHL and Web-of-Science. The search was not restricted to certain languages or years of publication. The last search was performed the 30th of August 2017.

In Medline and EMBASE, the search strategy was based on the Medical Subject Heading (MeSH) terms: laparotomy, wound closure, sutures and abdominal wall hernias. The detailed search term for Medline was: ((“triclosan” [MeSH Terms] OR “triclosan” [All Fields]) AND coated [All Fields] AND (“sutures” [MeSH Terms] OR “sutures” [All Fields])) AND (“surgical wound infection” [MeSH Terms] OR (“surgical” [All Fields] AND “wound” [All Fields] AND “infection” [All Fields]) OR “surgical wound infection” [All Fields]) OR “surgical” [All Fields] AND “site” [All Fields] AND “infection” [All Fields]) OR “surgical site infection”[All Fields]).

Evaluation of papers and data extraction

Firstly, the records were screened by title and abstract by two assessors independently (NAH, LV). Secondly, the full-texts were evaluated by two authors (NAH, RF) independently for eligibility with the use of critical appraisal checklist for randomized controlled trials developed by the Scottish Intercollegiate Guidelines Network (SIGN) [23]. Only papers rated as ‘acceptable’ or ‘high quality’ by SIGN were included to limit the risk of bias. Any disagreement of the two assessors was settled by discussion with a third evaluator (FM). Data were extracted by two authors independently regarding the predefined outcomes (NAH, FM) and checked by a co-author (ED).

Selection of outcomes to be included in the meta-analysis and trial sequential analysis (TSA)

In the meta-analysis and TSA, all triclosan-coated sutures versus uncoated sutures were evaluated. Furthermore, the sutures were divided into triclosan-coated slowly absorbable PDS sutures versus uncoated slowly absorbable PDS sutures and triclosan-coated fast-absorbable Vicryl sutures versus uncoated fast-absorbable Vicryl sutures, respectively.
Statistical analysis

The outcomes were pooled in conventional meta-analyses and reported as weighted odds ratios (OR) with 95% confidence intervals (95% CI) using the random effects model and illustrated with forest plots. Heterogeneity was explored using $I^2$ statistics. The Cochrane risk of bias tool was used to assess the risk of bias. Meta-analyses increase the power of the estimated effects, but can obtain false positive results. If a meta-analysis includes too few randomized participants, there may be insufficient statistical power to assess the effect of an intervention. Further, there is a risk of multiple significance testing when accumulating data in meta-analyses. The TSA technique is a way to account for these problems with calculation of the required information size (RIS). RIS is like sample size calculation and is compared with the accrued information size (AIS). RIS is defined as the number of participants required to detect or reject an assumed intervention effect in a meta-analysis [24]. The risk of type I and II errors was set to 5% and 20%, respectively. The control event rate (CER-baseline risk) was calculated in all meta-analyses as the median of the proportion of events in the control group. The effect size (OR) was estimated from the included trials. We used the $I^2$ present in the included trials as the estimate for the heterogeneity. Statistical analyses were performed with Review Manager Software version 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark) and TSA was performed using the TSA software.

Results

Literature search

Out of 79 citations, a total of 8 RCTs with 3641 patients were included in the meta-analyses (Fig. 1). All studies were published in peer-reviewed English-language journals from 2009 to 2015. Study characteristics are listed in Table 1.

Risk of bias

Five of the studies were considered high quality with the SIGN critical appraisal checklist, and the overall risk of bias was low. The most frequent source of bias was performance.

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Fig. 1 PRISMA flow diagram of study selection
bias. In two of the studies [25, 26], the surgeons were not blinded to the intervention, and in three of the studies [27–29] it was not reported whether participants or personnel were blinded to the intervention.

Most of the studies were large RCTs with at least 140 patients in each arm [25–27, 30, 31]. However, three of the RCTs were quite small [28, 29, 32]. Mingmalairak et al. [32] stated that the manuscript was a preliminary safety report, however, no newer study was to be found, and it was not possible to get in contact with the author.

<table>
<thead>
<tr>
<th>Bibliographic citation [reference]</th>
<th>Quality assessment</th>
<th>Type of study</th>
<th>Number of patients (group A/group B)</th>
<th>Patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Method of evaluating outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baracs et al. [26]</td>
<td>High quality</td>
<td>Multi-center RCT</td>
<td>385 (188/197)</td>
<td>Elective open colorectal surgery</td>
<td>PDS Plus</td>
<td>PDS II</td>
<td>‘Signs of SSI’, clinical examination during hospital stay and telephone follow-up at day 30</td>
</tr>
<tr>
<td>Diener et al. [29]</td>
<td>High quality</td>
<td>Multi-center RCT</td>
<td>1185 (587/598)</td>
<td>Elective midline laparotomy</td>
<td>PDS Plus</td>
<td>PDS II</td>
<td>SSI according to CDC criteria, clinical examination and photograph evaluation at day 10/day of discharge and at day 30</td>
</tr>
<tr>
<td>Justinger et al. [30]</td>
<td>High quality</td>
<td>Single-center RCT</td>
<td>856 (485/371)</td>
<td>Emergency or elective laparotomy</td>
<td>PDS Plus</td>
<td>PDS II</td>
<td>SSI according to CDC criteria, clinical examination during hospital stay and at day 14</td>
</tr>
<tr>
<td>Mattavelli et al. [24]</td>
<td>High quality</td>
<td>Multi-center RCT</td>
<td>281 (140/141)</td>
<td>Elective open colorectal surgery</td>
<td>PDS Plus</td>
<td>PDS II</td>
<td>SSI according to CDC criteria, weekly clinical examinations until day 30</td>
</tr>
<tr>
<td>Mingmalairak et al. [31]</td>
<td>Acceptable</td>
<td>Single-center RCT</td>
<td>100 (50/50)</td>
<td>Open appendectomy</td>
<td>Vicryl Plus</td>
<td>Vicryl</td>
<td>‘Presence of SSI’ at day 1, 3, 7, 14 and 30, 6 and 12 months follow-up</td>
</tr>
<tr>
<td>Nakamura et al. [25]</td>
<td>High quality</td>
<td>Single-center RCT</td>
<td>410 (206/204)</td>
<td>Elective colorectal surgery</td>
<td>Vicryl Plus</td>
<td>Vicryl</td>
<td>SSI according to CDC criteria, daily clinical examination during hospital stay, weekly clinical examination until day 30</td>
</tr>
<tr>
<td>Ruiz-Tovar et al. [28]</td>
<td>Acceptable</td>
<td>Multi-center RCT</td>
<td>101 (50/51)</td>
<td>Laparotomy due to fecal peritonitis</td>
<td>Vicryl Plus</td>
<td>Vicryl</td>
<td>SSI according to CDC criteria, clinical examination at day 5, 30 and 60</td>
</tr>
</tbody>
</table>
Type of sutures

All studies reported the use of the same suture material and suture technique in both arms with the only difference being the triclosan-coating. Four studies [26, 28, 29, 32] used Vicryl sutures for fascial closure and four studies used PDS sutures [25, 27, 30, 31].

Type of surgeries

The majority of the studies included only elective surgery (Table 1). Four of these [25–28] included only colorectal procedures, whereas Diener et al. [30] included all types of elective procedures through a midline laparotomy. Justinger et al. [31] included both elective and emergency laparotomies, whereas Ruiz-Tovar et al. [29] only included cases with fecal peritonitis and Mingmalairak et al. [32] studied patients undergoing open appendectomies.

Primary outcome—surgical site infection

The majority of the studies [25, 26, 29–31] used the Center for Disease Control and Prevention (CDC) definition for SSI. Most studies examined the patients during their hospital stay and included a 30-day examination in the outpatient clinic [25–27, 29, 30, 32]. One study also included a 60-day examination [29] and Justinger et al. [31] examined the patients 2 weeks after hospital discharge. Rasic et al. [28] defined SSI simply as ‘presence of wound infection’ during hospital stay and after hospital discharge; readmissions and reoperations were recorded.

In an overall comparison including both triclosan-coated Vicryl and PDS sutures, the rate of SSI was 13.5% (230/1705) for uncoated sutures and 10.1% (182/1797) for triclosan-coated sutures. Thus, overall triclosan-coated sutures were superior in reducing the rate of SSI (OR 0.67; 0.46–0.98, $P = 0.04$), (Fig. 2a). When evaluating PDS sutures separately, the SSI rate was 11.4% (159/1400) for PDS Plus and 13.5% (177/1307) for uncoated PDS, meaning that there was no effect of triclosan-coating on the rate of SSI (OR 0.85; 0.61–1.17, $P = 0.31$), (Fig. 2c). Triclosan-coated Vicryl sutures were superior (SSI rate: 5.8%) to uncoated Vicryl sutures (SSI rate 13.3%) in decreasing the rate of SSI (OR = 0.41, 95% C.I. 0.21–0.79, $P = 0.008$), (Fig. 2b).

TSA showed that for triclosan-coated PDS sutures an AIS of 2707 patients was obtained, but the RIS was estimated to be 18,693 patients (Fig. 3a). For triclosan-coated Vicryl sutures, the RIS of 797 patients was almost reached with an AIS of 795 patients (Fig. 3b).

Discussion

This meta-analysis including 8 RCTs evaluated the effect of triclosan-coated sutures on SSI for abdominal fascial closure, and discriminated between the use of triclosan-coated PDS and Vicryl sutures. Triclosan-coated PDS sutures failed to reduce the rate of SSI. On the other hand, triclosan-coated Vicryl sutures for abdominal fascial closure significantly reduced the rate of SSI.

In recent global guidelines to prevent SSI, triclosan-coated sutures were recommended to decrease SSI rate for any type of surgery [15]. This recommendation was inspired by meta-analyses by Edmiston and Daoud et al. [17, 19], where RCTs evaluating all types of surgical procedures were included and no separate evaluation between PDS and Vicryl sutures was performed [17, 19]. In a newly published meta-analysis and TSA, also including all types of surgical procedures, it was also concluded that there is moderate quality of evidence to conclude that triclosan-coated sutures do decrease SSI and that further studies are not likely to alter the effect [20]. Interestingly, in a subgroup analysis on triclosan-coated PDS sutures, there was no significant effect on SSI rate [20]. Additionally, in a thorough literature review by the Canadian Agency for Drugs and Technologies it was concluded that the efficacy of triclosan-coated sutures was inconsistent [33]. Further, two recent meta-analyses including RCTs on colorectal surgery concluded that there was no effect on SSI rate with the use of any type of triclosan-coated suture [34, 35]. This was supported by a meta-analysis on all types of surgical procedures which reported that for colorectal surgery specifically, triclosan coating did not reduce SSI [36]. These conflicting conclusions suggest that it is essential to assess specific surgical procedures and suture types separately.

This current meta-analysis evaluated the use of triclosan-coated sutures in abdominal surgery only and distinguished between Vicryl and PDS sutures. The triclosan-coating was only effective in reducing SSI when using Vicryl sutures corresponding to the subgroup analysis of de Jonge et al. [20] Vicryl is a braided suture with a greater surface area increasing the risk of bacterial colonization and biofilm formation in comparison to monofilament suture material [13]. Thus, it is possible that the concentration of triclosan is higher on the braided suture compared to a monofilament suture. This could be a reason for the effect of triclosan-coating on Vicryl sutures. Indeed, if comparing the overall SSI rate in the Vicryl control group with the PDS control group, the rates are equal, 13.3% versus 13.5%, respectively.

TSA was performed to evaluate the statistical power of the meta-analysis. According to the TSA, another 16,000 patients need to be randomized to triclosan-coated PDS sutures, before there is sufficient statistical power to finally accept or reject the effect of the intervention. The reason
why so many more patients are required in the PDS group compared to the Vicryl group is explained by a difference in the relative risk reduction and $I^2$ for PDS Plus and Vicryl Plus. However, 16,000 patients are quite a lot to randomize and unknown whether this would alter the results of the meta-analysis. For triclosan-coated Vicryl sutures the RIS was already reached, and no further RCTs on triclosan-coated Vicryl sutures are needed.

Incisional hernias are a frequent complication of laparotomies, and SSI is a well-known risk factor for incisional hernia formation [4, 37]. Possibly, incisional hernias are preceded by SSI in up to 40% of the cases [38–41]. When a wound is colonized by bacteria, its healing potential is compromised thereby increasing the risk of incisional hernia formation [42]. Unfortunately, none of the RCTs included in this meta-analysis evaluated the incisional hernia rate in a 12-month follow-up.

The abdominal fascia is subject to high tension and it takes somewhere between half a year to several years before the fascia has regained its strength after surgery [42]. In guidelines on incisional hernia prevention by the European Hernia Society, it is recommended to close the fascia with a slowly absorbable monofilament suture [43]. In a recently published RCT concerning the closure of a midline laparotomy using PDS in small versus large bite-technique, there was no significant difference on SSI rate in both groups, but significant less incisional hernia formation in the small bite group after 1 year [44].

Fig. 2 Forest plot of surgical site infection rates using a triclosan-coated sutures versus uncoated sutures, b triclosan-coated PDS versus uncoated PDS sutures and c triclosan-coated Vicryl versus uncoated Vicryl sutures
This meta-analysis is strengthened by the fact that it includes only one type of surgery and it analyses Vicryl and PDS sutures separately. However, the meta-analysis does have some limitations. Publication bias was not assessed since less than 10 RCTs were included [45]. In two RCTs [25, 26], the surgeons were not blinded to the intervention, which could hypothetically have influenced the results, even though the investigators of SSI were blinded to the intervention. Two of the studies were industry funded [30, 31], of which the RCT by Diener et al. [30] had the highest weight.

**Fig. 3** Trial sequential analysis (TSA) curve for a triclosan-coated PDS versus uncoated PDS sutures and b triclosan-coated Vicryl versus uncoated Vicryl sutures. RIS required information size. The $Z$-curve marks the number of patients included in the randomized controlled trials included in this meta-analysis.
in the meta-analysis and found no effect of triclosan-coated PDS. Therefore, a bias in this case due to industry funding seems unlikely. The rate of SSI was reported to be 16% by Diener et al. [30] which may seem high in clean-contaminated cases, however, this rate is not high when compared to the reported rate in other high quality RCTs, where patients are thoroughly examined for SSI [2].

In accordance with the EHS guidelines [43], a slowly absorbable suture is to be preferred for fascial closure. When closing the abdominal fascia with a slowly absorbable suture, a triclosan-coated PDS suture does not seem to decrease SSI rate. But, in the case a Vicryl suture is used, the current systematic review advocates the use of a triclosan-coated suture.

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**Compliance with ethical standards**

**Conflict of interest**  NH, ED, LV, RF and JG declare no conflict of interest. MM declares conflict of interest not directly related to the submitted work: grants and personal fees (consultancy and speaker) from Medtronic and Dynamesh, grants and personal fees (speakership) from Intuitive Surgical.

**Ethical approval**  This study did not need approval from the local ethical committee.

**Human and animal rights**  This study does not contain any studies with participants or animals performed by any of the authors.

**Informed consent**  Informed consent was not required for this study.

**References**


