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Cutaneous Coating with Cyanocrilate for Heart Surgery Patients: A Systematic Literature Review

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Abstract: ***Objective*: To compare the effectiveness of conventional cyanoacrylate-based dressings / sutures to reduce mediastinitis in patients undergoing cardiothoracic surgery. *Method*: Systematic review based on Cochrane Handbook recommendations and PRISMA guide. Randomized controlled trials were sought, without language limitations and year of publication, were searched in the indexed or non-indexed databases, gray literature, Congressional ANAIS, specific bases of the studied subject and references of the references. *Results*: Were included four studies with 2092 participants, aged 45 to 81 years old, who used cyanoacrylate in sternotomies to reduce postoperative mediastinitis after cardiothoracic surgery. *Conclusions*: The use of cyanoacrylate-based sealants does not significantly influence the incidence of surgical site infection in general groups. However, the use of cyanoacrylate decreased the incidence of surgical site infection in obese, elderly patients with chronic diseases such as systemic arterial hypertension, diabetes mellitus and vascular diseases.***

Keywords: Sternotomy; Thoracic Surgery; Mediastinitis; Adhesives

1. Introduction

The loss of skin integrity, whether accidental or planned, predisposes to numerous damages and infections to the human species. These harmful effects have been reduced with the improvement of drugs, devices and surgical techniques, but they have not been eliminated.[1]

The opening of the sternum for cardiothoracic surgery was performed the first time to access the heart in 1897[4], however, even with the technological and surgical evolution, there is the occurrence of serious infectious conditions that challenge the competence of the surgical teams and the cardiological treatment centers.[1]

The incidence of mediastinitis in thoracic surgery and therefore in cardiac surgical procedures with sternotomy is small (0.4 to 5%)[5], however, the mortality of this complication is high, ranging from 14 to 47%[6], in addition to the considerable increase treatment costs after this complication, tripling its values.[7,8]

The main objective of treating a wound is to reduce the risk of infection and to prevent or minimize its complications[9] and for this purpose, several scientific advances have emerged related to wound closure, such as synthetic sutures, staplers, adhesive tape and more recently tissue adhesives.[10]

Surgical adhesives are an alternative to conventional sutures and have advantages such as technical ease, reduced intraoperative period by reducing the time spent on synthesis, reduced contamination risks and reduced surgical wound (SW) recovery period by facilitating the tissue synthesis.[11]

Cyanoacrylate is a generic term that refers to substances such as methyl-2-cyanoacrylate or 2octylcyanoacrylate, known as Dermabond® or IntegueSeal®. This adhesive was used in the industry and on a daily basis achieving success due to the adhesiveness it provides. In 1958, epoxy (or epoxylin) was used to join bone tissue in experimental fractures.[12] Shortly afterwards, polyurethane polymers were also used in fracture consolidation.[13]In 1958, cyanoacrylate had its synthesis reformulated by the Mckeever method and the surgical interest in this material grew, with positive prospects for results, for having good adhesion and being bactericidal.[14]

It is a sterile topical adhesive, applied to the wounds to keep the edges together. This therapy applied to keep the edges together or overlapping the conventional suture, has bacteriostatic action, favors tissue repair and inhibits the migration of inflammatory cells.[2]

The first report in the literature regarding the use of methyl cyanoacrylate in living tissues was highly successful when using the adhesive on stomach, trachea, spleen, bones, muscles and small intestine.[12] The ability to waterproof the skin is highlighted because it forms a protective film, dispense the use of covers, favoring the visualization of the wound and for being sterile. Among the main benefits are

sterility, waterproofing of the SW and visualization of the wound, without being open to the environment.[2]

This adhesive has also been used after conventional suture to seal the edges of the SW in order to prevent infection of the wound in the postoperative period, through its performance as a microbial barrier for exogenous bacteria. Studies have found that routine use of cyanoacrylate is associated with a significant reduction in infection rates for cardiovascular surgery patients.[15]

A study carried out by the Oxford University in 2010 showed that the rates of sternal dehiscence and post-sternotomy osteomyelitis were significantly reduced in cases in which cyanoacrylate was applied; it reduced hospitalization time, both in patients treated for recurrent mediastinitis and in patients with recovery without complications after cardiac surgery.[16]

Based on the scientific evidence of controlled and randomized clinical trials (RCTs), this study compared the advantages presented in relation to the use of cyanoacrylate in sternotomies, thus, the objective was to compare the effectiveness of conventional dressings and / or sutures with topical adhesive cyanoacrylate-based to reduce mediastinitis in patients undergoing cardiothoracic surgery. The study question consisted of: for patients who underwent sternotomy in cardiothoracic surgery, do cyanoacrylate-based patches reduce mediastinitis rates?

2. Method

Systematic literature review study conducted according to the recommendations of the Cochrane Handbook for Systematic Review of Interventions.[29] The PRISMA[30] protocol was used as a guide for the review and the PICO strategy was used for the elaboration of the question.[31]

For this study, the PICO strategy used was: P - Patients undergoing sternotomy in cardiothoracic surgery; I - Topical adhesives cyanoacrylate-based; C - Conventional dressings and / or sutures; O - Reduction in the rate of mediastinitis, decrease in treatment costs and reduction in hospital stay. Therefore, the question of the study consisted of: for patients who underwent sternotomy in cardiothoracic surgery, do cyanoacrylate-based patches reduce the rates of mediastinitis?

RCTs were included, with no limitations on language and year of publication, which evaluated interventions related to cyanoacrylate-based topical adhesives in the sternotomies of cardiothoracic surgery, at any duration and periodicity. Also, adult or elderly participants in the postoperative period of cardiothoracic surgery who underwent sternotomy.

The searches were carried out by two researchers who used a search protocol, containing the research question and search strategies, in the Latin American and Caribbean Health Sciences (LILACS), Medical Literature Analysis and Retrieval System databases online (Medline), Cumulative Index to Nursing and Allied Health Literature (CINAHL), National Library of Medicine (PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), Virtual Health Library (VHL), Web of Science, Science Direct, Central Cochrane Library and Repository of Gray Literature (Open Gray) using controlled and uncontrolled descriptors. Gray literature was also searched, manual search of references cited in selected articles, review of conference proceedings involving mediastinitis and dressings, search for clinical trials (http: //.clinicaltrialresults.org; http://www.clinicaltrial.gov) and on specific bases on the topic studied, such as http://www.cardiosource.com; http://www.theheart.org/index.do; http://www.acponline.org/; http://dermatology.cdlib.org/; http://dermatologytimes.com/ for the purpose of checking all the literature.

The terms and sets of terms were combined with the Boolean connectors AND and OR. The Boolean NOT was not used in order to prevent valid studies for the research from being excluded in the searches.

The two researchers independently evaluated the titles and abstracts of the studies, to select the studies that met the inclusion criteria. For the final selection of articles participating in this study, they were fully read, thoroughly. There was no need for a third reviewer, as there was no case of disagreement.

To extract the data present in the selected studies, a form designed for this study was used considering the instructions on content and appearance, recommended by the Cochrane Collaboration.[17] For its use, the instrument was subjected to a pilot test by the main reviewer and was carried out at extraction of data from selected studies, to ascertain items to be improved or modified.

The CONSORT (Consolidated Standards of Reporting Trials)[20] instrument was used in order to minimize bias, selecting clear, transparent studies and with the methodological steps properly described.

The author of the study included with incomplete data was contacted in order to obtain the necessary data and complementary information regarding the published article. The date of the communication was recorded, as well as the response obtained. The Cochrane Collaboration Risk Assessment Tool was used to assess the risk of study bias.[17]

The Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE) was used to assess the quality of the evidence body of the outcomes.[17,21-22]

3. Results

The initial search found 574 references in the following databases: 15 at American College of Cardiology, 23 at theheart.com, 05 at ACP, 04 at dermatologytimes.com, 05 at VHL Salud, 20 at Clinical Trials, 02 at Controlled Trials, 178 at CINAHL, 02 at Pubmed, 129 at Central Cochrane Library, 01 at Annals Thoracic Surgery, 134 at Science Direct, 25 at Web of Science, 08 at Open Gray and 07 at reference references. No studies were found in the American Literature and Caribbean Health Sciences (Lilacs), Scientific Electronic Library Online (SciELO) and

dermatology.cdlib.org databases. The five studies located by title in the VHL Salud were not found in full text, nor were the abstracts even when searched by the CAPES portal, being excluded due to the impossibility of analysis. After removing 16 duplicate references, titles and abstracts of 558 references were read, of which 528 were excluded because they did not meet the inclusion criteria. The remaining 30 references were considered relevant and potentially eligible. After reading the articles in full text and in-depth analysis, 26 references were excluded.

Thus, four completed articles were included (Dohmen 201123; Muhammet 201424; Schimmer 201725; Grauhan 201026). No studies were found in progress.

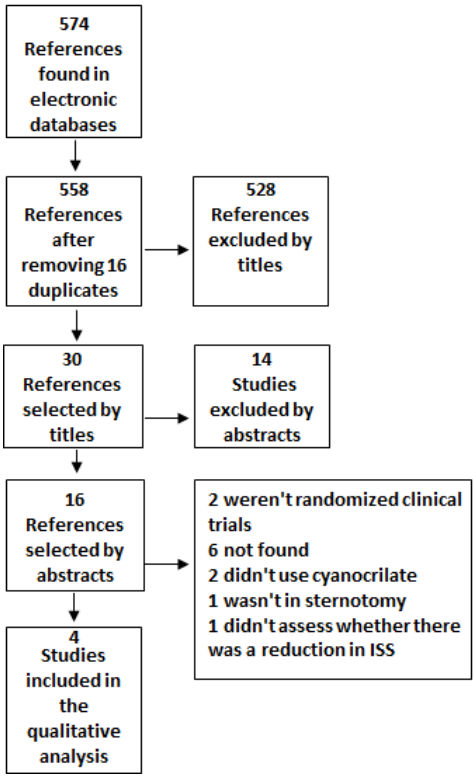


Figure I: Flowchart for selecting studies for the systematic review. São Paulo, Brazil.

The four studies included totaled 2092 participants aged between 45 and 81 years old. The main characteristics of the included RCTs are shown in Table 1.

After thorough full analysis of the studies, six articles were excluded. The reasons for excluding these studies are described in Table 2.

The risk of bias in the included studies was assessed according to the Cochrane Collaboration Risk Table and the domains were classified as “low risk”, “high risk” and “uncertain risk”.[17]The Cochrane Collaboration Review Manager 5.3 application was used to assist in assessing the risk of study bias.

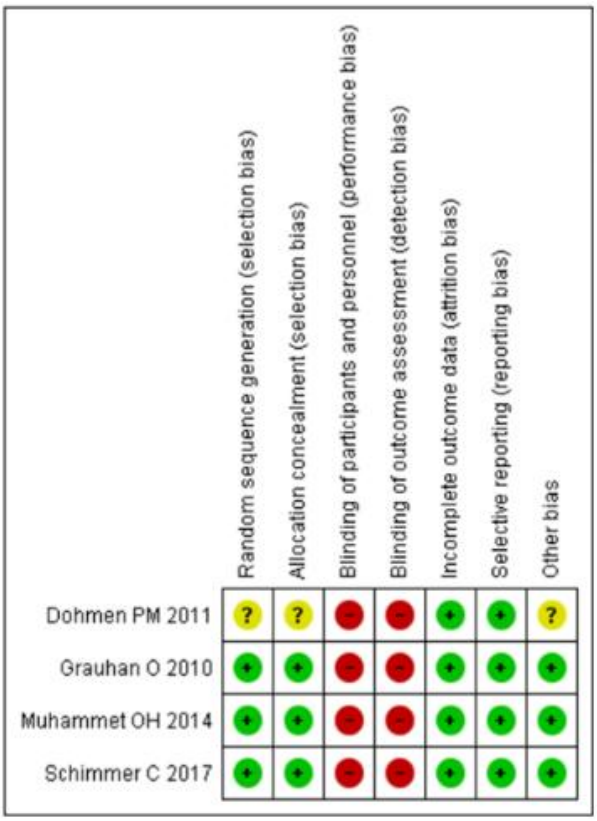
For items were classified as “uncertain risk of bias”. Contact was made with the correspondence authors for clarification, but there was no feedback.

In the evaluation of the selection bias (generation of the allocation sequence) the randomization process was clearly described in one of the studies found (Schimmer C 2017[25]), which used block randomization. Two studies (Grauhan O 2010[26]; Muhammet OH 2014[24]) report randomizations, but did not detail the process. Therefore, these three studies were classified as having a low risk of bias. The Dohmen PM 2011[23] study, despite working with a control group and an intervention group and leaving randomization implicit, does not use this term and does not describe how this process was carried out, being classified as having an uncertain risk of bias. For this case, contact was made with the corresponding author, but no reply was obtained.

In the assessment of selection bias (allocation secrecy), the four studies did not describe the type of strategy to maintain allocation secrecy. Thus, all studies were considered to be of uncertain risk of bias for the allocation confidentiality domain. In assessing the performance bias (blinding patients) it was found that, due to the nature of the intervention (surgical procedure), blinding patients and staff was too complex to be performed. The four studies did not blind those involved. Only the study of Schimmer C 2017[25] performed the blinding of the analyst of the collected data. All studies were considered to be “high risk of bias” for this domain.

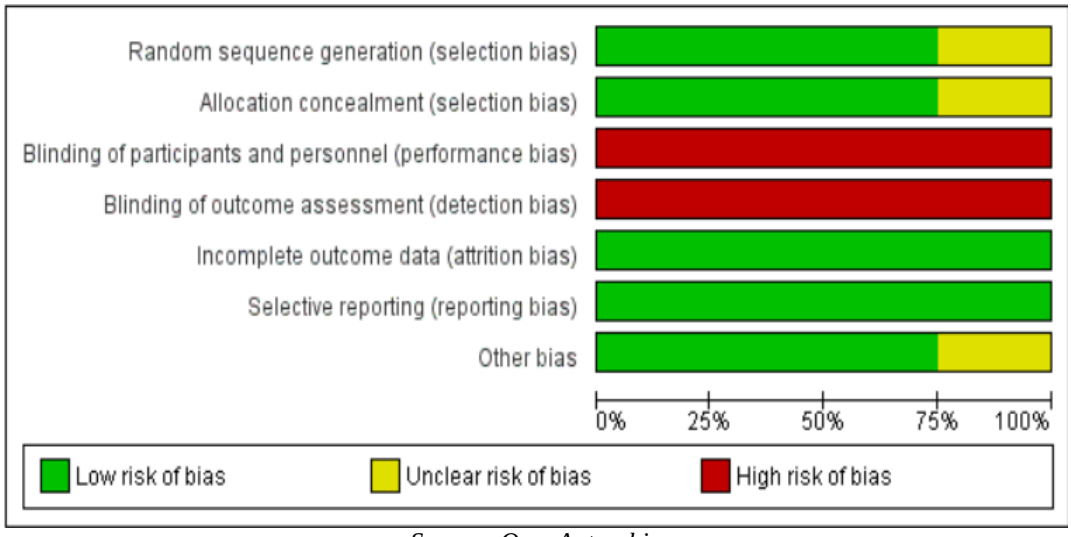
As for the attrition bias (incomplete outcome data), only one of the studies showed losses (Muhammet OH 2014[24]), however the loss was less than 15% and reported properly in the work method, causing no bias in the research. There were no losses in any of the other studies and all were classified as having a low risk of bias.

The four studies were consistent in terms of the proposed outcomes and published results. Thus, all studies were classified as low risk of bias for the domain related to reporting bias (selective reporting). The studies did not publish their protocols.



Source: Own Autorship

Figure II: Summary of the risk of bias in the studies included for each domain, according to the judgment of the authors of the review. São Paulo, Brazil.



Source: Own Autorship

Figure III: Graphical representation of the risk of bias in the studies included in each domain according to the judgment of the authors of the review. São Paulo, Brazil

Two studies reported a benefit in the use of cyanoacrylate and two reported that there were no differences between the use of cyanoacrylate when compared to conventional treatment. Dohmen 2011[23] concluded that the use of antimicrobial sealant decreased the incidence of SSI in patients undergoing cardiac surgery, especially in the elderly with chronic diseases such as arterial hypertension, diabetes mellitus or vascular diseases. Grauhan 2010[26] concluded that obese patients benefit from wound closure with cyanoacrylate as it offers tension-resistant closure with antimicrobial barrier properties.

Muhammet 2014[24] concluded that the use of cyanoacrylate-based sealant is equivalent to the traditional preparation of the skin in cardiac surgery. Likewise, Schimmer 2017[25] who compared conventional treatment, Gentamicin and Cyanoacrylate concluded that none of the interventions significantly influenced the incidence of the SSI rate, but demonstrated that there is a tendency for a benefit from using these prophylactic approaches.

4. Discussion

Median sternotomy has established itself as the standard approach for most open-heart surgery procedures since the technique was introduced in 1957.[3] Patients undergoing cardiac surgical procedures are particularly at risk for local infection, as the procedures are highly invasive and extended in duration.[27] A study[28] has shown that the incidence of mediastinitis varied between 1 and 5% and, a previous study[29] found that the incidence of superficial SSI postoperative and deep SSI in cardiac surgery ranged from 1.3 to 12.8%.

The low rates of mediastinitis are based on modern hygienic standards, the use of prophylactic antibiotics during and after the operative procedure and improvements in surgical and anesthetic techniques and in the development of intensive care.[28,30,31] Despite the low incidence, Surgical infection is a devastating complication in cardiac surgery after median sternotomy.[29] The mortality rate of patients with mediastinitis is three times higher than that of patients after cardiac surgery without deep SSI.[30-32]

The development of a sternal SSI is a multifactorial process, so studies have identified a multitude of clinical and perioperative variables as being contributory. The comparison of sternal infection rates after reported cardiac surgery included patients with different characteristics who underwent surgery, involving different specific procedures. However, large studies are useful to analyze risk factors as in a multivariate logistic regression analysis study of more than 9000 consecutive adult patients undergoing complete sternotomy[33], demonstrating that the presence of diabetes, the use of an artery graft (s) single or bilateral internal mammary, hospitalization in intensive care unit with more than five days, the surgical approach and the Body Mass Index (BMI)> 30 kg / m2, significantly increased the risk of deep SSI. Advanced age associated with the presence of Chronic Obstructive Pulmonary Disease (COPD) and renal failure are also established risk factors for SSI.[31,34,35] In this study, the interventions performed suggested that some groups may be at higher risk than others.

Diabetic patients undergoing cardiac surgery have increased rates of postoperative complications and mortality compared to non-diabetic patients. Also, the control of glucose levels reduces the rates of morbidity and mortality, since hyperglycemia contributes to the appearance of changes in skeletal and myocardial muscle metabolism, the increase in inflammatory mediators, platelet aggregation and thrombosis.[36]

The control of blood glucose levels in the pre, intra and postoperative periods is essential, since hyperglycemia is associated with an increased risk of SSI, since it promotes the proliferation of pathogenic microorganisms, impairs the function of neutrophils and may even cause other harm to the defense system.[37,38] The Global Guidelines for the Prevention of Surgical Site Infection recommends the control of perioperative glycemia in diabetic and non-diabetic patients to reduce the risk of SSI.[39]

Selected study[23]demonstrated a benefit in the use of cyanoacrylate-based sealant, applied to the skin before the surgical incision, in reducing SSI in elderly patients who suffered a variety of chronic disorders, such as hypertension, hyperlipidemia, diabetes mellitus and vascular disease. These patients had significantly elevated preoperative risk scores, therefore the highest incidence of SSI predicted. This study showed that prophylaxis with intravenous antibiotics as a normal practice, undoubtedly decreased the risk of SSI in cardiac surgical patients, but there is good evidence of antibiotic resistance that is directly linked to the duration of their prophylactic administration. The clinical consequences of infection with antibiotic-resistant bacteria are severe; patients experience a higher mortality rate, prolonged hospitalization and increased health costs compared to those with non-resistant infected organisms.

One of the studies selected for this review[26], found the presence of infection in the SW in obese patients, comparing the conventional suture and the suture associated with subsequent application of the sealant with cyanoacrylate. Obese patients are known to be a risk group for the development of mediastinitis and concluded that this group of patients benefited from the use of cyanoacrylate in wound closure as it offers tension-resistant closure with antimicrobial barrier properties.

In obesity, osteosynthesis may be exposed to special mechanical stress. After osteosynthesis, the bone and threads must be covered by closing the fascia and muscle[40]. In most cases, infection after sternotomy remains superficial as long as the soft layer of closure tissue on the sternum is maintained, highlighting the importance of meticulous closure of this layer. The skin incision after median sternotomy in obesity has two problematic aspects, related to the sitting position in which the skin suture is folded in the inframammary crease and the skin edges are forced to separate and the aspect related to the supine position, where the weight the adipose tissue pulls to both sides, beyond the edges of the skin, as this poses a problem, especially in the case of Heavy Mamma. Considering all these aspects, skin closure in obesity must guarantee resistance to mechanical traction forces, sufficient blood supply at the edges of the skin to guarantee the healing process and an immediate barrier to the penetration of skin flora.[26]

The joining of techniques with the purpose of preventing sternal infections is recent and in 1998 the first report was published regarding the use of cyanoacrylate glue in sternal closure after cardiac surgery, as a complement to the wiring in two cases of severe type III instability. from Hendrickson.[41]

Skin patches are intended for wound closure only at the edges of the skin, easily approached by small surgical incisions or clean traumatic lacerations, but in conjunction with, not in place of, deep skin points. However, there is recent evidence that longer incisions can also be closed by cyanocrylate.[15] In addition, wound closure by tissue adhesives offers an immediate antimicrobial barrier, as it prevents the migration of microorganisms from the skin flora to the surgical site.[15,42] The closure of the incision using the Donati suture pattern and the additional sealing of

the skin's edges by cyanoacrylate combines the advantages of both closure techniques, that is, it offers tension-resistant wound closure with immediate barrier properties and supports wound healing only by minimal impairment of cutaneous blood flow with increasing tension.

Closing the standard wound with severe wiring and layered suture, although used with various techniques, is still the first-line method established for incisions in the sternum. Studies differ widely regarding the advantages of using cyanoacrylate as an auxiliary method in the prevention of mediastinitis. A study[23] demonstrated that the use of cyanoacrylate, both preoperatively and postoperatively (in addition to severe spinning and in the replacement of skin sutures) decreased the incidence of deep and superficial SSI. Research[16] concluded that the reduced length of stay and decreased recurrence of infections attenuated the increased cost associated with the application of cyanoacrylate.

A study[23] included in this review, aimed to assess the impact of a cyanoacrylate-based microbial skin sealant to extend preventive measures in order to reduce SSI in cardiac surgery. It concluded that the inclusion of a microbial skin sealant before cardiac surgery significantly reduced the SSI rate and that the skin sealant can thus be an useful complement to the multimodal prevention approach needed to minimize bacterial contamination of surgical incisions.

Unicentric investigation study[43] using two prospective records to assess the prophylactic effect of a cyanoacrylate-based antimicrobial sealant (IntéguSeal®) on the incidence of postoperative mediastinitis or any other form of thoracic skin incision after elective cardiac surgery, concluded that the use of IntéguSeal® had no influence on the incidence of postoperative mediastinitis and SSI after cardiac surgery with median sternotomy. Corroborating this investigation, a study[44] gathered evidence from eight RCTs and a non-randomized trial, demonstrating that the preoperative application of antimicrobial sealants to the skin, in addition to the standard preparation of the surgical site, neither benefits nor harms the reduction in the SSI rate, being thus, it concluded that there are no advantages in using antimicrobial sealants.

Different prophylactic approaches are examined for the prevention of SSI in cardiac surgery. Local antibiotics, such as the gentamicin-collagen sponge, provide high local antimicrobial concentrations.[44]

Studies diverged in relation to the reduction in the SSI rate using the Genta-Coll ® sponge, such as the meta-analysis of 14 studies with 22135 patients that aimed to carry out comprehensive research to evaluate the efficacy of implantable gentamicin-collagen sponges in preventing sternal wound infection. concluded that there was a risk reduction for SSI in almost 40% of individuals with highly consistent evidence in randomized studies and observational data.[46] However, it demonstrated that the extent of this benefit can be mitigated in patients who received internal thoracic artery grafts bilateral and that the risk of death has not been changed.[46] On the other hand, an RCT[47] that involved 107 patients at high risk for sternal infection, patients with diabetes, high body mass index, or both undergoing cardiac surgery, the use of two gentamicin and collagen sponges, compared to no intervention, did not reduce the sternal wound infection rate in 90 days.

A study[25] selected for this review compared three different groups to analyze the incidence of SSI in patients with median sternotomy. It used conventional treatment, cyanoacrylate and gentamicin concluding that the application of gentamicin as well as cyanoacrylate did not significantly influence the incidence of SSI, however it showed a tendency towards a benefit of using these prophylactic approaches.

Reducing the risk of SSI has an important economic impact, where SSI costs generally cost 0.5% of the hospital's annual budget.[48] These costs result from prolonged hospitalization, additional surgical therapy, long-term antibiotic therapy, and use additional medical equipment.[49] The superficial SSI costs an average of US $ 3, 740.58, while the deep SSI costs an average of US $ 6, 850.93.[48] Studies report that these costs depend on the length of hospital stay and the chosen antibiotic therapy.[50,51] The cost of hospitalization for a patient with sternal infection is usually three times higher than a patient without SSI.[37]

The selected studies varied in terms of the time they followed up the patients. The Global Guidelines for the Prevention of Surgical Site Infection recommends that superficial SSI, namely, infection that occurs at the incision site and that involves only the skin or subcutaneous tissue, occurs within 30 days after surgery, however, in the case of Deep SSI, namely, defined as surgery-related infection involving deep soft tissues (muscle and fascial layers), can occur at the site of the operation within 30 days after surgery, if no prosthesis (foreign body not permanently derived from humans positioned on the patient during surgery) is left in place and within one year after surgery, if a prosthesis is left in place.[39,52] The selected studies carried out follow up of at least thirty days and at most one year, adopting the recommendations recommended by the Global Guidelines.

This study had as a limitation the difficulty of blinding found in RCTs due to the involvement of surgical procedures. However, the studies found showed a satisfactory number of participants for their analysis.

This review also found limited by the small number of clinical trials that met the inclusion criteria, suggesting the need for more primary studies on the subject.

5. Conclusion

The use of cyanoacrylate-based sealants does not significantly influence the incidence of SSI in general groups. However, the use of cyanoacrylate reduced the incidence of infection in more likely groups, namely: obese patients, elderly patients with chronic diseases, such as systemic arterial hypertension, diabetes mellitus and vascular diseases.

References

[1] Sampaio DT, Alves JCR, Silva AF, Lobo Jr. NC, Simões D, Faria W, Lobato A, Figueroa CCS–Mediastiniteemcirurgiacardíaca: tratament ocomepíploon. Rev Bras Cir Cardiovasc 2000;15 (1):23-31.http://dx.doi.org/10.1590/S0102-76382000000100006

[2] MoraesMAP,GonçalvesLF,WitkowskiMC,RodriguesJA(2012). Cicatrizaçãodaferidaoperatóriadecirurgiacardíacacomcianocrilato.Rev.enferm.UFSM.2012.2(1):32-38.http://dx.doi.org/10.5902/217976924347

[3] JulianOC,Lopez-Belio M, Dye WS. The median sternal incision in intra cardiac surgery with extra corporeal circulation: a general evaluation of its use in heart surgery. Surgery 1957.42:753-61.https://www.ncbi.nlm.nih.gov/pubmed/13467646

[4] Milton H. Media stinal surgery. Lancet1897.1:872-5.:http://dx.doi.org/10.1590/S0102-76382000000100006

[5] Sarr MG, Gott VL, Townsend TR. Mediastinal infection after cardiac surgery. Ann ThoracSurg 1984;38:415-23.:https://doi.org/10.1067/mtc.2003.74

[6] El Oakley RM, Wright JE. Post operative media stinitis: classification and management. Ann Thorac Surg 1996; 61:1030-6.https://doi.org/10.1016/0003-4975(95)01035-1

[7] Loop FD, Lytle BW, Cosgrove DM, Mahfood S, McHenry MC, Goormastic M, Stewart RW, Golding LA, Taylor PC. Sternal wound complications after isolated coronary artery by-pass grafting: early and late mortality, morbidity and cost of care.AnnThoracSurg1990;49:179-87.https://doi.org/10.1016/0003-4975(90)90136-T

[8] Nelson RM, Dries DJ. The economic implications of infection in cardiac surgery. AnnThorac Surg1986;42:240-6.https://doi.org/10.1016/S0003-4975(10)62726-9

[9] Forrest, RD. Early history of wound treatment.J.R.Soc.Med.1982,75:198,205DOI:10.1177/030006058000800613.

[10] TitoMG, Costa MAA, Tavares JR, Boechart S, Gomes OM.Curativo Oclusivo Utilizandooc–Cianoacrilato:"oc-Cyanoacrilateas an occlusive dressing".CardiovascSciForum2008;3(4):14-20. http://dx.doi.org/10.1590/S0100-69912008000300011

[11] Andrade JNBM, Cuevas SE, Maniscalco CL, Stefanes SA. Usodoetil-cianoacrilatonasínteseda parede vascular em cães. Ars vet. 2001; 17 (3); 172-176.http://www.arsveterinaria.org.br/arquivo/2001/v.17, %20n.3,%202001/172-176.pdf

[12] Inou T. Studies on the surgical use of plastic adhesive. Amjsurg.1962;13 (4):219-226.

[13] Souza M, Fagundes DJ, Gomes PO, Ascensão AM, Guimarães CA, Mendonça JRITM, Guimarães AC, Martins VL. Fiosdesutura: umarevisãohistórica.RevistadeCienciasBiologicas edaSaúde2001;2 (1):98-100.

[14] Borba CC, Rouband NetoE, ValRLR, BorbaJrCO, Soufen MA, Francisco Neto A, Sakotani AY. Usodoetilcianoacrilatonasíntesedepelederatos;trabalhodepesquisa experimental. Acta cir.bras. 2000; 15 (1):48-54.http://dx.doi.org/10.1590/S0102-86502000000100008

[15] Souza EC, Fitaroni RB, Januzelli DM, Macruz HM, Camacho JC, Souza MR. Use of 2-octyl cyanoacry late for skin closure of sternal incisions in cardiac surgery: observations of microbial barrier effects. Curr. med.res. opin. 2008;24:151-155.DOI:10.1185/030079908X253807

[16] Chambers A, Scarci M. Isskinclosure with cyanoacry late glue effective for the prevention of Sterna wound infections? Interact. cardiovasc. thorac. surg. 2010; 10: 793–796.DOI:10.1510/icvts.2009.230425

[17] Higgins JPT, Green S. Cochrane Hand book of Systematic Reviews of Interventions. Version 5.1.0. The Cochrane Collaboration 2011. Available from www.cochrane-handbook.org.DOI:10.1186/2046-4053-3-54

[18] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009; 6 (7):DOI:10.1371/journal.pmed.1000097.

[19] Santos CMC, Pimenta CAM, Nobre MRC. Aestratégia PICO para a construçãodaperguntade pesquisa e busca de evidências. Rev. latinoam. enferm. 2007; 15 (3): 508-511.http://dx.doi.org/10.1590/S0104-11692007000300023.

[20] Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomized trials. BMJ. 2010; 340:c 869. DOI:10.1016/j.jclinepi.2010.03.004

[21] Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, RaskobG, Lewis SZ, Schünemann H. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an american college of chest physicians task force.Chest.2006 Jan;129(1):174-81.DOI:10.1378/chest.129.1.174

[22] Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, Montori V, AklEA, Epidemiol.2011;64(4):407-15.DOI:10.1016/j.jclinepi.2010.07.017

[23] Dohmen PM, Weymann A, Holinski S, Linneweber J, Geyer T, Konertz W. Use of na antimicrobial skin sealant reduces surgical site infection in patients undergoing routine cardiac surgery. Surgical Infections 2011;12(6):475-481.DOI:10.1089/sur.2011.050

[24] Hanedan MO, Unal EU, Aksoyek A, Basar V, TakS, Tutun U, IsikH, Birincioglu CL. Comparison of two diferente skin preparation strategies for open cardiac surgery.JInfectDev Ctries2014;8(7):885-890.DOI:10.3855/jidc.3597

[25] Schimmer C, Gross J, Ramm E, Morfeld B-C, Hoffmann G, Panholzer B. Prevention of surgical Sitesternal infections in cardiac surgery: a two-centre prospective randomized controlled study. EurJ Cardiothorac Surg2017;51:67–72.DOI:10.1093/

[26] Grauhan O, Navasardyan A, Hofmann M, Muller P, HUmmelM, Hetzer R.Cyanoacrylate_sealed Donatisuture for wound closure after cardiac surgery in obese patients. Interactive Cardio Vascular and Thoracic Surgery 11 (2010)763–767.https://doi.org/10.1510/icvts.2010.247965

[27] vonEckardstein AS, LimCH,DohmenPM,Pêgo-Fernandes PM, Cooper WA, Oslund SG, Kelley EL. A randomized trial of a skin seal ant to reduce the risk of incision contamination in cardiac surgery.AnnThoracSurg.2011Aug;92(2):632-7.doi:10.1016/j.athoracsur.2011.03.132

[28] Kjaergard HK, TrumbullHR. Bleeding From the Sternal Marrow Can Be Stopped Using Vivost at Patient-Derived Fibrin Sealant Ann Thorac Surg 2000; 69:1173–5. DOI: https://doi.org/10.1016/S0003-4975(99)01560-X

[29] Fedak PW, Kieser TM, Maitland AM, Holland M, Kasatkin A, Leblanc P, Kim JK, King KM. Adhesive-

enhanced sternal closure to improve post operative functional recovery: A pilot, randomized controlled trial. Ann Thorac Surg.2011 Oct;92(4):1444-50.doi:10.1016/j.athoracsur.2011.05.014.

[30] Pachulski R, Sabbour H, Gupta R, Adkins D, Mirza H, Cone J. Cardiac device implant wound closure with2-octylcyanoacrylate.JIntervCardiol.2005Jun;18(3):185-7.DOI:10.1111/j.1540-8183.2005.04048.x

[31] Dohmen PM, Gabbieri D, WeymannA,LinneweberJ,GeyerT,KonertzW. A retrospective non-randomized study on theimpact of INTEGUSEAL, a preoperative microbial skin sealant, on the rate of surgical site infections after cardiac surgery. IntJInfectDis.2011Jun; 15(6):e395-400. doi:10.1016/j.ijid.2011.02.004.

[32] Waldow T, Szlapka M, Hensel J, Plotze K, Matschke K, Jatzwauk L. SkinsealantIntegu Seal has no impact on prevention of post operative media stinitis after cardiac surgery.J. hosp. infect.2012(81):278-282. doi:10.1016/j.jhin.2012.04.024

[33] Haas JP, Evans AM, Prest on KE, Larson EL. Risk factors for surgical site infection after cardiac surgery: the role of endogenous flora. Heart Lung. 2005;34(2):108–114.DOI:10.1016/j.hrtlng.2004.02.004

[34] Crabtree TD, Codd JE, Fraser VJ, Bailey MS, Olsen MA, Damiano RJJr. Multi variate analysis of risk factors for deep and superficial sterna infection after coronary artery bypass grafting at a tertiary care medical center. Semin Thorac CardiovascSurg 2004;16:53–61.DOI:https://doi.org/10.1016/j.athoracsur.2016.05.047

[35] Ridderstolpe L, Gill H, Granfeldt H, Ahlfeldt H, Rutberg H. Superficial and deep sternal wound complications: incidence, risk factors and mortality.EurJCardiothoracSurg2001;20:1168–75.https://doi.org/10.1016/S1010-7940(01)00991-5

[36] Stahle E, Tammelin A, Bergstrom R, Hambreus A, Nystrom SO, Hansson HE. Sternal wound complications—incidence, microbiology and risk factors. EurJCardiothoracSurg1997;11:1146–53.

[37] El Oakley R, Paul E, Wong PS, Yohana A, Magee P, Walesby R. Media stinitis in patients undergoing cardiopulmonary bypass: risk analysis and midterm results. J CardiovascSurg1997;38:595–600.doi:10.1186/1749-8090-2-23

[38] Gelape CL. Surgical wound infection following heart surgery.ArqBrasCardiol2007;89:e3–e9. http://dx.doi.org/10.1590/S0066-782X2007001300013

[39] Gummert JF, Barten MJ, Hans C, Kluge M, DollN, Walther T. Media stinitis and cardiac surgery—an update risk factor analysis in10,373 consecutive adult patients Thorac Cardiovasc Surg2002,50:87-91.DOI:10.1055/s-2002-26691

[40] Diez C, Koch D, Kuss O, Silber RE, Friedrich I, Boergermann J. Risk factors for media stinit is after cardiac surgery—aretrospectiveanalysisof1700patientsJCardiothoracSurg2007,2:23.DOI:10.1186/1749-8090-2-23

[41] Gårdlund B, Bitkover CY, Vaage J. Post operative media stinit is in cardiac surgery—microbiology and pathogenesis. Eur J Cardiothorac Surg 2002. 21: 825-830. DOI:https://doi.org/10.1016/j.athoracsur.2006.05.097

[42] Schmeltz LR, DeSantis AJ, Thiyagarajan V, Schmidt K, O'Shea- Mahler E, Johnson D, Henske J, Mc Carthy PM, Gleason TG, McGee EC, Molitch ME. Reduction of surgical mortality and morbidity in diabetic patients undergoing cardiac surgery with a combined intravenous and subcutaneous insulin glucose management strategy.DiabetesCare.2007Apr;30(4):823-8.DOI:10.2337/dc06-2184

[43] Sajja LR. Strategies to reduce deep sterna wound infection after bilateral internal mammary artery grafting. Int J Surg. 2015 Apr; 16(PtB):171-8.doi:10.1016/j.ijsu.2014.11.017

[44] Meszaros K, Fuehrer U, Grogg S, Sodeck G, Czerny M, Marschall J, Carrel T. Risk Factors for Sternal Wound Infection after Open Heart Operations Vary According to Type of Operation. Ann Thorac Surg.2016Apr;101(4):1418-25.doi:10.1016/j.athoracsur.2015.09.010.

[45] World Health Organization. (2016). Global Guidelines for the Prevention of Surgical Site Infection. World Health Organization.pg120.http://www.who.int/iris/handle/10665/250680

[46] Francel TJ, Kouchoukos NT. A rational approach to wound difficulties after sternotomy: the problem. Ann Thorac Surg 2001;72:1411–1418.DOI: https://doi.org/10.1016/S0003-4975(00)02009-9

[47] Demirtas MM, Akcar M, Sarikaya S. Avoidance of sternal non-union with cyanoacrylate gluing. AnnThorac Surg1998;66:304–306.DOI:10.1510/icvts.2009.230425

[48] Mertz PM, Davis SC, Cazzaniga AL, Drosou A, Eaglstein WH. Barrier and antibacterial properties of 2-octylcyanoacrylate-derived wound treatment films.JCutanMedSurg2003;7:1–6.DOI:10.1177/120347540300700101

[49] Fowler VGJr, O'Brien SM, Muhlbaier LH, Corey GR, Ferguson TB, Peterson ED. Clinical predictorsofmajorinfectionsaftercardiacsurgery.Circulation2005;112:358–365.DOI:10.1161/CIRCULATIONAHA.104.525790

[50] Abu-OmarY, Kocher GJ, Bosco P, Barbero C, Waller D, Gudbjartsson T, Sousa-UvaM, Licht PB, Dunning J, Schmid RA, Cardillo G. European Association for Cardio-Thoracic Surgery expert consensus statement on the prevention and management of media stinitis. EurJ CardiothoracSurg2017;51:10–29.DOI:10.1093/

[51] Waldow T, Szlapka M, Hensel J, Plotze K, Matschke K, Jatzwauk L. Skinsealant Integu Seal (R) has no impact on prevention of post operative mediastin it is after cardiac surgery. JHospInfect 2012;81:278-282.DOI:10.1016/j.jhin.2012.04.024

[52] Raja SG, Salhiyyah K, Rafiq MU, Felderh of J, Amrani M. Impact of gentamic in-collagen sponge (Collatamp) on the incidence of sternal wound infection in high-risk cardiac surgery patients: A propensity score analysis. Heart Surg Forum 2012;15:E257 DOI:10.1532/HSF98.2012103

[53] 53-Bennett-GuerreroE,FergusonTBJr,LinM,GargJ,MarkDB,ScavoVA Jr.Effectofan implantable gentamicin-collagen sponge on sternal wound infections following cardiac surgery: A randomized trial.JAMA2010;304:755–62.DOI:10.1001/jama.2010.1152

[54] FryDE. The Surgical Infection Prevention Project: Processes, Outcomes, and Future Impact. Surgical Infections 2006.7(3):17-26.DOI:10.1086/505220

[55] Coskun D, Aytac J, Aydinli A, Byaer A. Mortality rate, length of stay and extra cost of sternal surgical site infections following coronary artery bypass grafting in a

private medical centrein Turkey. JHosp Infect 2005; 60:176–179.DOI:10.1016/j.jhin.2004.10.017
[56] Mangram AJ, Horan TC, Pearson ML, et al. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. AmJInfect Control1999;27:97–132.DOI:10.1086/501620

Table I: Characteristics of the included studies. São Paulo, Brazil

Study	Dohmen 2011[45]	Muhammet 2014[46]	Schimmer 2017[47]	Grauhan 2010[48]
Study country	Germany	Turkey	Germany	Germany
Population	910	96	996	90
Groups	Control Group = 721 Intervention Group = 189	Control Group = 28 Intervention Group = 68	Control Group = 332 Genta Coll Group = 336 InteguSeal Group = 328	Control Group = 45 Intervention Group = 45
Interventions	The cyanocrilate sealant was applied after the preoperative preparation of the sternum	The cyanocrilate sealant was applied after the preoperative preparation of the sternum	Genta Coll Group: the resorption sponge was placed between and under the sternum halves during osteosynthesis InteguSeal Group: the sealant was applied to the sternal area of the planned incision after skin disinfection	The skin was closed using a non-resorbable monofilament suture (Donati technique). The suture was sealed with cyanocrilate
Control	Conventional preoperative preparation (trichotomy and skin disinfection)	Conventional preoperative preparation (trichotomy and skin disinfection)	Cardiac surgery was performed without the use of additional prophylaxis devices for infection	The skin was closed with absorbable monofilament thread without sealing
Outcomes	Occurrence of superficial or deep SSI within 30 days after surgery and after one year	If the use of cyanocrilate sealant reduces the SSI index in cardiac surgery	1 - to analyze the incidence of superficial and deep SSI of the sternum after median sternotomy in the three groups 2 - determine the independent risk factors for an increase in the SSI rate in the sternum	Infection of the surgical wound
Follow up	30 days of follow-up or one year in case of implantation during surgery	6 months	3 months preoperative	90 days
Inclusion criteria	Elective or emergency cardiac surgeries	Elective cardiac surgeries	Adults (> 18 years), indication for elective surgery and consent form	Adults, BMI> 30 kg/m2, median sternotomy
Exclusion criteria	It's unclear	Previous cardiac surgery, skin lesions at the surgical site and morbid obesity (BMI> 35) Emerging cases and patients with anesthetic risk> 3	Allergy or hypersensitivity to gentamicin, patients with associated cardiac surgery (eg valve replacement) or emergency cases	BMI <30
Source: Own Authorship				

Table II: Studies excluded from full analysis. São Paulo, Brazil.

Study	Reason for exclusion
Eckardstein 2011[49]	Didn't assess whether there was a reduction in SSI
Kjaergard 2000[50]	Didn't use cyanocrilate
Fedak 2010[51]	Didn't use cyanocrilate
Pachulski 2005[52]	Didn't apply cyanocrilate to sternotomies
Dohmen 2011[53]	There was no randomization
Waldow 2012[54]	There was no randomization
Source: Own Authorship	